

Hematological Changes in Typhoid Fever

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ABSTRACT

Background: Typhoid fever is caused by Gram Negative Rods called Salmonella Typhi and Salmonella Paratyphi. It is largely a disease of developing nations due to poor standards of hygiene. The most prominent feature of the Infection is fever which gradually rises to a high plateau. This infection affect hematological parameters of the patients. We carried this study to determine the changes in various hematological parameters in our study subjects.

Material and Methods: This study was conducted in Nangarhar University Teaching Hospital, Microbiology Department on 100 Patients from 2020 June to 2020 November. The study design was case control .A total of 50 patients (Cases) with confirmed Diagnosis of typhoid fever on the basis of Typhidot (IgG and IgM were seen) enrolled in the study, 50 other healthy people were enrolled in the study as control group that had negative typhidot result and no other complaint. Complete blood count was done for both group (Case and control). Considered hematological parameters includes hemoglobin (Hb), White Blood Cell count (WBC) and Platelet count (PLT). As well interview were done with each patient and a questionnaire were used. Various demographic parameters like sex, age, economic state, education and clinical symptoms were asked. Then collected Data was analyzed with SPSS version 16.

Results. In the current study, A total of 100 patients were enrolled (50 were case, and 50 were control group). The average age of the patients under the study were (Mean±SD) 38.74±15.22 years. The most common hematological changes observed were; Anemia (32%), Thrombocytopenia (24%), Leukocytosis (8%) & Leucopenia (22%). Fever were the most common presenting symptom (78%) and abdominal symptoms were about 38%. Most of the people were of lower socioeconomic status and were Uneducated.

Conclusion: This study shows that typhoid fever is bacterial infection and are acquired by enteral route. This disease commonly affects people of low socio-economical status and those that are un-educated. Fever were the most commonly presenting symptom in these patients. Typhoid fever causes changes in the hematological parameters which is probably due to bone marrow suppression, which is transient and shows response to therapy.

Keywords: *Overseeing, Mechanism, Implementation, Constitution, Model.*

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1. Introduction

Typhoid fever also known as enteric fever, is a potentially fatal multisystem illness caused by a gram negative bacilli (Rods) salmonella typhoid. The Gram-negative bacterium that causes typhoid fever is Salmonella enterica subspecies. enterica serovar Typhi. Based on MLST subtyping scheme, the two main sequence types of the S. Typhi are ST1 and ST2, which are currently widespread worldwide.[1] The global phylogeographical analysis showed dominance of a haplotype 58 (H58) which probably originated in India during late 1980s and now distribution through the world carrying multidrug resistance. [2] A recently suggested and more detailed genotyping scheme has been reported in 2016 and is being used widely since. This scheme re-classified the nomenclature of H58 to genotype 4.3.1 [3] .

Detailed study of enteric fever was presented by Bretonneau (1826) who identified intestinal lesions .The name typhoid fever was given by Louis (1829) to distinguish it from typhus fever. Eberth (1880) described typhoid bacillus [1]. The incidence of typhoid

fever annually and its role in the increasing mortality and morbidity rate is of a great concern as the World Health Organization (WHO) has reported over 25 million typhoid fever cases annually [1].

This strain of Salmonella affects only humans and can be asymptomatic in most cases. The infection is usually acquired through the ingestion of water or food contaminated by the urine or feces of infected carriers [2].

Unlike other strains of Salmonella, no animal carriers of typhoid are known.[3] Humans are the only known carriers of the bacteria [4]. *S. enterica* subsp. *enterica* serovar Typhi is spread through the fecal-oral route from individuals who are currently infected and from asymptomatic carriers of the bacteria[4]. An asymptomatic human carrier is an individual who is still excreting typhoid bacteria in their stool a year after the acute stage of the infection[4].

Symptoms may vary from mild to severe, and usually begin 6 to 30 days after exposure [5, 6]. Often there is a gradual onset of a high fever over several days.[1] This is commonly accompanied by weakness, abdominal pain, constipation, headaches, and mild vomiting[6,7] Some people develop a skin rash with rose colored spots[6]. In severe cases, people may experience confusion[7]. Without treatment, symptoms may last weeks or months[6]. Diarrhea is uncommon [7] other people may carry the bacterium without being affected, but they are still able to spread the disease to others [8] Typhoid fever is a type of enteric fever, along with paratyphoid fever.[9]

Classically, the progression of untreated typhoid fever is divided into four distinct stages, each lasting about a week. Over the course of these stages, the patient becomes exhausted and emaciated[10] In the first week, the body temperature rises slowly, and fever fluctuations are seen with relative bradycardia (Faget sign), malaise, headache, and cough. An epistaxis is seen in a quarter of cases, and abdominal pain is also possible. A decrease in the number of circulating white blood cells (leukopenia) occurs with eosinopenia and relative lymphocytosis; blood cultures are positive for *Salmonella enterica* subsp. *enterica* serovar Typhi. The Widal test is usually negative in the first week[11] In the second week, the person is often too tired to get up, with high fever in plateau around 40 °C (104 °F) and bradycardia (sphygmothermic dissociation or Faget sign), classically with a Dicrotic pulse wave. Delirium can occur, where the patient is often calm, but sometimes becomes agitated.

This delirium has led to typhoid receiving the nickname "Nervous fever". Rose spots appear on the lower chest and abdomen in around a third of patients. Rhonchi (rattling breathing sounds) are heard in the base of the lungs. The abdomen is distended and painful in the right lower quadrant, where a rumbling sound can be heard. Diarrhea can occur in this stage, but constipation is also common. The hepatosplenomegaly and tender, and liver transaminases are elevated. The Widal test is strongly positive, with anti-O and anti-H antibodies. Blood cultures are sometimes still positive at this stage. In the third week of typhoid fever, a number of complications can occur: Intestinal due to bleeding in congested Peyer's patches occurs; this can be very serious, but is usually not fatal. Intestinal perforation in the distal ileum is a very serious complication and is frequently fatal. It may occur without alarming symptoms until septicemia or diffuse peritonitis sets in Encephalitis Respiratory diseases such as pneumonia and acute bronchitis Neuropsychiatric symptoms (described as "muttering delirium" or "coma vigil"), with picking at bedclothes or imaginary objects Metastatic abscesses, cholecystitis, endocarditis, and osteitis The fever is still very high and oscillates very little over 24 hours. Dehydration ensues, and the patient is delirious (typhoid state). One-third of affected individuals develop a macular rash on the trunk. Low platelet count (thrombocytopenia) can sometimes be seen. [12]

Although, reports obtained over time shows that increasing morbidity and decreasing mortality rates have been observed over a few years now. Vaccines are available to aid the prevention of the illness; about 40–90% of typhoid fever cases are preventable for a period of two years using the vaccine, however these data include patients aged 3–44 years which makes it unsuitable for children under 2 years.[13]

Since blood complete is a picture is first to be ordered in any condition, this may provide a clue to the diagnosis. Apart from diagnosis, the hematological manifestations can help in monitoring the response to therapy and disease course. [14] Typhoid fever causes significant hematological changes which could be helpful in diagnosis. Pancytopenia, bicytopenia, unicytopenia are well known hematological manifestations of typhoid fever [15]. Bone marrow findings including marrow aplasia and of hemophagocytosis are also seen [16]

The objective of this study was to assess hematological parameters in patients with typhoid fever. This study may provide direction for further research to determine the prognostic role of hematological parameters.

2. Method and Material

This is a case control study. This study were conducted on OPD patients in Nangarhar university Teaching hospital. All of 100 patients were included in the study (50 were case group and 50 were of control group).

Inclusion Criteria: The age range of case and control groups were between 18 and 70 years. Both sexes were included. Patients with complaints of fever and other related symptoms of typhoid fever were investigated for typhoid. Diagnosis was confirmed

by a typhoidot test for typhoid. All patients diagnosed with typhoidot test were selected as case group and typhoidot negative were selected as control group.

Exclusion Criteria: Patients who had started antibiotic treatment before presenting to our hospital were excluded. Patients suffering from other major systemic illness - history of liver disease, renal disease, hematological disorders, immunocompromised status (drugs/HIV) and or malaria were excluded.

3. Data collection

An informed consent was taken and a detailed Clinical history was taken to rule out the confounding illnesses as listed above and also ask about the symptoms of current illness (typhoid). Information of subjects recruited for the study was obtained by using a questionnaire which contains age, sex, socioeconomic status, education. Symptoms are also asked and are added to the questionnaire. Using 5 ml disposable syringe, 3 ml of venous blood was drawn in from each patient for CBC and typhoidot test. Sample for CBC (complete Blood Count) was collected in EDTA tube. As Nangarhar is endemic for malaria, so a peripheral blood smear was prepared and studied in each case to study the general blood picture and presence of Plasmodium species. Blood were centrifuged and typhoidot test were done for all of them case group were typhoidot positive and control group were typhoidot negative. Also CBC were done for all of them. Collected data were then analyzed and following results are obtained. Anemia was diagnosed by Hb < 12 g/dl, while PLT count < $150 \times 10^9/l$ and WBC count < $4.0 \times 10^9/l$ were used respectively to determine thrombocytopenia and leukopenia.

4. Results

This is a case control study. Which is undergone by 100 subjects {50 of them were typhoid fever positive (case group) and 50 were typhoid fever negative healthy patients (control group)}. The age of patients in case group were (Mean \pm SD) (38.74 \pm 15.22) years. All of them were evaluated by doing blood hematological tests (Hemoglobin, TLC (Total Leukocyte Count), Platelet count, Typhoid fever antibody tests). Demographic parameters, clinical data and laboratory Parameter details were noted and analyzed using SPSS software version 16(SPSS Inc., Chicago, IL, USA).The results of them are as follows.

Table #1: Distribution of patients with Typhoid positive (Case) and Typhoid Negative (Control) in terms of Demographic characteristics.

Variables	Category	Case group(n=50)		Control group(n=50)	
		No. of patients	Percentage (%)	No. of patients	Percentage
Education	Educated	22	44	28	56
	Uneducated	28	56	22	44
Economics	Good	10	20	12	24
	Middle	17	34	18	36
	Low	23	46	20	40
Sex	Male	32	64	30	60
	Female	18	36	20	40

From the above table we conclude that both groups' subjects were having the same demographical parameters. From the case group we finds that 64% of the patients were male or in the other words we can say that male were two times more affected by typhoid fever. Also typhoid fever affected subjects belongs with the lower and middle economic class. In our study we see that uneducated peoples are more affected by typhoid fever.

Table #2: Comparison of clinical parameters among case and control groups.

Variables	Category	Case group(n=50)		Control group(n=50)
		No. of patients	Percentage (%)	No. of patients
Fever	Present	39	78	-
	Absent	11	22	50
Abdominal pain	Present	18	36	-

	Absent	32	64	50
Anorexia	Present	18	36	-
	Absent	32	64	50
Headache	Present	12	24	-
	Absent	38	76	50
Diarrhea	Present	13	23	-
	Absent	37	74	50

The table No-2 shows that all control group subjects had no clinical signs and symptoms, but in case group the results of clinical signs and symptoms are as follows. Fever was the most common presenting symptom in nearly all patients. Abdominal pain and anorexia were also present in about one third cases. Also diarrhea and headache were of the least presenting symptoms.

Table #3: Comparison of the various hematological parameters in both case and control groups

Blood test	Case group(n=50)		Control group(n=50)	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Hemoglobin<12gm/dl	16	32	5	10
WBC count>11000 cells/mm ³	4	8	3	6
WBC count<4000cells/mm ³	11	22	2	4
Thrombocytopenia <1.5 lac	12	24	1	2

Table-3 shows that in typhoid positive patients the anemia were present at 32% patients leukocytosis were more present in comparison to leukopenia, and thrombocytopenia were present at about 24% of patients which had significant difference with control group.

5. Discussion

Enteric fever has high incidence of mortality and morbidity in underdeveloped countries, especially among children [17] the bacilli spread via contaminated food, drink or water. Typhoid fever usually arises due to lack of personal hygiene. It is common in places where there is poor sanitation, but especially where the water supply is liable to be contaminated by human excreta. It is a systemic infection which can present in a multitude of ways. Characteristic presenting features include fever, headache, anorexia, relative bradycardia, diarrhea or constipation and abdominal pain [18] by this reason in our study cases were more in uneducated and of low economic state patients. And in our study also fever is the most common presenting symptom.

Diagnosis of enteric fever is based on clinical suspicion and confirmed by laboratory tests. Enteric fever is a short term febrile illness with few complications and 0.2% risk of mortality with proper treatment [19] in the present study, positive cases were commonly seen in young adults which agrees with the Wasfy et al study [20] In our study group males are more affected than females. This is true in other studies also.

The hematological changes are common in typhoid fever and these include anemia, leucopenia, leukocytosis, thrombocytopenia and sometimes pancytopenia. Bone marrow suppression and hemophagocytosis are considered to be an important mechanism in producing hematological changes [21] in most patient's hemoglobin is normal at the initial stages of the disease, but it declines slowly, by this reason various results are observed in different studies. In our study, 32% patients had anemia, which is concordance with the results shown by Ahmed et al (38%) [12] and Alam (31%) [22] However, lower than observed by Joseph et al (77.8%) and Rasoolinejad. et al (79.4%) [22]. Leukocyte [23] count was normal in most of the patients which is consistent with the earlier reports [24]. Leucopenia is said to be a common hematological finding in typhoid fever. In our study, leucopenia was observed in 22% of cases, whereas the frequency of leucopenia was observed in 18% and 11.2% by Ahmet et al [25] and Rasoolinad et al [8] respectively. Thrombocytopenia was present in 40% cases, a figure higher than reported by other the investigators (10% and 9.1%) [24, 25]

6. Conclusion

From our study, we concluded that typhoid fever is more common in males than women's. And this can be attributed to the fact that a higher level of predisposing factors that cause typhoid fever, occurs more among the male subjects, probably as a result of

their occupational and social practices, this tends to provide a greater immunity to this infection to the male subjects than in women. Typhoid fever is also tend to infect peoples of having low economic status and are uneducated. Fever is the most common presenting symptom and gastrointestinal symptoms are also sometimes present. Typhoid fever causes significant hematological changes in patients. These changes are transient and will respond to antimicrobial therapy.

7. Limitations

- Incomplete resources and small sample size affects research accuracy
- No interest of patients in participating research programs

8. Recommendations

- Further research is required to find hematological associations among positive blood culture patients for typhoid fever
- All patients living in endemic area should be examined for typhoid fever
- Personal hygiene is very necessary for the prevention of typhoid fever

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