Epidemiology of Human Salmonellosis

Subjects: Microbiology

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Salmonella is one of the most common zoonotic foodborne pathogens and a worldwide public health threat. *Salmonella enterica* is the most pathogenic among *Salmonella* species, comprising over 2500 serovars. It causes typhoid fever and gastroenteritis, and the serovars responsible for the later disease are known as non-typhoidal *Salmonella* (NTS). Among *Salmonella* infections, NTS infections are the most common cause of self-limiting illness. Enteric fever caused by typhoid *Salmonella* has a high mortality and morbidity rate and occurs more frequently in developing nations.

Keywords: foodborne ; food safety ; non-typhoidal Salmonella ; Salmonella

1. Epidemiology of Enteric Fever

Enteric fever (EF) is endemic in different regions of Asian and African nations and countries in Europe, Central and South America, and the Middle East. EF is rare in the U.S. and some other European countries, with fewer than 10 cases of salmonellosis per 100,000 people each year. Most reported cases in these countries are linked to international travel. Travelers returning from India, Africa, or Pakistan are often the source of this disease [1][2][3]. The rise in cases of *S.* Paratyphi infection raises concerns about the efficacy of current vaccines for typhoid fever and suggests the need for a more comprehensive study.

Enteric fever is prevalent in several Asian nations, such as Indonesia, India, Vietnam, China, and Pakistan, with yearly incidence rates surpassing 100 cases per 100,000 people [4]. Since the data collected by EF are from significant outbreaks, the global incidence of EF reports is more of an estimate. Because of the shortage of diagnostic facilities and effective surveillance technologies in many developing nations, predominantly in sub-Saharan Africa, the prevalence of EF is poorly characterized [5].

2. Epidemiology of Non-Typhoid Salmonella Infections

Despite advances in sanitation and hygiene, the number of NTS infections remains high, posing a problem in developed and developing nations [6][7][8]. Invasive NTS capable of spreading to extraintestinal sites is prevalent in developing countries, particularly in sub-Saharan Africa, with high incidence rates in children under three and HIV-positive individuals [7][9]. In Asia, the invasive illness produced by NTS is less common [10].

Inadequate cooking of foodstuffs, improper storage, and direct contact with raw ingredients are all considered significant causes of *Salmonella* outbreaks. Animal commodities, such as milk, poultry, eggs, and other foods, such as peanut butter and chocolate, are frequently linked to epidemics [11]. Most recently, onion has been implicated in salmonellosis outbreaks in the U.S. [12].

Animals are considered the primary reservoir of NTS [13]. Consumption of water or food contaminated with the excrement of infected animals, direct contact with infected animals, or ingestion of infected food animals can cause NTS infection in humans. The global incidence rate of NTS infection is high, as the strains may exist naturally and in wild and domestic animals, such as dogs, cats, amphibians, rodents, and reptiles [14]. Widespread distribution of food animals, wildlife, and various commodities are primary factors in salmonellae spread in the farm-to-fork food supply continuum.

3. Outbreaks of Salmonellosis in Humans

When two or more individuals are afflicted with the same sickness from the same source of contaminated drink or food, such a scenario is known as a foodborne outbreak. Likewise, when two or more individuals suffer from the same disease

from animal or animal products and associated environments, the event is classified as a zoonotic outbreak [15][16]. A brief overview of outbreaks of salmonellosis in humans on different continents is provided below.

3.1. Africa

In Africa, NTS infections appear to be endemic, and are one of the major causes of bacteremia, mostly in children, with 4100 deaths per year [8]. The prevalence rate is higher in areas where malnutrition, malaria, and HIV are prevalent. Nearly 85.8% of global iNTS deaths have been reported in sub-Saharan Africa [6]. About 14.3 million typhoid and paratyphoid fever cases in 2017 resulted in 135,900 deaths, 15.8% of which were in sub-Saharan Africa [17].

Salmonella Typhi is the leading cause of bloodstream infections in eastern and southern Africa, with reports of multiple outbreaks since 2012 [18]. Malawi has a very high incidence of 444 cases per 100,000 persons per year [19]. The primary infection source of people's exposure to *S*. Typhi is uncertain [20]. In Africa, iNTS is mainly associated with HIV patients (both adults and young children), malaria infection, and malnutrition [21]. Two *Salmonella* serotypes, Enteritidis and Typhimurium, have been reported to be the most common causes of iNTS in South Africa, Malawi, Mozambique, Kenya, and Mali, with *S*. Typhimurium Sequence Type (ST) 313 (ST313) and S. Enteritidis ST11 being the most frequently reported serovars [22]. In South Africa (2020 and 2021), although the total number of enteric fever cases across the country was similar to previous years (83 patients in 2020 and 110 patients in 2021), there was a relative upsurge in the number of cases reported from the northwest provinces and Western Cape [23]. In Nigeria, out of 372 humans screened, 77 (20.7%) were positive for enteric fever, 38 (20.4%) were isolated from non-poultry workers, and 39 (21.0%) were isolated from poultry staff in the three senatorial districts [24]. A recent study on 16,236 children from Kenya indicated that 1.3% of bloodstream infections was caused by *Salmonella* Typhimurium and Enteritidis, while *Salmonella* Typhi caused 1.4% of disease. *Salmonella* Enteritidis and *S*. Typhimurium were not significantly associated with rearing domestic animals. However, rearing chicken was linked to a high prevalence of *S.* Typhi (2.1%) infection. The rate of children infected with *Salmonella* Typhimurium and Enteritidis was significantly higher in households that used water pots as water storage containers compared to using water directly from the tap (0.6%) [25].

An extensive drug-resistant (XDR) strain of *Salmonella* Typhimurium was reported to cause millions of bloodstream infections per year in sub-Saharan Africa, including in the Democratic Republic of Congo (DRC) [26]. A recent study conducted in Burkina Faso indicated that among the 106 *Salmonella* isolates (77 human stools; 14 sandwiches), O antigen-positive *Salmonella* was confirmed in 86% (91/106) of the samples, and serogroup O:4,5 was the most common serogroup detected (40%; 36/91). *Salmonella* Enteritidis and Typhimurium represented 5.5% (5/91) and 3.3% (3/91), respectively, and were identified only from clinical isolates. Furthermore, 14 serotypes of *Salmonella* (12/91 human strains and 2/15 sandwich strains) were evocative of Kentucky and Bargny serotypes [27]. In Ethiopia (from 2010 to 2020), the pooled prevalence of *Salmonella* among human stools and animal-origin foods was 4.8% and 7.7%, respectively [28].

3.2. Middle East and North Africa

Several reports indicate a worrisome rising trend of NTS cases in developing countries, including the Middle East and northern Africa (MENA) [29][30]. A systematic review and meta-analysis study conducted on the prevalence of enteric NTS in humans in the MENA countries indicated that there were 6356 *Salmonella*-positive cases associated with 252,831 human samples. The pooled *Salmonella* prevalence in MENA was estimated at 6.6%. The highest pooled prevalence of *Salmonella* reports were in Tunisia (10.2%), Morocco (17.9%), and Sudan (9.2%), while the lowest were in Oman (1.2%), Jordan (1.1%), and Palestine (1.2%) [31].

A recent study in Iran indicated that nearly 94% of *Salmonella* isolates were recovered from ≤5-year-old patients, and 99% were NTS. The author found extensive diversity among *Salmonella* isolates; serogroup D (46%) was predominant, and *Salmonella* Enteritidis (41%) was the most common serotype that showed the highest antimicrobial susceptibility rate (>96%). *S*. Newport from human specimens was isolated for the first time in Iran. Most isolates were sensitive to all antimicrobials tested, but 35% of isolates were not-typed (NT), which showed the highest resistance, with 48% being resistant to ≥1 antimicrobial tested [32].

Malaeb et al. [33] reviewed published data from Lebanon on *Salmonella* susceptibility/resistance patterns and its clinical complications. The estimated incidence was 13.34 cases per 100,000 individuals, and most cases occurred in the 20–39 age group with no significant gender variation. Poor and less developed districts of Lebanon had the highest number of cases, and the peak incidence was in summer [33].

A case-control study conducted in central Israel indicated that in 18 years (2001–2018), 34 cases of NTS were identified in the bloodstreams of infected patients. The median age was 59 years, with 20% of patients below 20 years of age [34].

Salmonella infection in Saudi Arabia is highly prevalent during the Hajj and Umrah seasons due to the gathering of many pilgrims [35]. A retrospective descriptive study conducted in King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia, between May 2017 and December 2018, indicated 22 patients with invasive *Salmonella* infection. Fifteen (68%) were females, and seven (32%) were males. The range of ages was from 8 months to 74 years [36].

3.3. Latin America

Typhoid is broadly accepted to be endemic in parts of Latin America; the region has a medium incidence of typhoid fever (53 per 100,000 people), corresponding to >273,000 cases annually [37]. Using cases reported to the National Public Health Surveillance System in Columbia between 2012 and 2015, typhoid salmonellae was found in 836 patients, with the majority (676/836; 80.1%) of reported cases originating from only 7 departments. They further characterized 402 *S*. Typhi isolates with available corresponding data recovered from various departments of Colombia through antimicrobial susceptibility testing and molecular subtyping. The majority (235/402; 58.5%) of these typhoid cases occurred in males aged between 10 and 29 years (218/402; 54.2%), with 3 deaths (0.74%). The overwhelming preponderance (339/402; 84.3%) of *S*. Typhi were susceptible to all tested antimicrobials. The organism showed the most resistance against ampicillin (30/402;7.5%), followed by nalidixic acid (23/402, 5.7%) [38].

In Brazil, serotyping of 3113 *Salmonella* isolates collected by the National Reference Laboratory for Enteric Diseases between 2011 and 2020 revealed 61 serogroups [39]. Calarga et al. [40] studied the prevalence of the antimicrobial-resistant phenotype in 789 NTS strains collected between 2000–2019 in São Paulo, Brazil. Among the non-susceptible isolates, 31.55, 14.06, and 13.18% were resistant to aminoglycosides, tetracycline, and β-lactams, respectively. Moreover, 68 and 11 isolates were MDR and extended-spectrum β-lactamase (ESBL) producers, respectively, whereas one isolate was colistin-resistant [40].

3.4. USA

The Centers for Disease Control and Prevention (CDC), USA, estimates that approximately 1.35 million illnesses, 26,500 hospitalizations, and 420 deaths occur due to NTS infection each year in the U.S., resulting in an estimated $400 million in direct medical costs [41]. Between 2009 and 2011, antibiotic-resistant *Salmonella* strains that had developed resistance to 5 or more antibiotics caused over 66,000 illnesses in the U.S. [42]. According to CDC, antibiotic-resistant NTS infections are on the rise, approaching an estimated 10% for ciprofloxacin, 3% for ceftriaxone, and 1% for azithromycin [41]. Prolonged hospitalization and increased risk of bloodstream infections, treatment failure, and excess mortality have been associated with antimicrobial drug-resistant NTS infections [43].

In late 2022, a multi-country outbreak of *Salmonella* Typhimurium was reported in the USA and UK. The outbreak was associated with chocolate produced in Belgium and was distributed globally to over 113 countries and territories across all WHO regions. While 150 of 151 known cases have been reported in Europe, 1 case has been reported in the U.S. Additional cases are likely reported from other countries, given the broad distribution of the products during the Easter holiday [44].

3.5. Europe

Salmonellosis remains the second most common zoonotic disease in humans in the European Union (EU). The incidence of human salmonellosis has decreased steadily in recent years. Nevertheless, in 2014, 88,175 confirmed human salmonellosis cases, causing 9830 hospitalizations and 65 fatalities, were reported across the EU. Among these, 16,000 cases of human salmonellosis were reported in Germany. As in previous years, *S.* Enteritidis was the predominant serovar (44.4% of all isolates), followed by *S.* Typhimurium (17.4%) and a monophasic *S*. Typhimurium variant (7.8%) [45].

After a considerable decrease in salmonellosis cases recorded from 2007 to 2014, the incidence was stable between 2015 and 2019. The number of cases in 2020 was significantly lower than in previous years, mainly due to the COVID-19 pandemic. All but two countries reported a decrease in the number of patients due to various factors, including people avoiding hospital and/or clinic visits for mild sickness for fear of the risk of exposure to COVID-19 in healthcare facilities, lower laboratory services because of the reallocation of resources to SARS-CoV-2, limited restaurant visits, frequent hand washing practices, and limited human movement and personal contacts due to travel restrictions [16].

Notification rates for human salmonellosis also differ between member states in the EU, including area coverage, quality of data, disease severity, surveillance systems, sampling and testing, the prevalence in the food-producing animal population, food and animal trade between member states, and the proportion of travel-associated cases [46].

In 2020, the majority (58%) of foodborne outbreaks were caused by *S.* Enteritidis, similar to previous years. The four most commonly encountered food vehicles in confirmed foodborne outbreaks associated with salmonellosis include 'eggs and egg products', 'pig meat and products thereof' and 'bakery products", as in previous years. Nearly 29 countries reported 53,674 cases, of which 53,169 were classified as confirmed. The number of notifications per 100,000 population was 14.2, considerably fewer than in 2019. Age-standardized notification rates did not differ substantially from crude rates. Of 35,715 cases with known outcomes, 61 were reported to have died, accounting for a case fatality of 0.17%. The highest prevalence was reported by the Czech Republic (98.4 cases per 100,000 population) and Slovakia (62.1), followed by Malta (34.2) and Hungary (30.3) [16]. Some of the recent outbreaks of human salmonellosis reported from different geographic regions associated with various foodstuffs are summarized in **Table 1**.

Table 1. Summary of worldwide *Salmonella* causing diarrheal diseases (from 2019–2022).

Year	*Salmonella enterica* Serovar	No of Cases	Source of Country	Food Source (s)	References
2018	Concord	NA	Israel	Tahini products	[47]
2018	Unidentified serovar	NA	Australia	Chicken sandwich	[47]
2019	Unidentified serovar	NA	USA	Backyard poultry	[47]
2021	Oranienburg	1040	USA	Onion	[12]
2022	Typhimurium	324	Europe and USA	Chocolate products	[48]
2022	Enteritidis	NA	Canada	Exposure to live mice	[49]
2017 and 2019	Multiple serovars	325	United States	Whole, fresh Maradol papayas	[50]
2019	Heidelberg	164 (48.5%)	North West Province, South Africa	School lunch at public primary day school	[51]
2019	Newport	25	Sweden	Imported frozen cooked crayfish in dill brine	[52]
2019	Oranienburg	26	USA (14 states)	Contact with pet turtles	[53]
2019	Six different serovars: Amsterdam, Havana, Kintambo, Mbandaka, Orion, and Senftenberg)	121	Five EU/EEA countries	Imported sesame-based products (originating from Syria)	[16]

NA—not available.

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