Typhoid Fever

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Key points:

- Introduction
- Transmission and Risk Factors
- Causes and Symptoms
- Diagnosis
- Treatment via Vaccine and Antibiotics
- Conclusion

Introduction

Typhoid fever is a systemic febrile illness resulting from infection with the gram-negative bacterium Salmonella enterica serovar Typhi (S. Typhi). Other serovars of S. enterica are also clinically significant; S. Paratyphi causes paratyphoid fever, whereas non-typhoidal serovars—particularly Enteritidis, Typhimurium, and Dublin—are major causes of invasive non-typhoidal salmonellosis.[1] Typhoid fever is an acute systemic febrile illness that usually persists for about three to five weeks.[12] The Global Burden of Disease Study estimated that, in 2021, there were over seven million cases of typhoid fever worldwide, resulting in more than 93,000 deaths.[13]

Transmission

Typhoid fever primarily occurs through the fecal-oral route, most often as a result of ingesting contaminated food or water.[1] The transmission of S. Typhi occurs predominantly via the gastrointestinal tract, commonly through the ingestion of food or water contaminated with the feces or urine of infected individuals or asymptomatic carriers.[9] Two principal pathways are involved in S. Typhi transmission: the short-cycle and the long-cycle routes. The short-cycle pathway entails direct contamination of food and water by bacteria shed from temporary or chronic carriers, often facilitated by inadequate hygiene and poor sanitation, particularly during food handling. In contrast, the long-cycle pathway occurs when human feces contaminate unsafe or untreated water sources or when untreated fecal matter is used as fertilizer for agricultural crops.[9]

Risk Factors

The risk of infection has been associated with factors such as contact with contaminated water, improper waste disposal, poor hygiene practices, and living in overcrowded urban slum areas.[1] Additional risk factors include those related to water, sanitation, and hygiene. Waterborne transmission accounted for 41.3% (45/109), while sanitation and hygiene practices contributed 31.2% (34/109). Other factors included travel-related risks at 17.4% (19/109), antimicrobial use at 12.8% (14/109), climate-related influences at 13.8% (15/109), environmental factors at 8.3% (9/109), typhoid carriers at 10.1% (11/109), and host-related factors at 5.5% (6/109).[2] Risk factors also included contact with contaminated water, contact with typhoid carriers or infected individuals, inadequate hand hygiene, lack of vaccination, hot climatic conditions, and the presence of mechanical vectors. Control

efforts were further challenged by increasing antimicrobial resistance, limited data availability, and constraints related to vaccines.[3]

Cause

Typhoid fever is a systemic febrile disease caused by the gram-negative bacterium Salmonella enterica serovar Typhi (S. Typhi).[1]

Symptoms

Typhoid fever is an acute infection of the small intestine characterized by prolonged fever lasting more than a week, often accompanied by gastrointestinal disturbances and, in severe cases, a decreased level of consciousness.[4] Most patients presenting to general hospitals and public health centers exhibit symptoms of typhoid fever, such as headache, fever, nausea, diarrhea, a progressively increasing temperature that may exceed 40°C (104°F), excessive sweating, and gastroenteritis.[5] Liver function abnormalities are commonly associated with enteric fever; therefore, it should be considered in the differential diagnosis of patients presenting with fever and jaundice.[6] Active gastric ulceration has been reported in patients with enteric fever; therefore, the possibility of upper and lower gastrointestinal bleeding should be considered, particularly in cases associated with relapsing bacteremia.[7]

Diagnosis

For a definitive diagnosis of typhoid fever, the World Health Organization (WHO) recommends isolation of the causative bacterium from blood or bone marrow samples.[8] Additional diagnostic investigations for typhoid fever include stool and urine cultures, along with other relevant laboratory tests.[8] Molecular techniques, such as polymerase chain reaction (PCR), can be employed for the detection of antibiotic-resistant strains of Salmonella Typhi.[8]

Treatment

Three licensed vaccines are currently available for the prevention of typhoid fever: typhoid conjugate vaccines (TCVs), the live attenuated oral Ty21a vaccine, and the Vi capsular polysaccharide (Vi-CPS) vaccine. The uptake of Ty21a and Vi-CPS vaccines has been limited due to factors such as multidose administration schedules, relatively short durations of protection, and constrained financial support from Gavi. Unlike these earlier vaccines, TCVs address several of these limitations and provide important immunological and programmatic advantages. Notably, TCVs are suitable for administration in children younger than two years of age, enabling their incorporation into routine childhood immunization programs. In contrast, both the Ty21a and Vi-CPS vaccines are not recommended for this age group. The Vi-CPS vaccine is indicated for children aged two years and older because of its low immunogenicity in younger children. Similarly, the oral Ty21a vaccine is recommended only for children aged five years and above due to reduced tolerability and limited immunogenic response in younger age groups. TCVs can be administered from infancy because the Vi polysaccharide antigen is conjugated to a carrier protein, which induces a T-cell-dependent immune response and results in enhanced immunogenicity and immunological memory in young children.[9]

Third-generation antibiotics such as cephalosporins are commonly utilized as second-line therapeutic agents in the management of typhoid fever. Among this class, ceftriaxone and cefixime are the most frequently used agents, with ceftriaxone considered the most cost-effective option.[10] Due to the widespread emergence of resistance to traditional first-line antimicrobials, the World Health Organization (WHO) currently recommends the use of azithromycin, ciprofloxacin, or ceftriaxone for the treatment of typhoid fever.[11]

Conclusion

Typhoid fever is a common infectious disease in many countries. It can be caused by poor hygienic

conditions, including contaminated food and water. Maintaining good personal hygiene, ensuring access to safe drinking water, and practicing proper sanitation are essential for preventing the disease. Once typhoid fever is diagnosed, prompt treatment should be initiated to prevent serious complications, as the disease can become life-threatening if left untreated.

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