

# An Extensive Review on the Exploration of Non-Typhoidal *Salmonella* and its Associated Infections

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## Abstract

Nontyphoidal *Salmonella* infections are common and remain a significant public health problem. The increasing cases of non-typhoidal *Salmonella* confirmed cases in past years from the United States, Europe, and low-income countries indicated that control programs aimed at inhibiting the contamination of food animals along the food chain had been largely ineffective. The majority of non-typhoidal *Salmonella* infections are mild gastroenteritis that rarely demands antimicrobial treatment. *Salmonella* is a gram-negative, multidrug-resistant, facultatively anaerobe bacterium. *Salmonella* is composed of approximately 2500 serotypes among which *Salmonella enterica* is responsible for more than 99% of human salmonellosis and morbidity. *Salmonella enterica* is an enteropathogenic foodborne bacteria isolated from animals that are responsible for zoonotic infections in humans, animals, and birds. Children who are young or immunocompromised, as well as those with underlying health issues like sickle cell disease, are highly susceptible to invasive disease. Antimicrobial treatment might be needed in case of invasive infections like meningitis, bacteremia, and osteomyelitis. Resistance to third-generation cephalosporins and fluoroquinolones in non-typhoidal *Salmonella* is a worrying concern in the 21st century. This review specifies various non-typhoidal *Salmonella* serotypes infections and their cases.

**Keywords:** Antibacterial, Bacteraemia, Gastroenteritis, Immunocompromised, Osteomyelitis

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## INTRODUCTION

*Salmonella* terminology is immensely complicated and has been a concern of immense controversy for many years. In the end, estimating the species and subspecies that represent the *Salmonella* genus is incredibly challenging.<sup>1</sup> Facultative cellular anaerobic characteristics and Gram-negative rod nature of *Salmonella enterica* induce 1.3 billion illnesses year after year. It is representative of the Enterobacteriaceae family. *Salmonella* is an enteroinvasive bacterium that, when consumed, dodges gastric protection, multiplies, and breaches the mucosal surfaces of the intestinal epithelium. Intense gastroenteritis infection is the prevalent type of *Salmonella* infection. The period of incubation might variegate between 4-72 hours after consuming deteriorated food and water too. Critical bacterial fever & chills, vomiting, seasickness, diarrhoea, and abdominal discomfort are perhaps the most typical signs and symptoms. If fever occurs it normally dwindles within 72 hrs. Diarrhoea with blood typically limits itself and lasts for 3-7 days. This bacterium is removed from the body through faeces after inflammation, which can take up to 5 weeks. In youngsters, excretion may be prolonged. *Salmonella* excretion that lasts for more than 8 weeks after the infection is unusual in young patients and adults. The optimal amount of bacteria required to make a healthy individual ill is 10<sup>6</sup>-10<sup>8</sup> non-typhoidal *Salmonella*.

To date, approximately 2500 unique serotypes or serovars of *Salmonella bongori* and *Salmonella enterica* have already been found. *Salmonella* is a commonly encountered and persistent which may persist for several weeks or months in dry and moist situations. Although all serotypes induce illness in people, some are specific to a particular host and can only be identified in either one or some species of animals, which includes *Salmonella enterica* serotype Dublin in cattle and *Salmonella enterica* serotype Choleraesuis in pigs. Generally, such serotypes induce gastroenteritis, which is typically benign and does not require medical attention; nevertheless, sickness could be acute in youngsters, aged people, and compromised immune systems individuals. *Salmonella enterica* serotype Enteritidis and Typhimurium, are the

prevalent *Salmonella* serotypes transmitted to humans from infected animals in various regions around the globe. It is typically distinguished by an immediate onset of acute fever, abdominal discomfort, diarrhoea, uneasiness, and in rare cases vomiting. Humans get infected with non-typhoidal *Salmonella* infections by coming in contact with different farm animals, pets, reptiles, and broilers.<sup>2</sup>

*Salmonella* is perhaps the most frequently isolated pathogen after *Campylobacter* when a presumptive diagnosis of diarrhoea is sought. The well-known *Salmonella* enteric serovar Heidelberg strain is ubiquitous and is regularly acquired from victims of salmonellosis in the North American region.<sup>3</sup> *Salmonella* can thrive on plants; thus, fruits and vegetables could be a way for *Salmonella* to enter the food chain.<sup>4</sup> NTS infection in animal-based foods occurs as a consequence of contamination in the feed or even the environment.<sup>5,2</sup> It is the most predominant bacterial source of food contamination across the globe.<sup>6</sup> Non-typhoidal salmonellosis is probably minor; however, in youngsters, the aged, and individuals with disabilities, it can cause life-risking consequences. The extent of NTS infection is determined by the host immune response, *Salmonella* serotype, and infective dosage. There is a matter of discussion that the evolution of *Salmonella* has not been properly researched to explain various complications within or across subspecies, and hence the ability to cause foodborne sickness or even more serious invasive illness remains unexplored.<sup>7</sup>

In the study of Taliha et al.<sup>8</sup> three patients were detected with invasive non-typhoidal *Salmonella* infections in which one patient was suffering from a urinary tract infection and spondylodiscitis which was given medical treatment and surgery. The second patient was detected with an abdominal prosthetic aortic aneurysm which was given long-term antimicrobials. The third patient was detected with a thoracic aortic aneurysm and cutaneous abscesses which were treated with antimicrobials and surgery. For future research, the study suggests application of antimicrobials in the field of agriculture and veterinary should be encouraged to avoid the emergence of antimicrobial resistance. A vaccine against NTS that is both effective and safe

is anxiously awaited.

Recent Study of Marchello et al.<sup>9</sup> provided current information on the fatalities and complications related to the global burden of non-typhoidal *Salmonella* invasive disease, including in regions lacking up-to-date and strong national research data. A lacuna of this study is the inability to investigate the relationship between non-typhoidal *Salmonella* invasive disease and other comorbid conditions besides HIV and malaria.

Based on the findings of Rule et al.<sup>10</sup> the patient was detected with acute bacterial meningitis. To treat the most common causes of bacterial meningitis, empiric antibiotic therapy with intravenous ceftriaxone was given. To minimize intracranial inflammation and avoid long-term neurological sequelae, dexamethasone intravenous corticosteroid therapy was incorporated. However, a limitation of the approach was the incapability to provide handling clinicians with quick microbiological results. Due to this conventional culture was conducted on this patient's CSF, resulting in a four-day turnaround time before final identification.

In the study of Albert et al.<sup>11</sup> NTS bacteremia was detected in 30 of 53,860 and 31 of 290,36 blood cultures in two hospitals of Kuwait. 13 different serovars were cultured in both hospitals and the majority of the cases were due to *S. Enteritidis* (all sequenced type (ST11) and *S. Typhimurium* (all ST19). Ampicillin, ciprofloxacin and tetracycline were the most prominent antibiotics and showed 36.1% to 50.8% prevalence. Limitations showed that the hospitalized cases didn't represent community cases where a wide range of the severity of cases can occur, and the community population at risk was not defined clearly. Therefore polymerase chain reaction (PCR) and conventional blood cultures methods may not be sensitive enough to recognize all true positive cases.

The study investigated by Sanni et al.<sup>12</sup> stated that 150 samples were accumulated from three local areas of government in every five states of the North Central zone of Nigeria. Besides of *Salmonella enterica*, *Klebsiella pneumoniae* was found in 92.9% of the specimens, *Salmonella arizonae* in 0.2%, *Lactobacillus bulgaris* in 0.9%, *S. paratyphi* in 1.9% and *S. typhi* in 2.3% of

all specimens. Mixed infections with *Lactobacillus bulgaris*, *S. arizonae*, *Klebsiella pneumoniae*, and *S. paratyphi* were reported in 392 of the 416 *S. enterica*-positive specimens (94.5%). There were some limitations in this work. Firstly no complete serotyping of all categorised confirmed cases was conducted, as this could have revealed all of the *Salmonellae* serotypes collected during the 18-month period. Secondly, many laboratories were used to ascertain NTS positivity, and not all farm cases were forwarded for laboratory analysis, among which some may have been salmonellosis. This resulted in misclassification which may have increased or decreased the overall prevalence calculated in the study. The objective of the present study is to give a detailed comprehensive review of non-typhoidal *Salmonella* infections and their consequences in humans.

#### **Non-typhoidal *Salmonella* antimicrobial-resistant property**

Antimicrobial resistance condition is a worldwide issue in the management of human and animal health care. Assessments of AMR pathogen transmission between humans and animals might provide insight into an essential pathway through which AMR pathogens invade humans. However, determining the transmitting path can be difficult (either pass on from animals to people or people to animals). Furthermore, AMR *Salmonella* illnesses exacerbate the situation by increasing the likelihood of blood infections due to treatment inefficacy.<sup>13</sup> Although salmonellosis from pets has been proposed as a potential AMR transmission pathway, there is a lack of concrete data for this fact.<sup>14</sup> Pet dogs can get *Salmonella* via ingestion of contaminated food or coming into contact with infectious waste or other diseased animals. Humans might be infected because of getting in contact with a diseased dog. According to one investigation, 107 (84 per cent) of the 128 *Salmonella*-infected individuals previously had interacted with dogs before becoming ill.<sup>15</sup>

#### **Intrinsic and iatrogenic susceptibility of the host**

Salmonellosis of the gastrointestinal system and its chronic complications are linked to a broad range of ailments and therapies that are mainly accountable for the several defence mechanisms against intestinal and

intracellular pathogenic organisms. Hypoacidity in newborns, pernicious anaemia, or brought about by antacids and H-2 blockers can make people more susceptible to salmonellosis. Multiple perilous aspects can lead to salmonellosis which includes changes in the endogenous intestinal microbiota, rheumatological illnesses, diabetes, tumours, and reticuloendothelial blockade because of sickle-cell disorder, malaria, and bartonellosis. Therapeutic immunosuppression of all types and HIV infection are major reasons for salmonellosis. Various anatomical disruptions, such as UTIs, atherosclerotic endovascular lesions, kidney stones, gallstones, schistosomiasis, and prosthetic devices, could be the sole cause of persistent *Salmonella* disease.

### Non-typhoidal *Salmonella* infections of key serotypes

Reptiles, poultry, and amphibians are widely known reservoirs for *Salmonella* spp. disease.<sup>16</sup> However, in a few patients, the causative agent is unknown.<sup>17,18</sup> According to a Chinese investigation conducted between 2005-2011, *S. newport* was among the ten leading serovars involved in clinical patient trials.<sup>19</sup> Salmonellosis is a complicated disorder having a myriad of causes influencing death rates. Various serotypes appear to be related to specific spreading channels according to their roles in naturally occurring ecological systems.<sup>20</sup> *Salmonella Enteritidis* was mostly linked to the ingestion of turkey, eggs, chicken, and sprouts, while *Salmonella Typhimurium* was linked to beef, dairy products, pork, and vegetables, while *S. Newport* to fruits & veggies.<sup>21</sup> Although these are self-limiting, zoonotic infections can also induce irritable bowel syndrome problems, ulcerative colitis illness, and Crohn's disease too, as well as extra-intestinal consequences such as rheumatoid arthritis, Guillain-Barre, and reactive arthritis.<sup>22</sup>

*S. Heidelberg* promotes many invasive human illnesses, such as dilated cardiomyopathy and septicemia.<sup>23</sup> The condition can sometimes present as a feverish invasive disease, typically without diarrhoea, with bacteremia, meningitis, or focal disorders that can be fatal if left untreated or incorrectly managed.<sup>24-26</sup> In 2017, the disease accounted for an estimated 535000 non-typhoidal *Salmonella* invasive illnesses and 77500 fatalities.<sup>27</sup>

Among six subspecies of *S. enterica* the foodborne illnesses are most often observed in 1 subspecies, notably *S. enterica* subspecies I. Some other *S. enterica* subspecies are II (salamae), IIIa (arizonae), IIIb (diarizonae), IV (houtenae), and VI (indica). It is very rare when subspecies II-IV lead to disease, but they hardly seem like people's clinical care hazards and are also correlated with professions comprising wildlife, animals, and reptiles that are rarely eaten.<sup>28-30</sup>

Selection for just the fittest *Salmonella enterica* subspecies I serotype able to produce food-related ailments is obvious in a particular subspecies. It's also known that many *S. enterica* serotypes can induce sickness under ideal circumstances; hence, all food and feedstuff components must pass quality control tests for humans and domestic animals. In the United States annually, very few serotypes, principally *S. infantis*, *S. typhimurium*, *S. newport*, *S. enteritidis*, and *S. javiana*, are the reason for 80% of reported salmonellosis cases.<sup>31,32</sup> Microbiological studies demonstrated a higher prevalence of *S. newport*, *S. Mississippi*, and *S. javiana* in western Tennessee countries in comparison to all other Tennessee countries.<sup>33</sup> Surprisingly, a similar pattern was documented in Louisiana, as per the credentials of the Louisiana Office of Public Health.<sup>34</sup> *Salmonella* type III and type IV secretory systems are some of its major virulence factors (T3SSs, T4SSs). These key *Salmonella* virulence factors influence host cell physiology to promote illness.<sup>35</sup>

Non-typhoidal serotypes, like *S. enteritidis* and *S. Typhimurium*, are commonly encountered serotypes linked to foodborne outbreaks. They have enormous epidemiologic importance because they survive in food production environments and have the tendency to expand extensively and fast throughout communities. Contamination of domestically marketed ice cream, chocolate cake, and smoked salmon outbreaks involving cucumbers are a few instances.<sup>36-39</sup> Non-typhoidal *Salmonella* species are associated with 550 million diarrheal diseases around the globe.<sup>40</sup> NTS can reside in infected individuals for extended periods without showing clinical manifestations.<sup>41</sup> Asia's Southeast region is a key hub for salmonellosis caused by non-typhoidal *Salmonella*. As per the data, this region accounted for 20.69 per cent of cases and 26.93 per cent of deaths of whole world

non-typhoidal salmonellosis.<sup>42</sup>

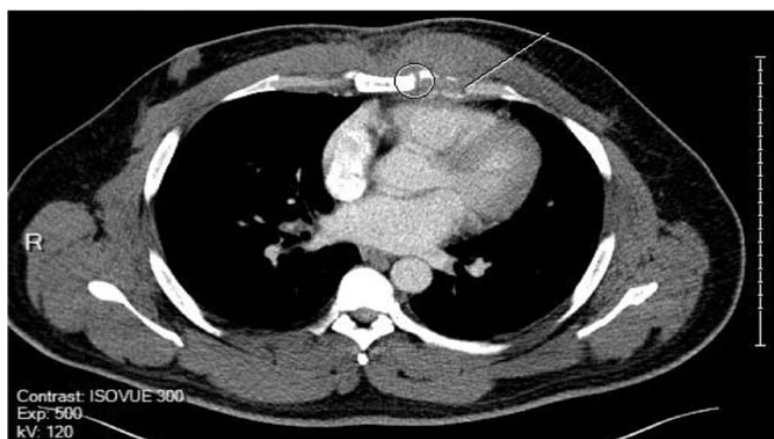
### Infections of the gastrointestinal tract instigated by non-typhoidal *Salmonella*

Gastroenteritis is the foremost reason for morbidity in children globally, particularly in developing nations, accounting for roughly 1.87 million deaths in children under the age of five per year.<sup>43</sup> It typically begins 12-38 hours after the pathogen is consumed, with cramping of the abdomen, nausea, diarrhoea, and 100.5-102.2 °F fever. Although the faeces is runny, it also has a paste-like mucilaginous consistency and contains a modest amount of polymorphonuclear leukocytes and occult blood. Stool culture continues to remain positive after 4 to 5 weeks also. Mild leucocytes

could be found. Around 70% of patient populations will experience fever. Tenderness is discovered during an abdominal investigation. Typically, the ailment is relatively benign and last for 1-4 days. Many serious, long-term illnesses occur frequently. When diarrhoea stops, reactive arthritis affects 10-30% of adult human populations and can last for several weeks or months. This condition causes pain & inflammation in the knees, hips, and Achilles tendon also. *Salmonella enteritis* may progress more slowly in susceptible hosts. Preterm infants, premature children, and children with primary/secondary immune deficiency may experience problems for several weeks. *Salmonella enteritis* can induce toxic megacolon formation, bowel incursion, systemic toxicity, and



a. Sagittal CT scan; abscess indicated by white line



b. Axial CT scan; abscess indicated by white line

**Figure 1.** Both Sagittal & Axial CT scans of the chest of an infected individual<sup>44</sup>

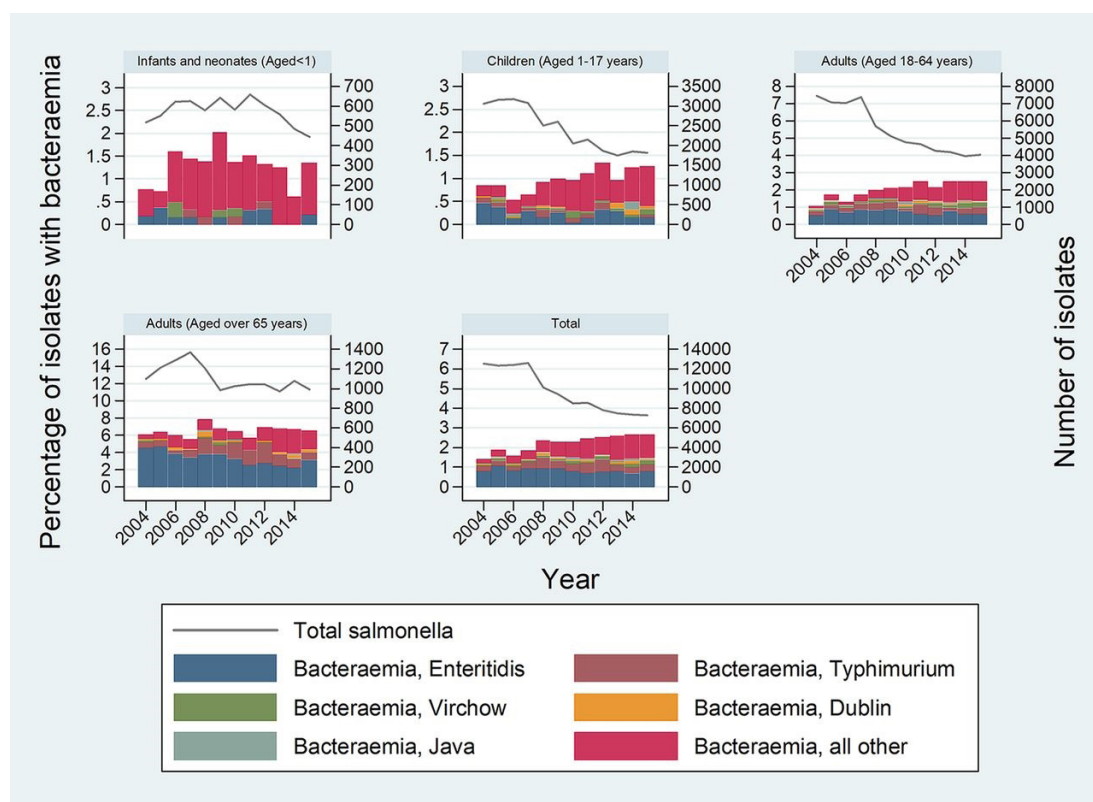


even death in sick individuals with inflammatory bowel disorders, especially active ulcerative colitis. In immunocompromised adults, *Salmonella* gastroenteritis is a self-limiting infectious disease. A case report of Castlemain et al.<sup>44</sup> stated that a healthy man 39-year-old who was previously successfully treated with *Salmonella* gastroenteritis and bacteremia was found *Salmonella* Oranienburg positive. *S. Oranienburg* is a serovar responsible for the current gastroenteritis breakout linked to interaction with a pet turtle. Figures 1a and b showed a chest CT scan of a patient infected with *S. Oranienburg*.

### Non-typhoidal *Salmonella* extraintestinal focal infections (EFI)

NTS extraintestinal focal infections are entirely unusual and have unknown danger variables. Pleuropulmonary infection, spinal osteomyelitis, and mycotic aneurysm are all some

examples of EFIs.<sup>45</sup> When possible, these infections must be depleted. For the cure of a medically eliminated focus of soft tissue in a normal host, a minimum period of 14 days of antimicrobial prophylaxis is recommended. Because *Salmonella* species are known to persist in polluted areas, treatment for 4-6 weeks is usually recommended. Osteomyelitis and joint-related infections are more refractory to treat in sickle-cell anaemic individuals. Bacteremia or focal infection tends to affect 8% of people (which are septic arthritis, osteomyelitis, and meningitis). Focal infections, most prevalently in the bones and central nervous system, can happen in newborns (particularly those under 3 months old) and immunocompromised children.<sup>46</sup> However, NTS disease is linked to a variety of illnesses besides enteritis, with a broad range of severity in particular risk groups like extraintestinal manifestations (meningitis, osteomyelitis, deep soft tissue, septic arthritis, pneumonia, and



**Figure 2.** The Overall number of non-typhoidal *Salmonella* reported cases by age category, proportion to bacteremia, and the five major serovars.<sup>47</sup>

bacteremia.

### **Bacteremia and Endovascular Disorder: Intense Complications**

Bacteremia is much more likely to happen in immunocompromised hosts. Bacteremia, a life-threatening condition, affects about 5% of people who have a gastrointestinal disorder resulting from non-typhoidal *Salmonella*. Non-typhoidal *Salmonella* bacteremia is more noxious. *S. Choleraesuis*, *S. Heidelberg*, and *S. Typhimurium*, on the other hand, can normally cause a detrimental bacteremia syndrome which can last for 1 week and is characterized by a protracted fever, malaise, headache, and shivers but scarcely diarrhoea. *Salmonella* may cause recurrent bacteremia or other invasive infections like septic arthritis in hosts. In adults, the progression of infective endarteritis, particularly embolism of the abdominal aorta, is a frightening contraindication to *Salmonella* bacteremia.

Bacteremic *Salmonella* is typically treated with a particular antimicrobial agent, such as third-generation cephalosporin, quinolone 2001, and ampicillin. Figure 2 depicts total NTS instances over a specific period by age category and proportion of infectious bacteremia infection.<sup>47</sup> Bacteremia is the most widely known systemic infection, with the occurrence of *Salmonella enteritis* ranging from 2% to 47% depending on the region.<sup>48</sup> Despite the overall reduction in salmonellosis incidence during the last five years due to better hygiene, *Salmonella* persists as the second leading source of bacteremia in youngsters between the age of 3-59 months, as per the largest multicenter study on pediatric invasive bacterial infections in South Korea.<sup>49</sup>

### **Non-typhoidal *Salmonella*: Reason behind meningitis in children with immune deficiency**

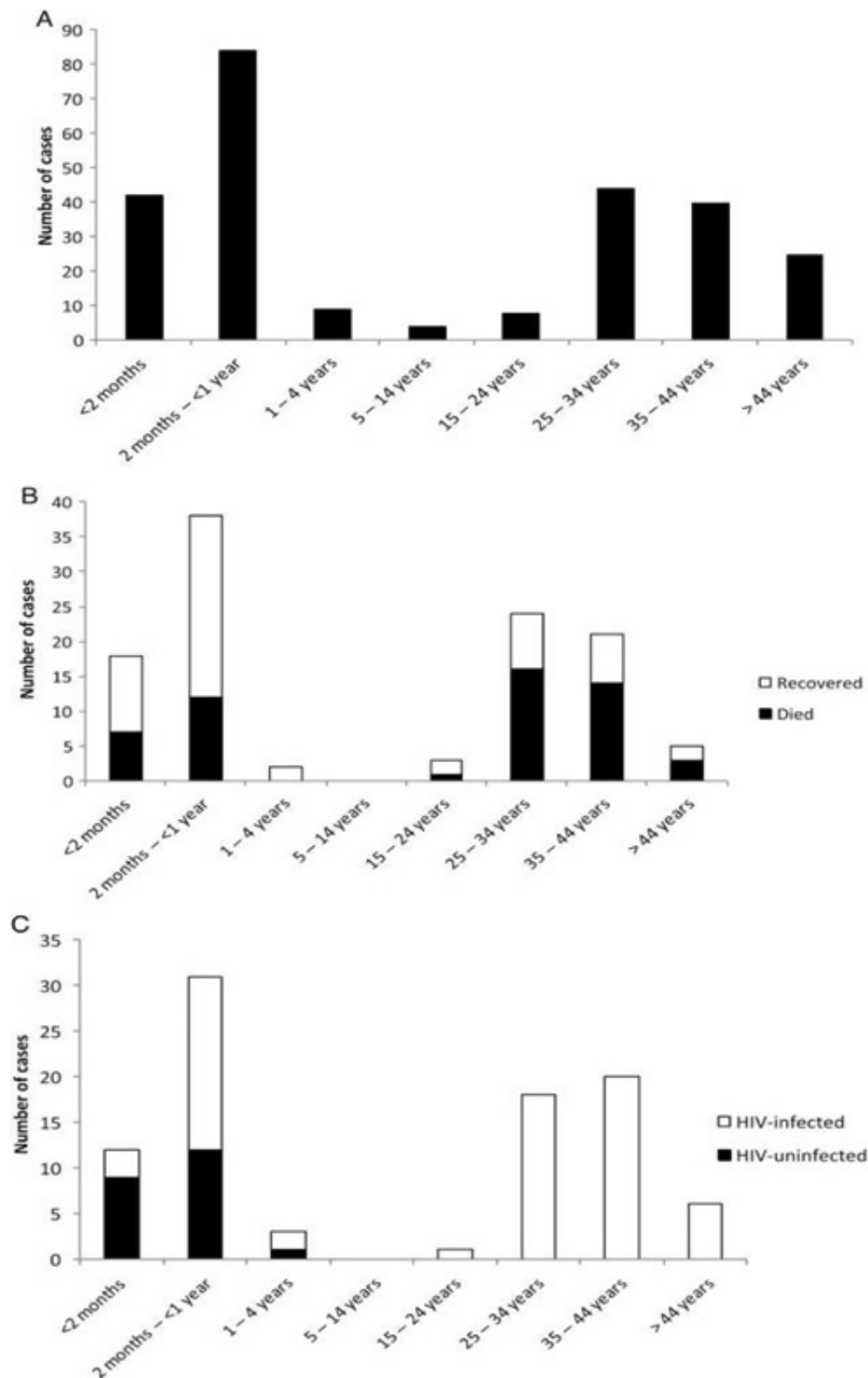
A leading source of chronic bacterial meningitis in newborns and infants in developing countries is non-typhoidal *Salmonella*. Abscesses, subdural empyema, Seizures, and hydrocephalus are common complications of NTS meningitis in youngsters, and children may experience serious delayed development and impairment. Meningitis caused by NTS has an elevated mortality rate and long-term neurologic disorders.<sup>50</sup> Meningitis caused by NTS is much less common, and the

exact prevalence is uncertain. Little research on meningitis caused by NTS or *S. enterica* ser. Typhi in children has already been publicly released, and most of them involved infants and malfunctioned children. All three pediatric sufferers were given meropenem to treat multidrug non-typhoidal *Salmonella*, and there was a significant improvement. Even after antibiotic therapy, the survival rate of NTS meningitis can range from complete recovery to fatality, and neural complications like epilepsy, focal problems, and cerebral palsy usually occur.<sup>51</sup> Various inflammation peaks were detected in youngsters of age five and adults fifteen. In 196 sick people, NTS had been secluded from the cerebrospinal fluid, and in 82 sick people from feces, blood, or any other body spots. During the period, the mean rate of infection of NTS meningitis was 5 per 10000000 annually as shown in Figure 3.<sup>52</sup>

Because NTS meningitis has an elevated morbidity & mortality rate, it is pivotal to administer relevant antibiotics as soon as possible. Adult HIV-positive people are at a significantly greater risk of getting salmonellosis, which can progress to severe complications like meningitis even after antibiotic prophylaxis.<sup>53</sup> Third-generation cephalosporins, luckily are frequently used as an early empirical antimicrobial prophylaxis in children with suspected bacterial meningitis. In a report by Monica et al.,<sup>54</sup> a two-month-old Italian boy infant was admitted as he was suffering from loss of appetite, elevated fever, irritability, and blood traces were present in diarrhoea when investigated showed the presence of *Salmonella enteritidis*. Brain ultrasound confirmed periencefalic purulent suffusion, which was affirmed by brain imaging technique i.e., MRI (Figure 4a). A third brain MRI indicated some re-absorption of the frontal collection at the end of the prophylactic antibiotic treatment (Figure 4b). Adult meningitis has also been linked to *S. Virchow*.<sup>55</sup>

### **Complications of osteomyelitis caused by Non-Typhoidal *Salmonella***

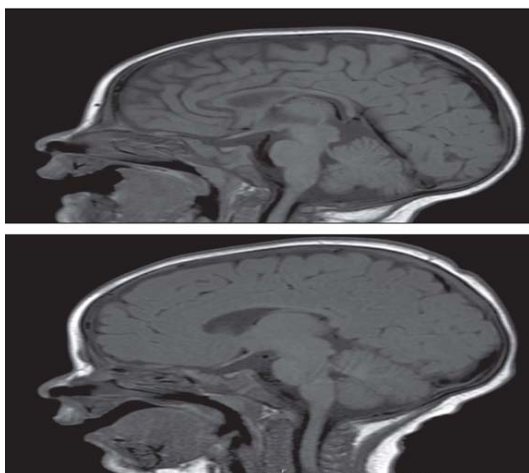
Vertebral osteomyelitis is a very infrequent NTS complication with an undiscovered global prevalence.<sup>56</sup> *Salmonella* osteomyelitis, an unusual typhoid infection, can happen because of hematogenous damage to the joints and



**Figure 3.** From 2003 to 2013, there were 256 incidents of nontyphoidal *Salmonella* meningitis [n=256]. B) Total NTS meningitis incidents (n=111) by category of age and morbidity from 2003 to 2013. Single patients who retrieved had no age registered. C) Total NTS meningitis instances (n=91) by category of age and condition of HIV, 2003-2013. The age of a single HIV-diagnosed host was not registered.<sup>52</sup>

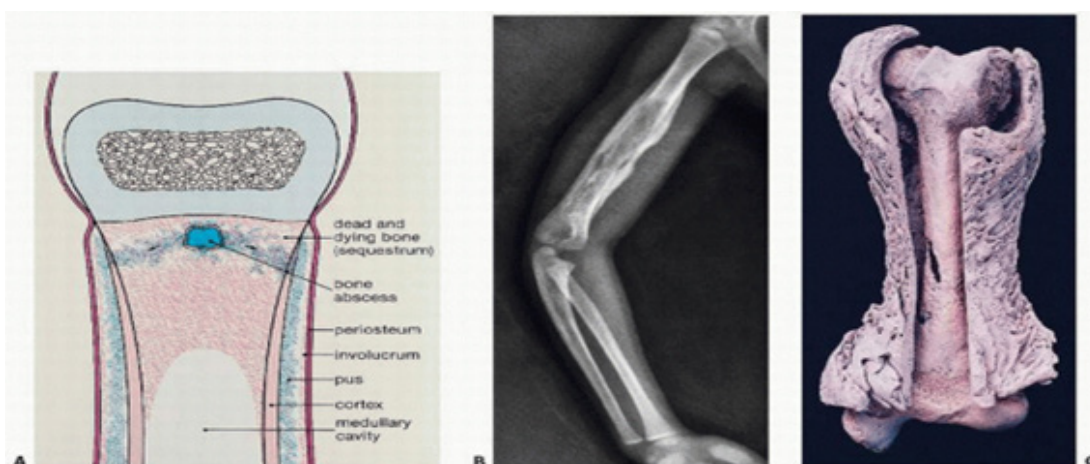


bones caused by a bacterial episode. It can also be dispersed from infected areas nearby or through penetrating trauma. Distress in the



**Figure 4.** In a report of two month old boy who suffered from *Salmonella* enteritidis, the results of the first brain MRI, which were supported by the cerebral ultrasound, showed periencephalic purulent suffusion (figure 4a) and a last brain MRI after the antibiotic treatment ended showed a slight resorption of the frontal accumulation (figure 4b)

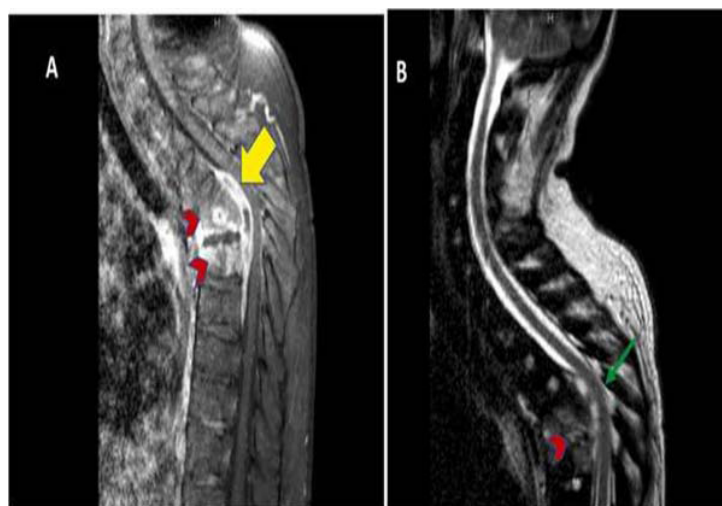
particular bone which has upper redness, elevated body temperature, and paleness are possible symptoms. Diagnosis and treatment must be done as soon as possible because if not, it can result in long-lasting functional impairment afterwards. *Salmonella* osteomyelitis can be seen infrequently in hospitals, accounting for 0.8 per cent of all infections caused by *Salmonella* and only 0.45 per cent of overall osteomyelitis are triggered by NTS, primarily in sickle cell anaemic hosts.<sup>57</sup> Capillary obstruction by intravascular sickling might desiccate and siege the gastrointestinal tract in patients with sickle cell anaemia, allowing *Salmonella* bloodstream incursions and raising the risk of osteomyelitis. A role for the complement system and impaired opsonization has also been proposed.<sup>58,59</sup> In immunocompromised individuals with no hemoglobinopathy, non-typhoidal *Salmonella* osteomyelitis is unusual. Surgical debridement and long-term antibiotics are part of the healing process. In the United States, out of 0.04 per cent, 51,964 cases of NTS infections remained closely linked to bone and joint illnesses. It has also been related to other scenarios such as connective tissue disorders, prior trauma, and immunocompromised conditions such as cancer malignancies, (Figure 5).<sup>60</sup>



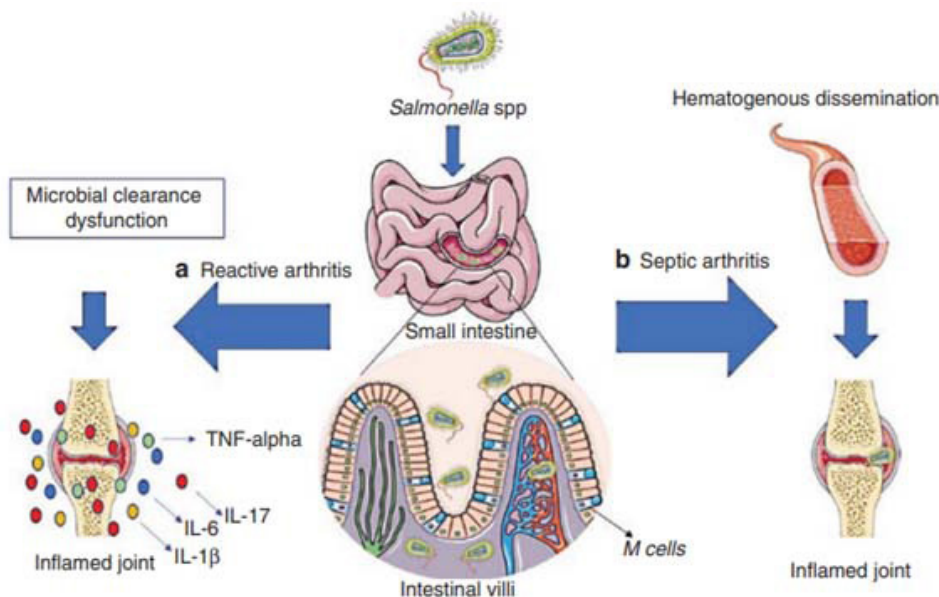
**Figure 5.** Osteomyelitis. Within the bone, an infection nidus disperses through the medullary (cancellous) and cortical bone, causing periosteal growth of new bone [A]. The diseased bone finally dies (sequestrum) and is surrounded by a shell of periosteal new bone (involucrum). Roentgenogram of the humerus [B]; remember that the whole femur is necrotic, with extensive new periosteal bone wrapping and forming a new shell contour in a gross femur of a cow [C] (involucrum)<sup>60</sup>

Patients suffering from sickle cell illness are prone to acquire osteomyelitis. Osteomyelitis clinical manifestations in sickle cell illness are equivalent to vasoocclusive crisis, with little or no diagnostic standard. It has been reported in the study of Weisman et al.<sup>61</sup> that twenty-

eight children who were suffering from sickle cell disease were treated for osteomyelitis. Based on the results of MRI, and other clinical diagnoses revealed that osteomyelitis was confirmed in 3 patients, and the probability was in 6 patients and assumed in 19 patients. Another sickle cell illness



**Figure 6.** A contrast MRI of the spine revealed focal spondylodiscitis in level T5-T6 with a multiloculated intraspinal epidural lesion stretched from level T4-T7 underneath the unaffected posterolateral longitudinal ligament, compacting the cord with a modest spinal canal with modest stenosis of the spinal canal, vertebral obliteration with prevalent kyphosis, and a huge bilateral paraspinal phlegmon with lesions.<sup>62</sup>



**Figure 7.** Pathophysiology of Salmonella arthritis. (a) After intestinal colonization and infection, a person with genetic and environmental sensitivity related to factors that affect microbial clearance will result in reactive arthritis. (b) After intestinal colonization and infection, hematogenous dissemination can occur, leading to the development of Salmonella bacilli and finally causing septic arthritis.<sup>73</sup>



**Figure 8.** Chronic occluding calculi in the distally present left ureter.<sup>78</sup>



**Figure 9.** Left kidney oedema and hydronephrosis.<sup>78</sup>

sufferer mentioned in Elnour et al.<sup>62</sup> study needed surgery to cure vertebral-related osteomyelitis and an epidural inflammation, healed by 4 weeks of IV ceftriaxone treatment, and 2 weeks of trimethoprim/sulfamethoxazole treatment. This increased his chances of contracting an intricate *Salmonella* infection (Figure 6).

#### **Septic arthritis: A rare cause of non-typhoidal *Salmonella***

*Salmonella* arthritis is a relatively uncommon joint ailment that accounts for about 1% of total infected case scenarios.<sup>63</sup> Organisms that induce the problem of septic arthritis can often be a non-typhoidal *Salmonella* species, and it typically manifests as one of the metastatic illnesses in children and young adults who have previously experienced bacteremia.<sup>64</sup> *Salmonella* septic arthritis is commonly caused by hematogenous spread. Hardly 10 to 15% of rare situations result in a positive blood culture of specimens.<sup>65</sup> Many non-typhoid *Salmonella* serotypes have already been known to trigger septic arthritis or osteomyelitis in humans, which would include *S. Enteritidis*, *S. Typhimurium*, *S. Typhi*, *S. Newport*, *S. Choleraesuis*, *S. Virchow*, and *S. Ohio*.<sup>66,57,67-71</sup> Genomic identification of *Salmonella* Virchow monophasic variant in the study of Wang et al.<sup>72</sup> showed that this variant was responsible for knee joint septic arthritis. Surgical treatment and antimicrobial therapy are common treatments. Acute septic arthritis is relatively uncommon in immune-competent children. Bacterial infections that begin in the skin (after cutaneous lesions) or throat are the leading triggers

(like *Staphylococcus* or *Streptococcus* species). *Salmonella* species exhibit reactive and septic arthritis in the joints. (Figure 7) shows how *Salmonella* species invade the small intestine and how inflamed joints lead to septic arthritis and reactive arthritis.<sup>73</sup>

#### **Urinary tract infections**

Urinary tract infection by NTS is uncommon and is also typically linked with degenerative changes in the genitourinary tract, immunodeficiency, and chronic conditions like diabetes. Immediate urethral inflammation, which is likely to occur in females, and hematogenous dispersal from gastroenteritis illness are the modes of inflammation.<sup>74</sup> Serious diseases that increase the risk of *Salmonella* UTI involve cardiovascular or liver problems, cancer, and acute hemodialysis.<sup>74-76</sup> The much more widely known *Salmonella*-caused UTI illnesses are nephrocalcinosis and nephrolithiasis. Primary hyperparathyroidism is associated with an increased risk of nephrolithiasis. Furthermore,<sup>77</sup> indicated that 25-33% of non-typhoidal salmonellosis in those patients who have undergone kidney transplants had urinary tract infections, whereas no individuals with a heart transplant had non-typhoidal salmonellosis-acquired urinary tract infections. Non-typhoidal *Salmonella* UTI is primarily linked to tract structural abnormalities. The CT scan report of the abdomen/ pelvis disclosed chronic occluding calculi in distally present left ureter, left renal oedema, and hydronephrosis, Figure 8 and Figure 9.<sup>78</sup>

## CONCLUSION

Only a few investigations have been undertaken to ascertain the etiology of NTS in people. Recognition of serotype dispersion, and also drug sensitivity patterns is critical for developing effective therapeutic and control strategies. This article guides us about different infections which are triggered by NTS, how they affect our body, and the way our body encounters them. Recent advancements in sequencing and bioinformatics, as well as the emergence of new versions to review interrelations between host and cell, have granted critical perceptions in understanding the gene's role and their regulation process, which might help in providing explanations of resistance against *Salmonella* infections. The immense population of sufferers is children under the age of five. Both experimental outcomes and medical outcomes indicate that this pathogen is highly adaptable to various antimicrobial selective pressures.<sup>79</sup> *Salmonella* vigilance in both people and animals is mandatory to effectively control the associated infections.

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None.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## AUTHORS' CONTRIBUTION

NC and PR conceived the study. PR, VC, and JC performed literature review. PR wrote the first draft. PR, VC and JC worked on subsequent drafts. NC reviewed and revised the manuscript. All authors read and approved the final manuscript for publication.

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None.

## DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

## ETHICS STATEMENT

This article does not contain any studies with human participants or animals performed by

any of the authors.

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