Research Article

Study of leukocyte profile in patients of fever with splenomegaly

Khushboo Garg[1], Anju Bharti[2], Sandip Kumar[2], Lalit Prashant Meena[1], Jaya Chakravarty[1], Madhukar Rai[1]

[1]Department of General Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India, [2]Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

Correspondence to: Lalit Prashant Meena, E-mail: drlalitmeena@gmail.com

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ABSTRACT

Background: There are many different possible etiologies of fever with splenomegaly; few patients with prolonged fever will remain undiagnosed despite an intensive diagnostic work-up. The presence of splenomegaly in patients with fever narrows down the differential diagnosis. **Objectives:** The objectives of this study were as follows: (I) To evaluate the causes of fever with splenomegaly and (II) to study the leukocyte profile which includes pattern of total leukocyte count and differential leukocyte count (DLC) in various diseases presenting as fever with splenomegaly. **Materials and Methods:** A total of 100 patients with fever and splenomegaly were included in the study. Complete hematological study such as complete blood count provided with main focus on total leukocyte count and DLC including neutrophil, basophil, eosinophil, lymphocyte, and monocyte and peripheral blood smear to especially note the morphology of white blood cells (WBCs) and to determine their relative percentage in blood. **Results:** A total of 100 patients of fever with splenomegaly with male and female ratio of 1.7:1 were included in the study. While considering age-wise distribution, the highest percentage of cases was fell in the age group of 21–30 years. Infectious causes constituted 55% of cases, followed by hematological malignancies constituting 33% of cases. Other causes included 12% of cases. Kala-azar was the most common cause of fever with splenomegaly in our study followed by malaria and acute myeloid leukemia. Pancytopenia was found in 29% of cases and followed by 38% of bicytopenia cases in our study. About 32% of cases presented with normal total leukocyte count, 39% of cases showed leukopenia, and 29% of cases showed leukocytosis. Leukopenia was commonly found in kala-azar followed by hypersplenism. Neutropenia was most commonly present in kala-azar. **Conclusion:** This study helps in understanding the distribution of leukocyte count and DLC pattern in various diseases presented as fever with splenomegaly and also the variable presenting signs and symptoms of these diseases so that the patients of fever with splenomegaly investigated and treated in a proper manner.

KEY WORDS: Leucocyte; Splenomegaly; Fever

INTRODUCTION

There are many different possible etiologies of fever with splenomegaly, most commonly infectious, but neoplastic and inflammatory or autoimmune disorders may also be a possibility. Some patients with prolonged fever will remain undiagnosed despite an intensive diagnostic work-up. The presence of splenomegaly in patients with fever narrows down the differential diagnosis, for example, infectious causes such as bacterial (typhoid fever, *Mycobacterium tuberculosis* [disseminated tuberculosis (TB)], AIDS, etc.), fungal (histoplasmosis), parasitic (malaria and leishmaniasis), and viral (infectious mononucleosis, i.e., Epstein–Barr virus and cytomegalovirus, and hepatitis). Hematologic causes such as leukemia (acute, chronic, lymphoid, and myeloid) and lymphoma and other causes.[1] Leukocyte count number and distribution have varied presentation in different diseases.[2,3] The pattern of leukocyte distribution in a particular

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geographical area may provide a direction to investigate the patients in a proper manner. Hence, the main focus of our study is on the study of leukocyte profile which includes pattern of total leukocyte count and differential leukocyte count (DLC) in various diseases presented as fever with splenomegaly.

Objectives

The objectives of this study were as follows:

I. To evaluate the causes of fever with splenomegaly and
II. To study the leukocyte profile which includes pattern of total leukocyte count and DLC in various diseases presenting as fever with splenomegaly.

MATERIALS AND METHODS

The study conducted from November 2016 to June 2018 in the Department of General Medicine in collaboration with the Department of Pathology and Department of Community Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi (Uttar Pradesh). A total of 100 patients fulfilling the inclusion criteria, i.e., (a) confirmed diagnosed cases of fever (history and recorded) with splenomegaly (palpable/radiologically detected spleen) and (b) patients more than 12 years of age and given informed written consent were included in the study. The study was approved by the ethical committee of institute. Patients below 12 years of age and those who do not give consent were excluded from the study. All the patients were subjected to thorough physical examination including the relevant clinical history. Palpable spleen graded from Grade 0 to V on the basis of Hackett's classification which is the WHO accepted.[4] Grades I and II were considered as mild splenomegaly, Grade III as moderate splenomegaly, and Grades IV and V as massive splenomegaly. Complete hematological study like complete blood count provided with main focus on total leukocyte count and DLC including neutrophil, basophil, eosinophil, lymphocyte and monocyte, and peripheral blood smear to especially note the morphology of WBCs and to determine their relative percentage in blood. According to provisional diagnosis on the basis of history and clinical examination, patient was investigated further for the cause which includes liver function test, renal function test, blood culture and sensitivity, sputum microscopy, *Leishmania donovani* bodies in bone marrow aspirate, rapid antibody-based kit test for malaria, RK-39 kit test, typhi-dot test, Leptocheck test, immunoglobulin M (IgM) anti-hepatitis A virus and IgM anti-hepatitis E virus, and others. Bone marrow aspiration/biopsy, lymph node biopsy and flow cytometry were performed in selective cases.

Statistical Analysis

All data were recorded, compiled, and statistically analyzed on SPSS for Window (version 16) using *t*-test, *Z*–test, and χ^2-test considering $P < 0.05$ as statistically significant.

RESULTS

A total of 100 patients of fever with splenomegaly with male and female ratio of 1.7:1 were included in the study. While considering age-wise distribution, the highest percentage of cases was fell in the age group of 21–30 years. Hackett's Grade I splenomegaly was present in 20% of patients, Grade II was present in 44% of patients, Grade III in 25% of patients, and Grades IV and V in 11% of patients. Massive splenomegaly, i.e., Hackett's Grades IV and V was present in only 11% of cases [Table 1]. Infectious causes constituted 55% of cases, followed by hematological malignancies constituting 33% of cases. Other causes included 12% of cases [Table 2]. Hypersplenism was present in 7% (n = 7) of cases, of which four cases were diagnosed as chronic liver disease and three cases were remain undiagnosed on evaluation. Kala-azar was the most common cause of fever with splenomegaly in our study followed by malaria and acute myeloid leukemia (AML). Generalized weakness was present in majority of cases of fever with splenomegaly. Altered sensorium was present in five cases of malaria and in one case of disseminated TB due to tubercular meningitis. The left upper quadrant heaviness was present in 24 cases due to massive splenomegaly. Weight loss present in 16 cases mostly comprised lymphomas and chronic infections such as TB. Pallor was the most common physical finding in cases of fever with splenomegaly. Icterus was present in 13 cases, of which nine cases were of malaria. The 18 cases showed lymphadenopathy mostly constituted by lymphomas (n = 11) followed by disseminated TB (n = 4). Hepatomegaly was found in 40 cases constituted by 18 cases of infections and 16 cases of hematological malignancy (leukemia and lymphoma). Pancytopenia was found in 29% of cases and followed by 38% of bicytopenia cases in our study. In 30% of cases, there was only single lineage involvement constituted by 27% of anemia, 1% of leukopenia, and 2% of thrombocytopenia. About 32% of cases presented with normal total leukocyte count, 39% of cases showed leukopenia, and 29% of cases showed leukocytosis. Leukopenia was commonly found in kala-azar (n = 14) followed by hypersplenism (n = 7). Of nine cases of Hodgkin's lymphoma (HL), four cases present with leukocytosis. In DLC, 33% of cases showed normal neutrophil count, 25% of cases showed neutrophilia, and 32% of cases showed neutropenia. Neutropenia was most commonly present in kala-azar. About 52% of cases normal lymphocyte count on DLC, 15% of cases showed lymphocytosis mostly present in hematological malignancies, and 33% of cases showed lymphopenia, of which most cases were of disseminated TB. Monocytosis was present in 25% of cases. Eosinophilia and basophilia were present in 5% and 6% of cases, respectively, mostly in cases of chronic myeloid leukemia (CML) [Tables 3 and 4].

DISCUSSION

The pattern of leukocyte distribution in cases of fever with splenomegaly in a particular geographical area may provide

Table 1: Grading of spleen in broad categories of various etiologies of fever with splenomegaly

Etiology	Hackett's grade			
	I (*n*=20) N (%)	II (*n*=44) N (%)	III (*n*=25) N (%)	IV and V (*n*=11) N (%)
Infections (*n*=55)	10 (50.0)	23 (52.3)	16 (64.0)	6 (54.5)
Hematological malignancy (*n*=33)	7 (35.0)	17 (38.6)	5 (20.0)	4 (36.4)
Others (*n*=12)	3 (15.0)	4 (9.1)	4 (16.0)	1 (9.1)

Table 2: Distribution of causes of fever with splenomegaly in broad categories in our study

Infection	N (%)	Hematological malignancy	N (%)	Others	N (%)
Kala-azar	17 (31.0)	Acute myeloid leukemia (AML)	14 (42.4)	Hypersplenism	7 (58.3)
Malaria	14 (25.4)	Acute lymphoid leukemia (ALL)	1 (3.03)	Systemic Lupus erythematous	3 (25.0)
Disseminated tuberculosis	12 (21.8)	Chronic myeloid leukemia (CML)	4 (12.1)	Adult-onset Still's disease	1 (8.3)
Typhoid	3 (5.45)	Chronic lymphocytic leukemia (CLL)	3 (9.0)	Hemophagocytic lymphohistiocytosis	1 (8.3)
Leptospirosis	2 (3.63)	Hodgkin's lymphoma (HL)	9 (27.2)		
Infective endocarditis	2 (3.63)	Non-Hodgkin's lymphoma (NHL)	2 (6.0)		
Splenic abscess	2 (3.63)				
Viral hepatitis	1 (1.82)				
Tropical splenomegaly syndrome	2 (3.63)				
Subtotal	55		33		12
Grand total					100

Table 3: Total leukocyte count in various causes of fever with splenomegaly

Causes	Total (*n*=100)	Leukopenia N (%)	Normal leukocyte count N (%)	Leukocytosis N (%)
Kala-azar	17	14 (82.4)	3 (17.6)	-
Malaria	14	4 (28.6)	7 (50)	3 (21.4)
Disseminated tuberculosis	12	4 (33.3)	7 (58.3)	1 (8.4)
Typhoid	3	2 (66.7)	1 (33.3)	-
Leptospirosis	2	-	-	2 (100.0)
Infective endocarditis	2	-	1 (50.0)	1 (50.0)
Splenic abscess	2	-	1 (50.0)	1 (50.0)
Viral hepatitis	1	-	1 (100.0)	-
Tropical splenomegaly syndrome	2	2 (100.0)	-	-
Acute myeloid leukemia	14	-	5 (35.7)	9 (64.3)
Acute lymphoid leukemia	1	-	-	1 (100.0)
Chronic myeloid leukemia	4	-	1 (25.0)	3 (75.0)
Chronic lymphocytic leukemia	3	-	-	3 (100.0)
Hodgkin's lymphoma	9	2 (22.2)	3 (33.3)	4 (44.4)
Non-Hodgkin's lymphoma	2	1 (50.0)	1 (50.0)	-
Hypersplenism	7	7 (100.0)	-	-
Systemic lupus erythematosus	3	2 (66.6)	1 (33.3)	-
Adult-onset Still's diseases	1	-	-	1 (100.0)
Hemophagocytic lymphohistiocytosis	1	1 (100)	-	-

a direction to investigate the patients in a proper manner. In our opinion, none of the study related to leukocyte profile in patients of fever with splenomegaly is conducted previously. However, the studies related to leukocyte count number and distribution in different diseases taken in our study are done previously in India and other western countries. Here, the current study on 100 patients having fever with splenomegaly was conducted to analyze the various etiologies of fever with splenomegaly and the study of leukocyte profile which includes pattern of total leukocyte count and DLC. The resulting statistical data obtained were consolidated and compared with pre-existing studies.

In our study, infectious causes constituted 55% of cases, followed by hematological malignancies constituting 33% of cases. Other causes which include cases of hypersplenism,

Table 4: Study of differential leukocyte count in various causes of fever with splenomegaly

Causes	Total (*n*=100)	Neutropenia N (%)	Neutrophilia N (%)	Lymphopenia N (%)	Lymphocytosis N (%)	Monocytosis N (%)	Eosinophilia N (%)	Basophilia N (%)
Kala-azar	17	13 (76.5)	1 (5.9)	8 (47.1)	-	-	-	-
Malaria	14	2 (14.3)	3 (21.4)	4 (28.6)	-	3 (21.4)	-	-
Disseminated tuberculosis	12	2 (16.7)	1 (8.3)	10 (83.3)	-	2 (16.7)	-	-
Typhoid	3	2 (66.7)	-	-	-	-	-	-
Leptospirosis	2	-	2 (100)	-	-	-	-	-
Infective endocarditis	2	-	1 (50)	-	-	-	-	-
Splenic abscess	2	-	1 (50)	-	-	-	-	-
Viral hepatitis	1	-	-	-	1 (100)	1 (100)	-	-
TSS	2	2 (100)	-	1 (50)	-	-	-	-
AML	14	3 (21.4)	5 (35.7)	-	5 (35.7)	10 (71.4)	-	1 (7.1)
ALL	1	-	1 (100)	-	1 (100)	1 (100)	-	0 (0.0)
CML	4	-	3 (75)	-	3 (75)	4 (100)	3 (75)	4 (100)
CLL	3	1 (33.3)	2 (66.7)	-	3 (100)	2 (66.7)	-	-
Hodgkin's lymphoma	9	-	4 (44.4)	2 (22.2)	2 (22.2)	2 (22.2)	1 (11.1)	-
Non-Hodgkin's lymphoma	2	1 (50)	-	-	-	-	-	-
Hypersplenism	8	5 (71.4)	-	5 (71.4)	-	-	-	-
SLE	3	1 (33.3)	-	2 (66.6)	-	-	-	-
Adult-onset Still's disease	1	-	1 (100)	-	-	-	1 (100)	1 (100)
HLH	1	-	-	1 (100)	-	-	-	-

AML: Acute myeloid leukemia, ALL: Acute lymphoid leukemia, CML: Chronic myeloid leukemia, CLL: Chronic lymphocytic leukemia, HL: Hodgkin's lymphoma, NHL: Non-Hodgkin's lymphoma, SLE: Systemic lupus erythematosus

systemic lupus erythematosus (SLE), adult-onset Still's disease, and hemophagocytic lymphohistiocytosis constituting 12% of cases. Agarwal and Mittal study on 50 patients with splenomegaly found that the infections were the most common cause of splenomegaly in adults followed by hematological causes. Hypersplenism was found in 8% of cases in this study mostly due to liver cirrhosis.[4] Among 55 cases of infectious etiology, kala-azar constituted 17 (31%) cases followed by 14 (25.4%) cases of malaria and 12 (21.8%) cases of disseminated TB and others. In 33 cases of hematological malignancy, majority of cases were acute leukemia, i.e., 15 cases (14 AML and 1 acute lymphoid leukemia [ALL]) followed by 11 cases (9 HL and 2 non-HL [NHL]) of lymphomas and 7 cases (4 CML and 3 chronic lymphocytic leukemia [CLL]) of chronic leukemia. Agarwal and Mittal study on 50 patients with splenomegaly found that the malaria was the most common cause among infections and acute leukemia among hematological causes. As eastern Uttar Pradesh is also an endemic zone for visceral leishmaniasis, kala-azar is the most common cause of fever with splenomegaly in our study. Among 12 cases of TB in our study, majority of patients (58.3%) shows normal leukocyte count, 4 cases (33.3%) show leukopenia, and 1 case (8.4%) had leukocytosis. In DLC, one case had neutrophilia and two cases show monocytosis. Pancytopenia presents in two cases. Yaranal *et al*. study to evaluate the hematological parameters in 100 patients of TB shows that, in spite of the infection, 71 patients had a normal leukocyte count. Leukocytosis as a response to infection was observed in 26 patients and three patients had leukopenia. Patients with leukocytosis mostly had neutrophilia and some had monocytosis.[5] Two patients had pancytopenia. Sinha *et al*. study in 20 cases of disseminated TB showed that leukocytosis with neutrophilia was present in 52.5% of patients and none of patients had monocytosis. Moreover, the leukopenia was seen in 47% of patients.[6] The present study showed leukocytosis in both cases of leptospirosis. Adiga *et al*. in patients with leptospirosis showed the mean total leucocyte counts rise till day 2 in mild illness and up to day 5 in severe illness.[7] De Silva *et al*. study in patients with leptospirosis found leukocyte counts and absolute neutrophil counts showed a decline over the first 5 days of illness and on day 3 of fever, the majority of patients had normal leukocyte counts and leukopenia was an uncommon finding.[8] Among three cases of typhoid in our study, two cases had leukopenia and one case had normal total leukocyte count. Neutropenia was present in two cases. Rasoolinejad *et al*. study in typhoid patients showed that leukocyte count was normal in most of the

patients.[9] Leukopenia is said to be a common hematological finding in typhoid fever by the previous studies of Ahmed *et al*. and Rasoolinejad *et al*.[9,10] Bone marrow suppression and hemophagocytosis are considered to be an important mechanism in producing hematological changes.[11] In cases of infective endocarditis, anemia and leukocytosis with neutrophilia present in one case of two cases. Baddley *et al*. study reported anemia in 79–90% of cases and leukocytosis in 20–30% of studied cases of infective endocarditis. In our study, both the cases diagnosed on the basis of modified Duke criteria. *Staphylococcus aureus* grown on blood culture in both the cases.[12]

In our study, malaria cases clinically presented with varied presentation such as icterus, cough, altered sensorium, pain abdomen, pallor, hepatomegaly, and pedal edema. Among 14 cases of malaria in our study, majority of cases (50%) shows normal leukocyte count, leukocytosis present in 3 (21.4%) cases, and 4 (28.6%) cases had leukopenia. In DLC, neutrophilia was present in 3 (21.4%) cases, neutropenia in 2 (14.3%) cases, lymphopenia in 4 (28.6%) cases, and monocytosis in 3 (21.4%) cases. Four cases had pancytopenia. Lathia and Joshi and Wickramasinghe and Abdalla studies showed that the decrease in lymphocyte counts associated with malaria is due to reflect redistribution of lymphocytes with sequestration in the spleen.[13,14] Akhtar *et al*. conducted a study on hematological changes in malaria found that some patients had monocytosis and neutrophilia.[15]

Tesfaye *et al*. conducted a study to assess hematological abnormalities in 414 visceral leishmaniasis patients found that 95.4% of patients shown leukopenia, 90.1% showed neutropenia, and 37.9% showed lymphopenia. In our study, 17 cases of kala-azar were present, of which 82.4% of cases showed leukopenia, 17.6% of cases showed normal leukocyte count, 76.5% showed neutropenia, and 47.1% showed lymphopenia. Pancytopenia present in 70.5% of patients of our study.[16] Hamid and Gobah conducted a study in 64 kala-azar patients showed that the presence of peripheral pancytopenia was in 70.3% of patients, while the remaining patients had anemia plus either leukopenia or thrombocytopenia.[17] Among cases of HL, according to Ann Arbor staging system, majority of patients were in Stage III. On histopathological examination of lymph node biopsy, mixed cellularity type was present in most of the studied cases. In nine cases of HL, leukocytosis and leukopenia were present in four and two cases, respectively. Neutrophilia was present in four cases, monocytosis in two cases, and lymphopenia in two cases. One case had eosinophilia. Reid *et al*. study showed that neutrophilia and lymphopenia are sometimes seen in Hodgkin's lymphoma patients, with the latter having a poor prognosis.[18] Samoszuk and Nansen study found that the eosinophilia present in HL patients is related to the production of interleukin-5 by the tumor cells.[19] Conlan *et al*. found that the survival in NHL patients was not affected by the presence of leukopenia or mild leukocytosis, but, in patients without marrow lymphoma, leukocytosis with a leukocyte count >20 × 10^9/L was associated with short survival length.[20] Bloomfield *et al*. study showed a significant increase in total WBCs, neutrophils, and monocytes of the NHL and a significant decrease in lymphocytes and eosinophils. These increased white cells could elicit the production and release of cytokines and chemokines which will affect the prognosis of the malignancy.[21] In our study, of two cases of NHL, none of the patient had leukocytosis. One patient had normal leukocyte count and the other one had leukopenia with neutropenia. Among 14 cases of AML included in our study, all patients had fever, generalized weakness, and splenomegaly. Bleeding manifestations such as gum bleeding and gastrointestinal bleeding were present in 4 cases (28.5%) associated with extreme degree of leukocytosis and thrombocytopenia and with coagulopathy as associated with monocytic type of AML. Chang *et al*. study in 107 patients of AML found that the clinically majority of the patients 81% presented with fever, pallor, and weakness, weight loss in 53 patients (49%), bleeding and swollen gums in 13% patients, and hepatosplenomegaly in only 15 (14%) of patients. In the above-mentioned study, majority of patients of AML showed leukocytosis accounting to 84.1%, while 6.5% had leukopenia.[22] In our study, of 14 cases of AML, 64.3% off cases showed leukocytosis and 35.7% of cases had normal leukocyte count. Anemia and thrombocytopenia were present in all 14 cases. One young male patient presents in our study diagnosed as acute lymphoblastic leukemia presented with generalized weakness and hepatomegaly along with fever and splenomegaly. In complete blood count, total leukocyte count was raised with neutrophilia, lymphocytosis, and monocytosis in DLC. Pahloosye *et al*. study in 100 patients with ALL found that 25% had abnormal WBC count at presentation, 37% had leukopenia, and 38% had leukocytosis. WBC count was above 50,000/mm^3 in 22% of cases.[23]

Of four cases of CML in our study, three were male. In clinical presentation, anemia (100%), hepatomegaly (50%), left upper quadrant heaviness (50%), and weight loss (25%) were present in CML patients. Three of four cases of CML in our study had leukocytosis. Basophilia and eosinophilia present in majority of cases. Two patients were in blast crisis, one patient in accelerated phase and one patient in chronic phase of CML. Patients presented in blast crisis and accelerated phase had severe anemia. The splenic size, duration of illness, and phases of CML correlate with severity of anemia at the time of diagnosis. Thrombocytopenia and thrombocytosis were present in one case each and the other two cases had normal platelet count. Korubo *et al*. study in 105 CML patients reported that all of the patients had leukocytosis and anemia in 61.8% of cases. In this study, there was no case of thrombocytopenia, but 9 (26.5%) had thrombocytosis.[24] Leukocytosis and lymphocytosis were present in all three cases of CLL

included in our study. According to Rai staging of CLL, two cases were in Stage III and one case in Stage IV at the time of diagnosis. Anemia was present in all cases and only one patient had thrombocytopenia, i.e., platelet count <100,000/μL. Among three patients of SLE, leukopenia and lymphopenia were present in two cases each. Shoenfeld and Ehrenfeld study found the prevalence of lymphopenia in SLE ranges from 20 to 81% and its degree may correlate with disease activity.[25] One case in our study diagnosed as hemophagocytic lymphohistiocytosis, presented with high-grade fever and splenomegaly. In complete blood count, pancytopenia was present, i.e., all three cell lines affected. Two patients diagnosed as tropical splenomegaly syndrome presented with intermittent fever, anemia, and splenomegaly. One patient presented with pancytopenia. Leukopenia and neutropenia were present in both the cases. Splenic trapping leads to neutropenia and thrombocytopenia. Fakunle study found that the most common presenting symptoms are chronic abdominal swelling (64%) and pain (52%) in tropical splenomegaly syndrome patients.[26] One patient of adult-onset Still's disease included in our study diagnosed by Yamaguchi *et al*. criteria presented with fever, typical rash and arthralgia, and hepatosplenomegaly. Leukocytosis >10,000/μL was present.[27]

Because this study was conducted in a limited regional area, the data cannot be generalized. However, further studies with large sample size are needed to verify the study findings.

CONCLUSION

This study helps in understanding the distribution of leukocyte count and DLC pattern in various diseases presented as fever with splenomegaly and also the variable presenting signs and symptoms of these diseases so that the patients of fever with splenomegaly investigated and treated in a proper manner. This study also helps in making the early diagnosis of these patients to reduce the morbidity, mortality, and cost of treatment associated with these diseases if there was a delay in early initiation of the treatment.

REFERENCES

1. Ghalaut PS, Atri SK, Gaur N, Jain S, Chahal A, Pahuja I, *et al*. To Study the clinical profile and etiological spectrum of patients with splenomegaly in a tertiary care center of North India. IJSRP 2016;6:120-3.
2. Chandanwale SS, Gupta K, Vishwanathan V, Jadhav R, Mishra N, Patel AR, *et al*. Hematological profile in splenomegaly a study of 50 cases. Int J Pharm Bio Sci 2015;5:368-78.
3. Dabadghao VS, Diwan AG, Raskar AM. A clinic hematological profile of splenomegaly. Bombay Hosp J 2012;54:10-8.
4. Agarwal D, Mittal A. hematologya diagnostic tool in cases of splenomegaly. Int J Biomed Adv Res 2016;7:413-7.
5. Yaranal P, Umashankar T, Harish S. Hematological profile in pulmonary tuberculosis. Int J Health Rehabil Sci 2013;2:50-5.
6. Sinha KN, Krishnamurti S, Chatterji JC. Disseminated tuberculosis and abnormal haemopoietic response. Indian J Tub 1977;24:110-5.
7. Adiga DA, Mittal S, Venugopal H, Mittal S. Serial changes in complete blood counts in patients with leptospirosis. J Clin Diagn Res 2017;11:21-4.
8. De Silva NL, Niloofa MJ, Fernando N, Karunanayake L, Rodrigo C. Changes in full blood count parameters in leptospirosis: A prospective study. Int Arch Med 2014;7:31.
9. Rasoolinejad M, Esmailpoor NB, Mogbel BA. Salmonella hepatitis (analysis of hepatic involvement in 107 patients with typhoid fever). Acta Med Iran 2003;4.161-3.
10. Ahmed Y, Idris Y, Selahattin K. Clinical and laboratory presentation of typhoid fever. Int Pediatr 2001;4:227-31.
11. Khosla SN, Anand A, Singh U, Khosla A. Haematological profile in typhoid fever. Trop Doct 1995;25:156-8.
12. Baddley JW, Benjamin DK Jr., Patel M, Miró J, Athan E, Barsic B, *et al.* Candida infective endocarditis. Eur J Clin Microbiol Infect Dis 2008;27:519-29.
13. Lathia TB, Joshi R. Can hematological parameters discriminate malaria from nonmalarious acute febrile illness in the tropics? Indian J Med Sci 2004;58:239-44.
14. Wickramasinghe SN, Abdalla SH. Blood and bone marrow changes in malaria. Baillieres Best Pract Res Clin Haematol 2000;13:277-99.
15. Akhtar S, Gumashta R, Mahore S, Maimoon S. Hematological changes in malaria. A comparative study. IOSR J Pharm Biol Sci 2012;2:15-9.
16. Tesfaye E, Fissehatsion K, Terefe B, Enawgaw B. Haematological abnormalities in visceral leishmaniasis patients attending Gondar university hospital; retrospective study. Int J HIV/AIDS Prev Edu Behav Sci 2017;3:48-53.
17. Hamid GA, Gobah GA. Cilinical and hematological manifestation of visceral leishmaniasis in Yemen children. Turk J Hematol 2009;26:25-8.
18. Reid TJ 3rd, Mullaney M, Burrell LM, Redmond J 3rd, Mangan KF. Pure red cell aplasia after chemotherapy for hodgkin's lymphoma: *In vitro* evidence for T cell mediated suppression of erythropoiesis and response to sequential cyclosporin and erythropoietin. Am J Hematol 1994;46:48-53.
19. Samoszuk M, Nansen L. Detection of interleukin-5 messenger RNA in reed-sternberg cells of hodgkin's disease with eosinophilia. Blood 1990;75:13-6.
20. Conlan MG, Armitage JO, Bast M, Weisenburger DD. Clinical significance of hematologic parameters in non-hodgkin's lymphoma at diagnosis. Cancer 1991;67:1389-95.
21. Bloomfield CD, McKenna RW, Brunning RD. Significance of haematological parameters in the non-hodgkin's malignant lymphomas. Br J Haematol 1976;32:41-6.
22. Chang F, Shamsi TS, Waryah AM. Clinical and hematological profile of acute myeloid leukemia (aml) patients of Sindh. J Hematol Thrombo Dis 2016;4:s239.
23. Pahloosye A, Hashemi A, Mirmohammadi SJ, Atefi A. Presenting clinical and laboratory data of childhood acute lymphoblastic leukemia. Iran J Pediatr Hematol Oncol 2011;1:71-7.
24. Korubo KI, Omunakwe HE, Nwauche CA. Chronic myeloid leukemia: Clinical and laboratory features at presentation to a referral hospital in Southern Nigeria. Blood 2013;122:5174.
25. Shoenfeld Y, Ehrenfeld M. Hematologic manifestations. In:

Schur PH, editor. The Clinical Management of Systemic Lupus Erythematosus. 2nd ed. Philadelphia, PA: Lippincott; 1996.
26. Fakunle YM. Tropical splenomegaly. Part 1: Tropical Africa. Clin Haematol 1981;10:963-75.
27. Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, *et al*. Preliminary criteria for classification of adult still's disease. J Rheumatol 1992;19:424-30.

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