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Editorial

Typhoid Fever

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Abstract:

Typhoid fever constitutes a major global health problem, with an estimated 21.7 million cases and 200,000 deaths annually. Typhoid fever is a significant contributor to infectious disease mortality and morbidity in low- and middle-income countries, particularly in South Asia. Enteric fever like typhoid showed the highest morbidity in Asia with approximately 93 % of global episodes has been contributed by this region. Poor hygiene, poor sanitation and sewerage system, over population are the key contributing factors.

Keyboard: typhoid, Salmonella typhi, Fever, Epidemiology

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Introduction:

Typhoid Fever

Enteric fever, caused by the bacterium *Salmonella enterica* serovars Typhi and Paratyphi, has a long history and impact on human lives.

Historical records teach us a great deal about typhoid fever—the high disease burden and deadly consequences of the disease; the major routes of transmission; and the potential impact of vaccines.

As early as 430 BC , a pernicious plague annihilated half the population of Athens, bringing to an end the "Golden Age of Athens," and is now believed to have been typhoid fever based on DNA examination of dental pulp.

With increasing antimicrobial resistance, commonly used treatments are less effective and risks increase for complications and hospitalizations.[1,2]

Salmonella Typhi

Global disease burden estimates of *Salmonella enterica* serovar Typhi range between 19.1 and 20.6 million cases and 200000 and 600000 deaths annually. Approximately 90% of these deaths occur in

Asia. In South Asia, it is estimated that 23% of the population (approximately 400 million persons) lives in high-risk conditions for waterborne diseases.

While the primary source of *S.* Typhi infection is through contaminated food and water, a number of factors contribute to disease burden in endemic settings. These factors include poor sanitation, contact with carriers, living near bodies of stagnant water, climatic conditions, and socioeconomic contexts (eg, literacy rates, food and water consumption patterns).[3, 4]

Typhoid fever is a systemic disease caused by *Salmonella enterica* serovar Typhi, a Gram-negative bacterium. Humans are the only host, and transmission most commonly occurs through ingestion of water or food contaminated by feces from an acutely ill or convalescent patient or an asymptomatic carrier. The incubation period is usually 1 to 2 weeks but can range from 3 to 60 days. The illness presents with sustained fever and a constellation of other symptoms including dry cough, fatigue, abdominal pain, diarrhea, and constipation. Case fatality ratios range between 10 and 30% if untreated but fall to 1–4% with appropriate and timely antimicrobial treatment. [4, 5]

The gold standard laboratory diagnosis of typhoid fever requires isolation of *S.*. Typhi from blood, stool, bone marrow, or other tissue or bodily fluid by bacterial culture. Other tests with moderate sensitivity and specificity include the Widal test and TUBEX® TF test which involve detection of antibodies against *S.* Typhi antigens. Typhoid fever is a major cause of mortality and morbidity worldwide. In endemic areas, the disease is most commonly found in children 5–19 years of age.

International visitors from non-endemic areas are also at risk if unvaccinated. The global burden of the disease in low- and middle-income countries in 2010 was estimated to be 11.9 million cases, including 129,000 fatalities, after adjusting for water-related risk factors.[5, 6]

Antimicrobial Resistance

Multidrug resistance to first-line agents including ampicillin, trimethoprim-sulfamethoxazole, and chloramphenicol has been followed by reported resistance to fluoroquinolones.

Antimicrobial resistance has decreased typhoid fever treatment efficacy and increased treatment cost and risk of complications. Hospitalization for typhoid fever occurs in 10%–40% of cases. Complications including gastrointestinal bleeding and intestinal perforation occur in 1%–4% of cases. [7]

Prevention of Typhoid Fever

Prevention of typhoid fever requires improved water and sanitation infrastructure in endemic regions, ongoing surveillance, early identification of cases through blood culture and other reliable technologies, and health education and community outreach programs. And also excluding disease carriers from handling food. In addition, the World Health Organization has advocated for the vaccination of high-risk population groups in endemic settings and the use of vaccines to control outbreaks.[8, 9,10]

Epidemiology:

Typhoid and paratyphoid fever are enteric infections caused by the bacteria *Salmonella enterica* serovar Typhi (*S.* Typhi) and Paratyphi A, B, and C (*S.* Paratyphi A, B, and C), respectively, collectively referred to as typhoidal *Salmonella*, and the causes of enteric fever. Humans are the only reservoir for *Salmonella* Typhi with disease transmission occurring via the fecal–oral route, usually through the consumption of food or water contaminated by human feces. An estimated 17 million cases of typhoid and paratyphoid fever illnesses occurred globally in 2015, mostly in South Asia, Southeast Asia, and sub-Saharan Africa, with both the largest burden and incidence occurring in South Asia (Figure 1).

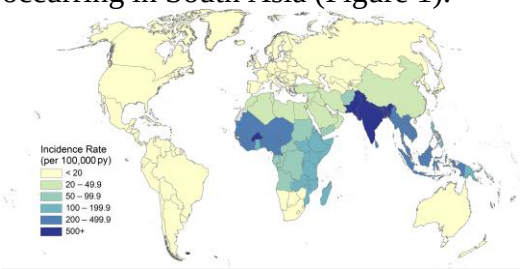

Fig 1.*Estimated incidence of typhoid and paratyphoid fevers by country per 100,000 population, 2015.*

Although considerable literature exists on typhoid fever incidence, most endemic countries do not have well-established population-based national surveillance systems for typhoid fever. In addition, some countries that use passive surveillance use clinical diagnoses with limited ability to confirm typhoid fever cases by blood culture. Although improvements in water, sanitation infrastructure, and public health measures have led to the virtual disappearance of typhoid fever transmission within the developed world, residual cases largely occur in travelers returning from countries where typhoid fever remains endemic. Knowledge of local disease burden, risk factors for acquisition, transmission characteristics, and implemented control measures are essential in developing strategies for prioritized and optimally targeted typhoid and paratyphoid fever control, and elimination.[10, 11,12]

Typhoid Toxin

Salmonella Typhi is the cause of typhoid fever, a major global health concern. An essential virulence factor of this pathogen is typhoid toxin. Unlike infections with most other *Salmonellae*, which result in self-limiting gastroenteritis, typhoid fever is a life-threatening systemic disease. Furthermore, in contrast to most *Salmonellae*, which can infect a broad range of hosts, *S.* Typhi is a strict human pathogen. The unique features of *S.* Typhi pathogenesis and its stringent host specificity have been a long-standing puzzle. The discovery of typhoid toxin not only has provided major insight into these questions but also has offered unique opportunities to develop novel therapeutic and prevention strategies to combat typhoid fever.[13]

In contrast to most AB-type toxins, typhoid toxin is exclusively expressed by intracellular bacteria. The regulatory networks that ensure this unique gene expression pattern are unknown. However, it is found that there is a regulatory mechanism that allows a bacterial pathogen to exclusively express a virulence factor when located within a specific intracellular compartment.[14, 15]

Vaccines for Typhoid Fever

Typhoid fever and paratyphoid fever continue to be important causes of illness and death, particularly among children and adolescents in south-central and Southeast Asia.A notable feature of typhoid is the carrier state – asymptomatically infected

individuals who continue to shed *Salmonella* Typhi in their stool or urine for many years, thereby sustaining transmission. Despite a recommendation by the World Health Organization in 2008 that typhoid vaccination be considered for the control of endemic disease and outbreaks, programmatic use remains limited. Typhoid vaccination is an important component of typhoid fever prevention and control, and is recommended for public health programmatic use in both endemic and outbreak settings. Two typhoid vaccines are widely available, Ty21a (oral) and Vi polysaccharide (parenteral). Newer typhoid conjugate vaccines are at varying stages of development and use. The World Health Organization has recently recommended a Vi tetanus toxoid (Vi-TT) conjugate vaccine, Typbar-TCV, as the preferred vaccine for all ages.[16,17]

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