

Clinical and Haematological Manifestations of Typhoid Fever in Children in Eastern Turkey

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ABSTRACT

Objective: Typhoid fever can involve various organs, leading to a wide range of presentations: from uncomplicated to complicated typhoid fever. The haematological changes are common in typhoid fever and include anaemia, leucopaenia, thrombocytopaenia and bleeding diathesis. This study was undertaken in order to determine the clinical and haematological presentation of typhoid fever in children.

Methods: In this study, records of children and adolescents with typhoid fever aged under or equal to 16 years, admitted to Yuzuncu Yil University Hospital between 2010 and 2014, were analysed retrospectively.

Results: The cases (56%) were admitted to our hospital in July and October. Major symptoms of patients were abdominal pain (24%), arthralgia (21%) and fever (11%). In our study, decreased mean platelet volume (31%), eosinopaenia (20%), abnormal platelet count (19%), anaemia (16%), leucocytosis (16%) and eosinophilia (12%) were the most common haematological findings in the children.

Conclusions: Typhoid fever is predominant in children at school age with a slight male predominance. Decreased mean platelet volume and abdominal pain might be useful as early diagnostic clues.

Keywords: Child, mean platelet volume, typhoid fever

Manifestaciones Clínicas y Hematológicas de la Fiebre Tifoidea en Niños al Este de Turquía

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RESUMEN

Objetivo: La fiebre tifoidea puede involucrar varios órganos, conduciendo así a una amplia variedad de manifestaciones, que van desde la fiebre tifoidea sin complicaciones a la fiebre tifoidea con complicaciones. Los cambios hematológicos son comunes en la fiebre tifoidea e incluyen leucopenia, trombocitopenia, anemia y diátesis hemorrágica.

Métodos: En este estudio se analizaron retrospectivamente las historias clínicas de niños y adolescentes de edades menores o igual a 16 años, ingresados por fiebre tifoidea en el Hospital Universitario de Yuzuncu Yil, entre 2010 y 2014.

Resultados: Los casos (56%) fueron ingresados a nuestro hospital en julio y octubre. Los síntomas principales de los pacientes fueron dolor abdominal (24%), arthralgia (21%) y fiebre (11%). En nuestro estudio, la disminución del volumen promedio de plaquetas (31%), la eosinopenia (20%), el conteo anormal de plaquetas (19%), la anemia (16%), los leucocitosis (16%) y la eosinofilia (12%) fueron los hallazgos hematológicos más frecuentes en los niños.

Conclusiones: La fiebre tifoidea es predominante en niños en edad escolar, con un ligero predominio masculino. La disminución promedio del volumen de plaquetas y el dolor abdominal pueden ser útiles como pistas para un diagnóstico temprano.

Palabras claves: Niño, volumen promedio de plaquetas, fiebre tifoidea

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INTRODUCTION

Typhoid fever is a common and widely distributed food-borne disease that is a global major public health problem. It affects approximately 21 million people each year, which results in 200 000 to 600 000 deaths annually (1).

Typhoid fever can involve various organs, leading to a wide range of presentations from uncomplicated to complicated typhoid fever involving multiple organs (2). Fever, physical findings and medical history are suggestive but can neither confirm nor exclude typhoid fever (2). Blood culture is the gold standard for diagnosis but this is impeded by the cost of the cultures and administration of prior antibiotics. As such, there is a dependence on alternative forms of diagnosis. The Widal test is commonly used in Turkey (3, 4).

The haematological changes are common in typhoid fever and include anaemia, leucopaenia, thrombocytopenia, bleeding diathesis and subclinical disseminated intravascular coagulation (5). Although these changes are transient and respond favourably to the appropriate antimicrobial therapy, they can lead to potentially life-threatening complications (5).

This study was undertaken in order to determine the clinical and haematological presentation of typhoid fever in children.

SUBJECTS AND METHODS

In this study, records of children and adolescents with typhoid fever aged under or equal to 16 years, and admitted to Yuzuncu Yil University Hospital between 2010 and 2014 were analysed, retrospectively. Patients who were known to have any acute or chronic systemic disease other than typhoid fever were excluded from the study. In addition to personal/family history and physical examination, complete blood count and Widal test of all children were analysed. Over this time period, 99 patients with typhoid fever were diagnosed.

The diagnosis of typhoid fever was made based on a compatible clinical picture with typhoid fever together with positive Widal test titres ($> 1:200$ O antigens) or isolation of *Salmonella typhi* from blood.

Haematological disorders were defined as: anaemia – haemoglobin level of < 11 g/dL, thrombocytopenia – platelet count of $< 150.000/\text{mm}^3$, leucopaenia – leucocyte count of $< 4.000/\text{mm}^3$, leucocytosis – leucocyte count of $> 11.000/\text{mm}^3$, neutropaenia – neutrophil count of $< 1.500/\text{mm}^3$, eosinopaenia – eosinophil count of $< 0.1\%$, low mean platelet volume (MPV) – MPV of < 7.4 fL and elevations in MPV – MPV of > 10.4 fL.

RESULTS

In this study, 99 patients (52 males, 47 females) with typhoid fever were analysed. The male/female ratio was 1:1 and the mean age was 10.6 ± 4.2 years (range: 1–16 years). Ten (10%) patients were 0–4 years of age, 35 (35%) were 5–10 years of age and 54 (55%) were 11–16 years of age. The cases (56%) were admitted to our hospital in July and October. The distribution of typhoid fever in the spring, summer, autumn and win-

ter was 12.1%, 31.3%, 46.5% and 10.1%, respectively. The seasonal distribution of cases is shown in the Figure.

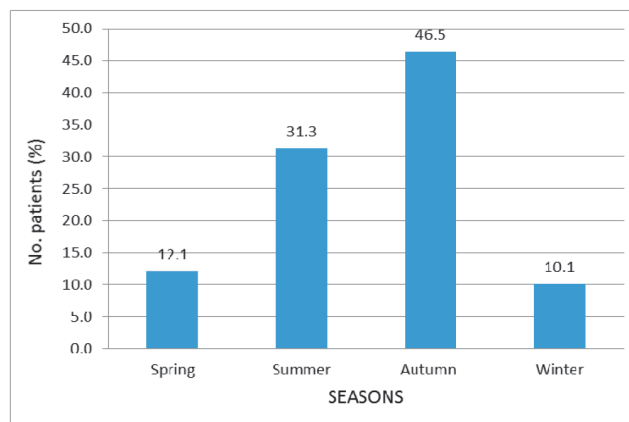


Figure: Seasonal distribution of cases.

Major symptoms of patients were abdominal pain (24%), arthralgia (21%), fever (11%), headache (9%) and malaise (4%). The most frequent clinical findings were peripheral arthritis (3%), hepatomegaly (2%) and splenomegaly (2%). The main clinical symptoms, findings and their frequency are demonstrated in Table 1.

Table 1: The clinical symptoms and findings of typhoid fever cases

Clinical symptoms and findings	No. of patients
Symptoms	
Abdominal pain	24
Arthralgia	21
Fever	11
Headache	9
Malaise	4
Dizziness	4
Diarrhoea	3
Sore throat	3
Nausea and vomiting	2
Loss of appetite	2
Fatigue	1
Drowsiness	1
Weight loss	1
Findings	
Peripheral arthritis	3
Hepatosplenomegaly	2
Cardiac souffle	2
Eruption	1

In our study, low MPV (31%), eosinopaenia (20%), abnormal platelet count (19%), anaemia (16%), leucocytosis (16%) and eosinophilia (12%) were the most common haematological findings in the children. Anaemia was present in 16 (16%) patients; haemoglobin presented as $6.8\text{--}16.4$ g/dL (12.6 ± 4.5 g/dL). Three (3%) patients had a leucocyte count below 4.5×10^9 cells/dL. Eight (8%) patients had neutropaenia (ANC $< 1500 \times 10^6$ cells/dL), 14 (14%) patients had lymphopaenia (lymphocyte $< 1500 \times 10^6$ cells/dL), 12 (12%) patients had

eosinophilia (eosinophil count $> 0.4 \times 10^9$ cells/dL) and 20 (20%) patients had eosinopaenia (eosinophil count $< 0.1 \times 10^9$ cells/dL).

Platelet count ranged from $35\text{--}1057 \times 10^9/\text{L}$ ($311.8 \pm 139.1 \times 10^9/\text{dL}$). Nineteen (19%) patients had an abnormal platelet count: 3 (3%) had thrombocytopenia (platelet count $< 150 \times 10^9/\text{L}$), while 16 (16%) had thrombocytosis (platelet count $> 450 \times 10^9/\text{dL}$).

Mean platelet volume was between 5.9 and 12 fL (8.1 ± 0.9 fL). Thirty-one (31%) patients had decreased MPV (MPV < 7.4 fL), two (2%) patients had increased MPV (MPV > 10.4 fL) and one of the children (1%) had pancytopenia.

The erythrocyte sedimentation rate (ESR) was considered high (above 20 mm in one hour) in 25 cases (25%). Examination for C-reactive protein (CRP) was performed in 30 cases (30%). Initial haematologic and serologic findings are listed in Table 2.

Typhoid fever in children under five years of age is uncommon and subclinical (11). Singh *et al* (12) found that the typhoid fever cases were seen most frequently in children between six and 10 years, followed by 11–16 years, and least frequently in children below five years of age. Among the study population, 81% were children at school age (12). In this study, 10% ($n = 10$) of patients with typhoid fever were under five years, and the most affected group 90% ($n = 89$) were school children, which was close to figures of other studies (13, 14). High prevalence in 5–16-year old children may be attributed to poor hygienic conditions, eating and drinking outside the home from street vendors and consuming creams and beverages which are prepared under unhygienic conditions.

The maximum prevalence of typhoid fever was recorded in summer and autumn while it was minimal in the winter season. A total of 31 ($n = 99$) patients were found serologically positive with 31% prevalence in summer as compared to 10%

Table 2: Initial laboratory findings of typhoid fever cases

Laboratory examination	n	%	Range	Mean values \pm SD	No. of performed test cases
Haematologic parameters					
Anaemia (Hb g/dL)	16	16	6.8–16.4	12.6 ± 4.5	99
Leucocytosis ($10^3/\mu\text{L}$)	16	16	2.9–20.1	8.1 ± 4.1	99
Thrombocytopenia ($10^3/\mu\text{L}$)	3	3.0	35–1057	311.8 ± 139.1	99
Leucopaenia ($10^3/\mu\text{L}$)	3	3.0	2.9–20.1	8.1 ± 4.1	99
Lymphopaenia ($10^3/\mu\text{L}$)	14	14	6.4–77.6	35.9 ± 19.3	99
Neutropaenia ($10^3/\mu\text{L}$)	8	8	0–1.5	0.5 ± 0.4	99
Eosinophilia ($10^3/\mu\text{L}$)	12	12	0–2.5	0.5 ± 0.4	99
Eosinopaenia ($10^3/\mu\text{L}$)	20	20	0–0.1	0.075 ± 0.04	99
High MPV (> 10.4 fL)	2	2.0	5.9–12	8.4 ± 3.8	99
Low MPV (< 7.4 fL)	31	31	5.9–12	8.4 ± 3.8	99
Pancytopenia	1	1.0			99

Hb: haemoglobin; MPV: mean platelet volume

DISCUSSION

Typhoid fever is a major public health problem in developing countries (6). The highest prevalence is among infants, children and adolescents, where poor sanitation and food handling practices continue to make typhoid a persistent public health issue (1). A number of factors ranging from poor nutrition, endotoxaemia and altered immune response have been incriminated in the causation of various complications (7). Endotoxins, even if not sufficiently released into circulation, may act locally in the liver, spleen and other reticuloendothelial organs to produce changes in the haematological profile (8).

Various haematological manifestations like anaemia, leucopaenia and thrombocytopenia have been observed in cases of typhoid fever but these are self-limited (5).

Typhoid fever was more common in the male population than in the female population (9). Ganesh *et al* found that the male-to-female ratio was 1:2 (10). In our study, the male/female ratio was 1:1.

($n = 10$) in winter. In congruence with seasonality patterns elsewhere, the peak occurrence was reported in summer months in other studies (15, 16).

Typhoid fever is among the most common febrile illnesses in developing countries. The advent of antibiotic treatment has led to a change in the presentation of typhoid, and the classic mode of presentation of a slow and “stepladder” rise in fever and toxicity is rarely seen (17). Typhoid fever has multisystem involvement but the commonest system to be involved is the gastrointestinal system (2). Children in this study group commonly presented with abdominal pain, 24% ($n = 24$), arthralgia, 21% ($n = 21$), fever, 11% ($n = 11$) and headache, 9% ($n = 9$).

Several haematological abnormalities like anaemia, leucopaenia, leucocytosis, thrombocytopenia and eosinopaenia have been observed in cases of typhoid fever, but these are self-limited (2). Leucopaenia, eosinopaenia, thrombocytopenia and anaemia in typhoid fever can be attributed to the myeloid maturation arrest, decrease in the number of erythroblasts and megakaryocytes and increased phagocytic activity of histio-

cytes in the bone marrow (8). Leucopaenia is said to be a common haematological finding in typhoid fever. In this study, leucopaenia was observed only in 3% of the cases, whereas the frequency of leucopaenia was observed in 4%, 6.6% and 11.2% by Abro *et al*, Ahmet *et al* and Rasoolinejad *et al*, respectively (2, 12, 18, 19). Singh *et al* (12), in their study, found that 72.5% (n = 100) had normal total leukocyte counts, only 11.5% (n = 16) of cases had leucopaenia and 16% (n = 22) of cases had leucocytosis. In our study, it was found that 80% had normal total leukocyte counts and leucocytosis was found in 16% of the cases. Neutropaenia in typhoid fever has been attributed to increased margination and defective granulopoiesis (20). Qamar (21) found neutropaenia in 48 (32%) patients and lymphopaenia in 12 (8%) patients. In our study, neutropaenia was found in eight (8%) patients and lymphopaenia in 14 (14%) patients.

Normocytic normochromic anaemia is most commonly found in typhoid fever (22). Anaemia was probably related to toxemia, haemolysis, or less often to intestinal haemorrhage. Anaemia in typhoid fever does not need to be treated energetically since it is related to endotoxaemia and improves during recovery (8). The prevalence of anaemia varies greatly according to different reports and has been found in 28% to 38% of newly diagnosed patients with typhoid fever (4, 23). In our study, of the 99 children with typhoid fever, 16 (16%) had anaemia.

Eosinopaenia has been reported in typhoid fever by previous investigators, similar to our series where 20% of children had eosinopaenia (10).

Prevalence of thrombocytopenia in typhoid fever is about 2% to 15% (2, 24, 25). In our study, thrombocytopenia was found in 3% of patients. Mean platelet volume has recently been recognized as an inflammatory marker in various conditions such as ulcerative colitis, chronic hepatitis B and diabetes (26). While some studies demonstrated a negative correlation between MPV and inflammatory activity, other investigators have reported an association between increased MPV and disease severity (26, 27). In our series, we found that 31 (31%) patients had a decreased MPV and two (2%) patients had increased MPV.

In conclusion, typhoid fever is predominant in children at school age with a slight male predominance. Most of the cases were admitted in July and October. Decreased MPV and abdominal pain might be useful early diagnostic clues. Haematological parameters can be employed in the effective diagnosis of typhoid fever and can provide a reliable and earlier diagnosis, thus leading to an early and timely management of the condition.

AUTHORS' NOTE

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