

PREVALENCE AND CLINICAL PROFILE OF TYPHOID FEVER IN BANGLADESH

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ABSTRACT

Typhoid fever is an acute bacterial infection caused by the gram-negative bacterium *Salmonella enterica serotype Typhi* (*S. Typhi*). It is common in regions with poor sanitation and hygiene practices and is spread through contaminated food and water. Symptoms include a high fever, headache, abdominal pain, and diarrhea. Treatment typically involves antibiotics and supportive care to manage symptoms. Typhoid fever can be prevented through vaccinations, proper sanitation, and avoiding risky foods and water sources. However, the emergence of antibiotic-resistant strains of the bacteria poses a growing concern for global health. Whereas new serologic markers are effective in detecting typhoid fever, it is unclear whether or not they can be used to correctly predict incidence in the general population. This paper reviews the global prevalence and patterns of typhoid fever, including incidence rates and demographic trends, the major factors that contribute to the spread of typhoid, including hygiene, access to clean water, and sanitation, highlighting recent outbreaks and epidemics of typhoid that have occurred in Bangladesh. Their causes and implications are also discussed.

KEYWORDS: Typhoid Fever; Prevalence, *Salmonella Enterica*, Prevention, Treatment.

1 INTRODUCTION

Typhoid fever is a major global health concern, particularly in areas with poor sanitation and limited access to clean water. It is estimated that over 11 million people are affected by typhoid fever each year, with the majority of cases occurring in developing countries.^[1] In addition to the high number of cases, typhoid fever also has a significant impact on mortality rates.^[2] It is responsible for the deaths of approximately 128,000 people annually a staggering statistic given that the disease is both preventable and treatable particular concern is the emergence of drug-resistant strains of *Salmonella typhi*. This has made treatment significantly more difficult and has increased the risk of complications and death for infected individuals. It is estimated that up to 20% of typhoid fever cases are resistant to standard antibiotic treatment.^[3] The impact of typhoid fever is not just limited to health outcomes. The disease can also have economic implications, particularly in developing countries where it can lead to lost productivity and missed work. In addition, it can be a significant burden on healthcare systems, particularly in areas with limited resources. Despite these challenges, there have been some significant strides in addressing the global impact of typhoid fever.^[4] Vaccination campaigns have been successful in reducing the number of cases in some areas, and there are ongoing efforts to improve sanitation and hygiene practices in at-risk communities. However, much more needs to be done to address the ongoing

threat of typhoid fever and its impact on global health.

1.1 Serotypes of *Salmonella enterica*

Salmonella enterica is a species of gram-negative bacteria that is responsible for a multitude of illnesses and can cause food poisoning in humans and animals.^[5] Within this species, there are over 2,500 known serotypes of *Salmonella enterica*, each distinguished by the specific antigens on their bacterial surface and each with unique genetic characteristics and abilities to cause illness. The most common serotypes that cause human illness include *S. Typhimurium* and *S. Enteritidis*. These bacteria are found in the intestines and feces of infected animals and can contaminate food products. These strains are typically transmitted through contaminated food or water and can cause symptoms such as diarrhea, fever, and abdominal pain.^[6] In severe cases, *Salmonella* infection can lead to dehydration, sepsis, and even death. Due to the diversity of serotypes and their varying pathogenicity, identifying the specific strain of *Salmonella enterica* involved is important in preventing and controlling outbreaks.^[7]

1.2 Symptoms and treatment of *Salmonella* infection

Symptoms of *Salmonella* infection include diarrhea, fever, and abdominal cramps, and can last up to a week. Most people recover without treatment, but severe cases may require hospitalization and antibiotic therapy. Prevention measures include proper food handling and

preparation, including avoiding cross-contamination and using safe cooking temperatures to kill the bacteria. The *Salmonella enterica* strain responsible for typhoid disease has specialized in infecting people. In crowded and inadequately sanitary environments, this pathogen is a leading cause of febrile sickness and mortality. Travelers to endemic countries are also at risk of contracting a disease because of the prevalence of contaminated water and food sources there.^[8] In addition, healthy people can contract typhoid by the consumption of contaminated food and drink that has been shed by an infected person or an asymptomatic person who has not practiced proper hand hygiene.^[9] Symptoms normally appear 1 to 2 weeks after infection. Persistent fever, sometimes reaching 103-104 degrees Fahrenheit (39-40 degrees Celsius), is a common symptom of *Salmonella Typhi* infection.^[10] As the illness progresses, diarrhea and a loss of appetite may also set in other symptoms include headache, cough, excessive weariness, constipation, and a lack of appetite. If ignored, intestinal and neuropsychiatric problems can occur 6 weeks after infection.^[11]

1.3 Progress of Infection

As a contagious infection caused by the bacterium *Salmonella typhi*, typhoid fever is spread through the ingestion of contaminated food or water. The bacteria live in the intestines and bloodstream of infected individuals and are shed in their feces and urine. Transmission can occur in several ways. In areas with poor sanitation and hygiene practices, contaminated food and water can be easily and unknowingly consumed by people. Additionally, people who are carrying the bacteria but are not infected themselves known as carriers can spread it to others through close contact, such as preparing food for others. Once the bacterium is ingested, it makes its way to the digestive system and enters the bloodstream. From there, it can spread to various organs throughout the body, including the liver, spleen, and lymph nodes. Attaching to and then invading mucosal cells is the initial step in colonization for bacteria in the small intestine. After entering the lamina propria through microfold cells or enterocytes, they rapidly activate an influx of macrophages that eat the bacilli but do not typically kill them. Some bacteria and bacilli escape the macrophages in the small intestine lymphoid tissue and travel to the intestinal lymphoid follicles and the draining mesenteric lymph nodes before entering the thoracic duct and the rest of the body's circulation.^[12]

Symptoms typically begin to appear within one to three weeks after exposure and can include fever, headache, abdominal pain, constipation or diarrhea, and a rash. In severe cases, typhoid fever can lead to complications such as intestinal bleeding, perforation of the bowel, and organ failure.

1.4 Prevention of infection

Preventing the spread of typhoid fever involves

improving sanitation and hygiene practices and providing access to clean water and proper medical treatment. Vaccination is also a highly effective way to prevent infection. It is important for individuals traveling to areas with a high prevalence of typhoid to take precautions such as avoiding raw and undercooked food, drinking only bottled or boiled water, and washing their hands frequently.^[13] Generally, preventing *Salmonella enterica* infections is an important public health concern. The following steps can reduce the risk of infection. The first is to practice good hygiene. Proper hand washing and personal hygiene can significantly reduce the risk of *Salmonella* infections. The second is to cook food thoroughly. Cooking meat, poultry, and eggs to a safe temperature can kill any *Salmonella* bacteria present. The third is to avoid raw or undercooked foods. Raw or undercooked eggs, meat, and poultry can potentially harbor *Salmonella* bacteria. The fourth is to keep food refrigerated. *Salmonella* bacteria can grow rapidly at room temperature, so refrigerate perishable foods and leftovers promptly. The fifth is to wash fruits and vegetables thoroughly. Wash all fruits and vegetables before consumption to remove any bacteria on the surface. The sixth is to separate raw and cooked foods. To prevent cross-contamination, keep raw meat and poultry separate from cooked foods and use separate cutting boards and utensils. Finally, be aware of food recalls. Stay informed of any food recalls related to *Salmonella* contamination and avoid consuming any affected products. By following these simple measures, individuals can help reduce their risk of *Salmonella enterica* infections and promote overall public health.^[14]

1.5 The burden of typhoid fever in Bangladesh

Young children, especially those who are immune-compromised or are otherwise younger than five, are significantly more at risk than adults. Communities that lack access to safe food, water, and sanitation are also at risk.^[15] Typhoid outbreaks have been linked to multiple climate conditions, including higher rainfall, river levels and temperatures, especially in Bangladesh, which receives an average of 2,200 mm of rainfall per year. Drainage issues and incorrect wastewater drainage contribute to the contamination of shallow water sources, which are typically used during droughts and by people living in rural regions or slum. This places a tremendous burden on water, sanitation, and hygiene infrastructures. Furthermore, in densely populated nations like Bangladesh, where individuals are exposed to a single contaminated source, the rise of typhoid cases is aggravated. The incidence of intestinal infections was higher among children and young adults. Pakistani and Bangladeshi typhoid patients, on average, are just 7 years old. Together, Pakistan, India, and Bangladesh are responsible for 85% of all reported cases. Patients may be infected with anything from one thousand to one million *S. Enteric* serotype typhi germs.^[16] Most important of all, the emergence of co-epidemics due to the pandemic has added to the strain on an already overburdened healthcare system. More than 110,000

people have died from typhoid, according to the Global Burden of Disease research, and an estimated 9 million cases are reported annually.^[17] A total of 1,135 typhoid cases per 100,000 people were reported in 2021 highlighting the financial burden inflicted on healthcare systems.^[18] Further, healthcare providers are having trouble distinguishing between COVID-19 and typhoid because of the overlap in nonspecific symptoms between the two diseases, such as fever, exhaustion, and body pains. It has been noted that symptoms of COVID-19 and *Salmonella enterica* infections can be difficult to differentiate. Both illnesses involve fever, fatigue, and gastrointestinal symptoms such as diarrhea and nausea. However, while COVID-19 primarily affects the respiratory system, *Salmonella enterica* infection focuses on the digestive tract. In some cases, patients with *Salmonella enterica* infections may experience additional symptoms such as abdominal pain and vomiting. It is important to seek medical attention and undergo testing to determine the cause of these symptoms and ensure appropriate treatment.^[19]

1.6 Risk factors for typhoid fever

Typhoid fever is a serious and potentially life-threatening disease, and several factors can increase an individual's risk of contracting it. The following are some of the major risk factors associated with typhoid fever.^[20] The first is Poor sanitation: The bacteria that cause typhoid fever can spread through contaminated food and water. Poor sanitation practices, such as inadequate handwashing and improper disposal of waste, increase the risk of transmission. The second is traveling to high-risk areas. Typhoid fever is more common in developing countries with poor sanitation and limited access to clean water. Traveling to these areas can greatly increase an individual's risk of contracting the disease. The third is age. Children are at particular risk of contracting typhoid fever, as they may be more likely to consume contaminated food or water and may not yet have fully developed immune systems. The fourth is weakened immune systems. Individuals with weakened immune systems, such as those with HIV/AIDS or undergoing chemotherapy, may be more susceptible to typhoid fever. Other factors, such as close contact with infected individuals and occupation, are also risk factors for this disease. Close contact with someone who has typhoid

fever, such as caring for them or sharing food or drink, increases the risk of transmission, while certain occupations, such as healthcare workers or those working in food service, may have increased exposure to typhoid fever. Therefore, it is essential to take preventative measures to reduce the risk of contracting typhoid fever. These include practicing good hygiene, ensuring that food and water are properly prepared and sanitized, and getting vaccinated before traveling to high-risk areas. By understanding the risk factors associated with typhoid fever, individuals can take steps to protect themselves and others from this dangerous disease.^[21]

2 Incidence rates of typhoid fever and typhoidal *Salmonella*

Salmonella enterica is a common bacterial pathogen that can cause gastroenteritis and other infections in humans. The clinical infection rate for *Salmonella enterica* varies depending on factors such as the strain of the bacteria and the population affected. According to the Centers for Disease Control and Prevention (CDC), there were an estimated 1.35 million cases of *Salmonella enterica* infections in the United States in 2018, resulting in approximately 26,500 hospitalizations and 420 deaths. High-risk groups such as young children, elderly individuals, and individuals with weakened immune systems are more susceptible to severe infection. Overall, proper food safety and hygiene practices are critical in preventing *Salmonella enterica* infections and reducing the clinical infection rate.^[22]

2.1 Typhoid *Salmonella* Seroprevalence and age distribution estimates

Figures 1 and 2 show the state of Typhoid fever in four different countries, including Bangladesh, Nepal, Pakistan, and Ghana.^[12] Figures are given for children ages 2 to 4 so that the serological figures match the way clinical monitoring is done by age group. Crude clinical rate reflects culture-confirmed *S. Typho* and *S. Paratypho* A cases divided by the number of people in the sampling area and the amount of time. An adjusted incidence takes into account the fact that blood cultures are not always accurate and how many cases of acute feverish illnesses are caught by the monitoring system.

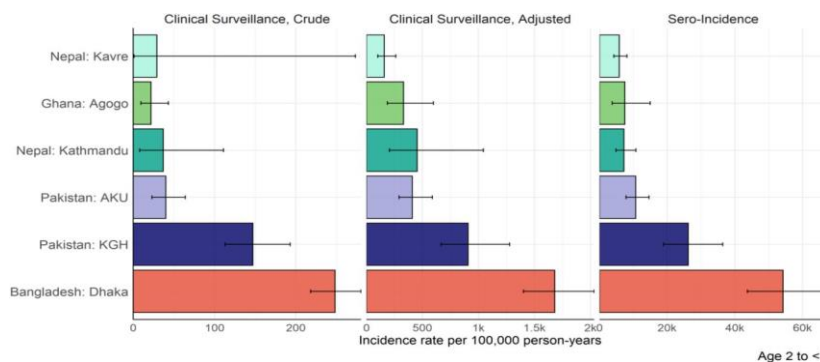


Figure 1 Clinical enteric fever incidence, including typhoidal *Salmonella* seroincidence, both unadjusted and adjusted in Bangladesh Dhaka. (Source: <https://www.medrxiv.org/content/10.1101/2021.10.20.21265277v2.full>)

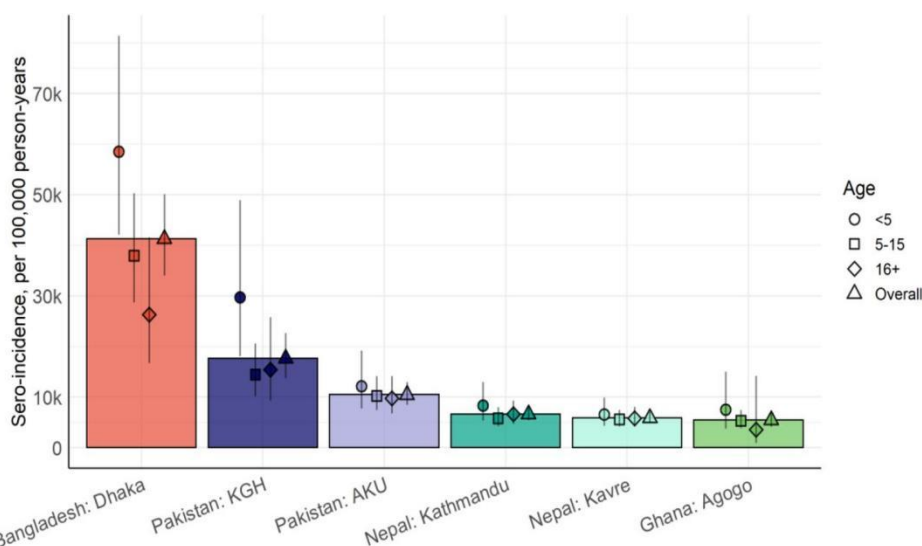


Figure 2 Typhoidal *Salmonella* sero-incidence rates estimated by study area and age group.

(Source: <https://www.medrxiv.org/content/10.1101/2021.10.20.21265277v2.full>)

(A dot shows the median for each age group, and the lines next to it show the 95% confidence ranges. The middle number from the population-based poll is shown by the height of the boxes.)

2.2 Clinical characteristics: significance of typhoid fever diagnosis

In poor nations, typhoid fever is one of the most typical febrile illnesses that doctors see. Fever and malaise appear at the beginning of bacteremia, which takes 7 to 14 days to develop. Patients often arrive at the end of the first week following the onset of symptoms and report fever, chills, and other symptoms resembling the flu, headache, malaise, and localized stomach pain in the case of anorexia, dry cough, and myalgia. Hepatomegaly, splenomegaly, a coated tongue, and a painful abdomen are frequent.^[23] The introduction of antibiotic therapy has caused a change in the traditional pattern of presentation. Nowadays, a slow and step-by-step rise in fever and toxicity is uncommon. The typhoid appearance may be unusual in regions where Schistosomiasis and malaria are predominant.^[24] It has been noted that even monoarthritis and polyarthritis appear. Typhoid manifests more dramatically in kids under the age of five, with increased incidence of complications and hospitalization. Infancy is also a time when diarrhea, toxicity, and consequences including disseminated intravascular coagulation are more prevalent. Miscarriage from typhoid fever during pregnancy is complex, however, antibiotic treatment has decreased the likelihood of this happening. Neonatal typhoid is a rare but serious and life-threatening illness that may result from vertical intrauterine transmission from an infected mother. 1% to 5% of patients develop long-term carriers who excrete the organism for longer than a year.^[25] Chronic carriage is more likely in older people, young women, and cholelithiasis patients. Schistosomiasis patients regularly expel their parasites. The common complication of typhoid fever included abdominal, hepatitis, cardiovascular, neuropsychiatric, bronchitis, pneumonia (*Salmonella enterica* serotype typhi, *Streptococcus pneumoniae*), respiratory, and others.^[26]

2.3 Sensitivity pattern of *Salmonella typhito* (*S. typhi*) to antibiotics

Salmonella enterica is a common bacterium that can cause foodborne illness in humans. Antibiotics are often used to treat infections caused by *Salmonella*, but the emergence of antibiotic-resistant strains has become a growing concern.^[27] In recent years, there have been reports of increased resistance to multiple antibiotics in clinical isolates of *Salmonella enterica*. This poses a significant challenge to the treatment of infections caused by this pathogen. The development of new antibiotics and the implementation of effective infection control measures are crucial in reducing the spread of antibiotic-resistant *Salmonella enterica* and improving clinical outcomes for infected individuals.^[28] Before the development of antibiotics, intestinal hemorrhage, and peritonitis were not common causes of death. Fever lasting more than a week and other mysterious illnesses accounted for the deaths of 15% of patients. Research conducted by the Department of Microbiology at Bangabandhu Sheikh Mujib Medical University (BSMMU) on antibiotic sensitivity in the population of Bangladesh. Culture sensitivity data of the Dept. of Microbiology of BSMMU showed 8.6% sensitivity to nalidixic acid, whereas ciprofloxacin is still 67% sensitive. Typhoid fever in both adults and children can be effectively treated with azithromycin at doses of 500 mg (10 mg/kg) once daily for 7 days. In adults, 5-day treatment was also proven to be efficient.^[29] Cefixime, demonstrated higher failure and relapse rates than fluoroquinolones in some trials. However, the BSMMU antibiotic sensitivity pattern demonstrated higher sensitivity of about 78.8%.^[30] Third-generation cephalosporins administered intravenously (Ceftriaxone, Cefixime, and Cefotaxime) are efficient with low recurrence (3% to 6%) and fecal carriage (3%) rates. Ceftriaxone is effective when taken orally once or twice daily in doses of 2-4 mg.^[31] Imipenem and aztreonam are

potential third-line medications as antimicrobial resistance spreads, fluoroquinolones, a class of first-line drugs, become less effective. Third-generation cephalosporins are more often employed now because of a decline in bacteria's resistance to ciprofloxacin and, more recently, fluoroquinolones. Ciprofloxacin is the most effective antibiotic, although it cannot be administered at standard dosages because of nalidixic acid resistance.^[32] Zithromax has shown efficacy in the treatment of fever in many regions of the globe, although research conducted in Bangladesh suggests that it has low sensitivity when used to treat fever.^[33] Ceftriaxone is quite effective, but it is essential to take all necessary measures while taking it to avoid potentially deadly adverse effects, such as hypersensitivity. There is growing awareness of cardiotoxicity as a possible adverse consequence. Ceftriaxone-resistant *Salmonella* strains are something to keep an eye out for because of the bacteria's ability to change its behavior in response to changed antibiotic use patterns over time. The testing of gatifloxacin sensitivity is essential. Antibiotic-resistant bacteria are more likely to develop when these drugs are used carelessly or in excess. Antibiotic usage should be directed by culture and sensitivity data, and antibiotics should no longer be sold over the counter if we're to avoid this nightmarish scenario.^[34]

2.4 Population-level incidence estimates

Despite wide variations in seroresponse curves from patient to patient, the median fitted peak antibody responses are similar across nations. Degradation occurs at different rates in different countries. Studies show that Bangladesh has one of the slowest rates while Ghana has one of the quickest. Two hypotheses are proposed to account for the discrepancy. The first is that regions with greater infection rates tend to have more occurrences of reinfection. Second, since sick people may be exposed to typhoid more often in areas with a greater frequency of the disease, secondary antibody responses may wane more gradually there. There is a severe lack of data on the temporal and geographical spread of typhoid. There has been some population-based research done in Dhaka, and although it has highlighted the high sickness burden, it has not addressed the geographical distribution of the individuals who are at risk.^[35]

2.5 Prediction of typhoid fever seroincidence

Prediction of typhoid fever seroincidence means forecasting or estimating the rate at which new cases of typhoid fever will occur in a population based on the presence of antibodies against the bacteria that causes typhoid fever in blood samples (seroincidence). It involves using statistical models and epidemiological data to predict the likely occurrence and spread of the disease over time. The goal is to help public health officials and healthcare providers prepare for and respond to potential outbreaks of typhoid fever. Immunoglobulin (IgG) responses to the Vi polysaccharide capsule have been employed in earlier typhoid seroepidemiological research. Even though anti-

Vi Immunoglobulin (IgG) had the lowest ratio of 28-day antibody responses among cases compared to population serosurvey participants and anti-HlyE IgG had the highest ratio, it showed that anti-Vi IgG had limited utility in distinguishing acute cases from earlier exposures. In addition, the study results corroborated those of prior research from Kathmandu that linked age not at all to serologic responses to Vi.^[36] Anti-Vi IgG responses rose with age, and this trend was seen in both the high and low-incidence groups, according to a study from Fiji.^[37] When added to vaccines as recommended by the World Health Organization (WHO), Vi will make it hard to discriminate between protection from a genuine ailment and that from a vaccine. All of these factors emphasize the importance of using additional antigens in enteric fever seroincidence estimation. Seroincidence estimates are considerably higher than population-based clinical incidence estimates for all catchment regions. When there are over 100 instances of clinical enteric fever per 100,000 person-years, it is called a "high" incidence. For all study locations, seroincidence is >4,000 per 100,000 person-years, with a rate ratio of 16-32 between seroincidence and clinical incidence. This coincides with the high proportion of asymptomatic and paucisymptomatic disorders seen in other infectious diseases.^[38]

2.6 Incidence of Typhoid fever caused by *S. paratyphi* A

Typhoid fever is caused by *S. paratyphi* A in 10%-20% of South Asians. Since *S. Paratyphi* A and *S. Typhi* only share O12 (has O9 and O12), it is not surprising that patients with *S. Paratyphi* A had lower *S. Typhi*-LPS seroresponses than *S. Typhi* cases. These cross-reactive interactions are likely due to the O12 antigen, which has a trisaccharide repeat backbone like *Salmonella* groups A, B, and D. Anti-HlyE antibody responses are extremely selective for the diagnosis of typhoid or paratyphoid, as shown by a previous study. The prevalence of *Salmonella typhi* and *S. paratyphi* must be accurately quantified, thus it should be discovered if an individual's immune response is unique to these two serovars.^[39]

2.7 Typhoid surveillance and subnational data on the disease's effects

There was no statistically significant difference in antibody kinetics between hospitalized and non-hospitalized cases of enteric fever that sought treatment suggesting that seroresponses were not dependent on the severity of the clinical disease. Antibody responses of asymptomatic patients or those treated in lower acuity facilities, such as pharmacies, could not be compared because of a lack of participants. Serosurveys can help estimate typhoid prevalence in low-resource settings, but they can't replace blood culture surveillance, which is the only way to track the worrisome rise in antibiotic resistance that's undermining the ability to treat the disease. There is an urgent need for information on the incidence of typhoidal *Salmonella* since the WHO

advises that countries with a high typhoid incidence include TCVs in national initiatives. Only in places with access to blood culture facilities is clinical monitoring for enteric fever possible, and even then, biases in care-seeking behavior, antibiotic usage, and varied diagnostic sensitivity may significantly impact incidence estimates.

2.8 Test Felix-Widal

The traditional Widal test dates back more than a century. It finds agglutinating antibodies to *S. enterica* serotype Typhi O and H antigens. Sera dilutions that have been doubled are used to measure the levels in a sizable test tube. This test has moderate sensitivity and specificity despite being reliable and straightforward to use. Its sensitivity and specificity are both claimed to be between 70 and 80 percent. Up to thirty percent of cases of typhoid fever that has been confirmed by culture may have a negative result. This is likely the result of a reduced antibody response that occurred after an earlier course of antibiotic treatment. In addition, individuals with typhoid fever could not exhibit any sign of an antibody response or an increase in their antibody titer.^[40] The cross-reactive epitopes and antigens of *S. enterica* serotype Typhi are unfortunately shared with other Enterobacteriaceae species. This might lead to the achievement of erroneously positive results. These kinds of results are also conceivably observable in other clinical settings, such as those involving cirrhosis, typhus, malaria, and several other types of bacterial illnesses that result in bacteremia. In areas where the disease is prevalent, the average person in the general population has a low baseline level of antibodies. It is difficult to define an appropriate cut-off point for a favorable result since it varies not only across places but also between times in certain regions. Because there is often only one acute serum available, it is essential to determine the antibody level in the local normal population to establish a cutoff threshold at which the antibody titer is regarded to be significant. This may be done by conducting an experiment in which the normal population is exposed to the acute serum. If matched serums are available, a diagnostic condition is indicated if there is a fourfold rise in antibody titer between convalescent and acute sera.^[41] Because of its relatively cheap cost, the Widal examination is likely to be the test of choice in a great number of less developed countries. This is permissible provided that the results of the test are properly interpreted in light of any previous typhoid infections and line with the appropriate regional cut-off values for the determination of positive.

3. Typhoid prevalence in Bangladesh

Studies revealed that out of a total of 33,136 patients who had blood cultures taken, 8,705 (or 26%) tested positive for typhoidal *Salmonella*. In Dhaka, the incidence of *S. Typhi* was 1,110 (95% confidence interval: 949-1,305) per 100,000 person-years when adjusted for population. Adjusted typhoid incidence rates in Nepal came in at 330 (95% confidence interval: 232-476) in Kathmandu and 271 (95% confidence

interval [CI]: 205-365) in Kavrepalanchok. Adjusted incidence rates per hospital site in Pakistan were 195 (95% confidence interval [CI]: 163-236) and 126 (95% [CI]: 106-151) respectively. Although they were lower than the rates of typhoid, the adjusted incidence rates of paratyphoid were as follows: 150 (95% [CI]: 127-177) in Bangladesh; 49 (95% [CI]: 38-65) and 82 (95% [CI]: 57-116) in the Nepal sites; 25 (95% [CI]: 21-31) and 1 (95% [CI]: 1-1) in the Pakistan sites; and 1 (95% [CI]: 1-1) in India. Overall, 32 percent of case patients were admitted to hospitals, which indicates that the frequency of hospitalization was high across all locations.^[42]

4. Limitations that should be considered when evaluating the results

When interpreting the results here, it is important to keep in mind several caveats. By fitting distinct kinetics models to each age group, the study was able to account for differences in antibody responses among individuals with enteric fever. Longitudinal decline curves that take into consideration age need further research. Although it is possible that asymptomatic individuals had different antibody kinetics, the study assumed that they were all the same for all patients. It may not be reliable if asymptomatic individuals have lower peak antibody responses and a more rapid drop over time. Antibody kinetics from secondary and tertiary exposures are expected to look and behave differently from those of primary infections, especially in high-transmission locations where individuals may be repeatedly re-exposed.

5. CONCLUSIONS

In conclusion, typhoid fever remains a significant public health concern, particularly in developing countries with poor sanitation and limited access to clean water. However, the disease is also a risk for travelers to these areas and those working in certain high-risk occupations.

Prevention is key to reducing the spread of typhoid fever. This can be achieved through improved sanitation practices, vaccinations, and education about how the disease spreads. Timely diagnosis and treatment are also essential to preventing severe illness and potential mortality.

While progress has been made in reducing the incidence of typhoid fever globally, there is still much work to be done in controlling and eradicating the disease. Typhoid fever morbidity and mortality drastically decreased in industrialized nations as a result of better housing conditions and the advent of drugs. However, many of the developing nations in the WHO's African, Eastern Mediterranean, South-East Asia, and Western Pacific Regions continue to struggle with the disease.

In Bangladesh vaccination programs, awareness campaigns, and infrastructure improvements are required to control typhoid fever effectively. The main challenges to eradicating typhoid fever include poverty, lack of

education and lack of awareness remain in Bangladesh. Future research and intervention are required for eradicating typhoid fever. Continued efforts in research, education, and public health interventions are needed to achieve this goal and ensure that typhoid fever is no longer a threat to global health.

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