



Diagnosis & Management of an Enteric Fever Case in a Small Setting- A Case Report

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Case Report

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Abstract

Enteric fever is an important public health problem in developing and underdeveloped countries. It is mainly caused due to contaminated food or water and poor personal and food hygiene. Despite a century-old history of the diseases, the progress in its diagnostic tools is limited, age-old Widal test and treatment by empirical Antibiotic therapy continues to be the choice. Here, we present one such case managed in a smaller setting with serological diagnosis and empirical Antibiotic therapy. A 26-year-old male working graduate with a one-week history of evening rise of temperature with chills, heaviness of head and pain abdomen lasting for about one hour, associated with loose stools (5-6times), Nausea, loss of taste and severe body ache in early March 2021. He gave frequent travel history and consumption of street food and poor sleep for a week before the presentation. Typhoid was suspected based on clinical features, Widal test and other supportive blood tests. The same tests were repeated three times over 2 weeks to monitor the prognosis of the condition. The case was treated by cephalosporin, Antipyretics, Fluoroquinolone and Macrolide, temperature became normal after 3 days of day-care, followed up after 5 days & 8 days and confirmed to be back to Normalcy.

Keywords: *S.typhi*; Typhoid fever; Paratyphoid; Serodiagnosis; Laboratory; Multidrug Resistance

Introduction

Enteric fever, also called Typhoid fever, is caused by Gram-negative bacterium *Salmonella enterica* serovar Typhi (*S. Typhi*) & *S. Para typhi*. Paratyphi A & B cause a disease that is Clinically Indistinguishable from Typhoid particularly in parts of Asia. Typhoid fever is endemic in Asia, Africa, Latin America, the Caribbean and Oceania, but 80% of cases come from Bangladesh, China, India, Indonesia, Laos, Nepal, Pakistan or Vietnam. Within each of these countries, typhoid fever is most common in underdeveloped areas & Socio-economical poorer population what was considered as the disease of over 5 years of age due to beginning of eating outside home. But is now seen among under-fives also

indicating towards poor hygiene of caretakers of the children. The only known natural hosts & reservoir of infection is human being.

Background

Enteric fever is a multisystemic illness that has been a public health problem, for over a century, especially in the developing world. It is one of the major causes of mortality and morbidity in overcrowded & unhygienic areas. It is also one of the serious infectious disease threats to public health on a global scale with great concern over the rapid & widespread emergence of resistance to multiple Antibiotics. Typhoid fever is an acute, febrile illness with a case fatality

rate of 10-30% among undertreated/untreated that can drop to 1-4% with appropriate treatment; young children are at greater risk of dying. Annual estimation of 11-21 million cases of enteric fever and approximately 128000-161000 deaths compared to an annual estimation of 6 million cases of paratyphoid fever and 54000 deaths. The majority of the cases occur in Southeast Asia and Sub-Saharan Africa [1]. Typhoid annual incidence per 100000 person-years among the age group of 5-10 years varied from 24.2 and 29.3 in sites of Vietnam & china respectively to 180.3 in sites in Indonesia and 412.9 & 493.5 in sites in Pakistan and India respectively [2]. According to the Medical Certification Of Cause of Death 2018 report, total deaths of typhoid and paratyphoid fevers were 947 (males-546, females-401) and Karnataka state total deaths were 19, (11 & 8 male, female deaths respectively) [3]. According to the National Health Profile 2019 Report, Total typhoid cases in India were 2264453 (males-1211346, females-1053107) and total deaths were 496 (males-304, females-192), Karnataka state status was, total cases were 137973 (males-72699, females-65274) and total deaths were 4, (4 & 0 males, females deaths respectively) [4]. According to the Central Bureau of Health Intelligence provisional report 2009-10, Total typhoid cases were 1099331 (Males-588280,

females-511051) and Total deaths were 436 (males-255, females-181), Karnataka status was total cases were 50434 (males-27372, females-23062) and Total deaths were 11 (males-4, females-7) [5].

According to the Central Bureau of Health Intelligence Provisional report 2009-10, despite the suspicion of under-reporting the national data reveals a doubling of the number of cases annually over 9 years. While CFR has reduced from 22 per lakh in 2018 as compared to 39.7% in 2009 that indicates improvement in case management and early seeking of the care. Karnataka also saw the same trend as cases increased by 273% and CFR reduced from 13.9/Lakh to 2.9/Lakh cases. Gender-specific rate reduced to 2% in males in 2018 as compared to 2009, In females, it increased by 2% in 2018 as compared to 2009. In Karnataka reduction by 2% in males in 2018 and increase by 2% in females as compared to 2009 was not significant change. However, a reduction of CFR by 42% in males and 48% in females in 2018 as compared to 2009 countrywide does indicate significant improvement case management. In Karnataka, CFR reduced to 61% in males and 100% in females in 2018 as compared to 2009 is encouraging.

| Country/State | Cases | | | Deaths | | |
|----------------|---------|---------|---------|--------|--------|-------|
| | Male | Female | Total | Male | Female | Total |
| India 2018 | 1211346 | 1053107 | 2264453 | 304 | 192 | 496 |
| India 2009 | 588280 | 511051 | 1099331 | 255 | 181 | 436 |
| Karnataka 2018 | 72699 | 65274 | 137973 | 4 | 0 | 4 |
| Karnataka 2009 | 27372 | 23062 | 50434 | 4 | 3 | 7 |

(Source – National Health Profile of India 2009 & 2018).

Table1: Comparative number of enteric fever cases and Deaths by gender in India & Karnataka in 2018 & 2009.

Enteric fever control has got inadequate attention by the international health authorities as it is a problem of developing countries and heavily dependent on the investment on infrastructure, diagnostic methods, sanitation especially drainage system in Towns & Cities, Unsafe sources of drinking water, open defecation & multidrug Resistance add to the problem.

The main purpose of this case report is to highlight the simple empirical way of the management of enteric fever cases. Advocacy for investment in lying of water and sewage pipes far apart in the urban areas to reduce cross-contamination. Municipal authority's oversight minimizing food and personal hygiene cannot be overemphasized.

Case Presentation

A 26-year-old Male working graduate reported to a General Practitioner in a taluka level day-care centre on

9th March 2021 with a one-week history of evening rise of temperature with chills, heavy headedness and pain in abdomen lasting for an hour after each meal. He also complained of loose stools (5-6 times/day), Nausea, loss of taste and severe body ache. He gave history of job-related travel, consumption of street food and poor sleep for a week before the episode.

Examination

Temperature- 102*3F, Blood Pressure – 110/70mmhg, pulse rate – 94/min, respiratory rate – 19/min, oxygen saturation – 96%.

Physical examination

The patient looked emaciated, dehydrated with dried lips and a white-coated tongue. Abdomen tenderness more below umbilicus.

Laboratory Investigations

Diagnosis was clinched based on the laboratory investigations on 9th march 2021, report findings were, Total count – 11,200 cells/mm³, Neutrophils – 60%, Lymphocyte – 26, Eosinophile – 4%, Haemoglobin – 14.6 gm%, Platelet

count – 2.46L/mm³, Widal Test – *S. Typhi* O – 1:320, *S. typhi* H – 1:160, *S. Paratyphi* O – 1:80, *S. Paratyphi* H – 1:80. Urine: PH- Acidic, Sugar- Nil, Colour-Yellow, Pus cells – 5-6/hpf, Red cells- Nil, Epithelial cells – 0-2/hpf.

| Investigation | 9 th march 2021 | 11 th march 2021 | 17 th march 2021 | Remarks |
|-------------------|----------------------------|-----------------------------|-----------------------------|---------------------|
| Widal Test | | | | |
| <i>S. Typhi</i> O | 1:320 | 1:160 | 1:80 | Reduction by 75% |
| <i>S. typhi</i> H | 1:160 | 1:80 | 1:80 | Reduction by 50% |
| <i>P. Typhi</i> O | 1:80 | 1:40 | 1:40 | Reduction by 50% |
| <i>P Typhi</i> H | 1:80 | 1:40 | 1:40 | Reduction by 50% |
| Total WBC | 11,200 | 7,500 | 5,000 | Reduction by 55% |
| Platelet Count | 2.46 | - | 3.6 | Increased by 32% |
| Urine Test | | | | |
| Colour | yellow | clear | clear | Improved |
| Pus Cells | 5-6 | 2-3 | 2-3 | Reduction by 50-60% |

Table2: Series of Laboratory Investigations done to monitor the prognosis.

Management

The patient was admitted to a Private day-care centre at taluka level treated by a General Physician with parental fluids, 3rd generation Xone (cephalosporin) injection 1gm BD dosage, Vomikind (Anti-emetic) injection 4mg OD dosage, PAN (Proton pump inhibitor) injection 40mg OD dosage, Eldervit (Multivitamin) injection OD dosage, Dynapar (NSAID) 75mg Injection, Medomol (Antipyretic) 650mg tablet on the requirement, Azibig (Macrolide) 500mg tablet OD dosage for 3 days.

Prognosis

The prognosis was good, as the temperature became normal by 3rd day of treatment and the patient was doing well. On 11th of March 2021, the blood investigation report was total count reduced to 7,500 cells/mm³, Widal test dilution reduced to *S. typhi* O – 1:160, *S. typhi* H – 1:80, *S. paratyphi* O -1:40, *S. Paratyphi* H- 1:40, Urine Examination report was Pus-Cells – 2-3/hpf and it was clear. Emaciation had decreased, dehydration corrected, the patient was having oral soft diet, the coated tongue was normal, fever, heaviness of head and loose stools symptoms had disappeared. Continued medicines, a combination of 3rd generation Starfix – OF Cefixime (Cephalosporin) tablet 200mg & Ofloxacin (Fluoroquinolone) 200 mg BD dosage, Pepticool (Proton Pump Inhibitor) 40mg tablet OD dosage, Neuralac (Multivitamins) tablet OD dosage, Medomol (Antipyretic) tablet 500mg TID dosage, for 5 days given. He was advised for regular frequent hand washing, to drink boiled water, take

oral fluids frequently and electrolytes and a soft diet. He was advised not to have outside foods and take only homemade food. A review after another 5 days without fail.

Follow-Up

Follow up on 17th March 2021, the Patient was feeling cheerful and all symptoms except heaviness of the head had disappeared. Investigations revealed Widal test- *S. typhi* O – 1:80, *S. typhi* H – 1:80, *S. Paratyphi* O – 1:40, *S. Paratyphi* H – 1:40, Total Count – 5000 cells/cumm, Platelet count – 3.6L/cumm, Urine examination- Pus cells – 2-3/hpf, Epithelial cells- 0-1/hpf and it was clear.

Advised for continuation of Combination of Cephalosporin 200 mg & Fluoroquinolone 200mg BD for another 3 days that included Proton pump Inhibitors 40 mg OD (3days), Multivitamins OD (5days). Advised for the continuation of frequent hand wash, drink boiled water, clean fruits, and vegetables before eating, maintenance of personal & surrounding environment hygiene and typhoid vaccination. After Re-joining for the Job, two weeks down the line consulted via Telephone for further suggestion and continuation of personal and food hygiene.

Discussion

Enteric fever is a huge public health problem especially in developing countries like India and mainly associated with poor hygiene and with low socioeconomic status; human beings are only known natural hosts and reservoir

of infection.

Pathophysiology

By taking contaminated food, the ingested bacillus invade the mucosa of the small intestine, these bacilli taken up by macrophage and are transported to the regional lymph node. *S.typhi* multiplies in the intestinal lymphoid tissue and intact with enterocytes and M cells during 1-3 weeks of the incubation period. Bacilli enter the bloodstream after the end of the incubation period, bacteria invade the gall bladder, Biliary system and lymphatic tissue of the bowel and it gets multiplies in high number and it passes into the intestinal tract (stool).

Clinical Features

During 1st week; Prodromal stage headache, malaise, cough & sore throat, the disease classically persists with step-ladder fashion rise in temperature (40-41°C) over 4 to 5 days, accompanied by headache, vague abdominal pain and constipation or pea soup diarrhoea. The second week; between a 7-10th day of illness, mild hepato-splenomegaly occurs in the majority of patients. Relative bradycardia may occur and rose spots may be seen, the Third week; the patient will appear in a typhoid state which is a state of prolonged apathy, toxemia, delirium, disorientation or coma. Diarrhoea will then become apparent. If left untreated, there is a high risk (5-10%) of intestinal haemorrhage and perforation. Rare complications seen are Hepatitis, Pneumonia, Thrombophlebitis, myocarditis, cholecystitis, Nephritis, osteomyelitis and psychosis.

Diagnosis Challenges

Cure for any disease starts with accurate and timely diagnostics, which are often not available, accessible, and affordable especially in rural India. In endemic and resource-poor settings, clinical diagnosis of typhoid fever has the preference over the diagnostic tests. The current diagnosis for typhoid largely prevalent is with Widal Test. The Widal test may be falsely positive in patients who have had previous vaccination or infection with *S.typhi*. Besides cross-reactivity with other salmonella species, the test cannot distinguish between current infection and previous infection or vaccination against typhoid. Isolation of *salmonella typhi* from bone marrow is the current gold standard method for confirming a case of typhoid fever. A diagnosis of typhoid fever can usually be confirmed by analysing samples of blood, stools or urine. These will be examined under a microscope for the *salmonella typhi* bacteria that cause the condition. The bacteria are not always detected the first time, so you may need to have a series of tests but rarely available at the Sub-district level in India.

Treatment Challenges

Chloramphenicol was the main stay for chemotherapy until a decade ago. But now Ciprofloxacin or ofloxacin, chloramphenicol, amoxicillin and co-trimoxazole are recommended for fully sensitive typhoid cases. However, the resistance to antibiotics such as chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole [multidrug resistance -MDR strains] and resistance to the fluoroquinolone drugs are encountered in recent years. For the MDR cases, ciprofloxacin or ofloxacin or cefixime or azithromycin or cefotaxime are recommended but for the want of culture facilities many practitioners have started using them as drugs of choice. In case of quinolone resistance, azithromycin, Rocephin, or cefotaxime are recommended.

Magnitude of the Problem

A community study conducted in an urban slum of India has the incidence of the disease as high as 2/1000 population/year under 5 year of age and in under 10 years of age, it was 5.1/1000 population/year. In north India, a study reported that most of the cases occurred in the children age group of 5-12 years were in 24.8% of cases were in children up to 5 years of age [6]. Sidrammappa, et al. study shows an isolation rate of 7% which was slightly higher (7.3%) in south Karnataka compared to north Karnataka (6.9%) [7]. Sur, et al. study findings were 0.53% were positive for *S. typhi/S. paratyphi*, a higher proportion of participants with *S.typhi* infection were hospitalized compared with these with *S.paratyphi* infection (44% v/s 35%)(8). Sudeepa Kumar M, et al. hospital-based Study findings were out of 292 isolates of salmonellae, 160 were *S.typhi* & 132 were *S. Paratyphi* both salmonella species showed male preponderance in all groups highest was in the age group 11-20 years followed by 21-30 years [9]. Olumide Ajibola, et al. study shows that typhoid fever disease burden assessment is limited by a lack of a high degree of sensitivity & specificity by many current rapid diagnostic tests. Some of the new technologies, such as PCR & Proteomics may also be useful but are difficult for low resource settings to apply as point-of-care diagnostics. Across endemic areas, weak surveillance systems may also contribute to the spread of multidrug-resistant salmonella serovar Typhi [10,11].

Immunization

Many studies have assessed the cost of hospitalization to be around 10,000 to 100,000 depending upon the complications developed, leading to a substantial financial burden in Asia and justify targeted vaccination. Typhoid Conjugate vaccines (TCVs) have been licenced for use is a single intramuscular dose for children over 6 months of age. Though WHO advisory group has recommended the

use of TCVs in routine immunization programs, and GAVI has supported the same in the countries it is supporting. 'Typbar-TCV' is developed by Bharat Biotech, Hyderabad and procured by UNICEF for some countries. The economics of typhoid burden and economic benefits of vaccination are not fully understood yet and therefore there are not enough evidence for introduction of vaccination in the national programs [12].

Conclusion

The incidence of Enteric Fever in developing countries including India is still pretty high. It is mainly due to the contaminated food & water, males, females & children are all susceptible to the disease. Diagnosis is based on serological tests for want of culture and sensitivity test facilities below district levels and similarly antibiotic therapy is based on empirical treatment.

It can be controlled by heavy investments in adequate sanitation facilities, proper personal & food hygiene practices; safe water supply, avoiding laying of sewage & water supply pipes in towns & cities and inspection of commercial food establishments especially with periodical testing for the servers and cleaners in the Restaurants are the mainstay, WASH Programme should be Strengthened with long-standing investments and sustained political commitment.

Take-Home Messages

- 1) Typhoid fevers with a century-old history, have Rudimentary diagnostic tools in developing country.
- 2) Typhoid fever causes significant morbidity & mortality in developing countries, with inaccurate estimates in countries affected, especially sub-Saharan Africa & Asia.
- 3) Disease burden assessment is limited by the lack of a high degree of sensitivity and specificity by many current rapid Diagnostic tests.
- 4) Most Typhoid-endemic countries employ serological tests that have low sensitivity and specificity making diagnosis unreliable.
- 5) Some of the new technologies, such as PCR & proteomics, may be useful but are difficult for low-resource settings to apply as point-of-care diagnostics.
- 6) Weak laboratory surveillance systems contribute to the spread of multidrug-resistant salmonella serovar Typhi across endemic areas.
- 7) Typhoid Conjugate Vaccines have been licenced recently for targeted vaccination, being supported by GAVI but there is not enough evidence to introduce the vaccination in national immunization programs
- 8) Developing countries led by India should invest in the control of this disease & better diagnostic tool & antibiotic sensitivity test facilities.

9) Sanitation, personal & food hygiene play a major role in reducing the burden of enteric diseases.

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