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ORIGINAL ARTICLE

Clinical Spectrum and Diagnosis of Enteric Fever: A Cross-Sectional Study

AMANULLAH LAIL[1], BISMAH MEMON[2], SHAHID LATIF[3], TAZEEM HUSSAIN[4], MUHAMMAD GHAZI ASAD KHAN[5], SAJID ALI[6]
[1]*Amanullah Lail, Assistant Professor pediatrics, DMC/DUHS Civil Hospital Karachi Pakistan*
[2]*Graduate, Isra University Hyderabad Pakistan*
[3]*General Practitioner, Primary & Secondary Healthcare Department, MOH, Kuwait*
[4]*Consultant Medicine, FM Academy & Department, King Saud Medical City Riyadh. KSA*
[5]*Graduate, Liaquat University of Medical and Health Sciences Jamshoro Pakistan*
[6]*General Practitioner, Primary & Secondary Healthcare Department, MOH, Kuwait*
Corresponding author: Amanullah Lail, Email: aman_lail@yahoo.com

ABSTRACT

Background: Enteric fever is also known as paratyphoid fever or typhoid fever. Approximately 14.3 million cases around the world were due to enteric fever. Typhoid leads to a number of complications as well as mortality. It is a multi-system disease that involves several organs.
Objective: To determine the clinical spectrum and diagnosis of enteric fever.
Study design: A cross-sectional study
Place and Duration: This study was conducted at DMC/DUHS Civil Hospital Karachi from December 2020 to December 2021.
Methodology: All of the participants in this research were aged from 18 years to 75 years. All of the participants had clinically suspected cases of enteric fever because they had a fever for more than 3 days. Blood samples were collected from all the patients. On the sample collected, the IgM antibody test, blood culture, Loop-mediated isothermal amplification, and Widal test were conducted. Moreover, every patient's detailed history, which includes demographics as well as prior medical history, was also obtained. All of the data was gathered using a pre-designed and pre-tested schedule.
Results: There were a total of 80 patients involved in this research. There were 44 females and 36 males. The majority of the participants' ages ranged from 21 years to 30 years. A total of 39 patients were treated as in-patients while 41 patients were treated as out-patients. Most patients had complaints about abdominal pain, headaches, and fever. There were 41 culture-negative patients and 39 culture-positive patients. The mean time period among culture-negative patients was 8.3 days, while it was 8.6 days among culture-positive patients. When blood was obtained between 6 and 10 days of fever, maximum blood culture positivity and maximum Widal positivity were observed.
Conclusion: Widal and blood cultures performed better between 6 and 10 days of fever, whereas IgM performed best in the first 5 days of fever.
Keywords: Enteric fever, adults, Blood C/S, Widal test

INTRODUCTION

Salmonella enterica serovars Typhi and Paratyphi A, B, and C are the causes of Enteric fever [1]. Enteric fever is also known as paratyphoid fever or typhoid fever. Approximately 14.3 million cases around the world were due to enteric fever [2]. This was found by the Global Burden of Disease Study (GBD). According to GBD, approximately 135.9 thousand deaths in 2017 were due to enteric fever [3]. Typhoid leads to a number of complications as well as mortality. It is a multi-system disease that involves several organs [4]. The gold standard for diagnosing enteric fever is a blood culture. In the first week of diagnosis, the sensitivity of the blood culture ranges from 40 percent to 80 percent, and the blood culture is 90 percent [5]. A promising molecular diagnostic method called Polymerase chain reaction (PCR) is 90% sensitive. However, it is costly. There is a serological test called Widal whose specificity ranges from 50% to 92% and whose sensitivity ranges from 47% to 77% [6]. Four Rapid-dot enzyme immunoassays (EIAs), such as Typhidot and IDL Tubex, are immunoassay techniques that find antibodies to a particular antigen of Salmonella Typhi.

The STY2879 gene of S. Typhi is targeted when Loop-mediated isothermal amplification is applied to diagnosis. This option excludes the need for multiple thermal cycles of PCR and is also a good option for rapid diagnosis [7]. Loop-mediated isothermal amplification is a very sensitive diagnostic method for genetic material with low copy counts [8]. A multidrug-resistant (MDR) strain is when typhoidal salmonella is resistant to all these drugs together: co-trimoxazole, chloramphenicol, and ampicillin [9]. Due to the widespread use of cefixime and ceftriaxone, there have been reports of an increasing defervescence time for these antibiotics [10]. There was a study conducted that revealed that 12% of S. Typhi isolates were resistant to ceftriaxone [11].

METHODOLOGY

All of the participants in this research were aged from 18 years to 75 years. All of the participants were clinically suspected of having enteric fever because they had a fever for more than 3 days. Those patients who had some other reason for a fever were not included in this research.

Blood samples were collected from all the patients who were volunteering for this study. Approximately 10 ml of blood was obtained from all participants. A clinical examination of each patient was done. Moreover, every patient's detailed history, which includes demographics as well as prior medical history, was also obtained. All of the data was gathered using a pre-designed and pre-tested schedule. Once the sample was collected, the IgM antibody test, blood culture, Loop-mediated isothermal amplification, and Widal test were conducted. Loop-mediated isothermal amplification assays were first carried out directly from blood samples, and later they were also carried out after 4 hours of blood incubation in blood cultures. The viability of the pathogen was detected when there was an increase in amplified products. Other necessary tests were also conducted.

The case was confirmed when the patient had a constant fever for 3 or more days and S. Typhi organisms (bowel fluid, blood, and bone marrow) were confirmed by the laboratory. This is a clinically compatible case that has been confirmed in the laboratory. A probable case was when the fever lasted for 3 or more days but there was no S. Typhi isolation. Instead, there was a positive diagnosis. This case was confirmed epidemiologically, which is linked to a confirmed case.

10 ml of blood samples were obtained from the participants, and they were mixed with 45 ml of brain heart infusion (BHI) media. These blood culture bottles were incubated for 1-2 days at 37°C. Later, they were sub-cultured on MacConkey agar plates for another day at 37°C. When the organisms were identified, they were incubated on TSI agar for serotyping.

Patients who were not admitted were followed up on alternate days after the completion of the antibiotic course. Those who did not show up for the follow-up were contacted through phone calls. The patients who were admitted were followed up every day until their discharge or antibiotics were completed. The patients' day of fever defervescence was inquired about, and they were checked for any health or medication complications. To analyse the data, t-tests and z-tests were used.

RESULTS

There were a total of 80 patients involved in this research. The majority of the participants were female (n=44), representing 55% of the total sample size. All the patients' ages ranged from 18 years to 75 years. The majority of the participants' ages ranged from 21 years to 30 years. Only 22.5% of patients' ages ranged from 18 years to 20 years. A total of 39 patients were treated as in-patients (48.75%), while the remaining patients were treated as out-patients. Those patients who were not able to take oral antibiotics or were hemodynamically unstable were admitted to the hospital. The time period of fever ranged from 1 day to 30 days, with an average of 10 days. Overall, 15 patients had a fever for more than 2 weeks.

Table 1: shows the presenting complaints of the patients.

Complaints	N	%
Vomiting	13	16.25
Only fever	24	30.00
Diarrhoea	12	15.00
Abdominal Pain	29	36.25
Myalgia	2	2.50
Hematochezia	1	1.25
Headache	24	30.00
Cough	13	16.25

Table number 2 shows the comparison of clinical and laboratory features of culture-positive and culture-negative patients.

Table 2: comparison of clinical and laboratory features of culture-positive and culture-negative patients.

Characteristics	Culture-negative patients (n=41)	Culture-positive patients (n=39)
Transaminitis		
AST>80 U/l	9	12
ALT>90 U/l	11	11
Leukopenia	14	12
ANC<1500 mm3	6/14	7/12
lymphopenia<1000 mm3	2/14	5/12
Anaemia		
Males	9/12	18/25
Females	21/29	7/14
Splenomegaly	12	11

The mean duration of hospitalization was 8.5 days. The mean time period among culture-negative patients was 8.3 days, while it was 8.6 days among culture-positive patients. S. Typhi growth was seen in 80% of the culture-positive patients, while S. Paratyphi growth was seen in the remaining 20%. When blood was obtained between 6 and 10 days of fever, maximum blood culture positivity and maximum Widal positivity were observed. Maximum IgM Typhi point positivity was seen in the first 5 days of fever. Table 3 shows a comparison of the tests conducted.

Table 3: comparison of the tests conducted.

Days of fever	Blood culture (%)	Widal test (%)	IgM Typhi point (%)
≤5	53.33	40	71.43
6-10	57.89	82.35	65
11-15	45.45	50	45.45
>15	0	57.14	28.57

DISCUSSION

In our research, 16.25% of patients had a cough. However, research conducted in Ethiopia revealed that 44.4% of patients had a cough [12]. Just like in other studies, typhoid hepatitis was seen in a large number of patients [13, 14]. According to Crump et al., blood culture positivity was seen in 40% to 87% of patients, which is similar to our research [15]. We have seen a decline in blood culture's ability to identify infections after the first week of fever in numerous earlier investigations [16, 17]. Our results are consistent with those of related research in terms of the high sensitivity, strong negative predictive value, and early detection of IgM Typhi. A recent study by Kaur et al. reported 100% sensitivity and specificity of loop-mediated isothermal amplification in diagnosing typhoid, which is consistent with the findings of our current study [18].

This diagnostic approach has the potential to be used in settings with low resources where cultural facilities are absent due to its equivalent sensitivity and specificity to culture. However, further research is necessary before drawing firm conclusions. The results of our investigation are consistent with recent literature, which shows a decline in initial treatment option resistance and a significant incidence of quinolone resistance among isolates currently in circulation [19]. It is because of the decrease in the use of co-trimoxazole, ampicillin, and chloramphenicol and the increase in the use of quinolones. In the current study, ceftriaxone was typically provided as the initial antibiotic for patients who were admitted. Of them, 31.43% started off with ceftriaxone and azithromycin combination therapy. A total of 45.71% of hospitalized patients received two antibiotics in combination at some point during their care. These results on the application of ceftriaxone and combination therapy are consistent with the research done by Rathod et al. [20].

In this study, Zithromax and cefixime were the two most often recommended medications in the outpatient department (OPD). Azithromycin 1 g/day and cefixime 400 mg twice a day were given as combination therapy to about 11% of the patients. Although the usage of combination therapy was relatively low in our study, the utilization of azithromycin was high, which is consistent with other studies. In our study, the combination of azithromycin 1 g/day and cefixime 400 mg twice daily produced the earliest reduction in fever, with an average of 2.5 days. This shows the possibility of using combination therapy in the near future to treat enteric fever more quickly. To investigate this further, however, larger and better-designed research is required.

CONCLUSION

Leukopenia, anemia, and transaminitis were common among the participants in our research. Widal and blood cultures performed better between 6 and 10 days of fever, whereas IgM performed better in the first 5 days of fever.

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