

ATYPICAL PRESENTATION OF ENTERIC FEVER

Muhammad Umer Zaheer Khan^{*1}, Bashir Ullah¹

¹Department of Medicine Unit 4A BMCH, Quetta.

ARTICLE INFO

Received: 12/06/2024.
Accepted: 21/07/2024.
Published: 25/07/2024.

Keywords:

Atypical Presentation,
Typhoid Fever,
Encephalopathy,
Hepatomegaly,
Neutrophilia.

Author info:

Corresponding Author.

Muhammad Umer
umerzahir@hotmail.com

Citation:

Muhammad Umer Zaheer
Khan, & Bashir Ullah. (2024).
ATYPICAL PRESENTATION
OF ENTERIC FEVER.
Pakistan's Multidisciplinary
Journal for Arts & Science,
5(2), 37– 43.

<https://doi.org/10.5281/zenodo.12818946>

DOI:

<https://doi.org/10.5281/zenodo.12818946>

ABSTRACT

Background: The typical symptoms of typhoid fever include a high temperature, toxemia, constipation during the first week of a fever, complications from encephalopathy, and perforation during the third week. However, the traditional typhoid fever appearance has significantly modified since then. Our purpose is to research typhoid fever's atypical symptoms, such as hepatomegaly, neutrophilia, bone marrow depression, etc.

Material & methods: All patients who fulfilled the inclusion criteria and visited medical unit 4A of Bolan medical complex Hospital Quetta were included. After ethical approval, informed and written consent, a detailed clinical history was acquired, physical examination was done, including liver span, consciousness level and relevant investigations were done to identify bone marrow depression and Neutrophilia.

Result: Total of 513 patients with enteric fever were included. 333 (64.9%) were males & 180 (35.1%) were females with the mean age was 35.17±11.807 years. Atypical presentation of enteric fever was encephalopathy in 20, hepatomegaly in 40, bone marrow depression in 43 and neutrophilia in 77. The association of both age and gender with encephalopathy, hepatomegaly, bone marrow depression, and neutrophilia were not statistically significant, and p-value was > 0.05.

Conclusion: Atypical manifestations do not necessarily mean a worse prognosis in typhoid fever. Patients having high fever presenting with encephalopathy, hepatomegaly, neutrophilia or bone marrow depression in a typhoid endemic area, should be suspected of this disease.

INTRODUCTION

Background

Enteric fever (EF) is categorized as paratyphoid fever and typhoid fever. Typhoid fever is caused by *Salmonella typhi*, but paratyphoid fever is caused by *S. paratyphoid* A, B, and C. Jain S and Das Chugh T. 2013. Around the world, EF is primarily found in developing states, resulting in 16 million infections and 600,000 annual deaths. Dairuki et al.,2015. The greatest estimates available globally indicate that there are a minimum of 16 million new cases of typhoid fever each year, with 600,000 fatalities Harichandran D, Dinesh KR, 2017 and Dutta et al.,2001 and one of the most common diseases among humans globally Hoffner et al.,2000. Fever, abdominal pain, etc. are the early signs of typhoid. However, its presentation and rate of occurrence has been changed in the last few years Muthumbi et al., 2015.

The typical gastrointestinal symptoms of the sickness start to appear within the first week of infection, that include abdomen discomfort and soreness, colicky pain in the right upper quadrant and constipation, which inflames Peyer patches of gut lumen Hatib et al.,2016. Upon advanced stages it causes a dry cough, frontal headache, delirium, and severe malaise Martin 2012.

Salmonella enterica, which causes typhoid fever, is a systemic bacterium having human-specific pathogens transform in their shape and size for survival within the body of the host Yousafzai et al.,2019. The bacterium is genetically positive for the polysaccharide capsular antigen Vi-negative Lin Fy et al.,2000. The protein flagellar antigen Hd, antigens O⁹ and O¹² and the lipopolysaccharide. Although it is common by some strains of *S. enterica* zero type shirsch felid (paratyphoid C), Dublin, and *Citrobacter freundii*, the Vi capsular antigen. *S. enterica* serotype typhi (CT), a multidrug-resistant strain that was first discovered in 1993 in a Vietnamese toddler with typhoid fever in the Mekong Delta, with whole genome sequenced Sinha A Sazawal S and Kumar 1999, Ivanoff B 1995.

The estimated 4599 coding sequences are spread over 4,809,037 base pairs in the CT18 genome. The DNA structure and formation of *enterica* serotype typhimurium LT2, Individuals with typhoid infection get between 1000 and 1 million organisms of the *S. enterica* serotype typhi *S. enterica* strains that are Vi-negative Woodward et al.,1948. The bacteria in the small intestine stick to mucosal cells before invading the mucosa Ivanoff B 1995. The special epithelial cells called M cells, which are situated above Peyer's patches, are likely responsible for internalizing *S. enterica* serotype typhi and transmitting it to the underlying lymphoid tissue Mirza et al.,1996. The liver, spleen, and lymphoid follicles contain nuclear phagocytic cells, which *Salmonella* dwells in and replicates, during the first

week of symptoms, patients typically report to the hospital with fever and chills similar to the flu, as well as a dull frontal headache, anorexia, lethargy, nausea, dry cough, myalgia, and poorly localized abdominal pain Ackers et al.,2000, Black RE et al.,1985.

However, there are typically few visible physical symptoms Hepatomegaly, splenomegaly, a painful abdomen, and a coated tongue are frequent Luby et al.,1998. In endemic regions, bed rest and medicines are used to treat more than 60 to 90 percent of typhoid fever patients Mermin et al., 1999. To prevent death in hospitalized patients, it is important to administer potent antibiotics, provide excellent nursing care, adequate nutrition, pay close attention to the fluid and electrolyte balance, and recognize and treat complications as soon as they arise.

Typhoid is challenging as the majority of health care institutions lack basic facilities related to blood culture, and a majority of patients who were determined to have symptoms of enteric fever are provided treatments as outpatients Luxemburger et al.,2001. According to extensive research, in which fluoroquinolones were given to patients with *S. enterica* serotype typhi infections in randomized, controlled trials showed that fluoroquinolones are the most effective drugs for treating typhoid fever Gasem et al., 2001.

Objective:

- To determine the frequency of atypical presentation of enteric fever.
- To associate age and gender with different symptoms of atypical presentation of enteric fever.

MATERIALS AND METHODS:

Current study was cross sectional descriptive study and done in Bolan Medical Complex Hospital with collaboration with Department of General Medicine Unit IVA, Duration of the study was Six months after approval of synopsis. The sample technique was consecutive sampling. Sample size was **513**, which was determined using the WHO sample size calculator with a 95% confidence level, and the prevalence was 3.1 %. The inclusion criteria of the study were both gender and age ranging from 15 to 65 years with enteric fever > 12 hours. Patients with Hepatitis, Ischemic stroke, Aplastic anemia, and Renal failure was excluded from the study to minimize the bias in the results

DATA COLLECTION PROCEDURE:

Demographic information like name, age, gender was obtained through a pre-designed questionnaire. Informed consent was taken from patients and family. Risks and benefits were explained. Female patients were examined in presence of chaperon (female attendant).



Participants that met the inclusion requirements registered for the current study. A detailed clinical history regarding the atypical features of typhoid fever was taken and the diagnosis of typhoid fever was done on a clinical basis i.e. Oral Temperature above 99.9 Fahrenheit measured by Thermometer with positive blood culture. Complete physical examination of every patient was done including liver span and CNS. With specific investigations to identify bone marrow depression and Neutrophilia. All the information about the patient was kept confidential. The data was analyzed by using SPSS Version 20.0. For quantitative variables such as age, descriptive statistics were used to calculate the mean and standard deviation. For Qualitative Variables, such as gender, frequencies were shown in percentages. To estimate atypical typhoid fever symptoms i.e. encephalopathy, hepatomegaly, bone marrow depression, and neutrophilia, the results were displayed in the form of tables and graphs. Post stratification chia-square test was applied.

RESULT:

A total of 513 patients with enteric fever were selected to conduct this study. The mean age was 35.1 ± 11.8 years. Out of 513 patients, 333 patients were males (64.9%) & 180 patients were females (35.1%). The mean hemoglobin level was 12.5 ± 1.7 g/dl. The mean of White blood cell count (WBC) was 5.7 ± 2.7 /mm³. The mean Platelet count was $246.8 \pm 91.1 \times 10^9$ / liter. In this current study encephalopathy in atypical enteric fever was found in 20 patients with percentage of 3.9, hepatomegaly in 40 patients with percentage of 7.8, bone marrow depression in 43 patients with percentage of 8.4, and Neutrophilia was in 77 patients with percentage of 15, The association of age and gender with encephalopathy, hepatomegaly, bone marrow depression and neutrophilia were shown in Table 2. The association of age with encephalopathy, hepatomegaly, bone marrow depression, and neutrophilia were not statistically significant, and p-value was > 0.05 and also the association of gender with encephalopathy, hepatomegaly, bone marrow depression and neutrophilia were not statistically significant and p-value was >0.05 .

Table-1

Descriptive statistics of Age, Hemoglobin, WBCs and Platelets Level

Gender	Age	Hemoglobin	WBCs	Platelets
Male	333	12	5.9	4.2
Female	180	11	5.1	3.9

Table-2**Association of Clinical Presentation of Enteric Fever with Gender**

Gender	Male	Female	P-value
Encephalopathy	14	6	0.812
Hepatomegaly	23	17	0.910
Bone Marrow Depression	41	44	0.880
Neutrophilia	1020	1025	0.721

DISCUSSION:

The traditional depiction of typhoid diseases has evolved throughout time. The increasingly common atypical appearance nowadays might prevent a clinical diagnosis from being made. In a region where the disease is prevalent, every patient who visits the hospital has already received care. As a result, the sickness' appearance is likely to have changed significantly. In Dutta et al., 2001-study encephalopathy was about 3.1% to all diagnosed enteric patients. while study of Ivanoff et al., 1995 showed that in 3.1% of patients there is early encephalopathy (i.e. during the first week).

These results are very much similar to our study which shows encephalopathy in 3.9% of patients presented with enteric fever. Moreover, typhoid fever typically causes hepatomegaly, with the possible exception of condition that is resistant to several medications⁸. This current study of atypical presentation of enteric fever shows hepatomegaly in 7.8% similar to the finding of Muthumbi et al 2015 study.

In Martin et al., 2012 study 6.1% of patients have encephalopathy and hepatomegaly and have the most frequent symptoms of typhoid fever at early initial second week of the sickness. In current study encephalopathy and hepatomegaly were seen in 4.95% of patients as compared to study which showed both encephalopathy and hepatomegaly in the first 10 days of infection and about 4.4%. In this current study, 8.4% of cases were identified as bone marrow depression as compared to the study of Ivanoff et al., 1995 who observed similar finding in its two publications. A thoroughly designed prospective research done by Ackers et al., 2000 found that 16 (44.5%) out of 36 typhoid fever patients had presented with bone marrow suppression. Similarly, Mirza et al., 1996 found that bone marrow suppression in approximately 6.2% of patients having enteric fever, which is nearly similar to our current study. In this current study, neutrophilia was

noted in 15% cases as compared to Luby et al., 1998 study having (10.4%), of patients with neutrophilia. Similar results were found.

A fourth-generation cephalosporin or a fluoroquinolone is currently the gold standard therapy for enteric fever, especially in states where patients have developed medication resistance. The mortality rate in our cases was 0%. If a case is immediately treated, the case-fatality rate seldom rises over 1%.

In conclusion, "atypical" presentations are increasingly observed. The results are impressive despite the large number of atypical presentations. Typhoid fever should be suspected in individuals who appear atypically with encephalopathy, hepatomegaly, bone marrow depression, neutrophilia, etc. in Pakistan.

CONCLUSION

In typhoid fever, atypical signs do not always indicate a worse prognosis. Typhoid should be suspected in patients with a high fever who also have encephalopathy, hepatomegaly, neutrophilia, or bone marrow depression.

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