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Typhoid Nephritis: Rare and Lethal Renal Manifestation of Widespread Infectious Disease

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Abstract

Typhoid fever is a widespread infectious illness, particularly in underdeveloped nations. It is unusual for typhoid fever to manifest as nephritis. Pyelonephritis and cystitis are the most frequent renal consequences of typhoid illness. Typhoid glomerulonephritis patients may also have hypertensive encephalopathy or nephritic syndrome upon presentation. Typhoid fever mortality rises to 20–30% when typhoid nephritis is present. Typhoid fever is a widespread infectious illness, particularly in underdeveloped nations. It is unusual for typhoid fever to manifest as nephritis. Pyelonephritis and cystitis are the most frequent renal consequences of typhoid illness. Typhoid glomerulonephritis patients may also have hypertensive encephalopathy or nephritic syndrome upon presentation. Typhoid fever mortality rises to 20–30% when typhoid nephritis is present.

Keywords

Typhoid glomerulonephritis, Typhoid fever, Nephritis, Acute renal failure

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1. Introduction

"Health burden estimates for a number of reasons, understanding the disease burden is important. First, it helps public health decision-makers by providing data on how the disease affects people's health and the local economy. Second, it helps resource managers by providing knowledge of local trends. Finally, it helps travelers by enabling them to make well-informed decisions." "Typhoid fever is defined as a symptomatic infection with the S Typhi bacteria. Global estimates for the burden of this disease are periodically published (26,9 million cases were reported in 2010)[1], and general fatality statistics are available from global and regional mortality studies (Figure 1).[2] However, there is still a lack of comprehensive local monitoring data from endemic areas. The material on typhoid fever in endemic areas of the world is updated in this piece as a follow-up to the previous seminar."

2. Typhoid Fever Diagnosis and Treatment

Typhoid fever's laboratory diagnosis is mostly based on the identification of organisms in blood by PCR (best suited to epidemiological surveys) or culture (sensitivity is still a problem, though). This is evident from recent studies of the diagnosis and treatment of typhoid fever[3,4.4-6] The Widal test for measuring antibody production is inaccurate, and modern serology assays like typhidot and tubex haven't shown to be trustworthy in Africa or Asia.[10,11] Typhoid-paratyphoid diagnostic assay[12], which locates IgA, is one novel test type that has promise. This technique uses ELISA11 to specifically identify circulating IgA for the diagnosis of typhoid fever and boosts sensitivity (to 100%) by isolating and incubating peripheral blood cells, which amplifies the signal.[13] Chloramphenicol is utilized in areas where susceptible strains are found in addition to fluoroquinolones, azithromycin, and third-generation cephalosporin medications as the primary forms of therapy (Panel 1).

2.1. S. Typhi's Genome

Despite the 90% genetic similarity between S entericaserovar Typhimurium and S Typhi, nothing is known about the genetic variations that explain S Typhi's capacity to induce enteric fever but not S Typhimurium's.[15] Large-scale transposon knockout libraries[16] enable scientists to analyze genome function and highlight variations between S Typhi and S Typhimurium.[17] Different regulatory networks and potential functional differences between the same genes in S Typhi and S Typhimurium may exist.[18] This innovative new technique may offer possibilities for the creation of vaccines and fresh antibacterial medications for S Typhi in areas where the disease is endemic. Two mouse studies for typhoid fever have been developed as a result of research into why S Typhi infects humans but not mice. One is based on mice that have received human haemopoietic stem cells[19], and the other is based on mice that have received bacterial flagella recognition cells with Toll-like receptor-11 knockouts.[20] The virulence gene gtgE, which is present in S Typhimurium but not in S Typhi and enables S Typhi to infect mice macrophages, has also been discovered as a result of research. These models, although they have not yet been confirmed, would make it feasible to investigate the etiology and immunology of this virus that only affects humans. The utilization of the humanized mouse model to explain the receptor-binding selectivity and delivery mechanisms for the typhoid toxin en-

coded by ctdB and pltA[21] and therefore to establish a possible new vaccination target highlights the significance of these novel models.

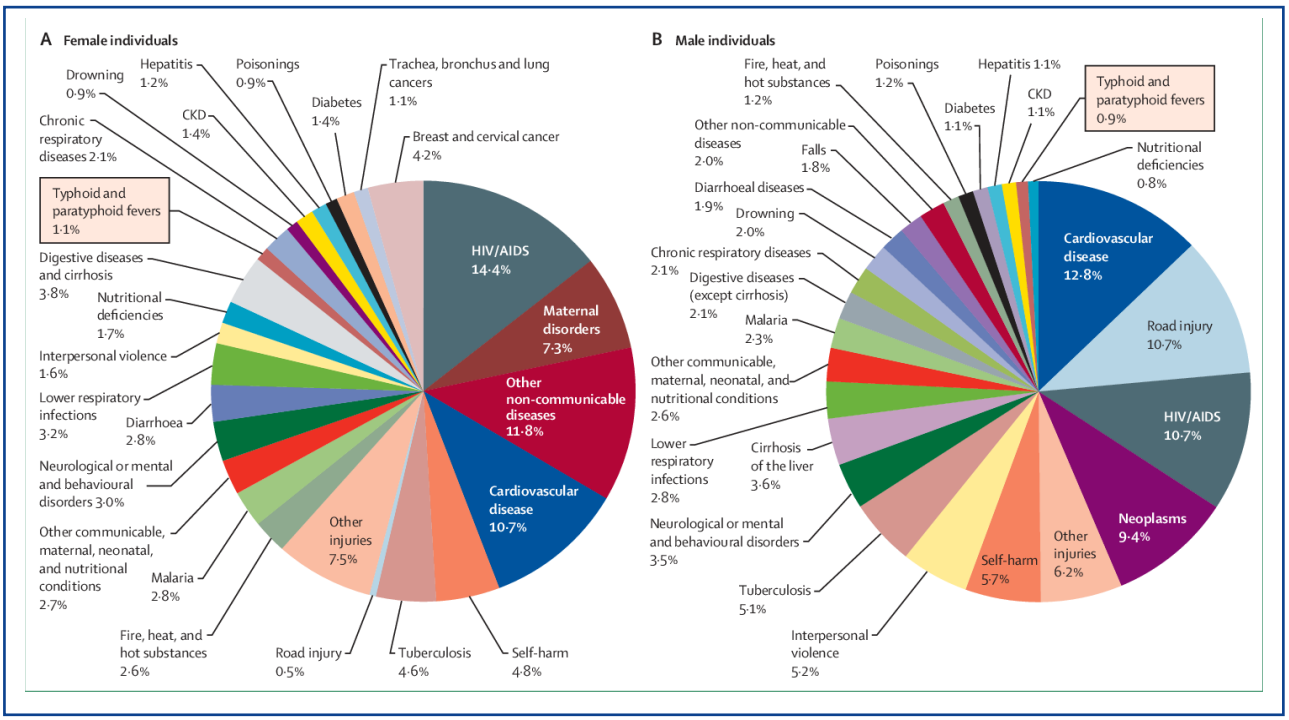

Figure 1. Mortality from enteric fever worldwide

Typhoid fever is thought to have sickened 26 million people (typhoid) and killed 190,000 people worldwide in 2010 due to enteric fever[2]. Economically underdeveloped countries, especially low-income ones in Asia and sub-Saharan Africa, where the majority of the population struggles to get clean water, adequate sanitation, and hygienic infrastructure, face the illness as a serious public health issue. Children under the age of 15 are often more vulnerable to the disease, possibly as a result of adults developing immunity to recurring infection and subclinical instances.

2.2. Contribution

2.2.1. Health Impact

The illness typhoid fever has the potential to be fatal. It causes high fever, severe headache, abdominal pain, and gastrointestinal symptoms such as diarrhea or constipation. In severe cases, it can lead to complications like intestinal perforation, internal bleeding, and organ failure. Typhoid contributes to morbidity and mortality rates, particularly in areas with limited access to clean water, sanitation facilities, and healthcare.

2.2.2. Economic Burden

Typhoid has a considerable economic impact on affected communities and countries. The disease can lead to prolonged hospitalization, increased healthcare costs, and loss of productivity due to illness or death. The financial burden extends to individuals, families, healthcare systems, and the overall economy, particularly in regions with a high prevalence of typhoid.

2.2.3. Impaired Quality of Life

Typhoid affects the quality of life of individuals and communities. The symptoms can be debilitating, causing physical discomfort and limiting daily activities. Additionally, the fear of contracting the disease and the need for preventive measures can impact social interactions and mental well-being.

2.2.4. Disease Transmission

Typhoid is a contagious disease that spreads through the fecal-oral route. Poor sanitation and hygiene practices, inadequate water treatment, and crowded living conditions contribute to its transmission. In communities with high typhoid prevalence, the bacterium can persist in the environment, leading to recurrent outbreaks and continued transmission.

2.2.5. Public Health Measures

The presence of typhoid highlights the need for public health interventions. Efforts to prevent and control the disease include improving access to clean water and sanitation facilities, promoting hygiene practices like handwashing, implementing vaccination campaigns, and enhancing surveillance systems to detect outbreaks. These interventions contribute to overall public health infrastructure development.

There is a dearth of information from research conducted in hospitals and communities in India. Only a few community-based studies and seven hospital-based studies in the past ten years have approximated the prevalence of typhoid fever, according to a comprehensive assessment of the literature on research on enteric fevers in India. In India's urban slums, a large-scale community survey found that the disease affects as many as 2/1000 children under the age of five and 5.1/1000 children under the age of ten per year[5]. According to comparable research from north India, the majority of cases affected children between the ages of 5 and 12 years old, with children under the age of 5 accounting for 24.8% of all cases[6]. Unfortunately, the effectiveness of preventative and control measures for enteric fevers has been reduced by the lack of estimates of the disease's burden at the national level.

3. Clinical Presentations

Abdominal discomfort and a high temperature are common symptoms of enteric fevers, with a high fever being the primary symptom at first. The typical incubation time is 1 to 14 days. Typhoid fever may be accompanied by a prodrome of vague symptoms including chills, a headache that won't go away, stomach pain, constipation, diarrhea, weakness, dizziness, nausea, and cough. Serious problems, including brain dysfunction, gut wall perforation, gastrointestinal hemorrhage, and shock, may result from delayed diagnosis or a patient's inability to react to therapy. The most frequent side effect of enteric fevers is terminal ideal perforation[1].

Re-infection only happens in cases when the first infection is treated with antibiotics early on in the process. Cell-mediated and humoral responses both work to protect against typhoid.7. Both serum and intestines produce antibodies in response to natural infection. If the bacilli that cause typhoid fever remain persistent in the environment and continue to offer ongoing low-level immunity, one assault may result in lifetime protection.

3.1. Diagnostics

3.1.1. The necessity of typhoid fever diagnosis and its function in prevention

Accurate and prompt diagnostics, which are frequently unavailable, accessible, and inexpensive in India, are the first step in treating any disease. Due to a lack of reliable and affordable quick diagnostic instruments, infrequent laboratory testing pro-

cedures, and inadequate illness-reporting systems, the exact prevalence of enteric fever sickness is still unknown in the majority of the world's nations. Typhoid fever clinical diagnosis, which is frequently erroneous, is preferred in endemic and resource-limited settings over diagnostic testing. The presence of other co-endemic acute febrile disorders makes the clinical diagnosis of typhoid challenging. A vital step in initiating suitable medicines is accurate laboratory diagnostics, which disclose the exact illness burden. It eliminates the possibility that needless therapy caused the problem with antimicrobial resistance to occur. Additionally, adequate diagnostics can determine the human natural history of infection and assess the effectiveness of the vaccination, which is a powerful disease control tool.

The assessment of disease burden is really hindered by the lack of diagnoses for enteric fevers. Despite improved and more continuous automated culture technologies, the gold standard for diagnosing typhoid fever remains the traditional blood culture, which has a poor sensitivity of 40–60%. With less specialized equipment and no scientific expertise, it is simple to carry out another frequently used serological Vidal test. The test performs poorly in terms of low sensitivity and specificity, and varied cut-off points employed by various laboratories in various locations sometimes make it difficult to interpret the results[9]. In addition, only one sample from the acute phase is used to start the treatment rather than samples from the convalescent period. The reliable but painful bone marrow culture test is dependent on laboratory resources and technical expertise, both of which are scarce in the majority of basic healthcare facilities in underdeveloped nations.

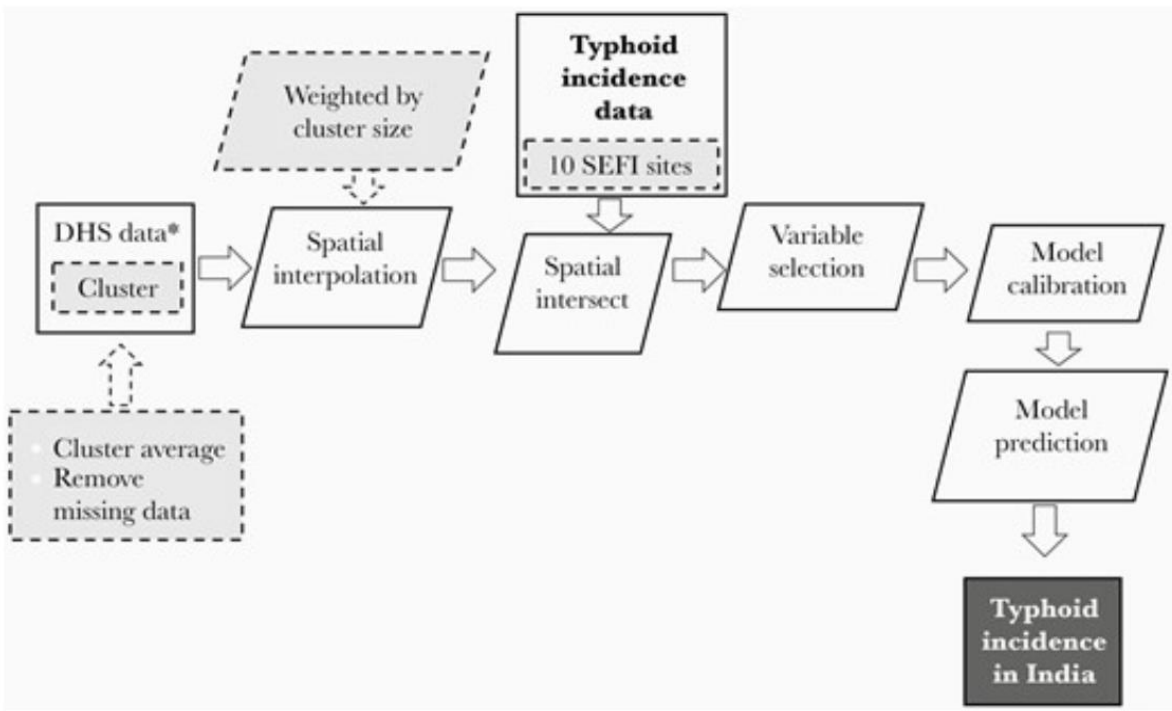

Figure 2. Summary of the study design for prediction of typhoid incidence in India.

3.1.2. India has practical difficulties with surveillance

It is clear that the current diagnostics platforms for enteric fevers have shortcomings in terms of sensitivity, time cycle, infrastructure need, etc.[12] This emphasizes the requirement for a precise and quick point-of-care (POC) diagnostic.

3.2. Test for paratyphoid typhoid (TPTest)

It recognizes immunoglobulin (Ig) IgA responses specific for Salmonella in the lymphocyte culture supernatant. Patients with suspected enteric fevers, patients with other diseases, and healthy controls are tested for typhoid paratyphoid (TPTest) in the three patient groups mentioned above. A simplified modified TPTest has been created that is perfect for use in developing-nation laboratories with sparse facilities and equipment.

Using time-of-flight mass spectrometry and gas chromatography: This two-dimensional test was run on plasma from S. Typhi- and S. Paratyphi A-infected patients and asymptomatic controls to look into metabolite signals linked to enteric fevers. This revealed 695 distinct metabolite peak locations. Highly significant metabolite profiles were used in conjunction with supervised pattern recognition to distinguish between the three groups. More precisely, a set of six metabolites served as systemic biomarkers that were serovar-specific and successfully identified the cause of the disease.

3.3. System for immunological cell capture (iMC2_)

The blood samples are maintained in broth medium for 6 to 8 hours in this locally created portable, completely automated device. The target cells are immunomagnetically enriched using the immunomagnetic cell capture (iMC2) apparatus. Two chambers make up the disposable capture chip of the apparatus. In the 5 ml sample compartment, pathogenic cells bind to antibody-coated magnetic nanoparticles and are transported by air to the 50-l recovery chamber. The detection of microorganisms is carried out using a lateral flow immunoassay. The test is more efficient and has good sensitivity and specificity.

A locally created test that uses S. Typhi's flagellin proteins is the strip-based typhoid fever diagnostic. These highly immunogenic flagellin monomers include a middle region that is serovar-specific. As a result, a collection of murine monoclonal antibodies (mAbs) was produced against this area. Leaving aside any cross-reactivity with other serovars, these mAbs demonstrated distinct specificity and strong affinity towards S. Typhi flagellin. The soluble form of the flagellin-bound mAbs on bacterial surfaces was suggestive of possibly better diagnostic.

3.4. India has practical difficulties with surveillance

Typhoid fever surveillance includes the early identification of patients, risk factors, and outbreaks. In addition, it envisions characterizing instances by genetic and serological methods to track variations in disease strains. Depending on the kind of monitoring, laboratory tests for illness documentation are necessary. In the event of hospital-based surveillance, for instance, blood cultures are advised. The preferred diagnosis, the self-limiting Vidal test, is accessible in outlying locations where there are no culture facilities. A vital component of any peripheral healthcare system should be laboratory support.

Despite the fact that India has carried out a variety of disease monitoring efforts, there are still a number of difficulties. First, only a small percentage of patients can precisely pinpoint the day when their fever started, which has an impact on the positive of typhoid diagnostic tests (mostly culture and Widal). Second, it takes time to report culture findings, and practitioners are limited in their ability to put off starting therapy. Since empirical therapy is the preferred approach, routine surveillance misses the positive typhoid cases. Additionally, diagnostic labs are few in rural and isolated places. Culture and other amenities are seldom available, even when they exist. Case detection may be hampered by laboratory staff that has received insufficient training. Other limitations, such as the seeming use of scarce financial resources for more high-prevalence diseases, restrict the need for further surveillance of underreported diseases like typhoid.

3.5. Water, sanitation and hygiene (WASH)

WASH initiatives were started as Sustainable Development Goals (SDG target 6)[23] in 1990. Basic water availability in India has grown from 80% in 2000 to 88 % in 2015, according to data from UNICEF on the WASH situation in that country. In 2014[23], 38% of people had access to basic sanitation. However, since its inception (in 2014), the Swachh Bharat Mission has contributed to a bettering of the condition in order to reach 95% coverage by 2019–24. Only 87.5% of people have access to facilities for washing their hands. Furthermore, there are still big differences between the country's urban and rural parts.

While better access to clean water and sanitation along with effective WASH practices are the cornerstones of typhoid management as well as other diarrheal illnesses, these demand extensive political commitment, long-term expenditures, and significant financial outlays. The majority of policymakers in developing nations use a comprehensive strategy that involves vaccination, combining a short-term remedy with long-term ones.

3.6. Resistance to Antibiotics in India

Despite the fact that adequate antibiotic medication is an efficient targeted treatment for enteric fevers, the frequency of antibiotic resistance is rising, which has an adverse effect on morbidity, mortality, and treatment costs.

3.6.1. Protocol for antibiotic treatment of enteric fevers

In accordance with WHO recommendations29, ciprofloxacin or ofloxacin is advised for completely sensitive typhoid infections; alternatively, chloramphenicol, amoxicillin, and co-trimoxazole are also advised. Resistance to antibiotics like ampicillin, trimethoprim-sulphamethoxazole, and chloramphenicol as well as resistance to fluoroquinolone medications have, however, also emerged as new types of drug resistance. It is necessary to utilize ciprofloxacin, ofloxacin, cefixime, azithromycin, or cefotaxime for MDR patients. It is advised to use azithromycin, rocephin, or cefotaxime in the event of quinolone resistance.

3.6.2. Multidrug resistance in Salmonella Typhi has emerged

Chloramphenicol resistance emerged in India in 1972, and by the 1990s, amoxicillin, co-trimoxazole, and chloramphenicol resistance had also emerged. The late 1990s saw the development of ciprofloxacin resistance30. As of right now, according to the National Treatment Guidelines for Antimicrobial Use in Infectious Diseases published by the National Center for Disease Control30, doctors recommend azithromycin or cefixime for straightforward cases and ceftriaxone for intravenous therapy. To prevent using last-line antibiotics in therapy, thorough monitoring, surveillance, and reporting of instances are essential due to growing resistance that increases illness severity, morbidity, and death.

3.7. From remain section we learn that

3.7.1. Cause

Salmonella enterica serotype Typhi is the bacterium that causes typhoid fever. It can be spread by tainted food or water or through intimate contact with an affected person.

3.7.2. Symptoms

High fever, headache, weakness, exhaustion, gastrointestinal discomfort, diarrhea, or constipation are all signs of typhoid fever, as is a rash with flat, rose-colored dots. Symptoms often show up one to three weeks following exposure.

3.7.3. Treatment

Typhoid fever is treated with antibiotics, which can usually cure the infection. However, some strains of the bacterium have become resistant to certain antibiotics, which can make treatment more difficult.

3.7.4. Prevention

The best way to prevent typhoid fever is to practice good hygiene and sanitation, including washing your hands frequently, drinking only clean water, and avoiding food and beverages from questionable sources. Additionally, tourists to regions where typhoid disease is prevalent can get vaccines.

3.8. Sign and Symptoms

Salmonella typhi, a bacterium, is the source of the bacterial illness known as typhoid fever. Typhoid symptoms can range in intensity and may appear gradually over days or weeks. Here are the common signs and symptoms of typhoid.

3.8.1. High Fever

A defining sign of typhoid is a persistent fever that can reach 103-104°F (39-40°C) in temperature.

3.8.2. Weakness and Fatigue

Feeling exhausted or tired, even with minimal activity, is common during typhoid fever.

3.8.3. Abdominal Pain

Pain and discomfort in the abdominal area, often around the belly button or on the right side, may be present.

3.8.4. Headache

Persistent and often severe headaches are a typical symptom of typhoid fever.

3.8.5. Loss of Appetite

A significant decrease in appetite, leading to weight loss, is commonly observed.

3.8.6. Diarrhea or Constipation

Some individuals may experience diarrhea, while others may have constipation or alternating episodes of both.

4. Conclusions and Future Scope

Typhoid fever is a serious disease that affects a large portion of India, with metropolitan areas having a greater frequency. This study endorses the Vi conjugate typhoid vaccine as a means of reducing the illness burden caused by typhoid fever in India.

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