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Study Of Various Aspects Of Typhoid Fever : A Review

[1]Ankit Jadhav, [2] Kiran Dhikale, [3]Akshay Gite,

Student[1], Student[2], Student[3].

Matoshri College Of Pharmacy, Eklahare, Nashik, Maharashtra, India

Corresponding Author E-mail :- ankitjadhav4033@gmail.com

Abstract

Typhoid fever is a globally spread infectious disease. Although there is a lot of information on Salmonella typhimurium infection in mice and the interaction of this serovar with human cell lines in vitro, information on S. typhi and the pathogenesis of typhoid fever is limited. We focus on three aspects in this review: adhesion to and penetration of gut epithelial cells, dissemination to systemic locations, and host cell survival and reproduction. We have included all relevant information about typhoid treatment and causes in this review.

Key Words : *Typhoid fever, Salmonella typhimurium, serovar*

Introduction.

Typhoid fever, diarrhoea, and vomiting are all symptoms of a bacterial infection called typhoid. It has the potential to be fatal. Salmonella typhi is the bacteria that causes it. The virus is spread by contaminated food and water, and it is more common in areas where handwashing is not practised. It can also be spread by carriers who are unaware that they are carrying the germs. Every year, around 5,700 instances of True Source are reported in the United States, with 75 percent of these cases beginning while travelling internationally. Typhoid affects around 21.5 million people worldwide each year. Typhoid can be successfully treated with antibiotics if found early; but, if not treated, typhoid can be fatalTrusted Source. Typhoid fever is a bacterial infection caused by Salmonella typhimurium (S. typhi). Humans have the bacterium in their intestines and bloodstream. It is communicated between people through direct contact with an infected person's faeces. Because no animals carry the disease, transmission is always from person to person. Typhoid can be fatal in one out of every five cases if left untreated. Fewer than 4 out of 100 cases are fatal after therapy.

S. typhi enters through the mouth and stays in the intestine for 1 to 3 weeks. It then makes its way into the bloodstream after passing through the gut wall. It spreads from the bloodstream to various tissues and organs. Because S. typhi may dwell within the host's cells, unnoticed by the immune system, the host's immune system has little ability to fight back. The presence of S. typhi in blood, stool, urine, or bone marrow samples is used to diagnose typhoid. [1]

Figure 1. Salmonella Typhi [13]

History

Both Salmonella typhoid and Salmonella paratyphoid have comparable clinical manifestations, though arthralgia is more prevalent in typhoid. To help with diagnosis, obtain a history of permanent residence, travel history (travel to endemic and outbreak areas), immunisation, socioeconomic position, lifestyle, onset and duration of sickness, and treatment history (malaria chemoprophylaxis, dose, and interval of the medicine). Excluding other infectious diseases is aided by a history of exposure and related activities such as contaminated drinking water, animal contact, insect bites, lodgings, and undercooked food. [2]

Typhoid is an infectious disease with a wide range of symptoms.After 12 to 48 hours of inoculation, patients have enterocolitis. They frequently begin with nausea and vomiting, which progresses to diffuse abdominal pain, bloating, anorexia, and diarrhoea (around 66 percent), which can range from mild to severe diarrhoea with or without blood, followed by a brief asymptomatic phase, which leads to bacteremia and fever (about 96 percent) with flu-like symptoms. Salmonella typhi causes greater enterocolitis than other Salmonella strains. Except in the elderly and extremely young, enterocolitis symptoms usually last a few days and are self-limited, requiring no medical intervention.Patients with HIV who are immunocompromised, especially those with low CD4 counts, are more likely to have severe diarrhoea and have more serious metastatic infections. The symptoms of classic typhoid fever appear around a week after the bacterium is consumed. Fever has a "step-ladder" design to it (i.e., fever rises one day, falls the subsequent morning, and continues to form peaks and troughs with insidious onset). Typhoid fever frequently causes abdominal pain. Constipation may predominate over diarrhoea in some circumstances due to Payer patch hypertrophy. [2]

The results of a physical examination can be vague. A recorded fever may be accompanied by a reduced heart rate in the first week. Findings like as abdominal distention are more common in the second week. Tenderness, rigidity, and guarding of the abdomen may be present when typhoid is worsened by ileal perforation. Typhoid fever is accompanied with visible rose spots (rose-colored macules on the abdomen), however they are uncommon. With sunken eyes, dry skin, and lethargy, the patient seems pale, somewhat agitated, and dehydrated. When a patient has gallstones or other biliary pathology, they may develop jaundice, which manifests as yellowish skin and sclera, pale faeces, and dark urine. On palpation, a swollen spleen may be seen.The patient is more toxic, anorexic, and has significant weight loss if the diagnosis is not made until the third week. With time, the risk of bowel perforation increases, worsening abdominal distension and peritonitis. On auscultation, the patient becomes tachypneic with crackles above the lung base. Metastatic problems start to show up. A dry cough owing to pneumonia, neck rigidity due to meningitis, or chest pain due to myocarditis and pericarditis are all possible symptoms.Patients from endemic countries, such as India and Africa, are more likely to experience neurologic symptoms such as delirium, psychosis, sleeplessness, disorientation, apathy, and, in rare circumstances, parkinsonism. Other atypical manifestations include pancreatitis-related severe epigastric pain extending to the back, osteomyelitis-related bone pain, and abscesses, which can arise anywhere in the body. [2]

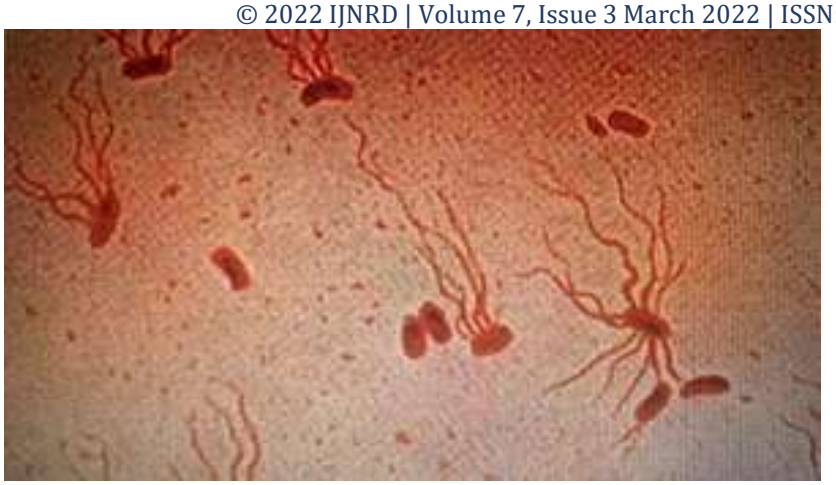

Figure 2. Salmonella enterica serological variant Typhi (shown under a microscope with flagellar stain) [18]

Global Impact Of Typhoid

In 2017, there were 14.3 million (95 percent uncertainty interval [UI] 12.5–16.3) cases of typhoid and paratyphoid fevers worldwide, down 446% (42.2–47.0) from 259 million (22.0-29.9) in 1990. From 439.2 (376.7–507.7) per 100 000 person-years in 1990 to 197.8 (172.0–226.2) per 100 000 person-years in 2017, age-standardised incidence rates fell by 54.9 percent (53.4–56.5). Salmonella enterica serotype Typhi was responsible for 76.3 percent (71.8–80.5) of enteric fever cases in 2017. In 2017, we calculated a global case fatality rate of 0.95 percent (0.54–1.53), with higher estimates for children and older individuals, as well as those residing in lower-income countries**.**As a result, we calculated 135.9 Thousand (76.9 – 218.9) deaths from typhoid and paratyphoid fever worldwide in 2017, down 41.0 percent (33.6–48.3) from 230.5 Thousand (131.2-372.6) deaths in 1990. Typhoid and paratyphoid fevers caused 9.8 million (5.6–15.8) DALYs in 2017, down 43.0 percent (35.5–50.6) from 17.2 million (9.9–27.8) DALYs in 1990. [3]

Epidemiology

Since 2008, the United States has reported only about 350 culture-confirmed cases of typhoid fever and fewer than 100 cases of paratyphi A per year, but enteric fever continues to be a major cause of illness around the world. Each year, nearly 26 million cases of typhoid fever and 5 million cases of paratyphoid infection result in around 215,000 deaths globally.Typhoid is more common in low- and middle-income nations in South Asia and Southern Africa than it is in developed ones. The majority of cases in developed countries are carried by travellers returning from endemic areas and visitors visiting relatives and friends, who are at a higher risk because they are less cautious with food and water sources.Those who are less inclined to seek immunisation and pre-travel advice are also at greater risk. In temperate and tropical regions, typhoid fever is more common. It is directly related with sanitation, sewage, and water treatment system. Salmonella typhi is more common than Salmonella paratyphi, and infections with Salmonella paratyphiA are more common than infections with Salmonella paratyphi B. Due to rapid population growth, pollution, and a lack of safe drinking water, the number of new cases of typhoid fever has been rising over the world.Despite developing multidrug resistance, death rates have dropped as a result of significant research, modifications in treatment techniques, and the introduction of new medications. Classic presentations are not often seen in the era of regular antibiotics. Splenomegaly and rose spots are only encountered in 10% and 1.5 percent of cases in the United States, respectively. [2]

Up to 4% of typhoid fever patients go on to become chronic carriers of the disease. After their acute therapy, these patients are asymptomatic, although they may excrete Salmonella in their stool for up to a year, or less frequently in their urine. Women and people with biliary disorders, such as cholelithiasis, are more likely to develop it. Susceptibility to S. typhi chronic carriage may also be associated to blood group antigens. [2]

Etiology

Salmonella typhi and Salmonella paratyphi, both members of the Enterobacteriaceae family, are the major causes of typhoid fever. Salmonella is a genus with two species, Salmonella entericaserovar and Salmonella enteritidis, which were recognised by multiplex quantitative polymerase chain reaction study (PCR). Salmonella enterica serotypes A, B, and C are both Salmonella typhi and Salmonella paratyphi (A, B, and C). Salmonella nontyphoidal (NTS) is more common in youngsters and is usually restricted to gastroenteritis. [2]

Salmonella is spread through contaminated water, undercooked foods, and infected individuals' fomites, and is more common in regions with overpopulation, social disorder, and poor sanitation. Because humans are its only host, HPV can only be spread from one infected person to another. Poultry, eggs, and, on rare occasions, turtles are major sources of salmonella. In one study, whole-

genome sequencing was used to look at the spread of salmonella isolates in chicken slaughterhouses in China, and 57 percent of the samples were positive. [2]

The normal flora of the gut protects you from infection. The use of antibiotics such as streptomycin damages the normal flora, which heightens its invasion. Malnutrition reduces the natural bacteria in the gut, making it more susceptible to infection. As a result, broad-spectrum antibiotics and poor nutrition increase the risk of typhoid fever. [2]

Risk Factor

Typhoid fever is a significant global danger that affects an estimated 27 million people each year. The disease has spread to India, Southeast Asia, Africa, South America, and other parts of the world.Children are at the highest risk of contracting the disease worldwide, while their symptoms are usually less than those of adults.If you reside in a place where typhoid fever is uncommon, you're more likely to contract it if you:

- Work in or travel to areas where typhoid fever is established
- Work as a clinical microbiologist handling Salmonella typhi bacteria
- Have close contact with someone who is infected or has recently been infected with typhoid fever
- Drink water polluted by sewage that contains Salmonella typhi [4]

Pathophysiology

When pathogenic Salmonella species are present in the gut, phagocytic cells engulf them, which then pass them through the mucosa and present them to the lamina proprietor's macrophages. Salmonellae that are not typhoidal are phagocytized throughout the distal ileum and colon. Macrophages identify pathogen-associated molecular patterns (PAMPs) such as flagella and lipopolysaccharides using the toll-like receptor (TLR)–5 and TLR-4/MD2/CD-14 complex. With interleukin 8 (IL-8), macrophages and intestinal epithelial cells attract T cells and neutrophils, generating inflammation and inhibiting infection. [5]

S Typhi and Paratyphi, unlike nontyphoidal salmonellae, enter the host's system largely through the distal ileum. They have specific fimbriae that stick to the epithelium over lymphoid tissue clusters in the ileum (Peyer patches), which serve as the main relay point for macrophages going from the gut into the lymphatic system. After that, the bacteria cause their host macrophages to attract other macrophages. [5]

The most prevalent ParatyphiSerova, Paratyphi A, possesses a VI capsular antigen that masks PAMPs, preventing neutrophil-based inflammation. This could explain why Typhi is more infectious than most of its cousins. [5]

Typhoidal salmonella uses the cellular machinery of macrophages to reproduce as it travels through the mesenteric lymph nodes to the thoracic duct and lymphatics, and then to the liver, spleen, bone marrow, and lymph nodes' reticuloendothelial tissues. They pause there and continue to multiply until they reach a critical density. After that, the bacteria cause macrophages to die, allowing them to enter the bloodstream and infect the remainder of the body. [5]

The bacteria subsequently infect the gallbladder through bacteremia or direct extension of infected bile into the gallbladder. As a result, the bacterium enters the gastrointestinal tract through the bile and infects Peyer patches once more. Bacteria that do not reinfect the host are usually shed in the stool and can later infect other people. [5]

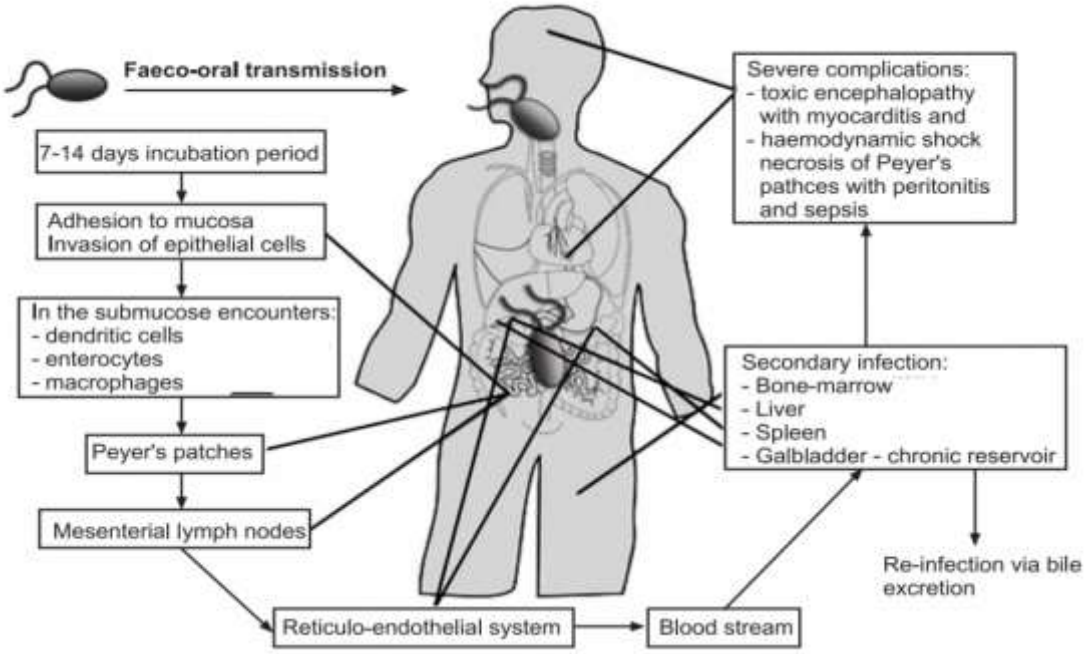

Figure 3.Life cycle of Salmonella typhi [5]

Transmission

Salmonella Typhi transmission is thought to be mostly indirect, with contaminated water or food being the most common mode of infection. Salmonella Typhi generally travels through water and food as a passive carrier. While Salmonella Typhi can survive for long durations on cars, it is uncommon for Salmonella Typhi to multiply in water or food [6]. Salmonella Typhi transmission has been divided into two major categories by several researchers. In short-cycle transmission, faeces shedding in the near surroundings contaminates food and water, and transmission is mediated by poor hygiene and sanitation. There is contamination of the broader environment in long-cycle transmission, such as human faeces pollution of untreated water supplies and the use of raw human excrement or untreated sewage as a crop fertiliser. Chronic carriers play a major role in short-cycle foodborne typhoid epidemics in countries with low typhoid incidence, as well as the potential for large-scale long-cycle waterborne transmission in many high-incidence settings, according to epidemiologic studies. The methods used to contaminate the source and the types of vehicles involved differ greatly from one place to the next, emphasising the significance of conducting local epidemiologic investigations to inform nonvaccine management approaches. [6]

Causes

Typhoid fever is caused by the Salmonella typhi (S. typhi) bacteria. The bacteria is transferred by contaminated food, drinks, or water. Salmonella typhi is carried in the intestinal tract and blood of those who have been infected. [7]

Salmonella typhi is excreted (expelled) in the faeces (stool). If you consume food or beverages prepared by someone who is shedding the bacterium and does not adequately wash their hands, you may contract typhoid fever. Sewage harbouring Salmonella typhi could contaminate local water systems in less developed countries.

People who have had typhoid fever in the past may still carry Salmonella typhi germs. These individuals are disease carriers. They can spread the sickness even if they don't show any symptoms (as in the case of "Typhoid Mary" in the United States). [7]

Signs & Symptoms

Untreated typhoid disease typically progresses through three phases, each lasting about a week. The patient grows fatigued and malnourished as these stages progress.

- The body temperature rises slowly in the first week, with relative bradycardia (Faget sign), lethargy, headache, and cough as symptoms. In a quarter of cases, a bloody nose (epistaxis) is noted, and abdominal pain is also a possibility. With eosinopenia and relative lymphocytosis, the quantity of circulating white blood cells (leukopenia) decreases; blood cultures are positive for S. enterica subsp. enterica serovar Typhi. In most cases, the Widal test is negative. [8]
- The person is frequently too weary to get up in the second week, with a high fever in a plateau about 40 °C (104 °F) and bradycardia (sphygmothermic dissociation or Faget sign), which is typically accompanied by a dicrotic pulse wave. Delirium is a condition in which the patient is usually calm but becomes agitated at times. Typhoid is known as "nervous fever" because of its delirium. In around a third of patients, rose patches occur on the lower breast and belly. In the base of the lungs, rhonchi (rattling breathing sounds) can be heard. The right lower quadrant of the abdomen is swollen and uncomfortable, with a rumbling sound. This stage might bring up diarrhoea, but constipation is also prevalent. The spleen

and liver are swollen and painful (hepatosplenomegaly), with increased liver transaminases. AntiO and antiH antibodies are found in the Widal test, indicating a strong positive result. Blood cultures can still be positive in some cases. [8]

- A number of complications can emerge during the third week of typhoid fever:
- The fever is still pretty high and hasn't changed much in the last 24 hours. The patient becomes delirious as a result of dehydration and starvation. A macular rash appears on the trunk in one-third of those who are affected.
- Intestinal haemorrhage can develop as a result of bleeding in clogged Peyer's patches; this can be life-threatening, but is typically not fatal.
- Intestinal perforation in the distal ileum is a dangerous and often fatal condition. It might happen without causing any noticeable symptoms until septicaemia or widespread peritonitis develops.
- Pneumonia and acute bronchitis are examples of respiratory illnesses.
- Encephalitis
- Picking at bedclothes or imaginary things, as well as neuropsychiatric symptoms (characterised as "muttering delirium" or "coma vigil").
- osteitis, cholecystitis, endocarditis, and metastatic abscesses
- Thrombocytopenia (low platelet count) is a common complication. [8]

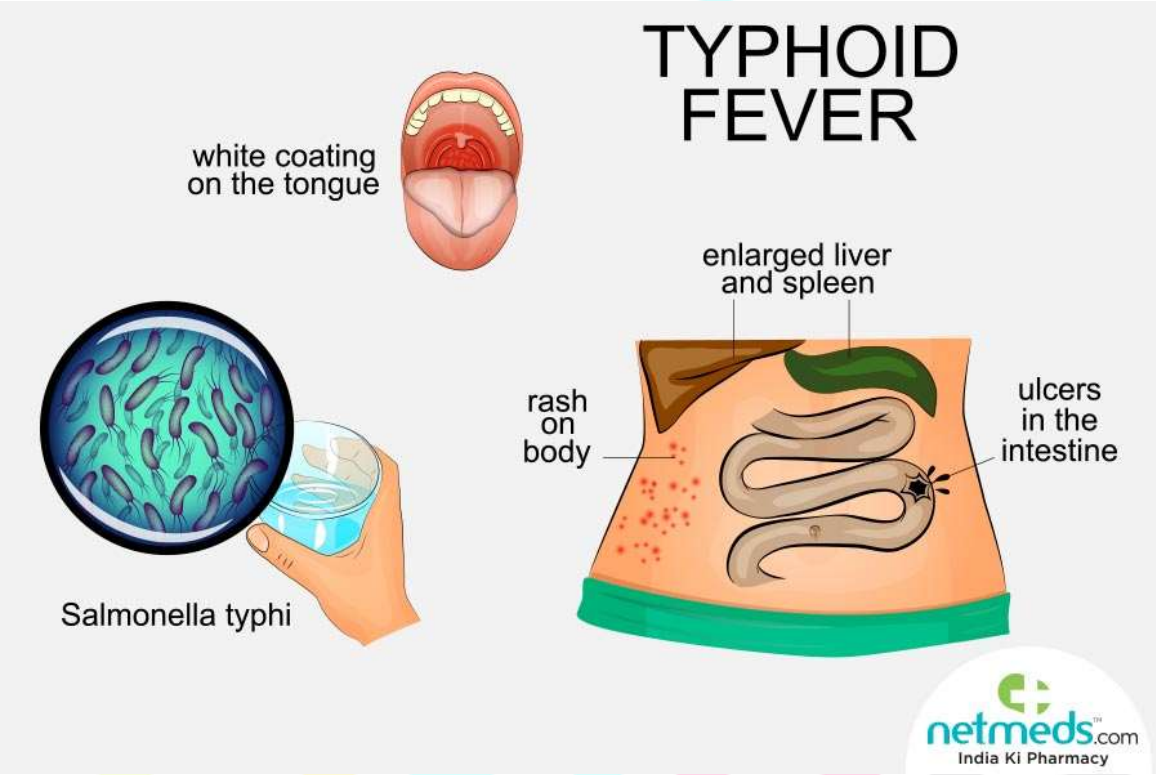

Figure 4. Sign & Symptoms [14]

Diagnosis

A positive culture from the blood or another anatomical site is used to diagnose typhoid fever. Blood cultures are positive in 40-60% of patients who are examined early in the disease's course, and stool and urine cultures are positive after the first week. During the incubation phase, the stool culture result is occasionally positive. However, in many regions of the developing world, the sensitivity of blood cultures in diagnosing typhoid fever is limited, as frequent antibiotic prescribing may make bacteriological confirmation problematic. While bone marrow cultures can help with bacteriological proof of typhoid, they are difficult to obtain and relatively intrusive. The advent of sensitive nested PCR diagnostic techniques in recent years has made it possible to diagnose typhoid fever with more sensitivity than blood cultures, raising issues about whether blood cultures can be considered the "gold-standard" for its diagnosis. [9]

Other laboratory tests aren't as specific. Although blood leukocyte counts are typically low in relation to fever and toxicity, there is a wide range of counts; leukocytosis is a common association in younger children and can vary from 20,000 to 25,000 cells per cubic millimeter. Thrombocytopenia is a sign of serious sickness and can occur in conjunction with disseminated intravascular coagulation. Despite the fact that liver function test results may be abnormal, severe hepatic impairment is uncommon. [9]

In endemic locations, the Widal test, which assesses antibodies against the O and H antigens of S. typhi, lacks sensitivity and specificity. Because many false-positive and false-negative results occur, the Widal test alone is prone to inaccuracy when diagnosing typhoid disease. Other, more recent diagnostic assays that use monoclonal antibodies to detect S. typhi-specific antigens in the serum or S. typhi Vi antigen in the urine have been developed. Only a few, however, have proven to be

sufficiently reliable in large-scale studies. Given the low amount of bacteremia in enteric fever, a nested polymerase chain reaction using H1-d primers was used to amplify specific S. typhi genes in the blood of patients; given the low level of bacteremia in enteric fever, it is a promising means of obtaining a quick diagnosis. Despite these advancements, clinical diagnosis of typhoid remains the gold standard in most developing countries, and numerous diagnostic algorithms have been tested in endemic areas. [9]

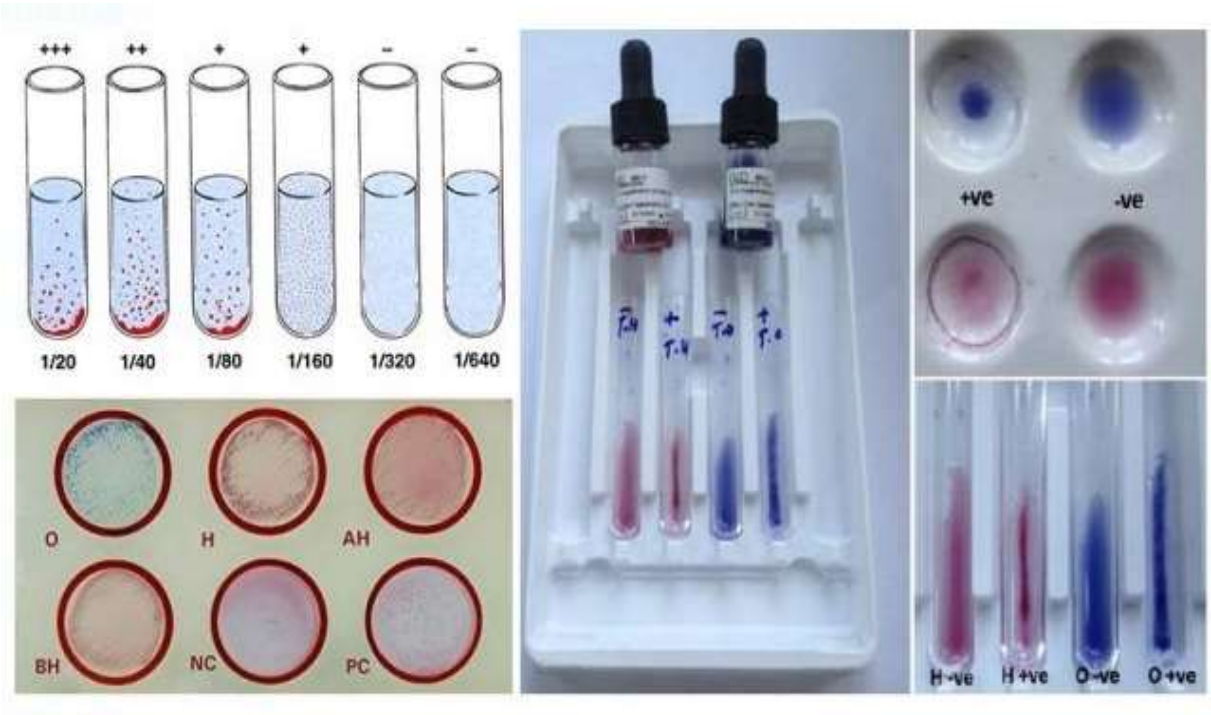

Figure 5. Widal Test [16]

Typhoid fever can mimic a variety of common febrile infections in endemic locations, with no distinguishing symptoms. Early stages of enteric fever in children with multisystem characteristics may be confused with other illnesses such as acute gastroenteritis, bronchitis, or bronchopneumonia. Malaria, sepsis with other bacterial pathogens, infections caused by intracellular microorganisms, such as tuberculosis, brucellosis, tularemia, leptospirosis, and rickettsial diseases, and viral infections, such as dengue fever, acute hepatitis, and infectious mononucleosis, are all included in the differential diagnosis. In developing nations, preliminary efforts are being made to create diagnostic techniques, such as a "fever stick," that could allow for the quick detection of a variety of febrile disorders. [9]

Treatment

More than 60 to 90 percent of typhoid fever cases in endemic disease areas are treated at home with antibiotics and bed rest. Effective antibiotics, appropriate nursing care, adequate nourishment, careful attention to fluid and electrolyte balance, and rapid diagnosis and treatment of problems are all essential for avoiding death in hospitalised patients. The fluoroquinolones are the most effective medications for treating typhoid fever, according to data. These medications have proven safe in all age groups and are quickly effective even with short courses of treatment in randomised, controlled trials including patients infected with quinolone-susceptible S. enterica serotype typhi (three to seven days). The average time it takes for a fever to go away is less than four days, and the cure rate is above 96 percent. Persistent faecal carriage or relapse affects less than 2% of treated patients. Fluoroquinolones are also associated with reduced rates of stool carriage than the usual first-line medicines (chloramphenicol and trimethoprim–sulfamethoxazole), according to the published data. [10]

Three key concerns about the use of fluoroquinolones in the treatment of typhoid fever have been raised: the potential for harmful consequences in children, the cost, and the evolution of resistance. Fluoroquinolones harmed the articular cartilage of juvenile beagles in preclinical testing. Long-term use of fluoroquinolones in children with cystic fibrosis, as well as short-term use of fluoroquinolones to treat typhoid fever and fluoroquinolones or nalidixic acid to treat bacillary dysentery in children, have all produced reassuring results. There has been no evidence of bone or joint toxicity, tendon rupture, or growth impairment in long-term follow-up. The manufacture of generic fluoroquinolones in Asia has significantly decreased the price. The evolution of quinolone resistance in countries where these medications are inexpensive and widely available, on the other hand, is likely to be the most significant constraint to their usage. Fortunately, complete resistance to fluoroquinolones is still uncommon. [10]

Fluoroquinolones are the current therapy of choice for all age groups in places where quinolone-resistant strains are infrequent. Short treatment courses (three to five days) are particularly effective at containing outbreaks. Patients with quinolone-resistant S. enterica serotype typhi infection who are treated for fewer than seven days had a higher rate of treatment failure than those who are treated for longer periods. In 90 to 95 percent of patients with resistant infections, treatment at the maximum prescribed doses (e.g., 20 mg of ofloxacin per kilogramme of body weight per day) for 7 to 10 days was successful. The time it takes for a fever to resolve (on average seven days) is protracted, and the rate of faecal carriage during convalescence might be as high as 20%.

(unpublished data). Fluoroquinolones should be given at the highest dose practicable for at least 10 to 14 days, and patients should be closely monitored to see if they have S. enterica serotype typhi in their faeces. Unfortunately, quinolone-resistant bacteria are frequently multidrug-resistant, limiting the treatment options to azithromycin or the more expensive cephalosporins. [10]

Typhoid is also treated with third-generation cephalosporins (ceftriaxone, cefixime, cefotaxime, and cefoperazone) and azithromycin. Fever clearance times averaged one week in randomised, controlled studies with third-generation cephalosporins, primarily ceftriaxone and cefixime, with treatment failure rates of 5 to 10%. Relapse rates were from 3 to 6 percent, with fecal-carriage rates of less than 3%. A cure rate of 95% was observed after five to seven days of azithromycin treatment. The fever went away in four to six days, and recurrence and convalescent faecal carriage were both less than 3%. Aztreonam and imipenem are two medications that could be used as a third-line treatment. [10]

In places of the world where the bacterium is still fully responsive to these medications and fluoroquinolones are not available or affordable, chloramphenicol, amoxicillin, and trimethoprim–sulfamethoxazole are still effective treatments for typhoid fever. These medications are low-cost, widely available, and have little side effects. They relieve symptoms, with defervescence usually happening within five to seven days; nevertheless, medication is required for two to three weeks, and adherence to a four-times-daily regimen during this time may be low. During a period of treatment, an adult may need to take more than 250 capsules of chloramphenicol. Although the cure rate is around 95%, the relapse rate is between 1 and 7%, and the rate of convalescent excretion is between 2 and 10%. [10]

There are limited studies on the treatment of typhoid in pregnant women. Beta-lactam antibiotics are thought to be safe. In addition, there have been several case reports of fluoroquinolones being used successfully. Despite the fact that these medications have been avoided in the past due to safety concerns, the general agreement is that they are likewise safe. [10]

The majority of the data from randomised, controlled trials comes from patients who were treated in disease-endemic areas. There are scant data from such treatment trials in patients who live in non-endemic areas or who are returning travellers. When deciding which antibiotic to employ, knowing the antibiotic susceptibility of the infecting strain is critical. If no culture is available, knowing the likelihood of sensitivity based on worldwide statistics may be informative. [10]

Ayurvedic Treatment

Langhana

Langhana is the most common jwara therapy. The word langhana usually refers to upavasa (fasting), which results in apatarpana (reduced nourishment of the body). The therapy tries to bring the body's dhatus and doshas into harmony, resulting in a sense of lightness.

Nirahaar (total abstinence from food) and phalahara (moderate abstinence from food) are the two types of fasting (eating only fruits). The fasting method is determined by the person's prakriti (constitution). The phalahara approach is better for a vata prakriti person, whereas the nirahaar fasting method is better for a pitta or kapha prakriti person. Fasting aggravates vata and agni (digestive fire), resulting in a catabolic state that aids in balancing the vitiated doshas in the body. This alleviates the accumulated kapha and malas, which are the root causes of typhoid fever. Other than typhoid, atisaar (diarrhoea), visuchika (cholera), vibhanda (constipation), alasaka (flatulence), chardi (vomiting), and other disorders are treated with langhana. Hemanta and Shishir, according to Charaka, are the greatest seasons for performing langhana (winter months). Langhana is not recommended for persons whose primary prakriti is vata. [19]

Typhoid ayurvedic herbs and medications

Typhoid Ayurvedic Herbs

- **Bilwaphal (golden apple):**
  Bilwaphal is a herb with astringent, nourishing, and aphrodisiac effects. It is a digestive stimulant because it promotes agni. Constipation, indigestion, and dysentery are all conditions that the herb can help with. When given early on, it can also assist to prevent typhoid fever. Bilwaphal is found in a variety of forms, including chyawanprash, as well as capsules and syrups. [19]

- **Jatamansi (muskroot):**
  Jatamansi possesses digestive, carminative, and aromatic effects. Flatulence, jaundice, stomach diseases, and typhoid are all treated with this herb. It also cleans the blood of contaminants. You can take jatamansi as a powder or as an infusion. [19]

- **Haritaki (chebulic myrobalan):**
  Haritaki is a herb that might help you feel refreshed. It works as a laxative, expectorant (removes phlegm), and body tonic. It aids in the treatment of a variety of ailments such as anaemia, jaundice, and fever. [19]

- **Guduchi:**
  Guduchi is a Sanskrit word that means "who guards the entire body." Many useful components, including as glycosides, alkaloids, and steroids, are abundant in the plant. For long years, it has been used in India's Ayurvedic and traditional medicinal systems. Guduchi is dahanashaka (cure for burning sensations), jwarahara (reduces fever), and mehanashaka, according to Ayurveda (cures metabolic syndromes). Guduchi is used to treat a variety of ailments, including diarrhoea and a variety of fevers, including periodic fever. [19]

Other Ayurvedic Medicines

- **Sitopaladi churna (powder):**
  1. Sitopaladi churna is thought to be the most effective treatment for flu and fever. Ela (cardamom), mishri (rock sugar), twak (cinnamon), vanshlochan (white-colored formations in bamboos), and pippali are used to make Sitopaladi churna (long pepper).
  2. Half a teaspoon of sitopaladi churna, mixed with warm water, is given to people with typhoid fever. [19]

- **Sudarshan churna :**
  1. Sudarshan churna is made up of 48 different herbs. Chirayata is the principal herb in the churna (bitterstick). This Ayurvedic medicine is known for curing all forms of fevers and was named after Lord Vishnu's sudarshan chakra, which can be seen on his index finger.
  2. Sudarshan ghana vati, a concentrated form of the drug accessible as a vati, is another option for this herbal mixture (tablet) [19]

- **Tribhuvankirti rasa :**
  1. Tribhuvankirti rasa is a herbal-mineral combination that is often used to cure fevers. Pippali (long pepper), maricha (pepper), shunthi (dry ginger), bhasma (borax), shuddha hingula (cinnabar), and other herbs make up this combination. Aqueous extracts of adrak (ginger), tulsi (holy basil), and dhattura (devil's snare) are combined with these herbs.
  2. Tribhuvankirti rasa has antipyretic (fever-reducing) and analgesic (pain-relieving) properties, as well as inducing perspiration in the body. [19]

- **Sanjivani vati :**
  1. Triphala (a blend of amalaki [Indian gooseberry], vibhitaki [belleric myrobalan], and haritaki), shunthi, vatsanabha (Indian aconite), guduchi, yastimadhu (mulethi), and bhallataka are among the plants found in Sanjivani vati (Indian nut tree). Aconite, which possesses fever-reducing qualities, is one of the vatsanabha's components.
  2. In the treatment of typhoid fever, sanjivani vati is combined with patoladi kashaya, kiratadisapta kashaya, and sudarshan ghana vati. Rashes, stomach disturbances, and fever are the main signs of typhoid, and this medicine's properties are aimed at lowering them. [19]

- **Kiratadisapta kashaya**
  1. Kiratadisapta kashaya is a herbal decoction created by boiling 20 g of the herbal mixture in 80 mL water and then reducing the liquid to 20 mL.
  2. The herb employed in this treatment, kiratatikta, has antipyretic, antihelminthic (kills parasitic worms), and hypoglycaemic (lowers blood sugar) characteristics that assist to relieve fever and strengthen the stomach. [19]

Vaccine

In the United States, there are two types of typhoid vaccine: an oral live-attenuated strain of Salmonella Typhi (Ty21a) and a Vi capsular polysaccharide vaccine (ViCPS). After a primary series, the two vaccinations provide protection of between 33% and 80%. Travelers travelling places where there is a higher risk of exposure to Salmonella enterica serotype Typhi should get a typhoid vaccine, according to the CDC. Typhoid vaccines are recommended for tourists who will be exposed to contaminated food and drinks in underdeveloped countries for an extended period of time, individuals who will be exposed to typhoid carriers for an extended period of time, and laboratory professionals who work with Salmonella Typhi. [11]

Figure 6. Typhoid Vaccine [15]

The oral vaccine comes in the form of an enteric-coated capsule that should be taken with cool beverage about 1 hour before a meal on alternate days. Refrigerate the four prescribed dosages until they're needed. Although the manufacturer recommends a fresh complete series every 5 years, there is insufficient data to make recommendations about the need for boosters with the oral vaccine. A single 0.5-mL dose of ViCPS is suggested. Every two years, boosters are suggested. Ty21a vaccination is not recommended for children under the age of six. The ViCPS is indicated for people aged 2 and up. Parenteral Vi vaccinations are generally well tolerated, according to evidence from trials and postmarketing investigations. In a manufacturer-funded postmarketing safety study done in 11 US travel clinics, injection site pain (77 percent), soreness (75 percent), and muscular pains were the most prevalent symptoms (39 percent). In less than 6% of recipients, the Ty21a and ViCPS vaccinations produce fever and headache. Abdominal discomfort, nausea, and vomiting are some of the most common side effects of the oral preparation. In 7% of recipients, local responses to the ViCPS have been reported. Immunocompromised people, particularly those with HIV infection, should not get the oral vaccine. If you're taking antibiotics, you shouldn't use Ty21a until at least 72 hours have passed since your last dose. [11]

Prevention

Typhoid fever is widespread in areas where sanitation is inadequate and there is no safe drinking water. Typhoid fever can be prevented by access to safe water and proper sanitation, as well as food handler hygiene and typhoid vaccine. [12]

For many years, two vaccinations have been used to protect people from typhoid fever:

- an injectable vaccine for people above the age of two years based on purified antigen
- For people over the age of 5, a live attenuated oral vaccine in capsule form is available.

These vaccines do not give long-term protection and are not recommended for children under the age of two.

In December 2017, WHO prequalified a novel typhoid conjugate vaccine with longer-lasting protection for use in infants as young as six months.

Typhoid fever is a danger for all visitors to endemic areas, however the risk is normally low in tourist and business centres with good standards of housing, sanitation, and food cleanliness. Travelers to areas where typhoid fever is a high risk should be administered typhoid fever immunisation. [12]

Figure7. Preventions Of TyphoidFever[17]

The following tips will assist you in staying safe when travelling:

- Ascertain that the dish has been properly cooked and is still hot when it is presented.
- Raw milk and raw milk-based products should be avoided. Milk should only be consumed after it has been pasteurised or boiled.
- Ice should only be consumed if it is made from safe water.
- If the safety of your drinking water is in doubt, boil it or, if that isn't possible, disinfect it using a dependable, slow-release disinfectant (usually available at pharmacies).
- Hands should be washed thoroughly and regularly with soap, especially after contact with pets or farm animals, or after using the restroom.
- Wash fruits and vegetables thoroughly, especially if they are to be consumed raw. Vegetables and fruits should be peeled if at all possible.[12]

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