Gastroenteritis in Human by Salmonella Infected Poultry: Establishment of Public Health Guidelines for Management and Control

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Abstract

Gastroenteritis is a zoonotic illness caused by digestive inflammation and irritation triggered by the immune system in humans in response to the consumption of *Salmonella*-contaminated poultry eggs or undercooked meat. The global burden of gastroenteritis is astonishing. Approximately 685 million cases have been reported annually. Non-typhoidal *Salmonella (S.) newport, S. enteritidis, S. typhimurium,* and *S. heidelberg* are most prevalent in poultry, leading to the zoonotic development of gastroenteritis in humans. Exposure to carrier animals, insects, contaminated chicken litter, feed, water, and aerosols transmit the *Salmonella* to poultry eggs and meat via two routes: horizontal and/or vertical. *Salmonella* infects poultry through multiple phases, including adherence and penetration of gastrointestinal epithelial cells, persistence, proliferation in the host cell, and extragastrointestinal propagation. After the consumption of contaminated eggs and poultry meat, plasmids, flagella, adhesion systems, endotoxins, exotoxins, and *Salmonella* pathogenicity islands (SPIs) participate in the pathogenesis of *Salmonella* in humans. Control of gastroenteritis is linked to the infectious rate of poultry, which can be regulated by practicing biosecurity measures and the proper use of antibiotics, probiotics, prebiotics, synbiotics, postbiotics, phytobiotics, bacteriophages, and vaccines.

Keywords: *Salmonella*, Gastroenteritis, Poultry, Zoonosis, Public health guidelines

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Introduction

Gastroenteritis is characterized as an ailment caused by gastrointestinal inflammation and irritation provoked by immune responses to viral, bacterial, or parasitic infection (Duncan, 2018; Flynn et al., 2024). Salmonella induces a kind of gastroenteritis called salmonellosis (Wilson et al., 2021), specifically in those cases documented for poultry utilization (Antunes et al., 2003). The global burden of gastroenteritis is astonishing. Approximately 685 million cases have been reported annually, resulting in 210,000 deaths globally, predominantly affecting children (Wang et al., 2023). Contaminated feed, inappropriate slaughtering techniques, and unfinished cooking are major determinants responsible for food-borne zoonotic transmission (Davies et al., 2010). Interestingly, despite successful Salmonella control practices, meat products are still considered the major cause of zoonotic infections worldwide (Ali & Alsayeqh, 2022). In various geographical regions, a transition in Salmonella serotypes associated with poultry farming has been reported (Authority, 2017). Additionally, antimicrobial resistance in non-typhoidal Salmonella is also responsible for hindrances in the control and management of salmonellosis (Antunes et al., 2016).

Escalating poultry consumption at the global level due to its economic feasibility and high protein value makes it crucial to understand the link between poultry and gastroenteritis. This chapter helps you understand the relationship between *Salmonella*-infected poultry and human gastroenteritis. It also offers an analysis of the disease's epidemiology, mechanism, diagnostic features, and control strategies, concentrating on establishing public health guidelines to lessen its impact.

Salmonella: its Classification, Types, and Epidemiology

Salmonella is a genus of rod-shaped, gram-negative, and pathologically significant population of bacteria belonging to the family Enterobacteriaceae (Su & Chiu, 2007). Over 2600 documented *Salmonella* serotypes are categorized under two main species, ***S. enterica*** and *S. bongori* (Ryan et al., 2017). The serotypes of *Salmonella* can be differentiated based on flagellar H (the Kauffman–White classification) and somatic O (lipopolysaccharide) antigens and classified into two categories, typhoidal *Salmonella* and non-typhoidal *Salmonella*. Typhoidal *Salmonella* is associated with typhoid, and non-typhoid *Salmonella* is usually related to mild gastrointestinal illness. However, clinical and epidemiological studies of different strains can be done by antibiotic sensitivity testing and other molecular biological techniques such as multilocus sequence typing, whole genome sequencing, and pulsed-field gel electrophoresis (Okoro et al., 2012).

Incidence of *Salmonella* in Poultry

The most prevalent clinically relevant poultry NTS serotypes associated with external egg contamination are *S. newport, S. enteritidis, S. typhimurium,* and *S. heidelberg,* and human infection through contaminated eggs is primarily associated with *S. enteritidis* (Howard et al., 2012; Chousalkar et al., 2018; Ricke et al., 2018).

Salmonella in Poultry

Exposure to carrier animals such as mice, cats, and insects is one of the several ways that poultry inhabits *Salmonella* during the production cycle. Furthermore, *Salmonella* is transmitted by contaminated chicken litter, feed, water, and aerosols (O'Bryan et al., 2022). It can contaminate poultry eggs in two ways: vertically and horizontally. In vertical or transovarial contamination, infection propagates in the egg's pre-laying albumen, yolk, and vitelline membranes from parent to offspring. For instance, *S. enteritidis* initiated an infection in reproductive organs such as the ovary and oviduct. Consequently, the pathogen penetrates the egg even before the formation of the eggshell in the oviduct (De Reu et al., 2006). In feco-oral or horizontal contamination, poultry becomes infected due to its direct exposure to the *Salmonella*-contaminated environment, water, and feed. Moreover, bacterial infection of the eggs also occurs by exposure to contaminated feces due to immature cuticles and few open pores in the initial period after oviposition. *Salmonella* proliferates and develops in fecal matter as it serves as the best nutrient supply, pollutes the surrounding atmosphere, and facilitates the spreading of infection to the other birds in the same facility (Hameed et al. 2024).

Pathogenesis of *Salmonella* in Poultry

Multiple phases of *Salmonella* pathogenesis exist, including adherence and penetration of gastrointestinal epithelial cells, persistence, proliferation in the host cell, and extra-gastrointestinal propagation. *Salmonella enteritidis* can infect a day-old chick with only 1–5 bacteria cells, a very low infectious dose. The period of incubation for *Salmonella* is typically 7 to 14 days. The ability of bacteria to tolerate 3.7 pH ensures their survival while passing through the acidic stomach (Tajkarimi, 2007). Once in the small intestine, fimbrial adhesins facilitate the penetration of *Salmonella* in the epithelial cells of the intestine. M cells of Peyer's patches assist the penetration of *Salmonella* in the mucosal layer of the intestine. Additional pathways involve dendritic cell internalization and enterocyte absorption aided by effector proteins related to virulence genes in SPI-1-TTSS (Broz et al., 2012; Higginson et al., 2016). *Salmonella* is actively transported to the underlying lymphoid follicles by M cells, characterized as antigen-sampling cells of the gastrointestinal epithelium, leading to the activation of systemic and mucosa immunity upon arrival of the *Salmonella* antigen to macrophages and dendritic cells (Kobayashi et al., 2019). It hinders the activity of macrophages by restricting the phagosomes from fusing with secondary lysosomes, demonstrating why macrophages can ingest the bacteria but cannot destroy it, thus increasing the bacteria's intracellular longevity (Gutiérrez et al., 2021). Inside the structure called the *Salmonella*-containing vacuole (SCV), *Salmonella* multiplies inside macrophages and slowly penetrates widely the draining mesenteric lymph nodes, where it develops bacteremia and attacks systemic organs such as the gallbladder, spleen, liver, and ovary (Gutiérrez et al., 2021). The *S. enteritidis* infects both young and adult birds. Adult birds are asymptomatic carriers after being invaded by the bacteria, young birds are inclined to acquire systemic disease with significant fatality rates (Velge et al., 2005).

Zoonotic Transmission and Pathogenicity of *Salmonella* in Humans

Consumption of contaminated eggs and poultry meat is the major source of *Salmonella* gastroenteritis in humans (Fearnley et al., 2011). A wide range of virulence determinants participate in the pathogenesis. These determinants include plasmids, flagella, capsule, adhesion system, and type 3 secretion systems (T3SS) expressed by *Salmonella* pathogenicity island SPI-1 and SPI-2 and other SPIs (Daigle, 2008; Sabbagh et al., 2010). Adhesion systems of *S. enterica* have many virulence factors, including invasions, hemagglutinins, endotoxins, exotoxins, fimbriae, and adhesins facilitating rapid colonization of the host (Kirti et al., 2024).

Salmonella Pathogenicity Islands (SPIs)

Various gene clusters known as *Salmonella* pathogenicity Islands (SPIs) present at specific areas of chromosomes are responsible for the expression of these virulence determinants and pathogenic properties (Foley et al., 2008). The SPI-1 helps in the penetration of the host cells and initiates macrophage apoptosis. SPI-2 induces bacterial proliferation in macrophages and systemic infection. SPI-3 promotes the development of *Salmonella* in magnesium-deficient conditions and its longevity in macrophages. SPI-4 contains genes that induce apoptosis and release toxins and promote survival in macrophages. SPI-5 contains genes that express various T3SS effector proteins, and SPI-6 functions by sending different proteins in the host cell in response to external signals (Amavisit et al., 2003; Foley et al., 2008; Foley & Lynne, 2008).

Plasmids

Different strains of *Salmonella* have serotype-particular plasmids containing virulence genes and vary in size from 50 to 100kb and number from 1 to 2 replicas per cell (van Asten & van Dijk, 2005). Expression of these genes in *Salmonella* organisms is essential for proliferation within the reticuloendothelial system (van Asten & van Dijk, 2005).

Fimbriae

Fimbriae are essential to *Salmonella* pathogenicity and serve as a source of variation among serovars by exhibiting unique functions and patterns (Dufresne & Daigle, 2017; Dufresne et al., 2018). Gene sets comprised of four to fifteen genes that express regulatory, structural, and assembly proteins constitute the fimbrial systems (Dufresne & Daigle, 2017). The functions of fimbriae in *Salmonella* are hemagglutination, biofilm synthesis, cellular penetration, macrophage interaction, and seroconversion (Jajere, 2019). Research on the roles of fimbrial genes in virulence is limited due to poor expression of *Salmonella* fimbriae *in vitro* investigations.

Flagella

In addition to enabling movement, flagella located on their cell surface in up to ten randomly positioned in *Salmonella* participate in pathogenicity. Certain *Salmonella* serovars exhibit flagellin phase variation, resulting in phenotypic heterogeneity of the flagellar antigens, as one of their strategies to reduce the host immunological response. It is still unknown how flagella (motility and rotational direction) operate in pathogenesis and maybe function in the adherence and penetration of mammalian cells (van Asten & van Dijk, 2005).

Endotoxins and Exotoxins

Salmonella serovars' pathogenicity is associated with the production of endotoxins and exotoxins. Endotoxins function in a variety of biological activities, whereas exotoxins consist of cytotoxins, and enterotoxins are linked to the destruction of mammalian cells (Munshi et al., 2021). Heat-labile trypsin-sensitive cytotoxins are identified in *S. choleraesuis* and *S. typhi,* known as salmolysin and *Salmonella* enterotoxin, and are expressed by *sly*A and *stn* genes identified in serovars such as *Enteritidis*, *Typhi,* and *Typhimurium* (Munshi et al., 2021; Bekoz et al., 2023).

These pathogenic activities of *Salmonella* activate the host's immune system and trigger various immunological responses against the bacteria, leading to the development of signs and symptoms of gastroenteritis in humans (Dougan et al., 2011). Figure 1. Represents the zoonotic transmission of *Salmonella* from poultry to humans, which leads to the development of gastroenteritis in humans.

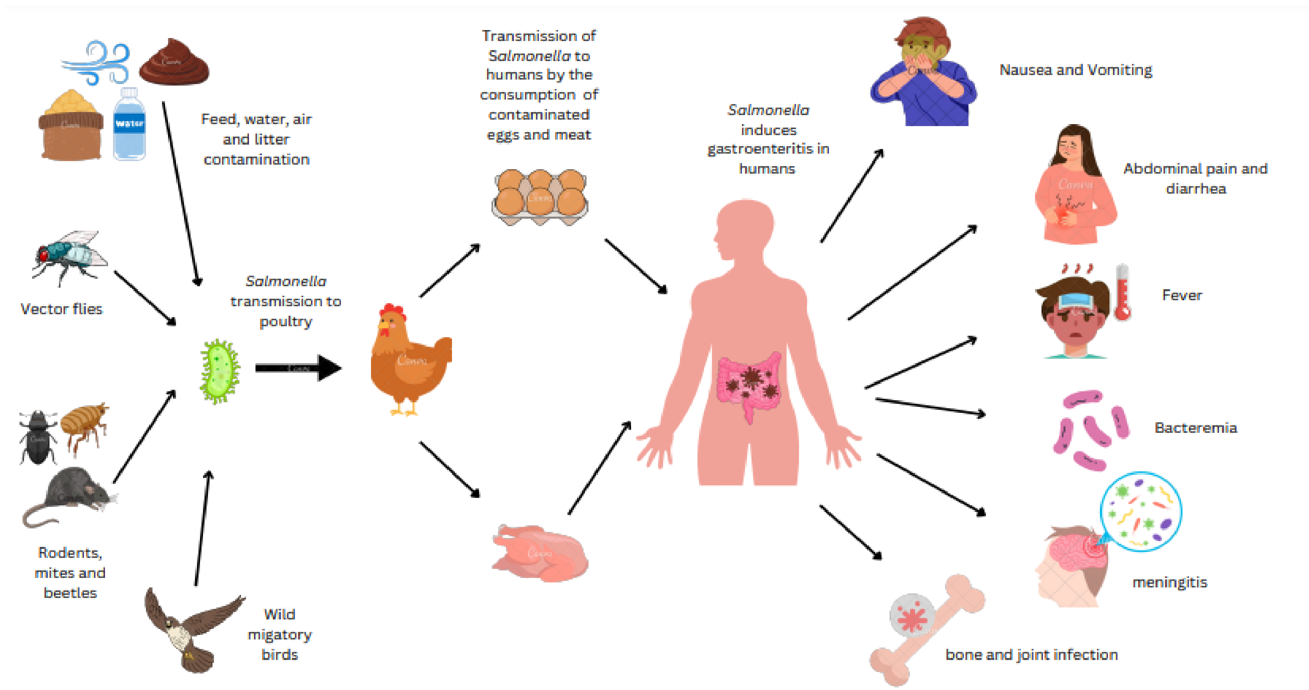

Fig. 1: Zoonotic transmission of *Salmonella* from poultry to humans

Clinical Symptoms, Diagnosis, and Treatment

The incubation period of *Salmonella* in humans is around 4 to 72 hours after ingestion of contaminated poultry products. The main clinical signs and symptoms of *Salmonella*-induced gastroenteritis are diarrhea, stomach cramps, blood in stool, vomiting, nausea, and fever, which appear 48 hours following bacterial intake. Bacteremia, meningitis, bone and joint infection, and recurrent or prolonged *Salmonella* infection in immunocompromised patients. When a *Salmonella* infection is suspected, fecal or blood culture and/or the identification of certain antibodies are utilized for early diagnosis (Hammack, 2012). The infection might cause dehydration, so oral or intravenous fluids may be essential. A brief course of oral antibiotics may be recommended for patients who are at a greater risk of developing a more fatal infection. Salmonellosis can be controlled by following appropriate sanitation and hygiene methods and avoiding undercooked or improperly handled food (Wilson et al., 2021).

Public Health Guidelines for Control and Management of Gastroenteritis

Since antibiotic residues are reported to contaminate dietary meat, substitutes for antibiotics are becoming more significant in the chicken farming industry due to the growth and development of multi-drug-resistant bacteria and related public health concerns (Abd El-Hack et al., 2022).

1. Biosecurity

Effective biosecurity measures for preventing the transmission of *Salmonella* in poultry and upgrading food quality include boot dips, employee hand sanitization, vaccinations, and facility cleanliness. Moreover, biological control, including red mite control, rodent and fly control, and *D. gallinae* control reduces the rate of infections at the farm level by interrupting the transmission cycle of *Salmonella* (Gosling et al., 2014; Sylejmani et al., 2016). Moreover, appropriate litter handling and recycling in poultry barns, reduced use of fresh wooden shavings, use of proper disinfectants, and implementation of strict measures to prevent seasonal incidence of infection are examples of biosecurity measures (Shaji et al., 2023).

2. Antibiotics

Since the 1940s, antibiotics have been considered an important part of poultry feed as they have proven beneficial for improving growth rate, minimizing gastroenteritis, and raising feed efficiency (Alagawany et al., 2018). Low concentrations of chloramphenicol, penicillin, and tetracycline antibiotics are utilized as feed additives to control enteric pathogens (Marshall & Levy 2011). However, rising antibiotic resistance in man challenges the use of antibiotics in chicken feed (Eckert et al., 2010). Resistance of *Salmonella* serotypes against cephalosporins, quinolones, and chloramphenicol antibiotics has been reported worldwide (Karon et al., 2007). Antibiotics can also lead to the deterioration of helpful gut bacteria that combat enteric pathogens. Therefore, in present times, probiotics, prebiotics, postbiotics, and synbiotics are used as substitutes for antibiotics.

3. Prebiotics

Prebiotics are described as "a substrate that is selectively utilized by host microorganisms conferring a health benefit" by the International Scientific Association for Probiotics and Prebiotics (Gibson et al., 2017). The exemplary prebiotic should be processed by the gut microbiota and be a targeted compound that facilitates the development of beneficial intestinal flora and can control pathogens while monitoring and regulating the immune responses in the host, thereby improving the overall host health status (Hajati & Rezaei, 2010). Prebiotics, including non-digestible oligosaccharides and polysaccharides, inhibit the growth and development of pathogens like *Salmonella* via the production of SCFA like butyrate and acetate in the ceca, reducing the pH of the gut (Bogusławska-Tryk et al., 2012). *Salmonella* propagation in poultry production units can be prevented by many efficient prebiotics such as yeast cell wall derived mannan oligosaccharides (MOS) (Fomentini et al., 2016), fructo-oligosaccharides (FOS), inulin (Adhikari & Kim, 2017), and xylo-oligosaccharides (Pourabedin et al., 2015).

4. Probiotic

Probiotics are defined as "non-viable food component that confers a health benefit on the host associated with modulation of the microbiota," according to the Food and Agricultural Organization (FAO) of the United Nations (UN) (Pineiro et al., 2008). Probiotic microbiota is utilized to fortify poultry such as spore-forming *Bacillus* spp. *Saccharomyces* yeast, *Enterococcus* spp. (Simon et al., 2001), *Bifidobacterium* spp. *Streptococcus* spp. and *Lactobacillus* spp. (Kabir et al., 2004). Single-species and multispecies probiotics are readily accessible in the market; the latter is recommended due to its capacity to produce a synergistic effect by targeting multiple sites (Krysiak et al., 2021). The supplementation of probiotics improves egg quality, egg harvesting, and egg weight (Menconi et al., 2014) as well as feed efficacy and intestinal T-lymphocytes in poultry (Bai et al., 2013). To ascertain the ideal circumstances for probiotic preservation and packaging, as well as to inquire about the emergence of antibiotic resistance in the gut microbiota, more investigation is required.

5. Synbiotics

Gibson and Roberfroid introduced the term "synbiotics" in 1995 to describe the synergistic combination of prebiotics and probiotics (Gibson & Roberfroid, 1995). By changing the microbiota of the gut, prebiotics in synbiotics facilitate the maintenance and nourishment of the probiotic microorganisms, enhancing their capacity to develop and limit pathogens from populating the gut epithelium (Khomayezi & Adewole, 2022). Useful intestinal bacteria including *Bifidobacterium spp*. and *Lactobacillus spp*. have been reported to multiply more effectively in broiler chickens when supplemented with synbiotic solutions containing *Lactobacillus spp*., *Saccharomyces cerevisiae* yeast, and inulin (Śliżewska et al., 2020). Furthermore, synbiotics may control immune responses against *Salmonella typhimurium* infection in broilers by activating immunoglobulins and enlarged bursal follicles and regulating lymphoid organs (spleen, bursa). (Villagrán-de La Mora et al., 2020). According to these investigations, synbiotics exhibit supporting effects and, therefore, can be utilized as promising growth boosters in the production of poultry.

6. Postbiotics

Postbiotics are metabolic byproducts or non-viable bacterial substances that are either derived from living bacteria or extracted from probiotic microbes after cell lysis and exhibit beneficial impacts on the host. Postbiotics mirror probiotics in their mechanism. Postbiotics include vitamins, peptides, organic acids, plasmalogens, enzymes, teichoic acids, SCFA, and muropeptide (Aguilar-Toalá et al., 2018). Moreover, *Salmonella* cecal colonization in broilers and layer pullets was prevented by postbiotics developed from *Saccharomyces cerevisiae* fermentation, making it a promising preharvest treatment to enhance food safety and production (Chaney et al., 2022; Chaney et al., 2023). As rising antibiotic resistance has emerged as a pressing concern, postbiotics can be utilized as a potential substitute against the enteric pathogen *Salmonella*.

7. Phytobiotics

Phytobiotics, also referred to as phytogenics or phytochemicals, originate from plants and are biologically and chemically active substances. They function by improving the health status, growth, development, and production rates of animals, particularly poultry, when utilized as feed additives. Flavonoids, alkaloids, saponins, and terpenoids are the main phytochemicals (Yang et al., 2015). By inhibiting the CASP6, IL6, IRF7, and IL8L2, and at day 23, the introduction of the phytobiotic known as Intebio to the food of growing birds infected with *S. Enteritidis* resulted in inhibiting the initial inflammatory response and restricted the pathogen multiplication (Laptev et al., 2019). Phytobiotics offer significant potential for commercial farm applications and as an antibacterial alternative against *Salmonella* in poultry.

8. Bacteriophages

Bacteriophages are viruses that invade bacteria and replicate inside the host cell by using the host's machinery. Following lysogenic penetration of their genetic material into the host cell, these phages reproduce and generate a new population of bacteriophages, triggering the lysis of bacteria and ultimately releasing new bacteriophages (Kasman et al., 2020). Because of their potential specific targeting behavior, fewer adverse side effects, and non-toxicity toward the host's natural flora, bacteriophages are utilized as antibiotic substitutes (Iqbal et al., 2016). *Salmonella* horizontal transmission was inhibited when viable eggs infected with *S. enteritidis* were transferred from incubators to hatchers, and a phage cocktail (F1055S, F12013S) was sprayed on them as an aerosol (Henriques et al., 2013). When broilers are infected with *S. enteritidis*, the treatment with CTCBIO phage dramatically decreases its stress in the cloacal swab, liver, and spleen (Kimminau et al., 2020). A combination of virulent and non-productive phages improved the survival chances of pandrug-resistant *S. typhimurium*-infected chicks by 100%. It did not lessen splenomegaly, enhance body weight, or recover the intestinal microbiota, but it did lower the bacterial stress in internal organs (Hao et al., 2023). However, the development of phage resistance is the primary problem of phage therapy (Luong et al., 2020).

9. Vaccines

Different vaccines that have been used to prevent *Salmonella* infection and increase the survival rate of poultry, by regulating the immune responses, are live-attenuated (Eeckhaut et al., 2018), killed or inactivated (Crouch et al., 2020), subunit vaccine (Sáenz et al., 2022) and ghost vaccine (Jawale & Lee, 2014).

In short, One Health techniques, contamination prevention strategies, and integrated surveillance, associated with human well-being, food security, and animal health, should be implemented thoroughly on a large scale to alleviate *Salmonella* transmission and contamination. Moreover, physicians need to evaluate the degree of *Salmonella* resistance worldwide and promote the most successful Salmonellosis treatment options, specifically for those following antibiotic medication (Antunes et al., 2016; Widodo et al., 2020).

Conclusion

Ensuring secure and clean poultry handling is crucial, considering the growing need for poultry-based products worldwide to minimize the potential risks of gastroenteritis. In the modern times of multi-drug-resistant *Salmonella*, more attention should be paid to a multifaceted strategy that lessens the bacterial load in poultry. Many approaches are currently accessible with the potential to diminish *Salmonella* contamination in poultry farming. However, precautionary measures must be implemented before practicing any of those methods on a wide scale. Furthermore, future research should be conducted to guarantee the integrity of all fresh control techniques accessible at present. More investigations should be done to study different vaccine mechanisms that can provide effective defense and target the zoonotic bacteria's different pathogenic mechanisms and thus control the zoonotic transmission of *Salmonella* into humans.

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