Making Food Safer in Palestine: A One Health Approach to Antimicrobial Resistance

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Said Fathi Abukhattab

From Ramallah, West Bank, Palestine

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Approved by the Faculty of Medicine on application of

Primary supervisor Prof. Dr. Jakob Zinsstag

Second supervisor PD Dr. med. Esther Künzli

External expert Prof. Dr. Gertraud Schüpbach-Regula

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Prof. Dr. Primo Leo Schär

Dean

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Executive summary:

Background

Foodborne diseases, combined with the growing threat of antimicrobial resistance (AMR), present significant public health challenges, especially in relation to climate change and the risks of zoonotic epidemics. Unsafe food consumption can cause various health issues, ranging from food poisoning to reproductive problems, and can contribute to the emergence of AMR, resulting in severe consequences such as cancer and death. The use of antimicrobials in food production raises safety concerns due to the presence of antibiotic residues, antibiotic-resistant bacteria (ARB), and antibiotic-resistant genes (ARGs) in animals, food products, and the environment.

Foodborne diseases caused by antibiotic-resistant bacteria from animals, such as foodborne urinary tract infections (UTIs), have recently attracted considerable attention. Resistant bacteria from contaminated food can colonize the human gastrointestinal tract, acting as a reservoir for further infections. This hinders infection prevention and control efforts, as well as antimicrobial stewardship programs in communities and hospitals.

The political unrest due to the conflicts and wars, such as in Palestine, have severe consequences for food safety and the spread of AMR. Infrastructure damage, limited resources for food safety programs, increased antibiotic use, hindered access to medical care, and displacement of individuals contribute to compromised food safety and the rise of AMR.

A comprehensive One Health approach is vital to tackle AMR throughout the entire food production process. It considers all relevant factors, from upstream to downstream, and includes an integrated surveillance-response system encompassing human and animal health, the environment, and food production. This holistic approach safeguards antimicrobial efficacy by ensuring food safety, preserving food security, and effectively combating communicable and noncommunicable diseases, benefiting future generations.

Objectives

This PhD thesis utilizes the One Health approach to examine zoonotic bacteria and AMR in the food production chain, particularly in conflict-affected regions. It aims to identify integrated One Health studies on Middle Eastern foodborne illnesses, assess food safety for an operational strategy in Palestine, and evaluate the benefits of implementing an integrated surveillance system for foodborne pathogens and AMR.

Methods

This PhD project tries to find a critical methodology to foster food safety by better understanding the zoonotic foodborne illnesses transmission and their resistance to antimicrobials in socio-ecological systems like in Palestine. The research conducted a systematic review and meta-analysis of scientific literature from 2010 to 2021 to assess the implementation of the One Health approach in the Middle East, with a particular emphasis on *Salmonella* and *Campylobacter* strains. Stakeholder perspectives were gathered through multi-stakeholder discussion groups, facilitating communication and identifying diverse viewpoints on the food production monitoring system in Palestine. Additionally, a semi-structured observation design was employed to evaluate hygiene practices in broiler farms, slaughterhouses, and meat stores, pinpointing potential transmission routes and contamination sources. The project also investigated the knowledge, attitudes, and practices of workers in the broiler production industry, to explore the relationship between their attitudes, practices, and hygiene knowledge regarding zoonotic diseases. Furthermore, a One Health integrated surveillance system for *Campylobacter* and *Salmonella*, including antimicrobial resistance analysis, was piloted in the central West Bank, Palestine, involving the collection and analysis of samples from various sources. This comprehensive approach provides valuable insights into the complex dynamics of food safety and antimicrobial resistance in Palestine's socio-ecological context.

Results

In the Middle East, a total of 41 studies were analyzed to determine the prevalence rates of non-typhoid *Salmonella* (NTS) and *Campylobacter*. The findings revealed that NTS had a prevalence of 9% among humans and 13% among food-producing animals, while *Campylobacter* had prevalence rates of 22% in humans and 30% in animals. The most common NTS serovars were *Salmonella* Enteritidis and *Salmonella* Typhimurium, and the predominant species of *Campylobacter* were *Campylobacter jejuni* and *Campylobacter coli*. Notably, both NTS and *Campylobacter* showed high resistance to multiple antibiotics, including erythromycin, amoxicillin, tetracycline, and more. However, the implementation of the One Health approach in the Middle East was limited, and data reporting varied across countries.

In Palestine, several challenges were observed in the food production chain, such as the scarcity of public slaughterhouses, inadequate coordination between authorities, and discrepancies in law enforcement. Hygiene practices also varied, with public slaughterhouses and meat markets demonstrating better hygiene compared to large-scale farms. While participants expressed awareness of zoonotic disease transmission and emphasized the importance of hygiene standards, there were conflicting findings between observations and survey results regarding actual hygiene practices.

In a cross-sectional study conducted in Palestine using integrated One Health surveillance, the positivity rate for *C. jejuni* in chicken manure samples was 24%, while *S*. enterica had a positivity rate of 6%. The dominant serotypes of both *C. jejuni* and *S*. enterica were found in chicken manure, chicken meat sold in markets, and the feces of asymptomatic farm workers, indicating genetic similarities across different sources. Strain turnover was observed in *C. jejuni* between 2021 and 2022. In 2021, *C. jejuni* isolates exhibited identical drug resistance gene patterns, including resistance to aminoglycosides, macrolides, quinolones, and tetracycline. In 2022, a different resistance gene pattern emerged, involving beta-lactamase and quinolone resistance genes. Among the *Salmonella* isolates collected, most belonged to *S.* enterica serotype Muenchen and showed multidrug resistance, facilitated by the pESI megaplasmid carrying resistance genes to multiple antibiotics, including aminoglycosides, fluoroquinolones, sulfonamides, tetracycline, and trimethoprim.

Conclusion

To effectively implement a One Health strategy in Palestine, the establishment of a technical committee is crucial. This committee would focus on food safety, zoonotic diseases, and AMR, promoting coordination, communication, and partnerships. Proposed measures include developing an integrated quality control system for food production, implementing product certification for broiler meat, and improving slaughterhouse capacity. Veterinary inspections, careful monitoring of antimicrobial use, and sharing of AMR data would further strengthen the food safety system.

Furthermore, implementing an integrated surveillance system and adopting a transdisciplinary approach are key to addressing AMR and enhancing the food safety system in Palestine. Sharing responsibilities and resources among relevant authorities is vital for successful AMR mitigation. The establishment of the Palestinian Integrated Program for Antimicrobial Resistance Surveillance (PIPARS) would lead to financial savings and a comprehensive approach. Employing efficient testing methods like whole genome sequencing enables early identification and timely response to AMR threats, serving as an essential tool for the One Health integrated surveillance system.

List of abbreviations

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
ANRESIS	Swiss Centre for Antibiotic Resistance
ARB	Antibiotic-resistant bacteria
ARGs	Antibiotic-resistant genes
CDC	United States Centers for Disease Control and Prevention
CIPARS	Canadian Integrated Program for Antimicrobial Resistance
DALYs	Disability-adjusted life years
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Program
DDDs	Defined daily doses
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
EMR	Eastern Mediterranean Region
EQA	Environmental Quality Authority
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FOPH	Swiss Federal Office of Public Health
G7	The group of seven largest economies
GAP	Global Action Plan on Antimicrobial Resistance
GBS	Guillain-Barre syndrome
GDP	Gross Domestic Product
GD-VSAH	General Directorate of Veterinary Services and Animal Health
GLASS	Global AMR Surveillance System
HACCP	Hazard Analysis and Critical Control Points
IACG	United Nations Interagency Coordination Group on Antimicrobial Resistance
ICPH	Institute of Community and Public Health at Birzeit University
IFIK	Institute for Infectious Diseases
iSRS	integrated Surveillance Response System
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
KAP	knowledge, attitudes and practices
LMICs	Low- and middle-income countries

MDR	Multidrug resistance
MDR	Multidrug Resistance
MENA	Middle East and North Africa
MGEs	Mobile genetic elements
MIAs	Medically Important Antimicrobials
MRSA	Methicillin-Resistant *Staphylococcus aureus*
NAP	National Action Plan
NARMS	United States National Antimicrobial Resistance Monitoring System
NGOs	Non-governmental organizations
NTS	Non-typhoid *Salmonella*
OECD	Organization for Economic Cooperation and Development
OHHLEP	One Health High-Level Expert Panel
PENGON	Environmental Non-Governmental Organizations Network
PIPARS	Palestinian Integrated Program for Antimicrobial Resistance Surveillance
PLO	Palestine Liberation Organization
PMQR	Plasmid-mediated quinolone resistance
PNA	Palestinian National Authority
PPEs	Personal protective equipment
PWA	Palestinian Water Authority
QRDRs	Quinolone-resistance-determining regions
SDGs	Sustainable Development Goals
SWEDRES-SVARM	Swedish Integrated AMR Surveillance Program
U5MR	Under-five mortality rates
UNEP	United Nations Environment Programme
UNRWA	United Nations Relief and Works Agency for Palestine Refugees in the Near East
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
USFDA	United States Food and Drug Administration
UTIs	Urinary tract infections
WAFA	Palestinian News and Information Agency
WaSH MP	Sanitation and Hygiene Monitoring Program
WGS	Whole-genome sequencing
WHO	World Health Organization
WOAH	World Organisation for Animal Health

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Part 1

INTRODUCTION, OBJECTIVES AND METHODOLOGY

1 Introduction

1.1 Infectious diseases and “acute gastroenteritis

Infectious diseases remain a major global source of mortality and morbidity despite substantial advancements in vaccinations, diagnostics, treatments, and infection control strategies (Gulati, Sharma, & Rao, 2021). Worldwide, infectious diseases rank first in terms of DALYs (disability-adjusted life years) and are the second most significant cause of death (Hay et al., 2017). Out of the 2.5 billion DALYs lost by all diseases globally, approximately 550 million DALYs were attributable to infectious diseases, according to the Global Burden of Disease Study (GBD) carried out in 2017. Among the top ten causes of disease burden globally, four were infectious diseases: lower respiratory tract infections (106 million DALYs), diarrhoeal diseases (81 million), HIV/AIDS (54 million), and malaria (45 million) (Gulati et al., 2021; Hay et al., 2017). Although the number of DALYs lost by communicable diseases declined while the number of DALYs lost by non-communicable diseases rose in 2016, "diarrhoeal diseases" remained ranked sixth globally in terms of leading causes of total DALYs (Gulati et al., 2021; Hay et al., 2017). Diarrhoea affects all locations and populations worldwide. However, a disproportionate amount of diarrhoeal morbidity and deaths occur in low-income countries, which have fewer resources and weaker infrastructure than high-income countries to handle the burden. In developing countries, factors such as limited clean water access, inadequate sanitation, poor hygiene practices, malnutrition, overcrowding, and limited healthcare contribute to the higher prevalence of diarrhoea and gastroenteritis diseases (Troeger et al., 2018).

Diarrhoeal diseases in children remain a major public health concern in countries of the Middle East and North Africa (MENA) region (A. Harb, O’Dea, Abraham, & Habib, 2019). According to the Global Burden of Disease Survey from 2015, around 103,692 diarrhoea deaths occurred in the MENA in 2015, with a mortality rate of 16.0 deaths per 100,000 persons. Children under the age of five (63.3%) accounted for the majority of these deaths ("Burden of diarrhea in the Eastern Mediterranean Region, 1990–2015: Findings from the Global Burden of Disease 2015 study," 2018). The number of DALYs attributable to diarrhoea in children under 5 years of age was estimated to be 6,058,681 in MENA regions (4,045,101–8,618,353) (A. Harb et al., 2019). Many countries in the MENA suffer from fragile healthcare systems due to decades of conflict, sanctions, and political instability (Ahmed et al., 2013). For example, diarrhoea is a major cause of death among children under 5 in war-torn Iraq. Due to the Gulf War in 1991 and subsequent sanctions, water treatment plants were unable to function properly, leading to untreated water in the supply. The damaged water distribution network resulted in an inconsistent water supply, forcing families to store water that often becomes contaminated. Maternal factors, such as education, nutritional knowledge, and economic status, also contribute to the problem (Alaa, Shah, & Khan, 2014; A. Harb et al., 2019; Siziya, Muula, & Rudatsikira, 2009). Pediatric diarrhoea has a significant financial and productivity impact on family's livelihood in MENA countries. For instance, in Oman, the total cost of hospital diarrhoeal disease treatment is estimated at $ 539 per child for three days in the hospital: a total of $1.8 million annually for all hospitals and outpatient clinics in the country (A. Harb et al., 2019). In addition, in the United Arab Emirates, the average cost of $ 64 is spent on medical care expenses for each case of diarrhoea in children (Howidi et al., 2012).

Acute gastroenteritis, a common condition affecting the digestive tract, is primarily attributed to viral, bacterial, or parasitic infections. Gastroenteritis outbreaks and sporadic cases are common throughout the year and significantly impact global public health. The main cause of foodborne or waterborne acute gastroenteritis is contamination with a pathogen and/or a pathogen toxin (Luo et al., 2019). Estimates indicate that viral, bacterial, and parasitic infections account for approximately 50-70%, 15-20%, and 10-15% of the infectious causes of acute gastroenteritis, respectively (Luo et al., 2019).

1.2 Food safety and foodborne disease

Food consumption and human disease were found to be related relatively early. Hippocrates (460 B.C.) asserted that there is a direct link between the food we eat and disease in humans (Bintsis, 2017). Eating food infected with bacteria, viruses, parasites, or chemicals like heavy metals can result in over 250 illnesses. Foodborne pathogens (e.g. parasites, bacteria, viruses) are biological agents that can cause a foodborne illness incident (WHO, 2023). Foodborne infection happens when a pathogen is consumed with food and establishes (and typically multiplies) in the human host or when a toxigenic pathogen establishes itself in a food product and creates a toxin, which the human host subsequently consumes. The duration between consumption and the onset of symptoms, the incubation period, is substantially greater for foodborne infections than foodborne intoxications (Bintsis, 2017). The main foodborne illnesses' symptoms, incubation period, and the pathogens or toxins that cause them are shown in Table 1-1.

The burden of foodborne disease hinders the achievement of the Sustainable Development Goals (SDGs), particularly the no poverty (SDG 1), zero hunger (SDG 2), aspirations to ensure health and well-being (SDG 3), clean water and sanitation (SDG 6), decent work and economic growth (SDG 8), responsible consumption and production (SDG 12), and partnerships for the goals (SDG 17) (Rush, 2019; WHO, 2022c). According to a report by the World Health Organization (WHO), approximately 600 million individuals, nearly 1 in 10 people worldwide, fall ill due to consuming contaminated food. Tragically, this leads to approximately 420,000 deaths annually and a loss of 33 million disability-adjusted life years (DALYs) (WHO, 2023). Unsafe food disproportionately impacts vulnerable groups of society, specifically infants, young children, the elderly, and immunocompromised individuals. This issue is particularly pronounced in low- and middle-income countries (LMICs), where the annual estimated expenses attributed to productivity losses, trade-related losses, and medical treatment costs due to the consumption of unsafe food amount to approximately US$110 billion (WHO, 2022c).

Table 1-1 The main foodborne illnesses' symptoms, incubation period, and the pathogens or toxins that cause them (Bintsis, 2017).

Associated pathogen or toxin	Predominant symptoms	Incubation Period
Staphylococcus aureus and its enterotoxins	Diarrhoea, vomiting, retching, abdominal pain, nausea, prostration	1–7 (mean 2–4) hours.
Bacillus cereus (emetic toxin)	Vomiting or diarrhoea, depending on whether diarrheic or emetic toxin present; abdominal cramps; nausea	8–16 hours (2–4 hours if emesis predominant)
Clostridium perfringens	Diarrhoea, abdominal cramps, sometimes nausea, vomiting, putrefactive diarrhoea	2–36 (mean 6–12) hours
Salmonella spp., *Shigella* spp., *E. coli*	Diarrhoea, abdominal cramps, fever, vomiting, headache	6–96 hours (often 1–3 days)
Vibrio cholearae (O1 and non-O1), *Vibrio parahaemolyticus*	Diarrhoea, vomiting, dehydration fever, abdominal cramps, headache, malaise, nausea,	6 h to 5 days
Campylobacter spp. (particularly *C. jejuni and C. coli*)	Diarrhoea (often bloody), fever, stomach cramps, nausea, arthritis, and vomiting	1-11 (median 2-5) days
Enterohaemorrhagic *E. coli*	Diarrhoea (mostly bloody), abdominal pain, nausea, malaise, vomiting, fever (uncommon with *E. coli* O157:H7)	1–10 (median 3–4) days
Yersinia enterocolitica	Diarrhoea, fever, abdominal pain	3–7 days
Clostridium botulinum and its neurotoxins	Weakness, vertigo, double or blurred vision, respiratory paralysis loss or light reflex, dry mouth, difficulty in swallowing, respiratory paralysis	2 hours to 6 days, often 12–36 hours
Listeria monocytogenes	Fever, chills, headache, prostration, arthralgia, malaise, swollen lymph nodes and other specific symptoms of the disease in question	Varying periods
Salmonella Typhi	High fever, fatigue, stomach pain, headache, abdominal pain, loss of appetite, cough, and constipation or diarrhoea.	6–30 days
Norovirus	Watery non-bloody diarrhoea, dehydration, vomiting, Nausea	12–48 hours
Rotavirus, Astrovirus, enteric Adenovirus	Diarrhoea (watery non-inflammatory),vomiting, , fever	3–5 days
Entamoeda histolytica	Abdominal pain, diarrhoea, constipation, headache, drowsiness, ulcers, variable—often asymptomatic	1 to several weeks
Toxoplasma gondii	Fever, myalgia, rash, headache	10–13 days
Trichinella spiralis	Gastroenteritis, perspiration, muscular pain, prostration, fever, chills, oedema around eyes, laboured breathing	4–28 days
Taenia saginata, *Taenia solium*	Nervousness, anorexia, weight loss, abdominal pain, sometimes gastroenteritis, insomnia, hunger pains	3–6 months

The MENA region ranked third in terms of the burden of foodborne illness per population, just after Africa and South-East Asia. According to that same WHO report, nontyphoidal *Salmonella*, *Campylobacter* spp., *Escherichia coli*, and Norovirus are responsible for 70% of the foodborne disease burden in the MENA region (WHO, 2015d). In the MENA region, determining the actual incidence of certain diseases, such as foodborne infections, can be challenging due to insufficient systematic surveillance efforts. This might be due to various factors, including inadequate healthcare infrastructure, limited resources, and political instability (Habib & Mohamed, 2022). Annually in Jordan, there are over 4.4 million cases of diarrhoea among individuals aged one year and above, with around 1.3 million seeking medical care for diarrhoea. The majority of Jordan's diarrhoeal illnesses are caused by contaminated food or water. It is estimated that for every individual diagnosed with a laboratory-confirmed *Shigella* or *Salmonella* infection, there are approximately 273 infected individuals within the Jordanian community (Hayajneh, Alnimer, Titi, & Abu-Zanat, 2016). In Lebanon, the most common foodborne pathogens are *Salmonella* spp., *Campylobacter jejuni*, *E. coli*, *Brucella* spp., *Staphylococcus aureus*, *Listeria monocytogenes*and, and *Yersinia* spp. (Serhan et al., 2009). Harb et al. (2020) argue that the massive spread of pathogenic bacteria in Lebanon shows that food safety practices in Lebanon are still under development and far from international standards. According to the study, the key causes of Lebanon's deficient food safety system are the weak laws regulating food safety, a lack of surveillance systems, insufficient monitoring systems, poor awareness, practices and attitudes in local communities, and a lack of research related to foodborne infections (C. Harb, Mouannes, Bou Zeidan, Abdel Nour, & Hanna-Wakim, 2020). In Egypt, the most common foodborne pathogens screened by central public health laboratories are *Salmonella* spp., *Campylobacter* spp., *Shigella*, *E. coli*, Staphylococcus *aureus*, *Bacillus cereus*, *Brucella* spp., *Listeria monocytogenese*, *Clostridium perfringens*, *Clostridium botulinum*, and *Vibrio parahaemolyticus*. According to Ibrahim et al. (2017), in Egypt, the organizational structure of the food safety system fits into the "many bodies system" concept, and the system lacks a clearly defined single strategic plan. Several bodies are involved in official food control, each with fully defined organizational structures and fields of operation. However, inter-ministerial coordination and communication bodies are not clearly defined. In addition, food laws are not founded based on risk analysis. Therefore, they do not require food industry to implement Hazard Analysis and Critical Control Points (HACCP) plans, which impacts the other detected factors because management is not done systematically (Ibrahim & Abdel-Haleem, 2017).

1.3 Palestine profile

The Eastern Mediterranean Region (EMR) comprises 22 countries and had a population of approximately 731 million people in 2021 (Talaat et al., 2022). Among the countries in the EMR, Palestine holds a significant historical position as part of the renowned "Fertile Crescent," often referred to as the birthplace of agriculture and a cradle of human civilization (Isaac, 1994).

However, the region currently faces a range of challenges due to its diverse economic, social, and demographic conditions. Civil unrest, conflicts, and population displacement have had a profound impact on approximately two-thirds of the countries in the EMR. These issues have led to significant health concerns and disruptions to healthcare systems (Truppa & Abo-Shehada, 2020; WHO, 2015c).

Palestine, situated at the centre of the ancient world where Eurasia and Africa converge (Sarsour & Nagabhatla, 2022), has a rich agricultural heritage. Historically, it has been classified as agricultural land, with the agricultural sector serving as the backbone of the state's economy and the main source of food security for its citizens (Kittaneh, 2020).

Palestine has been grappling with a complex web of political conflicts and environmental challenges for decades, and these issues are deeply intertwined (Isaac & Gasteyer, 1995). As a response to this unique situation, the Palestinian National Authority (PNA) was established in 1994 through the Oslo Accords, a series of agreements between the Israeli government and the Palestine Liberation Organization (PLO) aimed at resolving the Israeli-Palestinian conflict (Qumsiyeh & Albaradeiya, 2022). One outcome of the Oslo Agreements was the division of the West Bank into three distinct regions: A, B, and C. Area A, which constitutes 18% of the West Bank, is under the complete civil control of the Palestinian Authority. Area B, encompassing 22% of the West Bank, is administered by the Palestinians but with Israeli security oversight. The largest region, Area C, encompasses 60% of the West Bank and remains under full Israeli control (Lagerquist, 2004). The PNA was intended to be an interim self-governing body that would eventually establish a fully independent Palestinian state. Currently, the PNA exercises varying degrees of control over different parts of the West Bank, including East jeruslaem, and Gaza Strip (Figure1- 1 A). The population of the Palestine is estimated to be around 5 million in 2019, with approximately 3 million in the West Bank and 2 million in the Gaza Strip (Isaac & Gasteyer, 1995; Palestinian, 2003; "Statistical Yearbook of Palestine," 2017). Population density is extremely high in the Gaza strip and some West Bank areas, including East Jerusalem (Figure 1-1 B) (UNEP, 2020) .

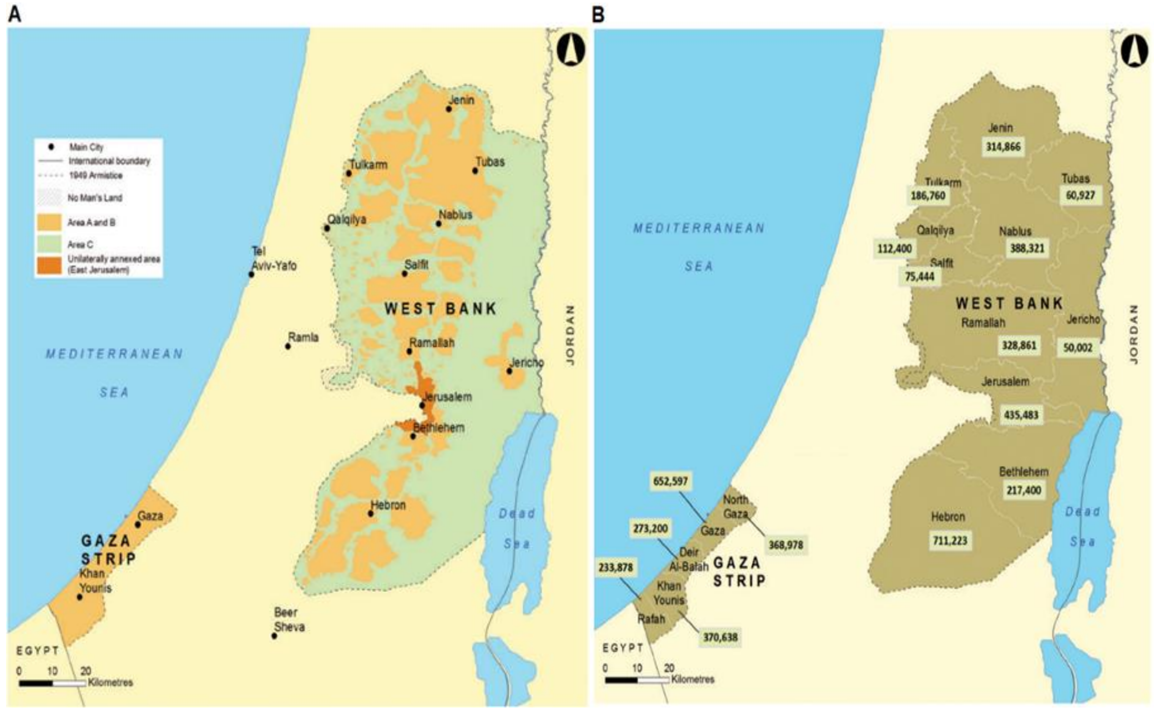


Figure 1-1 Map of the Palestine (West Bank and Gaza Strip). A): geopolitical map. B) Population by governorate, (Modified from (UNEP, 2020)).

1.3.1 Palestine health profile

Palestine which include the West Bank, East Jerusalem and the Gaza Strip, has undergone a significant demographic and epidemiological transition in recent decades (Husseini et al., 2009). This has resulted in an increase in life expectancy at birth, as reported by the World Bank. According to World Bank data, life expectancy at birth in the Palestine increased from 68 years in 1990 to 73 years in 2013 (WHO, 2017a).

The population growth rate in Palestine is expected to remain stable due to a combination of declining death rates and a high fertility rate of 4.06, which is one of the highest in the Arab world. However, there is a notable disparity between the Gaza Strip and the West Bank, with population growth rates of 4.5% and 3.6% respectively (UNFPA, 2023). While the overall fertility rate is still high, it has started to decrease in the past decade. According to a WHO report, the under-five mortality rates (U5MR) in Palestine between 2005 and 2014 were 21.7 per 1000 live births. These mortality rates were primarily attributed to infections, birth asphyxia, and congenital anomalies (WHO, 2017a).

The Palestine has a successful immunization program, some diseases, such as wild poliovirus, leprosy, schistosomiasis, and rabies, were historically eradicated. The national immunization schedule covers poliomyelitis, tetanus, hepatitis B, tuberculosis, diphtheria, rotavirus, pertussis, haemophilus influenza type B, pneumococcus, rubella, mumps, and measles. Since 2013, there has been consistently high vaccination coverage, ranging from 96 to 99% (WHO, 2017a).

In Palestine, the majority of deaths are caused by non-communicable diseases. Cardiovascular disease, complications related to diabetes mellitus, and cancer are the three leading causes of death (Table 1-2) (Manenti, Reinicke, MacDonald, & Donald, 2016; MOH, 2020; WHO, 2017a).

Table 1-2 Top ten causes of reported death, 2020 in Palestine (MOH, 2020).

Rank	Cause of reported deaths	% of all reported deaths
1	Cardiovascular diseases	24.7%
2	Diabetes mellitus complications	14.6%
3	Cancer	14.1%
4	COVID- 19	11.0%
5	Cerebrovascular diseases	10.7%
6	Respiratory diseases	5.5%
7	Perinatal conditions	4.7%
8	Accidents	3.7%
9	Chronic renal failure	3.4%
10	Congenital anomalies	2.7%

The Ministry of Health (MOH), non-governmental organizations (NGOs), the United Nations Relief and Works Agency for Palestine Refugees in the Near East (UNRWA), and the private sector provide health services in Palestine (Manenti et al., 2016; "Palestinian Health Accounts ", 2013). The Ministry of Health operates primary healthcare centers and hospitals in the West Bank and Gaza Strip. Non-Governmental Organizations play a significant role in delivering tertiary and rehabilitative care services. UNRWA provides health services to registered refugees through primary healthcare clinics and hospitals ("Health conditions in the occupied Palestinian territory, including east Jerusalem," 2014). The private health sector is growing, with private hospitals, pharmacies, laboratories, and rehabilitation centres. The domestic pharmaceutical industry supplies about half of the demand for prescription medicine. Additionally, the Ministry of Interior operates healthcare clinics and hospitals exclusively for military employees (Manenti et al., 2016).

According to World Bank reports, Palestinian health spending is close to 5% of Gross Domestic Product (GDP), which exceeds the average in low- and middle-income countries of 1.7% and the regional average of 2.6% of GDP (Bank, 2016). Health spending increased more than three times from 2000 to 2012, to $ 1.3 billion, more than 12% of GDP. Moreover, total health spending per capita more than doubled between 2000-2012, from $ 126 to $ 294, reflecting higher spending outside pocket expenses, mostly on pharmaceuticals (WHO, 2017a).

1.3.2 Palestinian animal health profile

Animal production is an integral part of the Palestinian agricultural sector and is socially and economically crucial at the national and household levels (Halawa, 2022). According to the results of the livestock survey conducted in 2021, the livestock population was estimated as follows: 71 million broilers, 3.6 million laying hens, 771 thousand sheep, 240 thousand goats, 68 thousand cows, and 64 thousand beehives (Figure 1-2). For thousands of Palestinian families, a direct food supply in the form of meat, milk, and eggs is the main source of income and food security. It also indirectly provides income to smallholders, savings, asset value and labor (Kittaneh, 2020; PCBS, 2022). Palestine's agricultural sector contributed 7.1% of the country's GDP in 2021. Around 46% of the agricultural GDP comes from the livestock industry (Halawa, 2022; WAFA, 2022).

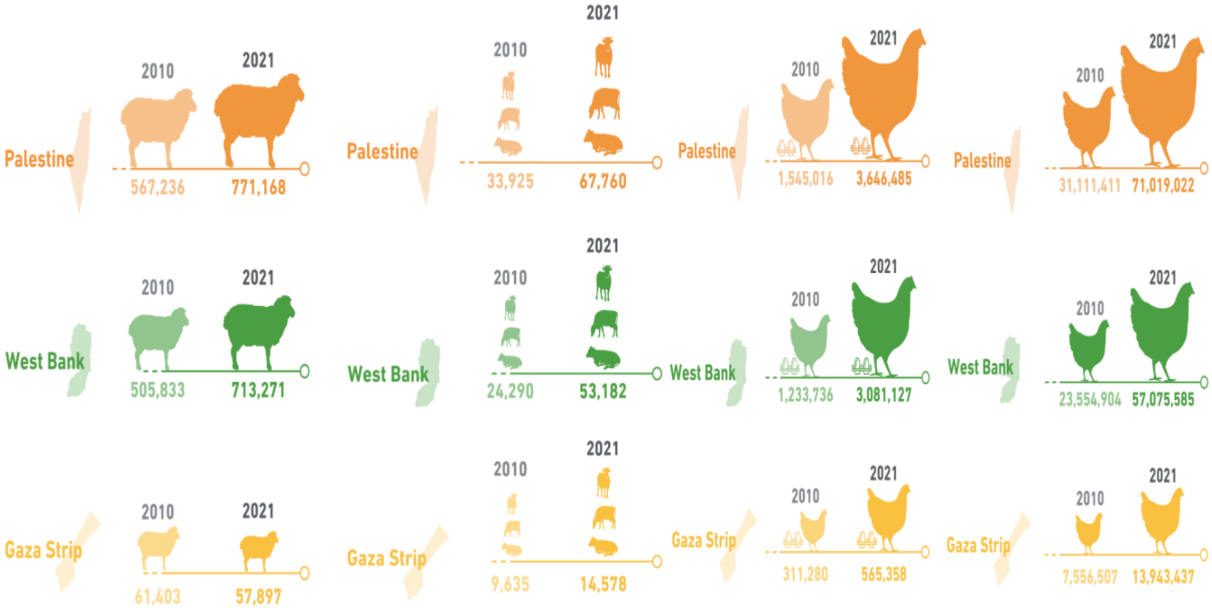


Figure 1-2 The changes in the livestock production, sheep, cattle, layers, and broilers numbers in Palestine between 2010- 2021 (PCBS, 2022).

The Ministry of Agriculture in Palestine is entrusted with the responsibility of overseeing animal healthcare through the General Directorate of Veterinary Services and Animal Health (GD-VSAH) (Ministers, 2023). The GD-VSAH has two main objectives: protecting Palestinian animals as a valuable national resource for ensuring food security and safeguarding human health by preventing zoonotic diseases (Ministers, 2023; WHO, 2020c). In relation to food safety, the GD-VSAH performs several key tasks, including the inspection of raw animal products to ensure their suitability for human consumption, conducting surveys to assess the safety of livestock products like milk, meat, and eggs, issuing veterinary certificates, and regulating the circulation of animal products (Gutkowski, 2021; WHO, 2020c).

Animal health is crucial for public health, food safety, sustainable agriculture, environmental conservation, and socioeconomic development. Prioritizing and investing in animal health programs and services yield numerous benefits, creating a healthier and more sustainable future for humans, animals, and the environment (Zinsstag, Schelling, Waltner-Toews, & Tanner, 2011). Therefore, veterinary services have a critical role in the management of highly contagious diseases and zoonotic infections, which have significant implications for both livestock and public health (Schelling, Wyss, Bechir, Moto, & Zinsstag, 2005; Zinsstag et al., 2011). Palestine's animal health sector suffers from challenges: 1. Insufficient quality and quantity of animal vaccines and medicines, contributing to the irrational use of antibiotics, 2. Weak institutions and organizations cause animal smuggling. 3. Most animal feed, 70% to 85% of the total production costs, is imported from Israel through a local intermediary without knowing the quality and quantity of this feed. 4. Shortage in veterinary health staff is a significant challenge; responsibilities on VSAH are continuously increased without corresponding staff expansion (FAO, 2017b; Gutkowski, 2021; WHO, 2020c). These issues are obstacles to completing whole responsibilities and forcing VSAH to deal with priorities.

1.3.3 Palestine environmental profile

According to a 2020 report from the United Nations Environment Programme (UNEP), various factors contribute to the state of the environment in Palestine, including socioeconomic factors, environmental governance restrictions, and the impact of climate change and underlying environmental conditions (UNEP, 2020). The high rate of population expansion is a significant driver of environmental change (Satterthwaite, 2009). A result of population growth and rising land values is the sale of land for urban infrastructure and the development of construction onto agricultural areas (Chitti & Moser, 2019; M. A. Hassan et al., 2010). Unfortunately, this urbanization process has been rapid and lacking proper planning, resulting in increased pressure on natural resources and strained service delivery systems. One consequence of this is the projected increase in solid waste generation in Gaza, expected to surpass 3,000 tonnes by 2030 compared to around 1,900 tonnes in 2015. Furthermore, the expansion of settlements in the West Bank and East Jerusalem further intensifies the strain on limited natural resources, leading to pollution of air, soil, and water (UNEP, 2020). Consequently, these factors, such as urbanization, settlement expansion, and building the separation wall, besides rapid population growth, has significantly intensifies pressure on food production (Figure 1-2) (PCBS, 2022). The intensive production system, such as the one depicted in Figure 1-2, increases competition for natural resources, specifically water, leading to increased land degradation, loss of biodiversity, greenhouse gas emissions, and the proliferation of transboundary diseases and antimicrobial-resistant pathogens (FAO, 2017a).

The political situation restricts the policy options for good environmental governance and makes it challenging to adopt best-practice solutions to deal with the problems of resource scarcity (Qumsiyeh & Albaradeiya, 2022). Based on the UNEP report, restrictions on environmental governance fuel environmental change in Palestine by restricting Palestinians' freedom of movement and access to land and by putting pressure on the infrastructure due to poor urban design, high population density, and deteriorating agricultural land. Additionally, the Palestinian Authority has trouble enforcing Palestinian legislation in Areas A and B and cannot do so in Area C (UNEP, 2020). As in Figure 1-1 A, the land classification has resulted in the fragmentation and restricted urban expansion of Palestinian cities, particularly those located near category C areas (Nassar, Levy, Keough, & Nassar, 2019). Palestinians have no planning authority in this region and are often prohibited, through military orders, from constructing buildings (Nassar et al., 2019). Consequently, irregular and fragmented urban forms emerge, mainly when available land for future development is severely limited (Abdelhamid, 2006). Simultaneously, there is an ongoing process of land confiscation for the construction of Israeli settlements, bypass roads, and the separation barrier (Wall). These actions exert additional pressure on the environment and natural resources while limiting opportunities for sustainable development within Palestinian communities (Abu Hammad & Tumeizi, 2012; Nassar et al., 2019; Raddad, Salleh, & Samat, 2010).

Moreover, the prolonged Israeli occupation has transformed significant portions of the Palestinian territory into desert-like areas. Evidence of desertification is prominent on the Eastern Slopes, which feature steep inclines that restrict agricultural practices to animal grazing (Alkhouri, 2010). With 85% of these zones closed off by the Israeli Occupying Authorities for military reasons, the remaining accessible areas for Palestinian herders have experienced severe overgrazing. This has led to the depletion of vegetation cover, increased soil erosion, and intensified desertification (Alkhouri, 2010; Isaac & Hilal, 2011).

Palestine, located in the Eastern Mediterranean, is recognized as a significant "hotspot" for global climate change. Given its diverse geographical features and the prevalence of extreme climate conditions, the effects of climate change in the region will be unequal and disproportionate (Hammad & Salameh, 2019; Lelieveld et al., 2012). Climate projections indicate that by the middle of the century, temperatures are expected to increase by approximately 1.2°C to 2.6°C in Palestine (UNEP, 2020). Climate change significantly impacts the water cycle by altering precipitation patterns and seasons, with projected decreases in average monthly precipitation of 8-10 mm by the end of the century and potential shifts in seasonal rainfall patterns, resulting in increased aridity (UNEP, 2020). The increase in temperatures and decrease in water availability have a cascading effect, leading to heightened salinity and land degradation (Gampe, Ludwig, Qahman, & Afifi, 2016). Consequently, farmers are compelled to cultivate crops that are more resilient to saline conditions. However, this shift in crop patterns negatively impacts the ecosystem and diminishes soil biodiversity (UNEP, 2020). Furthermore, climate change is expected to worsen the issue of desertification, particularly in the West Bank where approximately 45 percent of the land area is susceptible to soil degradation due to steep hills. Arid regions are particularly vulnerable to erosion caused by water and wind, as well as salinization (Isaac & Hilal, 2011; UNEP, 2020). Additionally, climate-related hazards, including droughts, floods, heatwaves, cyclones, and sand and dust storms, are anticipated to occur more frequently and intensively, posing greater risks to the region (WHO, 2022b).

1.4 The Silent Pandemic: Antimicrobial Resistances

Antimicrobial resistance (AMR) is a global issue that jeopardizes a century of medical advancement and progress toward SDGs (WHO, 2021). Regardless of socioeconomic status, AMR raises the number of fatalities, health complications, and medical costs in all countries (Allel et al., 2023). In 2019, an estimated 1.27 million deaths worldwide were attributed to bacterial AMR. The O’Neill report estimates that by 2050, 10 million lives could be lost annually from AMR with a total of accumulated costs of 100 trillion US dollar (Murray et al., 2022). In Europe, AMR leads to 670,000 cases and 33,000 fatalities, and an economic loss of 1.1 billion annually (WHO, 2022a). Bacterial AMR is a natural occurrence that can be caused by de novo mutations or by the horizontal gene transfer of genetic material generating resistant phenotypes (Allel et al., 2023; Burmeister, 2015). It is known that exposing pathogens to antimicrobial drugs promotes the development of resistant pathogens (Allel et al., 2023). The epidemiology of AMR involves tracking the emergence and spread of resistant pathogens across different populations and settings. This includes monitoring the prevalence of resistant strains in healthcare facilities, communities, and animal populations, as well as tracking trends in antimicrobial use and prescribing practices (Figure 1-3) (Canada, 2022). The emergence of AMR is driven by the overuse, misuse, and/or usage of inadequate antimicrobials in human and animal. However, the problem doesn't stop there. Once resistance develops, it can spread, and during this process, the environment serves as a reservoir for resistant microorganisms (Allel et al., 2023). Between 2000 and 2018, Browne et al. estimated the human consumption of antibiotics in 204 nations and territories. The results show that sub-Saharan Africa has the lowest overall antibiotic usage rates, and North Africa and the Middle East have the highest rates. According to the report, the world consumed 40.1 billion defined daily doses (DDDs) of antibiotics in 2018, which equates to an average of 14·1 DDD per 1000 population per day (Browne et al., 2021). In 2020, an estimated 99,502 tonnes of antibiotics were used for food-producing animals worldwide. This figure is projected to reach 107, 472 tonnes by 2030 (Mulchandani, Wang, Gilbert, & Boeckel, 2023). This increase in antibiotic usage is a result of rising consumer demand for meat products and over-the-counter antibiotic sales, particularly in LMICs, where populations are growing and economies are developing (Mulchandani et al., 2023).

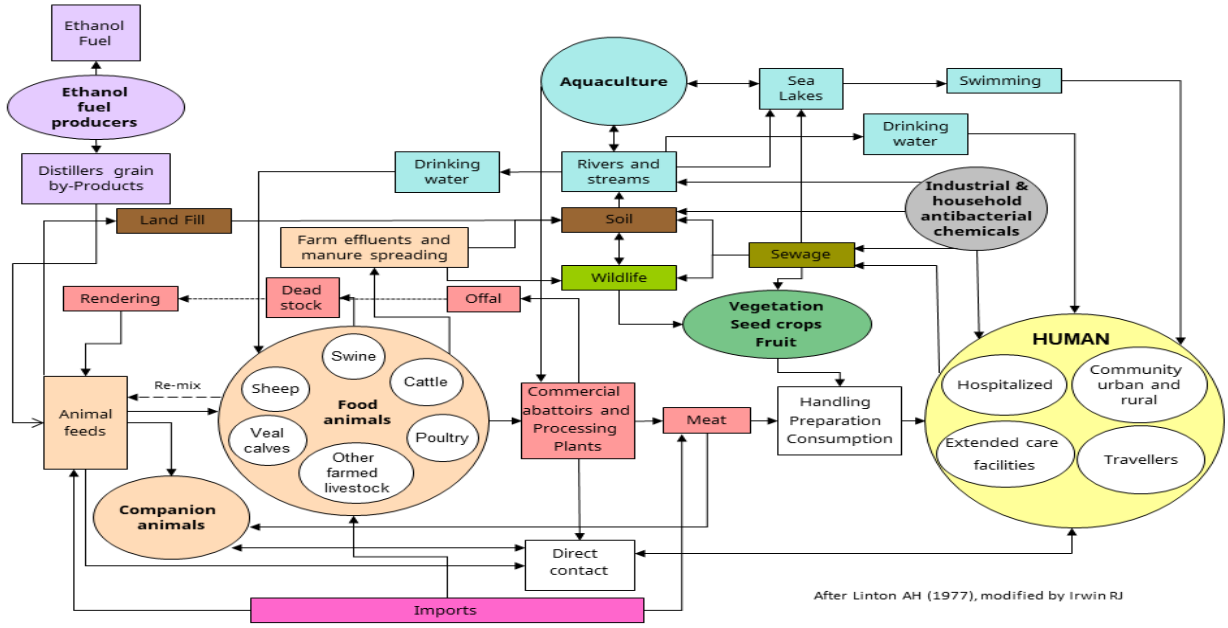


Figure 1-3 Epidemiology of AMR (Canada, 2022).

Various risk factors contribute to the emergence and spread of antimicrobial-resistant pathogens in LMICs. Some key risk factors include: 1. Misuse and overuse of antimicrobials including inadequate prescribing practices, inappropriate use of antimicrobials, and non-adherence to treatment regimens can contribute to the development of AMR (Byarugaba, 2004). 2. Lack of access to quality healthcare services, such as diagnostics, appropriate treatment options, and infection prevention and control measures, can facilitate the spread of resistant pathogens in LMICs (Sulis, Sayood, & Gandra, 2022). 3. The utilization of antimicrobials in livestock farming, aquaculture, and agricultural practices without adequate regulation and oversight can significantly contribute to the emergence and dissemination of AMR (Mulchandani et al., 2023; Sulis et al., 2022). 4. Poor sanitation and hygiene due to inadequate sanitation facilities, lack of clean water, and poor hygiene practices increase the risk of infections and transmission of resistant pathogens (Fletcher, 2015). 5. The absence of robust surveillance and monitoring systems in LMICs hinders the prompt detection, response, and implementation of effective interventions against AMR (Iskandar et al., 2021). 6.

Fragmented health systems, inadequate coordination, and limited resources can pose obstacles to the successful implementation of antimicrobial stewardship programs and control measures, impeding their effectiveness. (Cars et al., 2021).

As part of WHO's efforts to address rising AMR globally, the WHO published a list of 12 families of bacteria that are antibiotic-resistant and require novel medications urgently. The aim was "to guide and promote research and development of new antibiotics, as part of WHO's efforts to address growing global resistance to antimicrobial medicines" (WHO, 2017c). Microbes were categorized in the report as either critical, high priority, or medium priority. The critical category included the carbapenem-resistant pathogens *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae*, and ESBL-producing *Enterobacteriaceae*. Vancomycin-resistant *Enterococcus faecium*, clarithromycin-resistant *Helicobacter pylori*, fluoroquinolone-resistant *Salmonella* spp., *Campylobacter* spp., and *Neisseria gonorrhoea*, and cephalosporin-resistant *Neisseria gonorrhoea* were among the high priority pathogens, whereas ampicillin-resistant *Haemophilus influenza*, penicillin-non-susceptible *Streptococcus pneumonia*, and fluoroquinolone-resistant *Shigella* spp. are considered to be of middle priority (WHO, 2017c).

1.5 *Campylobacter* spp. and *Salmonella* spp. the leading pathogens of foodborne illnesses, gastroenteritis, and antimicrobial resistance.

1.5.1 *Campylobacter* spp.

Campylobacter is a genus of motile Gram-negative bacteria and has a curved, spiral or rod-shaped shape, often called an "S" or "seagull-shaped" (Kaakoush, Castaño-Rodríguez, Mitchell, & Man, 2015). *Campylobacter* is nutritionally fastidious and grows under strictly anaerobic or microaerobic settings. There are 26 species in the *Campylobacter* genus, two provisional species and nine subspecies (WHO, 2015b). The most well-known members are *C. jejuni* and *C. coli*, the major global contributor to bacterial gastroenteritis in humans (Kaakoush et al., 2015; Man, 2011). Although less frequently reported, other species, including *C. upsaliensis* and *C. lari*, have also been isolated from individuals with gastroenteritis (WHO, 2020a). Despite the fact that *C. jejuni* remains the most common cause of bacterial gastroenteritis in humans globally, developments in molecular biology and the emergence of novel culture methodologies have made it possible to identify and isolate a number of nutritionally unknown *Campylobacter* species, such as *C. upsaliensis*, *C. concisus*, and *C. ureolyticus* (Man, 2011).

Pathogenic *Campylobacter* species have been categorized as "emerging illnesses" because they cause 400-500 million cases of diarrhoea annually worldwide, and their capacity to adapt and evolve, resulting in the emergence of new strains exhibiting different levels of virulence and antimicrobial resistance (Chibwe, Odume, & Nnadozie, 2023). According to a report from the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC), *Campylobacter* accounted for the highest number of zoonosis cases in the EU in 2021 with 127,840 cases, a 2.1% rise in notification rate in the EU compared to 2020 (EFSA, 2022a). Additionally, *Campylobacter* is one of the leading causes of gastroenteritis especially among children, with the prevalence rate of 61%, 17%, 11%, 7%, 4% and 5% of gastroenteritis cases reported due to *Campylobacter* infections in Israel, Egypt, Iran, Kuwait, Morocco, and Palestine, respectively (Authority, 2018; A. Harb et al., 2019; Kaakoush et al., 2015).

The emergence of disease symptoms often happens 2 to 5 days after bacterial infection; however, it can range from 1 to 10 days. Acute watery or bloody diarrhoea, fever, weight loss, and persistent cramping are symptoms of *C. jejuni* or *C. coli* infections inpatients. Campylobacteriosis death is rare and mainly affects young children, elderly patients, or people with immunocompromised states (Kaakoush et al., 2015; WHO, 2020a). Extraintestinal infections caused by *Campylobacter* are uncommon in individuals with good overall health but are more likely to occur in individuals who are immunocompromised, elderly, or pregnant. Bacteremia, with or without accompanying diarrhoeal illness, is the most frequently observed type of extraintestinal *Campylobacter* infection (Fitzgerald, 2015). Patients who have experienced *Campylobacter* infections are at an increased risk of developing several postinfectious complications, including Guillain-Barre syndrome (GBS), reactive arthritis, and irritable bowel syndrome (Fitzgerald, 2015; Man, 2011; WHO, 2015b, 2020a). Among these, *C. jejuni* is the most frequently identified bacterial cause of GBS, preceding paralysis in approximately 30% of GBS patients (Yuki & Hartung, 2012). Reactive arthritis is estimated to occur in around 2% to 5% of patients, while irritable bowel syndrome affects approximately 33% of patients following a *Campylobacter* infection (Marshall, 2009; Pope, Krizova, Garg, Thiessen-Philbrook, & Ouimet, 2007).

Campylobacter genus members are ecologically diverse and readily colonize both humans and animals (Man, 2011). Campylobacteriosis is a zoonotic disease, which is a disease transmitted to humans from animals or animal products (WHO, 2020a). It is generally believed that the main route of transmission of *Campylobacter* is through food, meat products, and raw or contaminated milk. Cross-contamination from feces can lead to contamination of meat or carcasses with *Campylobacter* during the slaughtering process. Also, contaminated ice or water can potentially be a source of *Campylobacter* contamination (Prendergast et al., 2022; WHO, 2020a).

Poultry meat is recognized as a significant source of Campylobacteriosis; for example, in Canada, broiler chickens are a major source of *Campylobacter*. About 71% of Campylobacteriosis incidents in humans in Switzerland were also attributed to poultry in 2001-2012. According to data from the United Kingdom Food Standards Agency, from 2014 to 2015, 73% of fresh chickens were contaminated with *Campylobacter* (Kaakoush et al., 2015). Additionally, research from Kenya and Thailand indicates that 40% and 77%, respectively, of the poultry meat in these nations is contaminated with *Campylobacter* (Coker, Isokpehi, Thomas, Amisu, & Obi, 2002). Although broiler chicken meat consumption, handling, and preparation cause 20 to 30% of Campylobacteriosis cases in the EU, the poultry reservoir as a whole is responsible for 50 to 80% of human *Campylobacter* infections (Bless, Schmutz, & Mausezahl, 2017; Silva et al., 2011). *Campylobacter* is spread to broiler farms through interaction with rodents and wild birds, inadequate waste management techniques, particularly improperly disposing of dead birds, and a lack of hygienic habits among farmers and guests (Schmutz et al., 2017; Schmutz, Mausezahl, Jost, Baumgartner, & Mausezahl-Feuz, 2016). For instance, 40% of farms' broiler chickens in Jordan are contaminated with *Campylobacter* spp. (Hawileh, 2012).

Although the majority of *Campylobacter* infections are self-limiting, certain clinical cases involving severe illness or individuals at risk of serious complications, particularly those with impaired immune systems, may require antibiotics. In such circumstances, fluoroquinolones (e.g., ciprofloxacin) and macrolides (e.g., erythromycin and azithromycin) are typically considered the first-line treatment options when therapeutic intervention is deemed necessary (Shobo et al., 2016; WHO, 2020a). However, the rise of antibiotic-resistant strains makes managing *Campylobacter* infections challenging. The global reports of fluoroquinolone-resistant and macrolide-resistant *Campylobacter* spp., specifically *C. jejuni* and *C. coli*, highlight the impact of extensive and unrestricted use of these antibiotics on the development of resistance (Chibwe et al., 2023; Shobo et al., 2016). In the WHO's list on critical, high priority and medium priority bacterial pathogens, fluoroquinolone-resistant *Campylobacter* spp. were assigned to the high-priority group (number 2) (WHO, 2017c). This classification highlights the significant public health concern surrounding quinolone-resistant *Campylobacter* infections (Abraham et al., 2020; Béjaoui et al., 2022).

The fluoroquinolone resistance mechanism is chromosomally mediated through mutation of the *parC* gene and *gyrA* gene. In addition, the most prevalent efflux mechanism in *Campylobacter*, the *CmeABC* multidrug efflux pump, causes fluoroquinolone resistance in synergy with *gyrA* mutations (Shobo et al., 2016; Wieczorek & Osek, 2013). Macrolide resistance in *Campylobacter* is primarily linked to point mutations that occur in the peptidyl-encoding region of domain V within the 23S rRNA gene. These mutations affect the target site of macrolide antibiotics (Aleksić et al., 2021; Gibreel & Taylor, 2006). Additionally, in *Campylobacter*, the CmeABC multidrug efflux pump is a major contributor to macrolide resistance (Cagliero, Mouline, Cloeckaert, & Payot, 2006; Iovine, 2013; Wieczorek & Osek, 2013). The CmeABC efflux pump in *Campylobacter* is structurally similar to multi-drug efflux pumps found in Gram-negative bacteria of the resistance nodulation cell division superfamily (Corcoran, Quinn, Cotter, & Fanning, 2005). It comprises three components: CmeA, a periplasmic fusion protein; CmeB, an inner membrane drug transporter; and CmeC, an outer membrane protein. Together, these proteins form a membrane channel that actively expels various toxic substances, including antimicrobial agents, from *Campylobacter* cells (Gibreel & Taylor, 2006). Evidence suggests that a combination of efflux activity and mutations in the 23S rRNA gene contributes to the development of high-level macrolide resistance in *Campylobacter* spp.(Wieczorek & Osek, 2013).

Fluoroquinolone resistance in *Campylobacter* was initially described in the late 1980s, and since then, it has been spreading throughout various nations (Wieczorek & Osek, 2013). In a recent study conducted in Switzerland, *C. jejuni isolates* obtained from humans with gastroenteritis were examined over a span of 18 years, from 2003 to 2020. The study findings demonstrated that fluoroquinolones, particularly ciprofloxacin and nalidixic acid, had the highest rates of resistance (49.8%) (Ghielmetti et al., 2023). In the United Kingdom, the occurrence of fluoroquinolone resistance in *C. jejuni* strains isolated from patients has substantially risen over 20 years. In 1998, fluoroquinolone resistance was detected in 5% of the isolates, but by 2018, it had increased to affect 45% of all isolates (Veltcheva, Colles, Varga, Maiden, & Bonsall, 2022). In United States, use of fluoroquinolones in food-producing animals has been banned since 1997, however, ciprofloxacin resistance in *C. jejuni* isolates from cattle remained high or continued to increase, with beef isolates showing an increase from 14% in 2013 to 20% in 2015. In chicken isolates, ciprofloxacin resistance ranged between 22% and 28% from 2012 to 2015. Similarly, the prevalence of ciprofloxacin resistance in *C. coli* isolated from humans showed an increase, rising from 34% in 2012 to 40% in 2015 (NARMS, 2017; Veltcheva et al., 2022). In Latin America, recent research has shown high levels of resistance to fluoroquinolones, especially ciprofloxacin, in seven countries (Brazil, Argentina, Chile, Paraguay, Ecuador, Trinidad, and Peru) (Portes, Panzenhagen, Pereira dos Santos, & Junior, 2023). In Turkey, the prevalence of *C. jejuni* with quinolone resistance (human origin) increased from 1% in 1994 to 74% in 2013 (Kayman, Abay, Aydin, & Şahin, 2019). In China, among clinical samples, resistance to ciprofloxacin in *C. jejuni* increased from 78% (1994–2002) to 90% (2003–2010) (Zhou et al., 2016). Furthermore, a notable occurrence of fluoroquinolone resistance has been reported in *C. jejuni* strains of human origin in the United Arab Emirates (85%) and in strains of chicken origin in South Africa (91%) (Bester & Essack, 2008; Sonnevend et al., 2006).

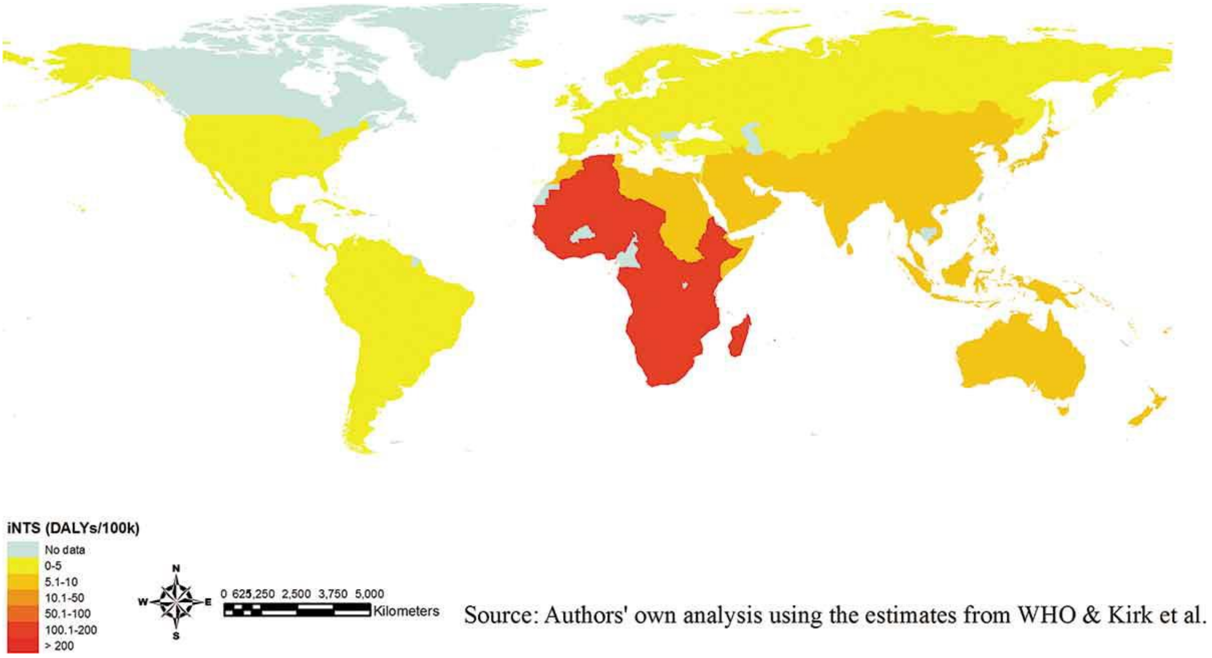
Nowadays, macrolides are considered the first line treatment for *Campylobacter* infections since, as mentioned above, fluoroquinolone resistance is common. However, there is also evidence that the prevalence of macrolide resistance in *Campylobacter* is gradually rising in some countries. Macrolide resistance in *Campylobacter* isolates is growing to be a significant public health concern (Wieczorek & Osek, 2013). In a study performed in China, *Campylobacter* isolates recovered from poultry and pig showed high resistance rates to erythromycin (75.3%) and azithromycin (66.7%) (Tang et al., 2020). In Poland, there was a statistically significant rise in the percentage of erythromycin-resistant *Campylobacter* isolates from poultry during the years 1994–1996 and 2005–2008 (49.3% and 88.9%, respectively) (Wieczorek & Osek, 2013). Erythromycin resistance has been reported with a high prevalence in *Campylobacter* isolates from poultry in Tunisia and Morocco, with 98% and 97% resistance rates, respectively (Béjaoui et al., 2022; Es-Soucratti et al., 2020). To date, *C. jejuni* from humans and animals in the European Union has shown a low level of macrolide resistance (Authority, Prevention, & Control, 2021).

1.5.2 *Salmonella* spp.

Salmonella spp. is a genus of rod-shaped gram-negative, motile, facultative anaerobic bacilli and is classified within the family Enterobacteriaceae. These bacteria grow under both anaerobic and aerobic conditions. *Salmonella* consists of two species: *bongori* and *enterica*. (Bula-Rudas, Rathore, & Maraqa, 2015). *Salmonella enterica* has six subspecies: *indica*, *houtenae*, *diarizonae*, *arizonae*, *salamae*, and *enterica* (Andruzzi, Krath, Lawhon, & Boudreau, 2020). Most recent DNA hybridization studies have led to the hypothesis that the majority of clinically relevant *Salmonella* organisms may belong to a single species, *Salmonella enterica* subspecies *enterica* (Bula-Rudas et al., 2015). Subspecies *enterica*, which has 2600 serovars and can be split into typhoidal and non-typhoidal *Salmonella* (NTS) serovars, is the most frequent cause of illness in mammals (Andruzzi et al., 2020; Bula-Rudas et al., 2015).

Non-typhoidal *Salmonella* (NTS) in humans is most often transmitted through the consumption of contaminated water and food of animal origin (mainly eggs, meat and dairy products) and this is facilitated by poor hygiene conditions (Bula-Rudas et al., 2015; WHO, 2018c). However, other foods, including green vegetables contaminated with manure, have been implicated in its transmission. Person-to-person transmission may also occur through the fecal-oral route (WHO, 2018c). Salmonellosis is usually characterized by abdominal cramps, bloody diarrhoea, severe onset of fever, nausea, and sometimes vomiting (Ehuwa, Jaiswal, & Jaiswal, 2021). Symptoms of the disease often appear 6-72 hours (usually 12-36 hours) after consuming *salmonella*, and the illness lasts 2 to 7 days (Bula-Rudas et al., 2015; WHO, 2018c). In most cases, symptoms of salmonellosis are relatively mild, and patients recover without specific treatment. However, in vulnerable population groups such as children and elderly patients, those with certain underlying conditions (e.g. haemoglobin disorders, malignancy, and HIV infection) have an increased risk of severe illness and death from complications (Bula-Rudas et al., 2015; Ehuwa et al., 2021; WHO, 2018c).

Invasive non-typhoidal *Salmonella* (iNTS) has emerged as a significant public health concern (Balasubramanian et al., 2019). An estimated 93 million intestinal infections and 155,000 related fatalities occur yearly due to NTS (Ao et al., 2015). Using data from the WHO at the regional level along with a linear random effect log model, WHO and Kirk et al. assessed the geographic distribution of the iNTS disease and presented their findings in (Figure 1-4) (Balasubramanian et al., 2019; Kirk et al., 2015; WHO, 2015a).



Source: Authors' own analysis using the estimates from WHO & Kirk et al.

Figure 1-4 Disability-adjusted life years due to iNTS illness (2010). The map is not suitable for interpretation at the country level; only regional estimates from WHO were used (Balasubramanian et al., 2019).

Multidrug resistance (MDR) in *Salmonella* refers to the ability of *Salmonella* to resist multiple medications, including commonly used first-line antibiotics such as ampicillin, chloramphenicol, and trimethoprim/sulfamethoxazole. *Salmonella* has a significant rate of MDR; hence second-line antibiotics are required (John A Crump, Sjölund-Karlsson, Gordon, & Parry, 2015; Cuypers et al., 2018). Fluoroquinolones, such as ciprofloxacin, and third-generation cephalosporin, such as ceftriaxone, are often recommended as the drugs of choice for treating invasive *Salmonella* infections, while the macrolides, such as azithromycin, can be used as a substitute (Cuypers et al., 2018; J. Li, Hao, Sajid, Zhang, & Yuan, 2018; Shane et al., 2017). However, there has been an increasing concern about the emergence and spread of fluoroquinolone-resistant *Salmonella* strains. The WHO included fluoroquinolone-resistant *Salmonella* in its list of high-priority antibiotic-resistant pathogens in 2017 (WHO, 2017c). This highlights the urgent need to address the growing challenge of antibiotic resistance in *Salmonella* (Cuypers et al., 2018).

The genetic basis of quinolone resistance in *Salmonella* is mutations in the quinolone-resistance-determining regions (QRDRs) of the chromosomal *gyr* and par genes, resulting in a lower quinolone-binding affinity of the topoisomerase enzymes (Figure 1-5) (Correia, Poeta, Hébraud, Capelo, & Igrejas, 2017; Cuypers et al., 2018; J. Li et al., 2018).

Salmonella's resistance to fluoroquinolones can also be attributed to other mechanisms, such as plasmid-mediated quinolone resistance (PMQR) (Figure 1-5), which requires the development of:

1. The *aac(6')-lb-cr* gene encodes a modifying enzyme that decreases quinolone activity (Sodhi & Singh, 2021).
2. Qnr genes (*qnrA*, *qnrB*, *qnrS*, *qnrC*, *qnrD*) encode topoisomerase-binding proteins that provide physical protection from quinolones (Redgrave, Sutton, Webber, & Piddock, 2014).
3. *oqxAB* and *qepA*, encoding quinolone efflux pumps (Correia et al., 2017).

Finally, upregulation and downregulation of multidrug efflux pumps or chromosome-encoded porins (such as *AcrAB-TolC*), respectively, lower the cellular quinolone concentrations (Figure 1-5) (Cuypers et al., 2018).

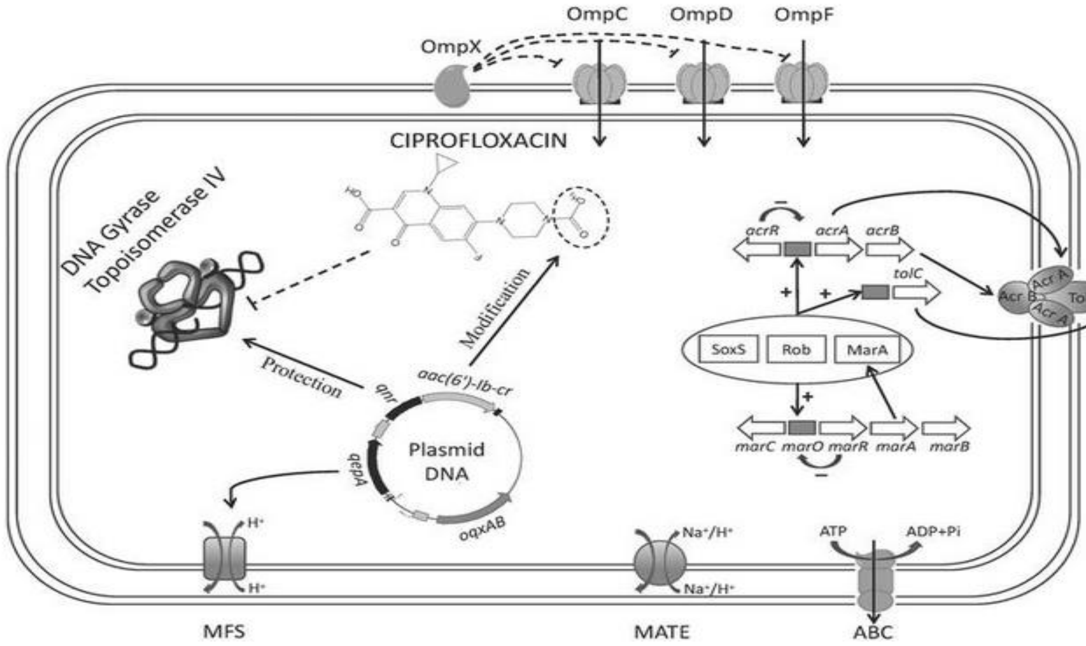


Figure 1-5 Mechanisms of quinolone resistance (J. Li et al., 2018).

Fluoroquinolone resistance in *Salmonella* can spread through horizontal gene transfer, where resistance genes are passed from one bacterium to another, allowing for the rapid dissemination of resistance in bacterial populations (Nadeem et al., 2020).

1.6 One Health approach

In the 1960s, the term One Medicine was coined by Calvin Schwabe, a veterinary epidemiologist, in order to draw attention to the commonalities between human and animal health concerns (Zinsstag et al., 2022). In 2004, the "One World, One Health" concept was introduced as a way to emphasize the interconnectedness of the health systems and to highlight the need for a coordinated and interdisciplinary approach to addressing global health challenges at a symposium organized by the Wildlife Conservation Society. The resulting manifesto, known as the Manhattan Principles, laid out a framework for collaboration between experts in public health, veterinary medicine, wildlife biology, and environmental science, among other fields (Trosko, 2017). One Health was first raised by Zinsstag and colleagues in 2005 in the peer-reviewed biomedical literature to highlight its potential to improve health systems (Zinsstag, Schelling, Wyss, & Mahamat, 2005). Zinsstag and colleagues described One Health as "*any added value in terms of human and animal health, financial savings or environmental benefit from closer cooperation of human and animal health sectors at all levels of organisation*"(Zinsstag, Schelling, et al., 2020). In 2019, the Berlin Principles were announced, which represent a comprehensive and forward-thinking framework for ecosystem management that emphasizes the interconnections between social, economic, and ecological, systems and highlights the importance of sustainable development for the well-being of people and the planet (Gruetzmacher et al., 2021). In addition to addressing urgent contemporary challenges, including climate change, disease spillover, and AMR, the Berlin Principles updated the Manhattan Principles by reintegrating ecological health and integrity (Gruetzmacher et al., 2021; Zinsstag, Kaiser-Grolimund, et al., 2023).

In 2020, the interdisciplinary One Health High-Level Expert Panel (OHHLEP) was established by four global partners; (WOAH, formerly the Office International des Epizooties), Food and Agriculture Organization of the United Nations (FAO), UNEP, and WHO. OHHLEP defined One Health approach as *"an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and interdependent"* (Adisasmito et al., 2022). Currently One Health is the most operationalized integrated health approach. The group of seven largest economies (G7) have adopted One Health as a strategic approach in the Carbis Bay declaration in 2021 (GOV.UK, 2021).

1.6.1 One Health approach for the understanding of Antimicrobial Resistance

The World Health Assembly passed the WHA67.25 resolution in 2014, which urged the creation of a worldwide action strategy to address the AMR problem. With collaboration from the FAO and WOAH, WHO led the creation of the GAP on AMR (Truppa & Abo-Shehada, 2020). The plan was officially adopted in 2015, aiming to ensure the continuous effectiveness of antimicrobial drugs and mitigate the emergence and spread of AMR. To achieve this, the plan established the Global AMR Surveillance System (GLASS), which facilitates robust evidence gathering and integrated data collection and surveillance across nations (Truppa & Abo-Shehada, 2020; WHO, 2018b).

Integrated surveillance of AMR and antimicrobial use (AMR/AMU) is a key component of efforts to combat the growing threat of AMR (Otto, Haworth-Brockman, Miazga-Rodriguez, Wierzbowski, & Saxinger, 2022). It involves the systematic collection, analysis, and reporting of data on the prevalence and patterns of AMR and AMU in human and animal populations, as well as in the environment. Integrated surveillance of AMR/AMU involves collaboration among multiple sectors and stakeholders, including healthcare providers, veterinarians, public health authorities, and researchers (Founou, Founou, & Essack, 2016). The aim is to provide a comprehensive picture of the emergence and spread of AMR and to inform policy decisions related to the appropriate use of antimicrobial agents (McDermott et al., 2016). The surveillance of AMR/AMU is critical to guiding the development and implementation of effective interventions to prevent and control AMR. By monitoring trends in resistance patterns and antimicrobial use, surveillance can help identify areas where interventions are most needed, guide the appropriate use of antimicrobial agents, and evaluate the impact of interventions over time (Ferri, Ranucci, Romagnoli, & Giaccone, 2017).

Globally, several countries have implemented integrated surveillance systems for AMR (Tacconelli et al., 2018) such as Sweden, Switzerland, USA, and Canada. The Swedish Integrated AMR Surveillance Program (SWEDRES-SVARM) and Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) were established in 1990s to monitor trends in antibiotic resistance in humans, animals, and food. The programs collect data on antibiotic use and resistance in in these sectors (Queenan, Häsler, & Rushton, 2016). Switzerland has implemented an integrated surveillance system for AMR known as the Swiss Centre for Antibiotic Resistance (ANRESIS). ANRESIS is a national program that was established in 2016 and is coordinated by the Swiss Federal Office of Public Health (FOPH) and Institute for Infectious Diseases (IFIK) of the University of Bern. ANRESIS collects data on antimicrobial susceptibility from clinical laboratories, veterinary diagnostic laboratories, and other sources. The program also conducts research on AMR, including the identification of new resistance mechanisms and the characterization of the genetic basis of resistance (IFIK, 2023). In United States, the National Antimicrobial Resistance Monitoring System (NARMS) is a joint program between the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA). NARMS monitors trends in antibiotic resistance in foodborne bacteria from humans, animals, and retail meat (Karp et al., 2017). Canadian Integrated Program for Antimicrobial Resistance (CIPARS) is a national surveillance program in Canada that monitors trends in antimicrobial use and resistance in food animals, food products, and humans. CIPARS was established in 2002 and is a collaboration between the Public Health Agency of Canada, Health Canada, the Canadian Food Inspection Agency, and provincial public health and agriculture agencies. The program collects data from multiple sources, including veterinary diagnostic laboratories, abattoirs, and hospitals (Figure 1-6) (Canada, 2022; WHO, 2017b). CIPARS has been instrumental in informing Canadian policies related to the use of antimicrobials in food animals, including restrictions on the use of Medically Important Antimicrobials (MIAs) for veterinary in 2018 (Canada, 2021). The program also provides valuable data for research on AMR and for international comparisons of resistance patterns (WHO, 2017b). Therefore, the advantages of implementing the One Health surveillance system, like in CIPARS, extend to a diverse range of professionals, including researchers, diagnostic microbiologists, pharmacologists, and clinicians, who can all benefit from its utilization (Guardabassi, Butaye, Dockrell, Fitzgerald, & Kuijper, 2020). The Canadian approach to AMR surveillance and management is considered a model for other countries to follow (Parmley et al., 2012; Zinsstag et al., 2011).

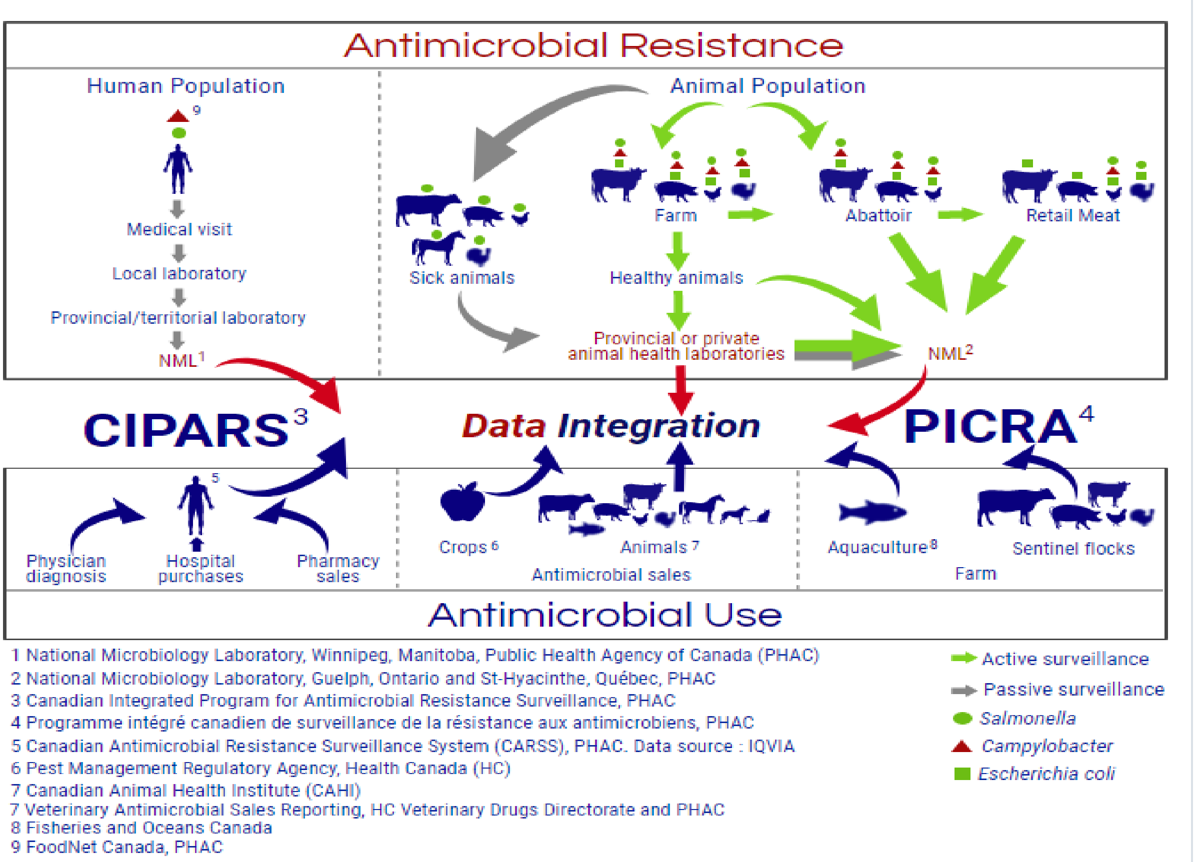


Figure 1-6 Canadian Integrated Program for Antimicrobial Resistance Surveillance components (Canada, 2022).

2 Rationale, Aim and Objectives

2.1 The rationale for applying the One Health surveillance system in a conflict-torn areas such Palestine

Foodborne illnesses are a significant regional public health concern, with high prevalence rates reported. Norovirus, Escherichia *coli*, *Campylobacter*, and NTS are among the most common pathogens responsible for causing foodborne diseases in the region, accounting for up to 70% of cases. This can result in a range of health issues, from minor gastrointestinal symptoms to severe illnesses and even death. Foodborne pathogens can be considered transboundary diseases, as they can easily spread across borders and affect multiple countries or regions (Todd, 2017). Unrest in the Middle East due to conflicts and wars has significantly influenced food safety and increased the risk of foodborne diseases due to 1) the disruption of food supply chains, which results in shortages, price spikes, and less availability of safe and nutritious food. 2) Damages to infrastructure (e.g. food production and processing facilities, transportation networks, and water and sanitation systems) lead to a decline in the quality and safety of food products and an increased risk of contamination due to the disruption of water supplies and sanitation services. 3) Limited resources for food safety programs such as surveillance, monitoring, and inspection programs. This can weaken the food safety system, making preventing and controlling foodborne illnesses more difficult (Alsayeqh, Baz, & Darwish, 2021; Faour-Klingbeil & CD Todd, 2020; Todd, 2022).

Unrest in the Middle East has also significantly impacted AMR. The following are some ways in which conflicts and wars can contribute to the spread of AMR: 1) Conflict and war can contribute to increasing the use of antibiotics, which includes both fighters and civilians. 2) Disruptive impact on health systems, causing interruptions in access to essential medical care, medications, and diagnostic tools. This, in turn, can result in inadequate treatment of infectious diseases, creating favorable conditions for the emergence and dissemination of resistant bacteria. 3) Conflict and war can result in the displacement and migration of individuals, forcing them to seek refuge in overcrowded and unsanitary conditions, such as refugee camps or temporary shelters. This heightened population density and inadequate sanitation facilities elevate the risk of infectious diseases, including those caused by resistant bacteria. 4) Unrest situation due to the conflict and war can significantly deplete resources allocated for the control of AMR in both human and animal settings. 5) Ongoing conflicts and wars often lead to reduced resources for public health measures, including immunization coverage. Factors such as population displacement, inadequate resources, disrupted supply chains, and restricted access further contribute to inequitable immunization coverage in areas affected by conflict.

This diversion of resources affects critical aspects such as surveillance, monitoring, and infection prevention and control measures. Consequently, the capacity of health systems to effectively respond to AMR threats is weakened, leading to limited access to appropriate and effective treatments (Abou Fayad et al., 2023; Grundy & Biggs, 2019; Mostafavi et al., 2022; Truppa & Abo-Shehada, 2020; WHO, 2020c).

2.1.1 Palestinian food safety profile

In Palestine, similar to Egypt and Lebanon, implementing preventive food safety and risk-based systems is typically optional and is still far from being addressed in terms of regulating the safety of locally sold goods (Faour-Klingbeil, Al-Busaidi, & Todd, 2022). In Palestine, several ministries are responsible for food safety, including the Ministry of Health, the Ministry of Agriculture, the Ministry of Local Governance, and the Ministry of National Economy. These ministries operate separately from each other (Figure 2-1) (FAO, 2017b). There is no single organization that regulates food safety, analogous to the United States Food and Drug Administration (USFDA) or the European Food Safety Authority (EFSA) (EFSA, 2022b; FAO, 2017b; " U.S. Food and Drug Administration ", 2022). This overlap in monitoring the food safety system prompted the Palestinian Authority to develop a food safety strategy in 2015. This strategy identified the following weaknesses in the Palestinian food safety system: Weakness in food safety-related legislation, poor coordination among the numerous formal institutions that monitor food safety, weak monitoring system across the production chain, including control of food-borne diseases, lack of risk analysis policy, and poor food safety culture (FAO, 2017b). Furthermore, the annual reports of the Palestinian Ministry of Health indicate that cases of foodborne diseases are significantly underreported (Todd, 2022). For instance, the 2020 annual health report mentioned that the environmental health department conducted 7669 food tests; however, the report did not disclose the specific outcomes or results of these tests (MOH, 2020). At the same time, the report revealed that brucellosis, a disease endemic in Palestine, had a human prevalence rate of 17.9 per 100,000 individuals, with rates of 31.2 and 0.1 per 100,000 in the West Bank and Gaza Strip, respectively (MOH, 2020). A recent study conducted in Palestine highlighted a significant rise in the average annual incidence rate of *Brucella* since 2013. This increase can be attributed to various factors, including the inadequate control and surveillance system. Weaknesses identified in the system include the lack of regular screening of animals (mainly sheep and goats) for *Brucella* disease, inadequate import control measures, increased smuggling across borders, insufficient awareness programs, and limited intersectoral collaboration between governmental and non-governmental organizations (Amro, Mansoor, Hamarsheh, & Hjaija, 2021).

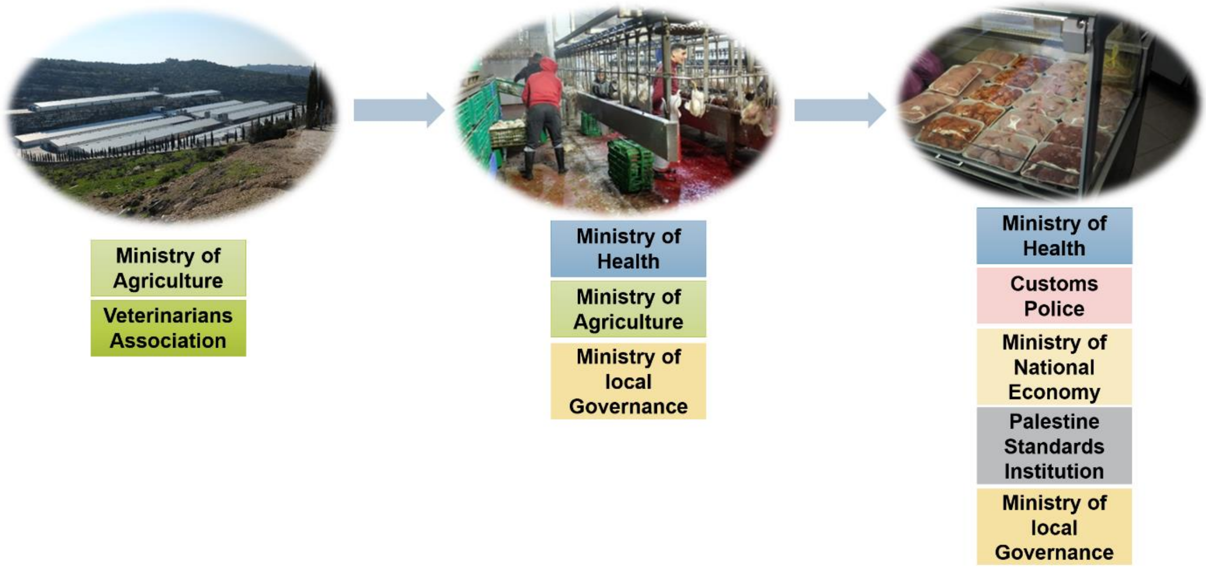


Figure 2-1 The monitoring system of the broiler meat production chain in Palestine. (Inspired from (FAO, 2017b)).

2.1.2 Palestinian Antimicrobial Resistance profile (human and animal)

The World Health Assembly adopted the Global Action Plan on Antimicrobial Resistance (GAP) in 2015. The GAP included the target that by 2017, all Member State would have a National Action Plan (NAP) aligned with the GAP's objectives (WHO, 2018a). In 2019, Palestine developed their NAP based on the GAP as recommended by WHO (WHO, 2020c). Palestine has identified five Goals for its National Action Plan (NAP) that closely align with the objectives outlined in the GAP (WHO, 2015b, 2020c). These goals include: 1. Raise awareness programs on AMR and the use of antimicrobials. 2. One Health surveillance system for AMR. 3. Prevent infection by implementing evidence-based infection control practices to mitigate the spread of resistant pathogens. 4. The optimal use of antimicrobial medication (human and animal). 5. Support and encourage operational research on AMR (WHO, 2015b, 2020c).

Based on Palestinian NAP, Palestine, like other LMICs, faces challenges in effectively managing infectious diseases through the use of safe and affordable antimicrobials. However, in Palestine, the absence of a comprehensive national surveillance system on AMR and insufficient data availability hinder the evaluation of the extent and nature of the AMR problem. Additionally, the quality of published data poses further obstacles in assessing the magnitude and dimensions of the AMR issue (WHO, 2020c). In response to the increasing incidence of AMR infections in Palestinian hospitals, mainly attributed to inadequate standardized infection prevention and control systems, the Quality Planning Department at the Ministry of Health collaborated with the United States Agency for International Development (USAID) in 2017.

They launched the Antimicrobial Stewardship project on a national scale, covering 22 hospitals. The primary objective of this initiative is to promote the responsible and rational use of antibiotics (USAID, 2018). In a study conducted in Palestine, it was observed that the availability of real-time antibiogram data was insufficient, resulting in clinicians relying on practical guidelines for the management of community-acquired pneumonia. Furthermore, the study found that clinicians demonstrated poor adherence to the current standards of care in terms of severity assessment and management for community-acquired pneumonia. Among the 18 different antibiotic regimens used, 81% of patients received combination therapy of β-lactam and macrolide, 49% were treated with β-lactam alone, and 32% were prescribed a combination of β-lactam with another antibiotic (Alyacoubi, Abuowda, Albarqouni, Böttcher, & Elessi, 2018).

In a survey study conducted in the two burn units of a teaching hospital, 28 samples from healthcare workers, 97 environmental samples, and 118 wound samples from burn patients were collected and cultured. *Pseudomonas aeruginosa* and *Enterobacter cloacae* were the most common pathogen isolated at 50% and 28.3%, respectively. The majority of pathogens were obtained from the environment, and patients exhibited resistance to nearly all antibiotics except piperacillin-tazobactam. Among the patients, approximately 60% of *Staphylococcus aureus* isolates were identified as Methicillin-Resistant *Staphylococcus aureus* (MRSA) (Elmanama, Al Laham, & Tayh, 2013).

In a study that targeted animals, samples of internal organs were collected from 83 flocks and tested for non-typhoidal *Salmonella*. High levels of resistance were detected in the antibiotic susceptibility profile against tetracycline (100%), amoxicillin (83%), ampicillin (83%), kanamycin (80%), ciprofloxacin (73%), and neomycin (70%) (WHO, 2020c).

2.2 Aim and objectives

This PhD thesis uses the One Health approach to assess the occurrence of zoonotic bacteria and their AMR in the food production chain, chicken meat production, and subsequently in humans in conflict-torn areas.

Objective 1: To identify existing integrated One Health studies on foodborne illnesses in the Middle East

a) To determine the prevalence, serovars, and AMR phenotypes and genotypes of *Salmonella* and *Campylobacter* strains among humans and food-producing animals.

b) To address the knowledge gap and summarize the available information about the situation of applying the integrated research to follow up *Salmonella* spp. and *Campylobacter* spp. in the Middle East.

Objective 2: To assess food safety from farm to public health toward an operational One Health strategy for Palestine.

a) To explore stakeholder perspectives on the food production control system in Palestine.

b) To assess hygiene practices along the chicken meat production chain in Palestine

c) To assess knowledge, attitudes and practices (KAP) related to hygiene by workers in the chicken meat production chain in Palestine.

Objective 3: To assess the added value of implementing an integrated foodborne pathogen surveillance system and AMR in conflict-torn areas.

a) To assess the prevalence rates of *Salmonella* spp. and *Campylobacter* spp. along the chicken meat production chain using the One Health survey (human, animal, and environment) in Ramallah/Al-Bireh and Jerusalem, Palestine.

b) To investigate *Salmonella* and *Campylobacter* serovars circulating over the chicken meat production chain in Ramallah/Al-Bireh and Jerusalem, Palestine.

c) To investigate the genetic resemblance between the *Salmonella* and *Campylobacter* isolates obtained from various sources and to compare them to clinical isolates found in Ramallah/Al-Bireh and Jerusalem, Palestine.

d) To comprehensively investigate the antibiotic resistance genes (ARGs) and mobile genetic elements (MGEs) shared in isolates from different sources (human, animal, environmental samples) in Ramallah/Al-Bireh and Jerusalem, Palestine.

e) To explore the risk factors associated with *Campylobacter* infection in chicken meat workers in Ramallah/Al-Bireh and Jerusalem, Palestine.

3 Planned activities, work plan

One Health can be defined as “any added value in terms of human and animal health, financial savings or environmental benefit from closer cooperation of human and animal health sectors at all levels of organisation” (Zinsstag, Schelling, et al., 2020). One Health has been validated in numerous case studies worldwide. So far, few existing studies in the Middle East have applied One Health; however, these studies need robust epidemiological study designs adequate for a One Health approach (Zinsstag, Schelling, et al., 2020). This PhD thesis will be the first to use the One Health approach on foodborne pathogens and their AMR in Palestine. We employ the new-generation sequencing technique to analyze the isolates genetically, which is the first time used within One Health in the Middle East to study foodborne pathogens, *Salmonella* and *Campylobacter*, and their circulating serotypes and AMR profiles.

Therefore, we used different epidemiological methods to achieve our objectives, starting with a systematic review and meta-analysis and mixed-methods, including multistakeholder discussion groups, semi-structured observational designs, and cross-sectional study designs.

3.1 Methodology for objective 1

Systematic review: The databases Web of Science, Scopus, and PubMed were searched for literature published from January 2010 until September 2021. Studies meeting inclusion criteria were included and assessed for risk of bias. To assess the temporal and spatial relationship between resistant strains from humans and animals, a statistical random-effects model meta-analysis was performed. Detailed descriptions of the methods applied for these research components are provided in chapter 4 (Abukhattab *et al*. [2022]) (Figure 3-1).

3.2 Methodology for objective 2

A mixed-method study: transdisciplinary approach, semi-structured observations, and survey.

The transdisciplinary approach included multi-stakeholder discussion groups and field visits to broiler farms, slaughterhouses, and meat stores in the Ramallah/Al-Bireh and Jerusalem districts using a semi-structured observational tool. A survey (a questionnaire) with

337 poultry producers and workers in slaughterhouses and meat stores was conducted to assess hygiene knowledge, attitudes, and practices during broiler meat production. Detailed descriptions of the methods applied for these research components are provided in chapter 5 (Abukhattab *et al*. [2022]) (Figure 3-1).

3.3 Methodology for Objective 3

Laboratory tests targeting the leading causes of foodborne Illness and AMR: *Salmonella* spp. and *Campylobacter* spp.

This cross-sectional study was conducted to examine the role of AMR at the human-animal-environmental interface and was performed in Ramallah/Al-Bireh and Jerusalem governorates of the central West Bank, Palestine. In 2021 and 2022, a total of 592 samples were collected and analyzed. From a total of 65 *C. jejuni* and 19 *Salmonella* spp. isolates DNA was extracted for whole genome sequencing using Oxford Nanopore Technologies MinION platform. Detailed descriptions of the methods applied for these research components are provided in Chapter 6 (Abukhattab *et al*. [2023]) (Figure 3-8).

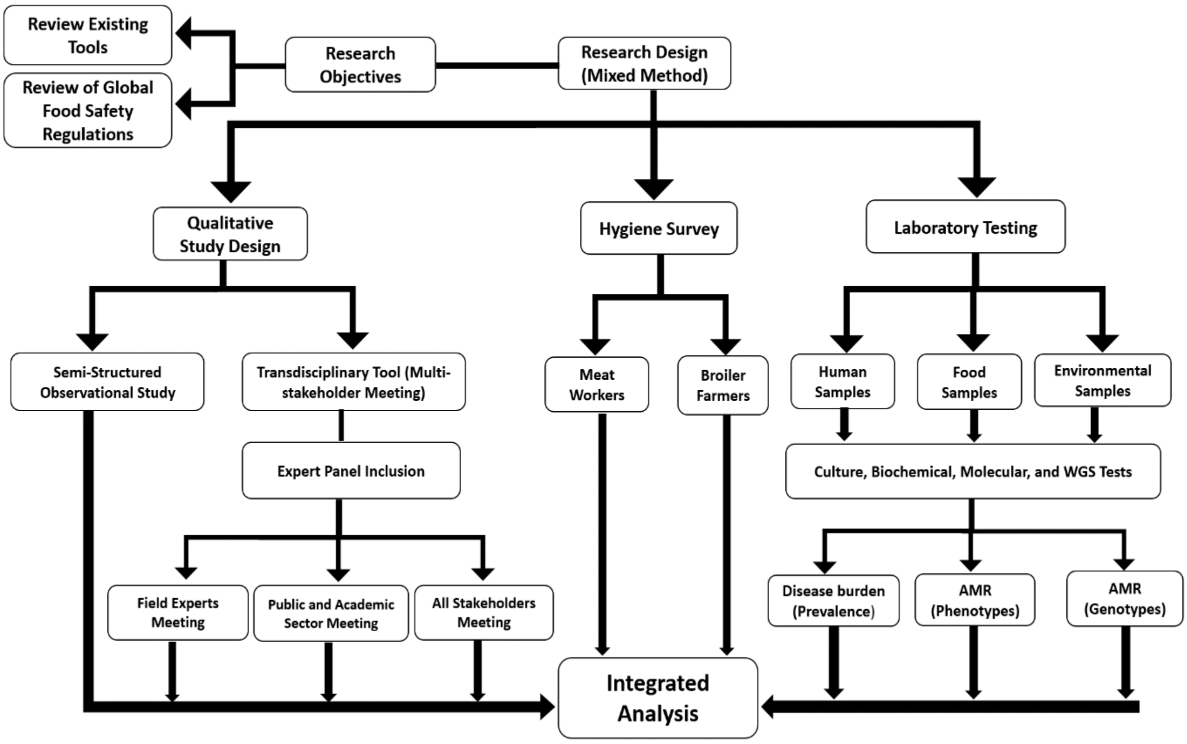


Figure 3-1 PhD Project Methodological Framework

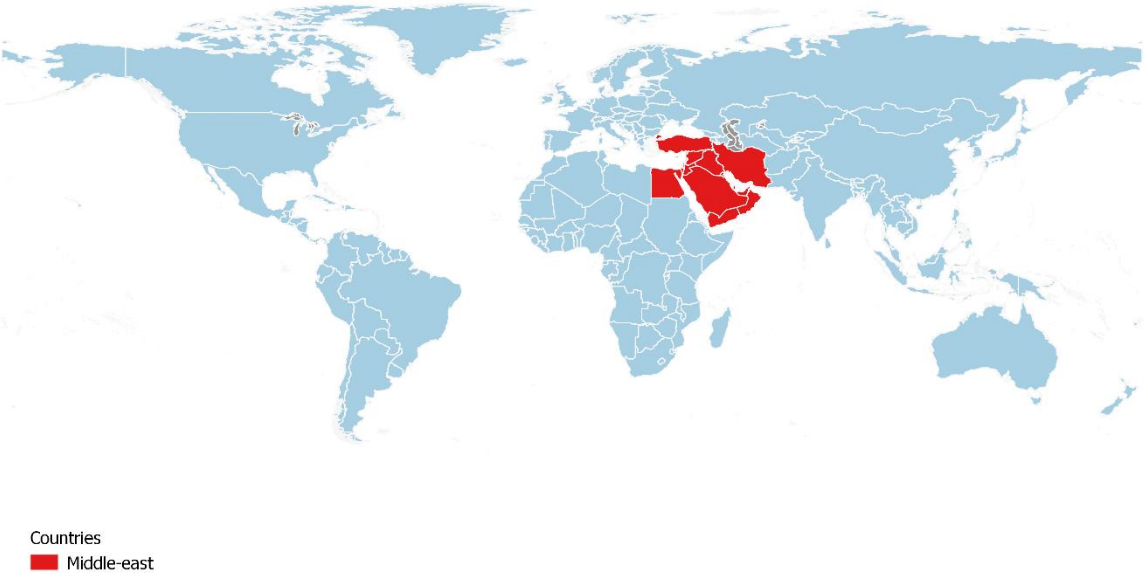
Abbreviations: AMR-Antimicrobial Resistance; WGS-Whole Genome Sequencing.

3.4 Ethical considerations

This PhD project was approved by the Northwestern and Central Switzerland Ethics Committee (Ethikkommission Nordwest- und Zentralschweiz, EKNZ) (Reference No: AO_2021-00021) and the Ethics Review Committee at the Institute of Community and Public Health (ICPH) at Birzeit University (Reference No: 2020 (12 – 1)). The project followed the ethical principles governing medical research, including the Helsinki Declaration and country-specific regulations. Local authorities were informed and have been involved in the project. The purpose and procedure of the study were explained to the potential participants to obtain their consent (Participant Information and Consent form). Tailored consent forms have been developed for broiler producers and meat workers to take samples to diagnose *Salmonella* and *Campylobacter*. The information and consent forms were translated into the Arabic language. Those who provided written informed consent participated in the study. Participants did not receive any compensation. If a participant was illiterate, a witness who could read and write, selected by the participant and without connection to the research team, was present while the information was explained. After establishing that the participant understood the study's terms, the participant confirmed the agreement with a thumbprint.

Confidentiality and anonymity were guaranteed for the participants involved in this research project, ensuring their privacy and protection. Information about the participants was coded to safeguard their privacy. Unless otherwise required by law, no information about the participant or information that could connect the participant to the study was disclosed to third parties without the participant's agreement. Only the study team has access to all password-protected electronic databases. However, for the purpose of reviewing data, the ethics committee, the appropriate authority, or a duly appointed sponsor representative may request direct access to some of the essential project records. Participants were informed that their names wouldn't be revealed and that published reports wouldn't make it possible to identify specific subjects

Part 3: Systematic Review and Meta-Analysis of Integrated Studies on *Salmonella* and *Campylobacter* Prevalence, Serovar, and Phenotyping and Genetic of Antimicrobial Resistance in the Middle East—A One Health Perspective



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Systematic Review

4 Systematic Review and Meta-Analysis of Integrated Studies on *Salmonella* and *Campylobacter* Prevalence, Serovar, and Phenotyping and Genetic of Antimicrobial Resistance in the Middle East—A One Health Perspective

Said Abukhattab [1,2], Haneen Taweel [3], Arein Awad [3], Lisa Crump [1,2], Pascale Vonaesch [4], Jakob Zinsstag [1,2], Jan Hattendorf [1,2] and Niveen M. E. Abu-Rmeileh [3]

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[1] Swiss Tropical and Public Health Institute, Kreuzstr. 2, CH-4123 Allschwil, Switzerland
[2] University of Basel, Petersplatz 1, CH-4001 Basel, Switzerland
[3] Institute of Community and Public Health, Birzeit University, West Bank P.O. Box 14, Palestine
[4] Department of Fundamental Microbiology, University of Lausanne, Bâtiment Biophore, CH-1015 Lausanne, Switzerland
* Correspondence: said.abukhattab@swisstph.ch

Abstract: Background: *Campylobacter* and *Salmonella* are the leading causes of foodborne diseases worldwide. Recently, antimicrobial resistance (AMR) has become one of the most critical challenges for public health and food safety. To investigate and detect infections commonly transmitted from animals, food, and the environment to humans, a surveillance–response system integrating human and animal health, the environment, and food production components (iSRS), called a One Health approach, would be optimal. **Objective**: We aimed to identify existing integrated One Health studies on foodborne illnesses in the Middle East and to determine the prevalence, serovars, and antimicrobial resistance phenotypes and genotypes of *Salmonella* and *Campylobacter* strains among humans and food-producing animals. **Methods**: The databases Web of Science, Scopus, and PubMed were searched for literature published from January 2010 until September 2021. Studies meeting inclusion criteria were included and assessed for risk of bias. To assess the temporal and spatial relationship between resistant strains from humans and

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animals, a statistical random-effects model meta-analysis was performed. **Results**: 41 out of 1610 studies that investigated *Campylobacter* and non-typhoid *Salmonella* (NTS) in the Middle East were included. The NTS prevalence rates among human and food-producing animals were 9% and 13%, respectively. The *Campylobacter* prevalence rates were 22% in humans and 30% in food-producing animals. The most-reported NTS serovars were *Salmonella* Enteritidis and *Salmonella* Typhimurium, while *Campylobacter jejuni* and *Campylobacter coli* were the most prevalent species of *Campylobacter*. NTS isolates were highly resistant to erythromycin, amoxicillin, tetracycline, and ampicillin. *C. jejuni* isolates showed high resistance against amoxicillin, trimethoprim–sulfamethoxazole, nalidixic acid, azithromycin, chloramphenicol, ampicillin, tetracycline, and ciprofloxacin. The most prevalent Antimicrobial Resistance Genes (ARGs) in isolates from humans included tetO (85%), Class 1 Integrons (81%), blaOXA-61 (53%), and cmeB (51%), whereas in food-producing animals, the genes were tetO (77%), Class 1 integrons (69%), blaOXA-61 (35%), and cmeB (35%). The One Health approach was not rigorously applied in the Middle East countries. Furthermore, there was an uneven distribution in the reported data between the countries. **Conclusion**: More studies using a simultaneous approach targeting human, animal health, the environment, and food production components along with a solid epidemiological study design are needed to better understand the drivers for the emergence and spread of foodborne pathogens and AMR in the Middle East.

Keywords: Middle East; One Heath; antimicrobial resistance; foodborne pathogens; *Campylobacter* spp.; *Salmonella* spp.; systematic review; meta-analysis

4.1 Introduction

Campylobacter spp. and *Salmonella* spp. are the leading causes of foodborne diseases worldwide (Devleesschauwer, Bouwknegt, Mangen, & Havelaar, 2017; Ferrari et al., 2019). According to a report published by the World Health Organization (WHO) in 2018, the global burden of food-borne illnesses is 1 in 10 individuals each year (Amuasi & May, 2019). Annually, non-typhoid *Salmonella* (NTS) is responsible for more than 155,000 annual deaths and 94 million annual cases worldwide (Majowicz et al., 2014). *Campylobacter* infection is a public health problem, causing about 8% of global diarrhoeal cases (Connerton & Connerton, 2017). Since 2005, *Campylobacter* has been the most reported gastrointestinal bacterial pathogen in humans in the European Union (EU) (Authority, 2018; Kaakoush et al., 2015).

The Middle East region has the third-highest prevalence of foodborne illness, with 100 million people estimated to be ill from foodborne illnesses each year. Norovirus, *Escherichia coli*, *Campylobacter*, and NTS are responsible for 70% of all foodborne diseases in the Middle East region ("WHO's first ever global estimates of foodborne diseases find children under 5 account for almost one third of deaths," 2015). The incidence rate of NTS among Jordanians was 124 per 100,000 in 2003–2004 and 30 per 100,000 among Israelis in 2009 (Bassal et al., 2012; D. Cohen et al., 2010). In addition, *Campylobacter* was identified in 61% of children with dysentery (63/99) in Israel, 33% (76/230) in Iran 4.7% (7/150) in Palestine, and 3.7% (13/356) in Egypt during the period 2005–2015 (Dayan, Revivo, Even, Elkayam, & Glikman, 2010; El-Shabrawi et al., 2015; Elamreen, Abed, & Sharif, 2007; Feizabadi, Dolatabadi, & Zali, 2007).

Antimicrobial resistance (AMR) is a major public health concern mainly resulting from the use and misuse of antimicrobial agents. AMR occurs when bacteria, fungi, parasites, and viruses change over time and are no longer susceptible to medicines, making infections difficult to treat and increasing the risk of spreading the infection, intensifying the severity of the disease, and raising death rates (Alsayeqh et al., 2021; Escher, Muhummed, Hattendorf, Vonaesch, & Zinsstag, 2021). After the bacteria has acquired resistance, AMR disseminates by clonal spreads of the bacteria and horizontal gene transfer (HGT), that is, by integrons or plasmids, leading to the accumulation of antimicrobial resistance genes (ARGs) in pathogenic and non-pathogenic bacteria within an individual organism (Escher et al., 2021). Rising antimicrobial use contributes to the sharing of resistant bacteria and resistance genes between food animals and humans through the food production chain (Alsayeqh et al., 2021). AMR in *Campylobacter* spp. and *Salmonella* spp. has been shown to be directly associated with antimicrobial use in animal production. Food-borne diseases caused by these resistant bacteria are well documented in humans (Alsayeqh et al., 2021).

Since humans and animals are in close contact and are intricately interconnected, food safety and AMR are fundamental One Health issues (Garcia, Osburn, & Jay-Russell, 2020; Racloz, Waltner-Toews, & DC, 2015). However, most of the current research in LMICs focuses on human or animal health risks separately and only a few studies have been conducted to understand the problem in an interconnected manner (King, 2013; Paul & Varghese, 2020). Additional components of human and animal health must be incorporated to make significant progress in reducing many foodborne diseases (King, 2013).

The Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) (www.jpiamr.eu, (accessed on 19 March 2022)) identified several critical knowledge gaps. First, the relative contributions of different sources of antibiotics and antibiotic-resistant bacteria into the environment are unmeasured. Second, the role of the environment, particularly the anthropogenic inputs, on the evolution of resistance is not understood. Third, the overall human and animal health impacts caused by exposure to resistant bacteria from the environment have not been studied. Finally, the efficacy of technological, social, economic, and behavioural interventions to mitigate environmental antibiotic resistance have not been evaluated (Larsson et al., 2018). A recent review of integrated studies on antimicrobial resistance in Africa concluded that data on AMR from a One Health perspective in Africa are scarce with only 18 studies meeting the minimal standards of addressing simultaneously at least two of the environment–animal–human realms (Escher et al., 2021).

This systematic review and meta-analysis aims to summarize the scientific literature published between January 2010 and August 2021 on the prevalence, serovars, and antimicrobial resistance phenotypes and genotypes (ARGs) of *Salmonella* and *Campylobacter* strains from integrated studies, studying at the same time humans and food-producing animals and their products in the Middle East region. In addition, it attempts to address the knowledge gap and summarize the available information about the situation by applying the integrated studies to follow up *Salmonella* spp. and *Campylobacter* spp. as the leading foodborne illnesses in the Middle East.

4.2 Methodology

The protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO ID: CRD42021277400).

4.2.1 Search Strategy

We conducted a systematic search on PubMed, Web of Science, and Scopus, limiting the search to the literature published from 2010 until 30 September 2021. Two reviewers performed the initial search, abstract screening, and data extraction, and any discordances were solved by a third reviewer. The exact search strategy used for each database is included in Supplementary Table S1.

4.2.2 Inclusion and Exclusion Criteria

We aimed to analyze the available information about prevalence, serovar distribution, and antimicrobial resistance phenotypes and genotypes of *Salmonella* and *Campylobacter* strains among humans and food-producing (terrestrial) animals and their products in the Middle East region. It included all peer-reviewed literature published from 1 January 2010, until 30 September 2021. The search included only studies that were published in English. We excluded publications published before 2010, grey literature, non-peer-reviewed literature, and studies with a different design than cross-sectional, cohort studies, and studies using survey system data (Routine data). In addition to information on *Salmonella* spp. and *Campylobacter* spp. isolates originating from companion animals, plant-based food, aquatic products (fish), water sources, and concerning *Salmonella* enterica serotypes Typhi and Paratyphi.

4.2.3 Study Selection

Two independent reviewers used Covidence software (www.covidence.org, (accessed on 23 September 2021)) for the title and abstract screening. Studies that were eligible for full-text review were further reviewed. Subsequently, risk assessment and data extraction were undertaken. Disagreements between reviewers in the title and abstract screening or full-text review were resolved through consultation with a third reviewer.

4.2.4 Data Extraction

Two independent reviewers extracted the data for the included papers, and the required data was entered into an Excel (Microsoft Inc.TM, Redmond, WA, USA) sheet. Data included author, publication year, year of data collection, collection country, study outcomes, study design, the validity and reliability of the study methodology, as well as details available regarding analysis, human and animal sample sizes, sample sources, isolated bacteria source, and prevalence. In addition, data regarding serotype prevalence, AMR gene prevalence, and NTS and *Campylobacter* AMR profiles were collected.

4.2.5 Risk of Bias Assessment

We used the risk of bias tool developed by Hoy et al., 2012 (Hoy et al., 2012) to assess the overall quality of the papers. Two independent reviewers performed the risk of bias assessment and disagreements were solved by consensus.

4.2.6 Data Synthesis

The number of studies remaining at each stage of the selection process is summarized in the flowchart in Figure 4-1.

The pooled prevalence rate of *Salmonella* spp. and *Campylobacter* spp. and their main serotypes for human and food-producing animals (live animals and products) were calculated separately based on the following Equation (1):

$$Prevalence\ rate = \frac{No.of\ isolated\ bacteria}{Total\ number\ of\ collected\ samples}. \tag{1}$$

AMR profile among NTS and *C. jejuni* was calculated using Equation (2):

$$Resistance\ rate = \frac{No.of\ resistance\ Isolates}{Total\ number\ of\ isoalted\ bacteria}. \tag{2}$$

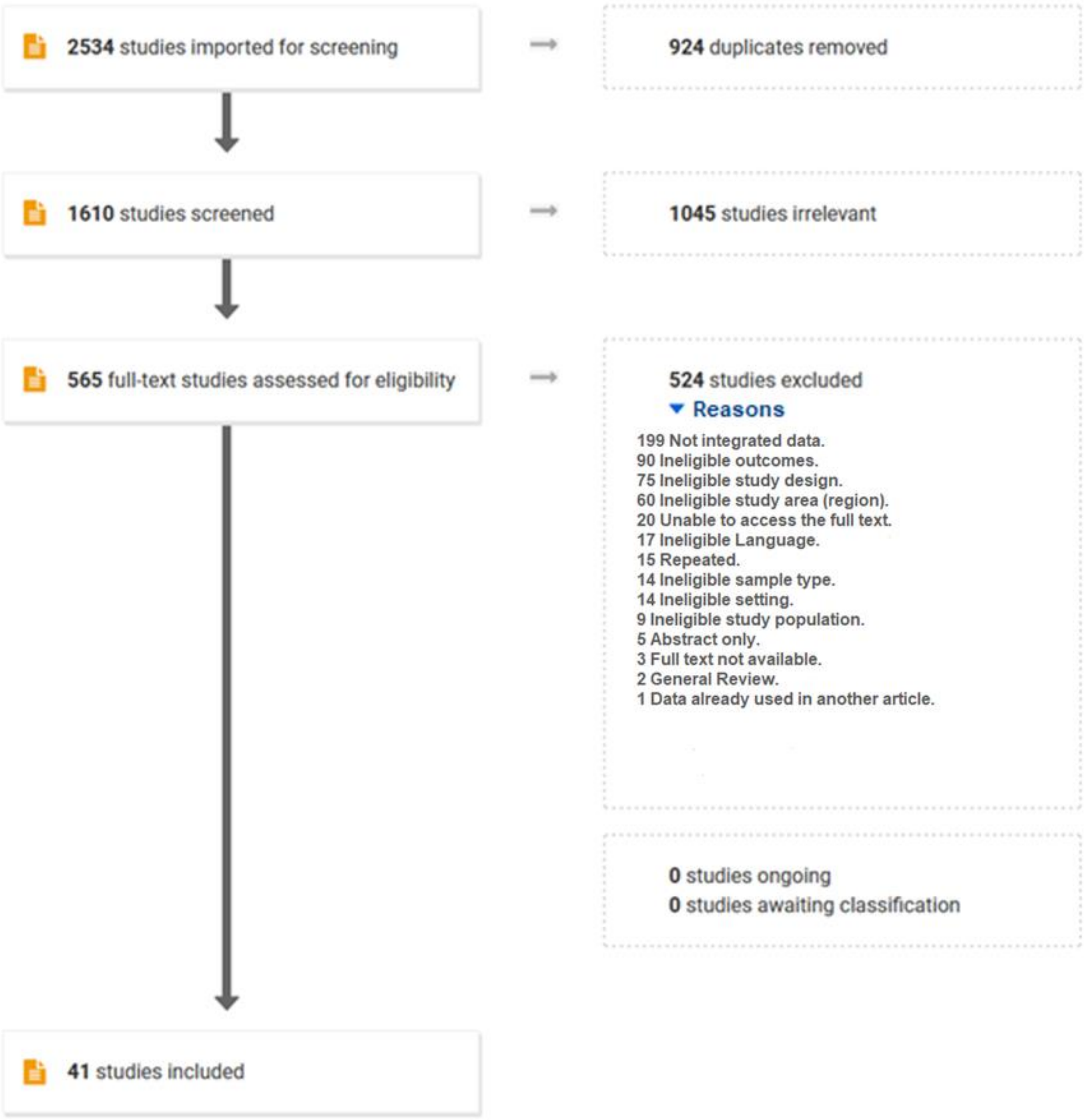


Figure 4-1 Search strategy and PRISMA flow diagram.

4.2.7 Statistical Analysis

Relative risks were assessed based on the total number of samples and the number of NTS, *Campylobacter* spp., and AMR positive samples (phenotype and genotype). Studies were stratified by bacterial species and sources. A pooled risk ratio (RR) was calculated separately for each bacterial species. The I^2 and r^2 statistics assessed heterogeneity. We exclusively used the random-effects model, irrespective of the heterogeneity results. For all statistical analyses, we used the R software environment version 4.0.3 and the “meta-package” version 4.14-0. We used the function ‘metabin’ using the Mantel–Haenszel method with inverse variance weighting for pooling (Mantel & Haenszel, 1959).

4.3 Results

4.3.1 Studies Identified and Included in the Final Analysis

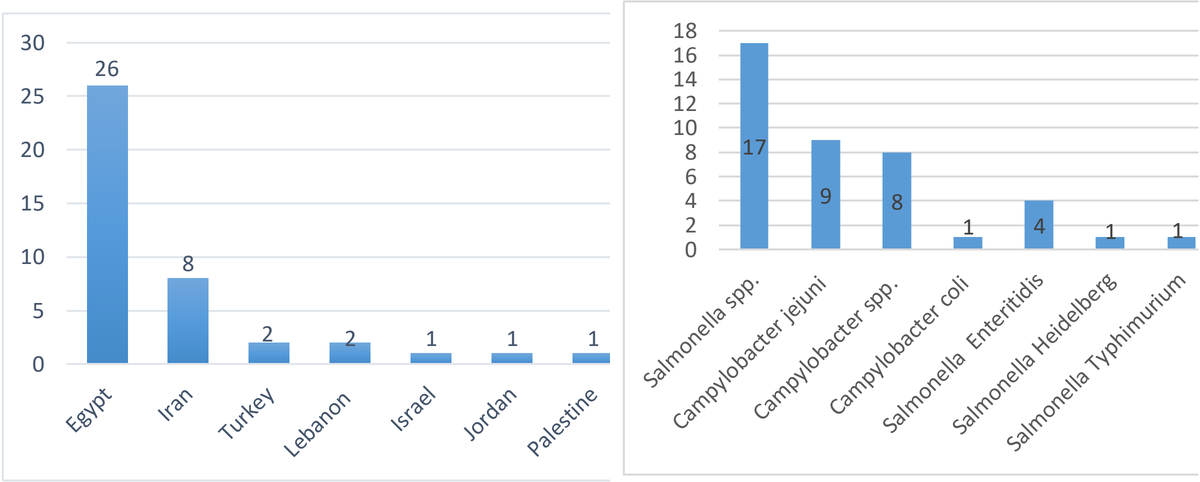
Based on the eligibility criteria, a total of 2534 publications were identified. After removing duplicates, we screened 1610 abstracts of which 565 were eligible for full-text screening. Out of 565 articles, 41 studies met the inclusion criteria for this meta-analysis (Figure 4-1). In total, 31 studies used a cross-sectional study design, and 10 studies used routine data (Supplementary Table S2).

The overall result of the risk assessment that was conducted for the included studies indicated that the majority of studies had an overall low risk of bias, and none of the papers had a high risk of bias. This result was based on the risk of bias assessment using the Hoy et al., 2012 tool (Hoy et al., 2012).

4.3.2 Overview of the Selected Studies

A total of 16 countries were included in this literature review: Qatar, United Arab Emirates, Bahrain, Saudi Arabia, Kuwait, Israel, Oman, Iran, Jordan, Lebanon, Palestine, Syria, Yemen, Turkey, Iraq, and Egypt. Of these, nine countries had no published literature matching the study inclusion criteria available (Qatar, United Arab Emirates, Bahrain, Saudi Arabia, Kuwait, Oman, Syria, Yemen, and Iraq), while seven countries had at least one article available (Egypt, Iran, Turkey, Lebanon, Israel, Jordan, and Palestine).

Of the included studies, 26 (63.41%) were conducted in Egypt, 8 in Iran (19.51%), 2 in Turkey (4.88%), 2 in Lebanon (4.88%), 1 in Israel (2.44%), 1 in Jordan (2.44%), and 1 in Palestine (2.44%) (Figure 4-2a). Of these, 17 reports (42%) included data about *Salmonella* spp. (the number of reports used for *Salmonella* spp is the same as that used for NTS), and 8 reports (20%) had data about *Campylobacter* spp. In addition, some articles focused on one of *Salmonella* and *Campylobacter* serovars; *Campylobacter jejuni* (nine reports, 22%), *Campylobacter coli* (one report, 2%), *Salmonella* Enteritidis (four reports, 10%), *Salmonella* Typhimurium (one report, 2%), and *Salmonella* Heidelberg (one report, 2%) (Figure 4-2b) and (Supplementary Table 3).



(**a**) (**b**)

Figure 4-2 Number of studies (**a**) per country and (**b**) per pathogen

4.3.3 Prevalence and Serotype Distribution of *Salmonella* spp. and *Campylobacter* spp. among Humans and Food-Producing Animals

Out of 41 eligible articles, 31 were cross-sectional studies. We used the cross-sectional data to calculate the prevalence rate for each pathogen separately. Of the 1317 human samples, 167 (13%) were positive for *Salmonella* spp. (14% in diarrhoea patients and 9% in high-risk population). In food-producing animals, out of 3520 samples, 585 (17%) were positive for *Salmonella* spp. (31% in poultry and poultry products and 4% in ruminants and ruminant products). Moreover, NTS was reported with a prevalence of 9% (109/1167) in humans (10% in diarrhoea patients and 6% in high-risk populations) and 13% (352/2718) in food-producing animals (33% in poultry and poultry products and 4% in ruminants and ruminant products). The two most common NTS serovars were *S.* Typhimurium with a prevalence of 5% (36/780) in humans (4% in diarrhoea patients and 6% in high-risk populations) and 3% (91/3038) in food-producing animals (7% in poultry and poultry products and 0.6% in ruminants and ruminant products) and *S.* Enteritidis with a prevalence of 2% (12/585) in humans (2% in diarrhoea patients and 2% in high-risk population) and 3% (87/2534) in food-producing animals (9% in poultry and poultry products and 0.3% in ruminants and ruminant products) (Tables 1-2).

Campylobacter spp. was reported with a prevalence of 22% (435/2008) in humans (23% in diarrhoea patients and 14% in high-risk populations) and 30% (1253/4122) in food-producing animals (39% in poultry and poultry products and 10% in ruminants and ruminant products). The two most commonly detected *Campylobacter* spp. serovars were *C. jejuni* with a prevalence of 16% (422/2693) in humans (16% in diarrhoea patients and 9% in high-risk populations) and 22% (1182/5472) in food-producing animals (25% in poultry and poultry products and 14% in ruminants and ruminant products) and *Campylobacter coli* with a prevalence of 4% (72/1938) in humans (3% in diarrhoea patients and 8% in high-risk populations) and 9% (367/4037) in food-producing animals (13% in poultry and poultry products and 2% in ruminants and ruminant products) (Tables 4-1 and 4-2).

Table 4-1 Overall prevalence of *Salmonella* and *Campylobacter* and main serotypes

Pathogens	No. of Isolated Bacteria from Humans	Total Number of Collected Samples from Humans	The Pooled Prevalence Rate among Humans (%)	No. of Isolated Bacteria from Animals	Total Number of Collected Samples from Animals	The Pooled Prevalence Rate among Animals (%)
Salmonella spp.	167	1317	13	585	3520	17
nontyphoidal *Salmonella*	109	1167	9	352	2718	13
S. typhimurium	36	780	5	91	3038	3
S. enteritidis	12	585	2	87	2534	3
Campylobacter	435	2008	22	1253	4122	30
C. jejuni	422	2693	16	1182	5472	22
C. coli	72	1938	4	367	4037	9

Table 4-2 Prevalence of *Salmonella* and *Campylobacter* and main serotypes based on the samples sources

Pathogens	N (%) Isolated Bacteria from Asymptomatic Humans	Total Number of Asymptomatic Humans Samples	N (%) Isolated Bacteria from Symptomatic Humans	Total Number of Symptomatic from Humans Samples	N (%) Isolated Bacteria from Poultry and Poultry Products	Total Number of Poultry and Poultry Products Samples	N (%) Isolated Bacteria from Ruminants and Ruminant Products	Total Number of Ruminants and Ruminant Products Samples
Salmonella spp.	29 (9%)	342	138 (14%)	975	492 (31%)	1597	76 (4%)	1717
Nontyphoidal *Salmonella*	11 (6%)	192	98 (10%)	975	259 (33%)	795	76 (4%)	1717
S. typhimurium	13 (6%)	205	23 (4%)	575	80 (7%)	1195	9 (0.6)	1637
S. enteritidis	1 (2%)	60	11 (2%)	525	82 (9%)	897	5 (0.3)	1637
Campylobacter	28 (14%)	206	407 (23%)	1802	1048 (39%)	2695	205 (10%)	1427
C. jejuni	21 (9%)	226	401 (16%)	2467	968 (25%)	3894	214 (14%)	1578
C. coli	18 (8%)	236	54 (3%)	1702	341 (13%)	2610	26 (2%)	1427

4.3.4 Microbial Resistance Patterns Detected by Phenotypic Screening

Based on the prevalence rate results and the number of eligible articles included in this review, NTS and *C. jejuni* were the two most prevalent representatives of *Salmonella* spp. and *Campylobacter* spp., respectively. The average resistance of NTS and *C. jejuni* was calculated for each pathogen separately depending on the source of the isolated bacteria (human or food-producing animals) (Supplementary Table S4).

For NTS, information on 13 different antibiotics was available and is summarized in Table 4-3. NTS isolated from humans showed resistance against erythromycin (100%), amoxicillin (71%), tetracycline (62%), ampicillin (52%), azithromycin (43%), amoxicillin–clavulanic acid (42%), streptomycin (40%), cefotaxime (31%), trimethoprim–sulfamethoxazole (24%), chloramphenicol (15%), ciprofloxacin (9%), imipenem (2%), and ceftriaxone (1%). NTS isolated from food-producing animals showed resistance against erythromycin (100%), amoxicillin (91%), tetracycline (50%), ampicillin (69%), azithromycin (9%), amoxicillin–clavulanic acid (70%), streptomycin (43%), cefotaxime (63%), trimethoprim–sulfamethoxazole (8%), chloramphenicol (12%), ciprofloxacin (17%), and ceftriaxone (7%). Amoxicillin–clavulanic acid was used more frequently in animal isolates (70%), with a pooled risk ratio (RR) of 1.09 (95% confidence interval (CI): 1.01–1.18) and with a heterogeneity of $I^2 = 34\%$ and $r^2 < 0.001$, while the pooled RR close to 1 in ampicillin and streptomycin suggests a similar probability of occurrence in humans and animals. For the other antibiotics, no clear pattern was detected (Table 4-3).

Table 4-3 Microbial resistance patterns detected by phenotypic screening among non-typhoidal *Salmonella*

	Non-Typhoidal *Salmonella*							
Antibiotic	**No. of Resistance Human Isolates**	**Human Isolates**	**Resistance Ratio/Human Isolates**	**No. of Resistance Animal Isolates**	**Animal Isolates**	**Resistance Ratio/Animal Isolates**	**Relative Risk**	**95% CI**
Amoxicillin–Clavulanic acid	53	126	42%	62	88	70%	1.09	[1.01;1.18]
Amoxicillin	50	70	71%	64	70	91%	4.02	[0.16; 103.61]
Ampicillin	97	186	52%	96	139	69%	1.10	[0.92; 1.31]
Azithromycin	32	75	43%	2	22	9%	0.21	[0.06; 0.82]
Cefotaxime	45	145	31%	58	92	63%	3	[0.23; 39.38]
Ceftriaxone	2	231	1%	9	131	7%	4.33	[0.93; 20.26]
Chloramphenicol	42	281	15%	21	181	12%	1.29	[0.86;1.96]
Ciprofloxacin	26	281	9%	30	181	17%	1.36	[0.73; 2.51]
Erythromycin	57	57	100%	52	52	100%	1	[0.96; 1.04]
Imipenem	3	194	2%	0	108	0%	0.45	[0.05; 4.02]
Streptomycin	50	126	40%	38	88	43%	1.09	[0.80; 1.49]
Tetracycline	142	231	62%	66	131	50%	0.79	[0.59; 1.06]
Trimethoprim–sulfamethoxazole	67	281	24%	15	181	8%	0.57	[0.18; 1.80]

Table 4-4 Microbial resistance patterns detected by phenotypic screening among *Campylobacter jejuni*

Campylobacter jejuni								
Antibiotic	**No. of Resistance Human Isolates**	**Human Isolates**	**Resistance Ratio/Human Isolates**	**No. of Resistance Animal Isolates**	**Animal Isolates**	**Resistance Ratio/Animal Isolates**	**Relative Risk**	**95%CI**
Amoxicillin–Clavulanic acid	283	416	68%	56	173	32%	0.79	[0.67; 0.95]
Amoxicillin	297	297	100%	52	52	100%	1	[0.96; 1.04]
Ampicillin	466	579	81%	142	223	64%	1	[0.97; 1.03]
Azithromycin	261	297	88%	52	52	100%	1.13	[1.04; 1.24]
Chloramphenicol	258	316	82%	50	73	69%	1.01	[0.89; 1.14]
Ciprofloxacin	460	627	73%	187	265	71%	0.92	[0.84; 1.01]
Erythromycin	393	608	65%	92	244	38%	1	[0.97; 1.03]
Nalidixic acid	558	627	89%	201	265	76%	0.89	[0.77; 1.02]
Streptomycin	213	544	39%	50	235	21%	1.02	[0.83; 1.26]
Tetracycline	248	330	75%	119	213	56%	0.94	[0.84; 1.05]
Trimethoprim–sulfamethoxazole	371	399	93%	85	103	83%	1.01	[0.97; 1.04]

For *C. jejuni,* we had data on 11 antibiotics. The phenotypic resistance results are summarized in (Table 4-4) *C. jejuni* isolated from humans showed resistance against amoxicillin (100%), trimethoprim–sulfamethoxazole (93%), nalidixic acid (89%), azithromycin (88%), chloramphenicol (82%), ampicillin (81%), tetracycline (75%), ciprofloxacin (73%), amoxicillin–clavulanic acid (68%), erythromycin (65%), and streptomycin (39%). *C. jejuni* isolated from food-producing animals showed complete resistance against amoxicillin (100%) and azithromycin (100%) and to a lesser extent resistance against trimethoprim–sulfamethoxazole (83%), nalidixic acid (76%), chloramphenicol (69%), ampicillin (64%), tetracycline (56%), ciprofloxacin (71%), amoxicillin–clavulanic acid (32%), erythromycin (38%), and streptomycin (21%).

Azithromycin was detected more frequently in animal isolates, with a pooled risk ratio (RR) of 1.13 (95% confidence interval (CI): 1.04–1.24) and a heterogeneity of I^2 = 72% and r^2 = 0.033. Amoxicillin–clavulanic acid was detected more frequently in human isolates, with a pooled risk ratio (RR) of 0.79 (95% confidence interval (CI): 0.67–0.95) and heterogeneity of I^2 = 53% and $r^2 < 0.001$. For the other antibiotics, no clear pattern was detected. Most phenotypic resistance had a pooled RR close to 1, suggesting a similar probability of occurrence in humans and animals (Table 4-4).

4.3.5 Assessment of Shared Antimicrobial Resistance Genes

Only six studies reported resistance genes targeted at three serovars of *Salmonella* spp. and *Campylobacter* spp. These serovars were *C. jejuni* (three studies), NTS (two studies), and *Salmonella Heidelberg* (one study). We calculated the average prevalence for every single resistance gene from food-producing animals and human sources separately. For human isolates, *tetO* was the gene with the highest prevalence (85%), followed by Class 1 Integrons (81%), *blaOXA-61 (53%)*, *cmeB (51%)*, *blaCMY-2 (38%),* Class 2 integrons (29%), *tetA (21%), blaOXA (21%), blaSHV (19%), AAC(6')-Ib (16%), blaCTXM-1 (16%), blaAMPc (13%),* and *blaTEM (13%)*. For food-producing animals, tetO was the most prevalent gene (77%), followed by Class 1 Integrons (69%), *blaOXA-61 (35%), cmeB (35%), tetA (30%),* Class 2 integrons (27%)*, blaCTXM-1 (22%), AAC(6')-Ib (22%), blaSHV (20%), blaTEM (15%), blaCMY-2 (11%), blaOXA (11%),* and *blaAMPc (3%)* (Table 4-5) (Supplementary Table S5a–c).

Resistance in *Campylobacter* spp. was exclusively reported as data for *C. jejuni* isolates. The three studies reporting data on resistance compromised 274 isolates (232 human isolates and 42 food-producing animals and their products). The most frequent genes were Class 1 Integrons (96%), *tetO* (85%), *blaOXA-61* (53%), *cmeB* (51%), and *tetA* (17%). For food-producing animals and their product isolates, the most frequently detected genes were Class

1 Integrons (100%), *tetO* (77%), *blaOXA-61* (35%), *cmeB* (35%), and *tetA* (30%). There was no evidence for a significant difference in the occurrence of the genes between human and food-producing animals and their products (Table 4-5) except for Class 1 integrons, which were detected more frequently in food-producing animals, with a risk ratio (RR) of 1.04 (95% confidence interval (CI): 1.01; 1.08) (Table 4-5). No clear pattern was detected for the other genes, with most of the genes having a pooled RR close to 1, suggesting a similar probability of occurrence in humans and animals (Table 4-5) (Supplementary Table S5a).

The two studies on NTS compromised 197 isolates (125 human isolate and 72 food-producing animals and their products). The most frequent genes were Class 1 Integrons (51%), Class 2 Integrons (29%), *blaSHV* (16%), *blaCTXM-1* (16%), *AAC(6')-Ib* (16%), *blaTEM* (10%), and blaAMPc (1%). For food-producing animal isolates, the most frequently detected genes were Class 1 Integrons (41%), Class 2 Integrons (27%), *blaSHV* (22%), *blaCTXM-1* (22%), *AAC(6')-Ib* (22%), and *blaTEM* (15%). No clear pattern emerged for the majority of the genes in the random effect models comparing frequencies in humans and animals (Table 4-5), suggesting there was no evidence for a significant difference in the occurrence of the genes between humans and food-producing animals (Table 4-5) (Supplementary Table S5b).

The single study including *Salmonella* Enterica Serovar Heidelberg compromised 33 isolates (24 human isolates and 9 food-producing animals and their products). In isolates from human sources, the most frequent genes were *blaAMPc* (50%), *blaCMY-2* (38%), *blaTEM* (29%), *blaSHV* (25%), and *blaOXA* (20%). For food-producing animal isolates, the most frequently detected genes were *blaAMPc* (11%), *blaCMY-2* (11%), *blaTEM* (11%), *blaSHV* (11%), and *blaOXA* (11%). There was no evidence of a significant difference in the occurrence of the genes between humans and food-producing animals (Supplementary Table S5c).

Table 4-5 Prevalence of AMR genes found in non-typhoidal *Salmonella* spp. and *Campylobacter jejuni*.

AMR Gen	Study ID	Pathogen	HN	HI	Prevalance_H	AN	AI	Prevalnce_A_	RR	95% CI	Lab Technique
blaAMPc	Besharati et al. 2020 and Elhariri et al. 2020	NTS and S. H	99	13	13.13%	31	1	3.23%	0.34	[0.07; 1.72]	PCR
AAC(6')-Ib	Youssef et al. 2021	NTS	50	8	16.00%	50	11	22.00%	1.38	[0.6; 3.13]	PCR
bla CMY-2	Elhariri et al. 2020	S. H	24	9	37.50%	9	1	11.11%	0.3	[0.04; 2.02]	PCR
bla CTXM-1	Youssef et al. 2021	NTS	50	8	16.00%	50	11	22.00%	1.38	[0.6; 3.13]	PCR
bla OXA	Elhariri et al. 2020	S. H	24	5	20.83%	9	1	11.11%	0.53	[0.07; 3.96]	PCR
											PCR
bla OXA-61	Divsalar et al. 2019	*C. jejuni*	80	42	52.50%	20	7	35.00%	0.67	[0.35; 1.25]	PCR
bla SHV	Youssef et al. 2021 and Elhariri et al. 2020	NTS and S. H	74	14	18.92%	59	12	20.34%	1.13	[0.49; 2.61]	PCR
blaTEM	Youssef et al. 2021, Besharati et al. 2020 and Elhariri et al. 2020	NTS, NTS, and S. H	149	19	12.75%	81	12	14.81%	0.91	[0.34; 2.44]	PCR
Class 1 Integrons	Besharati et al. 2020 and AbdEl-Aziz et al. 2020	NTS and *C. jejuni*	223	180	80.72%	42	29	69.05%	1.04	[1.01; 1.08]	PCR
class 2 Integrons	Besharati et al. 2020	NTS	75	22	29.33%	22	6	27.27%	0.93	[0.43; 2]	PCR
cme B	Divsalar et al. 2019	*C. jejuni*	80	41	51.25%	20	7	35.00%	0.68	[0.36; 1.29]	PCR
tet(A)	Divsalar et al. 2019	*C. jejuni*	80	17	21.25%	20	6	30.00%	1.41	[0.64; 3.11]	PCR
tet(O)	Divsalar et al. 2019 and Ghoneim et al. 2020	*C. jejuni*	84	71	84.52%	22	17	77.27%	0.92	[0.73; 1.16]	PCR

HN: Number of human isolates: HI: human isolates that have this gene; prevalance_H: prevalence among human isolates; AN: number of animal isolates; AI: animal isolates that have this gene; prevalance_A: prevalence among animal isolates; RR: relative risk; NTS: non-typhoidal *Salmonella*; S.H: *Salmonella* Heidelberg; *C. jejuni*: *Campylobacter jejuni.*

4.4 Discussion

Although 41 articles were eligible for inclusion in this systematic review and meta-analysis, there is an uneven distribution of the sources of the studies included. The majority (63%) of eligible studies were from Egypt and 20% from Iran. On the other hand, there are no published papers on applying a comprehensive One Health approach to study one of the two major foodborne diseases (*Salmonella* and *Campylobacter*) in 9 counties from the 16 Middle Eastern countries, and none came from those high-income countries members of the Gulf Cooperation Council.

Of the 41 studies included in this review, 31 were cross-sectional, and 10 were routine data studies. Studies allow a comparison between human and animal sources; they do not evaluate actual transmission methods because the few studies eligible for inclusion in this review suffered from insufficient statistical data on foodborne pathogens and AMR and assess only selected sections of the social ecosystem.

Furthermore, our systematic review and meta-analysis showed the prevalence of *Salmonella* spp. and *Campylobacter* spp., resistance rates, and antimicrobial resistance genes circulating in the Middle East region by using the random-effects model. The model showed high heterogeneity results, which indicate variability in the study data. This might be due to the study design (epidemiological study vs. routine data) or due to diverse sample types. The human isolates used in the studies were from different sources (symptomatic and asymptomatic participants), and the animal isolates used were from various sources (live animals and products). Finally, the small sample size in each study and, in particular, the human sample size could influence the results when measuring the prevalence and the relationship between the humans and animal settings. The heterogeneity might explain the insignificant relationship between animals and humans.

The low quantity (low sample size), uneven distribution in the reported data, and weak epidemiological study designs from a One Health methodological perspective (Zinsstag, Schelling, et al., 2020) in the studies that targeted foodborne illness and antimicrobial resistance in the Middle East can be explained by the food safety system's challenges in this region. These challenges are the lack of epidemiological and disease ecological capacity, diagnostic tools, and laboratory facilities. Moreover, there is a lack of quality control and standardization of microbiological identification and susceptibility testing techniques (Alsayeqh et al., 2021).

Our review demonstrates the prevalence of NTS and *Campylobacter* spp. and their serovars circulating in the Middle East. The pooled prevalence of *Campylobacter* spp. among humans was close to the higher estimate for the ranges reported in Sub-Saharan Africa: and

Northern Africa (2–27.5%) and more than the ranges reported in Southeast Asia (8%) (Asuming-Bediako, Parry-Hanson Kunadu, Abraham, & Habib, 2019; Gahamanyi, Mboera, Matee, Mutangana, & Komba, 2020; Wada & Abdul-Rahman, 2022). Additionally, the results show the prevalence of *Campylobacter* spp. in food-producing animals and their products (30%). For *Campylobacter* spp.*,* the prevalence rate is similar to the systematic review and meta-analysis results that targeted *Campylobacter* spp. globally, with approximately 30% of animal food products analyzed reporting *Campylobacter* spp. (Zbrun et al., 2020). Additionally, we looked at which *Campylobacter* serovars are circulating in the Middle East and found *C. jejuni* and *C. coli* to be the predominant serovars, similar to results that targeted *Campylobacter* in Africa as the *C. jejuni* and *C. coli* predominates in Sub-Saharan Africa (Hlashwayo et al., 2021).

We identified two systematic reviews conducted by Al-Rifai and his colleagues that targeted the Middle East and South African countries in 2019 and 2020; we will compare our results with these relevant studies. In this review, the pooled prevalence rates of NTS were 9% and 13% among humans and animals and their products, respectively. The pooled prevalence in humans is higher than the results in the Al-Rifai study (2019) which was 7% (Al-Rifai, Chaabna, Denagamage, & Alali, 2019). In addition, the prevalence of the food-producing animals in this review is more than the results of the Al-Rifai (2020) study, which was 9% (Al-Rifai, Chaabna, Denagamage, & Alali, 2020). Our findings are similar to Al-Rifai's studies of NTS serovars, in which *S.* Typhimurium and *S.* Enteritidis were the main NTS serovars reported in this region (Al-Rifai et al., 2020; Al-Rifai et al., 2019).

Furthermore, this systematic review showed *Campylobacter* and *Salmonella* serovars are highly prevalent in poultry and poultry products in the Middle East. The Campylobacter prevalence in animals was less than the prevalence reported in broiler meat in Poland, Slovenia, Spain, and Austria. Conversely, more than reported in Denmark and Finland (Skarp, Hänninen, & Rautelin, 2016). The *Salmonella* prevalence in animals showed results less than the prevalence reported in raw chicken at retail markets in China and more than reported in chicken carcasses in Spain (Capita, Alonso-Calleja, & Prieto, 2007; Yang et al., 2011). This endemic *Campylobacter* and *Salmonella* bacteria in animal food products can be explained, at least partially, by the changes in animal production systems that have tended to be more intense over the past decades (Zbrun et al., 2020). These findings are essential because transmission along the production chain is generally established as the most common pathway used by *Campylobacter* and *Salmonella* to generate human infection (Hlashwayo et al., 2021).

AMR is a transboundary public health problem. New types of AMR strains can expand worldwide following initial endemic emergence, as demonstrated by several resistant pathogens that spread globally (Cave, Cole, & Mkrtchyan, 2021). Our meta-analysis revealed a high NTS resistance against erythromycin, amoxicillin, tetracycline, and ampicillin for isolates from humans and food-producing animals. The isolates have similar resistance rates between humans and animals in erythromycin but are higher in isolates from animal sources for amoxicillin and ampicillin and higher in isolates from human sources in tetracycline. These results are close to those reported by Alsayeqh's systematic review in the Middle East region (Alsayeqh et al., 2021). In addition, the most recent report on AMR in the EU in 2019–2020 found that resistance of NTS to sulfonamides, ampicillin, and tetracycline was high in human isolates, while it ranged from moderate to very high in animal isolates (EFSA, 2022c).

AMR phenotypic results for *C. jejuni* isolates (human and food-producing animals) showed high resistance against amoxicillin, trimethoprim–sulfamethoxazole, nalidixic acid, azithromycin, chloramphenicol, ampicillin, tetracycline, and ciprofloxacin. These findings were close to Alsayeqh's systematic review for trimethoprim–sulfamethoxazole, nalidixic acid, and tetracycline. In comparison, it has a lower resistance rate for amoxicillin, chloramphenicol, ampicillin, and ciprofloxacin (Alsayeqh et al., 2021). Our results show that *C. jejuni* isolated from humans has a phenotypical resistance rate against nalidixic acid and tetracycline more than that reported in Italy and less against ciprofloxacin based on the same study results (Marotta et al., 2019). At the same time, our results show that *C. jejuni* isolated from animals has a phenotypical resistance rate against nalidixic acid, ciprofloxacin, and tetracycline more than that reported in broiler chicken in Belgium (Elhadidy et al., 2018). This systematic review demonstrated moderate to high resistance of *C. jejuni* to erythromycin. Conversely, the recent EU report on AMR found that *C. jejuni* resistance to erythromycin was either undetected or detected at very low levels in *C. jejuni* from food-producing animals and humans (EFSA, 2022c).

The WHO, Food and Agriculture Organization of the United Nations (FAO), and World Organization for Animal Health (OIE) recommend reducing antibiotic use in animal husbandry, particularly for those known to cause cross-resistance (WHO, 2021) However, some antimicrobials traditionally used in animal production as growth promoters and/or for treating gastrointestinal infections are also used to control human infectious diseases (e.g., tetracycline and quinolones) (Rodrigues, Panzenhagen, Ferrari, Paschoalin, & Conte-Junior, 2020). The misuse and overuse of antimicrobials in clinical and veterinary medicine and agriculture have increased antimicrobial resistance pathogens, including *Campylobacter* and *Salmonella* (Economou & Gousia, 2015). For instance, the Quesada study showed that *Salmonella* isolated from animal food has significant antibiotic resistance in Latin American countries (Quesada, Reginatto, Ruiz Español, Colantonio, & Burrone, 2016). The therapeutic and prophylactic use of antibiotics in animal production for long periods is likely contributing to the widespread resistance against antibiotics (Economou & Gousia, 2015). More integrated environmental–animal–human studies are needed in the region to ascertain its effect on public health. This way, microbiological and clinical evidence on the transmission of AMR between animals and humans can be ascertained in Middle Eastern countries (Economou & Gousia, 2015; Kim & Cha, 2021; Quesada et al., 2016).

Data on antimicrobial resistance genes (ARGs) among *Salmonella* spp. and *Campylobacter* spp*.* in the Middle East is limited. However, based on the reported information, we can argue that food-producing animals and their products in the Middle East are not the main drivers for the emergence of ARGs.

Based on our eligibility criteria, six studies targeted ARGs among *Salmonella* and *Campylobacter* as foodborne illnesses in the Middle East region (Besharati et al., 2020; Divsalar, Kaboosi, Khoshbakht, Shirzad-Aski, & Ghadikolaii, 2019; El-Aziz et al., 2020; Elhariri et al., 2020; Ghoneim, Sabry, Ahmed, & Elshafiee, 2020; Youssef, Abbas, El-Shehawi, Mabrouk, & Aboshanab, 2021). Besharati's study and Youssef's study were two studies that reported the ARGs among NTS. Besharati's study shows an association between the AMR phenotype results and ARGs results in Integron 1 and 2 classes and trimethoprim/sulfamethoxazole in Iran. Conversely, in Youssef's study, results from Egypt revealed no association between AMR phenotype results and ARGS.

Three studies reported the ARGs among *C. jejuni (*Abd-El-Aziz, Divsalar, and Ghoneim*)* (Divsalar et al., 2019; El-Aziz et al., 2020; Ghoneim et al., 2020). The results in Divsalar and Ghoneim could not show a significant association between the targeted ARGs and the AMR phenotype results. In turn, Abd-El-Aziz found an association between Class 1 integrons and aminoglycoside resistance.

We identified small-scale studies with a small sample size for the ARGs in the NTS and *C. jejuni*. The small sample size in the eligible studies might be responsible for the insignificant difference in the occurrence of the genes between humans and food-producing animals. Our results agreed with Escher's systematic review that targeted ARGs in Africa and found eligible studies characterized by small-scale studies and with a small sample size (Escher et al., 2021). Therefore, future studies should have an integrated approach to assess the ARGs and should have a suitable sample size.

Partial sequencing of *C. jejuni* and NTS were performed using conventional PCR to extract the ARGs. Therefore, there is a lack of laboratory techniques that determine the order of bases in an organism's genome in one process such as with Whole-genome sequencing (WGS), to follow the foodborne illnesses and ARGs. Undertaking WGS of isolates, especially those with high-level antibiotic resistance, is strongly encouraged to demonstrate the involved ARGs and their genetic localization (plasmid, chromosome, genomic islands, integrative and conjugative element, and transposon) as well as to detect the most prevalent resistant serovars (Collineau et al., 2019; EFSA, 2022c; Mouftah et al., 2021), detail their potential of horizontal transmission, and evaluate the different sources and comparison of human and animal isolates (Mourkas et al., 2019).

4.5 Conclusions

To the best of our knowledge, this is the first systematic review assessing integrated environment–animal–human studies using a One Health approach in the Middle East to pursue foodborne illnesses and antimicrobial resistance. The One Health approach was not rigorously applied in the Middle East countries. In addition to weak epidemiological study designs from a One Health methodological perspective, there is an uneven distribution in the reported data with about 60% of Middle Eastern countries having no published papers included in this review. More research on foodborne illnesses and AMR in the Middle East is urgently needed. The AMR phenotype results showed a high prevalence of resistance rate for the isolated bacteria that highlights the importance of antimicrobial stewardship in humans and animals in tandem. Furthermore, introducing new laboratory techniques that determine the order of bases in an organism's genome is essential to follow up the foodborne illness outbreak and ARGs.

A simultaneous approach that targets human and animal health in tandem with a solid epidemiological study design has a high potential to provide evidence for understanding the drivers for the emergence and spread of foodborne pathogens and AMR. A comprehensive One Health approach, integrating by a sound epidemiological design the spatio-temporal relationship of humans, animals, and their environment, will allow us to identify key transmission pathways, which are essential for designing more efficient food safety systems and AMR control policies.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/antibiotics11050536/s1, Supplementary Table S1: The search strategy used for each database., Supplementary Table S2: Overview of the selected studies, Supplementary Table S3: Summary of the selected studies showing the country and pathogens together, Supplementary Table S4: Phenotypic resistance to antibiotics for all isolated serovars, Supplementary Table S5. a, b, and c: Genotypic resistance to antibiotics for all isolated serovars.

Author Contributions: S.A., H.T., L.C., J.Z., P.V., and N.M.E.A.R., designed the search strategy and data-extraction form; S.A. and H.T. screened studies for selection; S.A., H.T. and A.A. extracted the data; S.A. and J.H. managed and analyzed the data; P.V. provided expert

microbiological and antimicrobial resistance advice; J.Z. provided expert One Health and epidemiology advice; N.M.E.A.-R. provided expert epidemiology advice; S.A. and H.T. wrote the first draft of the manuscript; A.A., L.C., J.Z., P.V., J.H., and N.M.E.A.-R. critically revised and finalized the manuscript. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

4.6 Supplementary Material

Supplementary Table S1: The search strategy used for each database.

Database	Full search strategy
PubMed	Poultry OR Chicken OR “Broiler chicken” OR meat OR Animal OR Livestock OR Human AND Campylobacter OR Salmonella OR “ non-typhoid Salmonella Enterica” AND antimicrobial resistance OR"antimicrobial susceptibility" OR "antibiotic resistance" OR resistome OR AMR OR "Multidrug Resistance" OR Serotype OR prevalence OR "prevalence rate" AND Middle East OR Eastern Mediterranean OR Near East OR EMRO OR Mediterranean Countries OR "Asia" OR Qatar OR United Arab Emirates OR Bahrain OR Saudi Arabia OR Kuwait OR Israel OR Oman OR Iran OR Jordan OR Lebanon OR Palestine OR "West Bank" OR "Gaza Strip" OR Syria OR Yemen OR Turkey OR Iraq OR Egypt OR “North Africa” OR “Africa”. AND (("2010"[Date - Publication] **Timespan:** January 1st, 2010, until September 30th, 2021
Web of Science	- **TITLE:** (- ("antimicrobial resistance" OR "antibiotic resistance" OR "antimicrobial susceptibility" OR "Resistome")) AND Salmonella Enterica OR “ non-typhoidal Salmonella Enterica” OR Campylobacter *AND* Poultry OR “Broiler chicken” *OR* Meat *OR* Animals OR Human *OR* **TOPIC:** ((Middle East OR“ East Mediterranean” OR “ Near East” OR EMRO OR Middetrenian Countries OR Asia OR Qatar OR United Arab Emirates OR Bahrain OR Saudi Arabia OR Kuwait OR Israel OR Oman OR Iran OR Jordan OR Lebanon OR Palestine OR "West Bank" OR "Gaza Strip" OR "Occupied Palestinian Territory" OR Syria OR

		Yemen OR Turkey OR Iraq OR Egypt OR “North Africa” OR “Africa.”
	-	**Timespan:** January 1st, 2010, until September 30th, 2021.
Scopus	-	(TITLE-ABS-KEY (*"antimicrobial resistance"* OR *"antibiotic resistance"* OR *"antimicrobial susceptibility"* OR *"Resistome"*) AND Salmonella Enterica OR “ non-typhoidal Salmonella Enterica” OR Campylobacter AND Poultry OR “Broiler chicken” AND Meat AND Animals AND Human *AND* TITLE-ABS-KEY (*Middle East OR“ East Mediterranean” OR “ Near East” OR EMRO OR Middetrenian Countries OR Asia OR Qatar OR United Arab Emirates OR Bahrain OR Saudi Arabia OR Kuwait OR Israel OR Oman OR Iran OR Jordan OR Lebanon OR Palestine OR "West Bank" OR "Gaza Strip" OR "Occupied Palestinian Territory" OR Syria OR Yemen OR Turkey OR Iraq OR Egypt OR “North Africa” OR “Africa”*) And
		AND DOCTYPE (*ar* OR *re*) AND PUBYEAR > *2010*

Supplementary Table S2: Overview of the eligible studies

ID	Reference	Country	Pathogen	Study design	Source	Outcomes of interest	Human sample size	Animal sample size
125	Aouf 2011; Resistance to -lactams of human and veterinary *Salmonella* isolates in Egypt and Algeria	Egypt	*Salmonella* spp.	Routine data-	Human with diarrhoea, poultry	1-Nontyphoidal s*almonella*_ AMR phenotypes 2-Nontyphoidal *salmonellae*-AMR genotypes	20 isolates	**20 isolates**
1056	Youssef 2021; Serotyping and Antimicrobial Resistance Profile of Enteric Nontyphoidal *Salmonella* Recovered from Febrile Neutropenic Patients and poultry in Egypt	Egypt	*Salmonella* spp.	Cross Sectional	Human with diarrhoea , poultry	1- Nontyphoidal *Salmonella*. Serotypes with prevelance rate. 2-Nontyphoidal *Salmonellae*. AMR phenotypes 4- AMR genotypes	300	**50 isolates**
109	Ammar 2021; Prevalence, Antimicrobial Susceptibility, Virulence and Genotyping of *Campylobacter jejuni* with a Special Reference to the Anti-Virulence Potential of Eugenol and Beta-Resorcylic Acid on Some Multi-Drug Resistant Isolates in Egypt	Egypt	*Campylobacter jejuni*	Cross Sectional	Human with diarrhoea (meat workers), poultry	1- *C. Jejuni* prevelance rate 2- *C Jejuni*. AMR phenotypes	100	**245**
634	Maysa 2015; Diversity and virulence associated genes of *Salmonella enterica* serovars isolated from wastewater agricultural drains, leafy green producing farms, cattle and human along their courses	Egypt.	*Salmonella* spp.	Cross Sectional	Human (Cattle Farm workers), Cattle	1-*Salmonella* prevelance rate 2-*Salmonella* serotypes	45	**52**

376	Gharieb 2015; Non-Typhoidal *Salmonella* in poultry meat and diarrhoeic patients: prevalence, antibiogram, virulotyping, molecular detection and sequencing of class I integrons in multidrug resistant strains	Egypt	*Salmonella* spp.	Cross Sectional	Human with diarrhoea , poultry meat	1- Nontyphoidal *Salmonella* prevelance rate 2- Nontyphoidal *Salmonella* serotypes 3-Nontyphoidal *Salmonella* AMR phenotype 4- Nontyphoidal *Salmonella* AMR genotype	50	**50**
381	Ghoneim 2020; Isolation and molecular characterization of *Campylobacter jejuni* from poultry and human stool samples in Egypt	Egypt	*Campylobacter jejuni*	Cross Sectional	Human with dirrhea and with contact with animal), poultry	*Campylobacter jejuni* prevelance rate	75	**360**
683	Morshed 2010; Drug resistance, plasmid profile and random amplified polymorphic DNA analysis of Iranian isolates of *Salmonella Enteritidis*	Iran	*Salmonella Enteritidis*	Routine Data	Human with diarrhoea, poultry and Cattle.	*Salmonella Enteritidis*_ AMR phenotype	9 isolates	**40 isolates**
1361	El-Tras 2015; *Campylobacter* infections in children exposed to infected backyard poultry in Egypt	Egypt	*Campylobacter* spp.	Cross Sectional	Children (Healthy, own poultry), poultry	*Campylobacter* prevelance rate *Campylobacter* serotypes	106	**379**
1390	Firoozeh 2012; Characterization of class I integrons among *Salmonella enterica* serovar Enteritidis isolated from humans and poultry	Iran	*Salmonella Enteritidis*	Routine data	Human with diarrhoea, poultry	1- *Salmonella Enteritidis* AMR phenotype 2- AMR genotype	58 isolates	**50 isolates**
1419	Ghoddusi 2019; Serotype Distribution and Antimicrobial Resistance of *Salmonella* Isolates in Human, poultry, and Cattle in Iran	Iran	*Salmonella* spp.	Routine data	Human with diarrhoea, poultry and Cattle	1- *Salmonella* serotypes and prevelance rates. 2- *Salmonella* AMR phenotype	109 isolates	**133 isoaltes**

2353	Mohamed 2011; Fecal Shedding of Non-typhoidal *Salmonella* Species in Dairy Cattle and their Attendants in Alexandria Suburbs	Egypt	*Salmonella* spp.	Cross Sectional	Human (Dairy Farms attendants), Cattle	1- *Salmonella* Nontyphoidal *Salmonella* prevelance rate 2- *Salmonella* Nontyphoidal *Salmonella* Serotypes 3- *Salmonella* phenotype	12	**450**
1678	Mohammed 2019; The prevalence of *Campylobacter* species in broiler flocks and their environment: assessing the efficiency of chitosan/zinc oxide nanocomposite for adopting control strategy	Egypt	*Campylobacter coli*	Cross Sectional	Human (poultry frams workers), poultry farms	*Campylobacter. coli* prevelance rate	30	**160**
1090	AbdEl-Aziz 2020; First Report of aacC5-aadA7Δ4 Gene Cassette Array and Phage Tail Tape Measure Protein on Class 1 Integrons of *Campylobacter* Species Isolated from Animal and Human Sources in Egypt	Egyp**t**	*Campylobacter* spp.	Cross Sectional	Human with diarrhoea, poultry, meat, milk, and milk products	1- *Campylobacter* prevelance rate 2- Campylobacter serotypes 3- *Campylobacter* AMR phenotype 4- *Campylobacter* AMR genotype	**30**	**520**
55	Ahmed 2020; Phylogenetic analysis of *Salmonella* species isolated from cows, buffaloes, and humans based on gyrB gene sequences	Egypt	*Salmonella* spp.	Cross Sectional	Human (healthy workers, and children with diarrhoea), buffaloes and cows (milk and feces).	*Salmonella* prevelance rate and serotypes.	160	**800**

17	Abdelmalek 2019; Occurrence of *Salmonella* infection and antimicrobial susceptibility for local *Salmonella* isolates from different sources in a cross-sectional study	Egypt	*Salmonella* spp.	Cross Sectional	Human with diarrhoea , grilled poultrys	1- *Salmonella* Nontyphoidal *Salmonella* prevelance rate 2- *Salmonella* Nontyphoidal *Salmonella* serotypes 3- *Salmonella* Nontyphoidal *Salmonella* AMR phenotype	75	**50**
301	El-Naenaeey 2021; Prevalence and antibiotic resistance patterns of *Campylobacter* species isolated from different sources in Egypt	Egypt.	*Campylobacter* spp.	Cross Sectional	Human (gastroenteritis patients), Polutry and cattle	1- *Campylobacter* prevelance rate and serotypes 2- *Campylobacter* AMR phenotype	44	**242**
497	Jaradat 2014; Comparative analysis of virulence and resistance profiles of *Salmonella Enteritidis* isolates from poultry meat and foodborne outbreaks in northern Jordan	Jordan	*Salmonella Enteritidis*	Cross Sectional	Human, poultry meat	1-*Salmonella Enteritidi* prevelance rate 2- *Salmonella Enteritidi* _ AMR phenotype	7 isolates	**302**
467	Ibrahim 2019; Prevalence, antimicrobial resistance and risk factors for Campylobacteriosis in Lebanon	Lebanon	*Campylobacter* spp.	Cross Sectional	Human with diarrhoea, meat (poultry, beef, lamb, and goat)	1- *Campylobacter* spp prevelance rate and serotypes 2- *Campylobacter* AMR phenotype	1000	**150**
3	Abay 2014; Genetic diversity and antibiotic resistance profiles of *Campylobacter jejuni* isolates from poultry and humans in Turkey	Turkey	*Campylobacter jejuni*	Cross Sectional-used Routine data	Human with diarrhoea, poultry carcasses	*Campylobacter jejuni* AMR phenotype	100 isolates	**100 isolates**

263	Divsalar 2019; Antimicrobial resistances, and molecular typing of *Campylobacter jejuni* isolates, separated from food-producing animals and diarrhoea patients in Iran	Iran	*Campylobacter jejuni*	Cross sectional	Human with diarrhoea, poultry and cattle (stool sample and meat)	1- *Campylobacter jejuni* prevelance rate 2- *Campylobacter jejuni* AMR phenotype 3- *Campylobacter jejuni* AMR genotype	74	**233**
54	Ahmed 2016; Characterization of Virulence-Associated Genes, Antimicrobial Resistance Genes, and Class 1 Integrons in *Salmonella enterica* serovar Typhimurium Isolates from poultry meat and Humans in Egypt	Egypt	*Salmonella typhimurium*	Cross sectional	pluck-shop markets workers, poultry meat	1- *Salmonella typhimurium* prevelance rate 2- *Salmonella typhimurium* AMR phenotype 3- *Salmonella typhimurium* AMR genotype	100	**500**
1839	Rokney 2020; WGS-Based Prediction and Analysis of Antimicrobial Resistance in *Campylobacter jejuni* isolates From Israel	Israel	*Campylobacter jejuni*	Routine data	Human clinical specimens, poultry and cattle	1- *Campylobacter jejuni* AMR phenotype 2- *Campylobacter jejuni* AMR genotype	239 isolates	**24 isolates**
401	Greige 2019; Prevalence and genetic diversity of *Campylobacter* spp. in the production chain of broiler poultrys in Lebanon and its association with the intestinal protozoan Blastocystis sp	Lebanon	*Campylobacter* spp.	Cohort and Cross sectional	Human (farm workers, vet, and diarrhoea patient), poultry meat (Farms and slaughterhouses)	1- *Campylobacter* prevelance rate 2-*Campylobacter* serotypes	100	**454**
421	Hamidian 2011; Prevalence of putative virulence markers in *Campylobacter jejuni* and *Campylobacter coli* isolated from hospitalized children, raw poultry, and raw beef in Tehran, Iran	Iran	*Campylobacter* spp.	Cross sectional	Human (hospitalized children), meat (poultry and beef).	*Campylobacter* prevelance rate	420	**378**

383	Ghoneim 2017; Zoonotic Importance of *Campylobacter jejuni* Isolated From Chicken Farms in Egypt	Egypt	*Campylobacter jejuni*	Cross sectional	Human (workers at poultry farms and shops), poultry	*Campylobacter jejuni* prevelance rate	20	**200**
382	Ghoneim 2020; *Campylobacter* Species Isolated from Chickens in Egypt: Molecular Epidemiology and Antimicrobial Resistance	Egypt	*Campylobacter jejuni*	Cross sectional	Human (workers at poultry farms and shops), poultry	1- *Campylobacter* prevelance rate 2- *Campylobacter* serotypes 3- *Campylobacter* AMR phenotype 4- *Campylobacter* AMR genotype	50	**360**
375	Gharieb 2019; Antibiogram, virulotyping and genetic diversity of *Escherichia coli* and *Salmonella* serovars isolated from diarrheic calves and calf handlers	Egypt	*Salmonella* spp.	Cross Sectional	human (hand swab from calf handlers), Calves with diarrhea	1- *Salmonella* Nontyphoidal AMR phenotype 2- *Salmonella* Nontyphoidal serotype	35	**80**
1066	Zeinhom 2021; Prevalence, Characterization, and Control of *Campylobacter jejuni* Isolated from Raw milk, Cheese, and Human Stool Samples in Beni-Suef Governorate, Egypt	Egypt	*Campylobacter jejuni*	Cross sectional	Human with diarrhoea, raw milk and cheese	1- *Campylobacter jejuni* prevelance rate 2- *Campylobacter jejuni* AMR phenotype	53	**200**
147	Awad 2020; Phenotypes, antibacterial-resistant profile, and virulence-associated genes of *Salmonella* serovars isolated from retail poultry meat in Egypt	Egypt	*Salmonella* spp.	Cross sectional	Human (retail workers), poultry carcasses	1- *Salmonella* serotypes and prevelance rate 2- *Salmonella* AMR phenotype	25	**200**

10	AbdEl-Hamid 2019; Genetic Diversity of *Campylobacter jejuni* Isolated From Avian and Human Sources in Egypt	Egypt.	*Campylobacter jejuni*	Cross Sectional	Human with diarrhoea , poultry (meat, and Cloacal Swab) and pigeon droplet	*Campylobacter jejuni* prevelance rate	270	**270**
155	Barakat 2020; Prevalence, molecular detection, and virulence gene profiles of *Campylobacter* species in humans and foods of animal origin	Egypt	*Campylobacter* spp.	Cross sectional	Human with diarrhoea Human incontact with poultry, poultry, milk and milk products	1- *Campylobacter* spp prevelance rate 2- *Campylobacter* serotypes	105	**1194**
53	Ahmed 2015; ERIC-PCR Genotyping of Some *Campylobacter jejuni* Isolates of poultry and Human Origin in Egypt	Egypt	*Campylobacter jejuni*	Cross sectional	Human with diarrhoea, poultry	*Campylobacter jejuni* prevelance rate	246	**287**
1234	Besharati 2020; Serogroups, and drug resistance of nontyphoidal *Salmonella* in symptomatic patients with community-acquired diarrhoea and poultry meat samples in Tehran	Iran	*Salmonella* spp.	Cross sectional	Human with diarrhoea, meat (poultry)	1- *Salmonella* Nontyphoidal prevelance rate 3- *Salmonella* AMR phenotype 4- *Salmonella* AMR genotype	400	**100**
337	Farahani 2018; Molecular Detection, Virulence Genes, Biofilm Formation, and Antibiotic Resistance of *Salmonella enterica* Serotype enteritidis Isolated from poultry and diarrhoea Samples	Iran	*Salmonella Enteritidis*	Routine data	Human, meat (poultry)	*Salmonella enteritidis* AMR phenotype	36 isolates	**195 isolates**

76	Al-Dawodi 2012; Antimicrobial resistance in non-typhi *Salmonella* enterica isolated from humans and poultry in Palestine	Palestine	*Salmonella* spp.	Routine data	Children, poultry	Nontyphoidal *Salmonella* AMR phenotype	71 isolates	**80 isolates**
1310	Derakhshandeh 2013; Association of three plasmid-Encoded spv Genes Among Different *Salmonella* Serotypes Isolated from Different Origins	Iran	*Salmonella* spp.	Routine data	Human with diarrhoea, poultry	*Salmonella* Nontyphoidal serotypes	5 isolates _	**30 isolates_**
296	Elhariri 2020; Virulence and Ant(Youssef et al., 2021)ibiotic Resistance Patterns of Extended-Spectrum Beta-Lactamase-Producing *Salmonella enterica* serovar Heidelberg Isolated from Broiler poultrys and poultry Workers: A Potential Hazard	Egypt	*Salmonella Heidelberg*	Cross Sectional	poultry workers, poultry with diarrhoea	1- *Salmonella Heidelberg* prevelance rate 2- *Salmonella Heidelberg*.AMR phenotype 3- *Salmonella Heidelberg* AMR genoptype	60	**300**
2175	Elsayed 2019; Tracing of *Salmonella* contaminations throughout an integrated broiler production chain in Dakahlia Governorate, Egypt	Egypt	*Salmonella* spp.	Cross sectional	Human (poultry Farms workers), poultry farms	*Salmonella* prevelance rate and serotypes	15	**395**
685	Mouftah 2021; High-throughput sequencing reveals genetic determinants associated with antibiotic resistance in *Campylobacter* spp. from farm-to-fork	Egypt	*Campylobacter* spp.	Routine data	Human with diarrhoea, poultry carcasses, milk and dairy product	1-*Campylobacter* AMR phenotype 2- *Campylobacte*r AMR genotype	57 isolates	**54 isolates**
25	Acar 2017; Phenotyping and genetic characterization of *Salmonella enterica* isolates from Turkey revealing arise of different features specific to geography	Turkey	*Salmonella* spp.	Cross sectional	Human with diarrhoea, bovine, ovine, goat, and poultry	1- *Salmonella* Nontyphoidal *Salmonella* prevelance rate 2- *Salmonella* serotypes 3-*Salmonella* AMR phenotype	50	**335**

						4- *Salmonella* AMR genotype		
380	Ghoneim 2017; Camel as a transboundary vector for emerging exotic *Salmonella* serovars	Egypt	*Salmonella* spp.	Cross sectional	Human (slaughterhouse workers), Camel	Nontyphoidal *Salmonella* prevelance rate	50	**206**

Supplementary Table S3: Summary of the selected studies showing the country and pathogens together:

	Country							
Pathogens	**Egypt**	**Iran**	**Turkey**	**Lebanon**	**Palestine**	**Jordan**	**Israel**	**Total**
***Salmonella* spp**	**12**	**3**	**1**	**0**	**1**	**0**	**0**	**17**
***S.* Heidelberg**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**
***S.* Typhimurium**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**
S. Enteritidis	**0**	**3**	**0**	**0**	**0**	**1**	**0**	**4**
***Campylobacter* spp**	**5**	**1**	**0**	**2**	**0**	**0**	**0**	**8**
C. jejuni	**6**	**1**	**1**	**0**	**0**	**0**	**1**	**9**
C. coli	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**1**
Total	**26**	**8**	**2**	**2**	**1**	**1**	**1**	**41**

Supplementary Table S4

	Nontyphoidal Salmonella								
	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95% CI	Heterogeneity
Amoxicillin–Clavulanic acid	53	126	42%	62	88	70%	1.09	[1.01;1.18]	(I^2 = 34%, r^2 =< 0,000)
Amoxicillin	50	70	71%	64	70	91%	4.02	[0.16 ; 103.61]	(I^2 = 83%, r^2 = 4,6834)
Ampicillin	97	186	52%	96	139	69%	1.10	[0.92; 1.31]	(I^2 = 25%, r^2 = 0,0111)
Azithromycin	32	75	43%	2	22	9%	0.21	[0.06; 0.82]	NA
Cefotaxime	45	145	31%	58	92	63%	3	[0.23; 39.38]	(I^2 = 73%, r^2 = 2,7125)
Ceftriaxone	2	231	1%	9	131	7%	4.33	[0.93; 20.26]	(I^2 = 0%, r^2 =0)
Chloramphenicol	42	281	15%	21	181	12%	1.29	[0.86;1.96]	(I^2 = 18%, r^2 =< 0,001)
Ciprofloxacin	26	281	9%	30	181	17%	1.36	[0.73; 2.51]	(I^2 = 0%, r^2 = 0,0811)
Erythromycin	57	57	100%	52	52	100%	1	[0-96; 1.04]	(I^2 = 0%, r^2 = 0)
Imipenem	3	194	2%	0	108	0%	0.45	[0.05; 4.02]	(I^2 = 0%, r^2 =<0)
Streptomycin	50	126	40%	38	88	43%	1.09	[0.80; 1.49]	(I^2 = 28%, r^2 = 0,0234)
Tetracycline	142	231	62%	66	131	50%	0.79	[0.59; 1.06]	(I^2 = 55%, r^2 = 0,0440)
Trimethoprim-sulfamethoxazole	67	281	24%	15	181	8%	0.57	[0.18; 1.80]	(I^2 = 77%, r^2 = 1,4708)

	Campylobacter jejuni								
	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95%CI	Heterogeneity
Amoxicillin–Clavulanic acid	283	416	68%	56	173	32%	0.79	[0.67; 0.95]	(I^2 = 53%, r^2 =< 0,000)
Amoxicillin	297	297	100%	52	52	100%	1	[0.96 ; 1.04]	(I^2 = 0%, r^2 = 0)
Ampicillin	466	579	81%	142	223	64%	1	[0.97; 1.03]	(I^2 = 11%, r^2 =< 0,001)
Azithromycin	261	297	88%	52	52	100%	1.13	[1.04; 1.24]	(I^2 = 78%, r^2 = 0,033)
Chloramphenicol	258	316	82%	50	73	69%	1.01	[0.89; 1.14]	(I^2 = 0%, r^2 = 0)
Ciprofloxacin	460	627	73%	187	265	71%	0.92	[0.84; 1.01]	(I^2 = 0%, r^2 = 0,0020)
Erythromycin	393	608	65%	92	244	38%	1	[0.97; 1.03]	(I^2 = 0%, r^2 =< 0,0001)
Naladixic acid	558	627	89%	201	265	76%	0.89	[0.77; 1.02]	(I^2 = 69%, r^2 =0,0230)
Streptomycin	213	544	39%	50	235	21%	1.02	[0.83; 1.26]	(I^2 = 0%, r^2 = 0)
Tetracycline	248	330	75%	119	213	56%	0.94	[0.84; 1.05]	(I^2 = 38%, r^2 = 0,0056)
Trimethoprim-sulfamethoxazole	371	399	93%	85	103	83%	1.01	[0.97; 1.04]	(I^2 = 0%, r^2 = 0)

	Salmonella Heidelberg								
	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95%CI	Heterogeneity
Amoxicillin–Clavulanic acid	16	24	67%	6	9	67%	1	[0.58; 1.72]	NA
Ampicillin	24	24	100%	8	9	89%	0.89	[0.72; 1.11]	NA
Ceftriaxone	22	24	92%	7	9	78%	0.85	[0.59; 1.23]	NA
Ciprofloxacin	5	24	21%	2	9	22%	1.07	[0.25; 4.55]	NA
Imipenem	18	24	75%	6	9	67%	0.89	[0.53; 1.49]	NA
Streptomycin	10	24	42%	5	9	56%	1.33	[0.63; 2.83]	NA
Tetracycline	9	24	38%	4	9	44%	1.19	[0.48; 2.90]	NA
Trimethoprim-sulfamethoxazole	12	24	50%	7	9	78%	1.56	[0.91; 2.65]	NA

	Salmonella Enteritidis								
	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95%CI	Heterogeneity
Amoxicillin–Clavulanic acid	5	82	6%	7	87	8%	0.86	[0.17; 4.22]	(I^2 = 0%, r^2 =< 0,000)
Amoxicillin	0	195	0%	8	36	22%	91,05	5.37; 1543.25]	NA
Ampicillin	31	340	9%	26	137	19%	2.37	0.41; 13.87]	(I^2 = 72%, r^2 = 3,1086)
Cefotaxime	1	237	0%	1	78	1%	1	[0.06;15.47]	NA
Ceftriaxone	14	322	4%	2	130	2%	0.65	[0.13; 3.11]	(I^2 = 0%, r^2 = 0)
Chloramphenicol	105	340	31%	46	137	34%	1.43	[0.79; 2.58]	(I^2 = 42%, r^2 = 0,1714)
Ciprofloxacin	126	295	43%	11	94	12%	0.45	[0.26; 076]	(I^2 = 4%, r^2 =< 0,0001)
Imipenem	0	82	0%	5	87	6%	NA	NA	NA
Streptomycin	28	127	22%	36	94	38%	1.54	[1.07; 2.21]	(I^2 = 0%, r^2 = 0)
Tetracycline	18	85	21%	10	52	19%	1.22	[0.58; 2.55]	(I^2 = 0%, r^2 = 0)
Trimethoprim-sulfamethoxazole	40	295	14%	41	94	44%	1.53	[0.35; 6.64]	(I^2 = 88%, r^2 =< 1,6285

Campylobacter coli

	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95%CI	Heterogeneity
Amoxicillin–Clavulanic acid	58	63	92%	0	4	0%	0.12	[0.01; 1.65]	NA
Amoxicillin	63	63	100%	4	4	100%	1	[0.72 ; 1.39]	NA
Ampicillin	63	63	100%	4	4	100%	1	[0.72 ; 1.39]	NA
Azithromycin	51	63	81%	4	4	100%	1.23	[1.09; 1.39]	NA
Chloramphenicol	46	63	73%	0	4	0%	0.15	[0.01; 2.08]	NA
Ciprofloxacin	46	69	67%	12	19	63%	0.67	[0.25; 1.79]	(I^2 = 23%, r^2 = 0,2730)
Erythromycin	67	69	97%	9	19	47%	0.81	[0.43; 1.51]	(I^2 = 49%, r^2 = 0,1179)
Naladixic acid	60	69	87%	17	19	90%	1.02	[0.77; 1.35]	(I^2 = 86%, r^2 = 0,0230)
Streptomycin	44	69	64%	5	19	26%	0.66	[0.16; 2.66]	(I^2 = 68%, r^2 = 0,7252)
Tetracycline	5	6	83%	11	15	73%	0.88	[0.55; 1.41]	NA
Trimethoprim-sulfamethoxazole	63	63	100%	4	4	100%	1	[0.72; 1.39]	NA

Salmonella typhimurium

	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95%CI	Heterogeneity
Ampicillin	15	49	31%	20	41	49%	1.59	[0.94; 2.69]	NA
Ceftriaxone	0	49	0%	0	49	0%	0	0	NA
Chloramphenicol	14	49	29%	19	41	46%	1.62	[0.93; 2.82]	NA
Streptomycin	18	49	37%	28	41	68%	1.86	[1.22; 2.84]	NA
Tetracycline	11	49	23%	13	41	32%	1.41	[0.71; 2.81]	NA

Salmonella Infantis

	No. of resistance isolates from Human sources	No. of isolates from Human sources	resistance ratio among isolates from Human sources	No. of resistance isolates from Animal sources	No. of isolates from Animal sources	resistance ratio among isolates from animal sources	Relative Risk	95%CI	Heterogeneity
Ampicillin	2	11	18%	1	11	18%	.0.50	[0.05; 4.75]	NA
Ceftriaxone	0	11	0%	1	11	9%	3	[0.14; 66.23]	NA
Chloramphenicol	8	11	73%	3	11	27%	0.37	[0.13; 1.05]	NA
Streptomycin	10	11	91%	7	11	64%	0.70	[0.43; 1.14]	NA
Tetracycline	10	11	91%	8	11	73%	0.80	[0.53; 1.20]	NA

Supplementary Table S5

		Table S5 a								
		C. jejuni								
AMR gen	**study id**	**pathogen**	**Human Source**	**Human Isolates**	**Human Prevelance rate**	**Animal/ Food Source**	**Animal/ Food Isolates**	**Animal/ Food prevelance rate**	**Relative Risk**	**95% CI**
bla OXA-61	Divsalar et al. 2019	C. jejuni	80	42	52.50%	20	7	35.00%	0.67	[0.35; 1.25]
class1integrons	AbdEl-Aziz et al. 2020	C. jejuni	148	142	95.95%	20	20	100.00%	1.04	[1.01; 1.08]
cme B	Divsalar et al. 2019	C. jejuni	80	41	51.25%	20	7	35.00%	0.68	[0.36; 1.29]
tet A	Divsalar et al. 2019	C. jejuni	80	17	21.25%	20	6	30.00%	1.41	[0.64; 3.11]
tet O	Divsalar et al. 2019 and Ghoneim et al. 2020	C. jejuni	84	71	84.52%	22	17	77.27%	0.92	[0.73; 1.16]

		Table 5 b								
		NTS								
AMR gen	**study id**	**pathogen**	**Human Source**	**Human Isolates**	**Human Prevelance rate**	**Animal/ Food Source**	**Animal/ Food Isolates**	**Animal/ Food prevelance rate**	**Relative Risk**	**95% CI**
bla AMPc	Besharati et al. 2020	NTS	75	1	1.33%	22	0	0.00%	1.12	[0.05; 26.52}
AAC(6')-Ib	Youssef et al. 2021	NTS	50	8	16.00%	50	11	22.00%	1.38	[0.6; 3.13]
bla CTXM-1	Youssef et al. 2021	NTS	50	8	16.00%	50	11	22.00%	1.38	[0.6; 3.13]
bla SHV	Youssef et al. 2021	NTS	50	8	16.00%	50	11	22.00%	1.38	[0.60; 3.13]
blaTEM	Youssef et al. 2021, and Besharati et al. 2020	NTS	125	12	9.60%	72	11	15.28%	1.25	[0.57; 2.75]
class1integrons.	Besharati et al. 2020	NTS	75	38	50.67%	22	9	40.91%	0.81	[0.47; 1.40]
class 2 integrons	Besharati et al. 2020	NTS	75	22	29.33%	22	6	27.27%	0.93	[0.43; 2]

Table S5 c

Salmonella Heidelberg

AMR gen	study id	pathogen	Human Source	Human Isolates	Human Prevelance rate	Animal/ Food Source	Animal/ Food Isolates	Animal/ Food prevelance rate	Relative Risk	95% CI
bla AMPc	Elhariri et al. 2020	S. H	24	12	50.00%	9	1	11.11%	0.22	[0.03; 1.47]
bla CMY-2	Elhariri et al. 2020	S. H	24	9	37.50%	9	1	11.11%	0.3	[0.04; 2.02]
bla OXA	Elhariri et al. 2020	S. H	24	5	20.83%	9	1	11.11%	0.53	[0.07; 3.96]
bla SHV	Elhariri et al. 2020	S. H	24	6	25.00%	9	1	11.11%	0.44	[0.06; 3.20]
blaTEM	Elhariri et al. 2020	S. H	24	7	29.17%	9	1	11.11%	0.38	[0.05; 2.68]
ESBL	Elhariri et al. 2020	S. H	24	16	66.67%	9	5	55.56%	0.83	[0.44; 1.6]

Part 5

Towards a One Health Food Safety Strategy for Palestine: A Mixed-Method Study

antibiotics

Article

5 Towards a One Health Food Safety Strategy for Palestine: A Mixed-Method Study

Said Abukhattab [1,2]*, Miriam Kull [1,3], Niveen M. E. Abu-Rmeileh [4], Guéladio Cissé [1,3], Lisa Crump [1,3], Jan Hattendorf [1,3] and Jakob Zinsstag [1,3]

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[1] Swiss Tropical and Public Health Institute, Kreuzstrasse 2, CH-4123 Allschwil, Switzerland

[2] Faculty of Medicine, University of Basel, Petersplatz 1, CH-4001 Basel, Switzerland

[3] Faculty of Science, University of Basel, Petersplatz 1, CH-4001 Basel, Switzerland

[4] Institute of Community and Public Health, Birzeit University, West Bank, Palestine; nrmeileh@birzeit.edu (N.M.E.A.R)

* Correspondence: author: Email: said.abukhattab@swisstph.ch

Abstract: Introduction: Foodborne diseases, together with increasing antimicrobial resistance (AMR), pose a threat to public health in an era of huge challenges with climate change and the risks of zoonotic epidemics. A One Health approach to foster food safety is a key for improvement, particularly in complex socio-ecological systems such as in Palestine, to examine human–animal-environment interfaces and promote intersectoral action. **Objectives:** This study aimed to assess food safety from farm to public health toward an operational One Health strategy for Palestine. This study evaluates the food production (broiler production) and monitoring system to better understanding the zoonotic foodborne illnesses transmission and their resistance to antimicrobials. **Methods:** The transdisciplinary approach included multi-stakeholder discussion groups and field visits to broiler farms, slaughterhouses, and meat stores in the Ramallah and Al-Bireh and Jerusalem districts using a semi-structured observational tool. A survey with 337 poultry producers and workers in slaughterhouses and meat stores was conducted to assess hygiene knowledge, attitudes, and practices during broiler meat production. **Results:** The stakeholders point out various challenges along the food production chain in Palestine, such as a striking scarcity of public slaughterhouses, insufficient coordination between authorities, a gap between public and private sectors, and inconsistent application of the law. From observations, it appears that, unlike traditional broiler production, the public slaughterhouses and meat markets have effective hygiene, while large-scale farms implement biosecurity measures. Overall, surveyed participants reported that they are aware of zoonotic disease transmission routes and value hygiene standards. Semi-structured observations and survey results are contradictory. Observations indicate poor hygiene practices; however, the vast majority of broiler meat production chain workers claim that hygiene standards are met. **Discussion and Conclusions:** Our study found that the overuse of antimicrobials, system fragmentation, insufficient infrastructure, a lack of regulations and controls, and poor hygiene practices are among the main obstacles to improving food safety in Palestine. Considering the risk of an important human health burden of food-related illnesses, enhancing food safety in Palestine is required using an integrated One Health approach. It is crucial to develop an integrated quality control system for food production along with promoting on-farm biosecurity and antimicrobial stewardship. Infrastructure, especially slaughterhouses and laboratories, must be built, training and education provided, and consumer awareness raised. As an important added value within a One Health strategy for better food safety in Palestine, research should be reinforced and accompany any future development of the food production monitoring system.

Keywords: Palestine: One Heath; food safety: antimicrobial resistance; zoonosis: foodborne pathogens; mixed methods

5.1 Introduction

The burden of foodborne disease hinders the achievement of the SDGs, particularly the aspirations to end poverty, achieve food security, and ensure health and well-being (WHO, 2015d). Nearly one in ten people, about 600 million worldwide, becomes sick after consuming food contaminated with harmful bacteria, viruses, parasites, prions, or chemicals annually (Pires et al., 2021; WHO, 2015d). In addition to threatening public health, foodborne illnesses also impose a financial burden that hinders socioeconomic development by depleting healthcare systems and harming national economies, tourism, and trade (WHO, 2015d).

Zoonotic pathogens can be transmitted to humans at all stages of the food production chain. For instance, *Salmonella* and *Campylobacter,* the most common foodborne bacteria, can be transmitted during food production, distribution, sale, or preparation if basic hygiene practices are not followed (WHO, 2018c, 2020a). However, the main transmission route is generally considered to be foodborne via consumption of contaminated food (WHO, 2018c, 2020a). Although improper preparation or handling at home, in food establishments, or markets account for a large proportion of food contamination, the World Health Organization (WHO) still assigns primary responsibility for preventing food contamination to food producers ("Food safety ", 2020). Nevertheless, contamination occurs along the entire food production chain, and disease transmission is sensitive to the growing and emerging threats from climate change and risks of zoonotic epidemics outbreaks (Zinsstag et al., 2018). The so-called “farm-to-fork” approach integrates all the processes from food production, transformation, transport, to marketing to assure a healthy product for the consumer (Fung, Wang, & Menon, 2018). A One Health approach extends the farm-to-fork concept to explicitly include human health and allows for assessing the full societal benefits of a systemic study of food-related health issues from a closer cooperation of human and animal health and other related sectors (Zinsstag, Schelling, et al., 2020).

A One Health and transdisciplinary perspective, considering human–animal–environmental interfaces, is central in the context of food safety as it embeds food production systems in their environmental, socio-economic, and public health contexts. Integrated One Health approaches add value in terms of optimized human, animal, and environmental health compared to frameworks that focus on individual elements of food safety only (Gordon, Alonso, Crump, Dominguez-Salas, & De Garine-Wichatitsky, 2020). WHO reports that prevention strategies implemented to reduce the prevalence of *Campylobacter* in live poultry have been associated with a similar decline in human cases (WHO, 2020a). This observation illustrates the interplay of the complex socio-ecological system and underlines the value of inter-sectoral action. To foster collaboration between different disciplines and also between science and society, transdisciplinary approaches promote dialogue between academic and non-academic actors (Mónica Berger-González, Pelikan, Zinsstag, Ali, & Schelling, 2020). Academic knowledge is complemented by valuing practical knowledge from the "life-world" to co-produce novel transformational knowledge (Hirsch Hadorn et al., 2008). Transdisciplinary approaches bring together academic and non-academic stakeholders. In this way, practical knowledge and perspectives of social domains complement scientific knowledge and contribute significantly to the success, quality, acceptance, and sustainability of interventions (Hirsch Hadorn et al., 2008; Stöckli, Wiesmann, & Lys, 2012).

Despite the fact that foodborne illnesses in Palestinians have been rarely reported, the population is exposed to pathogens on a regular basis. In the Gaza Strip, *Campylobacter* and *Salmonella* were detected in approximately 5% and 2% of stool samples from children with acute diarrhoea, respectively. These *Salmonella* isolates were resistant to several antimicrobials, including 62% to 78% ampicillin resistance and 89% doxycycline resistance. (Abu-Elamreen, Abed, & Sharif, 2008; Abu Elamreen, Abed, & Sharif, 2007; Abu Elamreen, Sharif, & Deeb, 2008). A study by Adwan and colleagues reported a prevalence of *Salmonella*, *Escherichia coli*, and *S. aureus* of 25%, 95%, and 30%, respectively, in different types of meat in Palestine (Adwan, Alqarem, & Adwan, 2015). The reported resistance rates in Palestine were 59% and 80% for tetracycline, 59% and 51% for ampicillin, and 59% and 45% for nalidixic acid in humans and poultry non-typhoidal *Salmonella* (NTS) isolates, respectively. The authors conclude that the high prevalence of resistant NTS, especially the frequent resistance to fluoroquinolones, has become a serious problem in Palestine (Al-Dawodi, Farraj, & Essawi, 2012). Moreover, the presence of antibiotic residues in up to 22% of raw dairy milk that reaches Palestinian consumers and in 24% of chicken breast samples collected from slaughterhouses in the Gaza Strip was confirmed (Al Zuheir, 2012; Albayoumi, 2015).

The lacking capacity for zoonotic disease surveillance, the insufficient fight against antimicrobial resistance (AMR), and the low number of education and awareness events in the Middle East and North Africa call for a One Health initiative in these regions (Abukhattab, Taweel, et al., 2022; Baradaran-Seyed & Pishraft-Sabet, 2019). In the absence of relevant data on the risk of AMR from environmental sources, the Eastern Mediterranean and African regions are counted among the least contributors to global research findings on AMR in the environment (Sweileh & Moh'd Mansour, 2020). To the best of our knowledge, food safety in Palestine has not been considered from a One Health perspective (Abukhattab, Taweel, et al., 2022). This research aims to identify the structure, strengths, obstacles, and limitations of the food production monitoring system in Palestine through multi-stakeholder discussion groups. Complementing the qualitative study, we evaluated hygiene practices at broiler farms, slaughterhouses, and meat stores in Palestine through quantitative and semi-structured observational studies. This assessment forms the basis for specifically adapted future developments of the monitoring system and associated improvements in food safety in Palestine using the One Health approach.

Conflict zones, such as the ongoing conflict situation in Palestine, can have a negative impact on social structures, including the family and community. Such conflict scenarios can be extremely complicated and have an impact on aspects such as the environment, nutrition, economy, and psychosocial factors (Rosenthal, 2021). The cost of war and violence results in environmental concerns in addition to psychological misery. Efforts to improve health care and public health will be hampered by this complicated socio-ecological system, which will also hinder social performance and economic progress (Diab et al., 2018; Rosenthal, 2021). In Palestine, 29.2% of the population, or more than one in three, were deemed to be living in poverty in 2017. In 2017, the poverty rate in the Gaza Strip was 53%, which was more than four times higher than the rate in the West Bank (PCBS, 2017). By 2020, the agricultural sector's value added in Palestine reached 7.1% of the gross domestic product (Bank, 2020). Broiler production was chosen as a prime example of food production in Palestine. In 2019, Palestine produced more than 70 million broiler chicks (PCBS, 2021a, 2021b). In 2020, poultry meat production accounted for more than 60% of the country's total meat production at 42,728 tons (Knoema, 2020). A better understanding of the structure, strengths, obstacles, and limitations of the food production monitoring system in Palestine and the context in which it is embedded is essential for developing the monitoring system and related improvements to food safety in Palestine

5.2 Results

5.2.1 Stakeholder Points of View on the Food Production Monitoring System

Various interest groups share numerous challenges and issues along the food production chain in Palestine. Some of the most commonly cited concerns include inadequate hygiene practices, scarcity of veterinary services, laboratories and public slaughterhouses, the uncontrolled use of antimicrobials, insufficient monitoring measures, coordination between authorities, communication between public and private sectors, and inconsistent application of the law. While stakeholders agree on some issues, such as the urgency of containing the spread of AMR, the multi-stakeholder discussion groups also revealed some major differences in perceptions of the various interest groups mainly related to lab testing and services.

The multi-stakeholder discussion group outcomes for each of the five key themes ("The current system for monitoring food production", "Regulatory authorities with responsibilities relevant to food safety", "Public health", "Available infrastructure and capacity building", and "Political and legal context") are presented in detail below (Supplementary Table S3).

5.2.1.1 The Current System for Monitoring Food Production

The multi-stakeholder discussion groups reveal that certain surveillance tools, such as monitoring proper food transport or testing for pathogens, already exist but with some limitations. For instance, the Ministry of Health asserts that the proper transportation of food is monitored: *"There was a case of transporting milk in plastic tanks that did not meet the conditions and standards, so a decision was given to destroy the milk"*. Meanwhile, one of the participating poultry farmers raises the issue of improper meat transportation: "*The meat transporting is not done in the right and proper way. Sometimes it is done in private cars or not a refrigerated car*".

Regarding examination for pathogens, the discussion groups indicate that pathogen testing is practiced in suspected cases by authority bodies. *"In the central veterinary laboratory, our main function is diagnostic services through surveys of certain animal diseases or animal products. Any veterinarian who suspects important diseases sends us samples for examination"*.

Challenges such as disease outbreaks seem to overwhelm the monitoring system in Palestine. Some stakeholders point out that the surveillance system is not able to contain disease outbreaks because identified disease cases are often not reported, properly identified, or followed up. According to a private veterinarian, follow-up of disease cases is not done, resulting in a *"permanent disorder"*. One of the participating private veterinarians agreed, describing the monitoring system fundamentally as *"weak"* and its outcome as *"almost zero".*

Stakeholders particularly criticize the poor implementation of monitoring tools such as the licencing of farms or veterinary health certificates. The issue of licensing, especially of small informal farms, so-called random farms, was raised by several stakeholders, including representatives of poultry breeders and the Ministry of Health: *"Random farms mean few are licensed, and therefore, it is difficult to control the market"*. The Ministry of Health explained that there were random farms that neither the veterinary services nor the health departments knew about and stressed the importance of monitoring the issue of licensing.

5.2.1.2 Regulatory Authorities with Responsibilities Relevant to Food Safety

Stakeholders from the academic, public, and private sectors agreed that some tasks are clearly assigned to the respective ministries. One participant asserted that there was no interference between the powers of the regulatory authorities. The role distribution between authorities, as confirmed by various stakeholders, assigned responsibility for live animals to the Ministry of Agriculture, which is in charge of field controls. The Ministry of Local Governance was responsible for slaughterhouses and once slaughtered, further processing up to the final product was the responsibility of the Ministry of Health. At the same time, the Ministry of National Economy supervised the marketing of food products.

While some responsibilities are assigned to a single regulatory authority, others were shared by multiple authorities. For instance, one public sector representative stated that although the Ministry of Health is the regulatory authority for food safety, it worked closely with other ministries for this purpose.

Other shared responsibilities include import and export or the health sector, which is in charge of three ministries, Local Governance, Health, and Agriculture. One stakeholder was struck by deficient coherence between these ministries to jointly decide and implement measures. In contrast, a representative of the Ministry of Health highlighted the presence of a joint committee between the Ministry of Agriculture and the Ministry of Health called the *"Zoonotic Committee"* as well as a monthly epidemiological report in which both ministries participated. *"Recently, there was a Brucella outbreak in Ramallah area which extended to one of the refugee camps. Direct coordination was made between the United Nations Relief and Works Agency for Palestine Refugees (UNRWA), the Ramallah Health Directorate, Preventive Medicine Department and Environmental Health Department at Ministry of Health and Veterinary Service Directorate at Ministry of Agriculture to reach the source of infection".*

Several stakeholders observed not only overlap but also conflict among regulatory authorities with adverse consequences, such as delayed application of the Palestinian food strategy which was issued in 2017 and AMR national action plan that was issued in January 2020. Both of them are still in infancy and need more participation, collaboration, understanding, and support at the national level.

5.2.1.3 Public Health

Stakeholders advocated for worker and consumer health and the need for prevention, surveillance, and control of foodborne pathogens. Some interest groups pointed out that not only consumers but especially workers who are in direct contact with animals and veterinary medicines are exposed to health risks: *"Hormones are used to gain weight in the fattening farms, which affects human fertility"*. Poor hygiene or contamination by water was, for example, a possible cause of *Salmonella* in poultry, explained the Ministry of Health. However, as multiple stakeholders agree, the adequate preparation of animal food products also plays a crucial role in the prevention of zoonotic disease transmission; the participants agreed the best example of this issue in Palestine is Brucellosis *"We are supposed to convince the consumer to eat what is pasteurized. If it is implemented, 80% of brucellosis cases in Palestine will be ended".*

In addition to foodborne pathogens, stakeholders were also concerned about antimicrobial residues in foods marketed for human consumption. As the AMR national action plan committee warns, humans may develop resistance to antimicrobials due to antibiotic residues in animal meat. One participant commented on this issue by saying: *"I suspect a high percentage of products of animal origin, whether poultry, sheep or cattle, contain antibiotic residues".* Antimicrobials can directly impact human health, as various interest groups agree, but the most feared impact is AMR, the emergence of bacteria that are resistant to antimicrobial drugs. According to the Ministry of Health, the issue of antimicrobial resistance has not yet been studied at the Palestinian level: *"In Palestine, we need to strengthen AMR surveillance by establishing AMR national surveillance system"*.

While AMR occurs naturally over time, as the public health laboratory acknowledged, the misuse and overuse of antimicrobial drugs accelerate its emergence. The AMR national action plan committee was in agreement with this, stating that "*antibiotic misuse leads to resistance*" and emphasizing that the prescription and use of drugs in veterinary and human medicine were critical. The Ministry of Health explained the misuse and overuse of antimicrobials through poor prescribing practices, improper drug selection, incorrect dosing, and self-medication practices: *"The person (health professionals) must have adequate attitudes and awareness; for example, use of third-generation antibiotics in the onset of disease without the use of sensitive test results"*. In animal production, as the as the Ministries of Agriculture and Health pointed out, misuse and overuse of antimicrobial medicines occur especially when they are administered for non-therapeutic purposes, such as prophylaxis or animal growth promotion: *"There are no restrictions on dispensing antibiotics or growth promoters; they are often handed out without a veterinarian's prescription".*

One of the participants from the government sector stated, "*In 2016, 201 samples from farms of laying and broiler chickens came to us on the basis that the farms had high mortality and no antibiotics were effective. When a sensitivity test was conducted, we found that more than 50% of isolated E. coli were extremely resistant to all antibiotics"*.

To slow the spread of AMR, stakeholders requested measures including: 1) Good manufacturing practices for antimicrobials; 2) avoidance of antimicrobial use in animal farms unless for treatment purposes; 3) prescription of antimicrobials for humans exclusively by physicians; 4) improvement of the antimicrobial surveillance system in Palestine; 5) networking of laboratories at the national level; 6) inspecting, testing, and controlling antimicrobial residues in animal feed products and food sources; 7) development of a national awareness program.

In addition, stakeholders questioned whether enough culture and susceptibility testing was being done and advised for the wider use of these tests. The department of epidemiology and preventive medicine acknowledged that culture-susceptibility testing was difficult to perform for each individual case in human medicine and that the procedure was performed in hospitals but not in private clinics.

5.2.1.4 Available Infrastructure and Capacity Building

Farmers and veterinarians did not seem to have much confidence in the sample collection, handling, and testing procedures followed in animal health laboratories and called for capacity building. Veterinarians were even convinced that samples did not arrive at the laboratory, and if they did, they were neglected and not examined: *“I sent 21 chicks to the government laboratory to check for mycoplasma after a week, and the answer was (the sample is not enough)”.* Another veterinarian said, *“I have not sent samples to the laboratory for more than 3 years... Samples were sent, and the result was that pathogens were not isolated, and all results were negative despite the high mortality rate with clinical symptoms, and in the end, all animals were dead. They have laboratory equipment, but they don’t use them”. “The vet himself does not trust in the government laboratory”.* The Ministry of Health agreed partially with the veterinarians, and called for a general expansion of diagnostic capacity in laboratories. This was supported by other stakeholders, including the public health laboratory. The public health laboratories complained about inadequately trained personnel, lack of certain equipment and materials, and insufficient national coordination, which entails duplicate sampling. The Palestinian authorities should better coordinate collaboration between the veterinary laboratory, public health laboratories, and laboratories at universities.

The discussion groups agreed that *“more than 70% of slaughtering takes place outside public slaughterhouses”*, which is explained by the lack of official slaughterhouses and limited control of the existing ones since not all cities, villages, and refugee camps in the country have poultry slaughterhouses. The Ministry of Agriculture as well as the Ministry of Health condemn slaughtering outside public slaughterhouses, arguing that hygiene practices in traditional slaughterhouses, known as *“Natafats”*, are not controlled. The ministries share concerns about contamination due to poor hygiene practices in traditional abattoirs. *“We must improve some practices during the slaughtering process, such as reusing materials and tools and personal hygiene in the Natafats, which will reduce carcass contamination*”. While the ministries require the presence of a veterinarian at the slaughterhouse to grant permission for operation, even in public slaughterhouses, stakeholders criticize the absence of veterinarians during the operations of these slaughterhouses: “*To improve control of the slaughter process,* *slaughterhouses should be run privately but remain under government control*". A representative of the Ministry of Health suggested, "S*laughterhouses should be equipped with cameras and be linked to the Ministry of Agriculture. In this way, not only could the veterinarians' presence be monitored, but also compliance with their duties*".

5.2.1.5 Political and Legal Context

From the discussion groups, it appeared that one obstacle to food safety in Palestine was the gap between the private and government sectors. Stakeholders argued, for instance, that food safety strategies failed in the past because only the government sector was involved. One of the poultry breeders, who has worked in poultry production for five years, raised the specific issue of missing communication between farmers and the Ministry of Agriculture. This poultry breeder criticized that "*the Ministry of Agriculture does not support farmers in matters of health, product safety, and poultry farms protection and is therefore of no concern to farmers, it is even non-existent*".

"*If there was an insurance and compensation system for farmers, a control system would be superfluous*", argues one of the poultry producers. Another farmer adds, "*Sometimes we look for medications that are the cheapest for treatment. Some medications have better treatment effectiveness, but if I use them, I lose the profit of my work." "Indeed, the lack of compensation forces farmers to slaughter animals regardless of the health status of the flock*", one of the veterinarians justified. Veterinarians should also be subject to legal protection, according to one of them: "*My colleague works in a slaughterhouse and after eliminating a calf unfit for human consumption; he was attacked by having his car set on fire and shot at. But currently, there is no criminal law that would deter criminals from committing such acts*". Another participant representing the government sector said, "*We frequently find antibiotics residues in broiler meat samples collected from traditional slaughterhouses. However, we are unable to proceed because we lack legal provisions to take any enforcement action against these facilities*".

Obstacles to the implementation of Palestinian law and deficient import controls at border crossings were cited as another impediment to food safety in Palestine. "*The Palestinian law, which was built, based on the Jordanian law, has been amended and updated many times, and this amendment has led to the weakening of the Palestinian law, as stated by one of the participants*". The problem of smuggling, especially the large number of uncontrolled poultry imported from Israel to Palestine, was raised by various stakeholders, such as the Ministry of Health and representatives of poultry production. The Ministry of Health referred to the regional differences in the implementation of the law in Palestine: *"The problem of smuggling is due to* *weak law enforcement outside the cities or on the border areas, which constitute more than 60% of the Palestinian Authority's land".* In all meetings, there was consensus among stakeholders that the law should be applied to all Palestinian Authority territories with the same effectiveness.

5.2.2 Semi-Structured Observational Study: Hygiene Practices along the Broiler Production Chain

5.2.2.1 Hygiene Practices in Broiler Farms

Large-scale farms visited had biosecurity and modern technologies at their disposal (Supplementary Figure 1a). On the other hand, farms with smaller production lacked automatic ventilation systems, temperature control, or even closed buildings (Supplementary Figure 1b). While floors were usually concrete, sometimes they were covered with loose, dry bedding, soil, or both. Nearly all farmers reported that dead chickens were either fed to pets or deposited in municipal open dumps (Supplementary Figure 1c), and that manure was used as fertilizer for olive trees (Supplementary Figure 1d). Farms were run by workers who often live on site. The bedroom, kitchen, and toilet were usually located near the chicken farm, often even in the same building, separated only by a door. On only one large- and one small-scale farm visited were the workers living in separate buildings. All but one of the facilities had running water, but soap was rarely seen, and a towel was available in only one establishment. Kitchen and toilet cleanliness at the time of visit ranged from dirty to very clean and smoking shisha or cigarettes inside the rooms was the norm (Supplementary Figure 1e) and (Supplementary Figure 1f). Overall, workers' personal hygiene and accommodation cleanliness seemed better in larger agencies than in small farms.

5.2.2.2 Hygiene Practices in Poultry Slaughterhouses

The procedure of slaughtering was similar in traditional abattoirs and public slaughterhouses, but public slaughterhouses made use of modern technologies at all processing steps, while traditional abattoirs relied on simple equipment only. Slaughter in traditional slaughterhouses depended directly on demand as consumers came to the abattoir to select the live animal that is kept right inside the abattoir. Public slaughterhouses started work at 10:00 p.m., working all night so that the fresh poultry could be transported to the markets before they opened around 6:00 a.m. The public slaughterhouse we visited had the capacity to process up to 30,000 broilers every night (Supplementary Figure 2).

5.2.2.3 Hygiene Practices in Poultry Meat Stores

Selling points of poultry meat in Ramallah city and surrounding villages were highly similar. Chicken was kept fresh by cooling but was never frozen, as there was no demand for frozen poultry meat. Poultry was sold either as whole or cut into breasts, thighs, wings, kidneys, and livers (Supplementary Figure 3). Overall, the poultry meat stores visited appeared clean and well maintained, and hygiene, such as hand washing, seemed adequate

5.2.3 Knowledge, Attitudes, and Practices of Hygiene among Broiler Production Chain Workers

5.2.3.1 Sociodemographic Characteristics of the Study Population

Overall, 337 workers in the broiler meat production chain from 175 locations, from farms to meat stores, participated in the survey. The sociodemographic characteristics of the poultry meat chain interviewed are summarized in Table 5-1. It is noticeable that almost all respondents were male (98.2%) and lived in the countryside (89.3%). Most were married (69.9%) with up to 13 family members. The majority had at least completed junior high school (94.3%), and 27.0% had attended university. Respondent experience in broiler production differed greatly, varying between 6 months and 60 years. The monthly income median was 4000 NIS (New Israeli Shekel), equivalent to about 1200 U.S. dollars, and varied strikingly, with minimum of 1000 NIS and maximum of 8000 NIS.

Table 5-1 Stratified the sociodemographic characteristics of the broiler workers surveyed based on workers' profession/occupation

	Farmers N (%)	**Meat Workers N (%)**	**Overall N (%)**
Gender			
Male	160 (97%)	171 (99.4%)	331 (98.2%)
Female	5 (3%)	1 (0.6%)	6 (1.78%)
Age (years)			
15-30	41(24.9%)	85 (49.4%)	126 (37.4%)
31-45	58(35.2%)	65(37.8%)	123 (36.5%)
46-60	43(26%)	15(8.7%)	58(17.2%)
> 60	23(19.9%)	7(4.1)	30 (8.9%)
Marital status[a]			
Single	30(18.3%)	68(39.5%)	98 (29.2%)
Married	133(81.1%)	102(59.3%)	235 (69.9%)
Divorced	1(0.6%)	2(1.2%)	3 (0.9%)
Family Size [median (IQR)]	6(3)	5(2)	5 (3)
Residence			
Urban	5(3%)	29(16.8%)	34 (10.1%)
Rural	159(96.4%)	142(82.6%)	301 (89.3%)
Refugee camp	1(0.6%)	1(0.6%)	2 (0.6%)
Education level			
Illiterate	3(1.8%)	2(1.2%)	5(1.5%)
Elementary school (≤ 5 years of education)	7(4.2%)	7(4%)	14 (4.2%)
Junior high school (≤ 9 years of education)	37(22.4%)	49(28.5%)	86 (25.5%)
Senior high school (10–12 years of education)	62(37.6%)	79(45.9%)	141 (41.8%)
University (≥ 13 years of education)	56(34%)	35(20.4%)	91 (27%)
Experience in farming (years) [median (IQR)]	10(15)	6(7)	8 (11)
Monthly income (NIS)[b] [median (IQR)]	4500(3000)	4000(2200)	4000 (3000)

N, number of respondents; IQR, interquartile range. [a]: One missing data in the marital status variable. [b]: Sixteen missing data in the monthly income variable.

5.2.3.2 Reported KAP of Hygiene in Broiler Production

Interview results suggested that respondents were aware of zoonotic disease transmission routes and valued hygiene standards such as thorough hand washing or personal protection, especially when in contact with sick or dead chickens (Table 5-2). The survey results also revealed that stricter hygiene measures and regular disinfection of workplaces were introduced since the SARS-CoV pandemic (Table 5-3). With 84.3% of respondents having heard of it before, zoonotic diseases seem to be a concept for most participants, while 6.8% of them were infected with one of the zoonotic diseases related to their works. About

94% of respondents believed in promoting proper hand hygiene and 82.5% considered that personal protective measures when in contact with poultry could prevent zoonotic disease infection. According to the surveys, about 11.3% washed their hands without soap, while the rest used soap and or disinfectants. In fact, 95% declared that they had introduced frequent hand washing since the emergence of the SARS-CoV pandemic. In addition, 50.5%, 65.0%, and 68.0% disclosed that they had adopted wearing overalls, masks, and gloves, respectively, since SARS-CoV emerged. In addition, 75.8% reported using a tissue when sneezing since the outbreak of the pandemic (Table 5-3).

Table 5-2 Hygiene and zoonotic diseases-related knowledge and practices[1]

		Farmers N (%)	**Meat Workers N (%)**	**Overall N (%)**	***p*-Value for Difference[1]**
Do you think promoting proper hand hygiene can prevent infection with zoonotic diseases?	Yes	150 (91%)	166 (96.5%)	*316 (93.8%)*	*0.03*
	No	15 (9%)	6 (3.5%)	*21 (6.2%)*	
Do you think touching sick or dead poultry can cause infection with zoonotic diseases?	Yes	124 (75.2%)	140 (81.4%)	*264(78.3%)*	*0.007*
	No	37 (22.4%)	20 (11.6%)	*57 (16.9%)*	
	Don't know	4 (2.4%)	12 (7%)	*16(4.8%)*	
Do you think increase the frequency of cleaning and disinfection and make sure there is adequate ventilation in shared spaces can prevent infection with zoonotic diseases?	Yes	158 (95.8%)	162 (94.2 %)	*320 (95%)*	*0.37*
	No	2 (1.2%)	6 (3.5%)	*8 (2.4%)*	
	Don't know	5 (3%)	4(2.3%)	*9 (2.6%)*	
Do you think personal protective measures when in contact with poultry can prevent infection with zoonotic diseases?	Yes	132 (80%)	146 (84.9%)	*278 (82.5%)*	*0.06*
	No	28 (17%)	16 (9.3%)	*44 (13%)*	
	Don't know	5 (3%)	10 (5.8%)	*15 (4.5%)*	
How do you wash your hands?	Carefully, without soap	6 (3.6%)	32(18.6%)	*38 (11.3%)*	*<0.0001*
	With soap or hand disinfectant	159 (96.4%)	140 (81.4%)	*299(88.7%)*	
Did you touch sick or dead poultry with your hands in the last month?	Yes	105 (64%)	59 (34%)	*164 (48.8%)*	*<0.0001*
	No	59 (36%)	113(66%)	*172 (51.2%)*	

Did you take preventive measures when you touched sick or dead poultry?	Yes	60 (58.8%)	28 (47.5%)	*88 (54.7%)*	*0.16*
	No	42 (41.2%)	31(52.5%)	*73 (45.3%)*	
Have you ever heard about zoonotic diseases?	Yes	145 (88%)	139 (80.2%)	*284 (84.3%)*	*0.08*
	No	20 (12%)	33 (19.2%)	*53 (15.7%)*	
Have you experienced a disease problem regarding chicken health (zoonotic)?	Yes	11 (6.7%)	12 (7%)	*23 (6.8%)*	*0.91*
	No	154 (93.3%)	160(93%)	*314 (93.2%)*	
How are the remains of slaughter and dead chickens handled?	Burned	18 (10.9%)	5 (2.9%)	23 (6.8%)	*<0.0001*
	Buried	11 (6.7%)	28 (16.3%)	39 (11.6%)	
	Fed to pets (dog or cat)	54 (32.7%)	23 (13.4%)	77 (22.9%)	
	Released into the wild	45 (27.3%)	32 (18.6%)	77 (22.9%)	
	Collected by the municipality	32 (19.4%)	77 (44.8%)	109 (32.3%)	
	Other	5 (3%)	7 (4%)	12 (3.5%)	

[1] Chi2 test. N, number of respondents.

Table 5-3 The impact of SARS-CoV on hygiene practices among farmers and meat workers in the chicken meat production chain

What Protective Measures Have You Adopted in Your Work After SARS-CoV Emerged?			
protective measures	**Farmers N (%)**	**Meat workers N (%)**	**Overall N (%)**
Wearing masks	86 (52.1%)	133 (77.3%)	219 (65.0 %)
Wearing gloves	87 (52.7%)	143 (83.1%)	230 (68.2%)
Wearing overalls	74 (45.0%)	96 (55.8%)	170 (50.5%)
Frequent hand washing	149 (90.9%)	170 (98.8%)	319 (95.0%)
Sanitizing with disinfectant after finishing work	140 (84.9)	127(73.8%)	267 (79.2%)
Increasing the frequency of disinfection at the workplace	114 (69.1%)	162 (94.7%)	276 (82.1%)
Ventilation at the workplace	127 (77.0%)	160 (93.0%)	287 (85.2%)
Using a handkerchief when sneezing	108 (65.5%)	144 (83.7%)	252 (75.8%)

N, number of respondents.

While 264 of 337 respondents believed touching sick or dead poultry could transmit a zoonotic disease, 164 admitted to touching sick or dead poultry with their hands in the past month. Of these 164, 88 respondents reported taking preventive measures, such as thorough hand washing after contact with the animal. A total of 95.0% of respondents believed that increasing the frequency of cleaning and disinfection and ensuring adequate ventilation in common, spaces could prevent zoonoses. Since the emergence of COVID-19, there has been a 79% rise in sterilization with disinfectant after finishing work, an 82.1% increase in disinfection frequency, and an 85% increase in ventilation in the workplace (Table 5-3).

About 22.9% of dead chickens and slaughter waste were fed to pet animals, without any treatment, while 22.9% were released in the wild, and municipalities collected 32.3%. The rest reported that they burn or bury dead animals. Few respondents specified that they burned dead chickens if they had a disease and fed them to pets if they were healthy before they died.

An association between poultry farmers' practices and their attitudes could not be demonstrated in the survey results. Table 5-4 shows the frequencies of respondents by attitude and related practice regarding hand hygiene and contact with poultry. These results indicated no strong association between attitudes and related practices. Assuming that respondents' practices correlate with their attitudes, we would expect consistent responses to the questions "Do you think promoting proper hand hygiene can prevent infection with zoonotic diseases?" and "How do you wash your hands?", for instance. In this case, we would expect that respondents who believe that proper hand hygiene prevents zoonotic disease transmission are more likely to wash their hands with soap and or disinfectants than respondents who do not believe that proper hand hygiene does prevent zoonotic diseases. A univariable logistic regression estimated a non-significant OR of 0.82 (95% CI [0.18, 3.66]) was associated with the responses to the two questions, and hand hygiene practices appear to be independent of farmers' attitudes toward hand hygiene. The comparison between individuals who believe that touching sick or dead poultry can cause zoonotic infection and those who do not believe or do not know reveals a non-significant OR of 0.69 (95% CI [0.41, 1.17]) related to the response to the question "Did you touch sick or dead poultry with your hands in the last month?". With an OR of 1.15 (95% CI [0.5, 2.6]), no association can be found between the questions "Do you think personal protective measures when in contact with poultry can prevent infection with zoonotic diseases?" and "Did you take preventive measures when you touched sick or dead poultry?". Based on the questions analyzed in this study, we could not validate the consistency between respondent attitudes and practices.

Table 5-4 Number and row percentage of respondents (N (%)) stratified by attitude and related practice regarding hand hygiene and contact with poultry.

		How do you wash your hands?		
		Carefully, without soap	With soap or hand disinfectant	*Total*
Do you think promoting proper hand hygiene can prevent infection with zoonotic diseases?	Yes	36 (11.4%)	280 (88.6%)	*316 (100%)*
	No	2 (9.5%)	19 (90.5%)	*21 (100%)*

		Did you touch sick or dead poultry with your hands in the last month?		
		Yes	No	*Total*
Do you think touching sick or dead poultry can cause infection with zoonotic diseases?	Yes	134 (50, 8%)	130 (49.2%)	*264 (100%)*
	No	24 (42.9%)	32 (57.1%)	*56 (100%)*
	Don't know	6 (37.5%)	10 (62.5%)	*16 (100%)*

		Did you take preventive measures when you touched sick or dead poultry?		
		Yes	No	*Total*
Do you think personal protective measures when in contact with poultry can prevent infection with zoonotic diseases?	Yes	74 (55.2%)	60 (44.8%)	*134 (100%)*
	No	8 (53.3%)	7 (46.7%)	*15 (100%)*
	Don't know	6 (50%)	6 (50%)	*12 (100%)*

5.2.3.3 Determinants of broiler production chain workers knowledge about zoonotic diseases

Our analysis identifies education level and years of experience working in the broiler meat production chain as likely determinants of poultry farmer and meat worker knowledge about zoonotic diseases. The examination of the proportion of respondents who have heard or have never heard of zoonotic diseases by education level suggests a relationship between respondent education and their knowledge (Figure 5-1). For instance, 3 out of 5 illiterate participants (60.0%) had not heard of zoonoses, while the majority of individuals within each other educational category knew about zoonotic diseases. About 71%, 66%, 90%, and 96% of respondents who graduated from elementary school, junior high school, senior high school, and university, respectively, had heard of zoonotic diseases. For participants with more than nine years of education (completed senior high school or university), zoonotic diseases seemed to be a familiar concept. Years of experience working in broiler meat production appeared to be another determinant of zoonotic disease knowledge.

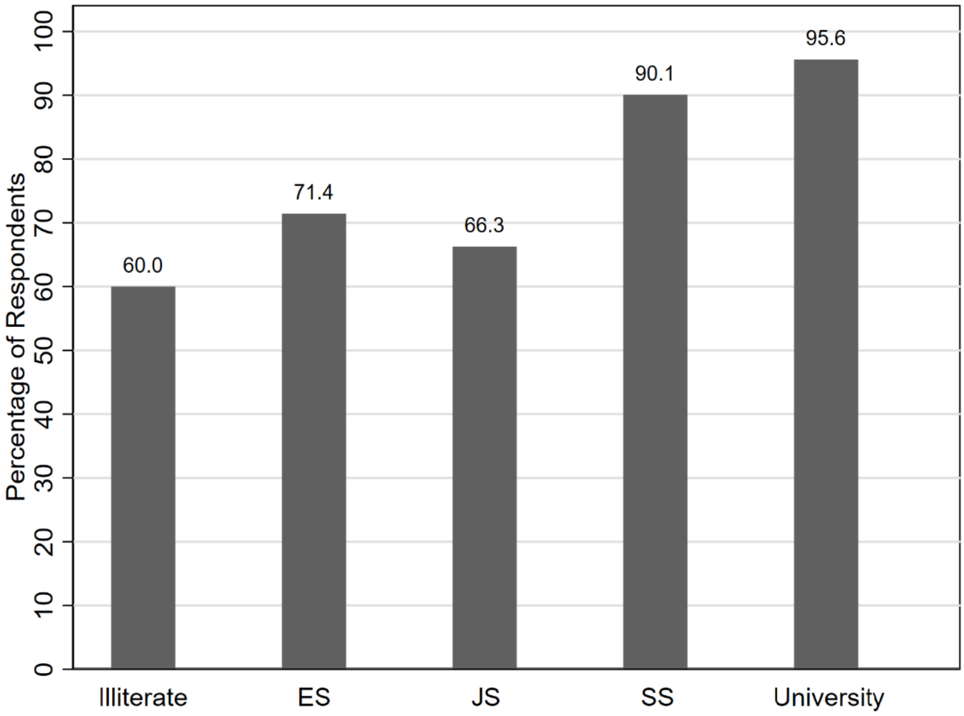

Figure 5-1 Percentage of respondents who have heard of zoonotic diseases by education level

Abbreviations: ES, Elementary school; **JS**, Junior high school; **SS**, Senior high school.

As shown in Figure 5-2, workers (farmers and meat workers) who knew about zoonotic diseases tended to be more experienced in broiler meat production (median years of experience working in the broiler meat production chain = 9 years) than those who had never heard of zoonotic diseases (median years of experience = 4 years). The results of a multiple logistic regression supported the suggested dependence of zoonotic disease knowledge on education level and years of experience working in the broiler meat production chain. The odds of having heard of zoonotic diseases were 4.54 (95% CI [2.28, 8.99]) and 10.88 (95% CI [3.69, 32.06]) times higher for education levels of senior high school and university, respectively, compared to individuals who were illiterate or whose highest level of education was elementary or junior high school. Further, for every one-year increase in experience in working in broiler meat production, the odds of having heard of zoonotic diseases increased by a factor of 1.13 (95% CI [1.06, 1.20]). Thus, our model suggested that education level and years of experience working in broiler meat production were likely determinants of zoonotic disease knowledge.

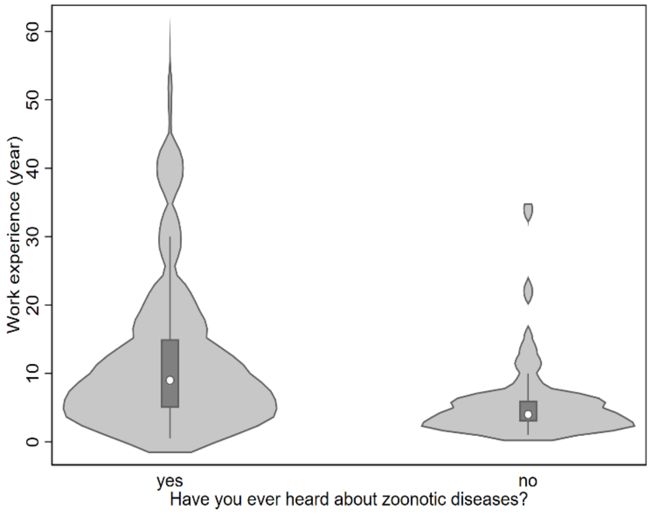

Figure 5-2 Years of experience working in the chicken meat production chain, by whether respondents have heard of zoonotic diseases or have never heard of them before

5.3 Discussion

5.3.1 Toward an Operational One Health Strategy for Palestine

Although a national food safety strategy was developed, unclear roles and poor communication among regulatory authorities as well as between private and public sectors appear to be impeding progress in improving food safety in Palestine. The division of responsibilities among ministries, as determined by the national committee for the formulation of the Palestinian strategy for food safety, is consistent with the reports of the multi-stakeholder discussion groups we conducted (FAO, 2017b). Our results regarding the role distribution between regulatory authorities could thus be confirmed. The Palestinian food safety strategy agrees that the main responsibility for monitoring food safety, including hygiene guidelines for service providers, food safety inspections, and prohibiting the marketing of unregistered foods until they have obtained the necessary permits, or disease control measures, lies with the Ministry of Health (FAO, 2017b). However, as mentioned in the discussion groups, the Ministry of Health is expected to collaborate with other stakeholders to develop control mechanisms, ensure workplace safety, or inspect imported food (FAO, 2017b). At the same time, the responsibility to regulate imports and exports of foods is assigned to the Ministry of Agriculture (FAO, 2017b). We assume that these shared responsibilities bear the risk of misunderstandings and often fail due to insufficient communication and coordination between regulatory authorities and poor communication between the private and government sectors.

Our findings suggest that there is a lack of adequate resources and personnel to implement a One Health strategy for improved food safety in Palestine. These findings are consistent with the results of Abuzerr and colleagues and Al-Khatib and colleagues who identified a lack of policy coherence, poor governance and leadership, limited financial resources and the lack of explicit national food safety requirements and standards as major barriers to implementing the One Health integrated surveillance system (Abuzerr, Zinszer, & Assan, 2021; Khatib & Al Mitwalli, 2009). In the specific context of implementing *Brucella melitensis* control programs in Palestine, for example, based on the FAO report, the program is challenged by weak infrastructure, scarce resources, insecurity, political instability, vaccine quality, farmer attitudes, and deficient traceability of animal movements (FAO, 2009). Under these circumstances, the organization notes, improving occupational and food hygiene, monitoring disease outbreaks in humans and animals, and implementing animal movement control are particularly challenging. A test and slaughter policy, for instance, should only be considered if farmers are fully compensated for their slaughtered animals, cooperate, and accept the slaughter policy (FAO, 2009).

Rigorous, evidence-based strategies should guide hygiene practices in Palestinian animal food production from farm to final food preparation. It has been shown that on-farm biosecurity measures could reduce the prevalence of *Campylobacter* infection in broilers by more than 50% (Gibbens, Pascoe, Evans, Davies, & Sayers, 2001; Van de Giessen, Tilburg, Ritmeester, & Van Der Plas, 1998). Thus, renovating traditional poultry farms in Palestine or constructing new buildings should be supported and encouraged. A simple measure such as the use of screens to keep flies out has been associated with a reduced prevalence of *Campylobacter* from 51.4% in the control houses to 15.4% in the intervention houses (Hald, Sommer, & Skovgård, 2007). We hypothesize that such a reduction in infection of zoonosis pathogens in live poultry will also reduce the risk of transmission to humans by reducing occupational hazards for workers who are in direct contact with animals or meat products. On the other hand, better product quality prevents the transmission of zoonoses to consumers.

The stakeholders expressed particular concern about misuse and overuse of antimicrobials and the associated acceleration of antimicrobial resistance. The researchers agree that critical steps for mitigating antimicrobial resistance and maintaining future efficacy of antimicrobials requires a comprehensive, system-wide, multidisciplinary, and multisectoral strategy to promote, monitor, and evaluate judicious use of antimicrobials (Majumder et al., 2020; Sweileh & Moh'd Mansour, 2020). Appropriate precautions, such as biosecurity measures and a national action plan for antimicrobial stewardship (AMS), may mitigate the impact of foodborne pathogens and AMR, but these challenges remain and require an integrated One Health approach. Biosecurity measures reduce but cannot exclude the risk of *Campylobacter* infections in broiler flocks because chickens are exposed to "constant contamination pressure" (Hermans, Van Deun, Messens, et al., 2011). Van de Giessen and colleagues record that positive cases reappeared after the successful elimination of *Campylobacter* (Van de Giessen et al., 1998). When it comes to AMS, the United Nations Interagency Coordination Group on Antimicrobial Resistance (IACG) cautions that most countries do not fail to develop a national action plan for AMS but rather to implement and sustain it (WHO, 2018a). Challenges to implementing AMS include technical capacity, necessary finances, political will, and regional cooperation to prevent poor implementation of measures in one region from undoing progress in other regions (WHO, 2018a). In the long term, IACG insists governments must allocate resources to implement their national action plans to ensure sustainability and achieve effective AMS (WHO, 2018a). Meanwhile, IACG asserts that allocating resources to address AMR is one of the most profitable investments a country can make (WHO, 2018a).

During our research, we realized that incorporating legal, political, and social dimensions as part of a One Health initiative for improved food safety in Palestine is indispensable. Current legislation regulating food safety in Palestine is fragmented and does not cover all aspects of food safety at all levels of the food chain (FAO, 2017b). Due to the Israeli occupation, uncontrolled trade takes place on borders and in "Zone C", which covers more than 60% of the West Bank where Palestinian authorities are prevented from enforcing their policies (FAO, 2017b). Given decades of conflict, war, and unrest, developing the political will for international cooperation for disease prevention and AMS presents one of the greatest challenges in Palestine.

A limitation of this study is that the composition and participation of the multi-stakeholder discussion groups have an impact on the outcomes. We tried to be inclusive by inviting all relevant sectors. However, the multi-stakeholder discussion groups had an imbalance of power since not all invited interest groups were equally active and engaged. For instance, in the

Ministry of Local Governance, the municipalities did not actively participate in the first discussion group, leaving the discussion early.

5.3.2 Methods to Assess Hygiene Practices

Focusing on farms and broiler production, we propose utilizing various approaches to evaluate hygiene practices. Even though some direct observations were confirmed by the questionnaire responses, we noted poor agreement of survey results and data collected through observations. Observations and interviews agreed that dead chickens were most often fed to pets or disposed of at the municipal dump. In contrast, observations and survey results were contradictory on hand washing, protective clothing, disinfection, and ventilation at workplaces, and visitor hygiene regulations. According to the surveys, about 90% reported to wash their hands with soap, but we rarely found soap near the sink during site visits. A significant percentage of respondents reported wearing protective clothing, but workers were rarely wearing uniform clothing, tall boots, or masks during our visits.

Although field observations are considered one of the most appropriate tools for measuring hygiene behaviour at the community level, their validity and reliability must be questioned (Curtis et al., 1993). In a few cases, our field visit was announced beforehand, so staff were present to show us around. This needs to be considered as the announcement could allow workers to prepare and adapt, for instance, getting rid of dead animals or cleaning the facilities. Observation at a single time point might miss individual behaviour that varied over time (Cousens, Kanki, Toure, Diallo, & Curtis, 1996). However, because most of our observations examined facilities and equipment, such as the presence of a disinfecting footbath or the type of bedding in the poultry farm, they were not particularly susceptible to variability. In contrast, the reliability of observations related to the cleanliness of toilets, for example, maybe more vulnerable. Although time-consuming and costly, repeated observations could increase the reliability and validity of semi-structured observations, provided that farms became accustomed to the presence of researchers.

Over-reporting of good KAP may limit the validity of survey results on hygiene practices in broiler production. As reported in several studies assessing sanitary practices, we assume that KAP perceived as good tends to be over-reported in surveys (Curtis et al., 1993; Manun'Ebo et al., 1997; Stanton, Clemens, Aziz, & Rahman, 1987). The resulting overestimation of the frequency of good hygienic KAP affects the validity of survey results in that they may not accurately reflect reality. To avoid this point, a written questionnaire could also be considered instead of a verbal interview so that participants would not be influenced by direct interaction with interviewers. In addition to validity, the generalizability of surveys must also be questioned due to the restricted study area and the corresponding study population. The evaluation of associations between survey responses is limited by the sample size. For instance, the low number of respondents affected by a zoonotic disease transmitted by chickens, only 23 interviewees, makes it difficult to identify KAP as a risk factor. To examine KAP as risk factor for health outcomes, the study area and thus the sample size would need to be dramatically increased.

While the low correspondence between observations and survey results is noteworthy, we expected such inconsistencies due to our study design. We also assume that respondents may be over-reporting good hygienic KAP. Al-Khatib and Al-Mitwalli noticed in 2009 a similar divergence between survey results and field observations regarding food sanitation practices in restaurants of Ramallah and Al-Bireh district of Palestine (Khatib & Al Mitwalli, 2009). For example, 76.5% of respondents reported washing their hands with soap, while the authors found that in 14.2% and 37.3% of cases, respectively, there was no cleaning material near the hand-washing sink in the kitchen and the toilet. Generally, data collected through direct observation of hygiene practices, as Curtis and colleagues in Burkina Faso, Manun'Ebo and colleagues in Congo, and Garayoa and colleagues in Spain, are less prone to overestimate the frequency of good practices than those through questionnaires (Curtis et al., 1993; Garayoa, Vitas, Díez-Leturia, & García-Jalón, 2011; Manun'Ebo et al., 1997). Nevertheless, the authors emphasize that there is no gold standard for measuring hygiene practices, because just as participants can adjust their responses to a questionnaire to correspond to what they perceive as good, they can also adjust their behaviour in the presence of observers to show an image they consider desirable.

5.3.3 Impacts of Food Supply Chain Actor KAP on Public Health

To the best of our knowledge, this is the first study attempting to describe the knowledge, attitude, and prevention practices of zoonotic disease in Palestine. Interest groups of the multi-stakeholder discussion groups emphasized that KAP are critical to preventing foodborne pathogens and fighting AMR at all levels of the food supply chain, from farm to fork. Farmers are considered end users of antimicrobials, which explains the importance of their KAP to mitigate the spread of AMR (M. M. Hassan et al., 2021). Similar to our results suggesting that farmer and meat worker education level and years of experience might be related to KAP of hygiene in broiler production, Hassan and colleagues demonstrate that in Bangladesh, farmer socioeconomic demographics, such as education, source of income, and age, have a major impact on KAP in the context of antimicrobial use and AMR (M. M. Hassan et al., 2021). Wambui and colleagues in Kenya and Martins and colleagues in Portugal also found a significant effect of education level on hygiene practice among meat workers (Martins, Hogg,

& Otero, 2012; Wambui, Karuri, Lamuka, & Matofari, 2017). Thus, their findings confirm our hypothesis that sociodemographic characteristics are likely determinants of KAP. The KAP results in this study revealed that personal hygiene, such as proper hand washing, is close to those reported by Osaili and colleagues in Jordan and higher than those reported in Kenya, Turkey, and Egypt (Abd-Elaleem, Bakr, Hazzah, & Nasreldin, 2014; Osaili et al., 2013; Wambui et al., 2017). Conversely, a higher proportion was reported by Neil and colleagues, who found that all South African meat workers who took part in their study indicated that they always washed their hands with soap while at work (Nel, Lues, Buys, & Venter, 2004).

We also looked at knowledge of zoonoses diseases, and a high percent of respondents had heard of the term "zoonoses" prior to this study. These results are close to those reported in India (80%) and lower than those reported in Greece (99%) (Moutos, Doxani, Stefanidis, Zintzaras, & Rachiotis, 2022; Singh et al., 2019). While studies in Malaysia and Nepal found that the proportions of prior knowledge of zoonotic diseases among the farmers were 42% and 74%, respectively (Niraulaa, Sharmaa, & Dahalb, 2021; Sadiq et al., 2021).

The global economy and health have both been severely impacted by the SARS-CoV epidemic. Even though most firms were completely shut down due to government regulations, the food industry across the supply chain still operates to feed the nations. In such a challenging time, maintaining worker safety and health is essential, as is upholding a high standard of food safety and consumer confidence (Nakat & Bou-Mitri, 2021). Personal protective equipment (PPEs), along with good personal hygiene and hand washing habits, are strongly recommended by health institutions such as WHO and the Centers for Disease Control for food business to minimize the spread of both cross-infection (SARS-CoV) and cross-contamination (food safety) (WHO, 2014, 2020b). Therefore, it is now more pressing than ever to have higher compliance with hygiene practices and protective measurements (Nakat & Bou-Mitri, 2021; WHO, 2020b). This strictness in applying hygiene practices in markets and meat factories, along with the hygiene awareness program to limit the spread of coronavirus within the Palestinian territories, was reflected in our KAP study that was carried out in the midst of the pandemic.

5.4 Methods

The study used methods to capture attitudes, views, opinions, interests, and needs of all relevant stakeholders involved in the food production chain. The exchanges between these stakeholders were facilitated, and their coordination and cooperation promoted. For these purposes, the study combined the use of multi-stakeholder discussion groups and semi-structured observations (Figure 5-3).

Furthermore, this study examined the hygiene practices of broiler meat production chain workers and the underlying KAP. An attempt was made to explain and understand current hygiene practices in broiler production. Of particular interest was the coherence between attitudes and practices in broiler production. In addition, sociodemographic characteristics, namely education level and years of experience in farming, were tested as determinants of the workers' knowledge about zoonotic diseases. At best, broiler meat worker KAP can be identified as risk factors for health outcomes, measured by the proportion of respondents affected by a zoonotic disease transmitted by working in the broiler meat production chain (Figure 5-3).

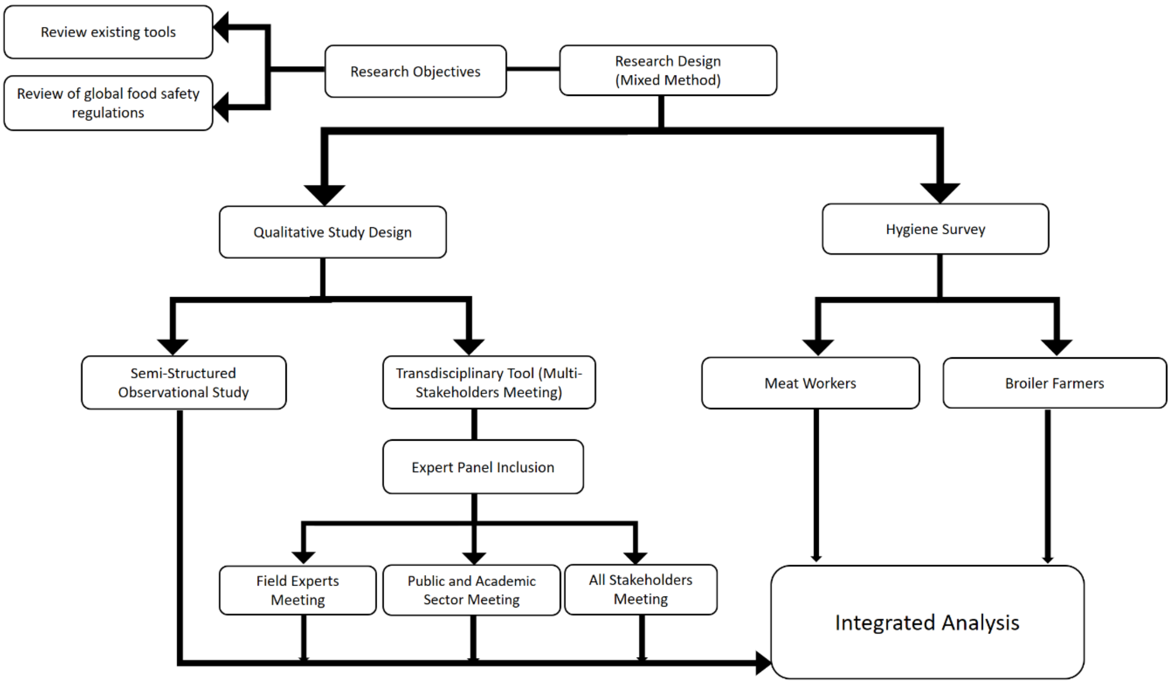

Figure 5-3 Methodology framework to assess the hygiene practices from farm to fork

5.4.1 Multi-Stakeholder Discussion Groups

This research projected adopts principles of transdisciplinarity to assess stakeholder points of view on the food production monitoring system in Palestine by incorporating contextual conditions, interests, knowledge, and expectations. The "multi-stakeholder discussion group" tool provided by the transdisciplinarity network (TD-net, transdisciplinarity.ch), a forum initiated by the Swiss Academies of Arts and Sciences, served as a guideline for the stakeholder meetings. This method brought together stakeholders and civil society to identify the problem at hand and facilitate a common understanding of different perspectives, mutual learning, successful co-production of knowledge, and building trust (Fry, 2021).

Discussion groups were conducted at Birzeit University in Palestine between July 2021 and February 2022 and included the public, private, and academia sectors. After identifying the social groups relevant to the project, representatives of key institutions, associations, networks, and stakeholders were invited to participate in a discussion group in July 2021. Representatives of the public and academic sectors attended the multi-stakeholder discussion group on July 7, 2021, composed of 11 stakeholders. Eight stakeholders involved in or overseeing food production were invited to participate in a second-day multi-stakeholder discussion group from July 8, 2021. These two initial discussion groups clarified the roles of the stakeholders and identified the various perspectives on the Palestinian food production monitoring system. The first multi-stakeholder discussion group included stakeholders from the public sector and academia to create the most favorable climate for authentic reporting. While participants in the second discussion group were private interest groups and stakeholders directly involved in monitoring food production. A third multi-stakeholder discussion group with 15 participants in February 2022 sought dialogue between the public and private sectors, academia, and civil society. Participant details in the three meetings are described in Supplementary Table S1.

The participant sociodemographic characteristics were considered. Participants ranged in age from 30 to 70 years, with between 5 to 45 years of experience in their field. The majority of participants in the first and second stakeholder discussion groups were male, while 30% of participants in the last discussion group were female.

5.4.2 Semi-Structured Observations

To assess hygiene practices, a semi-structured observational tool was based on a survey developed by Hawileh (2012) (Supplementary Table 2) (Hawileh, 2012). This tool served as a basis for reporting hygiene practices at broiler farms, abattoirs, and meat selling points. Between February 8 and 17, 2021, a total of five farms, three abattoirs, and two meat stores within Ramallah area were visited. Sites were chosen so that the various types of farms and abattoirs, from traditional small-scale to modern, highly technological large-scale agencies were taken into account. Observations were not limited to hygiene practices during work, but also considered essential infrastructure: buildings and facilities, water availability, waste management, and worker personal hygiene. All field visits and observations were documented with handwritten notes and, when permission was provided, supplemented with photographs.

5.4.3 Surveys on Chicken Meat Production Chain Worker Hygiene Knowledge, Attitude, and Practices

A cross-sectional survey looked at the knowledge, attitudes, and practices (KAP) of workers involved in the broiler meat production chain under the hypothesis of inadequate implementation of hygiene practices in broiler production in Palestine. Ramallah and Al-Bireh and Northwest Jerusalem districts were chosen as the study area so that a complete analysis of the broiler production chain, from breeding farms to slaughterhouses and meat stores, could be implemented. Ramallah and Al-Bireh governorate is the administrative and economic capital of the Palestinian Authority and is among the governorates with the most breeding broiler chickens, with nearly 10 million birds in 2021 (PCBS, 2022).

Based on data from the Palestinian Ministry of Agriculture and Ministry of Local Government, the study population was designated as all broiler keepers, and slaughterhouse and meat store workers in Ramallah and Al-Bireh governorate, and Northwest Jerusalem region (175 sites in total). The study excluded farms that did not raise broiler chickens in the preceding year (May 2020 to May 2021). The structured questionnaire was based on a survey developed by Hawileh (2012) (Hawileh, 2012). With a response rate of 85% among all workers on the broiler production chain in the targeted area, 165 participants from broiler keepers and 172 broiler meat workers (in total 337) were surveyed between June 9, 2021, and September 2, 2021. Prior to the interviews, we trained Arabic-speaking interviewers for two days about the study objectives, ethical considerations, and the Mobile Data Studio program for data collection. To reduce interviewer bias, we did not share the hypothesis that hygiene practices in broiler production might be inadequate with the interviewers. All data were collected electronically using the software program Mobile Data Studio and regularly transferred to a second electronic database and backup in Palestine and Switzerland.

5.4.4 Data Management and Analysis

All multi-stakeholder discussion groups from July 2021 were transcribed in Arabic and translated into English. The software program MAXQDA 2018 allowed for computer-assisted qualitative data analysis. Using a deductive approach, themes, categories, and codes were developed and assigned to the corresponding contents.

Data collected through surveys were managed using Stata version 16.1. (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC). The KAP of hygiene in the broiler production chain was assessed through descriptive analysis. Additionally, we examined the coherence between attitudes and practices using simple logistic regressions. For these simple logistic regressions, responses “No” and “Don’t know” to questions “Do you think avoiding contact with poultry can prevent infection with zoonotic diseases?” and “Do you think personal protective measures when in contact with poultry can prevent infection with zoonotic diseases?” were combined into one category. Further, using multiple logistic regression, education level and years of experience in farming were examined as determinants of respondent knowledge about zoonotic diseases. For this multiple logistic regression, the educational levels of “illiterate,” “elementary school”, and “junior high school” were grouped together and served as the reference category. Supplementary KAP of hygiene in broiler production were examined as risk factors for contracting chicken-borne zoonotic disease through simple logistic regressions.

5.5 Conclusions and Recommendations

Our study found that the overuse of antimicrobials, system fragmentation, insufficient infrastructure, a lack of regulations and controls, and poor hygiene practices are among the main obstacles to improving food safety in Palestine. To support the One Health Initiative in Palestine, we recommend promoting education, training, and awareness campaigns. One Health knowledge should be taught in multidisciplinary programs at universities. Furthermore, target groups such as farm workers, slaughterhouse and restaurant staff, households, and health workers should be educated and trained in sanitation practices and in the use of antimicrobials. Meanwhile, the general public’s awareness of food safety, zoonoses, and AMR needs to be raised through awareness campaigns.

Any development of the food safety system in Palestine should be accompanied by conducting research to demonstrate the added value of applying a One Health approach and to consider the growing challenges of climate change and the risks of epidemics. To effectively and sustainably monitor and control outbreaks of zoonotic diseases and the spread of AMR in Palestine, a national surveillance system must be established. Human, animal, and environmental samples need to be collected regularly and tested for zoonotic pathogens and their resistance rates, as well as for antimicrobial residues. Efficient testing relies on sufficiently sensitive detection methods to enable early detection, notification, and timely response.

As the next steps toward an operational One Health strategy for Palestine, we propose to further promote exchanges between stakeholders and establish an integrated quality control system for food production. These discussion groups aim to clarify the roles of all actors, establish communication pathways, and foster cross-sector partnerships. A One Health strategy for Palestine does not require new ministries or other institutions, as they are already in place and operational. Ideally, however, a governing body with representatives from the private and public sectors as well as academia should be established to oversee food safety in Palestine.

Supplementary Materials: The following supporting information can be downloaded at: https: //www.mdpi.com/article/10.3390/antibiotics11101359/s1, Supplementary Table S1: Details of participants in the three meetings. Supplementary Table S2: The semi-structured observational tool. Supplementary Table S3: Codebook of multi-stakeholder discussion group outcomes. Supplementary Figure F1 (a to f): Semi-structured observational study: Hygiene practices in broiler farms. Supplementary Figure F2: Semi-structured observational study: Hygiene practices in poultry slaughterhouses. Supplementary Figure F3: Semi-structured observational study: Hygiene practices in poultry slaughterhouses.

Authors Contributions: Conceptualization, S.A., N.M.E.A.-R., J.H., and J.Z.; Data curation, S.A., M.K. and N.M.E.A.-R.; Formal analysis, S.A., M.K., and J.H.; Funding acquisition, S.A., N.M.E.A.-R., and J.Z.; Investigation, S.A., M.K., N.M.E.A.-R., and J.Z.; Methodology, S.A., N.M.E.A.-R., J.H., and J.Z.; Supervision, S.A., G.C., N.M.E.A.-R., J.H., and J.Z.; Writing—original draft, S.A. and M.K.; Writing—review & editing, S.A., N.M.E.A.-R., G.C., L.C., J.H., and J.Z. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement:

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Northwestern and Central Switzerland Ethics Committee (Ethikkommission Nord-west-und Zentralschweiz, EKNZ) (Reference No: AO_2021-00021) and the ethical review committee at the Institute of Community and Public Health (ICPH) at Birzeit University (Reference No: 2020 (12 – 1)).

Informed Consent Statement: All the participants provided written informed consent for using their de-identified data for research purposes.

Data Availability Statement: The data presented in this study are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest

5.6 Supplementary Materials

Supplementary Figure S1:

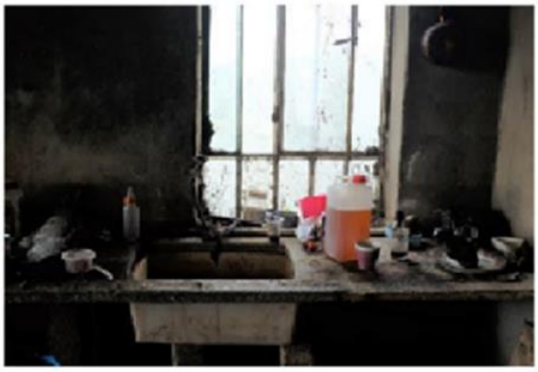
Supplementary Figure 1. a: Closed highly modernized buildings of a large-scale farm with biosecurity.

Supplementary figure 1. b: Simple small-scale farm with poor biosecurity.

Supplementary Figure 1. c: Municipal dam, where among other things also dead animals are disposed of.

Supplementary Figure 1. d: Olive trees for which chicken manure is used as fertilizer.

Supplementary Figure 1. e: Staffroom with kitchen and toilet in a separate building next to one of the large-scale farms visited



Supplementary Figure 1. f: Sink without soap or towel in a staffroom, which is separated from the small-scale farm only by a door

Supplementary Figure S2:

Supplementary Figure 2. a: Chickens kept in the interior of a traditional abattoir, ready to be selected for slaughter by consumers.

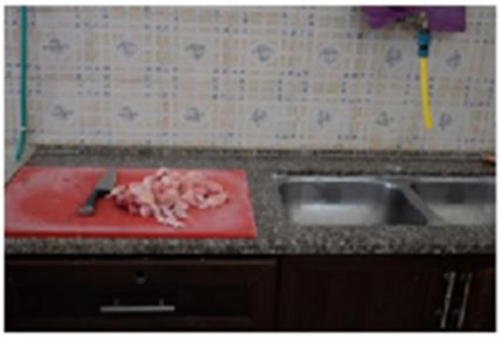
Supplementary figure 2. b: Chickens are delivered to public slaughterhouses in plastic boxes.

Supplementary Figure 2. c: Poultry meat or waste products such as chicken feet packed in plastic bags in a traditional abattoir.

Supplementary Figure 2. d: Fresh assorted poultry packed in plastic boxes in a public slaughterhouse.

Supplementary Figure S3:

Supplementary Figure 3. a: Poultry is sold assorted, packaged, and refrigerated in meat stores.

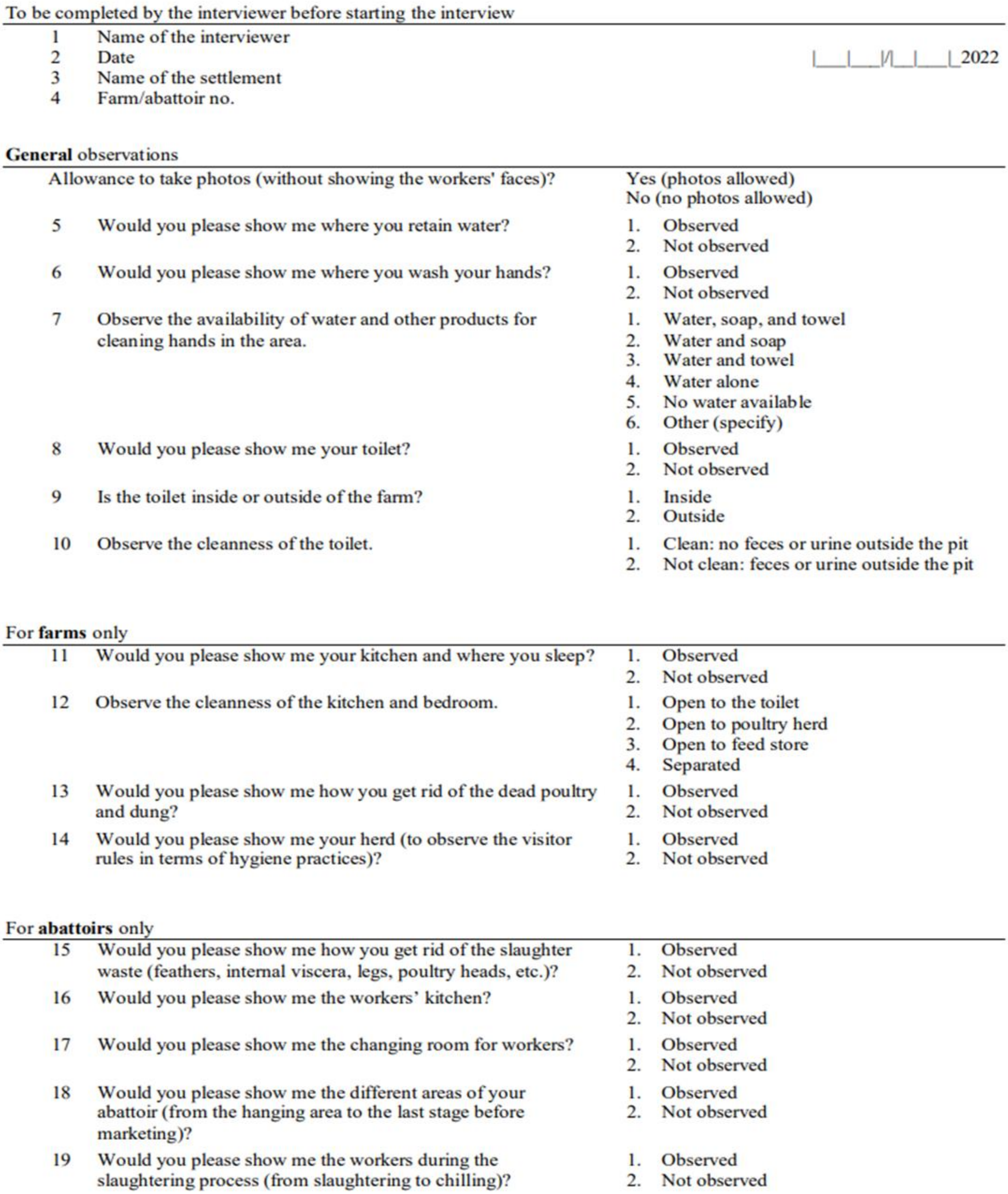


Supplementary Figure 3. b: Poultry remains lying next to the sink, which the meat seller tried to hide during our visit

Supplementary Table S1: Participants in the multi-stakeholder discussion groups who represented the relevant sectors.

Date	Discussion group	Relevant sectors	No. of participants
July 7, 2021	First discussion group	Ministry of Health	3
		Ministry of Agriculture/ Veterinary Services	2
		Ministry of Local Governance	2
		Ministry of National Economy	1
		Academic sector	3
July 8, 2021	Second discussion group	Ministry of Health/ Environmental Health Department	2
		Palestinian Veterinarians Syndicate	1
		Private veterinarians specialize in poultry disease	2
		Poultry producers	3
February 9, 2022	Third discussion group	Ministry of Health/ Environmental Health Department	2
		Ministry of Agriculture / Veterinary Services	2
		Ministry of Agriculture / Monitoring and Control Department	2
		Ministry of Local Governance	1
		Non-Government Organizations	2
		Academic sector	3
		Industrial sector	3

Supplementary Table S2. Semi-structured observational tool



To be completed by the interviewer before starting the interview

1	Name of the interviewer	
2	Date	|___|___|/|___|___|2022
3	Name of the settlement	
4	Farm/abattoir no.	

General observations

	Allowance to take photos (without showing the workers' faces)?	Yes (photos allowed) No (no photos allowed)
5	Would you please show me where you retain water?	1. Observed 2. Not observed
6	Would you please show me where you wash your hands?	1. Observed 2. Not observed
7	Observe the availability of water and other products for cleaning hands in the area.	1. Water, soap, and towel 2. Water and soap 3. Water and towel 4. Water alone 5. No water available 6. Other (specify)
8	Would you please show me your toilet?	1. Observed 2. Not observed
9	Is the toilet inside or outside of the farm?	1. Inside 2. Outside
10	Observe the cleanness of the toilet.	1. Clean: no feces or urine outside the pit 2. Not clean: feces or urine outside the pit

For **farms** only

11	Would you please show me your kitchen and where you sleep?	1. Observed 2. Not observed
12	Observe the cleanness of the kitchen and bedroom.	1. Open to the toilet 2. Open to poultry herd 3. Open to feed store 4. Separated
13	Would you please show me how you get rid of the dead poultry and dung?	1. Observed 2. Not observed
14	Would you please show me your herd (to observe the visitor rules in terms of hygiene practices)?	1. Observed 2. Not observed

For **abattoirs** only

15	Would you please show me how you get rid of the slaughter waste (feathers, internal viscera, legs, poultry heads, etc.)?	1. Observed 2. Not observed
16	Would you please show me the workers' kitchen?	1. Observed 2. Not observed
17	Would you please show me the changing room for workers?	1. Observed 2. Not observed
18	Would you please show me the different areas of your abattoir (from the hanging area to the last stage before marketing)?	1. Observed 2. Not observed
19	Would you please show me the workers during the slaughtering process (from slaughtering to chilling)?	1. Observed 2. Not observed

Supplementary Table S3.

Codebook

Theme 1: The current system for monitoring food production

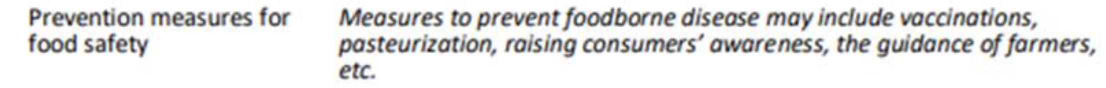
Category	**Code**	***Code description***
Epidemiological investigations	Pathogen testing and case detection	*Animals, meat, humans, and the environment can all be tested for pathogens. The results need to be properly communicated for case detection.*
	Follow-up of confirmed cases (test & slaughter)	*Once a case is detected, action must follow.*
Surveillance tools	Periodic examinations (from farm to fork)	*Regularly conducted examinations (by eye or laboratory testing) without suspicion at different stages along the food production chain: farms, transport, slaughter, markets, and food products.*
	Licensing of farms	*Palestinian law requires licensing of all farms, but many farms are unlicensed (random farms).*
	Veterinary health certificates	*Veterinary health certificates must be issued by a recognized veterinarian before slaughter.*

Theme 2: Regulatory authorities with responsibilities relevant to food safety

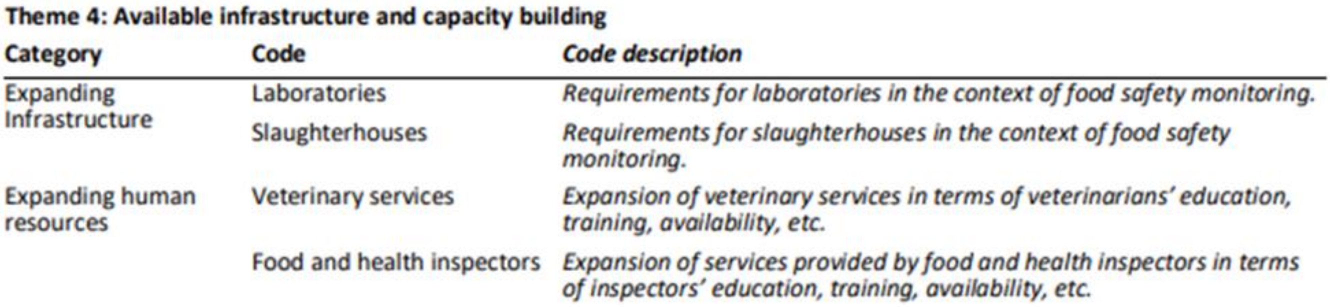
Category	**Code**	***Code description***
Organization of regulatory authorities	Responsibilities of the regulatory authorities	*Clear role distribution between regulatory authorities.*
	Cooperation between regulatory authorities	*Regulatory authorities working together on a particular issue.*
	Overlaps/conflicts between regulatory authorities	*Lack of clear role distribution between regulatory authorities.*
Initiatives and strategies	Toward a national food safety surveillance	*Advances toward a national food safety surveillance plan and its implementation.*
	Toward a national AMR surveillance	*Advances toward a national AMR surveillance plan and its implementation.*

Theme 3: Public health

Category	**Code**	***Code description***
Drugs in human and veterinary medicine	Human medicine: drug prescription and use	*Standards, regulations, and usage of drugs, especially antimicrobials, in human medicine.*
	Veterinary medicine: drug prescription and use	*Standards, regulations, and usage of drugs, especially antimicrobials, in veterinary medicine with a focus on adherence to the safety period/withdrawal period.*
	Drug residues and AMR	*Drug residues in meat or the environment and the associated growing AMR.*
Worker health and safety	Health insurance	*Health insurance system for workers involved in the food production chain (farmers, butchers, traders, veterinarians, etc.).*
	Financial insurance and economic incentives	*Financial insurance system for workers involved in the food production chain (farmers, butchers, traders, veterinarians, etc.) In the context of their economic incentives.*
	Legal protection	*Legal protection of workers involved in the food production chain (farmers, butchers, traders, veterinarians, etc.).*
Consumer health and safety	Hygiene practices and contamination (along the food production chain)	*Hygiene practices and associated contamination from farm to fork (farms, transport, slaughter, markets) threatening consumer health and safety.*
	Salmonella as an indicator of inadequate hygiene practices (in poultry production)	*Salmonella contamination in poultry production as a prime example of consumer health and safety hazards.*

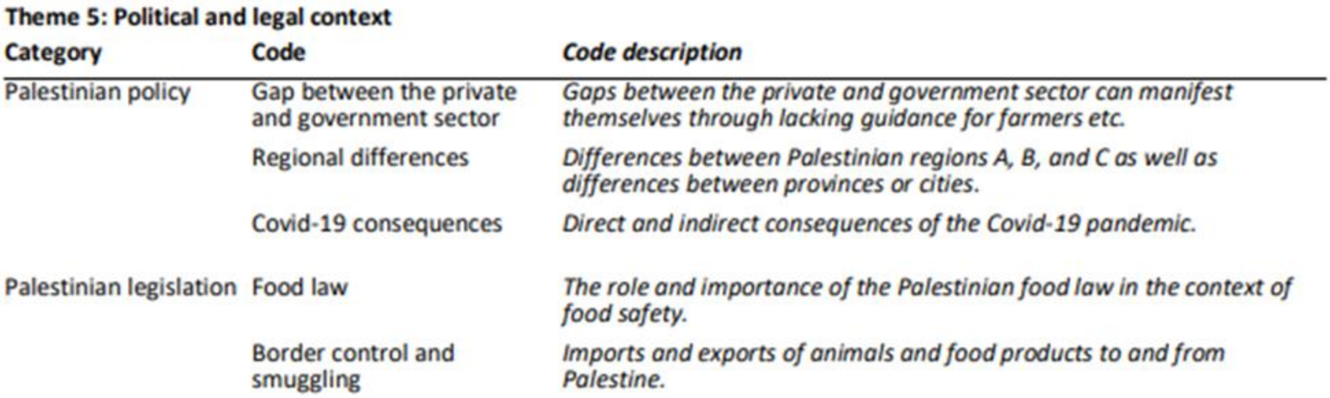


Category	Code	Code description
	Prevention measures for food safety	*Measures to prevent foodborne disease may include vaccinations, pasteurization, raising consumers' awareness, the guidance of farmers, etc.*



Theme 4: Available infrastructure and capacity building

Category	**Code**	***Code description***
Expanding Infrastructure	Laboratories	*Requirements for laboratories in the context of food safety monitoring.*
	Slaughterhouses	*Requirements for slaughterhouses in the context of food safety monitoring.*
Expanding human resources	Veterinary services	*Expansion of veterinary services in terms of veterinarians' education, training, availability, etc.*
	Food and health inspectors	*Expansion of services provided by food and health inspectors in terms of inspectors' education, training, availability, etc.*



Theme 5: Political and legal context

Category	**Code**	***Code description***
Palestinian policy	Gap between the private and government sector	*Gaps between the private and government sector can manifest themselves through lacking guidance for farmers etc.*
	Regional differences	*Differences between Palestinian regions A, B, and C as well as differences between provinces or cities.*
	Covid-19 consequences	*Direct and indirect consequences of the Covid-19 pandemic.*
Palestinian legislation	Food law	*The role and importance of the Palestinian food law in the context of food safety.*
	Border control and smuggling	*Imports and exports of animals and food products to and from Palestine.*

Part 6

Whole Genome Sequencing for One Health Surveillance of Antimicrobial Resistance in Conflict Zones: A Case Study of *Salmonella* spp. and *Campylobacter* spp. in the West Bank, Palestine

AMERICAN SOCIETY FOR MICROBIOLOGY | Applied and Environmental Microbiology

| **Spotlight Selection** | Epidemiology | Full-Length Text

6 Whole-genome sequencing for One Health surveillance of antimicrobial resistance in conflict zones: a case studyof Salmonella spp. and Campylobacter spp. in the West Bank, Palestine

Said Abukhattab[1,2], Salome Hosch[1,2], Niveen M. E. Abu-Rmeileh[3], Shadi Hasan[4], Pascale Vonaesch[5], Lisa Crump[1,2], Jan Hattendorf[1,2], Claudia Daubenberger[1,2], Jakob Zinsstag[1,2], Tobias Schindler[1,2]

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AUTHOR AFFILIATIONS See affiliation list on p.125.

Editor Christopher A. Elkins, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Address correspondence to Said Abukhattab, said.abukhattab@swisstph.ch.

Said Abukhattab and Salome Hosch contributed equally to this article. The order was established through consensus and in alphabetical order.

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Abstract: Antimicrobial resistance (AMR) is a critical global concern driven by the overuse, misuse, and/or usage of inadequate antibiotics on humans, animals' agriculture, and as a result of contaminated environments. This study is the first One Health survey in the Middle East that incorporated whole-genome sequencing (WGS) to examine the spread of AMR in *Campylobacter* spp. and *Salmonella* spp. This cross-sectional study was conducted to examine the role of AMR at the human-animal-environmental interface and was performed in Ramallah/Al-Bireh and Jerusalem governorates of the central West Bank, Palestine. In 2021 and 2022, a total of 592 samples were collected and analyzed. From a total of 65 *Campylobacter jejuni* and 19 *Salmonella* spp. isolates, DNA was extracted for WGS using Oxford Nanopore Technologies MinION platform. We found that the dominant serotypes of *C. jejuni* and *Salmonella enterica* were present in chicken manure, chicken meat sold in markets, and feces of asymptomatic farm workers, with high genetic similarities between the isolates regardless of origin. Additionally, our results showed rapid strain turnover in *C. jejuni* from the same sites between 2021 and 2022. Most of the positive *Salmonella* spp. samples were multidrug-resistant (MDR) *S. enterica* serovar Muenchen carrying the plasmid of emerging *S. infantis* (pESI) megaplas- mid, conferring

resistance to multiple antibiotics. Our findings highlight the spread of MDR foodborne pathogens from animals to humans through the food chain, empha- sizing the importance of a One Health approach that considers the interconnections between human, animal, and environmental health.

Importance: Prior to this study, there existed hardly an integrated human-animal-envi- ronmental study of Salmonellosis and Campylobacteriosis and related AMR in Middle Eastern countries. The few existing studies lack robust epidemiological study designs, adequate for a One Health approach, and did not use WGS to determine the circulating serotypes and their AMR profiles. Civil unrest and war in Middle Eastern countries drive AMR because of the breakdown of public health and food security services. This study samples simultaneously humans, animals, and the environment to comprehensively investigate foodborne pathogens in the broiler chicken production chain in Palestine using WGS. We show that identical serotypes of *C. jejuni* and *S. enterica* can be found in samples from chicken farms, chicken meat sold in markets, and asymptomatic broiler chicken production workers. The most striking feature is the rapid dynamic of change in the genetic profile of the detected species in the same sampling locations. The majority of positive *Salmonella* spp. samples are MDR *S. enterica* serovar Muenchen isolates carrying the pESI megaplasmid. The results demonstrate a close relationship between the *S. enterica* serovar Muenchen isolates found in our sample collection and those responsible for 40% of all clinical *Salmonella* spp. isolates in Israel as previously reported, with a sequence identity of over 99.9%. These findings suggest the transboundary spread of MDR *S. enterica* serovar Muenchen strains from animals to humans through the food chain. The study underscores the importance of combining integrated One Health studies with WGS for detecting environmental-animal-human transmission of foodborne pathogens that could not be detected otherwise. This study showcases the benefits of integrated environmental-animal-human sampling and WGS for monitoring AMR. Environmental samples, which may be more accessible in conflict-torn places where monitoring systems are limited and regulations are weak, can provide an effective AMR surveillance solution. WGS of bacterial isolates provides causal inference of the distribution and spread of bacterial serotypes and AMR in complex social-ecological systems. Consequently, our results point toward the expected benefits of operationalizing a One Health approach through closer cooperation of public and animal health and food safety authorities.

Keywords: Palestine, *Campylobacter*, *Salmonella*, AMR, WGS, One Health

6.1 Introduction

The global spread of antimicrobial resistance (AMR), often referred to as the "silent pandemic" is one of the major challenges to public health in the 21st century. The O'Neill report estimates that by 2050, 10 million lives could be lost annually due to AMR (O'Neill, 2016). The problem of AMR is exacerbated in conflict-torn regions, such as the Middle East, where overuse of antibiotics, fragmented monitoring systems, inadequate infrastructure, and a lack of regulations and controls contribute to the rise of AMR. This includes both community and nosocomial transmission, which raises the incidence of AMR in these areas (Devi, 2019). Evidence is accumulating that prolonged and intense conflicts, as in the Palestine territories, lead to social and environ-mental conditions that foster emergence of AMR (Truppa & Abo-Shehada, 2020). In Palestine, the lack of comprehensive national surveillance for antimicrobial resistance and weak published data hinder the ability to assess the extent of the problem and its risk factors. Furthermore, as a religious tourist destination, Palestine poses a potential risk for the emergence and international spread of AMR bacteria through the visitors.

Salmonellosis and Campylobacteriosis are leading causes of foodborne diseases (Havelaar et al., 2015). With an estimated 100 million individuals falling ill from foodborne infections each year, the Middle East has the third-highest prevalence globally (Abukhattab, Kull, et al., 2022). Due to the rapid spread of AMR, fluoroquinolone-resistant *Salmonella* (FRS) and *Campylobacter* (FRC) were declared as high priority pathogens for research and development of new antibiotics by the World Health Organization (WHO) (WHO, 2017c). Multidrug resistant (MDR) foodborne pathogens are found widespread across the entire ecosystem and can spread to humans through food, environmental contamination, or direct contact with the animals (Ngobese, Zishiri, & El zowalaty, 2020). The excessive use of antimicrobials in the food-producing animal industry fuels the emergence and spread of AMR (Chantziaras, Boyen, Callens, & Dewulf, 2014). In 2017, approximately 73% of all antimicrobial usage worldwide was reported in animal agriculture (Van Boeckel et al., 2017). Based on recent projections, the global usage of antimicrobials in food-producing animals will further increase by 2030 (Mulchandani et al., 2023). According to the agricultural census in 2021 by the Palestinian Central Bureau of Statistics (PCBS), there has been a significant growth in the industrial production of broiler chicken meat in Palestine. From 2010 to 2021, a remarkable increase of 128% was reported. This surge in production resulted in a total of 71 million broiler chickens being produced in 2021 (PCBS report in Arabic is available at (https://www.pcbs.gov.ps/Downloads/book2606.pdf). The industrialized meat production in Palestine goes along with excessive use of antibiotics (Abukhattab, Kull, et al., 2022; Mulchandani et al., 2023) and likely contributes to the spread of AMR.

Early detection and comprehensive understanding of drug resistant pathogens, including their reservoir, spread and genetic diversity is therefore crucial to adopt intervention measures to combat AMR (Holmes et al., 2016). This complexity highlights the importance of the One Health approach, which recognizes the interconnection between human, animal, and environmental health and focuses on demonstrating an incremental benefit of a closer cooperation between human and animal health and related sectors (Zinsstag, Kaiser-Grolimund, et al., 2023). Implementing this approach in the surveillance, prevention, and control of AMR in food animal production is vital in safeguarding human health and curbing the spread of AMR via the food supply chain. An integrated surveillance response system (iSRS) (Zinsstag, Utzinger, Probst-Hensch, Shan, & Zhou, 2020) for AMR should include continuous collection and testing of bacteria from various sources, such as animals, environment, food and humans, in combination with surveillance tools like whole genome sequencing (WGS). Whole genome sequence data enables in-depth investigations into the transmission dynamics of AMR strains that circulating between animals, food, the environment and humans (Wee, Muloi, & van Bunnik, 2020). We used an iSRS approach complemented with WGS to investigate in the Ramallah/Al-Bireh and Jerusalem districts the two leading endemic foodborne pathogens, Salmonella enterica and Campylobacter jejuni in humans, chicken and the environment.

6.2 Results and Discussion

To our knowledge, this is the first integrated One Health survey supported by next-generation sequencing (NGS) that reports on the emergence and spread of *Campylobacter* spp. and *Salmonella* spp. AMR in the Middle East. AMR is a serious global public health concern, and surveillance has historically been concentrated in clinical settings in high-income countries. Outside clinical settings, resistant bacteria can circulate largely undetected in healthy humans, animals and the environment, particularly in low- and middle-income countries (Maciel-Guerra et al., 2023). Very few studies exist that study the human-animal-environmental interface simultaneously (Meier et al., 2023). Our approach combines a One Health study design and WGS to identify the source and spread of foodborne pathogens and their AMR. Integrating WGS data from pathogens collected in the same place and time from humans, animals, and their environment using a One Health iSRS can lead to effective AMR control policies by identifying critical transmission routes and population dynamics (Zinsstag, Kaiser-Grolimund, et al., 2023). NGS technologies, such as Oxford Nanopore Technologies' Min-ION sequencing, have revolutionized clinical microbiology (Leggett et al., 2020). Switching to NGS from traditional microbiological methods has a wide range of benefits, such as simultaneous identification of pathogens, assignment of serotypes and detection of AMR markers. Therefore, integrating WGS-derived information into iSRS will help to design and guide control interventions and support monitoring of their effectiveness leading to reduced morbidity and mortality as well as saving health system resources (Abukhattab, Taweel, et al., 2022).

6.2.1 A high positivity rate and distinct risk factors associated with *Salmonella* spp. and *Campylobacter* spp. characterize the broiler chicken production chain in Palestine

Three hundred and nineteen (319) specimens of *Campylobacter jejuni* were collected from chicken manure (n=126), chicken meat (n=92), and human stool (n=101). Two hundred and seventy-three (273) specimens of *Salmonella* enterica were collected from chicken manure (n=91), chicken meat (n=81), and human stool (n=101). All samples which were culture positive for *Campylobacter* spp. were identified as *C. jejuni*, and all samples which were culture positive for *Salmonella* spp. were identified as *S. enterica*. The species identification of all positive samples was confirmed by PCR (Figure 1A). In chicken manure samples, the positivity rate for *C. jejuni* was 30.1% (39/126) and for *S. enterica* 7.7% (7/91). Among chicken meat samples, the positivity rate for *C. jejuni* was 19.6% (18/92) and for *S. enterica* 9.9% (8/81). Among faecal samples of broiler chicken production workers, we found a positivity rate of 19.8% (20/101) for *C. jejuni* and 1.0% (1/101) for *S. enterica*, respectively. Figure 1B shows risk factors for infection with *C. jejuni* among workers' sociodemographic characteristics, with higher education decreasing the risk of infection (OR = 0.23, p<0.005).

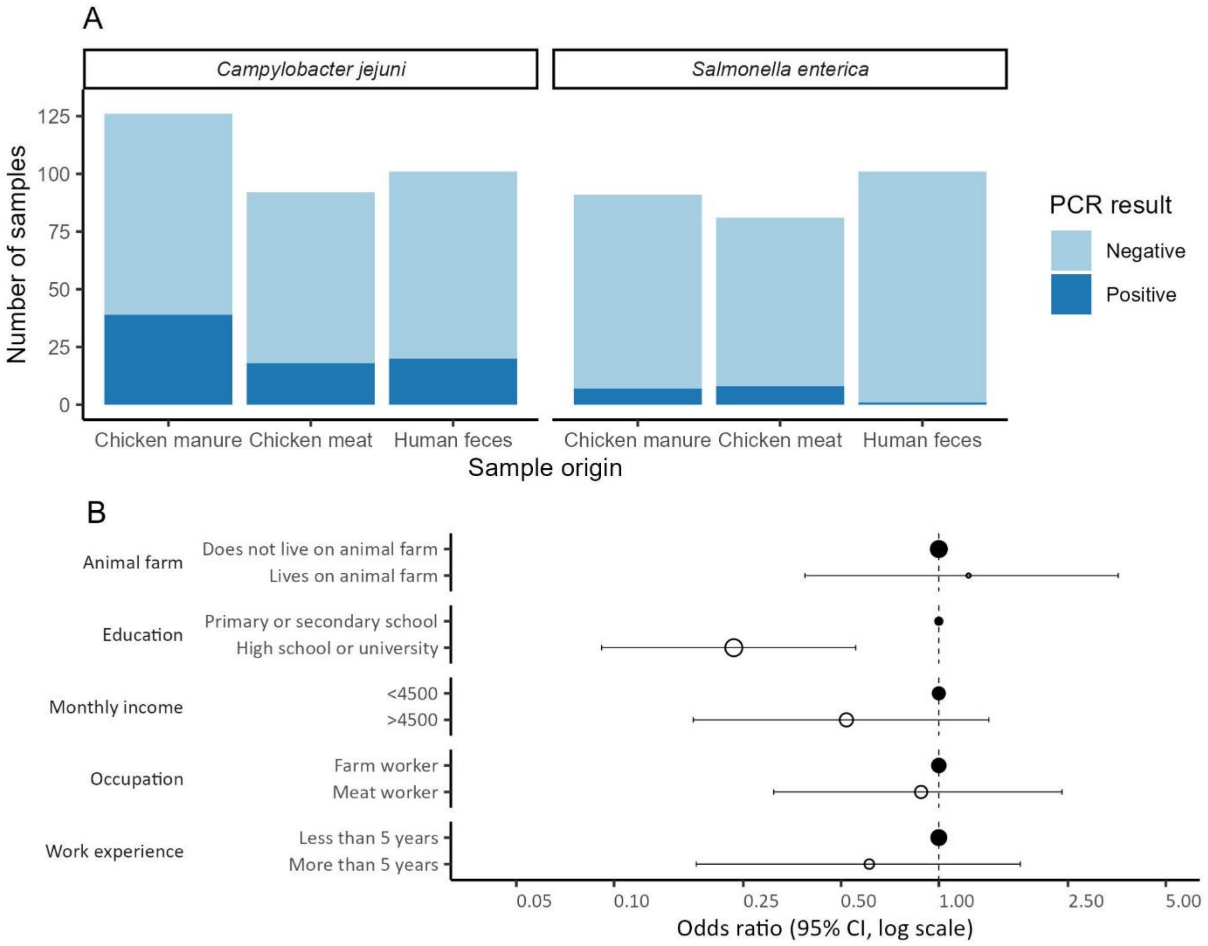

Figure 6-1 Epidemiology of *C. jejuni* and *S.* enterica in broiler chicken production chain in Palestine**.** A) Positivity rate of *C. jejuni* and *S.* enterica among samples tested from different sources. B) Univariable analysis of risk factors for C. jejuni infection among workers' sociodemographic characteristics and health status. Filled circles are the reference group.

The high positivity rate of *Campylobacter* spp. and *Salmonella* spp. in the investigated samples, especially from chicken manure and meat, highlights the need for better hygiene control in chicken farms and the need for better food safety measures throughout the food production chain. A study on food safety in Palestinian territories found that poor hygiene practices, monitoring system fragmentation, a lack of regulations and controls, and overuse of antimicrobials were obstacles to improving the food safety system (Abukhattab, Kull, et al., 2022). These results reflect the socio-economic challenges in the region, including chronic conflict, population pressure, limited economic development, rapid urbanization, intensive agriculture, and difficulty enforcing policies and regulations (UNEP, 2020). In conflict-torn places, collecting sam-ples from the environment can have significant advantages, especially when access to human patients is limited. Environmental samples, such as chicken manure, can provide important information about the presence of foodborne pathogens and AMR, as these pathogens often persist in the environment long after the animals have left (Parvin, Ali, Mandal, Talukder, & Islam, 2022).

The survey result showed that meat production workers with higher education level have a lower risk of infection with *Campylobacter*. These results are consistent with a recent study that showed that education level was a determinant of zoonotic disease knowledge among workers in the production chain in Palestine and significantly influenced hygiene practices among them (Abukhattab, Kull, et al., 2022). Therefore, to address the challenges in food safety, zoonotic diseases, and AMR in Palestine, we recommend several strategies focusing on education, training and awareness campaigns. Specific groups such as farm workers, slaughterhouse and meat shop employees, families and health professionals should be the focus of targeted education and training initiatives to enhance their knowledge and skills.

6.2.2 A rapid strain and AMR profile turnover is observed in samples positive for *C. jejuni*

Regardless of the sample origin, all 47 *C. jejuni* isolates collected in 2021 were highly similar with an average nucleotide identity (ANI) of 99.95% (range: 99.90-99.98%). The same was observed for 16 *C. jejuni* isolates collected in 2022, for which an ANI of 99.98% (range: 99.97-99.99%) was determined. Comparing the isolates collected in 2021 and 2022 revealed an ANI of only 97.84% (range: 97.80-97.93%) (Figure 2A). A phylogenetic tree based on 1000 single copy genes was created using 10 representative isolates from Palestine (Figure 2B). For comparison, 29 closely related genomes from BV-BRC and 22 genomes with the same ST as identified in PubMLST were added. All 47 isolates collected in 2021 were assigned to sequence type (ST) 11040 by Multi Locus Sequence Typing (MLST). Only one other isolate with the same ST was found in the PubMLST database, a human blood culture isolate collected in 2015 in Israel. These isolates did not match closely with any known genomes and showed a distinct AMR pattern. All samples collected in 2021 consisted of a single chromosome with a median length of 1,670,867 base pairs (range: 1,670,766-1,671,976 bp) and had identical drug resistance gene patterns, consisting of the aminoglycoside resistance genes *APH(2")-IIIa*, *ANT(4')* and *ANT(6)-Ia*, OXA beta-lactamase *bla-OXA184*, macrolide resistance gene *ermB*, quinolone resistance mutation T86I in *gyrA* and tetracycline resistance gene *tetL*. No plasmid was detected. The closest WGS we found had an ANI of only 98.39% (range: 98.27-98.44%). The co-resistance conferred by the combination of AMR markers to both aminoglycosides and macrolides is worrisome, as these drugs are typically the first line of treatment for human cases (Lopez-Chavarrias et al., 2021). The 16 isolates collected in 2022 were assigned to ST 305, which has a total of 95 entries in PubMLST. The majority of sequences with available WGS data (53.1%, 17/32) were submitted by the United Kingdom, while only one isolate originated from the Middle East. These isolates consisted of a chromosome with a median length of 1,677,345 bp (range: 1,677,331-1,677,357 bp) and a plasmid with a median length of 51,587 bp (range: 51,584-51,589 bp). Isolates collected in 2022 had a resistance gene pattern consisting of OXA beta-lactamase *bla-OXA61* and quinolone resistance mutation T86I in *gyrA* on the chromosome and the plasmid-encoded tetracycline resistance gene *tetO*. The *C. jejuni* isolates collected in 2022 did not have AMR markers conferring resistance to aminoglycosides or macrolides. Establishing an iSRS to address large annual fluctuations in bacterial strains and resistance characteristics requires enhanced collaboration and partnerships among relevant stakeholders (WHO, 2017b). Implementation of standardized protocols for data collection, testing and reporting is essential, supported by a robust data management system for centralized data collection and analysis (WHO, 2017b). Regular monitoring activities also play a vital role in observing dynamic patterns, while collaborative research efforts can help identify factors that contribute to these changes (Hattendorf, Bardosh, & Zinsstag, 2017). In addition, capacity building through introducing new laboratory techniques such as WGS, training programs, and effective sharing of information and communication among stakeholders are pivotal (Abukhattab, Taweel, et al., 2022; Seale, Gordon, Islam, Peacock, & Scott, 2017). If successfully implemented, these approaches could result in an immediate response and intervention to effectively address emerging AMR threats. A recent study identified Palestine as a global hotspot for veterinary antimicrobial consumption (Mulchandani et al., 2023), underscoring the problem of antibiotic overuse in intensive animal production. This issue is particularly prevalent in broiler production, where lower levels of biosecurity measures lead to heavy reliance on antibiotics. This excessive use could be a contributing factor to the rapid shift in the *C. jejuni* strain observed between 2021 and 2022.

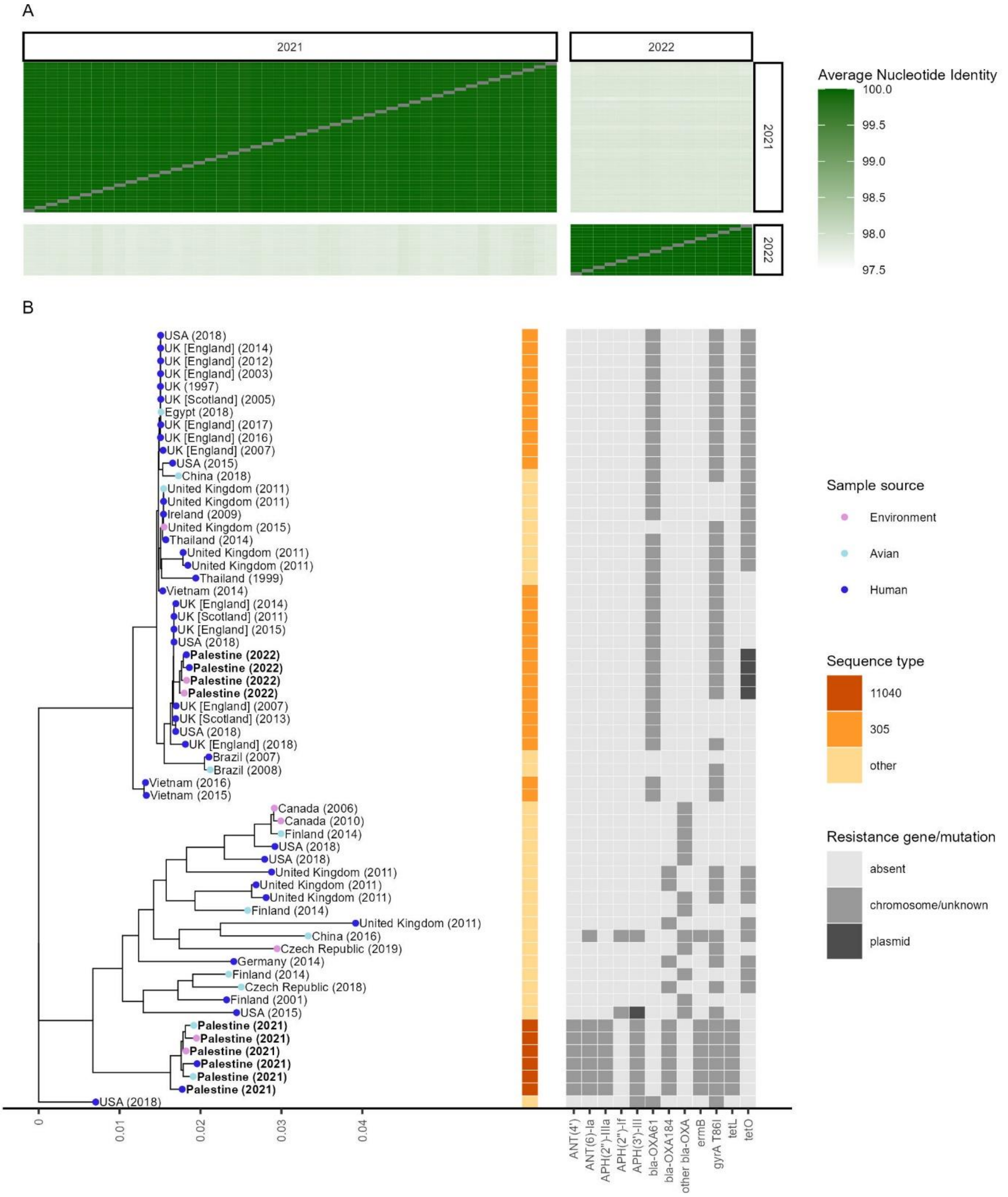

Figure 6-2 Phylogenetic analysis of *C. jejuni* isolates**.** A) Average nucleotide identities between all 47 isolates collected in 2021 and all 16 isolates collected in 2022. B) *C. jejuni* phylogenetic tree with 10 representative genomes from Palestine and 51 closely related genomes from different countries collected between 1997-2019. MLST based sequence types are shown for the sequence types represented by Palestinian isolates. The presence of AMR markers is shown in light grey if located in the genome or an unidentified contig or dark grey if located on a plasmid. Sample sources are depicted by colored, filled circles. Genomes generated in this study are in bold text. All human isolates collected in 2021 are from broiler chicken production chain workers, while all four human isolates collected in 2022 are from hospitalized gastroenteritis patients.

6.2.3 The MDR isolates *S. enterica* serovar Muenchen are found across the entire broiler chicken production chain

A phylogenetic analysis based on 1000 single copy genes for *S. enterica* revealed that 12 out of 14 *S. enterica* isolates collected in 2021 were assigned to *S. enterica* serovar Muenchen (Figure 3A). These twelve isolates had a median chromosome length of 4,857,056 bp (range: 4,856,898-4.857,070 bp) and a median plasmid length of 285,076 bp (range: 285,070-285,085 bp). The isolates show a high similarity across all samples with an ANI of 100.00% (range: 99.99-100.00 %). The two other isolates were sampled from chicken meat in 2021 and assigned to *S. enterica* serovar Paratyphi B. The two *S. enterica* serovar Paratyphi B isolates had chromosome lengths of 4,697,034 bp and 4,697,043 bp and chromosome encoded aminoglycoside resistance genes *AAC(6')-Iy* and *ANT(3")-Ia*, quinolone resistance mutation S83F in *gyrA*, trimethoprim resistance gene *dfrA1* and the *mdsABC* efflux pump. Additionally, they have the plasmid-encoded beta-lactamase *blaTEM-1*, phenicol resistance gene *floR*, sulfonamide resistance gene *sul2* and tetracycline resistance gene *tetA*. They were closely related to *S. enterica* serovar Paratyphi B isolates collected from environmental and avian sources in Europe and Israel. Additionally, three confirmed *S. enterica* clinical isolates obtained from humans in 2022 were added as positive controls. These three isolates had a median chromosome size of 4,720,112 bp (range: 4,720,107-4,720,159 bp), a plasmid with a median length of 37,698 bp (range: 37,698-37,699 bp) as well as a plasmid with a median length of 59,372 bp (range: 59,372-59,373 bp). The *S. enterica* serovar Enteritidis isolates contain the chromosome-encoded aminoglycoside resistance gene *AAC(6')-Iy* and the *mdsABC* efflux pump. They were closely related to *S. enterica* serovar Enteritidis strains isolated from humans globally. All twelve isolates assigned to *S. enterica* serovar Muenchen shared an identical pattern of molecular markers for AMR with resistance markers, including the aminoglycoside resistance gene *AAC(6')-Iaa*, the fluoroquinolone resistance mutation T57S of *parC* and the *mdsABC* efflux pump encoded on their chromosome (Figure 3B). Additionally, on the 285,077 bp (range: 285,070-285,085 bp) megaplasmid that was 99.99% (99.97-100.00) similar to 'plasmid of emerging S. Infantis (pESI)' described from Israel (E. Cohen et al., 2022), aminoglycoside resistance gene *ANT(3")-Ia*, sulfonamide resistance gene *sul1*, tetracycline resistance gene *tetA* and trimethoprim resistance gene *dfrA14* are located (Figure 3C).

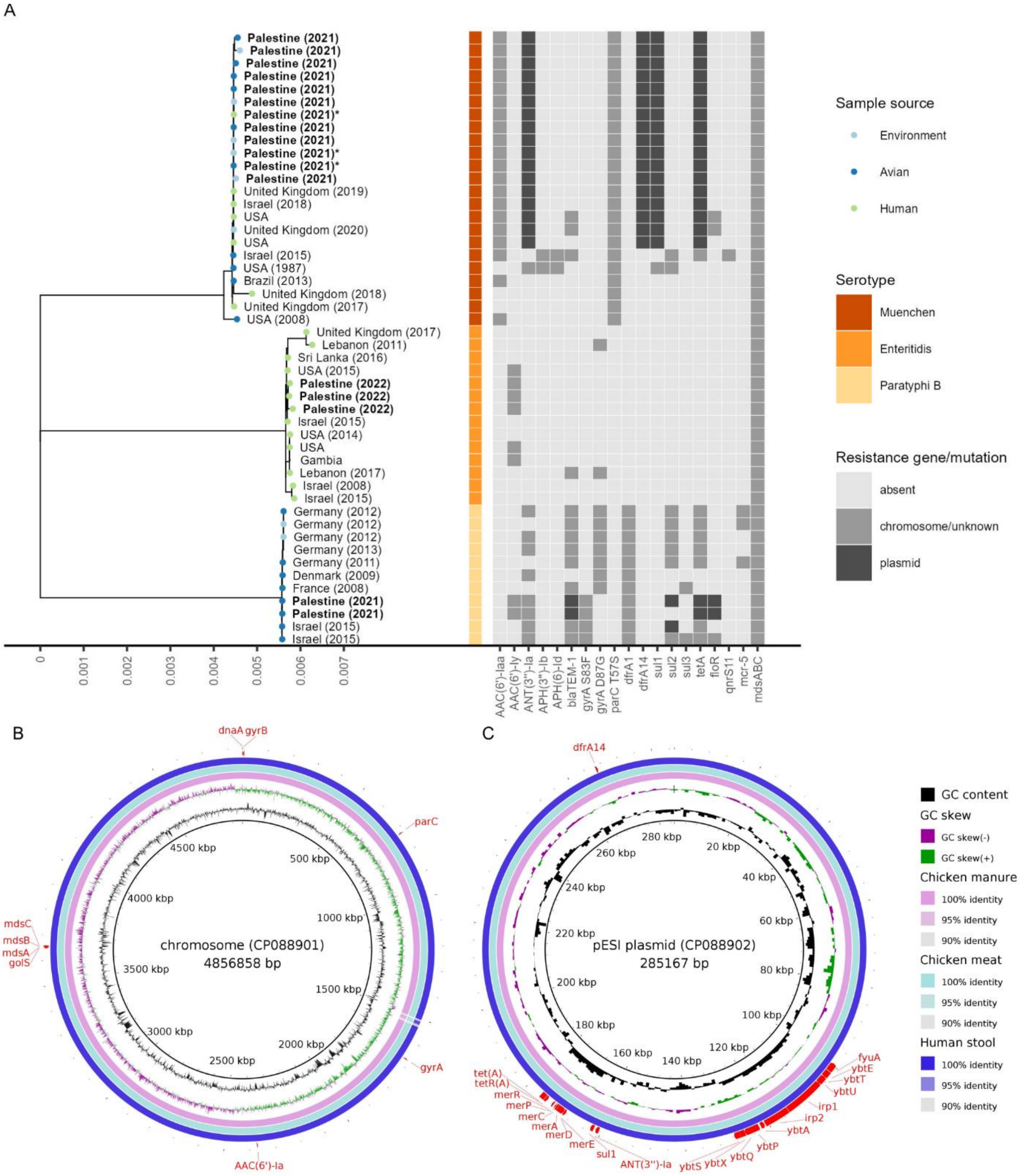

Figure 6-3 Phylogenetic analysis of *S.* enterica isolates**.** A) Phylogenetic tree for *S.* enterica with 17 genomes from Palestine and 31 closely related genomes belonging to the three serotypes found in this study from different countries collected between 1987-2020. The presence of AMR markers is shown in light grey if located in the genome or an unidentified plamid or dark grey if located on a plasmid. Sample sources are depicted by colored, filled circles. Genomes generated in this study are in bold text. Genomes used for Figures 3B and 3C are marked with an asterisk. Comparison of Palestinian *S.* enterica serotype Muenchen chromosome (B) and pESI plasmid (C) pESI plasmid from chicken manure and human faeces as well as meat with clinical isolate from Israel collected in 2018. The presence and location of antibiotic resistance genes is shown in red. The human isolate collected in 2021 is from a broiler chicken production chain worker, while all three human isolates collected in 2022 are from hospitalized gastroenteritis patients.

Our study shows that the MDR *S. enterica* serovar Muenchen isolates are found in the entire chicken meat production chain. Among the *S. enterica* serovar Muenchen isolates, we found genotypical resistance markers to at least five classes of antibiotics, including Aminoglycosides, Fluoroquinolones, Aminocoumarines, Sulfonamides and Tetracyclines. Given the significant clinical importance of *S. enterica* infections, with a global annual incidence of over 27 million cases of enteric fever (John A. Crump, Luby, & Mintz, 2004) and 78.7 million cases of gastroenteritis (Havelaar et al., 2015), the AMR monitoring as part of a One Health iSRS is of utmost importance.

All twelve isolates identified as *S. enterica* serovar Muenchen in our study showed a close relationship to an emerging clinical isolate reported in Israel (E. Cohen et al., 2022). In addition, this study identified 19 additional *S. enterica* serovar Muenchen isolates from the United States, the United Kingdom, and South Africa containing the pESI plasmid with high genetic similarity (E. Cohen et al., 2022). These *S. enterica* serovar Muenchen isolates were obtained from human clinical samples or avian sources. This noteworthy similarity among globally sourced isolates is likely to be attributed to the widespread and synchronized dissemination of breeding stocks contaminated with the bacteria, due to centralized sourcing practices and international trade. Similar patterns have been observed for *Salmonella enterica serotype Enteritidis* (S. Li, He, Mann, & Deng, 2021) highlighting the role of global trade in facilitating the spread of such MDR bacterial strains.

The researchers from Israel noted an increasing prevalence of a MDR strain of *S. enterica* serovar Muenchen among their clinical *Salmonella* spp. isolates (E. Cohen et al., 2022). These isolates displayed significant sequence similarity to the isolates described in our study. This suggests that there may be a regional spread of this particular MDR strain. This could be due to importing some of the raw materials used in animal feed production from Israel, intersecting distribution networks, and sharing the same ecosystem (Gutkowski, 2021; UNEP, 2020). Moreover, the prolonged and intense conflicts in the Palestinian territories contributes to a weak control system, which leads to cross-border smuggling (Abukhattab, Kull, et al., 2022; Gutkowski, 2021). The discovery of a dominant MDR strain emphasizes the need for continuous monitoring and open data sharing in real time to understand the epidemiology of AMR across borders and political systems.

6.3 Materials and Methods

6.3.1 Study design, setting, and participants

This cross-sectional study was performed in Ramallah/Al-Bireh and Jerusalem governorates of the central West Bank, Palestine. Between June and October 2021, five hundred fifty-seven (557) samples were collected and 284 samples were tested for the presence of for *Campylobacter* and 273 samples for *Salmonell*a. The samples came from abattoirs (n=50, fresh chicken meat), large-scale broiler chicken farms with single batch at a time (all-in, all-out) system (n=91), chicken manure and asymptomatic chicken meat production workers (n=101, faecal samples). In August 2022, an additional 35 chicken manure samples were collected from the same farms addressed in 2021 to investigate the persistence or replacement of *C. jejuni* strains over time. Furthermore, four *C. jejuni* isolates and three *S. enterica* isolates were isolated from gastroenteritis patients in 2022 after confirmation by VITEK® 2 and PCR, preserved in the hospital laboratory to be used as positive control isolates at one of the targeted region's hospitals to compare the pathogens isolated in our study to those reported in the hospitals. To investigate the risk factors for the presence of *Salmonella* spp. and *Campylobacter* spp. along the broiler chicken production chain, a questionnaire in Arabic was used to collect information on workers' sociodemographic characteristics and health status related to infection with gastroenteritis infections. All sampling sites were selected using a random sampling approach and using authorities' records about farms, abattoirs, meat stores, and workers. All study participants signed a written consent form.

6.3.2 Microbiological laboratory procedures

The faecal samples from humans and chicken manure were grown directly on Campylobacter Selective Agar (Oxoid, UK) for *Campylobacter* selection and Xylose-Lysin-Desoxycholat Agar (Oxoid, UK), MacConkey (Oxoid, UK), and Sheep Blood Agar Base (Oxoid, UK) for *Salmonella* selection. Agar plates were incubated at 37 °C and checked for the presence of colonies after 24-48 hours. The chicken meat samples were pre-processed according to the ISO 10272-1:2017 guidelines for *Campylobacter* and ISO 6579-1:2017 guidelines for *Salmonella*. From all samples suspected colonies for each of the species were selected for microbiological confirmation by the VITEK® 2 NH ID card for *Campylobacter* or VITEK® 2 GN ID card for *Salmonella* using the Vitek® 2 compact automated system (BioMerieux, France). All isolates which were confirmed as *Salmonella* or *Campylobacter* by the VITEK® 2 microbial testing system were subjected to further confirmation by PCR. Molecular species identification for *Campylobacter* spp. was performed using the PCR protocol published by Nayak et al. (Nayak, Stewart, & Nawaz, 2005) while for *Salmonella* spp. the procedure published by Paião et al was used (Paião et al., 2013).

6.3.3 DNA extraction and WGS

From a total of 65 *C. jejuni* and 19 *Salmonella* spp. isolates DNA was extracted using QIAamp DNA Mini Kit (Qiagen, Germany) and Quick-DNA Fungal/Bacterial Miniprep kit (Zymo Research, USA), respectively. Extracted DNA shipped to the Swiss Tropical and Public Health Institute. DNA was quantified with the Qubit dsDNA HS Assay Kit (Invitrogen, Germany). Samples with DNA concentrations >33 ng/µL were selected for whole genome sequencing using MinION platform (Oxford Nanopore Technologies, UK). The sequencing library was prepared according to manufacturer's instructions using the Native Barcoding Kit 96 and loaded onto the R10.4 flow cell and sequenced on the MinION Mk1C using super-accurate basecalling.

6.3.4 Bioinformatics and statistical analysis

De novo assembly was conducted using Flye 2.9.1 (Kolmogorov, Yuan, Lin, & Pevzner, 2019) and Trycycler v0.5.3 (Wick et al., 2021) at the scientific computing core facility of the University of Basel. The Bacterial and Viral Bioinformatics Resource Centre (BV-BRC) was used for annotation and phylogenetic analysis of the assemblies. The assemblies were annotated using the RAST 2.0 toolkit (Brettin et al., 2015). Only assemblies with less than ten contigs were considered for further analysis. Sequence type (ST) and serotype of assembled contigs were determined using Multi Locus Sequence Typing (MLST) (Larsen et al., 2012) and SeqSero (Zhang et al., 2015), respectively. Phylogenetic trees were generated by aligning protein and nucleotide sequences using MUSCLE (Edgar, 2004), MAFFT (Katoh, Misawa, Kuma, & Miyata, 2002) and RAxML (Stamatakis, 2014). The 20 most closely related genomes from BV-BRC were selected for each *C. jejuni* ST. Additionally, all available WGS for the respective ST were obtained from the public databases for molecular typing and microbial genome diversity (PubMLST). The 10 most closely related genomes from BV-BRC were selected for each S. enterica serotype. Additionally, four selected S. enterica serotype Muenchen genomes containing the pESI plasmid were obtained from the National Center for Biotechnology Information (**GCA_008248485**, **GCA_009444355**, **GCA_010825065**, **GCA_019543295**). C. jejuni and S.enterica genomes were filtered to contain high-quality genomes with available data for collection year, country, and sample origin.

Closely related isolates from the Middle East collected after 2008 were selected for *S. enterica*. Genome-wide Average Nucleotide Identities (ANI) were determined with FastANI (Jain, Rodriguez-R, Phillippy, Konstantinidis, & Aluru, 2018). Resistome analysis was performed using CARD (6.0.0) (Brian P. Alcock et al., 2023) and ResFinder (4.2.2) (Bortolaia et al., 2020). The comparison of *S. enterica* serotype Muenchen genomes was visualised using

BRIG (Alikhan, Petty, Ben Zakour, & Beatson, 2011). Risk factors for *C. jejuni* infections among study participants were calculated using median-unbiased estimates to calculate univariate odds ratio using the R software environment version 4.2.2 and the package epitools.

6.4 Acknowledgments

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S.A., N.M.E.A-R., P.V., J.H., and J.Z. conceptualized the epidemiological study. S.A., S.H.o., N.M.E.A-R., S.H., J.H., C.D., and T.S. curated the data. S.A., S.H.o., and T.S. did the formal analysis. S.H.o. and T.S analyzed and visualized the genomic data. S.A., N.M.E.A-R., and J.Z. acquired funding. S.A., N.M.E.A-R., S.H.o., and T.S. did the investigation. S.A., S.H., S.H.o., and T.S. wrote the methodology. S.A., N.M.E.A-R., J.Z., and T.S. did the project administration. S.A., N.M.E.A-R., J.Z., C.D., and T.S. supervised the study. S.A., S.H.o., and T.S. wrote the original draft. S.H., P.V., L.C., J.H., C.D., and J.Z. critically revised the manuscript. All authors were responsible for the reviewing and editing of the manuscript. All authors had access to the data presented in this study and had final responsibility for the decision to submit for publication.This study was supported by the Swiss Agency for Development and Cooperation— Jerusalem Office.The authors declare no conflict of interest.

6.5 Author's affiliations

1 Swiss Tropical and Public Health Institute, Allschwil, Switzerland

2 University of Basel, Basel, Switzerland

3 Institute of Community and Public Health, Birzeit University, Birzeit, Palestine

4 Master program in Clinical Laboratory Sciences, Birzeit University, Birzeit, Palestine

5 Department of Fundamental Microbiology, University of Lausanne, Lausanne, Switzerland

6.6 Author's ORCIDs

Said Abukhattab
http://orcid.org/0000-0003-1670-0143

Salome Hosch
http://orcid.org/00000001-9290-3589

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6.8 Data Availability

The data that support the findings of this study are available from the authors upon reasonable request. The genome assemblies and raw sequence reads are available on Genbank under BioProjects **PRJNA942086** *(S. enterica)* and **PRJNA942088** (*C. jejuni).*

6.9 Ethical Approval

The study was approved by the Northwestern and Central Switzerland Ethics Committee (Ethikkommission Nordwest- und Zentralschweiz, EKNZ) (Reference No: AO_2021-00021) and the ethical review committee at the Institute of Community and Public Health (ICPH) at Birzeit University (Reference No: 2020 (12 – 1)).

Part 7

DISCUSSION

7 Discussion

One Health recognizes that the health of humans, animals, and ecosystems are interconnected, and it promotes a collaborative and integrated approach to addressing complex challenges. A key component of the One Health framework is transdisciplinarity (TD), which transcends disciplinary boundaries to foster collaboration and knowledge production (Mónica Berger-González, Stauffacher, Zinsstag, Edwards, & Krütli, 2016; Zinsstag, Kaiser-Grolimund, et al., 2023; Zinsstag, Pelikan, et al., 2023). Through the integration of experts from diverse fields, sectors, and stakeholders, transdisciplinarity enables the exploration of innovative solutions and the formulation of policy recommendations that are locally tailored and acceptable for addressing societal issues. This approach has been acknowledged by the Organization for Economic Cooperation and Development (OECD) as an effective means of problem-solving (Peña-López, 2020; Zinsstag, Pelikan, et al., 2023; Zinsstag, Schelling, et al., 2020). Essentially, in a transdisciplinary process academic and non-academic actors join their knowledge to generate transformational knowledge for societal problem solving (Zinsstag, Pelikan, et al., 2023).

One Health Integrated Surveillance System is a comprehensive approach that recognizes the interconnectedness of human, animal, and environmental health and aims to collect, analyze, and disseminate information from these three sectors considering the spatial and temporal linkages between them. The system would combine human, animal, and environmental health data to provide a complete picture of pathogens transmission and AMR dynamics and facilitate early detection of disease outbreaks (Zinsstag, Schelling, et al., 2020; Zinsstag, Utzinger, et al., 2020). This PhD research project showed the components crucial for an effective One Health integrated surveillance system which include: 1. Cross-sectoral collaboration by establishing partnerships and collaboration between human, animal, and environmental health sectors. This collaboration is crucial for the success of a One Health integrated surveillance system. 2. Integrated data collection and analysis: collecting and analyzing data on pathogens and their AMR occurrence in humans, animals, food, and the environment in an integrated manner would provide a more comprehensive understanding of their transmission dynamics and facilitate the early detection of disease outbreaks and AMR transmission ways. 3. Risk assessment: conducting risk assessments to identify and evaluate the risk of disease transmission between humans, animals, and the environment would enable the development of targeted surveillance strategies. 4. Early warning systems: developing early warning systems for AMR in humans, animals, and the environment using new technology, e.g. whole genome sequencing technique, would facilitate rapid response and control measures. 5. Capacity building: developing the capacity of health professionals and veterinarians in One Health surveillance and response would enable the implementation of effective One Health integrated surveillance systems. 6. Information sharing: sharing information and data between sectors and countries would improve surveillance systems and response.

In Chapter 4, we presented evidence indicating that the Middle East countries have not effectively implemented the One Health approach. Notably, there are limitations in the epidemiological study designs from a One Health perspective, and the available data is unevenly distributed, with approximately 60% of Middle Eastern countries lacking published papers included in the systematic review used as the method in Chapter 4. Urgent research is required to address the gaps in understanding foodborne illnesses and AMR in the Middle East. Specifically, *Campylobacter* spp. and *Salmonella* spp. have been reported with high prevalence rates compared to other regions worldwide. The findings of the AMR phenotype analysis revealed a significant prevalence of resistance among the isolated bacteria, underscoring the importance of implementing antimicrobial stewardship in both human and animal contexts. Moreover, the adoption of novel laboratory techniques for genetic sequencing plays a pivotal role in effective monitoring of foodborne illness outbreaks and antimicrobial resistance genes (ARGs). It provides improved accuracy, rapid detection, comprehensive surveillance, insights into molecular epidemiology, and supports antimicrobial stewardship efforts.

In Chapter 5, Palestine was selected as one of the Middle East countries with a socio-ecologically complex system for studying the country's food safety and AMR control systems. The findings revealed several significant barriers hindering the improvement of food safety and AMR monitoring in Palestine, including antimicrobial overuse, system fragmentation, inadequate infrastructure, lack of regulations and controls, and poor hygiene practices. Based on the study, it was concluded that establishing a national integrated surveillance system following the One Health approach is crucial for enhancing food safety and AMR monitoring in Palestine. The primary objective of Chapter 6 was to assess the effectiveness of this integrated system recommended in Chapter 5, specifically for Palestine. Moreover, the study utilized the latest generation of WGS technology, namely the Oxford Nanopore Technologies MinION platform, as a tool for the One Health integrated surveillance system, as suggested in Chapter 4. The results demonstrated the advantages of integrated environmental-animal-human sampling and WGS in AMR monitoring. Environmental samples proved to be a valuable solution for effective AMR surveillance, particularly in conflict-affected areas with limited monitoring systems and weak regulations. By conducting whole genome sequencing of bacterial isolates, it becomes possible to establish epidemiological relationship between the distribution and transmission of bacterial serotypes and AMR in complex socio-ecological systems. Consequently, our findings highlight the anticipated benefits of implementing a One Health approach through close collaboration among public health, animal health, and food safety authorities.

7.1 Qualitative research for food safety: One Health perspective

The behaviour of "Homo sapiens" plays a critical role in the epidemiology of emerging or re-emerging zoonotic diseases (Macpherson, 2005; Zinsstag, Schelling, et al., 2020). The aim of qualitative research is the creation of concepts that aid in comprehending social phenomena and human behaviour in their contexts, focusing on the meanings, experiences, and perspectives of those involved and impacted (Degeling & Rock, 2020). Human behaviour can influence the spread of zoonotic diseases in several ways. For instance, the destruction of natural habitats, deforestation, and climate change might drive animals to relocate or change their behaviour, bringing them into closer contact with humans and increasing the risk of disease transmission (Cascio, Bosilkovski, Rodriguez-Morales, & Pappas, 2011). Additionally, poor food safety practices, such as improper food handling and preparation, can also contribute to the spread of zoonotic diseases (Abebe, Gugsa, & Ahmed, 2020). In chapter 5, we used the transdisciplinary tool, multi-stakeholder discussion group, in parallel with semi structural observational study. The transdisciplinary method was used to bring together diverse perspectives and expertise to develop research questions, design research methods, and interpret the survey and laboratory findings. The semi-structural observational study design was also being used to investigate human behaviour and interactions by observing and recording hygiene behaviour in a structured and systematic manner to interpret the survey and laboratory findings in Chapters 6.

The use of qualitative research methods, multi stakeholder discussion group and observations, are effective when conducting food safety research (Arendt et al., 2012). The qualitative finding in Chapter 5, explored in-depth the various factors influencing food safety practices, such as compliance with monitoring systems, hygiene behaviours, and motivators and barriers to following food safety practices among consumers, traders, butchers, farmers and other actors in the food chain. Through observations and discussions with stakeholders, insights were obtained about the contextual factors, social norms, and individual attitudes that shape food safety behaviours. Harris and colleagues contend that observation produces a deeper comprehension of the phenomena than focus groups or interviews, since phenomena may be viewed in context (Harris et al., 2009). Field observations are widely recognized as valuable methods for assessing community-level hygiene practices. However, it is important to acknowledge that like any research method, the validity and repeatability of field observations should be critically evaluated (Curtis et al., 1993). The reliability of observations depends on the consistency and accuracy of the measurements made by the observers. Inter-rater reliability, which is the agreement between different observers, can be a challenge in observational studies. Additionally, the validity of the data collected may be influenced by the subjective interpretation of the observers and the potential for errors or omissions (Curtis et al., 1993). However, because the majority of our observations focused on facilities and equipment, such as the availability of soap near the sink, the presence of a footbath for disinfection, or visiting the municipality dam; thus, they are less subject to variability. In contrast, the reliability of observations related to the wearing protective clothes or cleanliness of toilets, for instance, may be more vulnerable.

Qualitative studies often involve restricting the generalizability of the findings to broader populations due to sample size, which limits the study's external validity (Ferguson, 2004). For logistical and safety considerations, the places visited in the observational study were only chosen because they were in the Ramallah/Al-Bireh region. Selection bias cannot be ruled out, and generalizability may be constrained. Nevertheless, a variety of farms and abattoirs—from conventional to highly modernize—as well as a number of meat stores, were visited. To enhance the reliability and validity of the findings, triangulation using other research methodologies, multi-stakeholder discussion groups and surveys (questionnaire and laboratory) were used to support the observations and provide a deeper understanding of the subject of interest (Noble & Heale, 2019).

Multi-stakeholder discussion groups were part of the triangulation process to provide valuable opportunities to engage stakeholders, gain diverse perspectives, reflect on the complexities and nuances of real-world contexts, and generate in-depth insights on food safety systems and AMR issues. However, this methodology may be limited in power dynamics. Participants in multi-stakeholder discussion groups may have different levels of power and influence, which can impact the dynamics of the discussions (Faysse, 2006). Power imbalances can result in certain voices dominating the conversation while others may be marginalized or hesitant to express their opinions (Faysse, 2006). For this reason and others e.g. certain groups or perspectives may be underrepresented, we applied the KAP survey to interview the workers of the poultry meat production chain.

7.2 Quantitative analysis of KAP toward food safety and hygiene: One Health perspective

A survey was carried out among workers engaged in the broiler production chain, specifically in farms, slaughterhouses, and meat stores, to evaluate their KAP regarding hygiene during broiler meat production (Chapter 5). In contrast to qualitative study methodologies, KAP surveys offer quantitative data that can be statistically evaluated, enabling comparisons and revealing patterns and trends in hand hygiene knowledge, attitudes, and behaviours (Abdulkader Mohamed, Abdul Rahim, Mohamad, & Ahmad Yusof, 2022). Furthermore, KAP surveys frequently seek to gather information from a large number of respondents, offering a more comprehensive representation of the target demographic (Abdulkader Mohamed et al., 2022).

Self-reporting bias considers one of the KAP survey limitations due to its reliance on self-reported information. Respondents may overstate or understate their knowledge or practices due to social desirability bias or recall bias (Bauhoff, 2014). An over reporting of good KAP may hamper the validity of survey findings on hygiene practices in broiler production. We assume that KAP considered as good tends to be over-reported in surveys, as observed in various research examining hygienic practices (Curtis et al., 1993; Manun'Ebo et al., 1997; Stanton et al., 1987). In addition, overestimation can occur due to the social desirability bias; respondents may provide answers they believe are socially acceptable rather than reflecting their true knowledge or behaviours. This bias can lead to overestimating hand hygiene practices or adherence to recommendations, which affects the validity of survey results (Harvey, 2018; Stanton et al., 1987). Overestimating can also occur due to direct questions about "usual" behaviour, like "Do you clean and sanitize the chicken coop after each cycle?" run the risk of receiving an automatic "yes,”. In order to avoid this, the authors suggest adopting an alternative strategy and rephrasing queries like "Did you clean and disinfect the chicken coop after the last cycle?"(Curtis et al., 1993; Manun'Ebo et al., 1997). However, recall bias will always be inherent in these types of questions, exactly like in the example question "Have you been experienced disease problem regarding chicken health (zoonotic)?”. A written questionnaire in place of a verbal interview might be considered to ensure that participants wouldn't be influenced by direct interaction with interviewers, which leads to over-estimating.

In addition to validity, the generalizability of surveys must also be questioned due to the restricted study area and the corresponding study population. The KAP results might not be easily generalizable to all of Palestine because the study was restricted to Ramallah/ Al-Bireh and northwest Jerusalem regions. In fact, (Bonita, Beaglehole, & Kjellström, 2006) highlight that the representativeness of surveys may be limited to a small population within a specific area. The sample size restricts the analysis of survey response correlations. For instance, it is challenging to identify the KAP as risk factors given the small number of respondents (23 interviewees) who have been affected by a zoonotic disease spread by poultry. Therefore, it would be necessary to significantly expand the study region and sample size to explore KAP as risk factors for health outcomes. To mitigate these limitations, a concurrent triangulation design, mixed-method approach, is recommended. In a concurrent design, quantitative and qualitative data are collected simultaneously, analyzed separately, and integrating the findings at the interpretation stage (Pantha et al., 2022).

7.3 Inconsistencies between qualitative and quantitative results regarding hygiene practices

The KAP survey method is used alongside qualitative research, to provide a more comprehensive understanding of the drivers of foodborne pathogens and AMR in Palestine. The results of some of the responses to the questionnaire agreed with direct observations. For example, observations and interviews agree that the vast majority use chicken manure as fertilizer and that dead animals are often fed to pets or disposed of in a municipal dam. On the other hand, we note that the agreement between some survey results and the data collected through observations is weak. For instance, when it comes to hand washing, protective clothing, footbath disinfectant at the entrance to the poultry house, or visitor hygiene regulations, the observations and survey results are contradictory. Even though less than 10% of people wash their hands without soap, we rarely spotted soap next to the sink during site visits. Although a sizable portion of respondents claims to wear protective clothes, we rarely, if ever, observed workers wearing uniforms, long boots, or masks during our inspections. According to Curtis and colleagues and Manun'Ebo and colleagues, there is no gold standard for measuring hygiene practices. Participants can alter their responses to a questionnaire to reflect what they deem to be positive, and they can also adjust their behaviour in the presence of observers to show an image they consider desirable (Curtis et al., 1993; Manun'Ebo et al., 1997). To address low correspondence between observations and KAP survey results, we used multiple methods to triangulate the data and gain a more comprehensive understanding of hygiene practices. This includes, in Chapter 6, bacterial contamination assessment using One Health integrated surveillance in parallel with using WGS to compare genetically the bacteria, *Campylobacter* and *Salmonella*, that were isolated from workers in the production chain, animal (poultry), and environment (chicken manure) to validate self-reported hygiene practices. Additionally, in Chapter 5, qualitative research methods (multi-stakeholders discussion groups) were used to explore the underlying attitudes and beliefs influencing hygiene practices.

7.4 One Health integrated surveillance system

In Chapter 4 and Chapter 6, using the One Health approach, we assessed the prevalence of the leading foodborne pathogens, *Campylobacter* spp. and *Salmonella* spp., in the Middle East and Palestine, respectively. In addition, we investigated the circulating serotypes for each pathogen. Comprehensively investigating foodborne pathogens and their AMR in the production chain by simultaneously sampling humans, animals, and the environment is essential for understanding the sources and transmission dynamics of resistance and developing effective interventions to prevent its spread and to protect public health (Zinsstag, Schelling, et al., 2020). In Chapter 4, the model showed high heterogeneity results, which indicates variability in the study data. This might be due to the study design (epidemiological study vs routine data) or due to diverse sample types. The human isolates used in the studies were from different sources (symptomatic and asymptomatic participants), and the animal isolates used were from various sources (live animals and animal products). On the other hand, Chapter 6 of the study conducted in Palestine employed a comprehensive approach by simultaneously collecting samples from humans, animals, and the environment to investigate foodborne pathogens in the white meat production chain. Comprehensively investigating foodborne pathogens in the white meat production is essential for several reasons: first, foodborne illnesses are often caused by a complex interplay of factors, including cross contamination at various stages in the production chain (Golden, Rothrock Jr, & Mishra, 2021). By examining the entire production chain, we can better understand the sources of contamination and implement effective preventative measures (Chapter 6). Second, understanding the zoonotic nature of food-borne pathogens is crucial for implementing effective preventive measures. It underscores the importance of proper food handling, hygiene practices, and the implementation of appropriate surveillance and control measures in both human and animal populations. By addressing the zoonotic aspect of food-borne illnesses, we can work towards reducing the risk of transmission and protecting both human and animal health (Chlebicz & Śliżewska, 2018; Karesh et al., 2012). Simultaneously sampling both humans and animals can help us to better understand the infections' transmission mechanisms and create tailored strategies to stop their spread (Chapter 6). Thirdly, the misuse/overuse of antibiotics in animal production can contribute to the development of AMR, and this resistance can then be transmitted to humans through food or environment (Van Boeckel et al., 2017). By examining both animals and humans, we can identify the extent of this problem and take appropriate measures to mitigate it (Chapter 6). Fourth, the environment can also play a role in transmitting pathogens and AMR through horizontal transmission. For example, contaminated water or soil can lead to the spread of ARB (antibiotic-resistant bacteria), ARGs, or/and mobile genetic elements (MGEs). By examining the environment, we can identify potential sources of contamination and resistance and take steps to mitigate them (Escher et al., 2021).

Antimicrobial resistance is a serious global concern, and AMR surveillance has historically been concentrated in clinical settings and high-income countries. Outside clinical settings, resistant bacteria can circulate largely undetected in healthy humans, animals, and environmental contexts, particularly in many low- and middle-income countries (Maciel-Guerra et al., 2023). I present a comprehensive approach based on a One Health study design in combination with cutting-edge next-generation sequencing of bacteria to understand the emergence and spread of AMR better. We are convinced that only a One Health iSRS that integrates WGS data from bacteria collected simultaneously among humans, animals, and their environment will enable the identification of critical transmission routes and subsequently the development of more effective AMR control policies (Escher et al., 2021). I believe that integrating genomic surveillance tools, based on high-resolution WGS, into iSRS is a critical step towards changing how we think about monitoring zoonotic diseases, foodborne pathogens, and AMR. Switching to NGS from traditional microbiological methods has a wide range of benefits, such as the combined simultaneous identification of pathogens, serotypes and molecular AMR markers. Integrating WGS-derived information on pathogens into iSRS will guide interventions to control infection and AMR, which could break the chain of transmission of pathogens and their resistance genes, leading to reduced morbidity and mortality and saving limited health system resources in conflict zones (Abukhattab, Taweel, et al., 2022; Sugden, Kelly, & Davies, 2016; WHO, 2020c).

7.5 Piloting One Health integrated surveillance system for Foodborne pathogens

Based on the Chapter 4 results, the approach used in Chapter 6 is the first integrated One Health survey supported by pathogen WGS that reports on the prevalence of *Campylobacter* and *Salmonella* in a real-world dataset in the Middle East. The high positivity rate of *Campylobacter* spp. and *Salmonella* spp. in the investigated samples, especially from chicken faeces and meat, highlights the need for better hygiene control in chicken farms and the need for better food safety measures throughout the food production chain. These results approved the hypothesis generated in Chapter 5. These results also demonstrate the importance of including environmental and human samples in AMR surveillance.

The observed prevalence of asymptomatic *C. jejuni* colonization in humans was 20%, a figure considerably higher than the reported prevalence of asymptomatic *C. jejuni* in Chapter 4, Cambodia, and Mexico (Osbjer et al., 2016; Zaidi et al., 2012). It has been well established that the primary source of human Campylobacter occurs during the handling or consumption of contaminated food, especially poultry meat. *Campylobacter jejuni* colonizes the cecum and colon at high levels (generally around 10^6 to 10^8 cfu/g), and poultry remains colonized until slaughter (Cardoso, Ferreira, Truninger, Maia, & Teixeira, 2021; Hermans, Van Deun, Martel, et al., 2011). The low prevalence of *Salmonella* among the chicken production chain workers in Palestine is similar to those reported in different countries such as China and Vietnam, (Trung et al., 2017; Xu et al., 2019).

The prevalence of *C. jejuni* and *Salmonella* in the environment samples, chicken manure, was 31% and 8%, respectively. *Campylobacter jejuni* prevalence is higher than those reported in Greece and Burkina Faso (Kagambèga, Thibodeau, Soro, Barro, & Fravalo, 2021; Marinou et al., 2012) and less than those reported in South Africa and Malaysia (Ngobese et al., 2020; Saleha, 2002). *Salmonella* occurrence in the environment in this study, is consistent with the findings reported in Vietnam and Japan (Duc et al., 2019; Nguyen et al., 2021). However, our results indicate a higher occurrence compared to the findings reported in India (Shivaning Karabasanavar et al., 2020).

Chicken and its products have been identified as a significant source of Campylobacteriosis and Salmonellosis in humans (Abukhattab, Taweel, et al., 2022). The occurrence of *C. jejuni* and *Salmonella* among chicken meats included in this study were 20% and 10%, respectively; these results are close to those reported in the Chapter 4. *Campylobacter jejuni* occurrence in chicken meat was higher in France and Poland, (Andrzejewska, Szczepańska, Śpica, & Klawe, 2015; Guyard-Nicodème et al., 2015). Conversely, *C. jejuni* occurrence in chicken meat in Palestine is higher than that reported in China and Brazil (da Silva, Tejada, Blum-Menezes, Dias, & Timm, 2016; Jun, Guo, & Ning, 2013). *Salmonella* prevalence in chicken meat in this study is lower than reported in Nigeria (Adeyanju & Ishola, 2014). While it is higher than the pooled prevalence of *Salmonella* reported in European countries (Gonçalves-Tenório, Silva, Rodrigues, Cadavez, & Gonzales-Barron, 2018). Pathogenic contamination of chicken meat mainly occurs by horizontal transmission: due to a contaminated environment or during the slaughter process. Slaughter facilities and birds' gastrointestinal tracts have been identified as the main reservoirs of poultry meat contaminants (Gonçalves-Tenório et al., 2018).

7.6 One Health integrated surveillance system for AMR

In Chapter 6, *C. jejuni* phenotypic results showed high resistance rates to macrolides (e.g. erythromycin, azithromycin, etc.), which is in agreement with rates reported in Chapter 4 and the recent EU report on AMR (EFSA, 2022c). In contrast, we detected considerably higher resistance rates than those observed in China, Japan, Poland, and Turkey (Cokal, Caner, Sen, Cetin, & Karagenc, 2009; Haruna et al., 2012; Maćkiw, Korsak, Rzewuska, Tomczuk, & Rożynek, 2012; Zhong, Wu, Zhang, & Shen, 2016). While, these results indicated low resistance rates among *C. jejuni* isolates to fluoroquinolone (e.g. ciprofloxacin, levofloxacin, etc.) consistent with findings previously reported in Chapter 4, as well as in the United States and Brazil (Aquino et al., 2002; Wang et al., 2011). Conversely, we detected considerably lower rates than those observed in a recent EU AMR report, China, and Jordan (Alaboudi, Malkawi, Osaili, Abu-Basha, & Guitian, 2020; EFSA, 2022c; Han et al., 2016). In 2021, a strain with the ST 11040 genotype was found to be dominant. These isolates did not match closely with any known genomes and showed a distinct AMR pattern. The co-resistance conferred by the combination of AMR markers to both aminoglycosides and macrolides is worrisome, as these drugs are typically the first line of treatment for human cases (Lopez-Chavarrias et al., 2021). The *C. jejuni* isolates collected in 2022 did not have AMR markers conferring resistance to aminoglycosides or macrolides. These results emphasize the critical role of continuous monitoring to identify the emergence of MDR strains.

Salmonella isolates showed a high prevalence of resistance for trimethoprim and sulfamethoxazole, and ampicillin. The ampicillin resistance rates observed in our study align with the reported rates in Turkey and Ethiopia (Abdi et al., 2017; Arslan & Eyi, 2010). However, our study showed higher ampicillin resistance compared to the rates reported in the EU, United States, United Kingdom, and Ghana (Andoh et al., 2016; EFSA, 2022c; Neuert et al., 2018; Velasquez et al., 2018). *Salmonella* resistance to trimethoprim and sulfamethoxazole was similar to that reported in Egypt and Ethiopia (Abd-Elghany, Sallam, Abd-Elkhalek, & Tamura, 2015; Abdi et al., 2017), but higher than the rates reported in Chapter 4, as well as in the EU and UK (EFSA, 2022c; Neuert et al., 2018). Our study revealed that MDR (multi-drug resistant) *S.* enterica serovar Muenchen isolates were present throughout the entire chicken meat production chain. Among the *S.* enterica serovar Muenchen isolates, we found genotypical resistance markers to at least five classes of antibiotics, including aminoglycosides, fluoroquinolones, aminocoumarines, sulfonamides and tetracyclines. Given the significant clinical importance of *S.* enterica infections, with a global annual incidence of over 27 million cases of enteric fever (John A. Crump et al., 2004) and 78.7 million cases of gastroenteritis

(Havelaar et al., 2015), the AMR monitoring as part of a One Health iSRS is of utmost importance.

Recently, a team in Israel reported a high prevalence of an MDR strain of *S.* enterica serovar Muenchen among clinical *Salmonella* spp. isolates carrying the pESI megaplasmid (E. Cohen et al., 2022). These isolates had a very high sequence similarity with the isolates described in Chapter 6. This suggests that there may be a regional spread of this particular MDR strain. The discovery of a dominant MDR strain emphasizes the need for continuous monitoring and open data sharing in real time to understand the epidemiology of AMR across borders and political systems.

These results could be explained by the environmental situation in the occupied Palestinian territory, which is influenced by anthropogenic factors such as population pressure and economic development. Urbanization, intensive agriculture production, overgrazing, unplanned industrial distribution, pollution, and contaminants all contribute to environmental deterioration and threaten biodiversity, posing societal hazards such as spread of AMR across bacteria that evolve by the horizontal transmission of MGEs between human, animal, and environment (Nadimpalli et al., 2020; UNEP, 2020).

While the environment plays a role in antibiotic resistance, both during the evolution of resistance and as a means of transmission, it can also offer solutions for managing it (Larsson & Flach, 2022). Environmental microorganisms, including as fungus and bacteria, have produced a large number of unique candidate antibiotic compounds, advancing the field of drug development (Lewis, 2013). Additionally, various waste streams contain a constant and extensive environmental emission of germs linked to humans and animals. The relatively recent development of antibiotics as clinical treatments have drastically altered the conditions for the emergence and spread of resistance by introducing unprecedented selection pressures, particularly on the microbiota of people and domestic animals, but also in heavily antibiotic-polluted environments (Larsson & Flach, 2022). Various ARGs have been mobilized and horizontally transferred due to this selection pressure (Brian P Alcock et al., 2020). The introduction of additional ARGs into pathogens raises concerns. However, it is essential to consider the modifications occurring in the genetic background surrounding ARGs, as they can have significant implications for the degree of resistance, co-selection dynamics, pathogenicity, and transmission potential. These modifications further complicate the issue of antibiotic resistance. The effects of evolutionary events leading to the establishment of pathogens with novel and effective resistance genotypes, facilitated through these mechanisms, exhibit distinct characteristics compared to transmission events involving widely disseminated genotypes. The emergence of pathogens harbouring new resistance genotypes presents unique challenges, as they can exhibit modified phenotypic characteristics in comparison to prevailing strains (Andersson et al., 2020; Bengtsson-Palme, Kristiansson, & Larsson, 2018; Berendonk et al., 2015; Escher et al., 2021; Graham et al., 2019; Larsson & Flach, 2022; Singer, Shaw, Rhodes, & Hart, 2016). This is because bacteria and genes often cross environments and species boundaries. Critical evolutionary events, in contrast to transmission, are uncommon and, to some extent, unique in nature, which makes them harder to forecast (Larsson & Flach, 2022).

Antibiotics reach the environment through human and domestic animal excretions (urine and faeces) (Larsson & Flach, 2022; Tran, Reinhard, & Gin, 2018), improper handling and/or disposal of unused drugs (Cabello et al., 2013), direct environmental contamination in aquaculture, or plant production, and waste streams from antibiotic production (Anwar, Iqbal, & Saleem, 2020; Bielen et al., 2017; Larsson, 2014; Taylor & Reeder, 2020). Utilization and excretion of antibiotics result in the most widespread emissions and very possibly the majority of antibiotics that are released. However, exposure levels through this method are always influenced by factors, including the fraction of the population using the antibiotic at any particular moment, the doses utilized, and human or domestic animal metabolism (Larsson & Flach, 2022). Faecal pollution of the environment increases opportunities for gene exchange between naturally occurring environmental bacteria and bacteria adapted to human or domestic animal intestinal tracts by bringing them into physical contact. In addition, a lot of intestinal bacteria are known to carry genetic elements (plasmids, integrative conjugative elements, insertion sequences, transposons, or integrons) that can help pathogens acquire genes and transfer them to other organisms (Gillings, Paulsen, & Tetu, 2017; Klümper et al., 2015). In Palestine, the World Bank report reveals that wastewater treatment capacity is much less than the amount of wastewater produced and that this gap is anticipated to reach 72 million m3 by 2030 unless more capacity is constructed. Sewage networks gather only 30% (or 21 mcm) of the 69 mcm of wastewater collected on the West Bank, and only 9.5 million m3 is treated. Simultaneously, 40 million m3 is disposed of in streams or absorption pits (UNEP, 2020; Zohud & Alam, 2022). Therefore, determining the amount and distribution of antibiotic resistance in the environmental microbiota could offer a chance to forecast the regional resistance situation and, indirectly, reveal clues about past antibiotic use (Aarestrup & Woolhouse, 2020; Hendriksen et al., 2019; Larsson & Flach, 2022). This is similar to the primary goals of traditional clinical resistance surveillance, which is essential for directing empirical treatment, assessing therapies, and identifying geographical and temporal trends of resistance.

7.7 Deploying whole genome sequencing in One Health approach

The profiling of clinical and environmental pathogen communities has been revolutionized by NGS, such as the MinION by Oxford Nanopore Technologies (Leggett et al., 2020). Rapid nanopore sequencing can detect a pathogen and its associated resistance profile within hours. However, detecting ARGs with molecular methods is not ideal because genotypic resistance does not always correlate with phenotypic resistance, as in Chapter 6 (Burnham, Leeds, Nordmann, O'Grady, & Patel, 2017). The complexity and multifaceted nature of many resistance mechanisms necessitate further comprehensive understanding. With the new technique, WGS is becoming more inexpensive, and genotypic testing is quick and repeatable (Leggett et al., 2020). In addition to AMR, sequencing provides molecular-type data to aid in outbreak detection and helps infection control professionals to better understand transmission dynamics. Optimization of metagenomic methods and bioinformatics tools may enable identifying at-risk patients, profiling infectious pathogens, and tailoring therapy (Burnham et al., 2017; Leggett et al., 2020). For these reasons, the implementation of sequencing technologies, including metagenomics, can contribute to the establishment of an effective surveillance system within the socio-ecological complex context, such as that in Palestine and the Middle East.

In this PhD thesis, I demonstrated that deploying WGS in a One Health approach can considerably improve the surveillance and management of infectious diseases as well as our understanding of the interconnectivity of human, animal, food, and environmental health. Whole genome sequencing enables comprehensive characterization of pathogens at the genomic level. By sequencing the entire genome of a pathogen, researchers can identify specific genetic markers, including genes associated with antibiotic resistance or virulence factors. This knowledge not only aids in identifying transmission routes but also facilitates the recognition of identical strains in different compartments. Understanding the presence of identical strains across various sources assists in pinpointing the routes of transmission, determining the sources of infection, and enhancing our understanding of the likelihood of zoonotic spillover (Chapter 6).

Furthermore, WGS enables precise identification and monitoring of AMR genes in infections. By studying the genetic makeup of bacteria, including AMR genes, researchers can determine resistance profiles and assess the potential for AMR transmission between humans, animals, food, and the environment (Chapter 6). This involves analyzing gene similarity, MGEs, virulence genes, and conducting phylogenetic analysis. These approaches provide valuable insights into the resistance profiles, help identify routes of transmission, and assess the likelihood of AMR spread between different reservoirs. Additionally, the use of phylodynamics, which combines phylogenetics with epidemiology, allows for the tracing of transmission pathways, estimation of evolutionary rates, and understanding of disease outbreak patterns. By sequencing and studying the genomes of pathogens (Chapter 6), researchers can rapidly identify novel strains or mutations that may pose risks to human and animal health. This information is vital for the development of efficient AMR mitigation measures, optimization of antibiotic usage, and implementation of effective strategies for monitoring foodborne illnesses and zoonotic diseases..

7.8 Operationalized One Health approach to activate the food safety strategy and national action plan for antimicrobial resistance in Palestine

Although a national food safety strategy and national Palestine action plan for AMR (NAP for AMR) have been developed, unclear roles and poor communication among regulatory authorities as well as between private, academic, and public sectors appear to be impeding progress in improving food safety in Palestine (FAO, 2017b; WHO, 2020c).

The division of responsibilities among ministries, as determined by the national committee for the formulation of the Palestinian strategy for food safety, is consistent with the reports of the multi-stakeholder discussion groups we conducted (FAO, 2017b). Our results regarding the role distribution between regulatory authorities could thus be confirmed.

The Palestinian food safety strategy recognizes the Ministry of Health as the primary entity responsible for monitoring food safety. This includes enforcing hygiene guidelines for service providers, conducting food safety inspections, prohibiting the marketing of unregistered foods without proper permits, and implementing disease control measures (FAO, 2017b). However, as discussed in the focus groups, it is expected that the Ministry of Health collaborates with other stakeholders to develop control mechanisms, ensure workplace safety, and inspect imported food (FAO, 2017b). Simultaneously, the Ministry of Agriculture is assigned the responsibility of regulating the imports and exports of plant and animal-based food products (FAO, 2017b). We assume that these shared responsibilities carry risks of misunderstanding and frequently tumble due to inadequate communication and coordination between regulatory authorities. Moreover, there appears to be a communication gap between the private, academic and government sectors. For example, while regulatory authorities assign the Ministry of Agriculture primary responsibility for food production from animal sources and field control, one poultry farmer highlights and criticizes the lack of communication between the Ministry of Agriculture and farmers.

In animal food production, the implementation of appropriate precautions, such as biosecurity measures, plays a crucial role in promoting the responsible use of antimicrobials and enhancing food safety and public health (Gozdzielewska et al., 2020). Based on our findings, we strongly recommend the adoption of rigorous, evidence-based strategies to guide hygiene practices in Palestinian animal food production, from farm to final food preparation. Previous studies have demonstrated that implementing on-farm biosecurity measures can significantly reduce the prevalence of *Campylobacter* infection in broilers by more than 50% (Gibbens et al., 2001; Van de Giessen et al., 1998). Such measures may include standardized cleaning and disinfection of poultry houses between production cycles, vermin control, promotion of hand washing before and after contact with poultry, and the establishment of a comprehensive hygiene protocol for all individuals entering the farm. The latter could involve the use of protective clothing such as boots and overalls, as well as regular maintenance of the disinfecting footbath at the entrance. Several studies have identified well-maintained broiler houses as a critical factor in protecting against *Campylobacter*, as they serve as a physical barrier to potential contamination, while also incorporating ventilation and temperature control systems (El-Saadony et al., 2023; Georgiev, Beauvais, & Guitian, 2017; Kittler, Shakeri, Peh, & Plötz, 2021). Therefore, supporting and encouraging the renovation of traditional poultry farms or the construction of new buildings is essential. Even the simple use of fly screens to prevent flies from accessing broilers has been associated with a significant reduction in the prevalence of *Campylobacter*, from 51.4% in control houses to 15.4% in intervention houses (Hald et al., 2007). We hypothesize that such a reduction in zoonotic pathogen infection in live poultry will subsequently decrease the risk of transmission to humans. On one hand, this reduces the occupational risk for workers in direct contact with animals or meat products, and on the other hand, it enhances product quality and prevents the transmission of zoonotic diseases to consumers. However, biosecurity measures can reduce the risk of *Campylobacter* infections in broiler flocks, it is important to note that they cannot completely eliminate this risk due to the "constant contamination pressure" that chickens are exposed to (Hermans, Van Deun, Messens, et al., 2011; Kittler et al., 2021). Therefore, it is crucial to emphasize that addressing these challenges requires the adoption of a holistic One Health approach that integrates efforts across sectors. Without such an approach, the challenges associated with biosecurity measures, including the persistent risk of *Campylobacter* infections in broiler flocks, will persist and often positive cases of *Campylobacter* reappeared after successful elimination (Gölz et al., 2014; Hermans, Van Deun, Messens, et al., 2011; Van de Giessen et al., 1998).

The current Palestinian NAP aligns well with the WHO's GAP for AMR. The plan addresses the five main objectives for enhancing Palestine's AMR leadership outlined in the GAP and pledges to address key policy and regulatory concerns about the use of antibiotics in accordance with the "One Health approach" (WHO, 2020c). **In Chapter 6, we emphasized the crucial role played by the environment in the transmission and spread of AMR within the Palestinian territory. However, it is noteworthy that the environmental sector in Palestine, including both governmental and private entities such as the Palestinian Water Authority (PWA), the Water, Sanitation and Hygiene Monitoring Program (WaSH MP), the Environmental Quality Authority (EQA), and the Environmental Non-Governmental Organizations Network (PENGON), was poorly represented in the five technical working groups that contributed to discussions and drafting of NAP for AMR. While this committee was limited to the health (private and public) and agriculture sectors, along with the veterinary general directorate, the involvement of the environmental sector is crucial to ensure comprehensive strategies addressing AMR in Palestine.** Developing containment measures for AMR requires a transdisciplinary approach involving the government, civil society, academia, business, and media sectors. Applying a transdisciplinary approach will enhance the new national strategies in Palestine to contain AMR mitigation program in all relevant sectors, e.g., National Water and Wastewater, food safety, and environmental strategies. This will solve the issue of lack of financial allocation, which remains the most significant challenge for the implementation of NAPs in many low- and middle-income countries (Ranjalkar & Chandy, 2019). Once the NAP's implemented, authorities ought to emphasize monitoring and evaluating all of the goals, setting up suitable governance structures, and creating accountability systems so that they may plan how best to attain these outcomes in various contexts. Additionally, the NAP for AMR must be implemented with a robust political commitment as well as support from many private and academic stakeholders are essential for implementing the NAP for AMR (Ranjalkar & Chandy, 2019). The existing literature concurs with the NAP for AMR, emphasizing the importance of taking comprehensive, system-wide, multidisciplinary, and cross-sectoral steps to mitigate AMR and preserve the future efficacy of antimicrobials (Godman et al., 2021; Majumder et al., 2020; Sweileh & Moh'd Mansour, 2020). The Interagency Coordination Group on Antimicrobial Resistance (IACG) cautions that while many countries have developed NAPs, the main challenge lies in their implementation and sustainability (WHO, 2018a). Challenges in implementing NAPs for AMR include technical capacity, financial resources, political commitment, and regional cooperation to ensure that progress in one region is not undone by poor implementation in others (WHO, 2018a). In the long term, as emphasized by IACG, governments need to allocate resources to effectively implement their national action plans, ensuring sustainability and achieving effective AMR control program. Additionally, IACG asserts that investing resources to address AMR is one of the most beneficial investments a country can make, highlighting the long-term benefits and cost-effectiveness of such actions (WHO, 2018a).

Based on our findings in Chapter 5, it is evident that there is a shortage of resources and human capacity to effectively implement a One Health strategy aimed at improving food safety and controlling AMR in Palestine. Of particular surprise and concern, as reported in all multi-stakeholder discussion groups, is the insufficient infrastructure, such as the scarcity of public slaughterhouses and laboratories (Veterinary and food safety laboratories). Public slaughterhouses, along with meat inspection, fall under the jurisdiction of the Ministry of Local Governance (FAO, 2017b). Currently, Palestine only has ten modern chicken slaughterhouses, both public and private, and as the committee for Palestinian food safety strategy regrets, most meat products marketed for human consumption are not subject to the food safety authorities (Veterinary and Ministry of Health) inspections (FAO, 2017b). Furthermore, infrastructure scarcity includes the veterinary and food safety laboratories, as only two are in the Palestine. Veterinary laboratories are vital in the fight against AMR by providing essential diagnostic, surveillance, research, and educational services. Their contributions help to identify and respond to AMR in animals, promote responsible antimicrobial use, safeguard food safety, and protect public health by reducing the risk of transmission of resistant bacteria from animals to humans. As part of the One Health integrated surveillance system, it is essential to integrate data from animal pathogens collected by veterinary diagnostic laboratories into other human and environmental AMR surveillance activities (Ceric et al., 2019).

In this PhD thesis, we have come to recognize the essentiality of incorporating legal, political, and social dimensions into a comprehensive One Health initiative aimed at enhancing food safety and NAP for AMR in Palestine. It is evident that the current legislation pertaining to food safety in Palestine is fragmented and fails to encompass all aspects of food safety across the entire food chain (FAO, 2017b). Furthermore, due to the Israeli occupation, unregulated trade occurs at borders and within "Zone C," which encompasses over 60% of the West Bank and restricts Palestinian authorities from implementing their policies (Araj, 2010; FAO, 2017b). Given the prolonged conflicts, wars, and instability in the region, establishing the necessary political will for international cooperation in disease prevention and AMR mitigation poses a significant challenge in Palestine (WHO, 2020c). Therefore, employing an integrated One Health surveillance system in conjunction with a transdisciplinary approach that actively involves the civil community in these areas emerges as the most optimal solution for constructing an effective monitoring system. The spearheading of the Canadian program against AMR, CIPARS, exemplifies a comprehensive approach to monitoring AMR within a complex human-environment or social-ecological system (Zinsstag et al., 2011). This approach encompasses multiple sectors and employs various surveillance methods. Passive surveillance involves professionals from veterinary, environmental, and health sectors who observe and report data as part of their regular duties. Active surveillance, on the other hand, entails dedicated staff collecting samples from humans, animals, food, and the environment, while also gathering information about the population's health status. Each surveillance method serves distinct objectives. By employing this multi-faceted approach, CIPARS can effectively evaluate different facets of AMR. When data from all components are integrated and analyzed collectively, a comprehensive understanding of AMR in Canada is achieved. This holistic perspective yields valuable insights and facilitates informed decision-making (Zinsstag et al., 2011).

In Palestine, the successful implementation of One Health and food safety measures goes beyond surface-level understanding and requires a deep appreciation for the socio-cultural and spiritual norms that shape the community's relationship with food. Education and awareness campaigns should be thoughtfully crafted to incorporate religious teachings and principles, such as "Halal" (permissible) and "Baraka" (blessing). These campaigns should emphasize the importance of food safety within the framework of religious values, connecting hygiene, health, and well-being. Moreover, integrating traditional knowledge and practices into modern food safety concepts is essential (Ahmad, Abaidah, & Yahya, 2013; Conficoni, Zaghi, Rossin, Brscic, & Giaccone, 2022). Traditional food preservation, preparation, and storage methods often have deep-rooted cultural significance and must be recognized and valued. By incorporating traditional knowledge into training programs and guidelines, a more inclusive and culturally sensitive approach to food safety can be fostered (Conficoni et al., 2022).

Adapting regulatory frameworks and standards to align with the socio-cultural context is vital to contextual adaptation. This involves finding a delicate balance between honouring cultural practices and upholding fundamental food safety principles. Collaborative efforts between regulatory authorities, researchers, and local communities are crucial for developing practical solutions that respect cultural traditions while ensuring public health. Engagement with the community and stakeholders is key. By actively involving community members, religious leaders, and relevant organizations, a collective dialogue can be established to identify culturally appropriate strategies. This participatory approach ensures that the community's voice is heard and respected, leading to higher acceptance and engagement in implementing One Health and food safety measures (Fischer, De Jong, De Jonge, Frewer, & Nauta, 2005; Zinsstag, Pelikan, et al., 2023; Zinsstag, Schelling, et al., 2020).

For example, during the religious occasion, "Eid Al Adha" (Qurban), the traditional practice of slaughtering ruminant animals is commonly conducted in households, particularly in rural areas, due to the absence of dedicated slaughterhouses, as previously discussed in Chapter

5. Additionally, this practice holds cultural significance and is considered a way to seek "Baraka" or blessings. To address this particular scenario, the One Health approach offers a potential solution by integrating a transdisciplinary approach. This can be accomplished through the active involvement of local authorities, such as municipalities, religious leaders, civil communities, and relevant government entities like the Ministries of Health, Agriculture, and Environmental authorities. One possible measure to consider is the establishment of designated areas within each village that are specifically designated for the purpose of animal slaughtering during the "Eid Al Adha" season, overseen and guided by local authorities (Conficoni et al., 2022). The participation of religious leaders plays a crucial role in influencing and garnering community acceptance of this concept. Furthermore, religious leaders can actively engage in awareness campaigns to address irresponsible antimicrobial use in humans and animals (Jack & Broom, 2020).

Taking into account the socio-cultural and spiritual context and tailoring food safety measures accordingly allows for the implementation of impactful and enduring interventions in Palestine. This approach not only improves health outcomes but also ensures that the community embraces and appreciates these initiatives, creating a lasting positive influence on the well-being of individuals, animals, and ecosystems.

Part 8

CONCLUSIONS

AND

RECOMMENDATIONS

8 Conclusion and Recommendations

In order to effectively implement an operational One Health strategy in Palestine, the establishment of a One Health technical committee plays a crucial role in addressing key areas such as food safety, zoonotic diseases, and AMR. In Palestine, One Health strategy does not require new ministries or other institutions, as they are already in place and operational. This committee should be formed following further promotion of exchanges between stakeholders and the establishment of an integrated quality control system for food production. The primary objective of the committee is to foster clarity on the roles of different actors, establish effective communication pathways, and facilitate cross-sector partnerships.

Regarding food safety in Palestine, we propose to establish an integrated quality control system for food production: while existing ministries and institutions are already functioning, we recommend the formation of a governing body comprising representatives from the private sector, the public sector, and academia. This body would be monitoring food safety in Palestine and take on responsibilities such as developing a comprehensive quality control system throughout the food production chain. Their tasks would include setting clear guidelines for inspections and laboratory testing, enforcing necessary sanctions or corrective actions when needed, and implementing new public health laws. By implementing these measures, we aim to ensure effective governance and coordination in the realm of food safety in Palestine without requiring the creation of new ministries or institutions. This approach will help establish a robust quality control framework and contribute to successfully implementing a One Health strategy in the region.

Under the authority of the newly formed entity, we propose the implementation of product certification, which could be accomplished through the use of a label. This label would assure that broilers have been raised, transported, and slaughtered under hygienic conditions, with a focus on respecting animal welfare, and ensuring responsible antimicrobial use, especially antibiotics. Given that the current slaughtering practices in Palestine often fail to meet hygiene standards, it is crucial to prioritize the development of slaughterhouse capacity. Furthermore, all meat products entering the market must undergo veterinary inspections to guarantee their safety. The use of antimicrobials must be carefully monitored, with thorough record-keeping and strict adherence to withdrawal periods. If a certification label for broiler meat products is successfully established, it could be expanded to include other animal-derived foods or even general food products, thereby enhancing overall food safety and consumer confidence.

Our findings indicate that implementing an integrated surveillance system and adopting a transdisciplinary approach can effectively address AMR and improve the food safety system in the Palestinian territory. By sharing responsibilities and financial resources among relevant authorities, the mitigation of AMR and foodborne pathogens can be significantly improved. For example, if the Ministry of Higher Education prioritizes AMR research and the academic sector aligns with their regulations (active integrated surveillance), while the local municipalities and the environmental authorities incorporate AMR mitigation strategies into their wastewater treatment plans and environmental programs, and the Ministries of Health and Agriculture share AMR data through their passive surveillance systems, it would ensure a sustained and comprehensive approach to addressing AMR. Establishment the Palestinian Integrated Program for Antimicrobial Resistance Surveillance (PIPARS) (Figure 7-9), will lead to financial savings compared to single-sector AMR surveillance. Savings will be expected from the focused design (reduced and optimal sample size), centralized field and institutional organization, centralized laboratory components, IT infrastructure and data management, training, communication and evaluation. Additionally, as part of the integrated surveillance system, efficient testing methods are crucial. It is essential to employ highly sensitive detection methods, such as whole genome sequencing, that enable early identification, prompt notification, and timely response to AMR and other threats to food safety.

Overall, the combination of an integrated surveillance system, collaborative efforts among stakeholders, and the use of advanced detection methods will contribute to a more effective and comprehensive approach in addressing AMR and enhancing the food safety system in Palestine.

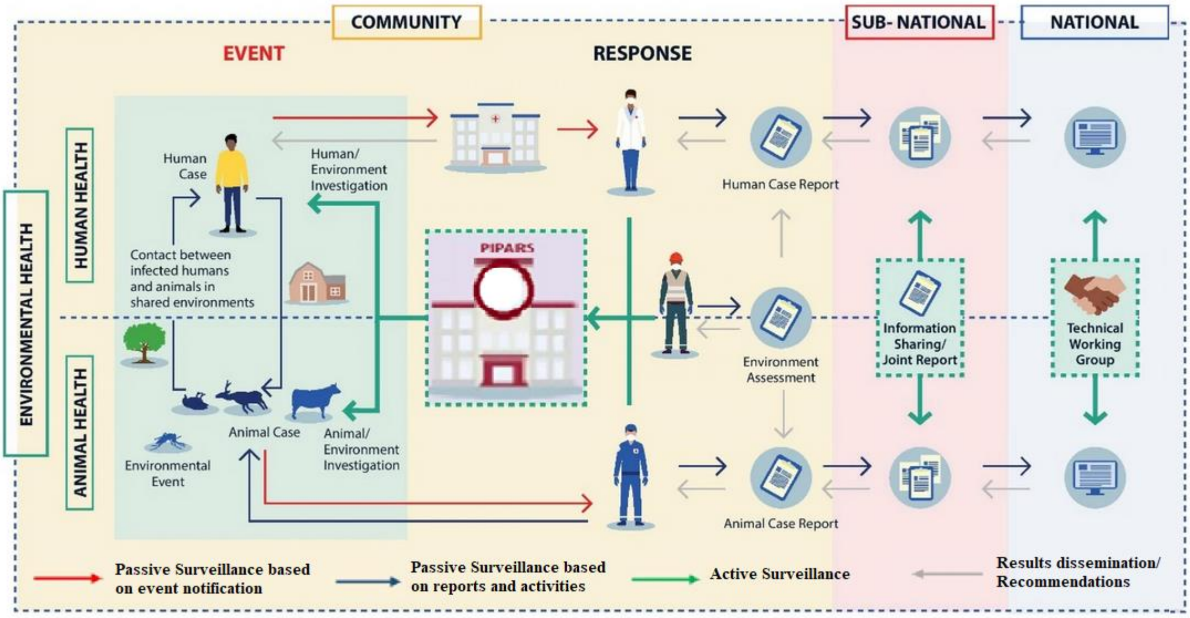

Figure 8-1 Generalized proposal to visualize the PIPARS framework. (Inspired from (Zinsstag et al., 2011) and (Ghai et al., 2022)). **Abbreviations:** PIPARS: Palestinian Integrated Program for Antimicrobial Resistance Surveillance

8.1 Recommendation for implementation One Health for zoonotic diseases and AMR in Palestine

In order to effectively develop prevention and control plans for zoonotic diseases in Palestine, several key steps should be taken:

1. Prioritization of a list of zoonotic pathogens of most national importance: in Palestine, since resources are frequently insufficient to meet all requirements for zoonotic disease control, it is vital to prioritize zoonotic diseases when allocating resources. A systematic, objective prioritization approach that includes equal involvement and input from all stakeholders will provide the additional benefit of assisting in establishing One Health's commitment and cooperation.
2. Establishing a Baseline: It is crucial to gather baseline information on the current status of zoonotic diseases, including their burden and epidemiological situation. This may require conducting new investigations, such as serological surveys or pilot studies, to establish the baseline epidemiology, including primary hosts, reservoirs, circulating species or strains, and prevalence in human and animal populations and their environments using the whole genome sequencing technique.
3. Developing a transdisciplinary One Health strategic plan: This approach is essential in developing context-specific policy recommendations for addressing societal challenges through a One Health framework. Chapter 5 of this Ph.D. thesis has already initiated such a transdisciplinary process. To further enhance this approach, it is crucial to engage local authorities, NGOs, community representatives, private businesses, and farmers in order to develop tailored policy recommendations for preventing the spread of AMR and zoonotic diseases within the local context. The ultimate goal is to have a significant societal impact by generating policy recommendations that effectively control and reduce AMR based on a comprehensive understanding of its distribution and transmission. This, in turn, can lead to a decrease in morbidity and mortality rates among both humans and animals. Additionally, implementing these recommendations can result in substantial cost savings for society as a whole.
4. Conducting Economic Assessments: Assessing the cost-effectiveness of the proposed program is essential for securing funding. Understanding the financial burden of the disease compared to different scenarios of investment in control and elimination can increase the program's chances of success. Economic assessments and decision

analyses involving all stakeholders are necessary to determine the societal cost of the disease and the benefits of prevention and control measures.

5. Developing a Multisectoral, One Health Strategic Plan: The development of a strategic plan is essential for enhancing collaboration among various government sectors. This involves evaluating the existing frameworks of the ministries of health and agriculture in terms of zoonotic disease reporting and control. By identifying any gaps or shortcomings, a strategic plan can be formulated to establish a unified vision with achievable goals and objectives. These strategic plans should have a long-term perspective, typically spanning 5 to 10 years, and should ensure equal participation and engagement from all relevant sectors.
6. Soliciting, Acquiring, and Allocating Resources: The program's cost will determine how available resources, including human, financial, and physical resources, will be distributed. Efforts should be made to secure missing resources through strategies such as lobbying campaigns and approaching non-traditional funding partners. Exploring international agencies or creating regional alliances for support can also be beneficial. Sufficient resources should be identified before implementing each phase to prevent early program terminations.
7. Implementing Plans, Protocols, and Procedures: With budgeted and funded strategies, One Health systems or zoonotic disease-specific programs can be gradually implemented using available resources. The aim is to establish an efficient system that minimizes resource utilization while achieving desired outcomes, such as reducing morbidity and mortality rates in humans and animals.
8. Monitoring and Evaluating Systems and/or Programs: Monitoring and evaluation should be incorporated from the planning phase to track implementation results and assess program accomplishments, challenges, scope, and size. Developing a framework for monitoring and evaluating One Health systems provides valuable information for decision-making.
9. Palestinian Integrated Program for Antimicrobial Resistance Surveillance (PIPARS): As a sustainable outcome of the establishment of One Health in Palestine, PIPARS is proposed (Figure 9). This program is expected to yield financial savings compared to single-sector surveillance approaches. PIPARS will leverage a focused design, centralized field and institutional organization, centralized laboratory components, IT infrastructure, data management, training, communication, and evaluation. One of the key features of PIPARS will be the establishment of a centralized sample archives, also known as a biobank. This repository will enable the storage and preservation of samples for future analysis and research purposes. Additionally, PIPARS will

implement public-facing dashboards to facilitate standardized data analysis, reporting, and sharing of information.

10. We propose promoting education, training, and awareness campaigns as key strategies: to begin with, incorporating One Health knowledge into multidisciplinary programs at universities would be beneficial in the future. Additionally, targeting specific groups for education and training is essential, such as farm workers, slaughterhouse and meat store staff, households, and health workers. These individuals should be provided with knowledge and training on sanitation practices and the appropriate use of antimicrobials. Furthermore, raising public awareness regarding food safety, zoonoses, and AMR is crucial. This can be achieved through comprehensive awareness campaigns that target the general population. We recommend conducting regular observational studies to assess the impact of the training and awareness campaigns on the knowledge, attitudes, and practices (KAP) related to hygiene and the use of antimicrobial drugs throughout the food production chain. These observations can be complemented by questionnaires, similar to the methodology employed in this thesis. By implementing these measures, Palestine can foster a culture of One Health, ensuring that individuals from various sectors are equipped with the necessary knowledge and skills to contribute to the prevention and control of diseases, as well as the promotion of food safety and responsible antimicrobial use.

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