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A Comprehensive Study on One Health Strategy and Public Health Effects of Salmonella

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A COMPREHENSIVE STUDY ON ONE HEALTH STRATEGY AND PUBLIC HEALTH EFFECTS OF SALMONELLA

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ABSTRACT

Salmonella poses a significant public health challenge due to its antibiotic resistance, zoonotic transmission, and diverse clinical manifestations. Over 60 % of human diseases are zoonotic, influenced by ecological dynamics and human activities such as land use changes, population growth, and international travel. Foodborne diseases, particularly those caused by Salmonella spp., have a substantial global impact, especially in low-income countries. Salmonella is divided into two species, *Salmonella enterica* and *Salmonella bongori*, with more than 2000 serotypes and six subspecies within *S. enterica*. This bacterium is highly adaptable, surviving extreme conditions such as drying, high salt concentrations, and acidic environments. Detection methods typically involve pre-enrichment, followed by specific enrichment, plating, and identification through serological and molecular techniques like PCR. Severe cases, especially in vulnerable populations, often require antimicrobial treatment. Salmonella's pathogenicity is driven by its ability to invade, persist, and replicate within host cells, facilitated by Salmonella pathogenicity islands (SPIs) and type III secretion systems. Epidemiological data reveal a global distribution of enteric fever, with high incidence and mortality rates in Africa, Asia, and South America, while lower rates are reported in developed regions, often linked to international travel. This study adopts a One Health approach, examining Salmonella's resistance, zoonotic transmission, and public health impact, while suggesting innovative strategies for detection and control to mitigate its global effects.

Keywords: Antibiotic resistance, one health, salmonella, public health, zoonosis.

INTRODCTION

Zoonoses are infectious diseases that can be spread from animals to people either through direct contact or indirectly. The zoonotic spread of diseases to humans elicits concerns due to its consequences for clinical care. On the other hand, reverse zoonoses, which involve the transmission of illnesses from humans to animals, can provide substantial risks to species conservation. More than 60 % of illnesses that affect people can also be observed in wild or domesticated animals (Taylor et al., 2001). The occurrence of zoonotic illnesses arises from the interaction between ecological and evolutionary factors, as diseases adjust to new host species and take advantage of new ecological habitats. Human activities, including as shifts in the usage of land, extraction of resources, population increase, animal husbandry techniques, use of antibiotics and vaccinations, worldwide travel, and business, have a substantial impact on the elements that allow entry to these new habitats (Karesh et al., 2012).

According to their pathogenesis, a large range of infections, including anthrax, salmonellosis, tuberculosis, Lyme disease, brucellosis and plague, can be categorized as bacterial zoonoses (Rehman et al., 2020). Zoonoses can be classified into different categories based on their origin and transmission. Anthropozoonoses are diseases, like rabies, that start in animals and spread to people. On the other hand, diseases known as zooanthroponoses such as tuberculosis in cats and monkeys are spread from humans to animals. Amphixenoses involve bidirectional transfer between humans and animals, as seen in staphylococcal infections. Lastly, euzoonoses are parasitic disorders that require human hosts, for example, infections caused by Taenia solium and Taenia saginata (Hubalek, 2003).

Currently, foodborne diseases, acquired by consuming food and water which have been contaminated, have a substantial worldwide effect on both health and the economy. EFSA and ECDC (2017) reported that various kinds of Salmonella are the primary etiological agents responsible for foodborne illnesses in humans. Gastroenteritis is a global public health issue, with around 1.7 billion cases and 2.2 million fatalities occurring each year. It primarily impacts young children in countries with lower incomes. The zoonotic pathogens that were detected in the case of gastroenteritis in Pakistan in 2023 were Salmonella Typhi, Entamoeba histolytica, Giardia lamblia, and Buxtonella sulcata. These diseases were widespread in distinct regions of Karachi and District Faisalabad, respectively. The main causes of gastroenteritis were Salmonella Typhi, E. histolytica, and G. lamblia, with Typhoid fever being the most prevalent form of the illness. However, gastroenteritis mostly arises from the use of polluted water and food, exacerbated by inadequate sanitation and hygiene standards. This combination of factors poses a greater threat to young adults (Muhammad et al., 2015).

Salmonella

i. Classification and Taxonomy

The closely related group of bacteria known as salmonella poses a serious threat to public health and is a leading cause of disease and mortality worldwide. Salmonella infections, also known as salmonellosis, have significant economic consequences for both industrialized and economically disadvantaged countries. This is because of the costs associated with preventive treatment, monitoring, and surveillance. Numerous studies (Eng et al., 2015; Barnett, 2016; Colin, 2018; WHO, 2018; Qamar et al., 2022) that have the backing of the World Health Organization (WHO) highlight how urgently this health issue has to be addressed. Furthermore, in 1879, a patient with typhoid fever had a bacillus found in the spleen and abdominal lymph nodes, according to records made by Karl Joseph Eberth, a pathologist and physician affiliated with the University of Zurich (Popa and Papa, 2021). Originally designated as Eberth's Bacillus (Gryglewski and Chlipała, 2020), it was subsequently recognized by George Gaffky in 1884 as the pathogenic microorganism responsible for human typhoid fever (Barnett, 2016; Gryglewski and Chlipała, 2020). The term "Salmonella" was later introduced as a tribute to Daniel Elmer Salmon, an American veterinary pathologist who supervised the USDA Microorganism Research Program in the late 1800s (Barnett 2016). Salmon and Theobald Smith successfully isolated Salmonella from the intestines of hog cholera-stricken pigs in 1884 (Popa and Papa, 2021).

While, historical investigations conducted by historians and scientists indicate that many widespread illness outbreaks in ancient times, including typhoid infections, were probably caused by Salmonella bacteria (Littman, 2009; Monte and Sellera, 2020). In 430 B.C., an outbreak, formerly thought to be typhoid illness, caused a severe reduction of onethird of Athens' population (Barnett, 2016). Furthermore, according to Tindall et al., (2005), salmonella is a member of the genus Salmonella, the order Enterobacteriales, the class Gamma-Proteobacteria, the phylum Proteobacteria, the Kingdom Monera or Eubacteria, and the family Enterobacteriaceae. Two commonly used methods make up the name associated with the Salmonella genus, which has caused confusion and debate. Le Minor and Popoff suggested a system in the 1980s that deviates from the Bacteriological Code's guidelines, although it has been widely accepted (Le Minor et al., 1982). While the second system adheres to the Bacteriological Code, it is not widely employed (Brenner et al., 2000). The discrepancies were resolved in Opinion 80, which was issued by the Judicial Commission of the International Committee on the Systematics of Prokaryotes. Tindall et al., (2005) provided a clear interpretation of the organism's taxonomy, dividing the genus Salmonella into two distinct species. There is uncertainty in the classification due to the large number of Salmonella species, almost 2000 of which are identical. Salmonella bongori and Salmonella enterica are the two species that the CDC is aware about.

			Salmonella Serotype Subspecies Serogroup Typhoidal/Non-typhoidal Source	
S. Typhi	I	A	Typhoidal	Humans
S. Paratyphi A	I	A	Typhoidal	Humans
S. Paratyphi B	I	B	Typhoidal	Humans
S. Paratyphi C	I	C	Typhoidal	Humans
S. Choleraesuis	\mathbf{I}	C ₂	Non-typhoidal	Pigs, Humans
S. Typhimurium	\mathbf{I}	B	Non-typhoidal	Cattle, Poultry, Humans
<i>S. Enteritidis</i>	I	B	Non-typhoidal	Poultry, Eggs, Humans
S. Dublin	I	B	Non-typhoidal	Cattle, Milk, Humans
S. Virchow	П	D	Non-typhoidal	Cattle, Humans
S. Heidelberg	\mathbf{I}	E1	Non-typhoidal	Cattle, Poultry, Humans
S. Bovismorbificans	VI	E2	Non-typhoidal	Cattle, Humans
$+1,500$ others				

Table 1: Classification of Salmonella Serotypes by Subspecies, Serogroup, and Typhoidal/Non-typhoidal Status.

The World Health Organization (WHO) collaborating center for the reference and investigation on Salmonella has recently revised the White-Kauffmann-Le Minor scheme. This scheme classifies multiple serotypes and six subspecies of Salmonella enterica (Popoff 1997; Brenner and McWhorter-Murlin 1998; Popoff et al. 2004) (Table 1). Antigenic polymorphisms allow the over 2600 serovars of the Salmonella genus to be identified (Tindall et al., 2005). To maintain readability, names should be written in Roman script, beginning with a capital letter. According to Brenner et al. (2000), the standardized naming convention for Salmonella requires the genus, species, the term 'serovar' (or 'ser.'), followed by the individual serovar name. Based on host adaptability, Salmonella can be divided into three main categories, each of which has a wide host range (Bäumler et al., 1998). According to Baumler et al., (1998), Group 1 serovars are adapted to humans and higher primates, Group 2 serovars are primarily adapted to certain animal hosts, and Group 3 serovars have a broad host range.

ii. General Characteristics

Salmonella is a type of bacteria that has a rod-like structure and is classified as gramnegative. These organisms lack the ability to produce spores and have a size range of 0.7-1.5 x 2.0-5.0 μm. With the exception of certain types that do not move and harmful bird serovars such as Pullorum and Gallinarum, Salmonella generally utilizes peritrichous flagella for movement. This bacteria exhibits a remarkable ability to thrive in diverse settings, including those with and without oxygen, by deriving energy from organic substances. It is worth mentioning that Salmonella typically generates hydrogen sulfide rather than fermenting lactose. In addition, as stated by Bell and Kyriakides (2002), Salmonella has catalase activity while lacking oxidase and urease activity.

Salmonella, being mesophilic bacteria thrives best in temperatures ranging from 35 to 37°C. However, certain strains of Salmonella are capable of surviving in extreme temperatures as high as 54°C. The quick adaptation to temperature variations is facilitated by the activation of multigenic heat stress and cold shock responses, which are regulated by sigma factors. These mechanisms improve Salmonella's capacity to endure, particularly in food that is frozen or subjected to low water activity (aw) circumstances during heat treatment (Mattick et al., 2001; Dominguez and Schaffner, 2009). In addition, Salmonella is capable of surviving in extremely acidic settings with a pH range of 3.0-4.0, tolerating high levels of salt up to 4 % , and resisting drying out (Álvarez-Ordóñez et al., 2012; Li et al., 2012). The bacterium's adaptable reproduction and survival mechanisms allow it to persist in challenging environments, including excrement, soil, water, pastures, and food, for prolonged durations, even without living hosts (Winfield and Groisman 2003; Spector and Kenyon 2012).

iii. Detection isolation and conformation

Salmonella has the ability to thrive in both a simple glucose-salts solution and, to a greater extent, in highly fortified media due to its flexible nutritional requirements. The optimal method for identifying Salmonella consists of three primary stages: initially, a nondiscriminatory pre-enrichment phase; subsequently, enrichment in a specialized medium; and ultimately, culturing on two distinct selective media, following the ISO 6579-1:2017 recommendations. Pre-enriching liquid media, such as buffered peptone water or modified tryptone soya broth, improves the ability to identify small amounts, bacteria that are under stress, or bacteria that are partially damaged (Valentín-Bon et al., 2003). Specialised nutrientrich solutions, such as Müller-Kauffmann tetrathionate or Rappaport-Vassiliadis soy peptone, are then employed to facilitate the proliferation of Salmonella bacteria while suppressing the development of other microbes. The Rappaport-Vassiliadis medium, which is in a semi-solid state, is employed to distinguish Salmonella from other bacteria that are unable to move, in accordance with ISO 6579-1:2017.

Salmonella is grown on different types of solid medium that selectively promote its growth, such as MacConkey, Xylose Lysine Desoxycholate (XLD), Xylose Lysine-Tergitol 4 (XLT4), Brilliant Green, Hektoen-Enteric, or Salmonella-Shigella. This selection is determined by distinct attributes, such as the incapability to undergo glucose fermentation and the generation of hydrogen sulphide (Vigo et al., 2011). After being separated, Salmonella can be accurately identified at the subspecies level by the utilization of biochemical assays such as the MUCAP test, VITEK®2, and API-E20. For serovar identification, serological assays such as slide agglutination tests using commercially available antisera are employed. The serovar's precise antigenic formula is defined by the presence of O antigens in the lipopolysaccharide component of the outer membrane. The H antigens, located in the central region of the flagellin protein, distinguish between monophasic and diphasic serovars, which produce distinct variants of flagellin (Issenhuth-Jeanjean et al., 2014).

Every Salmonella serovar possesses a unique antigenic makeup that is determined by the presence of K antigens, which are polysaccharides located on the surface of the bacterial capsule, as well as Vi antigens, which are a specific subtype of K antigen. The presence of Vi antigens is limited to specific pathogenic serovars, including Dublin, Typhi, and Paratyphi C (Issenhuth-Jeanjean et al., 2014).

Moreover, molecular approaches that target the invA gene, like PCR or real-time PCR, offer a quick way to identify Salmonella in addition to the labor-intensive phenotyping methods (González-Escalona et al., 2012). These methods are highly sensitive and specific, but they cannot distinguish between living and dead cells. Thus, in some circumstances, it might be required to cultivate the sample in order to meet the detection limit threshold (Malorny et al., 2003).

iv. Clinical manifestation

Human salmonellosis presents itself in three separate clinical forms: gastroenteritis, bacteraemia, and enteric fever. Certain individuals may also carry persistent Salmonella infections without exhibiting symptoms. Gastroenteritis, primarily caused by nontyphoidal Salmonella (NTS) serovars, is the prevailing manifestation characterized by symptoms such as watery diarrhea, nausea, vomiting, stomach aches, myalgia, headache, chills, and fever. Gastroenteritis, although symptom severity may differ, usually resolves spontaneously during a period of two to seven days. Recovery can typically be achieved by adequately replenishing fluids and restoring electrolyte balance, without the need for antibiotic treatment in persons with a strong immune system. Certain populations, such as babies, the elderly, and individuals with weakened immune systems, are more susceptible to severe symptoms and complications, increasing their likelihood of experiencing such outcomes (WHO 2017).

Bacteremia occurs when invasive nontyphoidal Salmonella (iNTS) breaches the intestinal barrier, enters the circulation, and disseminates to other organs. Although several serovars have the capacity to invade, certain ones including Choleraesuis, Dublin, and Heidelberg are most inclined to result in hospitalization, systemic illnesses, or death. Bacteremia is marked by a substantial elevation in body temperature, which can potentially result in septic shock and severe problems in organs outside of the intestines. Potential complications include diseases of the liver, spleen, biliary tract, urinary tract, pneumonia, arthritis, endocarditis, and meningitis (Hohmann 2001). The prevalence of invasive nontyphoidal Salmonella (iNTS) diseases is elevated in underdeveloped nations, particularly in those with concurrent medical problems such as HIV, malaria, and malnutrition (Feasey et al., 2012).

Enteric or typhoid fever is serious systemic diseases caused by serovars Typhi and Paratyphi that can affect patients with or without immune system function. Initial signs of infections are followed by a fever that rises rapidly throughout the second week. Other symptoms that can be present include a slow heart rate (bradycardia), enlargement of the liver and spleen (hepatosplenomegaly), red spots on the skin (rose spots), signs of inflammation of the meninges (meningism), and manifestations related to the brain and nervous system (neuropsychiatric manifestations). Salmonella bacteremia cases may lead to many complications, including pancreatitis, hepatitis, cholecystitis, encephalopathy, and hemorrhage. Gastrointestinal bleeding and intestinal perforation are particularly dangerous hazards (Huang and DuPont, 2005).

In cases of severe infection or in people who have a high risk of acquiring an invasive disease, antibiotic treatment is recommended. Fluoroquinolones and third-generation cephalosporins are the initial therapies for the bacteria until its susceptibility to antibiotics is determined (Gilbert et al. 2017). There are currently two typhoid vaccines on the market that have been shown to be secure and efficient. Two vaccines that are part of this series are the injectable ViCPS and the oral Ty21a (WHO, 2008).

v. Pathogenesis

The severity of a Salmonella infection in an individual is contingent upon the particular serotype and the overall health condition of the host. Individuals in vulnerable demographics, such as children under the age of five, the elderly, or those with compromised immune systems, have a higher susceptibility to acquiring Salmonella infections and consequently have an increased risk of mortality compared to individuals in better health. Most Salmonella strains are harmful as they have the ability to infiltrate, multiply, and survive within human host cells, which can result in life-threatening infections. Salmonella possesses the distinct ability to intentionally induce its own phagocytosis, allowing it to invade human host cells that are not typically involved in phagocytosis (Hansen-Wester et al., 2002). Genetic foundation for this innovative approach is found inside Salmonella pathogenicity islands (SPIs), which are groups of genes located in specific locations of chromosomal DNA. Grassl and Finlay (2008) state that these genes include the instructions for the structures those are responsible for the invasion process. Salmonella usually infiltrates the epithelial cells of the intestinal wall when it enters the digestive tract via contaminated food or drink. SPIs are responsible for encoding type III secretion systems, which are intricate protein, structures enabling Salmonella to transport effectors over the membranes of intestinal epithelial cells and into their cytoplasm. Subsequently, these bacterial effectors initiate the restructuring of the actin cytoskeleton in the host cell by activating the signal transduction pathway. This reconfiguration induces the epithelial cell membrane to extend or fold outward, so facilitating the engulfment of the bacteria. The membrane ruffle structure that is formed bears a resemblance to the process of phagocytosis (Takaya et al., 2003).

The ability of Salmonella strains to reside within host cells is crucial for causing disease, as non-virulent bacteria do not possess this capability (Bakowski et al., 2008). Once taken up by the host cell, Salmonella becomes enclosed in a membrane-bound compartment called a vacuole, which is formed from the host cell membrane. Normally, when a foreign bacterial object is present, it would trigger the immune response of the host cell. This response would lead to the fusion of lysosomes and the subsequent release of enzymes that would degrade the bacterium within the cell. However, Salmonella modifies the vacuole by introducing additional effector proteins through the type III secretion system. This modification prevents the fusion of lysosomes with the vacuole, allowing the bacteria to persist and multiply within the host cells.

Salmonella's capacity to endure within macrophages enables them to go through the reticulo-endothelial system (RES) (Monack et al., 2004). This capability is crucial for the spread of illness throughout the body, as the bacteria may navigate via the body's immune defenses and establish infection in other organs.

vi. Epidemiology

According to a study done in 2000, there would be 22 million instances of enteric fever worldwide, which would result in 200,000 deaths. Most of these observations were made in developing nations (Crump et al., 2004). Variable regions have variable rates of disease occurrence and death; in some cases, the death rate might exceed 7 % even when antibiotics are used.

Enteric fever is widespread in Africa, Asia, Europe, South and Central America, and the Middle East. Conversely, the occurrence of Salmonella is less than 10 cases per 100,000 individuals per year in the USA and several European nations, where enteric fever is seldom. The majority of cases in these places are associated with travel, frequently brought in by individuals from Pakistan, India, or Africa who are either foreigners or repeat tourists (Molbak et al., 2002). From 1995 to 2003, the occurrence rate in Israel declined from 0.42 to 0.23 per 100,000 individuals. Nevertheless, the growing occurrence of S. Paratyphi as the primary factor behind typhoid fever raises doubts about the effectiveness of existing vaccinations, emphasising the necessity for further epidemiological investigations (Woods et al., 2006; Meltzer et al., 2006).

Enteric fever is widespread in several Asian countries, including China, India, Vietnam, Pakistan, and Indonesia, where the annual incidence rates exceed 100 cases per 100,000 inhabitants. Ochiai et al., (2008) found that Pakistan and India have the highest incidence rates among Asian countries, with 451.7 and 214.2 cases per 100,000 inhabitants, respectively. Accurately quantifying the worldwide occurrence is difficult due to the fact that major outbreaks receive more focus than isolated cases, and several underdeveloped nations, particularly in sub-Saharan Africa, have insufficient monitoring and diagnostic technologies. Infants, young children, and school-age children in areas where the disease is common are particularly vulnerable to enteric fever. Recent research suggests that there are approximately 25 instances of enteric fever per 100,000 children under the age of five per year in China and Vietnam. India and Pakistan have far higher rates, reporting roughly 450 occurrences per 100,000 people annually (Mweu and English, 2008).

vii. Virulence Factor

Numerous genes located on large plasmids and bacterial chromosomes are involved in the intricate genetic regulation of virulence factors in Salmonella. Salmonella pathogenicity islands (SPIs), which are dispersed throughout the genome and vary in size from 10 to 200 kilobases (kb), are the major locations of the virulence-associated genes. Salmonella pathogenicity islands (SPIs) exhibit a discernible G+C composition in contrast to the core genome of the host, suggesting that they are obtained via horizontal gene transfer from different species. These SPIs generally consist of mobile genetic components. Variations in the quantity and makeup of SPIs impact the diversity of Salmonella serovars, which in turn affects their favoured hosts and methods of disease spread. As of right now, scientists have identified a total of 21 distinct SPIs. Some Salmonella species, like SPI-1 and SPI-2, contain SPIs that are present everywhere, while others, like SPI-7 in S. Typhi, are specific to particular serovars (Sabbagh et al., 2010).

Nevertheless, SPI-1 consists of a minimum of 35 genes that encode the Type III Secretion System (T3SS) and a multitude of effector proteins. These components play a crucial role in enabling Salmonella to invade host cells. One of the bigger components of SPI-2 is a Type III Secretion System (T3SS). This mechanism releases effector proteins, which are necessary for Salmonella to survive and reproduce within a structure known as the Salmonella-containing vacuole (SCV). Additional SPIs, including SPI-3, SPI-4, and SPI-5, seem to augment the bacterium's capacity to infiltrate and endure within host cells. Nevertheless, recently identified SPIs exhibit distribution patterns across serovars and play functions in disease that remain incompletely comprehended. Aside from SPIs, virulence factors can also be encoded in smaller clusters referred to as pathogenicity islets, fimbrial operons, prophages, or dispersed sporadically across the genome. They can also be found on virulence plasmids (Pilar et al., 2012).

viii. Antibiotic Resistance

An important issue in global health is the growing occurrence of antibiotic resistance in Salmonella strains (Chiu et al., 2002). In the early 1960s, there was initial evidence suggesting that Salmonella was becoming resistant to the antibiotic chloramphenicol (Montville and Matthews, 2008). Consequently, there has been a significant increase in the prevalence of Salmonella strains that exhibit resistance to multiple antibiotics in some countries, such as Saudi Arabia, the United Kingdom, and the United States (Yoke-Kqueen et al., 2008). Often used as first treatments for Salmonella infections, common antimicrobial medications like ampicillin, chloramphenicol, and trimethoprim–sulfamethoxazole are Salmonella spp. that show resistance to multiple antibiotics are called multi-drug resistant (MDR). Multidrug resistance (MDR) is the ability to withstand multiple drug treatments. It has long been present in S. Typhi and, to a lesser extent, in S. Paratyphi (Rowe et al., 1997). Multi-drug resistance (MDR) strains of Salmonella Typhi are highly prevalent in Africa and Asia. According to a surveillance study carried out in five Asian countries India, Pakistan, Vietnam, Indonesia, and China multi-drug resistant isolates of Salmonella Typhi are more common in India, Pakistan, and Vietnam than in Indonesia and China (Ochiai et al., 2008). Other studies corroborate these results, demonstrating a notable prevalence of multi-drug resistance (MDR) strains of Salmonella Typhi in Pakistan, India, Nepal, and Vietnam. Conversely, the occurrence of MDR S. Typhi is very low in China, Indonesia, and Laos (Chuang et al., 2009).

Fluoroquinolones and extended-spectrum cephalosporins are now the preferred antimicrobial medicines for treating multidrug-resistant (MDR) S. Typhi because of the increasing resistance to traditional antibiotics (Sood et al., 1999). However, there is strong evidence pointing to a rise in the frequency of fluoroquinolone-resistant typhoid Salmonella infections. Hasan et al., (2008) discovered that S. Paratyphi is more resistant to fluoroquinolones than S. Typhi is in regions where drug-resistant strains are more common. With rates of 59 %, 57 %, and 44 %, respectively, nalidixic acid resistance—a marker of decreased sensitivity to ciprofloxacin and other fluoroquinolones—is notably common among isolates from Pakistan, India, and Vietnam (Ochiai et al., 2008).

Since the first MDR S. Typhimurium DT104 strains emerged in 1990, there has been an increase in the occurrence of non-typhoidal Salmonella (NTS) strains that exhibit drug resistance to multiple medicines (MDR phenotype) in different countries (Helms et al., 2005). 84 % of clinical isolates of NTS exhibited resistance to multiple medicines, while 4.1 % showed decreased susceptibility to cephalosporins, according to data from the National Antimicrobial Resistance Monitoring System (NARMS) in the United States between 2005 and 2006. The NARMS study, which ran from 1996 to 2007, found that the number of NTS isolates resistant to ceftriaxone and nalidixic acid had increased. Public health experts, who are committed to tackling matters of clinical care and infection control, expressed alarm over this (Crump et al., 2011). 135,000 clinical samples of NTS were analyzed in a comprehensive investigation carried out in Europe between 2000 and 2004, which found that 15 % of the samples had resistance to more than one medication and 20 % had resistance to nalidixic acid specifically (Meakins et al., 2008).

ix. Spread of Resistance

The widespread use of antibiotics in animal feed to promote livestock growth and in veterinary medicine to treat bacterial infections in animals is the main factor contributing to the spread of antibiotic resistance in Salmonella strains. The risk of zoonotic transmission to humans is increased when animals harbor strains of Salmonella that are resistant to multiple drugs (MDR). This can happen if someone consumes tainted food or water, comes into close contact with an infected animal, or eats products made from diseased food animals. Moreover, MDR strains of Salmonella have been found in the aquatic environments of certain exotic pets, like turtles and tortoises. This raises concerns about an increased risk of zoonotic diseases in humans due to close contact with these animals (Hyeon et al., 2011).

x. *Mechanism of Resistance*

Studies have demonstrated that multidrug-resistant (MDR) Salmonella serotypes are capable of producing multiple types of hybrid plasmids. Primarily, the plasmids comprise gene cassettes containing resistance genes, offering antimicrobial resistance to widely used antibiotics such ampicillin, tetracycline, chloramphenicol, and streptomycin (Guerra et al., 2002). Genetic alterations in specific regions of the gyrA gene have resulted in resistance against quinolone antibiotics for salmonella serotypes that have become less susceptible to ciprofloxacin (Chiu et al., 2002). Due to genetic changes that result in the production of extended-spectrum β-lactamases, some strains of Salmonella have developed resistance to broad-spectrum cephalosporins. The medicines cephalosporin and cephamycins, which contain β-lactam rings, can be broken down by the aforementioned enzymes (Carattoli et al., 2002).

Significance in a Medical Context

The efficiency of antibiotic treatment for Salmonella infections is significantly impacted by the emergence of multi-drug resistance in various strains of the bacteria. Because invasive serotype infections can be very deadly, prompt and effective antibiotic therapy is necessary. The preferred medications for treating infections brought on by multidrug-resistant Salmonella are quinolones and third-generation cephalosporins (Karon et al., 2007). However, a new challenge in treating infected individuals is the advent of Salmonella serotypes resistant to cephalosporins and quinolones. Increased rates of morbidity and mortality could be the consequence of an ineffective antibiotic treatment.

The emergence of multidrug-resistant (MDR) Salmonella has resulted in increased severity of bacterial infections in humans and animals. Research has shown that MDR infections are linked to more severe or prolonged symptoms when compared to susceptible bacteria. Travers and Barza (2002) have indicated that MDR strains exhibit higher pathogenicity than susceptible bacteria. The evidence also suggests that people infected with MDR strains of Salmonella have more severe symptoms and are more likely to experience sepsis when the disease initially appears. Typically, these symptoms include fever, spleen enlargement, liver enlargement, and increased body temperature.

One Health

The advancements in detection and genotyping techniques have greatly enhanced our comprehension of Salmonella epidemiology. Nevertheless, the presence of numerous enteropathogens with diverse reservoir hosts and sources of infection underscores the intricate nature of their transmission cycles. It is commonly recognized that consuming food that is contaminated is the main cause of disease. Identifying the exact source of environmental contamination is difficult due to the wide range of animal species that can transmit these zoonotic infections (Hoelzer et al., 2011; Whiley et al., 2013). Moreover, the ability of bacteria to resist the effects of soil, water, and different surfaces enhances the likelihood of these germs infecting new hosts (Winfield and Groisman, 2003). The existence of bacteria in reservoirs within humans, domestic animals, and the environment serves as an illustration of the One Health concept (Bronowski et al., 2014).

The idea of one health acknowledges the interconnectedness between the well-being of animals, humans, and the environments in which they coexist. While the idea put forth by Rudolf Virchow and other scholars in the late 1800s did not receive much attention at the time, it is now garnering significant recognition. The One Health concept has demonstrated great potential in addressing current public health challenges, particularly those related to emerging infectious and zoonotic illnesses (Zinsstag et al., 2011). Human salmonellosis continues to be a significant public health issue, despite the presence of regular surveillance systems and strong efforts to prevent and control these infections. Intervening at the primary production level, which is the foundation of the food chain, is crucial for decreasing the occurrence of chronic diseases in individuals.

Sources of the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) in 2017 indicate that the implementation of national control programs for Salmonella in poultry farms has led to a significant reduction in the number of human cases of salmonellosis in Europe. Nevertheless, there is an increasing prevalence of uncommon serovars that hold equal significance in the field of human medicine. Implementing biosecurity measures in chicken farms to minimize environmental exposure frequently leads to inadequate management of salmonella colonization in animals. This highlights the fundamental ecological principles that govern the natural habitats in which these infections reside. As such, without a full understanding of One Health, it is not possible to prevent some zoonotic infections. However, most studies examining the genetic epidemiology of Salmonella concentrate on human, domestic animal, and food source samples. On the other hand, very few studies uses samples taken from ambient Wild animals, including insects, rodents, mammals, and birds, can transmit bacteria to domesticated animals (Sahin et al., 2002). The growing interest in the involvement of animals in zoonoses (Greig et al., 2015) emphasizes the potential for germs to be transmitted from wild animals to domestic animals. Nevertheless, there is ongoing debate regarding the degree of unidirectional or bidirectional transmission and the function of wildlife as a reservoir. The topics mentioned have been addressed by Wales et al., (2010), Antilles (2014), and Meerburg and Kijlstra (2007). Zoonotic bacteria have effectively crossed species boundaries and adapted to new hosts by undergoing various horizontal transfers. This process has allowed them to acquire new combinations of virulence factors. Salmonellosis can be transmitted to humans through the consumption of wildlife meat, such as birds, reptiles, and wild boars, or through direct contact with these animals (Tsiodras et al., 2008). Furthermore, there is a suggestion that wildlife carriers, including rodents, insects, and birds, have the potential to contaminate nonanimal items, such as fresh produce, nuts, and vegetables (Jay-Russell, 2013).

i. Wild birds as reservoirs of zoonotic bacteria

Bengis et al., (2004) state that wild birds have a crucial impact on the spread and maintenance of zoonotic diseases in the environment, such as influenza A virus, West Nile virus, Borrelia, and enteric bacteria. Salmonella bacteria have been found in different quantities in several species of wild birds, including raptors, seagulls, crows, sparrows, pigeons, and waterfowl (Chuma et al., 2000; Molina-Lopez et al., 2011). The dietary preferences of birds seem to have a substantial impact on their vulnerability to certain zoonotic diseases. The danger of infection is higher when there is close proximity to grazing meadows and farms (Ramos et al., 2010; Hald et al., 2016). Enteropathogens are uncommon or absent in specific ecological groups, such as insectivores, granivores, and herbivorous birds. Nevertheless, it has been observed that ground-hunting raptors and opportunistic feeders exhibit a high prevalence of carrying diseases. When birds search for food on the ground, they could eat food that is contaminated or mollusks that feed on particles in habitats affected by sewage, therefore polluting their sources of food. Furthermore, raptors that consume carrion may obtain enteric bacteria from the intestines of their prey or carcasses.

According to Raven and Coulson (2001), opportunistic bird species that are attracted to trash dumps and sewage sludge may serve as harbors for harmful microorganisms. Due to their propensity for scavenging, seagulls are known to be carriers of Salmonella spp. This has been thoroughly investigated. A number of gull species have seen significant increases in population in Europe, North America, and Australia in recent years. These increases can be related to human activities that have increased the availability of food supplies. The increasing urbanization of coastal areas brings seagulls and people closer together, particularly at sites like farms, processing plants, landfills, and fishing boats (Hatch, 1996).

Seabirds are becoming more and more reliant on alternative habitats, such wastewater treatment plants, as a result of the global decline in natural wetlands. These behaviors may contribute to the transmission of gut bacteria resistant to antibiotics from human activity to wild birds. Seabirds play a crucial role in maintaining zoonotic bacteria within the ecosystem by regularly migrating between their feeding grounds and roosting or nesting areas. Because birds often perch on adjacent fields and pastures and wash in neighboring bodies of water, the germs they ingest during foraging are reintroduced into the food chain through excretion (Murray and Hamilton, 2010).

Moreover, seabirds, like other bird species, can effectively spread disease by fecal contamination when they travel great distances on their annual migrations. Approximately 19 % of extant bird species migrate across national and international borders each year. According to Reed et al. (2003), migration has the potential to create new areas where illnesses can spread. Bird migration follows predictable, yearly paths between breeding and wintering areas; these paths are called flyways. The availability of food is the main factor motivating these movements. Different species' migration patterns, as well as those within the same species, can be intricate and unpredictable. Importantly, birds migrate in large numbers. Arctic terns and other birds travel thousands of kilometers and come into contact with a variety of environments on their journeys. Birds are possible virus vectors because of their increased vulnerability to infectious diseases due to the physiological stress of migration. According to Hockey et al. (2005), migration may contribute to the spread of diseases and the emergence of antibiotic resistance, so posing a threat to the health and welfare of both people and animals.

CONCLUSION

The need of a comprehensive one health strategy becomes more apparent when zoonotic germs persistently traverse species boundaries and acclimatize to novel hosts. The emergence of multidrug-resistant variants poses a substantial obstacle in the treatment of Salmonella infections, underscoring the importance of intensified surveillance and antibiotic stewardship. This review emphasizes the need for thorough epidemiological research, especially in wild animal populations, to reduce the worldwide impact of these diseasecausing infections that can be transmitted between animals and humans. It is crucial to include information from several disciplines in order to create efficient approaches for controlling and stopping the transmission of Salmonella infections in both human and animal communities.

AUTHORS CONTRIBUTION

Conceived and designed: MM Rahimmon, AH Mirani and JK Sahito; Designed the title: MA, MM Rahimoon, PA Khoso and RA Leghari; Analyzed the data: MA and AA Ali, R bux; Contributed materials MA, AZ Khoso; Wrote the paper: MA

CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

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