

**A Review on Prevalence and Antimicrobial Resistance in
Salmonella Enteritidis and *Salmonella* Typhimurium in
Poultry**

By-

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A thesis submitted to the Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of Bachelor of Science in Microbiology

Department of Mathematics and Natural Sciences

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Declaration

It is hereby declared that

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2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis/project titled “**A Review on Prevalence and Antimicrobial Resistance in *Salmonella* Enteritidis and *Salmonella* Typhimurium in Poultry**” submitted by Kazi Jannatul Tasnim (17326002) of Summer, 2017 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Science in Microbiology on 9th November, 2023.

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Abstract

Salmonellosis poses an enduring global challenge, contributing significantly to foodborne illnesses and economic burdens. This review focused on the prevalence of *Salmonella* serovars Enteritidis and Typhimurium in poultry populations, their role as foodborne pathogens, and the complexities of antimicrobial resistance. Additionally, it explored the influence of climate change on *Salmonella* prevalence in poultry environments as increasing temperature and rainfall elevate the growth, spread and transmission of its serovars. Underscoring *Salmonella's* omnipresence is its importance in infectious gastroenteritis. While often linked to contaminated food, the review shed light on the potential for infection through contact with animals, especially live poultry, revealing intricate transmission dynamics within poultry populations. The substantial economic impact of salmonellosis in various countries was discussed, emphasizing its global significance. Notable attention was given to *Salmonella* Enteritidis and *Salmonella* Typhimurium due to their adaptability to avian hosts and status as zoonotic pathogens, which contribute significantly to foodborne outbreaks. Additionally, the emergence of antimicrobial resistance in these serovars put complexity on infection management. Notable resistance patterns in these serovars in poultry from around the world were discussed as it is matter of concern in every aspect. Comprehensive, collaborative efforts were highlighted, aiming to mitigate the risks associated with these serovars through effective strategies in poultry management and public health because continued surveillance and research are deemed vital in the ongoing battle against salmonellosis.

Key words: *Salmonella* Enteritidis, *Salmonella* Typhimurium, Poultry, Climate change, Antimicrobial resistance, Economic impact.

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List of Acronyms

Acronyms	Full form
SEM	Scanning Electron Micrograph
ECDC	European Centre for Disease Prevention and Control
WHO	World Health Organization
EU	European Union
CDC	Centers for Disease Control and Prevention
RNA	Ribonucleic Acid
PBP _s	Penicillin-Binding Proteins
ESBL _s	Extended-Spectrum Beta-Lactamases
RND	Resistance-Nodulation-Division
MFS	Major Facilitator Superfamily
ABC	ATP-Binding Cassette family
MDR	Multidrug-Resistant
AMR	Antimicrobial Resistance
USD	United States Dollar
COL	Colistin
CIP	Ciprofloxacin
GEN	Gentamicin
NAL	Nalidixic Acid
CAZ	Ceftazidime
CTX	Cefotaxime
AMP	Ampicillin
CHL	Chloramphenicol
TET	Tetracycline
MEM	Meropenem
AZM	Azithromycin
TMP	Trimethoprim
TMP/SMX	Trimethoprim / Sulfadimethoxine
TGC	Tigecycline
TMS	Sulfamethoxazole

Chapter 1: Introduction

Salmonellosis, a prevalent foodborne infection, is among the most commonly reported worldwide. Renowned as one of the most significant foodborne pathogens worldwide, *Salmonella enterica* subsp. *enterica* remains at the forefront as the predominant causative agent of infectious gastroenteritis [1]. It accounts for a substantial burden of gastroenteritis, with an estimated 93.8 million cases caused by various *Salmonella* species occurring globally each year. These infections lead to a significant number of fatalities, amounting to approximately 155,000 deaths annually [2]. Animal-derived food, particularly poultry products like raw chicken and eggs, is commonly associated with *Salmonella*-related foodborne illness, being a frequent cause of both sporadic cases and outbreaks in humans [3,1]. While most cases of salmonellosis stem from the consumption of contaminated food, it is worth noting that contact with animals, particularly live poultry such as chickens, ducks, geese, and turkeys, can also lead to the acquisition of this bacterial infection. The transmission of *Salmonella* to poultry can occur through various means, including the mingling of infected birds from different origins, the vertical transfer of the bacteria from infected hens to their offspring, or the exposure to contaminated feed [4]. Salmonellosis is prevalent in both developed and developing countries, affecting populations across diverse geographical regions [2]. It was estimated that 11% of foodborne illness in the USA is caused by *Salmonella* [2]. Based on information from The European Centre for Disease Prevention and Control (ECDC), *Salmonella* is accountable for a significant number of human infections, resulting in illnesses reported in 91,857 individuals within the European Union (EU) in the year 2018 [6]. Studies conducted in Bhutan have shown that *Salmonella* is the most prevalent pathogenic organism (42.86%) contributing to foodborne illness there

[7]. Similarly, as mentioned in Table 1, it was responsible for 23% of South Korea’s foodborne illnesses. During the period of 2008 to 2013 in France, *Salmonella* spp. constituted the third leading cause of foodborne illnesses, accounting for approximately 12% of the cases [6]. From the last reported data in the UK, *Salmonella* was the reason behind 14.6% of the foodborne illness [8]. Annual incidence rate in Canada of *Salmonella* spp. were 19.38% reported by FoodNet Canada's annual report for the year 2018 [9]. The comprehensive data regarding the prevalence of *Salmonella* in foodborne illnesses worldwide is presented in Table 1.

Table 1: Percentage (%) of *Salmonella* in foodborne illness around the world.

Countries	Percentage of foodborne illness caused by <i>Salmonella</i>	Year	Source
China	70-80%	2021	[10]
USA	11%	2010	[2]
European Union	19.3%	2022	[11]
Bhutan	42.86%	2021	[7]
South Korea	23%	2021	[12]
UK	14.6%	2022	[8]
Canada	19.38%	2018	[9]

Chapter 2: *Salmonella enterica* as a Bacterial Pathogen

Salmonella enterica is an Enterobacteriaceae-family gram-negative bacterial pathogen. It is known to cause a wide spectrum of diseases in individuals as well as animals, with contaminated poultry products being responsible for a substantial amount of these infections. *Salmonella enterica* comprises a heterogeneous assortment of serovars, each exhibiting distinctive attributes and virulence factors. Within this broad range of serovars, particular strains of *Salmonella enterica* have been specifically associated with chicken, which serves as a reservoir for these bacteria. Poultry, encompassing chickens, turkeys, and ducks, have been identified as carriers of *Salmonella enterica*, frequently without exhibiting symptoms, and excrete the bacteria through their feces. This fecal contamination represents a primary pathway for transmission to humans. In accordance with the nomenclatural system endorsed by the World Health Organization (WHO) Collaborating Centre system, the *Salmonella* genus is organized into two distinct species: *Salmonella enterica* (recognized as the type species) and *Salmonella bongori*. The differentiation between these species is primarily determined by disparities observed in their 16S rRNA sequence analysis. *S. bongori* and other *S. enterica* subspecies often cause infections in cold-blooded animals like reptiles and amphibians, they very rarely infect human hosts [13]. Furthermore, the type species, *S. enterica*, exhibits classification into six subspecies, based on their genomic relatedness and biochemical characteristics [14]. It consists of subspecies, namely *enterica*, *salamae*, *arizonae*, *diarizonae*, *houtenae*, and *indica*, encompassing a total of approximately 2,659 distinct serovars. In accordance with the clinical symptoms they induce, these serovars are classified as typhoidal or non-typhoidal *Salmonella*. Among these, the *enterica* subspecies accounts for approximately 1,547

serovars, and it is noteworthy that approximately 99% of these serovars have the potential to cause infections in both animals and humans [15]. *S. Typhimurium* and *S. Enteritidis* represent serovars within the subspecies *enterica* of *Salmonella enterica*. These particular serovars, classified as non-typhoidal or generalist serovars, are prevalent in human and frequently isolated from various domestic livestock populations, including various types of pets [16].



Figure 1: Colored Scanning Electron Micrograph (SEM) of *Salmonella enterica*, *Salmonella* Enteritidis serovars and *Salmonella* Typhimurium serovars [17, 18, 19]

This is based on variations in biochemical and genomic characteristics. The majority of *Salmonella* strains exhibit lactose fermentation, hydrogen sulfite production, and are oxidase-negative while being catalase-positive. Additional biochemical properties used for *Salmonella* identification include the ability to grow on citrate as the sole carbon source, decarboxylate lysine, and hydrolyze urea [5]. Gaining insight into the virulence mechanisms of *Salmonella enterica* is imperative for understanding its pathogenic nature. This bacterium harbors a diverse range of virulence factors, such as adhesins, invasins, and toxins, which facilitate its colonization and invasion of the host. Also, *Salmonella enterica* possesses the capability to persist and replicate within host cells, resulting in systemic infections. The study of these virulence factors and intracellular survival mechanisms has

been the subject of extensive research in various *Salmonella* serovars, providing valuable insights into the intricate interplay between the pathogen and its host. *Salmonella* is widely regarded as the most prevalent foodborne pathogen on a global scale. It has been consistently acknowledged as a significant zoonotic microorganism of economic importance in both animal and human populations particularly in developing nations [20]. Because of their ability to persist, potential for zoonotic transmission, and impact on human health, *Salmonella* Enteritidis and *Salmonella* Typhimurium remain a noteworthy issue in poultry populations globally. These specific *Salmonella* serovars, Enteritidis and Typhimurium, are commonly detected in poultry samples across the world.

2.1: Sources

Salmonella enterica has the potential to infiltrate poultry production through diverse sources and pathways. *Salmonella* serovars mostly live in the gastrointestinal tracts of people and farm animals. In addition, they appear in the gastrointestinal system of wild birds, reptiles, and sometimes insects. Feedstuff, soil, bedding, litter, and fecal matter are common sources of *Salmonella* contamination on farms. After infecting the digestive system, *Salmonella* bacteria are expelled in feces. This allows them to be carried by insects and other animals, spreading the infection to many different places often resulting in contamination of water sources [5, 21]. Within poultry flocks, each of these sources contributes to the transmission and endurance of *Salmonella enterica*, elevating the risk of contamination in poultry products and subsequent human infections. Below are the diverse origins of *Salmonella enterica* contamination in poultry, along with corresponding occurrences from different regions worldwide:

1. **Environment:** The outer surroundings of poultry farms, encompassing areas adjacent to the poultry houses, can potentially serve as a reservoir for *Salmonella enterica* contamination. This can transpire when wild birds, rodents, or other animals carrying the bacteria introduce it to the environment. Global incidents of environmental contamination have been reported, such as in England, R. H. Davies and C. Wray (1996) conducted a study where they discovered the survival of *Salmonella* Enteritidis outside poultry houses in small areas of litter and fan dust that remained after the site had been cleaned and disinfected. Additionally, in certain poultry units, *S. Enteritidis* was found in droppings from wild birds. According to the findings of Craven et al., (2000), it was determined that wild birds serve as reservoirs for *Salmonella*, thereby posing a risk of infection to poultry populations. The persistence of *Salmonella* contamination seemed to occur primarily in conjunction with dust particles swept from the floor and in food troughs. *Salmonella enterica* contamination can occur within the interior of poultry houses, predominantly through infected birds shedding the bacteria in their feces or respiratory secretions. The presence of rodents, including rats and mice, poses a significant risk to poultry flocks as they can contaminate feed and poultry living areas with urine and droppings. This introduces the potential for disease transmission to the birds. The epidemiology of avian salmonellosis is significantly influenced by rodents, as they serve as reservoirs for paratyphoid *Salmonella* like Enteritidis and Typhimurium within poultry facilities [24]. The spread of *Salmonella* Enteritidis, especially within the layer industry, has been attributed to the involvement of rodents, primarily mice [25]. Subsequently, this contamination

can spread among other birds within the flock. Annual and daily losses of feed and spillage caused by rodents have been reported in Norway and Punjab, India [26].

2. **Hatchery:** Hatcheries can act as a source of *Salmonella enterica* contamination in poultry. If eggs contaminated with the bacteria undergo processing and hatching in a hatchery, it can lead to transmission of the bacteria to the hatched chicks. In several instances in Great Britain, hatcheries have been identified as the originating point of *Salmonella* contamination in broiler flocks [27]. Withenshaw et al., (2021) found that specific practices and features within hatcheries, including higher utilization of hatcher, storage of trays in the process room, drying of set-up trolleys in the corridor, and the placement of skips in an enclosed area, contribute to increased susceptibility to *Salmonella* contamination. For instance, due to a combination of factors including bird owners lacking experience, the presence of the bacteria in various bird species, the stress induced during shipping, and a lack of awareness regarding the significance of proper hand-washing practices, multiple outbreaks of *Salmonella* occurred at a hatchery in Michigan between 1999 and 2001 [28, 29].
3. **Chicks:** Chicks hatched from contaminated eggs can carry *Salmonella enterica*, contributing to the dissemination of the bacteria within the flock. *Salmonella* contamination can occur in chicks, affecting their surface, respiratory tract, or gastrointestinal tract. During the hatching process, strong air currents in the hatcher can carry dust, which includes pathogens that may exist on or inside the eggs, repeatedly recirculating them throughout the cabinet in the final two days of incubation. Research by Cox et al., (1990) has demonstrated that eggshell

fragments can serve as a source of *Salmonella* contamination within hatching cabinets. Furthermore, the dust generated during hatching in commercial hatcheries has been identified as a potential factor in cross-contamination of pathogens to other areas of the hatchery.

4. **Feed and Water:** The introduction of *Salmonella* into poultry feed can occur through various routes, including the presence of contaminated ingredients such as grains or protein sources. When these feed components are contaminated with *Salmonella*, they can serve as a vehicle for bacterial transmission into the feed. Additionally, there is a risk of cross-contamination during the production, handling, and transportation of feed. This means that *Salmonella* from external sources can contaminate the feed, further contributing to the potential contamination. Furthermore, the inadequate implementation of sanitation and hygiene practices in feed mills can be a factor in the introduction of this bacteria into the feed. If proper hygiene measures are not followed, *Salmonella* can easily contaminate the feed during processing. On the other hand, water can also serve as a potential source of *Salmonella enterica* contamination in poultry. Contaminated water sources, which are used for drinking or processing in poultry facilities, can introduce *Salmonella* into the bird's environment. This contaminated water can then facilitate the spread of the bacteria among the poultry population. Additionally, cross-contamination can occur when water comes into contact with fecal matter or other contaminated surfaces, further leading to the contamination of water sources. Moreover, inadequate water treatment methods, such as ineffective disinfection or filtration, can fail to eliminate *Salmonella* from the water supply, posing a risk of

contamination for the poultry. For instance, The Centers for Disease Control and Prevention (CDC) reported that samples taken from the feed and egg water wash facility in Wright County Egg and Hillandale Farms of Iowa during the 2010 outbreak tested positive for *Salmonella*. These positive test results indicated that *Salmonella* contamination in the feed and egg water was a contributing factor to the outbreak [31].

5. **Feces and Litter:** Feces and litter within poultry houses can serve as a source of *Salmonella enterica* contamination. Infected bird feces can contain the bacteria, which, if not properly managed, can contaminate the litter. *S. enterica* can persist in the litter, contributing to the transmission risk within the flock. In the environment of poultry sheds, the presence of *Salmonella* can arise from feces from layer hens, insects, or feces from rodents. In Ouagadougou, Burkina Faso, the prevalence of *Salmonella* in fecal samples obtained from poultry was 52.4%. Similarly, in a poultry farm in South Africa, the prevalence of *Salmonella* in poultry feces was determined to be 12.4% [32, 33].



Figure 2: Environment, Hatchery, Chicks, Feed- water and Feces and litter act as source of *Salmonella* contamination in poultry [34, 35, 36, 37, 38].

2.2: Transmission

The predominant mode of transmission for *Salmonella enterica* in poultry populations encompasses various mechanisms. Vertical transmission, specifically through infected chickens passing on the bacteria to their offspring via eggs, is a prevalent means of spread. Additionally, horizontal transmission can occur through direct contact with contaminated feces, contaminated surfaces, or respiratory droplets from infected birds. Contaminated feed and water sources also have the potential to serve as vehicles for the transmission of *S. enterica* among chicken populations. *Salmonella* can induce clinical illness or subclinical infections in asymptomatic animals referred to as "**carriers**" within farm animal populations. Infected birds act as carriers and can continuously shed the pathogen, increasing the risk of widespread contamination. In the context of hens, a previous

investigation demonstrated that subclinical infections can endure for a period exceeding 22 weeks [39].

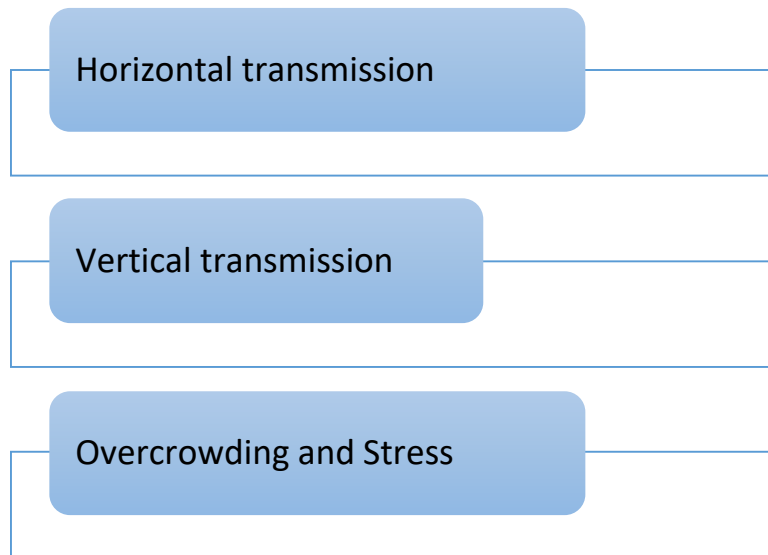


Figure 3: Modes of transmission for *Salmonella* in poultry [25, 40, 41, 42].

- **Horizontal transmission** in poultry refers to the spread of *S. enterica* among birds within the same flock. Horizontal transmission plays a significant role in the overall prevalence and persistence of *S. enterica* within poultry flocks. It plays a significant role in the dissemination and persistence of the pathogen within poultry populations. Several key aspects characterize horizontal transmission in poultry. Higher flock density increases the likelihood of direct contact between birds, facilitating the spread of this contamination. Close contact and interaction among birds provide opportunities for pathogen transfer along with environmental stressors, overcrowding, and poor management practices compromising the birds' immune system, making them more susceptible to *Salmonella enterica* infection and transmission [25]. The transmission can occur through-

Direct contact: Infected birds can transmit *Salmonella enterica* to susceptible birds through direct contact.

Fecal-oral route: Infected birds shed the bacteria in their feces, which can contaminate the environment and be ingested by susceptible birds through pecking or consuming contaminated feed, water, or litter.

Environmental contamination: The pathogen can persist in the poultry environment, including litter, dust, water sources, and surfaces, contributing to indirect transmission. Birds can come into contact with contaminated surfaces, leading to infection.

Amplification and maintenance: Once introduced into a flock, *Salmonella enterica* can undergo amplification and maintenance through horizontal transmission. Infected birds can shed the pathogen for an extended period, providing a continuous source of contamination [40].

- **Vertical transmission** occurs when *S. enterica* infects the reproductive organs of hens, such as the ovaries and oviducts [41]. Infected hens excrete the bacterium in their feces, which can contaminate the outer surface of the eggshell. Additionally, it has the ability to penetrate the eggshell through pores or cracks, reaching the internal contents of the egg, including the developing embryo. As a result, chicks can acquire the infection before hatching, carrying the bacterium in their gastrointestinal tract. The frequency of vertical transmission of *S. enterica* within poultry can fluctuate based on various factors. One significant factor is the prevalence of this bacterium in the breeding stock. In cases where hens are infected

with *Salmonella enterica*, they can introduce the bacterium into their reproductive tract, subsequently raising the probability of vertical transmission.

- In environments characterized by **overcrowding** and suboptimal conditions, **stress** can compromise the birds' immune systems, rendering them more vulnerable to *Salmonella* infections. Within such settings, the bacterium can flourish and propagate at an accelerated pace. In a research investigation carried out by Gomes et al., (2014) in Brazil, it was observed that overcrowding-induced stress resulted in reduced macrophage phagocytosis activity and an elevated presence of *Salmonella* Enteritidis in the livers of birds exposed to the pathogenic bacterium.

Chapter 3: *Salmonella* Enteritidis and *Salmonella* Typhimurium

3.1 Distribution and Prevalence in Poultry

Salmonella Enteritidis and *Salmonella* Typhimurium are highly prevalent in poultry populations globally due to their exceptional ability to adapt to avian hosts and persist within the poultry farm environment. Their capacity to colonize the gastrointestinal tract of birds leads to continual shedding in feces, facilitating their transmission. Vertical transmission from infected hens to their offspring through eggs further contributes to their sustained presence in poultry flocks. Both serotypes are primarily transmitted through the fecal-oral route, causing contamination of the surrounding environment, poultry feed, and water sources.

The survival capability of these serotypes in warm and humid conditions ensures their prevalence and re-infection within poultry. Additionally, as zoonotic pathogens, *S.* Enteritidis and *Salmonella* Typhimurium can pose a significant risk to human health

through the consumption of contaminated poultry products. The worldwide trade and movement of poultry facilitate their introduction and dissemination to new regions. Moreover, the stress and overcrowding inherent in intensive poultry farming create optimal conditions for their rapid transmission and amplification among flocks [25]. Typically, *S. Enteritidis* infections in hens primarily occur through vertical transmission, and contamination of eggs may result from trans ovarian infection. Conversely, *S. Typhimurium* and other serovars tend to contaminate eggs externally through the penetration of the eggshell [5]. Distinct *Salmonella* serovars exhibit varying reservoirs and pathogenic characteristics. The combination of these factors collectively contributes to the extensive and widespread occurrence of *Salmonella* Enteritidis and *Salmonella* Typhimurium in poultry populations across the globe. The reasons behind certain *Salmonella* serovars being responsible for a majority of human diseases remain inadequately understood, with a notable proportion of these serovars belonging to subspecies *enterica*. A comprehensive global survey conducted in the year 1995 revealed that serotypes Enteritidis and Typhimurium stood out as the most prevalent among all isolates [5]. Despite the continuous evolution of various serovars, *Salmonella* Enteritidis and *Salmonella* Typhimurium remain highly prevalent globally.

S. Enteritidis and *S. Typhimurium* have been widely recognized as prevalent serovars causing illness in both humans and animals worldwide for a considerable period. According to the Center for Disease Control and Prevention (CDC) report in 2013, *Salmonella* Enteritidis and Typhimurium were responsible for 27% and 14% of foodborne outbreaks in the US from 2007 to 2011, affecting humans. From investigations in poultry farm in the USA, *S. Enteritidis* (52%) showed highest prevalence (Figure 4) [44]. The

most frequently implicated food items associated with each serovars were eggs, chicken, and chicken, respectively, along with some other food products [44]. In Europe, both *S. Enteritidis* and *S. Typhimurium* have been identified as the most frequently encountered serovars in poultry. In 2017, *S. Enteritidis* was the reason behind 34% of salmonellosis outbreaks through food vehicles (poultry) [8]. Similarly, in China, *Typhimurium* and *Enteritidis* have been reported as the most prevalent serovars in poultry [45]. From Figure 4 and Figure 5 it can be seen that in China, raw poultry samples yielded the presence of *Salmonella Enteritidis* at a rate of 19.2%, while *Salmonella Typhimurium* was identified in 14.6% of the samples [46]. *S. Enteritidis* is responsible for over 70% of all documented cases of salmonellosis in Russia, indicating that the role of other *Salmonellae* in this observed pattern is quite limited [47]. In Sweden, *S. Typhimurium* has demonstrated the highest prevalence in both indoor and outdoor poultry settings which was 66.7% [48]. To add to that, in Australia, *Enteritidis* serovars is commonly associated with human gastroenteritis, while *Typhimurium* serovars is most frequently detected in egg farms. Remarkably, between 2001 and 2016, a striking 84% of Australia's foodborne outbreaks were attributed to *S. Typhimurium*. According to FoodNet Canada's annual report for the year 2016, *Salmonella Enteritidis* was the most prevalent cause of human salmonellosis and represents the serovar most frequently isolated from poultry (25.95%) whereas *S. Typhimurium* was second most prevalent for salmonellosis but found in 2.11% poultry [49]. On the other hand, *S. Typhimurium* ranked as the fourth most common isolate found in poultry products. In South Korea, 66.7% of the poultry samples tested positive for *S. Typhimurium*, making it the most prevalent serovar in that region [50]. From chicken samples in Iraq, 63.2% *S. Enteritidis* and 36.6% *S. Typhimurium* were detected [51].

During the period from 2008 to 2016 in Singapore, *S. Typhimurium* emerged as the most prevalent serovar found in food supply samples. Notably, in poultry, this serovar was more frequently isolated from fresh poultry samples compared to frozen ones (17.9% of the poultry samples). Meanwhile, *S. Enteritidis* ranked as the second most common serovar detected throughout this time frame, with a predominant association (20.12%) mainly observed in poultry samples [52]. Within Iran, a molecular confirmation process validated that *S. Enteritidis* was detected in 25.2% of the analyzed poultry samples [53]. *S. Enteritidis* (43.9%) and *S. Typhimurium* (30.3%) were present on the poultry samples of Pakistan [54]. In their study on poultry samples conducted in India, Mir et al., (2015) identified the presence of *Salmonella* Enteritidis at a rate of 28.13% (Figure 4), and *Salmonella* Typhimurium at a rate of 15.63% (Figure 5). These two serovars exhibited the highest occurrence among the detected strains. 23.1% of *Salmonella* Enteritidis were present in the chicken samples isolated from Saudi Arabia which is one of the most prevalent serovars there [56]. In Turkey, analysis of chicken samples revealed that *S. Enteritidis* accounted for 21.9%, and *S. Typhimurium* comprised 9.4%, ranking as the second and third most prevalent serovars [57]. Research conducted within Nepal reveals that, among the identified serotypes, Typhimurium (49%) and Enteritidis (36%) were the prevailing serotypes, raising significant public health concerns [58]. Strains derived from chosen poultry farms in Kwara State, situated as an intermediary area between the southern and northern parts of Nigeria, demonstrated that 16% of the samples were identified as *S. Typhimurium* which is shown in Figure 5, making it the third most prevalent among the various *Salmonella* serovars present [59]. Additionally, as per data from the World Health

Organization (WHO), Enteritidis stands out as the most commonly isolated serovars among non-typhoidal *Salmonella*, accounting for 65% of all cases.

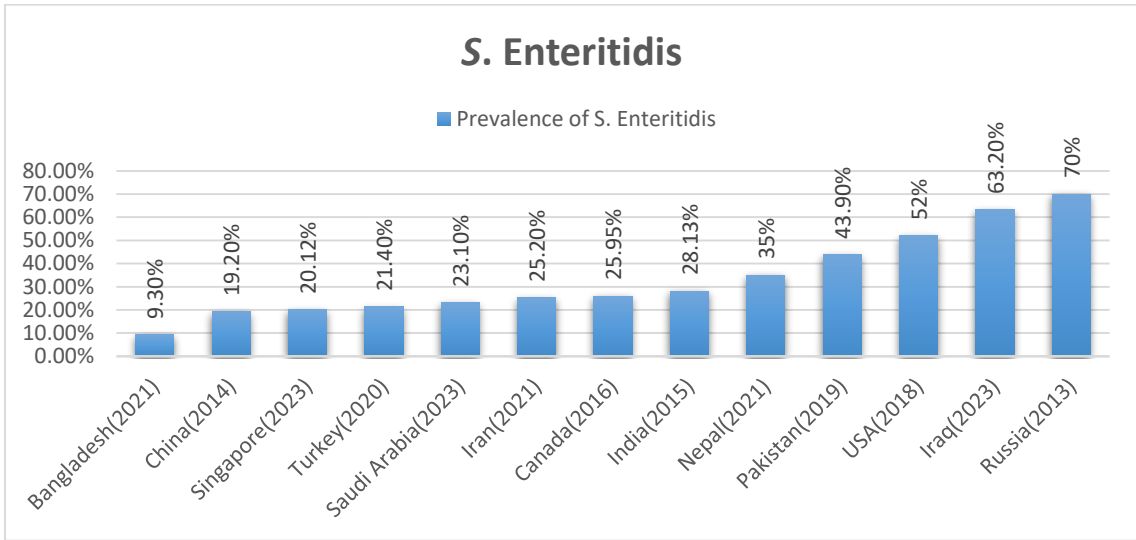


Figure 4: Prevalence of *S. Enteritidis* in poultry samples around the world.

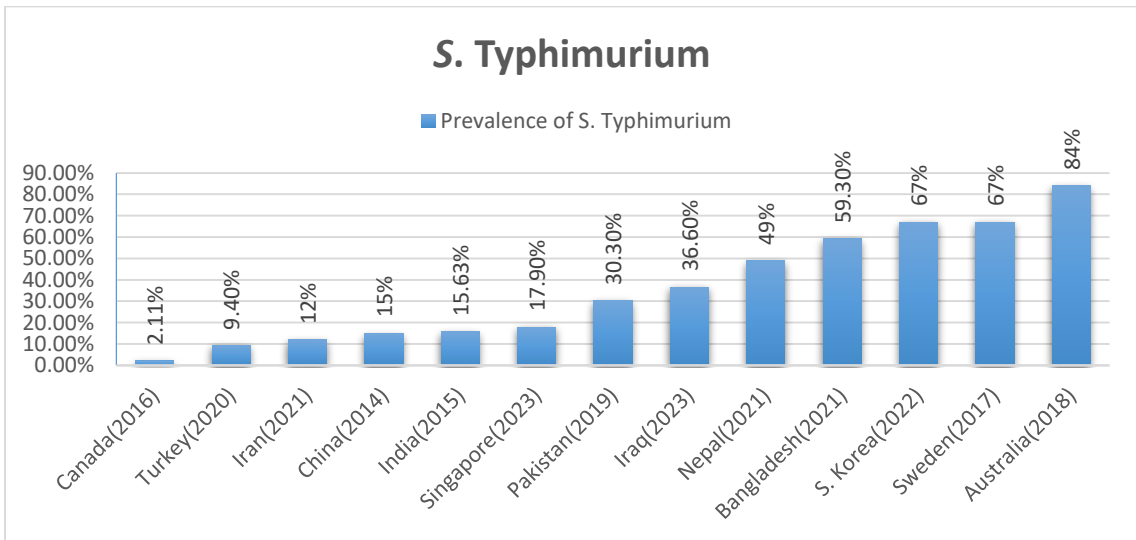


Figure 5: Prevalence of *S. Typhimurium* in poultry samples around the world.

3.2 Influence of Climate Change in the Prevalence

The rise of climate change presents a critical global challenge, influencing various ecological and environmental processes. Within this context, the prevalence of *S. Enteritidis* and *S. Typhimurium* in poultry populations has become a subject of significant concern. These zoonotic pathogens pose substantial health risks to both animals and humans, with potential implications for food safety, security, and the economic stability of the poultry industry. The association between climate change and the prevalence of *S. Enteritidis* along with *S. Typhimurium* in poultry is complex and intricate. As the world experiences escalating temperatures and unpredictable weather patterns, the environment within poultry farms undergoes notable transformations. These alterations have a profound impact on the behavior of the bacteria, affecting its transmission, prevalence, and dissemination among poultry flocks.

3.2.1 Warmer temperature and Changing rainfall patterns

S. Enteritidis exhibits a preference for warmer environments, where optimal conditions facilitate its growth and multiplication within poultry populations. *S. Enteritidis* demonstrates a remarkable ability to flourish in warmer environments, attributed to its adaptability and rapid multiplication under elevated temperatures. As global temperatures surge due to climate change, the bacterium capitalizes on these favorable conditions, establishing itself and spreading within poultry populations. Multiple mechanisms contribute to its success in these warmer climates:

Warmer temperatures expedite the growth and reproduction of *S. Enteritidis*, resulting in a rapid multiplication of the bacterium within infected hosts. In their study, Kynčl et al.,

(2021) demonstrated that, on average, each incremental rise of 1°C in monthly air temperature within their research region corresponded to a substantial escalation of 6.2% in reported cases of salmonellosis. This heightened reproductive rate leads to increased shedding of the pathogen in the feces of infected birds, elevating the likelihood of transmission to other birds within the flock. Elevated temperatures create an environment where *S. Enteritidis* can endure for extended periods outside the host. In these warmer conditions, the bacterium exhibits increased resilience, persisting on various surfaces, including feed, water, and equipment, thereby serving as potential sources of re-infection for the poultry flock. Warmer temperatures foster ideal conditions for the survival of intermediate hosts and vectors, promoting the transmission of the bacteria among birds and within the farm environment. Insects and rodents, known carriers of the bacterium, thrive in these warmer climates and play a significant role in the dissemination of the pathogen [62]. Higher temperatures can impact the immune response of birds, potentially weakening their defense mechanisms against *S. Enteritidis* infection. This compromised immune response may lead to increased susceptibility to the bacterium, resulting in a higher prevalence of the pathogen within the poultry population. *Salmonella* is classified as mesophilic, capable of surviving in temperatures ranging from 2°C to 54°C. Sigma factors, essential components of prokaryotic RNA polymerase, play a pivotal role in cellular responses by redirecting the initiation of transcription. Through sensing environmental changes, alternate sigma factors regulate bacterial gene expression. When exposed to high temperatures, a specific activation and transcription of *rpoH* genes occur, facilitating adaptation to heat stress. In the case of *S. Enteritidis*, the highest transcription of *rpoH* genes was observed at 42°C [5]. External stressors, including heat stress, can lead to the

spread of enteric pathogens like *Salmonella*, posing significant health concerns by potentially elevating animal pathogen presence and release [62]. During the summer months, with elevated temperatures, poultry farms often experience an upsurge in *S. Enteritidis* infections. Infected birds shed more bacteria in their feces due to the accelerated reproductive rate of the pathogen in warmer conditions. Exposure to heat stress has the potential to trigger enteritis in chickens that harbor *Salmonella* in their gastrointestinal tract, increasing the likelihood of bacterial dissemination to other organs [63]. Contaminated feces can subsequently spread throughout the environment, leading to cross-contamination of poultry feed and water sources. Additionally, variations in rainfall patterns and the occurrence of extreme weather events can lead to fluctuations in water availability, potentially aiding the dissemination of *S. Enteritidis* through contaminated water sources [64]. Furthermore, alterations in seasonal patterns may extend the duration of pathogen transmission, creating prolonged opportunities for infection within poultry flocks. As climate change influences the migratory patterns of wild birds, which are known reservoirs of *S. Enteritidis*, there is a possibility of introducing the bacterium to new regions, further contributing to its geographical spread. Climate change exerts a significant influence on *Salmonella* Typhimurium contamination in poultry by altering environmental conditions that affect the bacterium's survival, transmission, and prevalence. Rising temperatures create favorable conditions for the rapid growth and reproduction of *Salmonella* Typhimurium, leading to increased shedding by infected birds and higher contamination rates in the poultry environment. Changes in rainfall patterns can impact water availability and quality, potentially promoting the spread of *S. Typhimurium* through contaminated feed and water sources during excessive rainfall and flooding events [64].

Due to climate change leading to extended warm seasons, there is more time for *S. Typhimurium* to persist in the environment, thereby increasing the opportunities for poultry infection. Additionally, changes in migration patterns of wild birds and vectors can introduce the bacterium to new areas, elevating the risk of contamination in poultry farms.

All in all, environmental stressors induced by elevated temperatures and climate change can weaken the immune response of poultry, making them more susceptible to *Salmonella* infection. In various studies, researchers Murphy et al., (1999), Chen et al., (2013) and Churi et al., (2010) have reported on the elevated heat resistance and thermotolerance of *S. Typhimurium* and *S. Enteritidis* in chicken. The combined impact of these climate change-induced factors creates conditions that favor the survival, transmission, and prevalence of these serovars in poultry, leading to increased contamination rates and posing potential risks to both animal and human health. The intricate interactions between climate change and the prevalence of *S. Enteritidis* and *S. Typhimurium* underscore the imperative of comprehending and addressing the impacts of environmental shifts on foodborne pathogens. Given the substantial public health and economic implications of these serotypes' prevalence in poultry, the implementation of effective strategies to mitigate risks and ensure food safety becomes a paramount concern.

Chapter 4: Antimicrobial Resistance

Antimicrobial resistance, also known as AMR, pertains to the capacity of microorganisms, including bacteria, to endure the impact of antimicrobial medications, thereby diminishing their efficacy or rendering them entirely futile in combating infections induced by these resilient microorganisms. In simpler terms, the germs survive and keep multiplying instead

of being killed. Resistant bacteria persist in the presence of antibiotics, perpetuating their growth and resulting in prolonged illnesses or even fatalities. Infections caused by these resistant bacteria often demand increased medical attention and necessitate the use of alternative, costlier antibiotics, which may carry more pronounced adverse effects. This situation raises a considerable public health concern, as it curtails treatment alternatives and heightens the potential for prolonged and severe infections [68, 69]. *Salmonella* Enteritidis and *Salmonella* Typhimurium can develop resistance to antimicrobial drugs through several critical mechanisms, each playing a vital role in their survival and proliferation despite exposure to antibiotics which is generally the mechanism for many other pathogenic bacteria [70]. **The following are the key mechanisms through which these serovars acquire resistance:**

Enzymatic Inactivation: Antimicrobial resistance can occur through the enzymatic inactivation mechanism, where microorganisms produce enzymes that chemically modify or render antimicrobial drugs ineffective. This resistance is particularly pertinent to antibiotics like beta-lactams (e.g., penicillin, ampicillin) and cephalosporins. One type of enzyme, beta-lactamase, is produced by certain bacteria, including *Salmonella* Enteritidis and *Salmonella* Typhimurium. Beta-lactam antibiotics target bacterial cell wall synthesis by inhibiting penicillin-binding proteins (PBPs), essential for cross-linking peptidoglycan chains in the cell wall. However, beta-lactamase enzymes break down the beta-lactam ring in the antibiotic, leading to its ineffectiveness against the bacterium. Consequently, the bacterium can continue to grow and multiply despite exposure to the antibiotic. Different types of beta-lactamases, such as penicillinases, cephalosporinases, and extended-spectrum beta-lactamases (ESBLs), can inactivate specific classes of beta-lactam antibiotics. ESBLs

are of particular concern as they confer resistance to extended-spectrum cephalosporins, crucial antibiotics for treating severe infections in humans. Plasmids, small DNA fragments, can carry beta-lactamase genes and facilitate their transfer between bacteria through horizontal gene transfer. This rapid spread of resistance genes among bacterial populations contributes to the widespread dissemination of beta-lactam resistance [71]. Moreover, the presence of beta-lactamase genes on plasmids enables bacteria to develop resistance to multiple antibiotics simultaneously, exacerbating the complexity of treatment options. Clinically, the production of beta-lactamase enzymes by *Salmonella* Enteritidis and *Salmonella* Typhimurium poses a significant public health concern. It reduces the effectiveness of beta-lactam antibiotics, which are commonly employed to treat *Salmonella* infections in both humans and animals. The development of beta-lactam resistance can result in treatment inefficacy and more severe infections, particularly affecting vulnerable groups like young children, elderly individuals, and individuals with compromised immune systems. Consequently, addressing this resistance becomes crucial to maintaining effective antibiotic therapy and safeguarding public health.

Efflux Pumps: *Salmonella* can develop resistance through efflux pumps, specialized proteins that actively expel antimicrobial drugs out of the bacterial cell. By reducing the drug concentration within the bacterium, these pumps diminish the drug's efficacy. Efflux pumps confer resistance to various classes of antibiotics, including tetracyclines, fluoroquinolones, and others. Efflux pumps represent a crucial resistance mechanism utilized by bacteria, including *Salmonella* Enteritidis and *Salmonella* Typhimurium, to withstand antimicrobial agents. These specialized membrane proteins actively pump antibiotics and toxic substances out of bacterial cells, reducing their concentration inside

the cells and diminishing the efficacy of antibiotics. Active efflux enables bacteria to survive and thrive in the presence of antibiotics, leading to the development of multidrug resistance [72].

Efflux pumps are integral membrane proteins situated in the bacterial cell membrane, capable of recognizing and binding to specific antibiotics and other substances. Upon entry of drugs or toxic compounds into the bacterial cell, the efflux pump facilitates their transport across the cell membrane and expels them into the extracellular space. This pumping out of antibiotics lowers the intracellular drug concentration, thereby reducing its effectiveness in inhibiting bacterial growth and replication. Bacteria possess various types of efflux pumps, each with specificity for different classes of antibiotics or toxic compounds. One well-known family is the resistance-nodulation-division (RND) superfamily, including AcrAB-TolC in Enterobacteriaceae, such as *Salmonella*. Other significant families include the major facilitator superfamily (MFS) and the ATP-binding cassette family (ABC), which also contribute to antibiotic resistance. In the management of poultry infections, an array of substances is employed, encompassing not only fluoroquinolones but also β -lactams, macrolides, and tetracycline. All of these compounds encounter resistance facilitated by multidrug-resistant (MDR) efflux pumps [72]. Efflux pumps significantly contribute to multidrug resistance as they can expel multiple antibiotics with diverse chemical structures from bacterial cells. When bacteria carry genes encoding for efflux pumps on plasmids or other mobile genetic elements, these pumps can be easily transferred between bacterial strains and species through horizontal gene transfer, promoting the spread of resistance. Efflux pumps found in *S. Enteritidis* and *S. Typhimurium*, such as the AcrAB-TolC pump, play a critical role in the development of

antibiotic resistance. AcrAB-TolC comprises the periplasmic protein AcrA, the efflux transporter AcrB, and the outer membrane channel protein TolC [73]. These pumps actively transport antibiotics out of the bacterial cell, reducing the intracellular drug concentration and diminishing the antibiotics' effectiveness in inhibiting bacterial growth. For example, Fluoroquinolones- ciprofloxacin and levofloxacin, are important antibiotics for treating *Salmonella* infections. However, the AcrAB-TolC efflux pump in *Salmonella* can effectively pump out fluoroquinolones, reducing the drug concentration within the cell and leading to reduced susceptibility to these antibiotics [50]. Tetracyclines, including doxycycline and tetracycline, are commonly used to treat various bacterial infections, including *Salmonella*. The efflux pumps in these serovars can actively expel tetracyclines, reducing their concentration inside the bacterial cell and resulting in resistance to these antibiotics [50]. Aminoglycoside antibiotics, including gentamicin and kanamycin, are used to treat severe bacterial infections. However, efflux pumps in *Salmonella* can actively pump out aminoglycosides, leading to reduced drug levels inside the bacterial cell and resulting in resistance to these antibiotics [50]. Multidrug-resistant *Salmonella* strains, driven by efflux pump-mediated resistance, can lead to treatment failures and pose significant challenges to public health. Researchers are investigating the development of efflux pump inhibitors (EPIs) as potential therapeutic agents. EPIs can block the activity of efflux pumps, increasing the intracellular concentration of antibiotics and enhancing their effectiveness against resistant bacteria.

Target Modification: Target modification stands as a critical mechanism utilized by *S. Enteritidis* and *S. Typhimurium* to develop resistance to specific antibiotics, with fluoroquinolones serving as a notable example. In pursuit of this objective, bacteria have

developed varied strategies, encompassing safeguarding the intended target (preventing the antibiotic from reaching its binding site) and introducing alterations to the target site that lead to reduced affinity for the antibiotic molecule [72]. These antibiotics work by targeting essential bacterial enzymes, such as DNA gyrase and topoisomerase IV, which play vital roles in DNA replication and repair. Through interference with these crucial processes, fluoroquinolones induce bacterial cell death, effectively treating infections caused by susceptible bacteria.

An illustration of this resistance mechanism can be observed with the fluoroquinolone antibiotic, Ciprofloxacin, commonly used to treat infections caused by *S. Enteritidis* and *S. Typhimurium*. However, in resistant strains of these serovars, specific mutations occur in the genes encoding DNA gyrase and topoisomerase IV [2]. These genetic alterations lead to structural changes in these enzymes, resulting in reduced binding affinity of fluoroquinolones to their target sites. Consequently, the antibiotic's capacity to inhibit DNA synthesis is weakened, allowing the bacterium to continue its cell wall synthesis and replication despite the presence of fluoroquinolones [74]. As a consequence, the antibiotic's potency in treating the infection is diminished. The emergence of such resistance poses significant challenges in the management and control of *Salmonella* infections, both in terms of human health and in poultry populations.

Reduced Drug Uptake: Another mechanism through which *Salmonella* Enteritidis and *S. Typhimurium* develop resistance to antimicrobial agents is reduced drug uptake. These serovars have the capability to modify their cell membrane structure, which results in the limited entry or uptake of certain antibiotics into the bacterial cell. Consequently, the concentration of the drug inside the bacterium becomes insufficient to effectively exert its

antimicrobial effect [2]. An example of reduced drug uptake is observed with aminoglycoside antibiotics like gentamicin and kanamycin. Typically, aminoglycosides work by binding to bacterial ribosomes and disrupting protein synthesis, ultimately causing cell death. However, in resistant *Salmonella* strains, alterations in the cell membrane can hinder the entry of aminoglycosides, leading to a reduction in their ability to bind to the ribosomes and exert their bactericidal effects [75]. This alteration in drug uptake contributes to the development of resistance in these serovars, presenting a challenge for effective antimicrobial treatment.

Plasmid-Mediated Resistance: Plasmid-mediated resistance represents a significant mechanism utilized by *S. Enteritidis* and *S. Typhimurium* to acquire resistance to antimicrobial agents. Plasmids, small self-replicating pieces of DNA, play a crucial role in this process by carrying one or more resistance genes. These plasmids have the ability to exist independently within the bacterial cell and replicate autonomously, separate from the bacterial chromosome. Additionally, they facilitate the transfer of resistance genes between bacterial cells through horizontal gene transfer [76, 77]. *Salmonella* serovars have the capacity to acquire plasmids containing specific resistance genes, which confer resistance to particular antibiotics. These serovars may also possess additional mobile components like transposons and integrons. As a result, they enhance phenotypic variability and offer adaptive benefits in response to shifts in the environment. This dynamic allows the host to capitalize on prospects for expanding its ecological niche [2]. An illustrative example of plasmid-mediated resistance involves the acquisition of a plasmid containing the beta-lactamase gene. This particular gene encodes an enzyme known as beta-lactamase, which is capable of breaking down the beta-lactam ring present in beta-lactam antibiotics like

penicillin and ampicillin. When *Salmonella* Enteritidis or *Salmonella* Typhimurium acquires a plasmid carrying the beta-lactamase gene, the bacterium gains the ability to produce this enzyme. Consequently, when exposed to beta-lactam antibiotics, the produced enzyme degrades the antibiotic, rendering it ineffective in inhibiting bacterial growth and multiplication. This acquired resistance poses significant challenges in effectively managing *Salmonella* infections, particularly as antibiotics become less effective due to plasmid-mediated resistance mechanisms [71].

In the context of antibiotic resistance, *S. Enteritidis* and *S. Typhimurium* demonstrate a notable proficiency in employing a combination of resistance mechanisms simultaneously. This strategic utilization of diverse mechanisms renders them formidable adversaries against antibiotic treatment, enabling the bacteria to withstand the effects of multiple antibiotics. Frequently, these bacteria exhibit a combination of multiple mechanisms concurrently to guarantee comprehensive defense against the biologically active compounds they generate [78]. This amalgamation of resistance mechanisms confers a heightened level of protection to the bacteria against various classes of antibiotics. MDR *Salmonella* strains exhibit resistance to multiple classes of antibiotics, severely restricting the treatment options available to healthcare professionals. The emergence and spread of MDR *Salmonella* strains raise significant public health concerns, as infections caused by these resistant strains are harder to treat and may lead to more severe illness and increased mortality rates. The consistent growth of combination resistance in *Salmonella* Enteritidis and *Salmonella* Typhimurium can be attributed to the selective pressure imposed by the widespread use of antibiotics. Inappropriate usage of antibiotics in both human medicine

and agriculture has created an environment conducive to the selection and persistence of bacteria with multiple resistance mechanisms [51,79].

4.1 Antimicrobial Resistance in *Salmonella* Enteritidis and *Salmonella* Typhimurium Affecting Animal Lives

The rising occurrence of antimicrobial resistance (AMR), has sparked considerable concern due to its far-reaching impact on both animal health and public well-being. This heightened attention is driven by the significant consequences of AMR in various serovars, which affect the welfare of animals and the health of humans [80]. The anticipation is that by 2050, the issue of antimicrobial resistance (AMR) will lead to hundreds of millions of human fatalities, coupled with significant economic turmoil and extensive harm to livestock industries [81]. *Salmonella* Enteritidis and *Salmonella* Typhimurium are particularly noteworthy due to their significant roles as causative agents of infections in both human and animal populations worldwide. These serovars have demonstrated a remarkable capacity to adapt and persist across various host species, including poultry, making them a focal point for AMR monitoring and control efforts. To comprehensively assess the extent of AMR prevalence, numerous studies and surveillance initiatives have been carried out in diverse regions globally. These serovars are significant contributors to foodborne infections, causing a spectrum of symptoms ranging from mild gastrointestinal discomfort to severe illness. The rise of AMR within these bacterial strains adds complexity to treatment choices, rendering infections more challenging to control and potentially resulting in treatment failures [82]. This presents a considerable menace to public health by diminishing the efficacy of commonly employed antibiotics for managing such infections. Concerning animal well-being, AMR in *Salmonella* variants exerts an

influence on livestock, notably in poultry farming. Infected animals can harbor resistant strains, which may subsequently infiltrate the food chain, transmitting to humans through contaminated food items. According to earlier investigations, the utilization of antibiotics for non-therapeutic intentions in livestock such as poultry, swine, and cattle exceeded the quantities administered to humans by several magnitudes. The widespread application of antibiotics in animal husbandry for the aforementioned reasons has also played a role in fostering the emergence of bacteria resistant to drugs. The interconnectedness of these bacteria has additionally been recognized in the human food supply chain [83]. To add to that, AMR can lead to increased mortality rates in both humans and animals. In regions with limited access to effective antibiotics, such as certain parts of low-income countries, the impact of AMR can be particularly devastating [82]. The degree of resistance observed can be influenced by a range of intricate factors which are environmental elements like population density, rapid transmission due to mass travel, inadequate sanitation, ineffective infection control programs, and widespread agricultural use of antibiotics. Additionally, challenges related to drugs, such as the presence of counterfeit or substandard medications and unrestricted over-the-counter availability, contribute significantly. Patient-related factors, including non-compliance, poverty, limited education, self-medication, and misconceptions, play a substantial role. Lastly, the practices of healthcare providers, like inappropriate prescription practices, insufficient dosing, and outdated knowledge and training, also contribute to the complex landscape of AMR [84]. Crucially, the prevalence of AMR is not uniform and can exhibit significant variation not only between different countries but also within the same nation or among distinct poultry production systems. Considering the substantial role of poultry farming in global food production and

antimicrobial usage, it becomes imperative to address the evident increase in antibiotic administration within this sector. This step is crucial to enhance the responsible management of antimicrobials [80].

4.2 AMR's Global Statistics of *Salmonella* Enteritidis and *Salmonella* Typhimurium from Poultry

The issue of antimicrobial resistance (AMR) remains a substantial obstacle to worldwide health, food safety, and animal well-being. Notably, *Salmonella* Enteritidis is a significant bacterial pathogen, given its capacity to induce foodborne illnesses in both human and animal populations. The widespread emergence and dissemination of AMR in *S. Enteritidis* as well as *Salmonella* Typhimurium among poultry populations have elicited considerable apprehension globally. Infections caused by multidrug-resistant *Salmonella enterica* serotype Typhimurium have been correlated with an elevated likelihood of invasive infection, increased incidence and prolonged hospital stays, extended periods of illness, and heightened mortality risk in comparison to infections resulting from strains that are susceptible to treatment, as stated by the World Health Organization [60]. Antimicrobial resistance around the world has prompted the recognition of the imperative need for unified and collaborative endeavors to combat this overarching global risk. The intricate problem of antimicrobial resistance (AMR) is emphasized in the following comprehensive analysis spanning multiple countries across various continents-

Europe: In this context, the data compiled from various European countries shed light on the prevalence of antibiotic resistance in *Salmonella* Enteritidis strains isolated from different types of poultry. The information derives from the 'European Union Summary

Report on Antimicrobial Resistance (EUSR) in Zoonotic and Indicator Bacteria from Humans, Animals, and Food for the years 2019/2020': -

Among the antibiotics investigated, three displayed relatively high resistance rates across multiple countries and poultry types: colistin (COL), nalidixic Acid (NAL), and ciprofloxacin (CIP). NAL average resistance from total poultry population was 33.28%, CIP average resistance was 33.43% and COL average resistance was 10.43%. Notable resistance to these antibiotics was observed in various countries. colistin resistance ranged from negligible to relatively higher percentages. Countries such as Belgium, Greece, and Romania reporting resistance percentages as high as 60%. nalidixic Acid resistance was more pronounced, especially in fattening turkeys. On average, resistance was 44.5%, with Croatia, Cyprus, and Slovakia exhibiting resistance percentages over 90%. ciprofloxacin resistance rates were substantial across all three types of poultry, with broilers showing an average resistance of 53.1% (Table 2). Particularly high resistance percentages were reported in countries such as Austria, Greece, and Romania. Conversely, several antibiotics demonstrated minimal resistance across countries and poultry types: gentamicin (GEN), chloramphenicol (CHL), ampicillin (AMP), cefotaxime (CTX), and ceftazidime (CAZ) displayed very low resistance rates, often below 1%. Antibiotics like meropenem (MEM), tigecycline (TGC), azithromycin (AZM), trimethoprim (TMP), tetracycline (TET), sulfamethoxazole (TMS), and trimethoprim/ sulfadimethoxine (TMP/SMX) also exhibited minimal resistance. The lower resistance to other antibiotics points towards responsible antibiotic practices in the poultry industry within those region [85].

United of States of America: The provided data outlines the prevalent antimicrobial resistance phenotypes among *Salmonella* serovars isolated from the production and

processing of consecutive commercial broiler flocks in the USA. By emerging data mentioned in that study, in *Salmonella* Typhimurium following resistance rates were observed: 34.95% to streptomycin (STR), 13.25% to gentamicin (GEN), 14.55% to sulfadimethoxine (SMX), 11.3% to tetracycline (TET), 9.3% to trimethoprim/sulfamethoxazole (TMS), and around 13.9% of *S. Typhimurium* isolates were classified as multidrug resistant (resistant to three or more antibiotics). *S. Typhimurium* displayed higher levels of resistance, particularly to streptomycin [86]. From another conducted study, *S. Enteritidis* from poultry in the USA showed resistance to ceftriaxone + nalidixic acid, azithromycin + tetracycline and tetracycline [43].

China: The data extracted from raw poultry samples in China provided insights into the antibiotic resistance patterns of *Salmonella* Enteritidis and *Salmonella* Typhimurium isolates. The study by Yang et al., (2014) examined various antibiotics and revealed varying levels of resistance across different serotypes. Among the antibiotics tested, the highest resistance rates were observed for certain antibiotics. For *S. Enteritidis* isolates, the highest resistance rates were seen for sulfisoxazole (66.6%), followed closely by nalidixic acid (69.4%) and tetracycline (62.7%). Ampicillin also exhibited notable resistance at 54.2%. Similarly, resistance rates were relatively high for trimethoprim-sulfamethoxazole (41.9%) and amoxicillin-clavulanic acid (39.1%).

On the contrary, *S. Typhimurium* isolates displayed lower resistance percentages for most antibiotics compared to Enteritidis. Among the highest resistance rates in Typhimurium, tetracycline resistance was observed in 67.2%, followed by sulfisoxazole (70.9%), nalidixic acid (59.0%), and ampicillin (50.8%). As listed in Table 2, these findings emphasize that certain antibiotics, such as sulfisoxazole, nalidixic acid, and tetracycline,

showed consistently high resistance across both *Salmonella* Enteritidis and Typhimurium isolates. The varying resistance patterns among different antibiotics and serotypes highlight the complexity of antibiotic resistance in poultry samples [46].

Ethiopia: This following data shows antimicrobial resistance in *S. Typhimurium* in poultry farms in Ethiopia- All *S. Typhimurium* isolates showed resistance to cephalothin. *S. Typhimurium* displayed a high resistance rate of 100% to ciprofloxacin. There was no observed resistance to cefoxitin. Similarly, no resistance to gentamicin was observed and 66.7% of isolates were resistant to kanamycin. *S. Typhimurium* exhibited 100% resistance to sulfamethoxazole trimethoprim. All *S. Typhimurium* isolates were resistant to trimethoprim. A total of 33.3% of these isolates were resistant to tetracycline. 100% of the isolates displayed resistance to sulfisoxazole. Similarly, all isolates exhibited resistance to streptomycin. A portion of the isolates (33.3%) were resistant to nitrofurantoin and showed 100% resistance to nalidixic acid. No neomycin resistance was observed among them. Particularly, high resistance rates were evident for ciprofloxacin, sulfamethoxazole + trimethoprim, trimethoprim, sulfisoxazole, streptomycin, and nalidixic acid [87].

Iran: The antimicrobial resistance profiles of *Salmonella enterica* serotype Enteritidis and Typhimurium strains sourced from chicken samples in Iran reflect varying degrees of resistance against different antibiotics. Bahramianfard et al., (2021) reported some data that showcases the prevalence of resistance for each antibiotic. The investigation into antibiotic resistance patterns within *Salmonella* Enteritidis isolates from poultry and egg samples in Iran provides valuable insights into the prevailing landscape of resistance. Among the total of 63 *S. Enteritidis* isolates subjected to scrutiny, a diversity of antibiotic resistance profiles emerged, shedding light on the formidable challenges posed by these pathogens.

Noteworthy is the conspicuous prevalence of resistance to nalidixic acid, as evidenced by 55 out of the 63 isolates (87.3%) exhibiting this resistance. Another salient resistance pertained to trimethoprim-sulfamethoxazole, discernible in 13 isolates (20.6%). Furthermore, resistance to cephalothin was ascertained in 12 isolates (19.0%), while ceftazidime resistance was established in 7 isolates (11.1%). The findings additionally underscore resistance to colistin sulfate, with 15 isolates (23.8%) manifesting this resistance. Notably, kanamycin resistance was evident in 16 isolates (25.4%), contributing to the intricate tapestry of antibiotic resistance patterns observed [53].

Another research endeavor was undertaken by Nazari et al. (2023), within poultry meat establishments in Iran to evaluate the prevalence of *Salmonella* Typhimurium among poultry. This study also delved into the antimicrobial resistance patterns of the identified strains. The outcomes unveiled a range of responses encompassing resistance, intermediate susceptibility, and susceptibility to various antimicrobial agents. The resistance rate of tetracycline (TET) was observed to be 72.2%, ampicillin (AMP) resistance was observed in 16.7% of the isolates. cotrimoxazole (COT) resistance was noted in 66.7%. chloramphenicol (C) resistance was seen in 16.7%. gentamicin (GEN) resistance accounted for 11.2%. nalidixic acid (NA) resistance was found in 61.2%. nitrofurantoin (NIT) resistance was prevalent in 58.3%. meropenem (MRP) exhibited resistance in 13.4%. cefotaxime (CTX) resistance was detected at 11.2%. ciprofloxacin (CIP) resistance was noted in 19.5%. imipenem (IPM) resistance accounted for 16.7% and piperacillin/tazobactam (PIT) showcased resistance in 58.3% [88].

Bangladesh: Within the framework of Bangladesh, where the poultry industry's significance in ensuring food production and security is pivotal, the rise and dissemination

of antimicrobial resistance (AMR) among *Salmonella* serovars have escalated concerns. More specifically, the investigation carried out in the wet markets of Bangladesh yields valuable insights into the prevailing occurrence of and resistance tendencies exhibited by *Salmonella enterica* serovars Typhimurium and Enteritidis across diverse chicken populations. The analysis of AMR trends within these specific contexts furnishes indispensable insights for comprehending the intricate dynamics of resistance, the divergences observed among different serovars and chicken breeds, and the broader implications it engenders for the well-being of both animals and humans. The antimicrobial resistance (AMR) patterns of *Salmonella enterica* serovars, Typhimurium and Enteritidis, have been analyzed within different chicken populations, including broiler, sonali, and native breeds. The data reveals varying levels of resistance to different antimicrobials in these chicken populations.

-For *S. Typhimurium*: High resistance was observed to ciprofloxacin (100%), streptomycin (100%), tetracycline (86.7%), nalidixic acid (86.7%), and gentamicin (86.7%). Moderate resistance was observed to ampicillin (66.7%). Lower resistance rates were observed to azithromycin (13.3%), amoxicillin–clavulanate (40%), aztreonam (6.7%), ceftazidime (13.3%), ceftriaxone (13.3%), and cefotaxime (13.3%). Resistance was absent for sulfamethoxazole - trimethoprim, amikacin, meropenem, and chloramphenicol (Table 2).

-For *S. Enteritidis*: High resistance was observed to ciprofloxacin (80%), streptomycin (100%), tetracycline (80%), nalidixic acid (60%), and gentamicin (80%). Moderate resistance was observed to ampicillin (60%). Lower resistance rates were observed to azithromycin (20%), amoxicillin–clavulanate (20%), and ceftazidime (20%). Resistance

was absent for aztreonam, ceftriaxone, cefotaxime, sulfamethoxazole-trimethoprim, amikacin, meropenem, and chloramphenicol [89].

Iraq: An analysis from marketplaces in Iraq revealed varying levels of resistance to different antibiotics from chicken samples. Notably, antibiotics like sulfamethoxazole - trimethoprim and tetracycline exhibited a high resistance prevalence of 63.2%, while resistance to ciprofloxacin was relatively lower at 15.8% (Table 2). The combined resistance prevalence for *Salmonella* Enteritidis across all antibiotics was 58.9%, slightly higher than the 47.4% observed for *Salmonella* Typhimurium. Approximately 31.6% of the combined raw and frozen chicken meat samples showed resistance to amikacin. Around 24.0% of the analyzed chicken meat samples displayed resistance to gentamicin and the identified resistance indicates a notable proportion of *Salmonella* strains showing diminished susceptibility to this drug. In the case of cefoxitin, the resistance rate was 21.1% in the combined samples. Around 21.1% of the *Salmonella* isolates demonstrated resistance to ceftriaxone. The resistance prevalence for cefotaxime/clavulanic acid was also 21.1%. sulfamethoxazole - trimethoprim displayed the highest resistance rate at 63.2%. The significant resistance found indicates the potential limitations of its effectiveness. Around 42.1% of the analyzed samples exhibited resistance to aztreonam. A resistance rate of 47.4% was observed for ampicillin. Ampicillin is a commonly used antibiotic, and its relatively high resistance prevalence raises concerns. Approximately 37.9% of the samples showed resistance to chloramphenicol. Ciprofloxacin resistance was found in 15.8% of the samples. A notable resistance prevalence of 73.7% was observed for nalidixic acid. Similar to sulfamethoxazole - trimethoprim, tetracycline displayed a resistance rate of 63.2%.

tetracycline is a widely used antibiotic, and the significant resistance observed highlights the need for careful management of antibiotic use [51].

Brazil: *S. Typhimurium* and *Enteritidis* are two prevalent serovars found in Brazilian poultry production. These serovars have exhibited varying levels of resistance to a range of antibiotics. Phenotypic resistance has been reported in *S. Typhimurium* against the following antibiotics- aminoglycoside, ampicillin, aztreonam, cefepime, ceftriaxone, chloramphenicol, ciprofloxacin, colistin, doxycycline, fluoroquinolone, gentamicin, nalidixic acid, streptomycin, sulfamethoxazole, sulfonamide, tetracycline and trimethoprim. In *S. Enteritidis* resistance has been reported against the antibiotics which are gentamicin, nalidixic acid, streptomycin, sulfonamide, tetracycline and trimethoprim-sulfamethoxazole. These findings from this nation also indicate that both *S. Typhimurium* and *S. Enteritidis* exhibit resistance to a significant number of antibiotics commonly used for the treatment and prevention of this bacteria [90].

Nigeria: AMR in *S. Typhimurium* in poultry samples from Nigeria, revealed that all isolates displayed 100% resistance to ampicillin, cefotaxime, and neomycin, indicating the prevalence of resistance against these antibiotics which is listed in Table 2. Moreover, around 67% of the isolates exhibited resistance to chloramphenicol, ciprofloxacin, and streptomycin. Additionally, 56% of the isolates showed resistance to ceftazidime and gentamicin, while 33% demonstrated resistance to compound sulphonamides. Notably, 78% of the *S. Typhimurium* isolates were resistant to nalidixic acid and tetracycline [59].

South Korea: *Salmonella* serovars *Typhimurium* and *Enteritidis* are prevalent in South Korea's chicken, duck, pork, beef, etc. which covers a great proportion of their food source.

As a result of their prevalence foodborne illness frequently occurs in that country. Investigations in South Korea led by Kim et al., (2021), detected the prevalence of *Salmonella* serovars *S. Typhimurium* and *S. Enteritidis* from poultry. In this case, erythromycin and nalidixic acid showed 100% and 50% resistance respectively in *S. Typhimurium* isolates while other antibiotics showed less than 30% resistance. In case of *S. Enteritidis* ampicillin, erythromycin, nalidixic acid, tetracycline, kanamycin, gentamicin, cefotaxime, cefuroxime, cefuroxime, cefazolin, streptomycin, and ciprofloxacin showed resistance of 100%, indicating that all tested isolates were resistant to these antibiotics. All were multidrug resistant and 12 out of the 18 antibiotics showed 100% resistance which is a matter of concern. Trimethoprim/sulfamethoxazole, ciprofloxacin, cefepime, amoxicillin/clavulanic acid, amikacin and ceftiofur showed lower resistance in these serovars [91].

Saudi Arabia: The poultry sector in Saudi Arabia has witnessed substantial expansion, driven by a surge in demand for lean and protein-rich diets. This has resulted in a noteworthy rise in poultry consumption. Poultry holds a prominent position among animal protein choices in Saudi Arabia. However, meeting public demands requires effective disease management through rigorous animal husbandry practices, therapeutic interventions, including antimicrobial drug administration and vaccinations. As a result of increased consumer preference, the Saudi poultry industry faces the challenge of addressing diseases and infections while adhering to comprehensive strategies for sustainable production [56]. The data provided by Alzahrani et al., (2023) illustrates the antimicrobial resistance percentages observed in *Salmonella* Enteritidis isolated from chicken samples in Saudi Arabia. Among the antibiotics tested, the following resistance

rates were recorded: ampicillin (AMP) resistance was observed in 77.7% of the samples, nalidixic acid (NAL) resistance in 88.8%, tetracycline (TET) resistance in 88.8%, gentamicin (GEN) resistance in 11%, amoxicillin/clavulanic acid (AMC) resistance in 11%, sulfamethoxazole (SXZ) resistance in 11%, and cefoxitin (FOX) resistance in 11%. Specifically, 7 out of the 9 samples exhibited resistance to ampicillin, 8 out of 9 samples were resistant to nalidixic acid, tetracycline whereas gentamicin, amoxicillin/clavulanic acid, sulfamethoxazole, and cefoxitin resistance were shown by 1 out of the 9 samples each.

Table 2: Antimicrobial Resistance in Poultry from Various Countries

Country	<i>Salmonella</i> Serovar	Antibiotics with High Resistance	Year	Source
Europe	<i>S. Enteritidis</i>	nalidixic acid: 33.28%, ciprofloxacin: 33.43%, colistin: 10.43%	2022	[85]
United States of America	<i>S. Typhimurium</i>	streptomycin: 34.95%, gentamicin: 13.25%, sulfamethoxazole: 14.55%, tetracycline: 11.3%, sulfamethoxazole: 9.3%, Multidrug Resistant: 13.9%	2017	[86]
China	<i>S. Enteritidis</i>	sulfisoxazole: 66.6%, nalidixic acid: 69.4%, tetracycline: 62.7%, ampicillin: 54.2%, trimethoprim- sulfamethoxazole: 41.9%, amoxicillin–clavulanic acid: 39.1%	2014	[46]
Ethiopia	<i>S. Typhimurium</i>	ciprofloxacin: 100%, tetracycline: 86.7%, nalidixic acid: 86.7%, gentamicin:	2018	[87]

		86.7%, ampicillin: 66.7%, Multidrug Resistant: 100%		
Iran	<i>S. Enteritidis</i> , <i>S. Typhimurium</i>	nalidixic acid: 87.3%, trimethoprim- sulfamethoxazole: 20.6%, colistin sulfate: 23.8%. tetracycline: 72.2%, ampicillin: 16.7%, cotrimoxazole: 66.7%, nalidixic acid: 61.2%, nitrofurantoin: 58.3%, ciprofloxacin: 19.5%, piperacillin/tazobactam: 58.3%.	2021, 2023	[53, 88]
Bangladesh	<i>S. Typhimurium</i> , <i>S. Enteritidis</i>	streptomycin : 100%, ampicillin: 64%, gentamicin: 83%, tetracycline: 83%, ciprofloxacin: 90%	2021	[89]
Iraq	<i>S. Enteritidis</i> , <i>S. Typhimurium</i>	nalidixic acid: 73.3%, sulfamethoxazole- trimethoprim: 63.2%, tetracycline: 63.2%, ciprofloxacin: 15.8%	2023	[51]

Brazil	<i>S. Typhimurium</i> , <i>S. Enteritidis</i>	gentamicin, nalidixic acid, streptomycin, sulfamethoxazole, sulfonamide, tetracycline and trimethoprim. Multidrug resistant	2021	[90]
South Korea	<i>S. Typhimurium</i> , <i>S. Enteritidis</i>	nalidixic acid: 50%, and all other (erythromycin, nalidixic acid, ampicillin, tetracycline, kanamycin, gentamicin, cefotaxime, cefuroxime, cefuroxime, cefazolin, streptomycin, ciprofloxacin): 100%, Multidrug Resistant: 100%	2022	[91]
Saudi Arabia	<i>S. Enteritidis</i>	ampicillin: 77.7%, nalidixic acid: 88.8%, tetracycline: 88.8%, gentamicin: 11%, amoxicillin/clavulanic acid: 11%, sulfamethoxazole: 11%, cefoxitin: 11%	2023	[56]

All in all, across various countries from different continents around the globe, including Europe, USA, China, Ethiopia, Iran, Bangladesh, Iraq, Brazil, S. Korea, and Saudi Arabia, extensive studies have highlighted the concerning prevalence of antibiotic resistance in *Salmonella* strains isolated from poultry. In Europe, high resistance rates were observed for colistin (COL), nalidixic acid (NAL), and ciprofloxacin (CIP) across multiple countries and poultry types. Conversely, antibiotics like gentamicin (GEN), chloramphenicol (CHL), ampicillin (AMP), cefotaxime (CTX), and ceftazidime (CAZ) exhibited minimal resistance. The USA displayed varying resistance percentages in *Salmonella* Typhimurium, with higher levels of resistance observed for certain antibiotics. To add to that, in China, *Salmonella* Enteritidis isolates displayed higher resistance rates for sulfisoxazole, nalidixic acid, tetracycline, ampicillin, trimethoprim-sulfamethoxazole, and amoxicillin-clavulanic acid. On the other hand, *Salmonella* Typhimurium isolates exhibited lower resistance percentages for most antibiotics compared to Enteritidis, with tetracycline, sulfisoxazole, nalidixic acid, and ampicillin showing the highest resistance rates. In Ethiopia, *S.* Typhimurium exhibited resistance to multiple antibiotics, highlighting the need for prudent antibiotic management. Iran's studies highlighted the prevalence of resistance among different serovars, including *S.* Enteritidis, emphasizing the complex dynamics of antibiotic resistance. Iraq's research indicated variable resistance rates in chicken samples, raising concerns about the effectiveness of certain antibiotics. In Brazil, both *S.* Typhimurium and *S.* Enteritidis demonstrated resistance to several commonly used antibiotics. Nigeria's data underscored high resistance rates in *S.* Typhimurium isolates, particularly against ampicillin and tetracycline. South Korea reported concerning multidrug resistance in *Salmonella* serovars, indicating a significant public health

challenge. The Saudi Arabian poultry industry has expanded to meet consumer demands, necessitating effective disease management strategies through antimicrobial drug administration and vaccinations. Notably, Saudi Arabia exhibited resistance to multiple antibiotics in *Salmonella* Enteritidis, further emphasizing the urgency of tackling antibiotic resistance in the poultry sector. Among the antibiotics tested in various countries, several consistently showed higher levels of resistance across different *Salmonella* serovars isolated from poultry. Table 2 showed that notable patterns of higher resistance were observed for antibiotics such as ciprofloxacin, nalidixic acid, tetracycline and gentamicin. ciprofloxacin and nalidixic acid exhibited substantial resistance across multiple countries and poultry types. In Europe, ciprofloxacin and nalidixic acid resistance rates were noteworthy, with an average resistance of 33.43% and 33.28%, respectively. In Saudi Arabia, *Salmonella* Enteritidis isolates displayed 80% resistance to ciprofloxacin, while in *S. Typhimurium*, 100% resistance was observed. Similarly, high resistance to nalidixic acid was evident across various countries, with some strains reaching resistance levels over 90%. tetracycline resistance was consistently observed across several countries. In Europe, an average resistance of 88.8% was reported for tetracycline in *Salmonella* Enteritidis strains. In Saudi Arabia, tetracycline resistance was also 88.8% in *S. Enteritidis* isolates. Both *S. Typhimurium* and *S. Enteritidis* strains in Bangladesh showed substantial tetracycline resistance, reaching 83% on average for both of the cases. gentamicin resistance was another concern in different regions. Notably, in Saudi Arabia, 11% of *Salmonella* Enteritidis samples displayed resistance to gentamicin. In the USA, 13.25% of *S. Typhimurium* isolates showed resistance to gentamicin. In Iran, *S. Typhimurium* displayed resistance to gentamicin in 86.7% of cases (Table 2). The higher resistance rates

observed for these antibiotics across various regions and *Salmonella* serovars indicate the widespread challenge of antibiotic resistance in poultry. The recurrent resistance to ciprofloxacin, nalidixic acid, tetracycline, and gentamicin underscores the importance of prudent antibiotic use, rigorous disease management practices, and the need for continuous surveillance to mitigate the rise of antimicrobial resistance in the poultry industry.

Chapter 5: Impact of Salmonellosis in Economic Loss

Salmonellosis poses a significant economic burden in various countries, with costs extending into millions and billions of dollars annually. The economic ramifications of salmonellosis, a widespread bacterial infection caused by different *Salmonella* serotypes, are a critical concern on a global scale. The financial burden inflicted by this ailment, running into millions and billions of dollars yearly, profoundly impacts economies, industries, and public health systems. Across nations, the economic toll varies significantly.

For instance, Denmark experiences an annual cost of around 32.4 million USD due to salmonellosis [92]. Sweden documented a cost of illness amounting to 27.5 million USD attributed to salmonellosis, whereas the overall consumer well-being loss for Hungary was estimated to be approximately 8.56 million USD annually [93, 94]. The Netherlands follows closely with an economic impact of approximately 20.5 million USD [95]. Australia also faces substantial costs, totaling around 91 million USD each year [96]. The economic and societal impact of foodborne illnesses attributed to *Salmonella* in the UK amounts to an approximate annual cost of 264.2 million USD [97]. In Canada, the financial implications of salmonellosis are also more pronounced, reaching an annual cost of 211.6 million USD [98]. Ethiopia documented a cost-of-illness associated with non-typhoidal

Salmonella enterica infections amounting to 83.9 million USD [99]. Nigeria grapples with a higher economic toll, with salmonellosis accounting for an annual cost of 931 million USD [100]. The United States, however, bears the heaviest economic burden, with salmonellosis incurring an annual cost of about 4.1 billion USD [101]. These economic figures underscore the significant financial ramifications of salmonellosis across different nations. The substantial costs highlight the urgency of implementing effective prevention and control measures to address both the health and economic impacts of this disease.

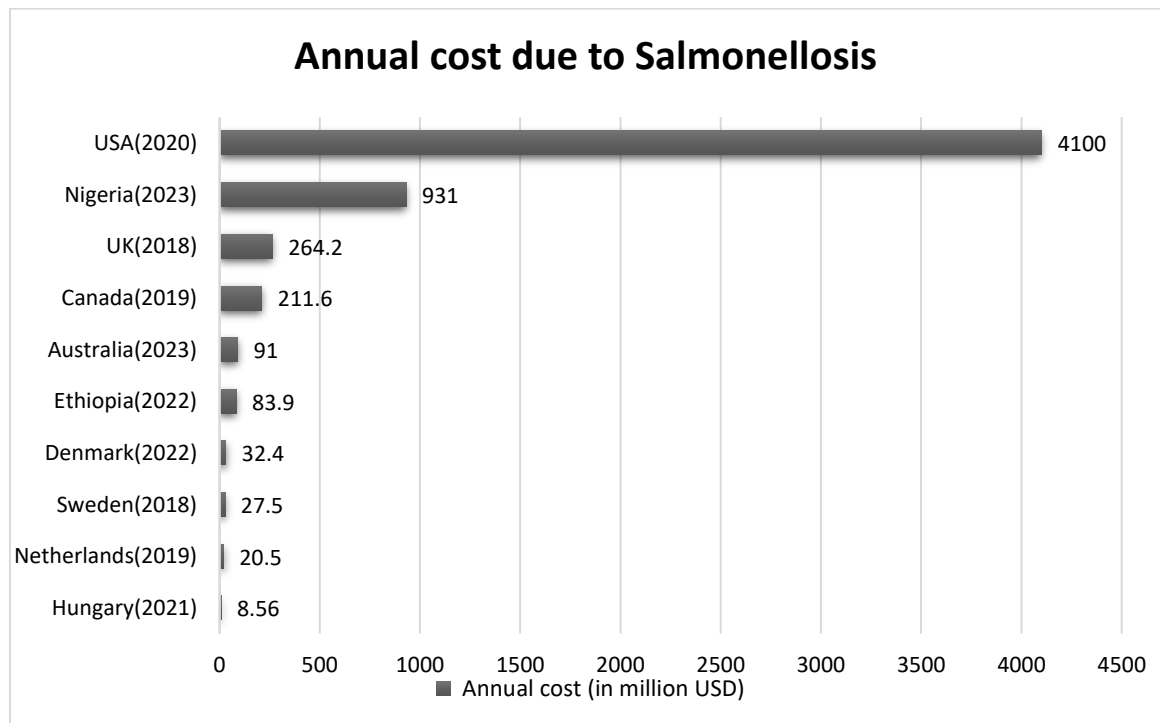


Figure 6: Annual cost burden in different countries due to Salmonellosis [92, 93, 94, 95, 96, 97, 98, 99, 100, 101].

Conclusion

Salmonellosis, primarily attributed to *Salmonella enterica* subsp. *enterica*, persists as an enduring and widespread global dilemma. It remains a prominent contributor to foodborne infections, resulting in significant human suffering and economic repercussions. The burden of salmonellosis is remarkably high, with an estimated 93.8 million cases annually and approximately 155,000 associated deaths across the globe. This underscores the pathogen's significance as a causative agent of infectious gastroenteritis. It is important to acknowledge that salmonellosis is not solely linked to the consumption of contaminated food; contact with animals, particularly live poultry, can also lead to infection. The transmission dynamics within poultry populations are intricate, involving both vertical and horizontal pathways, contaminated feed and water sources, and carriers that shed the pathogen over extended durations. Salmonellosis is a global issue, impacting nations at varying stages of development. Infections occur across diverse geographical regions, exerting a significant toll on public health. The financial burdens linked to salmonellosis are considerable, amounting to millions or even billions of dollars each year in various nations. Of particular concern are two specific serovars, *Salmonella* Enteritidis and *Salmonella* Typhimurium, due to their exceptional adaptability to avian hosts, their ability to persist in poultry environments, and their role as zoonotic pathogens. These serovars are responsible for a significant proportion of foodborne outbreaks, affecting both human and animal populations worldwide. Their capacity to colonize the avian gastrointestinal tract and their propensity for fecal shedding contribute to their continual presence in poultry flocks. The prevalence of antimicrobial resistance (AMR) in *Salmonella* Enteritidis and *Salmonella* Typhimurium adds complexity to the management of these infections. AMR

compromises the efficacy of antibiotics, making treatment more challenging and potentially leading to treatment failures. It is a global concern affecting both animal and human health. Climate change introduces another dimension to the prevalence of *Salmonella* in poultry. Rising temperatures and unpredictable weather patterns alter the poultry farm environment. Warmer conditions promote *Salmonella* growth and persistence, while changes in rainfall patterns and migratory bird behavior contribute to the pathogen's geographical spread. In conclusion, the prevalence of *S. Enteritidis* and *S. Typhimurium* in poultry populations, their role in foodborne infections, the challenges posed by antimicrobial resistance, and the influence of climate change emphasize the necessity for comprehensive and collaborative efforts to mitigate associated risks. Effective strategies in poultry management and public health are essential to address the health and economic implications of these pathogens. Continued surveillance, prudent antibiotic use, and research into innovative prevention and control measures are critical components of our ongoing battle against salmonellosis.

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