International Journal of Pharmacy and Pharmaceutical Science

ISSN Print: 2664-7222
ISSN Online: 2664-7230
IJPPS 2024; 6(1): 81-85
www.pharmacyjournal.org
Received: 05-12-2023
Accepted: 06-01-2024

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Typhoid disease its diagnosis procedure and antibiotic medicine care: Basic overview

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DOI: https://doi.org/10.33545/26647222.2024.v6.i1b.86

Abstract
A bacteria-related infection that can affect multiple organs and spread throughout the body is typhoid fever. It can be lethal and result in major complications. It is brought on by the Salmonella typhi bacteria, which is related to the germs that cause food poisoning. Enteric fever is another name for typhoid fever. It is a potentially multisystemic condition that has posed a challenge to public health, particularly in developing nations. Salmonella typhi and Salmonella paratyphi are the causes. The bacillus that was thought to be the source of typhoid fever was initially described by Karl Joseph Eberth in 1880. Pathologist Georg Gaffky identified the bacillus Eberthella typhi, which is now known as Salmonella typhosus (also known as Bacillus typhosus), four years after the pathologist first established this connection. Typhoid fever is quite frequent in India, with varying rates of transmission throughout the country and a higher incidence in urban areas. In this review study, we discuss the pathophysiology, epidemiology, therapy, diagnosis, and aetiology of typhoid.

Keywords: Typhoid, epidemiology, etiology, pathogenesis, medication

Introduction
Salmonella enterica serovar Typhi is the primary cause of typhoid disease, often known as enteric fever. S. Paratyphi A. also plays a minor role. S. enterica serotype Typhi belongs to the Enterobacteriaceae family. The polysaccharide capsular antigen Vi, the protein flagellar antigen Hd, and the lipopolysaccharide antigens O9 and O12 are all serologically positive for the bacteria. Though certain strains of S. enterica share its serotypes Hirschfeldii (paratyphi C) and Dublin, as well as Citrobacter freundii, the Vi capsular antigen is primarily limited to S. enterica serotype Typhi. Certain Indonesian isolates of S. enterica serotype Typhi possess a distinct flagella type called Hj. Studies using phage typing, pulse-field gel electrophoresis, and ribotyping have demonstrated that while a limited number of strains are typically responsible for outbreaks, locations with endemic disease typically have a large number of strains in circulation [1]. With over 16 million cases recorded annually, typhoid fever is still a serious public health concern in many parts of the world. Patients who have Salmonella enterica subspecies I serovar Typhi (S. typhi) infection and typhoid fever typically present to a healthcare provider with a history of fever, headache, stomach pain, and generalized lethargic behaviour [2]. These species have no other home than humans. The primary means of transmission are the faeces and urine of infected individuals, with contaminated food, water, and flies serving as significant intermediate vehicles. A foodborne or waterborne pathogen causes this gastrointestinal infection. The infectious dosage and the organism's pathogenicity are the primary factors that determine the disease's start and severity [3]. Fever is the primary presenting feature in the early stages of enteric fevers, with abdominal pain and high fever as typical symptoms. The incubation period is typically one to fourteen days. Non-specific symptoms, including chills, a lingering headache, stomach discomfort, constipation, diarrhoea, weakness, disorientation, nausea, and coughing may accompany typhoid fever. Serious side effects that could result from a delayed diagnosis or treatment failure include brain damage, intestinal perforation, bleeding in the gastrointestinal tract, and shock. The most frequent consequence of enteric fevers is terminal ileal perforation. Re-infection only happens in cases where early antibiotic intervention is used to treat the original infection. Both humoral and cell-mediated responses protect against typhoid. Antibodies are produced in the gut and serum by natural infection.

If the bacilli remain in the environment and cause persistently low levels of immunity, an outbreak of typhoid fever may result in lifetime protection [4-6]. Enteric fever is another name for typhoid fever. Multisystemic sickness has historically been a public health concern, particularly in developing nations. Salmonella typhi and Salmonella paratyphi are the causes. The phrase "enteric fever" refers to a combination of paratyphoid and typhoid fever. Typhoid fever and paratyphoid are used interchangeably since they are clinically similar. Although extensive research and public health initiatives have reduced the incidence, typhoid fever remains a leading cause of death and morbidity in crowded and unsanitary regions. The course of the disease might vary from early gastrointestinal pain to a generalized illness, but it can ultimately result in several problems. It's thought that the "four Fs"-flies, fingers, faeces, and fomites-are what spread salmonella. Usually occurring in a stepwise manner, fever is followed by headache and stomach pain [7]. Salmonella enterica serovar typhi and paratyphi (S. typhi and S. paratyphi) are estimated to have caused 14.3 million cases of enteric fever worldwide in 2017. S. Typhi was the cause of 11 million cases of typhoid fever and 120,000 deaths. Children under the age of 15 accounted for more than half of the deaths. The World Health Organization (WHO) has advised against typhoid immunization since 2008; nevertheless, because the vaccines were not suitable for use in young children, there was a limited uptake of the available shots. The WHO reaffirmed its recommendation for the currently accessible Vi polysaccharide-based typhoid conjugate vaccines (TCV) in 2018, giving priority to the nations with the highest burden [8]. Based on a 0.2% case-fatality rate, the yearly incidence of typhoid fever in India is 360 cases (95% confidence interval, 297-494) per 100,000 person-years. Additionally, we projected the number of fatalities (95%, 7360-12 260) and the number of cases (95% CI, 3.7-6.1 million) to be 4.5 million. Significant regional differences were seen in the incidence of typhoid across the nation, with a higher incidence in the southwestern states and northern urban centres. India has a high prevalence of typhoid fever, which varies greatly throughout the nation and is more prevalent in metropolitan areas [9].

Epidemiology

Even though the United States only records 350 cases of typhoid fever with a proven culture and less than 100 cases of paratyphi A year since 2008, enteric fever is still a major global source of sickness. Every year, around 26 million cases of typhoid fever and 5 million cases of paratyphoid infection occur worldwide, accounting for about 215,000 deaths. Typhoid fever is more prevalent in low and middle-income nations in southern Africa and south-central Asia than it is in developed nations. Travellers returning from endemic areas and those visiting family and friends are the main carriers of cases in industrialized countries because they are more likely to be careless with food and water sources. People who are less likely to get vaccinated and visit a doctor before travelling are also in danger. Tropical and temperate regions are more likely to see cases of typhoid fever. It is closely related to the water treatment system, sewage, and sanitation. It is more frequent to contract Salmonella typhi than Salmonella paratyphi, and infections with Salmonella paratyphi A are more common than those with Salmonella paratyphi B. Typhoid fever cases have been rising globally as a result of rapid population growth, pollution, and a lack of clean drinking water. Even so, despite rising multidrug resistance, death rates have declined as a result of thorough studies, modifications to treatment techniques, and the development of new medications. The traditional manifestations are not usually seen in the age of habitual antibiotic use. Only 10% and 1.5% of cases in the United States may exhibit splenomegaly or rose spots, respectively [10, 11]. Typhoid fever patients may become chronic carriers in as many as 4% of cases. Following their acute treatment, these individuals continue to show no symptoms; nonetheless, they may continue to excrete Salmonella in their stool or, less commonly, in their urine for up to a year. Women and people with biliary disorders, such as cholelithiasis, are more likely to experience it. Blood group antigens may also be connected to chronic carriage of S. Typhi susceptibility [12, 13].

Etiology

Salmonella typhi and Salmonella paratyphi, both belonging to the Enterobacteriaceae family, are the primary cause of typhoid fever. The two species of Salmonella in the genus, Salmonella enterica serovar and enteritidis, have been categorized after thorough examination using multiplex quantitative polymerase chain reaction (PCR). Salmonella enterica serotypes A, B, and C correspond to Salmonella typhi and Salmonella paratyphi, respectively. Salmonella that is not typhoidal (NTS) is more common in youngsters and is primarily associated with gastroenteritis. Salmonella is primarily found in places with overpopulation, social unrest, and inadequate sanitation. It is spread through the fecal-oral route and can also be contracted through undercooked food, polluted water, and the feet of infected people [14-17]. Its only host is humans, and it can only spread from one infected individual to another. Salmonella is primarily found in poultry, eggs, and infrequently, turtles. In one study, 57% of samples tested positive for salmonella isolates using whole-genome sequencing in Chinese chicken slaughterhouses. The gut's natural flora guards against illness. Antibiotics like streptomycin increase its invasion since they kill off the natural flora. Malnutrition also enhances the vulnerability to this infection since it reduces the natural gut flora. Thus, poor diet and the use of broad-spectrum antibiotics increase the risk of typhoid fever [18,19].

Pathogenesis

Numerous factors, such as the infectious species, host immunity, virulence, and infectious dosage, influence the pathogenesis of typhoid fever. The attack rate increases with increasing infectious dosage and decreases with decreasing incubation time. Patients with impaired immune systems, such as those with HIV (primarily paratyphi), those receiving glucocorticoid therapy, and those with altered phagocyte function (such as those suffering from sickle cell anaemia and malaria), are more susceptible to severe cases of typhoid fever. Except for a few resistant strains, salmonella is an acid-sensitive bacterium that, unless swallowed in high quantities, is usually killed in the stomach by gastric acid. Salmonella can colonize even at lower dosages in people with achlorhydria, antacid and antihistamine consumption, and other medical conditions. Additionally, food and drink serve as buffers against stomach acid, which makes it easier for germs to enter the small intestine (20). Typhoid toxin, flagellar H antigen,

liposaccharide O antigen, and Vi antigen (polysaccharide capsule) all indicate how virulent Salmonella is. Even with the same amount of microorganisms, strains positive for the Vi antigen had an attack rate twice as high as strains negative for the Vi antigen. Salmonella typhi and non-typhoidal salmonella (NTS) differ primarily in that the former has the Vi antigen, whereas the latter does not. The primary function of the Vi antigen is to inhibit macrophage activity by acting as an antiphagocytic agent, protecting the O antigen from antibodies that provide serum resistance. In the mucosa of the gut wall, the flagellar H antigen facilitates bacterial motility and adhesion. Flagella aids in the invasion of the gut wall, and the type III secretion system can penetrate the mucosa directly or transfer bacterial protein into enterocytes and M cells, which are specialized epithelial cells that present antigens in the gut mucosa or lymphoid tissue. Pinch off bacterial-containing cytoplasm to absorb bacteria adhering to M cells, and then expel those bacteria into the luminal area. M cells suffer damage during this process, and the basal lamina becomes visible. It makes germs easier to reach during the invasion, which exacerbates the illness. Patients with aberrant CFTR protein are resistant to typhoid because the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) is thought to play a significant role in the uptake of Salmonella. Through the recruitment of lymphocytes and mononuclear cells, bacteria cause the Payer patches to proliferate. They also cause necrosis and, ultimately, ulceration, which exacerbates the symptoms. Pathogens can enter the bloodstream and lymphatic system to reach the reticuloendothelial system. They can also enter through other organs, most frequently the gallbladder in nearly all cases. Because these bacteria are phagocytosed by macrophages and monocytes in the reticuloendothelial system, the early bacteremic phase (24-72 hours) is asymptomatic and brief. This condition is known as primary bacteremia. The ability of pathogens to proliferate within these immune cells is what distinguishes them, and the reticuloendothelial system's intracellular bacterial multiplication pushes the bacteria to re-enter the bloodstream, resulting in persistent bacteremia over days or weeks, a condition known as secondary bacteremia. The stage of the disease where symptoms appear is called secondary bacteremia [21-23].

Diagnosis

Any disease's first step toward a cure is an accurate and early diagnosis, which is frequently unavailable, expensive, and difficult to obtain in India. The true prevalence of enteric fever illness is still unknown in the majority of the world. This is because there are inadequate disease-reporting systems, few and expensive quick diagnostic instruments, and irregular laboratory testing procedures. Diagnostic tests are not as useful in endemic and resource-poor countries as the clinical diagnosis of typhoid fever, which is frequently erroneous. Nonetheless, the presence of other co-endemic acute febrile disorders makes the clinical identification of typhoid disease challenging. Crucially, precise laboratory diagnostics identify the actual disease load, which starts the proper therapies. the problem of antibiotic resistance emerging. Furthermore, suitable diagnostics can determine the human infection's natural history and assess the effectiveness of vaccinations, which is a useful disease control strategy. The assessment of disease burden is practically hampered by the failure to diagnose enteric fevers. Despite the advancements in automated culture methods, the gold standard for diagnosing typhoid fever remains the classical blood culture method, which has a low sensitivity of 40-60%. With simpler tools and little technical knowledge, one can effortlessly do another popular serological Widal test. However, inconsistent cut-off points between laboratories and locations frequently make it difficult to interpret data, and tests perform poorly in terms of low sensitivity and specificity. Furthermore, rather than starting the treatment with the convalescent phase samples, a single acute-phase sample is used. In most primary healthcare centres in underdeveloped countries, there is a lack of laboratory equipment and technical expertise necessary for the painstaking but reliable bone marrow culture test [24-27]. Typhoid patients should be treated with a clinical approach. Patients who have a history of travel from endemic areas, live in unsanitary or polluted places or have febrile sickness lasting more than three days together with gastrointestinal symptoms (pain, constipation, or diarrhoea) should be taken very seriously. Although diagnosing within the first week is challenging, several laboratory tests help. Blood culture: Blood culture is still the major method used to confirm a diagnosis of typhoid fever. Because it is not expensive or technically challenging, it is the most widely available and often conducted test. High-volume sample collection increases the blood culture's effectiveness. Though 30% to 50% of blood cultures may be mistakenly negative depending on the technique and time series, blood cultures performed during clinical signs of secondary bacteremia are more accurate. Stool culture: During the disease's bacteremic phase, stool culture is less effective. In the second and third weeks, stool culture is diagnostic. According to estimates, just 37% of patients receiving antibiotic therapy would see a positive outcome. The length of the sickness and the volume of the stool sample collected determine the sensitivity of the stool culture. Multiple samples should be obtained since chronic carriers occasionally transmit germs in their faeces for an extended period. Other metabolite biomarkers are being researched. Assay: Polymerase Chain Reaction (PCR): PCR is a DNA-based method for identifying genes of various serotypes, including the O and H antigen genes. However, because of the low bacterial counts during bacteremia, sensitivities may be minimal. In many locations with limited resources, this testing is also prohibitively expensive. Skin snip test: Up to 63% of positive cases with prior therapeutic antibiotic therapy may have punch biopsies from distinctive rose patches culture positively. The enzyme-linked immunosorbent assay, or ELISA, detects antibodies to the capsular polysaccharide Vi antigens and is rarely effective in the early stages of acute sickness. However, it may be beneficial in identifying carriers [28-33].

Medication

Treatment with antibiotics is the cornerstone of care. Multidrug-resistant strains that have emerged in many endemic locations, particularly in south-east Asia and India, have hampered the treatment. Treatment options vary depending on the disease's severity, course, spread, and consequences. Antibiotic therapy: Typhoid fever's serious consequences can be avoided by promptly administering the appropriate antibiotic medication. The choice of initial medication therapy is determined by the strains' susceptibility. Fluoroquinolones are the most effective

medication of choice in the majority of locations. Fluoroquinolones can be empirically given on clinical suspicion in cases of severe illnesses requiring immediate treatment, before the outcome of a diagnostic culture test. About 98% of cases are resolved with fluoroquinolones, and faecal carriage rates are less than 2%. Taking 500 mg of ciprofloxacin twice a day for five to seven days is the most efficient form of fluoroquinolone. Alternative treatments for adults in fully susceptible cases include amoxicillin (750 mg orally 4 times daily for approximately 2 weeks), trimethoprim-sulfamethoxazole (160 mg twice daily for 2 weeks) and outside of the United States, chloramphenicol (500 mg 4 times daily for 2-3 weeks). However, resistance to these medications is becoming more common. Oral antibiotics and antipyretics can be used at home to treat simple instances. Hospitalization is necessary for patients who have serious side effects including vomiting, diarrhoea, or distension of the abdomen. Up to five days following recovery, parenteral antibiotics, such as third-generation cephalosporins, and additional supportive care should be used. These measures should be guided by cultural sensitivities. In endemic locations, highly drug-resistant strains (XDR) and multidrug-resistant (MDR) have emerged. Bacteria are protected from external antibiotics by their intracellular nature. The best course of action in MDR cases is azithromycin combined with third-generation cephalosporins (ceftriaxone, cefotaxime, and oral cefixime 2g once daily for 2 weeks), with ciprofloxacin as a backup. These treatments have a failure rate of roughly 5% to 10% and a relapse rate of 3% to 6%. With a faecal carriage rate of less than 3%, these medicines alleviate fever in less than a week. When azithromycin and cefixime are added, the failure rate is decreased and hospital stays are shorter [23, 34, 35]. In 2017, the World Health Organization's Strategic Advisory Group of Experts on Immunization initially suggested that typhoid conjugate vaccines (TCVs) be administered to nations where the disease is endemic. Single-dose, intramuscular TCVs for patients aged six months and up are now registered in Nigeria, Nepal, India, and Cambodia. Further research is being done to see whether these vaccines may be used in endemic areas and during outbreaks. The TCV was shown to be safe for use in children between the ages of 10 and 6 months during an outbreak of extensively drug-resistant typhoid in Pakistan in 2018. When compared to the Vi polysaccharide unconjugated vaccine, TCVs are also preferable because they have the potential for a longer duration of protection, are safe for use in younger children, and have an improved immunogenicity profile. According to epidemiological data, typhoid is more common in low and middle-income nations, as well as in places with unsanitary conditions and bad drinking water. Sanitation, staying away from crowded areas, and access to clean drinking water all significantly lower the number of incidents [36-39].

Discussion and Conclusion

Our review articles begin with an overview of typhoid, including its various causes, epidemiology, pathophysiology, and alternative remedies. According to our research, medications (antibiotics) do provide full relief. The field of typhoid treatment needs more randomized controlled trials. In the future, we would like to conduct a preliminary investigation on typhoid. With the help of our colleagues, future counselling-based research in our country or state will assess the physical and mental health of patients and produce more accurate data about typhoid and its treatment.

Ethical statement

A health care professional uses tactful, considerate, and compassionate methods to promote each patient's well-being.

Acknowledgement

Authors would like to thank, Azad Institute of Pharmacy & Research, Lucknow, U.P, India, Lucknow, Uttar Pradesh, India for extending their facilities.

Conflict of interest

The authors attest that they are free of any known financial or personal conflicts of interest that would taint the findings of this study.

Informed consent

Using websites, review articles, and other sources to produce research content.

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