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Salmonellosis Remains the Hidden Menace in Our Global Food Supply: A Comprehensive Review

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Abstract Salmonellosis is a globally prevalent zoonotic disease that can occur in sporadic as well as in epidemic form. Disease is caused by *Salmonella*, which is a ubiquitous bacterium and one of the most frequently isolated foodborne pathogens. It is a major worldwide public health concern, contributing to the economic burden of both industrialized and underdeveloped countries through the costs associated with disease surveillance, prevention and treatment. As of now, over 2,500 *Salmonella* serotypes have been identified. Of these, more than half are categorized under *Salmonella* enterica subsp. enterica, which is the primary cause of *Salmonella* infections in humans. Salmonellosis remains a major foodborne zoonosis affecting around 93.8 million people with 230,000 deaths every year globally. This review aims to highlight the background information on *Salmonella* as a foodborne pathogen, illustrating its breaking point and its economic and public health burden. The pathogen naturally exists in the environment and, animals and its by-products. The primary cause of *Salmonella* infections is known to be food-borne transmission. Even though human infection occurs via ingestion of contaminated water and food with animal feces, and food-processing equipment, animal-origin food and their products are the commonest vehicles of *Salmonella* to humans. Poultry, pigs, and cattle, and their products like meat, eggs, and milk are most commonly identified as food sources responsible for outbreaks of human salmonellosis. To prevent bacterial contamination of food, it is essential to follow proper handling and cooking procedures. Risk factors such as raw animal product consumption, unstandardized slaughtering, and unhygienic food preparation and handling procedures may expose people to food-borne pathogens in general, and *Salmonella* in particular, in the country. The coordinated surveillance and monitoring system for food-borne pathogens like *Salmonella* should be done to design appropriate and effective control and prevention strategies against these pathogens in developing countries including Ethiopia. As a result, collaboration between human and veterinary practitioners is crucial for increasing disease awareness and education, particularly among susceptible risk groups. One Health approach seems imperative for the control of this major bacterial foodborne disease of global significance.

Keywords: *contamination, food producing animals, prevention, public health, salmonella, slaughter, surveillance*

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1. Introduction

Foodborne diseases (FBDs) are among the most widespread global public health problems of recent times, and their implication on health and the economy is increasingly recognized [1,2,3]. *Salmonella* is one of the most frequently isolated foodborne pathogens in the world [4] and it is estimated that 93.8 million cases of gastroenteritis due to *Salmonella* species occur globally each year, with 230,000 deaths [5,6]. In most recent years, the World Health Organization reports that the incidence and severity of cases of salmonellosis have increased significantly [7]. The most severe feature of *Salmonella* that makes it challenging to eliminate is its capacity for both vertical and horizontal transmission as well as its ability to acquire antibiotic resistance (AMR). The emergence and spread of such resistant strains among food animals is life-threatening and a global public health concern, as they are often non-treatable with currently available antimicrobials [8,9].

Salmonella is one of the most prevalent zoonotic pathogens in both developed and developing countries [10,11,12]. The genus comprises two species: *Salmonella enterica (S. enterica)* and *Salmonella bongori (S. bongori)* [13] under which over 2,500 serotypes were identified [14]. *S. enterica* is a major pathogen in humans as well as in animals [14,15]. However, *S. Typhimurium* and *S. Enteritidis* are more common [15,16].

The pathogen causes foodborne poisoning in humans and infection mainly occurs through the consumption of contaminated animal-derived food products that include eggs, meat, and milk and contact with infected animals [17]. Contamination of these foods can occur during production, processing, and distribution [18]. Poultry and other food animals are considered the common reservoirs of *Salmonella enterica* and consumption of undercooked poultry products is the major source of human infection with non-typhoidal *Salmonella*, which causes diarrhoeal and invasive disease [19].

As it has been revealed in different investigations, *Salmonella* serovars, which are most prevalent in humans are also common in poultry, suggesting a possible epidemiologic connotation that poultry could be a potential reservoir of human *Salmonella* infection. For instance, it was indicated in a study that *S. Enteritidis* and *S. Heidelberg* were the most frequently isolated serovars in the United States, which were also among the top serovars causing human infection [20]. Similarly, *S infantis*, *S. stanley*, and *S. kentucky* - all serovars originated from poultry meat- are also reported to be associated with human salmonellosis in European countries [3,21].

Generally, *Salmonella* infection remains a major public health concern worldwide, contributing to the economic burden of both industrialized and underdeveloped countries, through the costs associated with surveillance, prevention, and treatment of disease [22,23]. Apart from the morbidity and mortality costs in humans and animals, restrictions to trade and disposal of contaminated food are other significant socio-economic problems of the bacteria [9]. However, there is a lack of well-organized and documented information on food-borne diseases in general and *Salmonella* specifically in Ethiopia as well as in most developing countries. Therefore, the objectives of this review paper are:

1.1. General Objective

The general objective of this paper is to review *Salmonella* as a food-borne pathogen and its economic and public health importance.

1.2. Specific Objectives

- The specific objective is to update the status of *Salmonella* in the world, with special reference to its implications on epidemiology and public health, food chain and risk assessment, antimicrobial resistance, and control strategies.
- This review is an opportunity to collect significant and relevant information, using an integral approach, on Animal Health, Public Health, and the relationship between the two.

2. Literature Review

2.1. History and Nomenclature

Salmonella was first discovered and isolated from the intestines of porcine infected with classical swine fever, by Theobald Smith in 1855 and his colleague, Dr. Salmon after whom the bacteria was named [24].

The classification and nomenclature of *Salmonella* have been controversial for many years. The Centers for Disease Control and Prevention (CDC) currently adopts the *Salmonella* classification system recommended by the World Health Organization (WHO) Collaborating Centre [25,26]. This system divides the genus *Salmonella* into two species: *Salmonella* enterica (the type species) and *Salmonella bongori*, based on variations in their 16S rRNA sequences. *Salmonella* enterica, the type species, is further categorized into six subspecies based on genetic and biochemical characteristics. These are *S. enterica* subsp. e*nterica* (I), *S. enterica* subsp. s*alamae* (II), *S. enterica* subsp. a*rizonae* (IIIa), *S. enterica* subsp. d*iarizonae* (IIIb), *S. enterica* subsp. *houtenae* (IV) and *S. enterica* subsp. i*ndica* (VI) [13]. Out of these subspecies, *S. enterica subsp. enterica* (I) is found predominantly in mammals and contributes to approximately 99% of *Salmonella* infections in humans and warm-blooded animals [27]. As a result, human infection with the remaining five *Salmonella* subspecies and *S. bongori* is rare because these organisms are primarily found in the environment and cold-blooded animals [28].

In addition to classification into subspecies, the species are further sub-classified into serotypes using the Kauffman-White scheme, which is defined and maintained by the WHO collaborating centre for reference and research on *Salmonella* at the Pasteur Institute, Paris, France. The classification is based on the extensive diversity of lipopolysaccharide antigen (*O antigen*), flagellar protein antigen (*H antigen*), and capsular (K) antigens. Currently, there are more than 2500 serotypes of *Salmonella*, and new serotypes are listed on annual updates of the Kauffman-White scheme [13], out of which more than 150 serotypes can cause food-borne salmonellosis.

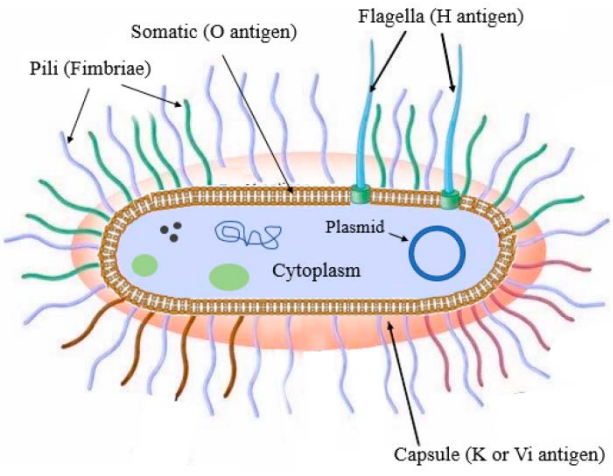

Figure 1. Schematic illustration of the structure of *Salmonella* (adopted from https://www.cram.com/flashcards/enterobacteriaceae-5178261 and modified using Biorendor software. (accessed on 28 August, 2024))

Salmonella serotypes can be identified by performing an agglutination test using antibodies unique to the O antigens to classify the organism into six serogroups, namely A, B, C1, C2, D, and E. This approach offers crucial evidence for epidemiological study and enables genus and/or species-level identification [29]. Thus, so far,

more than 2500 serovars have been identified; more than half of these serotypes are part of *S. enterica* subsp enterica, which is responsible for most human salmonellosis [30]. When describing *Salmonella* in the literature, their taxonomy and nomenclature should adhere to a standard format (*Salmonella* enterica subspecies enterica serovar Typhimurium, which is shortened as *S. Typhimurium*) [31]. More recently, a taxonomic classification was proposed based on whole genome sequence data to define a two-tier subtyping approach: multilocus sequence typing (MLST) followed by antigen prediction. Using this approach, the researchers classified 46,000 isolates of *Salmonella enterica* subspecies *enterica* that showed a 99.96% match to a serovar organized by the Kauffmann and White scheme [32].

2.2. Cultural and Biochemical Characteristics

Salmonella e are small, gram-negative, non-sporing rods, facultative anaerobic bacilli, and 2 to 3 by 0.4 to 0.6 μm in size [33]. Similar to other members of the family Enterobacteriaceae, they produce acid on glucose fermentation; reduce nitrates to nitrite, and are incapable of producing cytochrome oxidase. Most organisms, except *S.gallinarum* and *S.pullorum* are motile by peritrichous flagella [34]. Certain *Salmonella* serotypes can be distinguished by their distinct sugar metabolisms. It is observed that most *Salmonella* e do not ferment lactose whereas the only organism that does not release gas during the fermentation of sugar is *S.* Typhi.

Salmonella is non-capsulated except *S.* Typhi, *S.* Paratyphi, and some strains of *S.* Dublin. *Salmonella* grows between 8°C and 45°C (optimally at 37°C) and at a pH of 4 to 9. A temperature higher than 70°C rapidly kills the bacteria. These bacteria can resist dehydration for a very long time (Aw ≥ 0.93), both in faeces and in foods for human and animal consumption. In addition, they can survive for several months in saltwater with 20% salinity, particularly in products with a high protein or fat content, such as salted sausages. They are also resistant to smoking. *Salmonella* spp. has several virulence factors that contribute to diarrhea, bacteremia, and septicemia. These factors include the lipopolysaccharide of the outer wall, pili, flagella, cytotoxin, and enterotoxin [35].

2.3. Epidemiology of *Salmonella*

Salmonella is one of the biggest threats to public health, worldwide. It is the most common food-borne diseases in both developing and developed countries, although incidence rates vary according to the country [36] that affects both the humans and animals throughout the world [25,37,38]. Approximately, 93.8 million human cases of salmonellosis are reported annually around the world annually, with 155,000 deaths [5].

2.3.1. Distributions of typhoid Salmonella and non-typhoid Salmonella infections

Salmonella is one of the known food-borne pathogen with major public health and economic concerns all over the world. It is the most common food-borne disease in both developing and developed countries, although incidence rates vary according to the country [36,39].

The disease has been recognized in all countries but appears to be most prevalent in areas of intensive animal husbandry, especially poultry and swine production. Three categories can be used to classify *Salmonella* for epidemiological purposes: Those that exclusively infect humans: Include *S.* Typhi, *S.* Paratyphi A, and *S.* Paratyphi C. This group encompasses the bacteria responsible for typhoid and paratyphoid fevers, which are among the most serious diseases caused by *Salmonella*. The longest incubation period, highest body temperature, and highest death rate are all associated with typhoid fever. Before enteric fever, S. Typhi can be isolated from a victim's blood, urine, and occasionally their faeces. Compared to typhoid, paratyphoid syndrome is less severe. The host-adapted serovars include *S. Gallinarum* (poultry), *S. Dublin* (cattle), *S. Abortus-equi* (horses), *S. Abortus-ovis* (sheep), and *S. Choleraesuis* (swine). These are pathogenic for humans and other animals, and they include most food-borne serovars [40,41].

2.3.2. Source of Infection and Route of Transmission

The pathogen naturally occurs in the environment and animals and its by-products. Food-borne transmission is recognized as the major cause of *Salmonella* infections [42]. Even though human infection occurs via ingestion of contaminated water and food with animal faeces, and food-processing equipment, animal-origin food and their products are the commonest vehicles of *Salmonella* to humans [43]. Contaminated water or food acts as a major transmission route of enteric fever. Enteric fever is mostly transmitted through the fecal–oral route, which involves drinking water or consuming food contaminated by the faeces of chronic carriers. In endemic places, enteric fever is caused by carriers of *S.* Typhi and *S.* Paratyphi. [44] (Figure 2). Nearly 4% of enteric fever patients, including infants, the aging population, and women, may serve as chronic carriers [45]. On the other hand, a carrier state of NTS occurs in only 0.1% of patients, because animals are the primary source of NTS, rather than humans.

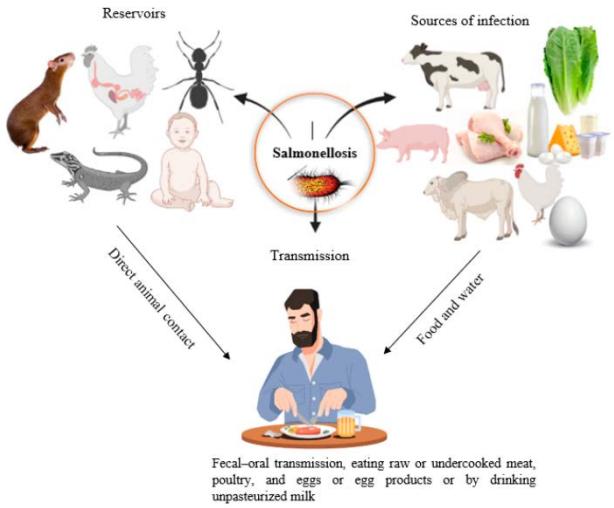

Figure 2. Diagram showing the primary reservoir, source of infection, and the transmission mechanism of human salmonellosis. Insects, reptiles, humans, and animals can serve as a reservoir for human salmonellosis. Uncooked, undercooked, and/or contaminated foods (poultry, beef, pork, egg, milk, milk products, vegetables, flour, nuts, etc.) are familiar sources of infection

Contaminated animal products generally result from infection in the animals used for food or from contamination of their carcasses or edible organs. The main source of human food-borne infections is fecal or intestinal contamination of carcasses, though *Salmonella* can also be directly transmitted into food products. Additionally, cross-contamination can occur during slaughtering processes [15]. Eggshells and egg contents can be contaminated by this bacterium during egg formation by fecal contact in the hen's reproductive system or from the environment [36]. It was indicated that the recently emerged *S.* Typhimurium DT104, which is known as a multidrug-resistant definitive type, is mainly transmitted through ingestion of contaminated beef [46].

2.3.3. Risk Factors for Animal Infections

Salmonella naturally occurs in the environment and can be found in both domestic and wild animals [47]. The widespread carrier status in animals is an important epidemiological factor. The primary habitat of *Salmonella* species is the intestinal tract of animals such as farm animals, humans, birds, reptiles, and insects. Animals are the reservoir of food-borne diseases caused by *Salmonella [48]*.

2.3.4. Risk Factors for Human Infection

Non-typhoidal Salmonella species (including all *Salmonella* strains other than *S.* Typhi and S. Paratyphi, - which are known as *typhoidal Salmonella*) [49] are zoonotic agents, and food products of animal origin are the main sources for their transmission [15]. Poultry, pigs, and cattle, and their products like eggs, meat, and milk are most commonly identified as food sources responsible for outbreaks of human salmonellosis [38,47,50] although the microorganism has also been found in other foodstuffs. Chicken products including eggs are widely acknowledged to be a significant reservoir of *Salmonella* and have been consistently implicated in sporadic cases and outbreak of human salmonellosis [43,51].

An outbreak of salmonellosis in humans has been linked to several factors, including the consumption of raw or unsafe food, improper food storage, cross-contamination, poor personal hygiene practices, inadequate cooling and reheating of food items, and a prolonged period between food preparation and consumption [42]. The bacteria can infiltrate the food chain at any stage during the production, processing, retailing, catering, and preparation of food for livestock. They can also withstand the normal refrigerated temperatures utilised for catering and proliferate when exposed to high temperatures [36]. Human and animal infections with antibiotic-resistant *Salmonella* are a global concern, especially in developing nations where the risk of infection is high due to unsanitary living conditions, animal-human close contact and house sharing, and customs involving the consumption of undercooked or raw animal origin food [42].

2.4. Pathogenesis

The severity of *Salmonella* infections in humans varies depending on the serotype involved and the health status of the animal and human host. Almost all strains of *Salmonella* are pathogenic as they can invade, replicate, and survive in human host cells, resulting in potentially fatal disease [27]. The pathogenicity of the organism is mediated by variables such host susceptibility, infectious dosage, route of infection, and strain virulence. Virulence factors such as virulence plasmids, toxins, fimbriae, and flagellae help in establishing an infection [43]. The product of several chromosomal genes mediates the complex invasion process, whereas growth within the host cell depends on the presence of virulence plasmids [48]. The microfold (M) cell is the target cell of *Salmonella* pathogenicity. Some of the mechanisms of pathogenesis are bacterial-mediated endocytosis, neutrophil recruitment and migration, epithelial cell cytokine secretion, fluid and electrolyte secretion, and systemic infection [43].

Salmonella avoids host defense in the stomach, reaches the intestines, and interacts with the non-phagocytic cells such as the epithelial cells of the intestinal mucosa. They adhere to the intestinal epithelial cells by fimbriae that promote binding and invade epithelial cells to provoke gastroenteritis [43]. Enteric infection is characterized by local damage without septicemia. This is followed by the ruffling of the target cell membrane, which results in the internalization of the bacteria in membrane-bound vacuoles. The ruffles facilitate the uptake of the bacteria in membrane-bound vacuoles or vesicles, which often coalesce [46,48]

2.5. Clinical Signs

The most common symptom of *Salmonella* infection is acute gastroenteritis. The incubation period varies widely from 4 hours to 72 hours after the ingestion of contaminated food or water. Symptoms are acute onset of fever which subsides in 72 hours, chills, nausea, vomiting, abdominal cramping, and diarrhea (Figure 3). Typhoid fever is usually manifested by gastrointestinal symptoms, but some cases may show various clinical syndromes like disseminated intravascular coagulation and acute respiratory distress syndrome. The clinical disease usually appears after 12-72 hours of infection and is characterized by diarrhea with fever, nausea, vomiting, abdominal pain, headache, bradycardia, and cough [52,53].

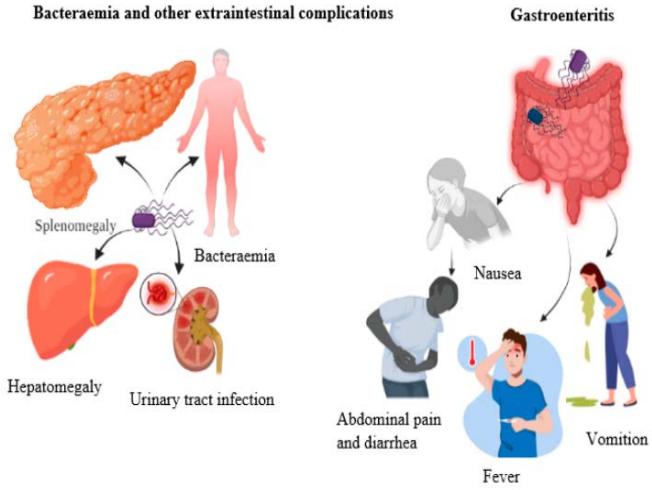

Figure 3. Source: Human Salmonellosis: A Continuous Global Threat in the Farm-to-Fork Food Safety Continuum by Addisu D. Teklemariam et al, 2023, *Foods* 2023, *12*(9), 1756; accessed from https:// doi.org/ 10.3390/foods12091756 on 31.08.2024

Non-typhoid *Salmonella (*NTS) infections are characterized by gastroenteritis or 'stomach flu', an inflammatory condition of the gastrointestinal tract which is accompanied by symptoms such as non-bloody diarrhea, vomiting, nausea, headache, abdominal cramps, and myalgias. Some cases of NTS show symptoms such as hepatomegaly and splenomegaly [54]. Compared to typhoid infections, NTS infections have a shorter incubation period (6–12 h) and the symptoms are usually self-limiting and last only for 10 days or less [23].

Gastrointestinal complications of NTS infections include cholecystitis, pancreatitis, and appendicitis, while the perforation of the terminal ileum has no association with NTS infections [54]. Infants, young children, elderly people, and immune- compromised patients are highly susceptible to NTS infections and develop more severe symptoms than normal individuals [55]. The infection always occurs through the ingestion of water or food contaminated with animal waste rather than human waste. The emergence of multidrug-resistant *S.* Typhimurium DT104 has been associated with outbreaks related to beef contamination and resulted in hospitalization rates twice that of another foodborne salmonellosis [46,56].

2.6. Diagnosis of *Salmonella*

2.6.1. Culture Method

Traditional techniques for identifying bacteria often involve assessing the microorganism's morphology and testing its capacity to grow in a range of mediums under a variety of conditions. These methods are very sensitive, inexpensive, and can give both qualitative and quantitative information on the number and the nature of microorganisms present in the food sample [57].

Although standard microbiological techniques allow the detection of single bacteria, implication of the signal is required through the growth of a single cell into a colony. Cultural methods of *Salmonella* typically involve the enrichment of a portion of the sample to recover sub-lethally injured bacterial cells due to heat, cold, acid, or osmotic shock [57]. Isolation of *Salmonella* by culture-based method is still the most widely used detection technique and remains the gold standard for the detection of *Salmonella* due to their selectivity and sensitivity [58].

The number of target cells is generally not uniformly distributed in foods, typically occurs in low numbers, and may be present in a mixed microbial population. Hence, the samples are usually inoculated into a non-selective pre-enrichment media, such as Buffered Peptone Water (BPW). Further, primary enrichment cultures are typically inoculated into secondary selective enrichment broths, such as Selenite Cysteine broth (SC), Rappaport Vasiliadis Soya broth (RVS), Tetrathionate broth (TT), or Muller Kauffmann Tetrathionate-Novobiocin broth (MKTTn) and incubated at elevated temperatures (37°C or 42°C for 18- 24 hours) before streaking onto selective agars such as Xylose Lysine Deoxycholate agar (XLD agar), Bismuth Iron Sulphate agar (BIS), Brilliant Green agar (BGA) with or without the addition of sulfadiazine or sulfa pyridine (BGS), modified semisolid Rappaport Vasiliadis (MSRV), *Salmonella* Shigella Agar, or Hektoen Enteric agar. There are several published standard methods utilizing combinations of media such as the current ISO horizontal method, ISO 6579:2002 for the detection of *Salmonella* spp.

Under circumstances in which high throughput screening is required for a large number of samples, the laborious and tedious culture-based methods may not be able to adequately address the need. The traditional techniques have been enhanced to provide quicker identification and detection of *Salmonella* while additionally reducing labour and expense. For example, chromogenic and fluorogenic growth media used for detection, enumeration, and identification directly on the isolation plate have shown to be more convenient, reliable, specific, and selective than conventional media [57].

Due to their affordability, convenience of use, high sensitivity and specificity, and dependability when compared to newly developing molecular-based technologies, conventional microbiological methods are the foundation for analysis in many food safety and public health laboratories. However, for performing these procedures, it is needed to prepare multiple subcultures required several identification steps, taking more than 5 days to complete isolation and confirmation. In addition, false positive results may occur due to competitive flora (e.g. proteus) [59]. Although some immunological rapid assays are available, these assays still require enrichment steps and give results in 18–48 hr. Enzyme-linked immunoassay (ELISA) [60] and polymerase chain reaction (PCR) are robust but require several lengthy steps, expensive laboratory instruments, and experienced operators [59].

2.6.2. Immunology-based Assays

Enzyme-linked Immunosorbent assay (ELISA): Different ELISA systems have been developed and are commercially available in kit form. An antigen specific to *Salmonella* species is coupled to the specific antibody and bound to a solid matrix in the ELISA assay. After forming the antigen-antibody complex, the concentration of the antigen and the presence of *Salmonella* can be measured through the change in color caused by the enzymatic cleavage of a chromogenic substrate. As an alternative, antigens coupled to the solid phase of ELISA can be used to identify the presence of antibodies in samples infected with *Salmonella* spp. Additionally, antibodies for the manufacturing of vaccines against *Salmonella* infections have been identified through ELISAs. At present, there is a lack of standardization of ELISA assays for non-typhoidal salmonellosis. A challenge with developing serologic tests for NTS is the diversity of non-typhoidal serovars globally, which will require empirically uniform and perhaps locally targeted, selection of LPS antigens to achieve adequate sensitivity. Additionally, it will be difficult for serologic diagnostics using current technologies to distinguish between the two syndromes NTS can cause: self-limiting gastroenteritis and invasive systemic infection [61].

Latex agglutination test: The agglutination technique employs latex particles coated with antibodies which react with antigens on the surface of *Salmonella* cells to form visible aggregates for identification of *Salmonella* positive samples [62]. The assays are specific, uncomplicated, and

reliable so that generally, they have been used as a confirmatory analysis technique, rather screening test for *Salmonella* organisms [63].

Immuno-diffusion assays: In this test, the sample is pre-enriched for 24 hours prior to being inoculated into the system unit, which is made up of two connected chambers. In the inoculation chamber, the enriched sample is injected with Tetrathionate brilliant green broth. After that, the bacteria leave the inoculation chamber and enter the mobility chamber, wherein a distal surface of a semisolid medium has been coated with an antibody. *Salmonella* in the mobility chamber is immobilized by forming an antigen-antibody complex. After incubation for 14 hrs, the readable three-dimensional immune diffusion band is produced. Modifications in an enrichment step before inoculation and an increase of incubation time improved the effectiveness of detection of *Salmonella* spp. [64].

2.6.3. Nucleic acid-based Assays

The nucleic acid-based assays (NADs) are *Salmonella* detection tests that utilize a specific nucleic acid target sequence within the organism [65]. The assays have been most intensively explored and developed for the past decade because they offer advantages of sensitivity, specificity, and inclusivity over other methods, rapidly identifying *Salmonella* without obtaining pure cultures. Direct hybridization (DNA probe) and amplification (PCR) methods are the two major techniques of the assays. The remarkable advancement of the assays allows the detection of very low numbers of organisms in the sample and high throughput of samples for routine analysis [66].

Polymerase chain reaction (PCR): Conventional methods for detection of *Salmonella* serovars in foods are generally time consuming and labor intensive. Several *Salmonella* specific target genes such as *ori*C, *fim*A, *him*A, *hil*A, and *stn* have been identified. However, none of the primer sets for these genes has been shown to be 100% accurate. This observation may be due to either the lack of species specificity of these genetic markers or the uneven distribution of these markers within the *Salmonella* population. The *Salmonella* invasion gene, *inv*A, has been shown to be involved in internalization of *Salmonella* Typhimurium in mammalian epithelial cells. This gene is unique to *Salmonella* , and the DNA sequence is highly conserved among *Salmonella* spp. These properties suggested that the *inv*A gene could serve as a reliable and accurate target gene for detection of *Salmonella* by PCR methods [67]. A real-time PCR method has been developed with custom designed primers and a Taq Man probe to detect the presence of a 262-bp fragment of the *Salmonella* -specific *inv*A gene [66].

However, the disadvantage of PCR is that the procedure is rather complicated and a very clean environment is needed to perform the tests. Further, PCR cannot distinguish between live and dead cells and hence providing more false negative results. Confirms positive *Salmonella* isolates from bovine and poultry origin by using multiplex PCR to amplify the pathogenic genes of *S.* Typhimurium, *S.* Enteritidis and *S.* Infantis by using specific primers for these genes. The method was highly specific in detecting *Salmonella* in spiked chili powder and shrimp samples, with a sensitivity of 0.04 CFU/g [68].

2.6.4. Biosensors

Biosensors are defined as an analytical device that integrates a biologically derived molecular recognition molecule such as antibodies, phages, or single-stranded DNA, with a suitable physicochemical transducing mechanism. Common transducing elements are optical, electrochemical, thermometric, piezoelectric, magnetic and others [69]. Biosensors produce an electronic or optical signal proportional to the specific interaction between the analytic and the recognition molecule present on the biosensor. Biosensors are capable of detecting a diverse array of targets, ranging from small protein molecules to large pathogens. In contrast to conventional methods, a biosensor is a device for pathogenic antigen detection that does not require highly skilled workers to operate. Further, if biosensor is highly sensitive and selective it provide results more rapidly than culture-based methods, making them ideal for practical and field applications [70]. In the food industry, biosensors are primarily employed for two key functions. The first involves the detection and quantification of compounds such as carbohydrates, alcohols, amino acids, amines, amides, and phenols, with a particular focus on applications within the liquor and beverage sectors. The second function is the identification of microorganisms present in food products. Among the diverse types of biosensors available, the industry predominantly utilizes enzyme-based biosensors and immunosensors for these purposes [71].

2.7. Treatment

Treatment of non-typhoidal *Salmonella* infection varies significantly from typhoidal infection. In treatment of non-typhoidal *Salmonella* infection, unlike typhoid, antibiotics should not be used routinely. Antibiotic should be used sparingly as infection with non-typhoidal *Salmonella* is usually self-limiting in nature and the duration of diarrhea and fever typically remains largely unchanged with the use of antibiotics. Antibiotic medication can potentially lengthen the duration of gastrointestinal carrier states and increase the risk of infection relapse. The main treatment should be aimed at correcting dehydration that may arise due to prolonged diarrhea by fluid and electrolyte replacement [72]. In case of patients with bacteremia and other complications, antimicrobials are used. Similarly, the treatment of enteric fever necessitates the use of antimicrobial drugs with chloramphenicol, ampicillin, amoxicillin, trimethoprim sulfamethoxazole and newer fluoroquinoazoles being drug of choice. Proper management of fluid and electrolyte balance is important in all patients with *Salmonella* gastroenteritis but is crucial in young children and elder individuals [73].

In animal treatment, supportive treatment with intravenous fluid is necessary for patients that have anorexia, depression, and significant dehydration. After an acid-base and electrolyte examination, a patient could be given aggressive treatment. Oral fluid and electrolyte solutions may prove to be a cost-effective alternative to intravenous fluids for mildly or moderately dehydrated cattle [74]. The efficacy of oral fluid therapy in cattle with salmonellosis may be partially diminished due to issues with malabsorption and maldigestion. However, it remains

a valuable treatment option. For cattle that can drink, adding specific electrolytes to the drinking water can aid in restoring electrolyte balance. The implementation of broad prophylactic strategies that are efficacious for all *Salmonella* e may be required in order to overcome the diversity of *Salmonella* serovars present on farms, and the potential for different serovars to possess different virulence factors [75]. Early intervention is crucial for managing septicemic salmonellosis; however, the use of antimicrobial agents for treating intestinal salmonellosis remains a subject of debate. Oral antibiotic may alter the intestinal micro flora and interfere with competitive antagonism and prolong shedding of the organism. There is also a concern that antibiotic resistant strain of *Salmonella* selected by oral antibiotic may subsequently infect human. Antibiotic such as ampicillin or cephalosporin lead to lysis of bacteria with the release of end toxin [76].

2.8. Food Borne Burden of Salmonellosis

People of all ages are affected by foodborne illnesses, although those under five and those residing in low-income areas of the world are disproportionately affected. Research has shown that foodborne illnesses are a major global cause of morbidity and mortality as well as a major barrier to socioeconomic development [77]. Between 2007 and 2015, the World Health Organization's Foodborne Diseases Epidemiology Reference Group (WHO-FERG) assessed the global burden of foodborne diseases, including incidence, mortality, and disability-adjusted life years (DALYs). Their findings indicated that, in 2010, 31 global hazards were responsible for approximately 600 million foodborne illnesses and 420,000 deaths. In that case, the initiatives recited that most frequent causes of foodborne illness were diarrhoeal disease agents. Foodborne diarrhoeal disease agents caused 230,000 deaths, which was particularly attributed to *non-typhoidal Salmonella enterica* [7].

Although NTS is the more common than Typhoidal salmonellosis, both the infections and are known to pose great food borne burden in different parts of the world. *Salmonella*e are widely distributed in nature [43] and they are the major pathogenic bacteria in humans as well as in animals. They are most frequently isolated bacterial agents of food-borne disease outbreaks [51], and they account around 93.8 million food-borne illnesses and 155,000 deaths per year worldwide [47]. NTS infections, which cause self-limited illness, are the most common *Salmonella* infections, and occur worldwide whereas the enteric fever, caused by typhoidal *Salmonella* , is associated with a high morbidity and mortality rate and occurs predominantly in underdeveloped countries [78]. More or less the emergence and spread of antimicrobial-resistant *Salmonella* strains have become a serious health hazard worldwide [79]. It is believed that the widespread use of antimicrobials in food-producing animals during rearing has contributed to the occurrence of *Salmonella* with decreased susceptibility to antimicrobials [80].

2.9. Antibiotic Resistance

The emergence of antimicrobial resistance in *Salmonella* strains is a serious health problem worldwide [81]. In the early 1960s, the first incidence of *Salmonella* resistance to a single antibiotic, namely chloramphenicol, was reported [82]. Since then, the frequency of isolation of *Salmonella* strains with resistance towards one or more antimicrobial agents has increased in many countries, including the USA, the UK and Saudi Arabia [83]. Antimicrobial agents such as ampicillin, chloramphenicol and trimethoprim–sulfamethoxazole is used as the traditional first line treatments for *Salmonella* infections. *Salmonella* species resistant towards these agents are referred to as multi-drug resistant (MDR). The widespread prevalence of multidrug-resistant (MDR) isolates has been recorded and this has influenced the impact of typhoid fever in developing countries [84].

In *S.* Enterica antimicrobial resistance (AMR) genes were detected in 68% of isolates from meat and dairy products [85]. Moreover, more than 43 isolates of *Salmonella* from chicken beddings and humans exhibited resistance to kanamycin and sulfamethoxazole-trimethoprim, nalidixic acid, ampicillin, cefoxitin, streptomycin, tetracycline, chloramphenicol, ciprofloxacin, and gentamicin [9]. Lately in 2019, demonstrated AMR genes in 76.7% of *S.* Enterica strains isolated from broiler chicken farms and chicken carcasses in retail shops at El-Sharkia province, in Egypt [86]. In a study carried out in Lower Egypt, AMR genes of *Salmonella* Typhi isolated from 29% patients showed resistance to chloramphenicol, ampicillin and trimethoprim-sulfamethoxazole [87].

To date, the emergence of *Salmonella* serotypes resistant to quinolones and cephalosporin poses a new challenge in treating infected patients, and the lack of an effective antibiotic therapy may lead to an increase in the morbidity and mortality rates [27]. The severity of bacterial infections in both humans and animals has risen as a result of the introduction of multidrug resistant Salmonella. Epidemiological studies indicate that MDR *Salmonella* strains are associated with more severe or prolonged illnesses compared to susceptible strains, implying that these MDR strains exhibit greater virulence [88]. Patients infected with multidrug-resistant (MDR) *Salmonella* strains often exhibit more severe illness and septic symptoms at the onset of the disease. This is typically accompanied by high fever, enlargement of the spleen and liver, and abdominal swelling [46].

2.10. Control and Prevention Methods

2.10.1. Reducing Animal Product Contamination

Food products may become contaminated along the food chain, mostly during the different stages of production, processing, distribution, preparation, and final consumption [89]. The likelihood of food contamination is mostly determined by the personal hygiene of the food handlers, the health status, personal cleanliness, knowledge, and practice of food handlers [90]. Food-borne microbes are major problems affecting food safety and cause infection following the consumption of animal products contaminated with microorganisms or their toxins. Therefore, minimization of food contamination is considered as mainstay in preventing the risk of *Salmonella* infection, which can be achieved at production,

transportation and service stages [46,47].

Implementing biosecurity and bio-containment measures in addition to enhanced food processing method and preparation and storage practices are required to control and prevent food spoilage due to *Salmonella* (48). Safe food preparation practices including thorough cooking, reheating of food, pasteurization (boiling) of milk, adequate refrigeration, and exclusion of pets and other animals from food-handling areas should be followed. Additional measures to control secondary contamination could be; prevention of contamination by cleaning and disinfection, hygiene of personnel, and proper processing [43]. Vulnerable groups are advised to avoid consuming undercooked meat and poultry, raw milk, eggs, and foods that contain raw egg [48]. Currently, there is no vaccine available for the prevention of salmonellosis in adult populations. However, a vaccine has been developed to protect against *Salmonella* typhi, particularly for children, though its efficacy is limited to approximately 60% [91].

2.10.2. Environmental Management

Contaminated water or food is the major route of transmission of enteric fever. Environments contaminated with *Salmonella* serve as a critical source of infection, as *Salmonella* can survive in these settings for prolonged durations. Further, bacterium is transmitted to vectors such as rats, flies and birds where it is shed in their faeces for weeks and even months. Following the direct transmission, animals such as pigs, cows and chickens act as the important risk factor for infection. These animal reservoirs are infected orally because *Salmonella* normally originates from the contaminated environment and contaminated feed [92]. Proper sanitation, correct sewage disposal and provision of clean water system can minimize the transmission of typhoid fever. The intervention strategies including *Salmonella e* monitoring programs along the farm-to-table continuum should be initiated in the environment surrounding susceptible population. Implementing environmental hygiene with respect to human and animal feces is an important approach to decreasing the environmental reservoir of pathogens, thus limiting the transmission to human beings [93].

2.11. Status of Salmonellosis in Ethiopia

In the 21st century, foodborne diseases have emerged as significant public health issues in both developed and developing nations. A substantial portion of the population is affected by illnesses or fatalities attributable to the consumption of unsafe food *Salmonella* infection most commonly occurs in countries with poor standards of hygiene in food preparation and handling and where sanitary disposal of sewage is lacking [94]. Studies indicated the widespread occurrence and distribution of *Salmonella* in Ethiopia. In Ethiopia, minced beef is usually used for the preparation of a popular traditional Ethiopian dish known as locally "*Kitfo*" and majorly, it is consumed raw or medium cooked. The consumption of raw meat and the detection of *Salmonella* in minced beef, along with substandard food handling practices, highlight significant public health risks associated with *Salmonella* in the country [95].

Investigations conducted in different parts of Ethiopia have confirmed the presence of *Salmonella* in human beings, different food animals, and food of animal origin. Despite existing reports on the prevalence and distribution of *Salmonella* species within the country, the issue of *Salmonella* contamination in animal-origin foods remains inadequately characterized. Furthermore, risk factors related to the contamination of animal products have not been well-documented, and incidence of food-borne salmonellosis is still unknown in the country [36,42]. Potential risk factors for Salmonella infection in the nation include the prevalence of raw meat consumption, the existence of carrier food animals, the illegal slaughtering of animals in open spaces, unsanitary slaughter procedures in abattoirs, etc. [96]. Few published findings on prevalence of non-typhoidal *Salmonella* in different parts of Ethiopia are shown in Table 1.

Table 1. Distributions of *Salmonella* in different parts of Ethiopia

Locations	Species	Prevalence (%)	Reference (s)
Central Ethiopia	shoats	1.8	[97]
Addis Ababa	cattle	10.76	[48]
Addis Ababa	shoats	1.04	[50]
Gondar	cattle	17.30	[98]
Holeta	cattle	5.60	[99]
Asella	cattle	6.50	[100]
Gondar	cattle	5.50	[42]
Addis Ababa	cattle	3.70	[101]
Dessie	cattle	4.95	[102]
Bahir Dar	cattle	70	[103]
Modjo and Bishoftu	shoats	17.21	[104]
Ambo	cattle	8	[105]
Wolaita Sodo	cattle	12.50	[106]
Addis Ababa	cattle	7.50	[107]
Addis Ababa and Mojo	poultry	2.9	[3]
Modjo	poultry	15.12	[99]
Central Ethiopia	poultry	11.5	[108]
Addis Ababa	cattle	1.6	[109]
	poultry	16.7	[9]

3. Conclusions and Recommendations

Food-borne pathogens are the leading causes of human illness worldwide with a great burden in developing countries resulting in huge economic loss in addition to public health issues. From this review, it is concluded that *Salmonella* is one of the most frequently isolated foodborne pathogens and salmonellosis is one of the major foodborne diseases in the world. It was estimated that 93.8 million cases of gastroenteritis due to *Salmonella* species occur globally each year, with 230,000 deaths. Food animals including poultry, pigs and cattle are recognized as the chief cause of human salmonellosis. This bacterium can enter into the food chain from production of food animals up to the final consumption of animal products. Additionally, the emergence of multidrug-resistant *Salmonella* strains has heightened public health concerns. The recommended methods for eliminating food contamination by bacteria include handling and cooking food properly. Risk factors such as the consumption of raw animal products, unregulated

slaughtering processes, and inadequate food preparation and handling procedures may increase susceptibility to foodborne pathogens in general, and *Salmonella* in particular, within the country. Based on the above conclusion, the following points are recommended:

- Good manufacturing practices, standardized slaughtering and pasteurization procedures, and hygienic animal product preparation techniques should be strictly implemented.
- Public awareness initiatives should be implemented to enhance understanding of preventive measures against *Salmonella* pathogens, thereby reducing their impact on both human health and animal well-being. Prevention strategies include proper handling of food and water, improved sanitation, public awareness, and government initiatives supported by surveillance systems.
- Collaboration between human and veterinary practitioners is very crucial to increase awareness and education about the disease importance especially among susceptible risk groups.
- Future control efforts should place a priority on regulatory strengthening, health promotion, investment in sanitation infrastructure, and dealing with health-related problems to decrease NTS infections effectively.
- There is a pressing need for having a strict biosecurity and regulation on the use of antimicrobials throughout the world to mitigate the problems of antimicrobial resistance.

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Contribution of Authors

All the authors contributed during the preparation of the manuscript.

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