



## Study of Typhoid Fever: A Review

**Prathmesh Siddheshwar Kaluse<sup>1</sup>, Neha Bhatt<sup>2\*</sup> and Nandkishor Bankar<sup>3</sup>**

<sup>1</sup>Datta Meghe Medical College, Nagpur, India.

<sup>2</sup>Department of Pathology, Datta Meghe Medical College, Shalinitai Meghe Hospital and Research Centre, Nagpur, India.

<sup>3</sup>Department of Microbiology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha, India.

### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i39A32172

#### Editor(s):

(1) Dr. Sawadogo Wantinga Richard, Scientific Research and Innovation, Burkina Faso.

#### Reviewers:

(1) Kawthar A. M. Ibrahim, Sudan University of Science and Technology, Sudan.

(2) Iwan Muhamad Ramdan, Mulawarman University, Indonesia.

(3) Chandra Shekhar Singh, Dr. Ram Manohar Lohia Avadh University, India.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/71200>

**Review Article**

**Received 24 May 2021**

**Accepted 29 July 2021**

**Published 31 July 2021**

## ABSTRACT

*Salmonella typhi* and *Salmonella paratyphi*, all members of the Enterobacteriaceae family, are the primary causes of typhoid fever. *Salmonella enterica* serovar and enteritidis are isolated by multiplex quantitative polymerase chain reaction PCR after detailed study. *Salmonella nontyphoidal* (NTS) is most frequent in infants, although the majority of cases are limited to gastroenteritis. *Salmonella* is spread by polluted water, raw food, and large groups of sick people, and is most prevalent in heavily populated cities, civil disorder, and inadequate sanitation. It can only be passed from one sick individual to another and humans are the only ones that can spread it. Chickens, milk, and uncommon tortoises are the most common causes of salmonella. The Patients went directly to the Observed Treatment in the Dept. of Medicine, at DMMC, SMHRC Nagpur. Enteric fever is still a major public health concern around the world, particularly in developing countries. Typhoid cases in cities are estimated to be about 800-900 per year, according to studies. While inexpensive and widely available, the Widal exam should be used with caution. Massive public awareness campaigns should be undertaken to inform citizens about the importance of taking preventative measures, vaccines, and seeing a doctor, among other items. Doctors should be

\*Corresponding author: E-mail: [nehabhatt1381@gmail.com](mailto:nehabhatt1381@gmail.com);

aware of the emergence of newer antibacterial agents that are both safe and reliable, as well as the gradual development of antibiotic resistance. Aside from that, the discipline should anticipate newer curative and preventative interventions.

**Keywords:** Typhoid; Widal; Salmonella; fever; antibiotic.

## 1. INTRODUCTION

Typhoid fever, also known as enteric fever, was a significant cause of illness and death in the Western Hemisphere some 200 years ago. Because of improvements in sanitation and general health, the deadly outbreaks of preceding decades are now rare in the United States and Europe. In developing countries, especially India, typhoid fever is still a deadly disease. Enteric fever is another name for typhoid fever. It is a multifaceted potential disease that has become a public health issue, especially in developed countries. *Salmonella typhi* and *Salmonella paratyphi* are the bacteria that cause it. Typhoid fever and paratyphoid fever are both classified as enteric fever [1]. Since the typhoid fever clinic does not understand paratyphoid, enteric and typhoid fever are used together. While comprehensive studies and public health initiatives have decreased the prevalence of typhoid fever, it remains one of the leading causes of death and disease in overcrowded and unsanitary environments. Disease trials can range from initial gut distress to a spontaneous infection, but can lead to a slew of complications over time. The 'four Fs' was said to spread Salmonella (flies, fingers, feces, fomites). Fever comes on in waves (i.e., rises and falls in different ways), and is accompanied by headache and stomach pain [2].

*Salmonella typhi* and *Salmonella paratyphi*, all members of the Enterobacteriaceae family, are the primary causes of typhoid fever. Salmonella enterica serovar and enteritidis are isolated by multiplex quantitative polymerase chain reaction PCR after detailed study. *Salmonella enterica* serotypes A, B, and C are both *Salmonella typhi* and *Salmonella paratyphi* (A, B, and C). Salmonella nontyphoidal (NTS) is most frequent in infants, although the majority of cases are limited to gastroenteritis [3].

Salmonella is spread by polluted water, raw food, and large groups of sick people, and is most prevalent in heavily populated cities, civil disorder, and inadequate sanitation. It can only be passed from one sick individual to another

and humans are the only ones that can spread it. Chickens, milk, and uncommon tortoises are the most common causes of salmonella. Another research found that 57% of the samples in a study on the spread of salmonella graded genome sequences in poultry slaughterhouses in China were correct [4].

While the disorder affects a significant percentage of children, it is also a leading cause of sickness and death in many adults. However, data on typhoid in India is not very accurate for a variety of reasons. The majority of flu patients are handled as outpatients; hospitals, especially in rural areas covering vast areas of the country, lack blood transfusion facilities; many clinics and even hospitals do not maintain accurate records; and comprehensive statistics for calculating the disease's burden are difficult to come by. Most cases of typhoid fever in India are now discovered in clinics or by non-stupid Widal checks. For any of these factors, a new study of recent advances in different types of typhoid fever, at least in the Indian sense, would be a major undertaking [5].

The results of the typhoid outbreak and associated diseases in third-world countries, especially in Africa, Asia, and Latin America, have shifted in recent years.<sup>6</sup> In unhealthy nations, more than 20 million cases occur each year. An approximate 85 % of all cases found worldwide are in Pakistan, India, and Bangladesh combined [6].

Children and young adults clearly carry the greatest prevalence of years with typhoid and related diseases. Typhoid fever patients in Pakistan and Bangladesh are seven years old, according to studies. Typhoid is a once-a-year illness that accounts for 45 percent of the overall number of cases recorded per year in the natural world. The disease is most common in South Asia between July and October, when there is a lot of rain. <sup>8</sup> As a result, proper placing of epidemiological tests on typhoid is recommended [7].

Buckle et al. performed a thorough analysis based on systematic testing procedures and 24

trials that looked at typhoid fever outbreaks and used blood culture as a screening tool. was spoken to. 35-39 years old there was also another recently published work that was included in the same way. Typhoid epidemiology evidence are distributed in 47 countries around the globe as a result of these standardized trials. Data was also gathered from population-based surveys and 13 countries' projected immunization rates. The rate of incidence of the remaining cases as reported by typhoid fever surveillance systems in many developing countries where standardized and systemic surveillance at the national level was the rule. only 9 countries provided data on paratyphoid fever prevalence, and despite having a developed and extensive surveillance network, the United States did not have a single case of paratyphoid fever during the study period [8].

## 2. MATERIALS AND METHODS

The Patients went directly to the Observed Treatment in the Dept. of Medicine, DMMC & SMHRC, Nagpur. This is a review article based on some literature searches.

### 2.1 Aetiology

Typhoid fever is an actively spread contagious agent caused by the bacteria *Salmonella typhi*. Drinking polluted water or consuming contaminated food are the most common causes. Typhoid is caused by toxins in surface water, such as sewage, drinking water, and ground water, since *S. typhi* bacteria can live in water for days. Another common source of typhoid transmission is defecation in public places. In most developing countries, cut fruits that have been left out for a long time are a major source of pollution. The cut surface of a papaya has a neutral pH, which allows a wide range of microorganisms to develop [9]. People who eat papaya, lettuce salad, and some typical raw foods were found to be a significant causative factor in a Turkish study (e.g. cig kofte). Typhoid fever is linked to living in a congested neighbourhood or household. Cleaning vegetables and defecating in a sanitary latrine have been found to help avoid typhoid once again. Eating food from street vendors was linked to paratyphoid fever in an Indonesian case-control report [10].

### 2.2 Bacteriology

*Salmonella enterica* serovar typhi, a bacteria, causes typhoid fever. The lipopolysaccharide

antigens O9 and O12, as well as the protein flagellar antigen Hd and the polysaccharide capsular antigen Vi, are all present in the bacterium. While the Vi capsular antigen is shared by certain strains of *S. enterica* serotypes Hirschfeldii (paratyphi C) and Dublin, as well as *Citrobacter freundii*, it is mostly confined to *S. enterica* serotype typhi. Polysaccharide capsule Vi's bactericidal effect on contaminated people's serum is covered [11].

### 2.3 Pathogenesis

The contagious dose of *Salmonella enterica* serotype typhi, also known as *S. enterica* serotype typhi, is estimated to be between 1000 and 1 million people. *S. typhi* variants that are Vi-positive are evidently more infectious and virulent than *S. enterica* serotype typhi strains that are Vi-negative. Since high gastric acidity is one of the most powerful defence mechanisms against *S. typhi* infection, a low gastric pH is an essential defence mechanism. Aging, gastrectomy, proton-pump inhibitors, and antacids are all potential causes of achlorhydria, a disorder that makes typhoid infection more difficult [12,13].

### 2.4 Symptomatology

In underdeveloped nations, typhoid fever is one of the most common febrile illnesses. After the incubation time has ended, fever and malaise occur 7 to 14 days later. Cold, fatigue, malaise, anorexia, nausea, vague stomach pain, dry cough, and myalgia are all symptoms of the fever. Coated tongue, swollen liver, hepatomegaly, and splenomegaly are the next symptoms to appear. This classic style of presentation has been changed by recent advances in antibiotic treatment, such as a slow and stepladder type of fever and toxicity characteristics that are rarely seen these days. In areas where malaria is endemic and Schistosomiasis is common, the appearance of typhoid may be unusual [14].

### 2.5 Diagnosis

In the developed world, typhoid is normally diagnosed based on clinical guidelines. In areas where typhoid is prevalent, any fever lasting more than one week with no apparent cause should be assumed to be typhoid unless proven otherwise. A differential diagnosis could include malaria, deep abscess, leukaemia, amoebic liver abscess, and encephalitis. Furthermore, the following typhoid symptoms should be held in

mind as they can be confounding during diagnosis and treatment:

### 2.5.1 Tests of liver function

It's possible that these are irrational. Though extreme hepatic dysfunction is rare, some studies and case reports have revealed hepatic derangement that mimicked acute viral hepatitis and manifested as a hepatic abscess.

### 2.5.2 Blood culture

This is the most popular method of diagnosis, with 60 to 80 percent of typhoid cases testing positive. Bone marrow culture is more vulnerable, with 80 to 95 percent of patients taking antibiotics for several days, regardless of how long they have been sick. Since there are less species in blood than in bone marrow, blood culture is less susceptible than bone marrow culture. The sensitivity of blood culture is increased by the volume of blood cultured in the first week of illness. Bacteremia is more common in infants than in adults.

### 2.5.3 Other cultures

Blood buffy coats, streptokinase-treated blood clots, intestinal secretion and skin snips with rose spots have also been used to make cultures. In 30% of patients with acute typhoid fever, stool cultures are positive. Urine society has a sensitivity of 0-58%.

### 2.5.4 Felix-Widal test

The Widal exam has been used for over a century. It detects agglutinating antibodies to *S. enterica* serotype typhi antigens O and H. The concentrations are determined by doubling dilutions of sera in a long test tube. It has a sensitivity of 70 to 80 percent and a specificity of 80 to 95 percent, according to the manufacturer. Because of a blunted antibody reaction caused by previous antibiotic use, it can be negative in up to 30% of culture-proven typhoid fever cases [15].

Furthermore, typhoid patients may have no detectable antibody reaction or antibody titre rise. Unfortunately, these antigens and cross-reacting epitopes are shared by other *Salmonella* serotypes and *Enterobacteriaceae* with *S. enterica* serotype typhi. As a result, there will be false positives. A fourfold increase in antibody

titre between convalescent and acute sera is diagnostic if paired serums are available. Because of its low cost, the Widal test is likely to be the preferred test in many developing countries. This is permissible as long as the test findings are carefully considered in light of a previous history of typhoid, for the determination of positivity, and in line with acceptable local cut-off principles [16].

## 2.6 Treatment

Patients with serious infection, such as frequent vomiting, severe diarrhoea, and abdominal distension, should be admitted to the hospital and given parenteral antibiotics. Following its release in 1948, chloramphenicol became the drug of choice for many decades. The development of plasmid-mediated resistance, as well as extreme side effects such as bone marrow aplasia, pushed this drug to the sidelines. To tackle chloramphenicol resistance, trimethoprim-sulfamethoxazole and ampicillin were used in 1970, but they were also abandoned due to the advent of plasmid-mediated resistance. In 1992, the emergence of multidrug-resistant enteric fever in Bangladesh was vigorously treated; a major study reported 36.58 percent cases. Ceftriaxone and ciprofloxacin were the drugs of choice in the 1980s. Fluoroquinolone resistance may be absolute or selective. When compared to nalidixic-acid-sensitive strains, the nalidixic-acid-resistant strain has a lower resistance to fluoroquinolone drugs. Although the isolates are nalidixic acid resistant, disc susceptibility testing shows that they are vulnerable to fluoroquinolones. Azithromycin, administered once daily for seven days at a dosage of 500mg (10 mg/kg). Cefixime, on the other hand, demonstrated higher rates of loss and relapse in certain studies than fluoroquinolones. In contrast, the antibiotic susceptibility pattern in BSMMU showed a higher sensitivity of about 78.8%. Cephalosporins of the third generation are efficient, with low rates of relapse (3–6%) and faecal carriage (3 percent). Ceftriaxone is effective when taken in single or divided doses of 2-4 grammes per day [17-20].

## 3. CONCLUSION

Enteric fever is still a major public health concern around the world, particularly in developing countries. Typhoid cases in cities are estimated to be about 800-900 per year, according to studies. While inexpensive and widely available,

the Widal exam should be used with caution. Massive public awareness campaigns should be undertaken to inform citizens about the importance of taking preventative measures, vaccines, and seeing a doctor, among other items. Doctors should be aware of the emergence of newer antibacterial agents that are both safe and reliable, as well as the gradual development of antibiotic resistance. Among the above are newer fluoroquinolones and macrolides in large doses, as well as third-generation cephalosporins in both oral and injectable forms. Apart from that, the field should prepare for newer curative and preventative approaches.

### CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

### ETHICAL APPROVAL

It is not applicable.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

### REFERENCES

1. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. *The New England Journal of Medicine*; Nov 28, 2002.
2. Alikhan NF, Zhou Z, Sergeant MJ, Achtman M. A genomic overview of the population structure of *Salmonella*. *PLoS Genetics*; 2018.
3. Buran T, Sanem Gökçe Merve Kılınc, Elmas Kasap. Prevalence of Extraintestinal Manifestations of Ulcerative Colitis Patients in Turkey: Community-Based Monocentric Observational Study. *Clinical Medicine and Medical Research*. 2020; 1(2):39-46. Available: <https://doi.org/10.52845/CMMR/2020v1i2a8>
4. Gu D, Wang Z, Tian Y, Kang X, Meng C, Chen X, Pan Z, Jiao X. Prevalence of *Salmonella* Isolates and Their Distribution Based on Whole-Genome Sequence in a Chicken Slaughterhouse in Jiangsu, China. *Frontiers in Veterinary Science*; 2020.
5. Osler W. *The principles and practice of medicine: Designed for the use of practitioners and students of medicine*. 8th Ed. New York: D. Appleton. 1912;1-46.
6. Daniel V, Daniel K. Diabetic neuropathy: new perspectives on early diagnosis and treatments. *Journal of Current Diabetes Reports*. 2020;1(1):12–14. Available: <https://doi.org/10.52845/JCDR/2020v1i1a3>
7. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bull World Health Organ*. 2004;82:346-53.
8. Whitaker RC, Pepe MS, Seidel KD, et al. Gestational diabetes and the risk of offspring obesity. *Pediatrics*. 1998;101:E9.
9. Murray CJL, Lopez AD. *Global burden of disease and injury series, 1<sup>st</sup> ed*. Boston (MA). Harvard University Press. 1996;1.
10. Breiman RF, Cosmas L, Njuguna H, Audi A, Olack B, Ochieng JB, et al. Population-based incidence of typhoid fever in an urban informal settlement and a rural area in Kenya: Implications for typhoid vaccine use in Africa. 2012;7:e29119.
11. Hosoglu S, Celen M, Geyik MF. Risk factors for typhoid fever among adult patients in Diyarbakir, Turkey. *Epidemiol Infect*. 2006;134:612-6.
12. Daniel V, Daniel K. Perception of Nurses' Work in Psychiatric Clinic. *Clinical Medicine Insights*. 2020;1(1):27-33. Available: <https://doi.org/10.52845/CMI/2020v1i1a5>
13. Vollaard AM, Ali S, Van Asten HAGH. Risk factors for typhoid and paratyphoid fever in Jakarta, Indonesia. *JAMA*. 2004;291:2607-15.
14. Background Document: The diagnosis, treatment and prevention of typhoid fever. department of vaccines and biological. Geneva: World Health Organizations. 2003;1.
15. Hornick RB, Greisman SE, Woodward TE, DuPont HL, Dawkins AT, Snyder MJ. Typhoid fever: pathogenesis and immunologic control. *N Engl J Med*. 1970;283(13):686-691 and 283(14):739-46.

16. Daniel V, Daniel K. Exercises training program: It's Effect on Muscle strength and Activity of daily living among elderly people. *Nursing and Midwifery*. 2020; 1(01):19-23.  
Available:<https://doi.org/10.52845/NM/2020v1i1a5>
17. Sahu, Preeti Rajendra, Kishor Madhukar Hiwale, Sunita Jayant Vagha, Samarth Shukla. Spectrum of lesions on upper gastrointestinal endoscopy and its correlation with histopathological evaluation. *Journal of Evolution of Medical and Dental Sciences-JEMDS*. 2020;9(32): 2301–6.
18. Ahasan HAMN, Islam QT, Choudhury MA, Azhar MA, Rafiquddin AKM, Hussain A, Kabir F. Hepatic manifestation of typhoid fever-report of four cases. *Bangladesh J Med*. 1993;4:19-21.
19. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. *N Engl J Med*. 2002;347(22):1770-82.
20. Background Document: The diagnosis, treatment and prevention of typhoid fever. department of vaccines and biologicals, Geneva: World Health Organizations. 2003;1.

---

© 2021 Kaluse et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*  
<https://www.sdiarticle4.com/review-history/71200>