KESANS: International Journal of Health and Science
e-ISSN: 2808-7178, p-ISSN: 2808-7380
Web: http://kesans.rifainstitute.com/index.php/kesans/index

Diagnostic Test and Management of Typhoid Fever with Family Medicine Approach: A Case Report

Gabrielle Glenis, Tirta Darmawan Susanto, Marshell Timotius Handoko
Faculty of Medicine University Pelita Harapan, Banten, Indonesia
ggtrisnadi@gmail.com

Article Information
Submitted: **15 August 2024**
Accepted: **17 August 2024**
Online Publish: **30 August 2024**

Abstract
A 24-year-old man with fever, decreased appetite, diarrhea, anxiety, cannot do his job properly because he feels weak and feels unwell, wants to be able to recover without having to be hospitalized, suspected of having typhoid fever. The patient often forgets to wash his hands before eating, 1 month ago the patient had a cough and runny nose, influenza, typhoid, dengue, pneumonia vaccines -, 8 years ago the patient had typhoid. The patient uses online food delivery, spends more time in the hospital than at home, is a major medical profession student, history of social service to Larantuka in May, experienced changes in family circumstances in 2019 so that adaptation and maturity are needed. This journal emphasizes supporting examinations and management carried out in accordance with a holistic family medicine approach in terms of promotive, preventive, curative, and rehabilitative aspects that focus on patients, families, and communities.

Keywords: Typhoid Fever; Teenagers; Family; Medicine;

How to Cite **Gabrielle Glenis, Tirta Darmawan Susanto, Marshell Timotius Handoko/Diagnostic Test and Management of Typhoid Fever with Family Medicine Approach: A Case Report, Vol. 3, No. 11, 2024**
DOI https://doi.org/10.54543/kesans.v3i11.310
e-ISSN/p-ISSN **2808-7178 / 2808-7380**
Published by **Rifa'Isntitute**

Introduction

Typhoid fever and paratyphoid fever are clinically indistinguishable multisystemic febrile illnesses caused by Salmonella enterica serotypes Typhi (S Typhi) and Paratyphi (S Paratyphi) A, B, and C that are major causes of bloodstream infections in South and Southeast Asia (Chattaway, Langridge, & Wain, 2021). In the Americas, typhoid fever is second only to malaria as a cause of severe and sometimes life-threatening infections in travelers (Van Camp & Shorman, 2023). Urbanization, climate change, and increasing antibiotic resistance have the potential to increase the global burden of typhoid and make typhoid more prevalent, especially in communities (WHO). Salmonella enterica subspecies enterica Typhi (S Typhi) and Salmonella enterica subspecies enterica Paratyphi (S Paratyphi) are exclusively human pathogens (Sanderson, Liu, Tang, & Johnston, 2015)

S Typhi and S Paratyphi are said to be spread by the fecal-oral route via the "4 Fs" (flies, fingers, feces, and fomites). They affect people living or traveling in low- and middle-income countries worldwide with poor access to clean water and sanitation. People who use pit latrines have a 50-fold increased risk of typhoid fever and the lack of handwashing facilities with soap and water increases the likelihood of getting typhoid fever by 2.3 times (Kim et al., 2023). According to the World Health Organization (WHO), access to clean water and adequate sanitation, hygiene among food handlers, and typhoid vaccination are all effective in preventing typhoid fever (WHO)

After an incubation period of 6 to 30 days, typhoid fever appears suddenly with a gradual onset of fever accompanied by fatigue, anorexia, headache, malaise, and abdominal symptoms. If treatment is delayed or inadequate, meningitis, sepsis, or intestinal perforation can occur. With a history of S Typhi and S Paratyphi strains rapidly developing antimicrobial resistance, treatment is very difficult and raises concerns (Lianou, Nychas, & Koutsoumanis, 2017)

Typhoid fever is more severe in debilitated and immunocompromised patients and in immunodeficiency diseases. Salmonella is the most common acid-sensitive bacteria and is destroyed in the stomach by gastric acid unless large doses are ingested (Basnyat, Qamar, Rupali, Ahmed, & Parry, 2021). Food and drink can reduce the exposure of Salmonella to gastric acid and the use of PPIs causes a decrease in gastric acid production (Heymans et al., 2018). The normal intestinal flora is protective against infection. The use of broad-spectrum antibiotics that destroy the normal flora allows for increased invasion. Malnutrition reduces the normal intestinal flora and also increases susceptibility to infection (Vos et al., 2020). Human genetics probably plays a role in susceptibility to typhus, with markers mapping to the HLA class II region strongly associated with typhoid resistance. Higher typhoid fever occurs with increasing temperature. Between 11° and 35° N, previous rainfall events are positively associated with typhoid fever incidence. Climate change is likely to increase the incidence of typhoid fever and other gastrointestinal diseases through increased flooding, drought, and temperature, endangering food and water security (Van Camp & Shorman, 2023)

Typhoid fever is a prime example of the "infection gap" between high-income countries (GNI per capita in 2021 of >$12,695) and low- and middle-income countries (≤$1046 and >$1047-$12,695, respectively) (Centers for Disease Control and Prevention, 2020). From a review of cases in major hospitals in Indonesia, suspected typhoid fever showed an increasing trend from year to year with an average morbidity of 500/100,000 population and a mortality rate of between 0.6–5%

In 2019, an estimated 9.2 million (95% CI 5.9–14.1) cases of typhoid fever and 110,000 (95% confidence interval; 53,000–191,000) deaths occurred worldwide. This compares with 11 to 21 million cases and 148,000 to 161,000 deaths in 2015. An estimated 3.8 million S Paratyphi infections occurred globally in 2019 (Nemhauser JB, 2023) at (Hancuh, 2023). The median ages for typhoid and paratyphoid cases were 26 and 24 years, respectively. No deaths were reported, although approximately 82% of cases for which data were available were hospitalized (Poudel, A.,) at (Ley et al., 2010)

The family medicine approach in handling typhoid fever in adolescents places the doctor as a provider of management and change that does not only focus on treatment but also promotive, preventive, curative and rehabilitative efforts by placing the family doctor as a partner for patients and families and an advocate for the community around the family so that the environment and habits of a community can also change. This must be supported by cooperation that can be realized through collaboration between family medicine and third parties such as the campus, local health center, and RT or RW head in the area where the patient lives. This report aims to implement holistic management through a family medicine approach that focuses on Patient Centered, Family Focused, and Community Oriented in 24-year-old adolescents with typhoid fever.

Case Report

Patient Mr. CC, 24 years old complained of fever from 3 days ago when returning from activities at the hospital. Fever occurs at night, hot with touch and shivering. When measured, the temperature reaches 38oC. During the day the fever goes down but does not reach normal temperature (37.6 oC), the patient can do activities as usual but the body feels unwell. The highest temperature reaches 38.8 oC on the night of the 3rd day of fever. Other complaints include headache, joint pain, diarrhea, and decreased appetite. Headache and joint pain are felt when the temperature increases at night. Joint pain is felt in the back, waist, and knees. Diarrhea only 1 time during regular bowel movements, a little, mucus-, blood-, odor- brown color and still pulpy. The patient only wants to eat food that is not too strong in taste because if it is too strong the patient will feel nauseous. The patient had typhoid fever 8 years ago. The patient had the flu 1 month ago and only recovered after 2 weeks of treatment by taking OBH Nelco, nasamex, and ciprofloxacin. The patient rarely takes stomach medicine and has no history of allergies. Neither the patient nor the patient's family has a history of influenza, typhoid, dengue, and pneumonia vaccines. The patient is a medical student who is undergoing a major. The busy activities cause fatigue and lack of sleep and sometimes the patient has difficulty sleeping because of irregular sleeping hours and the patient's habit of drinking 2-3

cups of coffee per day in the hope of not feeling weak. The patient did not have time to bring provisions from home so that the patient's nutrition was difficult to control, did not eat regularly and tended to buy food from online services. The patient often forgot to wash his hands before eating either using running water or hand sanitizer. The patient did not have time to exercise regularly and only drank alcohol at certain events. The patient lives with his parents, two siblings and grandfather (Figure 1). The relationship between family members is quite close and good so that they can rely on each other when in difficult situations (Figure 2).

This relationship is supported by the Family APGAR score with a value of 9 which indicates a very functional family. The SCREEM aspect and the HEEADSSS screening carried out showed that the patient's family environment is a religious environment so that the patient has good self-control over alcohol, free sex, and drug use. The patient experienced changes in 2019, namely his father retired in the middle of his college years and his grandfather had a stroke so he had to move to the patient's house which caused his mother's attention to be divided. In carrying out daily activities, the patient uses a car with a seat belt sensor so that it is certain that the patient will always use a seat belt when driving

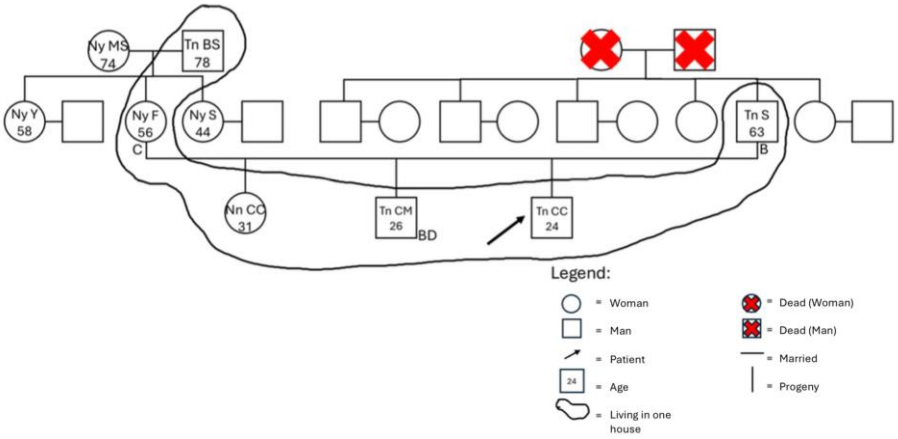

Figure 1. Family Genomics of Mr CC, 24 years old with typhoid fever.

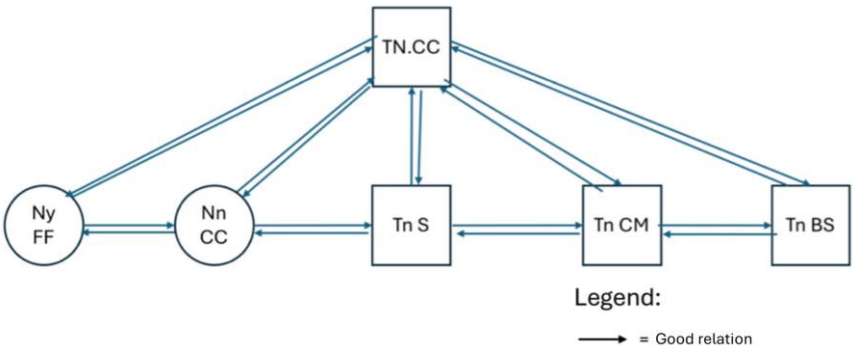

Figure 2. Family Map of Mr CC, 24 years old with typhoid fever

On physical examination, the general condition appeared moderately ill and weak; blood pressure 120/80 mmHg; pulse rate 70x/minute; respiratory rate 18x/minute; temperature 38oC; height 173 cm; weight 72 kg; body mass index 24.05 kg/m2; epigastric tenderness +. On supporting examination, leukocytosis 10,300/uL and Salmonella Typhii O and Paratyphii AO 1/320 were found. Other examination suggestions such as urinalysis, peripheral blood smear, SGOT, SGPT, direct indirect bilirubin, anti-hepatitis A were not performed.

The condition of the house is quite clean with running water from PDAM, a toilet with a septic tank system, good ventilation with many windows in the house, marble floors that are cleaned every day, the condition of the kitchen is cleaned after cooking, cutlery is washed and put back into the cupboard but some cooking utensils are put outside the cupboard. The patient's residential environment is quite beautiful and the road is quite wide with the condition of the gutter still open.

Based on anamnesis, physical examination and supporting examination, a holistic diagnosis was obtained which can be seen from the Personal Aspect: fever, decreased appetite, diarrhea, anxiety, not free to do his job because he feels weak and feels unwell, wants to be able to recover without having to be hospitalized; Clinical aspect: typhoid fever; Internal aspect: 24 year old male, rarely washes hands before eating likes to order food using online applications, eats non-nutritious food every day, and is exhausted from carrying out daily activities, influenza, typhoid, dengue, pneumonia vaccines -, 8 years ago the patient had typhoid; External Risk Aspect: spends more time in the hospital than at home, undergoes major medical profession education, history of social service to Larantuka in May, experiences changes in family circumstances in 2019 so that adaptation and maturity are needed; Functional degree aspect: 1 meaning that the patient can still do daily tasks as before being sick.

Interventions given to patients are divided into patient-centered, family-focused, and community-oriented. Patient-centered interventions include promotive aspects, namely vaccination education (influenza, typhoid, pneumonia), education on sleep hygiene methods such as regular sleep schedules, avoiding coffee at night, not playing with cellphones before bed and music therapy that will be implemented after education ends, education on balanced nutrition patterns and daily calorie needs, education on washing hands with running water and soap. In addition, it is advisable to buy food at the faculty canteen before closing time and buy food at places whose quality is known.

Preventive aspects are carried out by wearing masks when working or with friends and family, carrying hand sanitizer or wet tissues in the doctor's coat pocket so that it is more practical to wash hands, cleaning cutlery with tissue and water when the patient is outside, not drinking coffee at night or before bed and consuming multivitamins regularly.

The curative aspect is given at home because the patient refuses to be treated in the form of multivitamin and vitamin B infusion, Ondansetron 3x1 tablet before meals, Cefixime 2 x 200 mg for 7 days, Paracetamol 3 x 500mg if there is a headache and fever. The patient needs to avoid hard foods and foods that have strong flavors such as spicy, sour, and too salty.

The rehabilitative aspect is given in the form of follow-up to maintain hand hygiene and eating utensils used, maintain food with balanced nutrition, get enough rest, and advice to check for typhoid 1 year after being exposed to typhoid fever. Family-focused interventions, including family dynamics assessment, education and advice on influenza, typhoid, dengue, pneumonia vaccinations, education on balanced nutrition patterns and calculating daily calorie needs, education on washing hands with running water and soap before and after eating, education on the importance of maintaining the cleanliness of eating utensils and cooking utensils stored in the kitchen, and education on the cleanliness of cooking utensils by rinsing cooking utensils with running water before use. Community-oriented interventions include education on the importance of typhoid vaccination, education on balanced nutrition and maintaining the cleanliness of eating utensils, kitchen utensils and washing hands with soap by holding counseling before environmental prayers and approaching the campus dean so that the canteen can close later so that interns can still buy snacks at night.

Discussion

This case illustrates the problem of typhoid fever in adolescents with incomplete supporting examinations due to limited state insurance coverage. CDC, WHO, and Poudel said that the Widal test has several advantages, namely it is more affordable and accessible in developing countries compared to modern diagnostic methods that require sophisticated equipment, is easily accessible in various health facilities in developing countries, making it a diagnostic tool available to most people, and can provide rapid screening results, especially in early stages of examination (Poudel, A.,) at (Ley et al., 2010)

According to Islam et all. The Widal test has also been available for decades and can be performed using venous blood; unfortunately, the test has low sensitivity and specificity and optimally requires a comparison of samples taken in the acute and recovery stages of the disease. Thus, many clinicians and public health studies rely on other commercially available tests, such as Tubex and Typhidot which can be performed on small amounts of venous blood collected in the acute stage of the disease (Islam et al., 2016). Mawazo et al in his research said that the Widal examination has sensitivity, specificity, PPV and NPV of Widal titration in this study were 81.2%, 18.3%, 10.1 and 89.7 respectively. The Widal test has very low specificity and positive predictive value. This may be due to cross-reacting antibodies from other enterobacteria so that patients may suffer from diseases due to other causes and not really be sick from the suspected cause (Mawazo, Bwire, & Matee, 2019)

Research from Thiemer stated that Typhidot and Tubex TF do not support diagnostic enforcement so that blood culture and molecular biology techniques are more recommended as the reference method of choice even though there are many limitations (Thriemer, Ley, Menten, Jacobs, & Van Den Ende, 2013). Mogasale said in his research review that the sensitivity of blood culture was found to be 66% using bone marrow culture as the reference standard and 61% using blood culture (Mogasale, Ramani,

Mogasale, & Park, 2016). Around 1% to 4% of patients with typhoid fever become chronic carriers, indicating transmission for at least 12 months after completing appropriate antibiotic treatment. Chronic carriers are less common with adequate antibiotic treatment and S. Paratyphi infection and can be checked by culture examination (Kim et al., 2023), (Lianou et al., 2017). In this patient, a Widal examination was performed and other examinations such as a Tubex examination were not performed because they were hampered by state insurance regulations used when conducting supporting examinations, but it would be better if the Widal test was still confirmed using other tests that have higher sensitivity but are affordable for the patient.

In Indonesia, there are several recommended drugs that can be used to treat typhoid fever such as IV/IM ceftriaxone, cefixime, chloramphenicol, fluoroquinolones, ampicillin and amoxicillin, cotrimoxazole, and thiamphenicol. Recent data show that although susceptibility to chloramphenicol, ampicillin, and cotrimoxazole has re-emerged in some areas, these drugs are no longer recommended as first-line agents due to the threat of MDR (Marchello, Birkhold, & Crump, 2020). Cefixime can be an alternative to ceftriaxone, although its relative effectiveness may be lower than fluoroquinolones (Kuehn et al., 2022). In a recent systematic review study examining ceftriaxone, cefixime, chloramphenicol and fluoroquinolones against several aspects such as clinical failure, microbiological failure, relapse incidence, and time taken to reduce temperature. In the aspect of clinical failure, it was found that fluoroquinolone with a p value of 0.0003 had a higher clinical failure rate than cefixime, but fluoroquinolone had a microbiological failure rate that was not statistically significant as seen from the p value> 0.05 in each forest plot. Fluoroquinolone had a higher relapse rate based on statistical results with a p value of 0.04 compared to other drug classes, but fluoroquinolone had the ability to lower temperature in a shorter time based on statistical results with a p value of 0.0006 while ceftriaxone had a p value <0.00001 compared to other drug classes. From the data above, it was found that fluoroquinolone drugs had less good results statistically, so the use of fluoroquinolones to treat typhoid fever did not provide good results (Kuehn et al., 2022)

A study conducted by Patil and Mule in India on 251 typhoid fever patients stated that the sensitivity to ceftriaxone, cefixime, and azithromycin was like previous literature where Salmonella isolates showed 100% sensitivity to ceftriaxone and cefixime and 96.3–100% to azithromycin. Several studies have also reported that azithromycin is similar or superior to chloramphenicol, fluoroquinolones, broad-spectrum cephalosporins in the treatment of uncomplicated enteric fever with rapid resolution of clinical symptoms and low recurrence rates. Therefore, oral cephalosporins and macrolides are considered as first-line agents for empirical treatment of enteric fever cases in cases of decreased susceptibility to fluoroquinolones (Patil & Mule, 2019)

According to data taken from Amarullah et all, there are several antibiotics available in health centers in Indonesia such as amoxicillin, ciprofloxacin, cefadroxil, cefixime, clindamycin, metronidazole, erythromycin, thiamphenicol, chloramphenicol, azithromycin, doxycycline, and cotrimoxazole (Amarullah, Anwari, Dewi, & Sari, 2022). In the treatment of typhoid in health centers, there are several drugs in the study that

cannot be used in everyday life in primary health care facilities due to limited availability so in this case the author chose to use cefixime. Vaccination does not prevent the need for hand hygiene and food and water precautions. In endemic countries where typhoid vaccination is not integrated into the routine vaccination schedule, patients at higher risk of severe disease can get typhoid vaccination at their own expense (Lianou et al., 2017)

There are 2 types of typhoid vaccines, conjugated and unconjugated. There are 2 types of unconjugated vaccines, namely the inactivated Vi capsule polysaccharide vaccine (ViPS) and the live attenuated Ty21a S Typhi strain vaccine. These vaccines are approximately 50% to 60% effective in preventing typhoid fever (Muresu et al., 2020). The intramuscular Vi capsule polysaccharide vaccine is appropriate for those 2 years of age and older and a booster should be given every 2 years as directed by the CDC (Basnyat et al., 2021). The Ty21a vaccine is indicated for persons 6 years of age and older. One capsule every other day for a total of 4 doses is taken with a liquid not warmer than body temperature at least 1 hour before meals. The series should be completed at least 1 week before exposure, and a booster is indicated every 5 to 7 years. The oral vaccine is contraindicated in persons who are immunocompromised, acutely ill with gastrointestinal conditions, or breastfeeding. This vaccine should only be used in pregnant women if the attenuated injectable vaccine is not available and a careful risk assessment has been performed (Kim et al., 2023), (Basnyat et al., 2021)

WHO has prequalified 2 typhoid conjugate vaccines (TCVs): Typbar-TCV and TYPHIBEV. By combining a Vi capsule with a protein carrier (eg, tetanus toxoid), these vaccines induce a stronger and more durable T-cell-mediated immune response than previous vaccines; they can be used in children under 5 years of age and infants as young as 6 months (Mogasale et al., 2016). Given as a single intramuscular dose, TCV has been found to be 79% to 95% effective in the first 2 years after vaccination in studies involving more than 100,000 children at multiple sites. Antibody responses can persist for up to 7 years (Browne et al., 2024). Endemic countries have implemented TCV vaccines as part of routine immunization programs. However, these vaccines are not licensed in Europe or North America, and therefore are not suitable for travel. Typhoid vaccines can be given to patients who have previously had typhoid fever, especially those living in areas with high-risk factors. Trials have shown that treatment of typhoid patients in the first two weeks of illness can inhibit the development of a protective anti-Vi CPS antibody response, leading to general recommendations to administer typhoid vaccine 4 weeks after full recovery from the illness (Zaki, 2011)

Conclusion

Oral cephalosporins and macrolides are considered as first-line agents for empirical treatment of enteric fever cases in cases of decreased susceptibility to fluoroquinolones, but in primary health care facilities due to limited availability we use cefixime. Typhoid vaccines can be given to patients who have previously had typhoid fever, especially those living in areas with high-risk factors

References

Amarullah, Adinugraha, Anwari, Farida, Dewi, Aprilia Citra, & Sari, Eka Yuni Danam. (2022). KERASIONALAN PENGGUNAAN ANTIBIOTIK DI PUSKESMAS. *Journal of Pharmaceutical Care Anwar Medika (J-PhAM)*, *4*(2), 82–87.

Basnyat, B., Qamar, F. N., Rupali, P., Ahmed, T., & Parry, C. M. (2021). *Enteric fever. BMJ 372: n437*.

Browne, Annie J., Chipeta, Michael G., Fell, Frederick J., Haines-Woodhouse, Georgina, Hamadani, Bahar H. Kashef, Kumaran, Emmanuelle A. P., Aguilar, Gisela Robles, McManigal, Barney, Andrews, Jason R., & Ashley, Elizabeth A. (2024). Estimating the subnational prevalence of antimicrobial resistant Salmonella enterica serovars Typhi and Paratyphi A infections in 75 endemic countries, 1990-2019: a modelling study. *The Lancet Global Health*, *12*(3), e406–e418.

Centers for Disease Control and Prevention. (2020). National Typhoid and Paratyphoid Fever Surveillance annual summary, 2020. In *Centers for Disease Control and Prevention, Atlanta, GA*. Retrieved from https://www.cdc.gov/typhoid-fever/php/surveillance/annual-summary-2020.html?CDC_AAref_Val=https://www.cdc.gov/typhoid-fever/reports/annual-summary-2020.html

Chattaway, Marie A., Langridge, Gemma C., & Wain, John. (2021). Salmonella nomenclature in the genomic era: a time for change. *Scientific Reports*, *11*(1), 7494.

Hancuh, Molly. (2023). Typhoid fever surveillance, incidence estimates, and progress toward typhoid conjugate vaccine introduction-worldwide, 2018-2022. *MMWR. Morbidity and Mortality Weekly Report*, *72*.

Heymans, Raymond, Vila, Amir, van Heerwaarden, Caroliene A. M., Jansen, Claudia C. C., Castelijn, Greetje A. A., van der Voort, Menno, & Biesta-Peters, Elisabeth G. (2018). Rapid detection and differentiation of Salmonella species, Salmonella Typhimurium and Salmonella Enteritidis by multiplex quantitative PCR. *PloS One*, *13*(10), e0206316.

Islam, Kamrul, Sayeed, Md Abu, Hossen, Emran, Khanam, Farhana, Charles, Richelle C., Andrews, Jason, Ryan, Edward T., & Qadri, Firdausi. (2016). Comparison of the performance of the TPTest, Tubex, Typhidot and Widal immunodiagnostic assays and blood cultures in detecting patients with typhoid fever in Bangladesh, including using a Bayesian latent class modeling approach. *PLoS Neglected Tropical Diseases*, *10*(4), e0004558.

Kim, Chaelin, Goucher, Gerard R., Tadesse, Birkneh Tilahun, Lee, Woojoo, Abbas, Kaja, & Kim, Jong Hoon. (2023). Associations of water, sanitation, and hygiene with typhoid fever in case-control studies: a systematic review and meta-analysis. *BMC Infectious Diseases*, *23*(1), 562.

Kuehn, Rebecca, Stoesser, Nicole, Eyre, David, Darton, Thomas C., Basnyat, Buddha, & Parry, Christopher Martin. (2022). Treatment of enteric fever (typhoid and paratyphoid fever) with cephalosporins. *Cochrane Database of Systematic Reviews*, (11).

Ley, Benedikt, Mtove, George, Thriemer, Kamala, Amos, Ben, von Seidlein, Lorenz, Hendriksen, Ilse, Mwambuli, Abraham, Shoo, Aikande, Malahiyo, Rajabu, Ame, Shaali M., Kim, Deok R., Ochiai, Leon R., Clemens, John D., Reyburn, Hugh, Wilfing, Harald, Magesa, Stephen, & Deen, Jacqueline L. (2010). Evaluation of the Widal tube agglutination test for the diagnosis of typhoid fever among children admitted to a rural hdospital in Tanzania and a comparison with previous studies. *BMC Infectious Diseases*, *10*(1), 180. https://doi.org/10.1186/1471-2334-10-180

Lianou, Alexandra, Nychas, George John E., & Koutsoumanis, Konstantinos P. (2017). Variability in the adaptive acid tolerance response phenotype of Salmonella enterica strains. *Food Microbiology*, *62*, 99–105.

Marchello, Christian S., Birkhold, Megan, & Crump, John A. (2020). Complications and mortality of typhoid fever: a global systematic review and meta-analysis. *Journal of Infection*, *81*(6), 902–910.

Mawazo, Akili, Bwire, George M., & Matee, Mecky I. N. (2019). Performance of Widal test and stool culture in the diagnosis of typhoid fever among suspected patients in Dar es Salaam, Tanzania. *BMC Research Notes*, *12*, 1–5.

Mogasale, Vittal, Ramani, Enusa, Mogasale, Vijayalaxmi V, & Park, JuYeon. (2016). What proportion of Salmonella Typhi cases are detected by blood culture? A systematic literature review. *Annals of Clinical Microbiology and Antimicrobials*, *15*, 1–8.

Muresu, Narcisa, Sotgiu, Giovanni, Are, Bianca Maria, Cossu, Andrea, Cocuzza, Clementina, Martinelli, Marianna, Babudieri, Sergio, Are, Riccardo, Dettori, Marco, & Azara, Antonio. (2020). Travel-related typhoid fever: narrative review of the scientific literature. *International Journal of Environmental Research and Public Health*, *17*(2), 615.

Patil, Niranjan, & Mule, Prashant. (2019). Sensitivity pattern of Salmonella typhi and Paratyphi A isolates to chloramphenicol and other anti-typhoid drugs: an in vitro study. *Infection and Drug Resistance*, 3217–3225.

Sanderson, Kenneth E., Liu, Shu Lin, Tang, Le, & Johnston, Randal N. (2015). Salmonella Typhi and Salmonella Paratyphi A. In *Molecular medical microbiology* (pp. 1275–1306). Elsevier.

Thriemer, Kamala, Ley, Benedikt, Menten, Joris, Jacobs, Jan, & Van Den Ende, Jef. (2013). A systematic review and meta-analysis of the performance of two point of care typhoid fever tests, Tubex TF and Typhidot, in endemic countries. *PLoS One*, *8*(12), e81263.

Van Camp, Roscoe O., & Shorman, Mahmoud. (2023). Typhoid vaccine. In *StatPearls [Internet]*. StatPearls Publishing.

Vos, Theo, Lim, Stephen S., Abbafati, Cristiana, Abbas, Kaja M., Abbasi, Mohammad, Abbasifard, Mitra, Abbasi-Kangevari, Mohsen, Abbastabar, Hedayat, Abd-Allah, Foad, & Abdelalim, Ahmed. (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*, *396*(10258), 1204–1222.

Zaki, Syed. (2011). Re-infection of typhoid fever and typhoid vaccine (comment on 'An imported enteric fever caused by a quinolone-resistant Salmonella typhi'). *Annals of Saudi Medicine*, *31*(2), 203–204.