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HEMATOLOGICAL PROFILE IN SPLENOMEGALY – A STUDY OF 50 CASES

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ABSTRACT

Introduction: Palpable spleen in a symptomatic person is always significant. Splenomegaly is associated with a large number of disorders including hematological, infections, congestive states related to portal hypertension, lymphohematogenous disorders, immunological conditions, storage disorders and miscellaneous conditions. It can be an important diagnostic clue to the existence of an underlying disorder. Aims and objective: Present study is an attempt to find out the frequency of various causes of splenomegaly, to study its hematological parameters and to find out role of these parameters as a diagnostic or additional tool in elucidating etiopathogenesis of splenomegaly. Materials and methods: Hematological parameters were analyzed and correlated with clinical findings. P values were calculated using primer of biostats software in some routine hematologic parameters. **Results:** Males were affected more than females. The most common age group affected in males was 41-50 years and in females was 21-30 years. The maximum (50%) patients presented with moderate splenomegaly. Hematological causes (60%) outnumbered the non hematological causes (40%) in the present study. Anemia (30%) was found to be the most frequent cause. Hypersplenism was found in 36% cases. There was a significant association between the degree of hypersplenism and degree of splenomegaly. Discussion: Splenomegaly in a symptomatic person should always be investigated thoroughly as most of the common causes are treatable. Hematological causes outnumbered the non-hematological cause of splenomegaly. Hematological profile in cases with enlarged spleen are of utmost importance as a diagnostic or additional tool in elucidating the etiogenesis of splenomegaly.

KEY WORDS

Splenomegaly, Hematology, Parametres

INTRODUCTION

Splenomegaly can be an important diagnostic clue to the existence of an underlying disorder.[1] Splenomegaly is associated with a number disorders including large of haematological, infections, congestive states hypertension, related to portal lymphohematogenous disorders, immunological conditions, storage disorders and miscellaneous conditions.

Most of the chronic conditions like chronic malaria, myeloproliferative diseases, hemolytic anemias, Gaucher's disease and some of the lymphoid and myeloid neoplasms lead to massive splenomegaly.[1,2] In most of the acute conditions, patients present with a mild enlargement of spleen. Splenomegaly becomes more significant when associated with hepatomegaly or lymphadenopathy.[3]

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Very occasionally a palpable spleen may be present in an adult that may have no serious significance [3]. It is however, important to regard a palpable spleen as a significant physical sign and to investigate such a case, since most of the common causes are treatable.[4,5,6]

Palpable spleen in a symptomatic person is always significant. Splenomegaly can lead to cytopenias. 'Hypersplenism' is a term used for enlarged spleen with increase in normal destruction of blood cells.[7] It is characterized by splenomegaly, pancytopenia, presence of normal or hypercellular bone marrow, which is reversible after splenectomy, following which most of the patients present with an overwhelming response in the form of leucocytosis and thrombocytosis.[8-11]

Questions concerning the frequency, etiology and significance of finding a palpable spleen are raised from time to time. Present study is a humble attempt to find out the frequency of various causes of splenomegaly, to study its hematological parameters and to find out role of these parameters as a diagnostic or additional tool in elucidating etiopathogenesis of splenomegaly

MATERIALS AND METHODS

The present study is a cross-sectional study which was carried out from July 2012 -September 2014. Inclusion criteria: All clinically inquired cases of Splenomegaly, irrespective of age and sex. Exclusion criteria: Various systemic diseases and haematological conditions, where splenomegaly is not present. A written consent was taken for special hematological procedures such as bone marrow aspiration/biopsy. Findings of general and physical examination were noted. Blood was collected with aseptic precautions for routine and special hematological investigations.

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Hemoglobin estimation Complete Blood Count Platelet Count Red cell indices (MCV, MCH, MCHC, RDW) were done on fully automated cell counter (BeneSphera 5- part Hematology Analyzer H51). Blood smears were stained with Leishmann stain and studied in detail. Fresh bone marrow aspirate smears were prepared bedside and were stained with Leishmann stain, cytochemical stains and Pearls Prussian Blue stain wherever required. Sickle cell test, osmotic fragility, LE Cell test were also done in relevant cases.

Serological tests for malaria, dengue, human immunodeficiency virus (HIV) and Rheumatoid Arthritis Factor (RA) were carried out wherever required. Findings of Radiological investigations such as ultrasonography, 2D Echocardiography, barium studies, CT scan, MRI study were noted in cases, wherever indicated. Data collected was analysed to find out the etiology of splenomegaly, its hematological manifestations.

RESULTS

This is a cross-sectional study of 50 patients with clinically inquired splenomegaly.

Males were affected more than females. The most common age group affected in males was 41- 50 years and in females was 21-30 years. The incidence of male: female ratio was 1.5: 1. Table 1 shows detailed age and sex distribution in 50 cases. The 50%(n=25) patients presented with moderate splenomegaly followed by mild splenomegaly in 38% (n=19) and 12%(n=6) cases with severe splenomegaly. The 36% (n=18)) had associated hepatomegaly, splenomegaly in14%(n=7) and hepatomegaly and lymphadenopathy in 6%(n=3) cases.

Table 2 show detailed clinical diagnosis of 50 splenomegaly cases. Anemia was the most common clinical diagnosis (32%) followed by alcoholic liver disease (20%) and leukemia(18%). Table 3 show degree of

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splenomegaly in 50 splenomegaly cases. The moderate splenomegaly was seen in 50% (n=25) followed by mild splenomegaly in 38% (n=18) and and 12% (n=6) had severe splenomegaly.

98% splenomegaly cases (n=48) showed decreased hemoglobin concentration and one case (2%) of congestive splenomegaly presented with the normal hemoglobin concentration. Among the 15 cases of anemia commonest was iron deficiency anemia (n=9) followed by megaloblastic anemia(n=4) and dimorphic anemia (n=2).

The 50 %(n=25) cases presented with normal total leukocyte count (TLC), 36%(n=18) cases showed decreased TLC and 14%(n=7) cases showed increased TLC. Out of these seven cases, six cases were of hematological neoplasia and one case of rheumatoid arthritis presented with increased TLC.

The 66%(n=33) cases showed normal differential polymorph count, 6% (n=3) of congestive splenomegaly were associated with increased polymorphs and 28%(n=14) showed decreased polymorphs, of which 9 cases were of hematological malignancies. The 48%(n=24) cases showed normal lymphocyte count on DLC, the 36%(n= 18) showed increased lymphocytes, of which 4 cases each were of neoplastic and inflammatory pathology and 16%(n= 8) cases showed decreased lymphocytes on DLC. The 82%(n=41) cases showed normal eosinophil count and 18% (n=9) cases showed increased eosinophils on DLC. The 86% (n=43) presented with normal monocyte count and 14%(n=7) cases with decreased monocyte count on DLC.The 64%(n= 32) cases were associated with decreased platelet count, 30%(n=15) with normal platelet count and 6%(n=3) presented with increased platelet count. Table 4 shows platelet count in 50 splenomegaly cases.

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Table 5,6,7,8 show detailed status of red cell indices in 50 splenomegaly cases.

The 82%(n=41) cases splenomegaly cases show normal reticulocyte count, while 10%(n=5) showed decreased reticulocyte count and 8% (n=4) were associated with increased retic count.

The majority of the cases (96%) were associated with decreased RBC count, of which Anemia showed the most frequent association followed by hematological malignancy (20%), congestive causes secondary to liver cirrhosis (18%), infective causes (12%) and miscellaneous causes (6%) that are constituted by splenic cyst, splenic infarct and systemic lupus erythematosus one case each.

Table 9 show final diagnosis based on clinical and hematological profile. show final diagnosis based on hematological parameters.

Hypersplenism was found in 36% (n=18) cases . The most common cause of hypersplenism was alcoholic liver disease (n=7) followed by anemia(n=4), 2 each of malaria and lymphoma and 1 each of fever with anemia, leukemia and thrombocytopenia. Hypersplenism was associated with either normocellular or of hypercellular marrow. The 11 cases hypersplenism were associated with hypercellular bone marrow and 7 cases norm cellular bone marrow. Hypercellular bone marrow were complicated by associated disease.

The 18 cases (36%) of total 50 cases of splenomegaly were associated with hypersplenism. The most common cause of hypersplenism were the congestive causes secondary to liver cirrhosis (14%), followed by anemia (8%). 2 cases (4%) each of lymphoma and malaria and 1 case (2%) of Acute myeloid leukemia (AML), SLE and splenic infarct also presented with hypersplenism.

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There was a significant association between the degree of hypersplenism and degree of splenomegaly (p< 0.05). There was no significant correlation between hemoglobin and hypersplenism (p>0.05). There was a significant correlation between total leukocyte count (TLC) and hypersplenism (p<0.005). There was no significant correlation between Differential

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leukocyte count (DLC) and hypersplenism (p>0.05). Ther was a significant correlation between platelet count and hypersplenism (p < 0.0001). 8 cases in which splenectomy was done in our institution and showed subsequent normalization of the hematological parameters.

Age (Yrs)	Male (%)	Female (%)	Total (%)
0 - 10	1 (2)	0	1 (2)
11 – 20	5 (10)	3 (6)	8 (16)
21 – 30	4 (8)	8 (16)	12 (24)
31 – 40	4 (8)	4 (8)	8 (16)
41 – 50	9 (18)	3 (6)	12 (24)
51 - 60	4 (8)	1 (2)	5 (10)
61 - 70	2 (4)	0	2 (4)
>71	1 (2)	1 (2)	2 (4)
Total	30 (60)	20 (40)	50 (100)

Table 1: Age and Sex wise distribution of 50 splenomegaly cases.

Table 2: Clinical diagnosis in 50 cases of splenomegaly

Clinical diagnosis	No of cases	Percentage (%)
Acute Gastroenteritis	1	2
Alcoholic Liver Disease	10	20
Anemia	16	32
Arthritis	1	2
Fever with anemia	2	4
Leukemia	9	18
Lymphoma	3	6
Malaria	4	8
Pain abdomen	1	2
Bleeding diathesis	2	4
Viral fever	1	2
Total	50	100

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Table 3: Degree of splenomegaly 50 cases						
Diagnosis		Splenon	Splenomegaly			
Diagnosis		Mild	Moderate	Severe	n (%)	
Hematological (n=30)	Anemia	10 (20)	5 (10)	0	15 (30)	
	Neoplastic	0	6 (12)	5 (10)	11 (22)	
	Others	2 (4)	1 (2)	1 (2)	4 (8)	
Non Hematological (n=20)	Congestive	1 (2)	9 (18)	0	10 (20)	
	Infection	4 (8)	2 (4)	0	6 (12)	
	Inflammatory	1 (2)	0	0	1 (2)	
	Miscellaneous	1 (2)	2 (4)	0	3 (6)	
Total		19 (38)	25 (50)	6 (12)	50 (100)	

Table 4: Platelet count in 50 splenomegaly cases

Final diagnosis		Platelet count			Total
Final diagnosis		Normal	Increased	Decreased	n (%)
Hematological	Anemia	8 (16)	2 (4)	5 (10)	15 (30)
(n=30)	Neoplastic	3 (6)	1 (2)	7 (14)	11 (22)
	Others	2 (4)	0	2 (4)	4 (8)
Non	Congestive	1 (2)	0	9 (18)	10 (20)
Hematological	Infection	1 (2)	0	5 (10)	6 (12)
(n=20)	Inflammatory	0	0	1 (2)	1 (2)
	Miscellaneous	0	0	3 (6)	3 (6)
Total		15 (30)	3 (6)	32 (64)	50 (100)

Table 5: MCV in 50 splenomegaly cases

Final diagnosis		MCV (fl)	MCV (fl)		
Final diagnosis		Normal	Increased	Decreased	n (%)
Haematological	Anemia	1 (2)	4 (8)	10 (20)	15 (30)
(n=30)	Neoplastic	4 (8)	3 (6)	4 (8)	11 (22)
	Others	0	0	4 (8)	4 (8)
Non	Congestive	2 (4)	3 (6)	5 (10)	10 (20)
haematological	Infection	2 (8)	1 (2)	3 (6)	6 (12)
(n=20)	Inflammatory	0	0	1 (2)	1 (2)
	Miscellaneous	0	0	3 (6)	3 (6)
Total		9 (18)	11 (22)	30 (60)	50 (100)

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Table 6. MCH in 50 spielionlegaly cases					
Final diagnosis		MCH (pg)	MCH (pg)		
Final diagnosis		Normal	Increased	Decreased	n (%)
Hematological	Anemia	0	4 (8)	11 (22)	15 (30)
(n=30)	Neoplastic	1 (2)	5 (10)	5 (10)	11 (22)
	Others	0	0	4 (8)	4 (8)
Non	Congestive	1 (2)	4 (8)	5 (10)	10 (20)
hematological (n=20)	Infection	1 (2)	2 (4)	3 (6)	6 (12)
	Inflammatory	0	0	1 (2)	1 (2)
	Miscellaneous	0	0	3 (6)	3 (6)
Total		3 (6)	15 (30)	32 (64)	50 (100)

Table 6: MCH in 50 splenomegaly cases

Table 7: MCHC in 50 splenomegaly cases

Final diagnosis		MCHC (g/dl)	Total		
		Normal	Increased	Decreased	n (%)
Hematological	Anemia	3 (6)	3 (6)	9 (18)	15 (30)
(n=30)	Neoplastic	3 (6)	5 (10)	3 (6)	11 (22)
	Others	1 (2)	0	3 (6)	4 (8)
Non	Congestive	6 (12)	3 (6)	1 (2)	10 (20)
hematological	Infection	2 (4)	1 (2)	3 (6)	6 (12)
(n=20)	Inflammatory	0	0	1 (2)	1 (2)
	Miscellaneous	0	1 (2)	2 (4)	3 (6)
Total		15 (30)	13 (26)	22 (44)	50 (100)

Table 8: RDW in 50 splenomegaly cases

Final diagnosis		RDW (FI)	RDW (FI)		
Fillal diagnosis		Normal	Increased	Decreased	n (%)
Hematological	Anemia	0	15 (30)	0	15 (30)
(n=30)	Neoplastic	1 (2)	10 (20)	0	11 (22)
	Others	1 (2)	3 (6)	0	4 (8)
Non	Congestive	1 (2)	9 (18)	0	10 (20)
hematological	Infection	2 (4)	4 (8)	0	6 (12)
(n=20)	Inflammatory	1 (2)	0	0	1 (2)
	Miscellaneous	0	3 (6)	0	3 (6)
Total		6(12)	44 (88)	0	50 (100)

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Fina	l diagnosis		No of cases	Percentage (%)
	Anemia (n=15)	Iron deficiency anemia	9	18
_		Megaloblastic anemia	4	8
(30)		Dimorphic anemia	2	4
cal	Neoplastic (n=11)	CML	5	10
logi		AML	2	4
ato		ALL	1	2
Haematological (30)		Metastatic Lymphoma	3	6
На	Others (n=4)	ITP	2	4
		Thalassemia	1	2
		Multiple myeloma	1	2
ô	Congestive (n=10)	Liver cirrhosis	9	18
I (2		Budd chiari syndrome	1	2
Non haematological (20)	Infection (n=6)	Malaria	4	8
solo		Dengue	1	2
nato		HIV	1	2
aen	Inflammatory	Rheumatoid Arthritis	1	2
h h	(n=1)			
Š	Miscellaneous	SLE	1	2
	(n=3)	Splenic cyst	1	2
		Splenic infarct	1	2
	Total		50	100

Table 9: Final diagnosis based on hematological parameters in 50 splenomegaly cases

DISCUSSION:

Splenomegaly in symptomatic patients is of a considerable clinical significance. In this cross-sectional study, we analyzed hematological parameters of 50 cases of splenomegaly and correlated with clinical findings. Very few similar studies have been conducted in the past. [3,5,8,12]

In our study, males were affected more than females with male to female ratio of 1.5:1 and the most common age group in males was 41-50 years and in females 21-30 years. The Timite KM et al [13] observed male: female ratio of 1.4: 1, Hussain I et al [12] with the male: female ratio of 1.1: 1. In contrast Nadeem A et al [5] observed male to female ratio of 4:1 in their study. In the study conducted by Varsha S et al. [14] maximum cases were in age group of 21 - 40 years (46%). The male: female ratio was 1.2:1. Variation in the age group and sex possibly can be due to stage of the disease and geographical area.

In maximum cases (n=31), moderate to severe splenomegaly was present in our study possibly because of the more number of cases in chronic stage of the disease. Similar observations were made by Nadeem A et al.[5] . In contrast, Hussain I et al [12] had reported a large majority of patients with mild splenomegaly in their study possibly because of the early stage of the disease.

There was an associatedhepatomegaly in 36%cases followed by lymphadenopathy in14% andtheconcomitanthepatomegalywith

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lymphadenopathy in 6% cases. Findings in our study were comparable with the findings of Timite KM et al.[13] It will also depend on type of the disease process and chronicity in a particular study.

The 98% of splenomegaly cases in our study had decreased hemoglobin concentration. Varsha et al.[14] reported 21% cases of anemia while Timite KM et al [13] reported 72% cases of anemia in their study. The possible variation can be due to nutritional status of the individual. Our study suggests that there is no significant correlation between hemoglobin and hypersplenism (p>0.05).

There was a significant correlation between Total leukocyte count and hypersplenism (p<0.005). Patients with hypersplenism show decreased total leukocyte count (TLC) values. There was no significant correlation between Differential leukocyte count (DLC) and hypersplenism (p>0.05).

The red cell indices were quite helpful in the morphological classification of anemia. MCV, MCH and MCHC were found to be decreased respectively, in 60%, 64% and 44% cases of splenomegaly. Anemia constituted the most common cause, amongst which iron deficiency anemia (18%) was associated with decreased red cell indices while, megaloblastic anemia (8%) with increased red cell indices. RDW was found to be increased in 88% of the cases, of which anemia (30%) was the most common, followed by leukemia and lymphomas (20%) and congestive causes (18%). The retic count was found to be normal in most of the cases (82%).

Hematological causes (60%) outnumbered the non hematological causes (40%) in the present study. Anemia (30%) was found to be the most frequent cause, amongst which iron deficiency anemia accounted for 18% cases, megaloblastic for 8% cases and dimorphic anemia for 4%

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cases. These were followed by hematological neoplastic conditions (22%) that included chronic myeloid leukemia (10%), acute myeloid leukemia (4%), acute lymphoblastic leukemia (2%) and metastatic non-hodgkin's lymphoma (6%). Study by Varsha S et al [14] also reported 3 cases of CML, 2 cases of AML and 1 case of ALL in their study of 100 patients.

Amongst the non hematological conditions (40%), the most common cause of splenomegaly was congestive splenomegaly secondary to liver cirrhosis, hepatic and splenic vein thrombosis (18%) followed by infective causes (12%) that included malaria (8%), dengue fever (2%) and HIV (2%). This was comparable to the study by Hussain I et al [12] who reported cirrhosis of liver to be the most common cause (69%). In contrast, Nadeem A et al ^[5] concluded anemia, malaria, bacterial infections and hematological malignancies to be the common causes associated with splenomegaly. Ali N et al [3] found out hematological malignancies (37%) to be the most common cause followed by malaria (20.5%), megaloblastic anemia (13%), bacterial infections (9%). While, Varsha S et al [14] reported the commonest etiology to be inflammatory in 49% patients amongst which malaria was found to be the commonest etiology, followed by congestive causes (23%). The variability seems to reflect the higher prevalence of nutritional anemia in Indian subjects.

Hypersplenism is a condition in which the spleen becomes increasingly active and then rapidly removes the blood cells. It can result from any splenomegaly. It is most common with splenomegaly secondary to portal hypertension and hematological disorders.[11] It is characterized by reduction in one or more cellular elements of the blood leading to anemia, leucopenia, thrombocytopenia or any

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combination of these, normocellular or hypercellular marrow associated with hyperplasia of the respective marrow precursors of the deficient cell type and correction of the peripheral blood cytopenia by splenectomy.[6,9,10,11]

The present study showed that out of total 50 cases of splenomegaly, 18 cases (36%) presented with hypersplenism . Congestive splenomegaly secondary to liver cirrhosis (14%) was the most common cause of hypersplenism followed by anemia (8%) . Our findings were comparable to the study by Sundaresan BJ et al [10] that revealed hypersplenism in 28% patients. Congestive splenomegaly due to hepatic cause was found to be the most common cause of hypersplenism. Another retrospective study by O'Reilly RA [15] also concluded that hypersplenism remains a useful concept for the splenomegaly of liver diseases.

Bone marrow examination and biopsy were very useful either in confirming the diagnosis or in excluding a primary marrow involvement and suggesting alternative etiology.

In the present study, most of the cases of hypersplenism presented with moderate splenomegaly. Out of 18 cases (36%) of hypersplenism, 13 cases (26%) were associated with moderate enlargement of spleen while, only 5 cases (10%) presented with mild splenomegaly. There was significant а association between splenomegaly and hypersplenism (p< 0.05). While Sunderesan BJ et al [8] had reported in their study that though the prevalence of hypersplenism was found to be increased with increasing spleen size (p < p0.0001), they did not find any significant correlation between splenic size and severity of hypersplenism.

Hypersplenism had no significant correlation with hemoglobin (p> 0.05) in our study as majority of the cases (98%) of splenomegaly

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were associated with decreased hemoglobin levels . Total leucocyte count values were found to be significantly associated with hypersplenism (p< 0.005) while DLC values had significant correlation (p> 0.05 no Hypersplenism was significantly associated with decreased platelet count (p< 0.0001). Of the 18 cases of hypersplenism, there were 8 cases which were splenectomised in our institution and showed subsequent normalization of the haematological parameters.

USG study of splenomegaly was quite rewarding and we could confirm splenomegaly in all our cases. USG confirmation of splenomegaly has also been exercised by authors like Nadeem et al.[5] Interesting USG findings were noted in some of our cases which broadened our perspective on possibilities of etiology. According to Catalano et al [16] a real time sonography is considered a useful technique allowing the depiction of wide range of splenic abnormalities.

In the 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 and pertinent investigative workup. Workers like Nadeem et al [5] deliberately excluded cases of malaria, typhoid fever and liver diseases on pertinent investigations. Most of the studies reviewed are from tropical and developing countries [3,5,8] while few are from united states. [15,17,18,19] More such studies with large number of cases are required in future.

We conclude that splenomegaly in a symptomatic person should always be investigated thoroughly as most of the common causes are treatable. Given the multitude of functions of spleen, it is not surprising that

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splenomegaly occurs in a variety of conditions. There is an exhaustive list of differential diagnosis of splenomegaly. Hematological causes outnumbered the non-hematological cause of splenomegaly. The most frequent cause of splenomegaly was anemia followed by hematological neoplastic conditions and congestive causes. The commonest cause of hypersplenism was congestive splenomegaly secondary to liver cirrhosis. Degree of splenomegaly was significantly associated with degree of hypersplenism. Hematological profile in cases with enlarged spleen are of utmost importance as a diagnostic or additional tool in elucidating the etiogenesis of splenomegaly.

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