

Hematology – A diagnostic tool in cases of splenomegaly

Deepti Agarwal* and Aditi Mittal

Assistant Professor, Department of Pathology, Shri Ram Murti Smarak Institute of Medical sciences, Bareilly, India

*Correspondence Info:

Dr. Deepti Agarwal
MD Pathology
Assistant Professor,
Department of Pathology,
Shri Ram Murti Smarak Institute of Medical sciences, Bareilly, India
E-mail: dr.deeptiagarwal86@gmail.com

Abstract

Objective: To study hematological profile in patients with clinically palpable spleen and to find out the role of hematological investigations as a diagnostic tool in elucidating etiopathogenesis of splenomegaly.

Materials and methods: This cross-sectional study was conducted on 50 patients at a teaching hospital from Aug 2011 to 2013. Detailed clinical history including name, age, sex, chief complaints, clinical findings, X-ray and USG (if done) were noted. Grading of splenomegaly was done by Hackett's classification. Laboratory tests including peripheral blood smear, complete blood count and bone marrow examination (if required) were performed.

Results: In the present study, maximum numbers of patients were males in the age group of 0-15 years. The commonest cause of splenomegaly found was acute leukemia followed by malaria, hemolytic anemia, chronic myeloid leukemia, liver cirrhosis and infections. Hematological causes were the most common etiology of splenomegaly in this study. The commonest grade of splenomegaly was I and II (mild). There was also a case of congenital dyserythropoietic anemia type I (CDA), a rare autosomal recessive disorder. We also came across one case of plasmodium falciparum malaria with no evidence of parasite on peripheral blood smear which called for bone marrow study.

Conclusion: Splenomegaly is a subject of considerable clinical concern as spleen is not palpable under normal circumstances. When palpable, it may be associated with serious disorders from which no age is exempted. Thus, hematological evaluation becomes necessary to understand the etiopathogenesis of splenomegaly.

Keywords: Hackett's classification, hypersplenism, acute leukemia

1. Introduction

Spleen is a functionally diverse organ with active roles in immunosurveillance and hematopoiesis. The spleen combines the innate and adaptive immune system in a uniquely organized way.[1] Splenomegaly is a subject of considerable clinical concern as spleen is not palpable under normal circumstances. When palpable, it may be associated with serious disorders from which no age is exempted.

Clinically, if a spleen is palpable it means it has undergone enlargement by at least 2 folds. In most of the cases, splenomegaly is the first and the only sign of an underlying serious disorder. This makes it important to regard a palpable spleen as a significant physical sign and it also makes it imperative to investigate such a case.[2] A wide variety of diseases can lead to splenic enlargement. Most of the chronic conditions like chronic malaria, myeloproliferative diseases, haemolytic anaemias lead to massive splenomegaly while in most acute conditions, patients present with a mild enlargement of spleen.[2] Questions concerning the frequency, etiology and

significance of finding a palpable spleen are raised from time to time.

Our study was aimed to determine hematological profile in cases of clinically palpable splenomegaly and to find out the role of hematological investigations as a diagnostic tool in elucidating etiopathogenesis of splenomegaly.

2. Material and Methods

This cross-sectional study included 50 indoor patients of all age groups and was carried out at a teaching hospital from the year August 2011 to August 2013. The cases included were of clinically palpable splenomegaly alone or cases who had splenomegaly with hepatomegaly and/or lymphadenopathy. The exclusion criteria used was patients with splenomegaly detected only by radiological investigations and patients with splenomegaly along with tense ascites. Detailed clinical history including name, age, sex, chief complaints was noted. General examination to find out degree of pallor, presence of icterus, hepatomegaly,

lymphadenopathy and hemorrhagic manifestations was done. Grading of splenomegaly was done by Hackett's classification.

2.1 Grading (based on Hackett's classification) of splenomegaly

Grade 0: Spleen not palpable even on deep inspiration.

Grade I: Spleen palpable below costal margin, usually on deep inspiration.

Grade II: Spleen palpable, but not beyond a horizontal line halfway between the costal margin and umbilicus, measured by a line dropped vertically from the left nipple.

Grade III: Spleen palpable more than half way to umbilicus, but not below a line horizontally running through it.

Grade IV: Palpable below umbilicus but not below a horizontal line halfway between umbilicus and pubic symphysis.

Grade V: Extending lower than Grade IV

Hackett's grade I and II were considered as mild splenomegaly, grade III as moderate splenomegaly, and grade IV and V as massive splenomegaly.

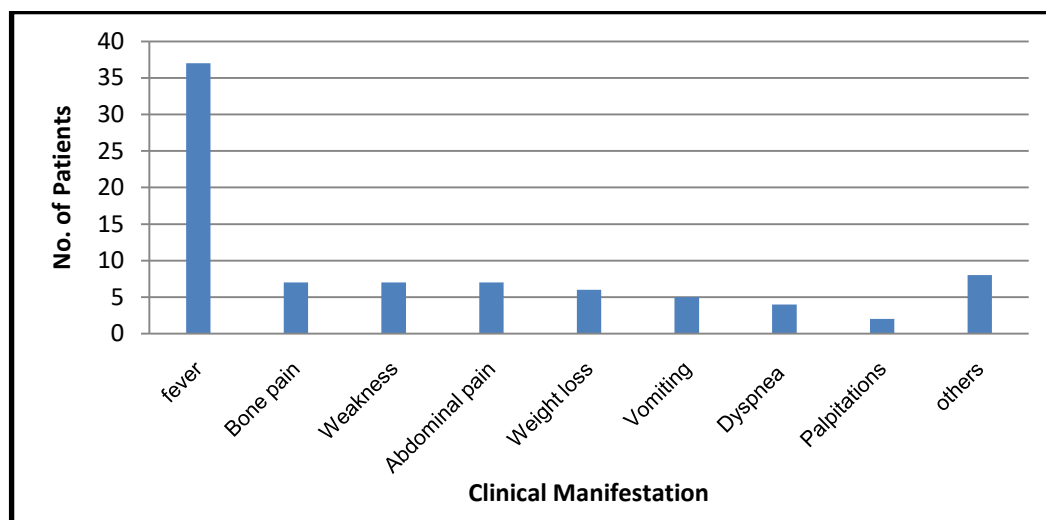
Results of pertinent investigations mainly USG, X-ray, CT scan (if done) were noted. Laboratory investigations including Peripheral blood smear, complete blood count and

bone marrow examination (if required) were performed. All peripheral blood smears were stained using leishman stain and bone marrow aspiration and imprint slides were stained using leishman-Geimsa stain. Special stains including retic stain, periodic acid schiff, leucocyte alkaline phosphatase, myeloperoxidase, reticulin stain were used if required. All slides were evaluated by two hematologists independently and final reports were issued.

An attempt was made to find out the etiology of splenomegaly and its correlation with hematological parameters. Reference ranges for various hematological parameters given in Dacie and Lewis, Practical haematology were used for comparison.[3] An attempt was also made to find the relation between degree of splenomegaly with degree of anemia and cytopenias in cases of hypersplenism.

3. Results

In this study, there were 31 males and 19 female patients; the male to female ratio was 1.6: 1. The age range in the present study was from 0.6 to 87 years. The maximum number of cases were under the age group of 15 (44%) and minimum were above the age of 61 (6%). The clinical manifestations of patients with splenomegaly were as shown in graph 1. The most common manifestation was fever.

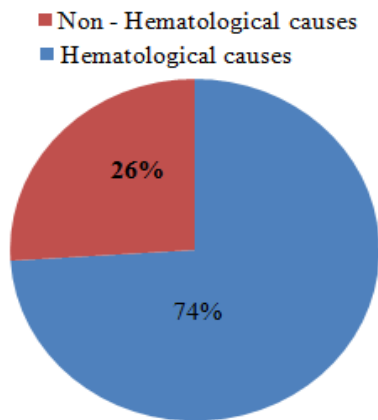


Graph 1: Distribution of cases according to the clinical manifestations

There were maximum number of cases of mild splenomegaly (56%), followed by moderate (34%) and massive (10%) splenomegaly. The most common causes of splenomegaly in our study in order of decreasing frequency were as follows: 13 cases of malaria; 11 cases of acute lymphoblastic leukemia; 5 cases acute myeloid leukemia; 3 cases each of thalassemia major, liver cirrhosis, tuberculosis and other bacterial infections; 2 cases each of chronic myelogenous leukemia and dengue and 1 case each of myelofibrosis, congenital dyserythropoietic anemia type I,

Evan's syndrome, enteric fever and non-cirrhotic portal hypertension.

For simplicity, we had divided the above causes into hematological and non-hematological causes of splenomegaly (Graph 2). In hematological causes, there were 18 cases were of leukemia, followed by malaria (13 cases), anemia (5 cases) and myelofibrosis (1 cases). Non-hematological causes included infections other than malaria, liver cirrhosis and non-cirrhotic portal hypertension.



Graph 2: Distribution of cases according to the hematological and non-hematological causes for splenomegaly

In the present study, hypersplenism was found in 8% of cases. The splenic enlargement noted in these cases was predominantly moderate to massive. The most common cause of hypersplenism in this study was liver cirrhosis (3 cases) followed by non-cirrhotic portal hypertension (1 case).

We have not offered a diagnosis of tropical splenomegaly in our study as we could not elicit history of malaria in the past and we have not done immunological investigations for malaria.

Splenomegaly associated with hepatomegaly and/or lymphadenopathy was seen in 26% and 10% patients. Moderate to severe anemia was noted in 68% of cases, leucopenia in 16% of cases and thrombocytopenia in 80% cases. Red blood cell count, hematocrit, Mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH) and Mean corpuscular hemoglobin concentration (MCHC) were decreased in 72%, 92%, 58%, 40% and 28% of cases respectively. Red blood cell distribution width (RDW) was increased in 86% of cases. Leucocytosis was seen in 44% of cases. In all the cases of hypersplenism, bone marrow was hypercellular with cytopenias on peripheral blood smears.

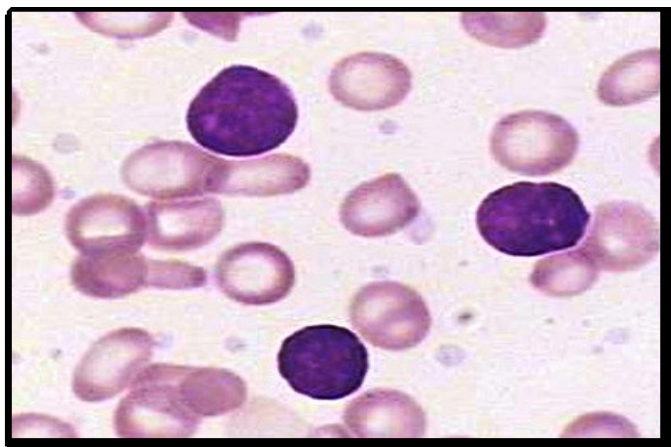


Fig 1: Photomicrograph of Acute lymphoblastic leukemia (L1) showing small, homogenous blasts with scanty cytoplasm and indistinct nucleoli (100x)

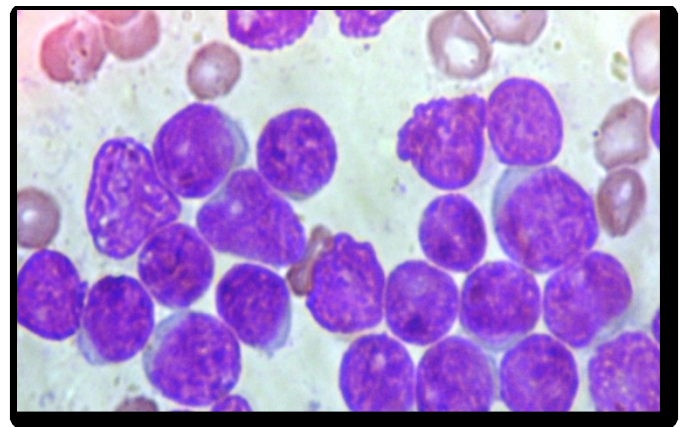


Fig 2: Photomicrograph of Acute lymphoblastic leukemia (L2) showing large, heterogeneous blasts, with one or more nucleoli and abundant cytoplasm (100x).

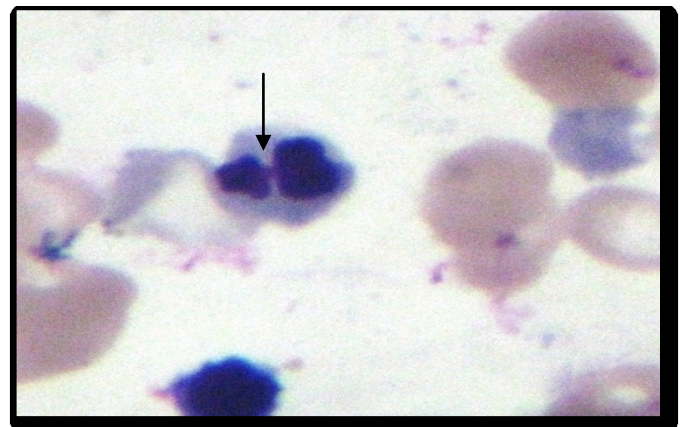


Fig 3: Photomicrograph of Congenital Dyserythropoietic Anemia type I showing normoblast with dumb-bell shaped nuclei with nuclear lobes joined by a thin chromatin bridge (arrow) (100x).

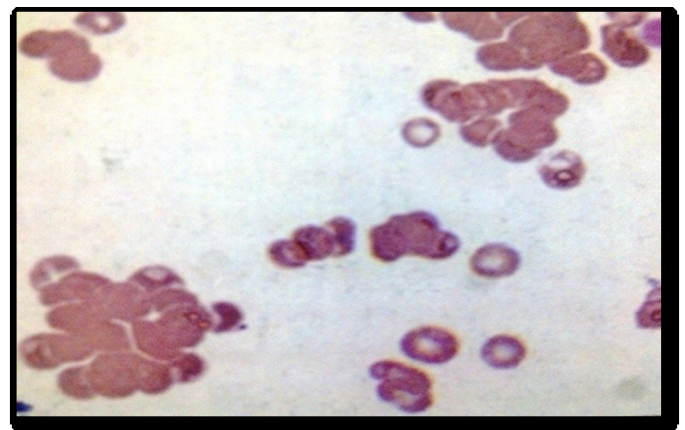


Fig 4: Photomicrograph of Evan's syndrome demonstrating red blood cells showing autoagglutination on peripheral blood smear (100x)

4. Discussion

Splenomegaly in a symptomatic patient is of considerable clinical significance. One needs to investigate a case of splenomegaly as many of the conditions causing splenomegaly are treatable.[2] In the present study we have studied cases of splenomegaly clinically and with pertinent

hematological investigations with special reference to cell counts and bone marrow studies; with the aim of finding etiology and hematological effects (element of Hypersplenism) of splenomegaly. More or less similar methodology has been adopted and aims have been attended by most of the studies reviewed in literature. In the present study 50 patients were studied. Maximum cases were in age group of 0-15 years (44%) and minimum were above the age of 61 (6%). Leukemia (11cases) and hemolytic anemias (5 cases) formed an important cause of splenomegaly in pediatric age group in our study. Similar observations are noted by Ali *et al.*[4] Infections (13 cases) were common causes of splenomegaly in adults in the present study. The male: female ratio was 1.6:1 in our study (Table 1). The experience is shared by various authors.

Table 1: Male to female ratio in cases of splenomegaly in various studies

	Nadeem <i>et al</i> [2]	Hussain <i>et al</i> [5]	Present study
M:F	4:1	1.1:1	1.6:1

M: Male, F: Female

The most common clinical manifestation in the present study was fever (Graph 1). This is comparable to a study by Nadeem *et al.*[2] There were maximum number of cases of leukemia and malaria in our study and fever is a common manifestation of these disorders. The second most common clinical manifestations was bone pain followed by weakness, abdominal pain, weight loss, vomiting, dyspnea, palpitations, pedal edema, cough with expectoration, gum bleed and tingling numbness in hands.

The most common causes of splenomegaly in our study in order of decreasing frequency were as follows: 13 cases of malaria; 11 cases of acute lymphoblastic leukemia; 5 cases acute myeloid leukemia; 3 cases each of thalassemia major, liver cirrhosis, tuberculosis and other bacterial infections; 2 cases each of chronic myelogenous leukemia and dengue and 1 case each of myelofibrosis, congenital dyserythropoietic anemia type I, Evan's syndrome, enteric fever and non-cirrhotic portal hypertension.

In the present study, hematological disorders formed an important and most frequent cause (74%) of splenomegaly which was comparable to the study by Nadeem *et al*[2], O'Reilly RA[6] and Swaroop *et al.*[7]

Table 2: Distribution of cases according to the hematological and non-hematological causes for splenomegaly:

Hematological causes	Non – Hematological causes
Acute lymphoblastic leukemia	Tuberculosis
Acute myeloid leukemia	Dengue
Chronic myeloid leukemia	Enteric fever
Malaria	Pneumococcal and other bacterial infections
Thalassemia Major	Liver cirrhosis
Congenital Dyserythropoietic Anemia	Non-cirrhotic Portal hypertension
Evan's Syndrome	
Myelofibrosis	

In hematological malignancies, there were maximum number of cases of acute lymphoblastic leukemia (11 cases), followed by acute myeloid leukemia (5 cases) and chronic myeloid leukemia (2 cases). Though chronic myeloid leukemia is the most frequent hematological condition associated with splenomegaly, only few cases were found in the present study. Splenomegaly is an important manifestation of myelofibrosis and was found in one case respectively.

In malaria, there were 7 cases of plasmodium falciparum and 6 cases of plasmodium vivax. We also came across one case of plasmodium falciparum malaria with no evidence of parasite on peripheral blood smear which called for bone marrow study.

There were 5 cases of anemia comprising of 3 cases of Thalassemia major and one case each of congenital dyserythropoietic anemia type I and Evan's syndrome. Congenital dyserythropoietic anemia Type I is a rare autosomal recessive disorder with upto 3% normoblasts displaying "dumb-bell" shaped nuclei with nuclear lobes joined by a thin chromatin bridge (pathognomonic feature). We also came across a case of Evan's syndrome which is characterized by Autoimmune hemolytic anemia along with autoimmune thrombocytopenia. Paucity of hemolytic anemia in the present study sample can be explained by the reason that it was readily diagnosed on clinical grounds and pertinent investigations and hence not referred under the heading of splenomegaly to us by clinicians.

In non-hematological group, infections other than malaria were found to be a causative factor in 9 (18%) cases. We have attributed definitive and specific infections which were sole cause of splenomegaly to this group. We came across cases of Tuberculosis (3 cases), pneumococcal and other bacterial infection (3 cases) followed by dengue (2 cases) and enteric fever (1 cases). In present study, we have evaluated only those cases of splenomegaly which were referred to us for extensive hematological workup. This is reflected in finding out infection as a cause of splenomegaly only in few cases, as these cases were already diagnosed by clinicians on clinical & pertinent investigative workup. Workers like Nadeem *et al*[2] deliberately excluded cases of malaria, typhoid fever and liver diseases on pertinent investigations.

In present study, hypersplenism was found in 8% of cases. The splenic enlargement noted in these cases was predominantly moderate to massive. The most common cause of hypersplenism in this study was liver cirrhosis (3 cases) followed by non-cirrhotic portal hypertension (1 case). The same experience has been shared by Swaroop *et al*[7], O'Reilly RA[8] and Sunderesan *et al*[9], who have shown liver diseases to be the important cause of hypersplenism. Sunderesan *et al*[9] have shown that there is no statistically significant correlation between degree of splenomegaly and hemoglobin level, total leucocyte count and platelet counts

amongst the patients of hypersplenism. Similar experience was shared by Erwa Elmakki.[10]

In the present study, the most common grade of splenomegaly was mild (Grade I and II, 56%) followed by moderate (Grade III, 34%) and massive (Grade IV, 10%) splenomegaly. This was comparable to a study by Hussain *et al* [5] and Nadeem *et al*. [2] In the present study, most cases of acute leukemia, malaria and other infections had grade I to II (mild) enlargement of spleen at the time of diagnosis. The most common causes of moderate and massive splenomegaly (Grade III and IV) in the present study were hemolytic anemia, myelofibrosis, chronic myeloid leukemia, liver cirrhosis, non-cirrhotic portal hypertension. Preponderance of hematological diseases in massive splenomegaly is also noted by Swaroop *et al* [7], O'Reilly R A. [8]

Table 3: Grade of splenomegaly in various studies

Grade of splenomegaly	Hussain <i>et al</i> [5]	Nadeem A. <i>et al</i> [2]	Present study
Mild	78%	83%	56%
Moderate	14%	8.3%	34%
Massive	8%	8.3%	10%

One case each of malaria, acute lymphoblastic anemia, acute myeloid leukemia, liver cirrhosis, chronic myelogenous leukemia, dengue, myelofibrosis, non-cirrhotic portal hypertension and congenital dyserythropoietic anemia had associated hepatomegaly. One case each of tuberculosis, acute lymphoblastic leukemia and acute myeloid leukemia has associated lymphadenopathy. Splenomegaly with both hepatomegaly and lymphadenopathy was seen in one case each of thalassemia major and bacterial infection. The cause on lymphadenopathy in a case of thalassemia major was concurrence of viral infection. Thus occurrence of multiple organomegaly is an important feature of infections and hematological disorders. Similar findings are also noted by other authors.[2,4,8] This consideration should help in clinical decision of etiology of splenomegaly.

Moderate to severe anemia was noted in 68% of cases, leucopenia in 16% of cases and thrombocytopenia in 80% cases. Red blood cell count, hematocrit, Mean corpuscular volume (MCV), Mean corpuscular haemoglobin (MCH) and Mean corpuscular hemoglobin concentration (MCHC) were decreased in 72%, 92%, 58%, 40% and 28% of cases respectively. Red blood cell distribution width (RDW) was increased in 86% of cases. Leucocytosis was seen in 44% of cases and the various causes were leukemia and infections. Red cell indices were useful in diagnosing various hematological conditions, for example, for distinguishing iron deficiency anemia from β thalassemia minor (low MCV with high RDW: iron deficiency anemia; low MCV with normal RDW: β thalassemia minor). Toghil and Green have studied red cell mass, splenic red cell pool and plasma volume and splenomegaly associated with hematological disorders. According to these, there is no significant relationship between red cell mass and splenic size

but the splenic red cell pool increases with increasing spleen size. Most of the studies reviewed in literature have led stress on etiological and clinical aspects of splenomegaly with hardly any mention of hematological features.

Bone marrow is an important investigation. In our study, bone marrow examination was helpful in diagnosing and confirming leukemia, hypersplenism, myelofibrosis and one case of malaria. In all the cases of hypersplenism, bone marrow was hypercellular with cytopenias on peripheral blood smears. In case of myelofibrosis, bone marrow biopsy with special stain was a pertinent investigation. We have also come across one case of *plasmodium falciparum* malaria with no evidence of parasite on peripheral blood smear and thus called for bone marrow study.

On the whole, present study on clinically palpable splenomegaly was quite rewarding and provided insight in to its etiology and hematological manifestations.

References

- [1] Mebius RE, Kraal G. Structure and function of spleen. *Nat Rev Immunol.* 2005; 5(8): 606-16.
- [2] Nadeem A, Ali N, Hussain T, Anwar M. Frequency and etiology of splenomegaly in adults seeking medical advice in combined military hospital Attock. *Journal of Ayub Medical College Abbottabad* 2004; 16(4): 44-7.
- [3] Bates I, Lewis S.M. Reference ranges and normal values. In: Bain B.j, Bates I, Laffan M.A, Lewis S.M. Dacie and Lewis, Practical Haematology. 11th edition. Churchill Livingstone Elsevier 2012:11-22.
- [4] Ali N, Anwar M, Ayyub M, *et al*. Hematological evaluation of Splenomegaly. *Journal of college of Physicians and Surgeons Pakistan* 2004; 14(7): 404-6.
- [5] Hussain I, Ahmed I, Mohsin A, Muhammad Z, Shah A. Causes of splenomegaly in Adult local population presenting at tertiary care centre in Lahore. *Pakistan Journal of Gastroenterology* 2002; 16(1): 12-6.
- [6] O'Reilly RA. Splenomegaly in 2,505 patients in a large university medical center from 1913 to 1995. 1913 to 1962: 2056 patients. *Western Journal of Medicine* 1998; 169(2): 78-87.
- [7] Swaroop J, O'Reilly RA. Splenomegaly at a University Hospital Compared to a Nearby Country Hospital in 317 Patients. *Acta Haematologica* 1999; 102:83-88.
- [8] O'Reilly RA. Splenomegaly at a United States County Hospital: diagnostic evaluation of 170 patients. *American Journal of the Medical Sciences* 1996; 312(4): 160-5.
- [9] Sundaresan JB, Dutta TK, Badrinath S, Jagdish S, Basu D. Study of Hypersplenism and Effect of Splenectomy on Patients with Hypersplenism. *Journal of Indian Academy of Clinical Medicine* 2005; 6(4): 291-6
- [10] Erwa Elmakki. Causes and Clinical features of patients with Hypersplenism: A case study conducted in Ibn Sina and Soba Teaching Hospitals, Khartoum, Sudan. *Journal of Biology, Agriculture and Healthcare* 2012; 2(9):55-59.