

Etiological Pattern of Splenomegaly in Adults at Tertiary Care Hospital Jamshoro Sindh

Mona Humaira, Atif Ahmed, Asadullah Memon, Sohail Ahmed Siddique, Pir Abdul Hayee, Mohammad Hanif Ghani, Rafi Ghouri

ABSTRACT

BACKGROUND: Splenomegaly is usually the result of an underlying disorder; causes ranging from infections to blood cancers. Primary diseases of spleen are uncommon. Etiology of splenomegaly varies according to the geographical areas studied and depends upon the endemic, genetic and hematological diseases in the particular region. Purpose of this study was to find out the causes of splenomegaly in a tertiary care hospital representing almost entire interior of Sindh.

MATERIAL & METHODS: This descriptive case series study was carried out at Department of Medicine Liaquat University Hospital Jamshoro from 1st March 2007 to 31st August 2007, over a period of six months. 100 Male and Female patients older than 13 years of age and admitted in ward with clinically enlarged spleen were selected for this study. Sampling technique was Non Probability convenient sampling. After getting informed consent from patients proforma was filled, elaborating history, important clinical findings and investigations like abdominal ultrasonography, CBC, LFT, HBsAg, Anti HCV etc were performed. Data analysis was carried out by SPSS 16 statistical software.

RESULTS: Among 100 patients with splenomegaly there was majority of male patients i.e.60%.The most common cause of splenomegaly found in our study was chronic liver disease i.e. 64% followed by malaria 16%, and hematological malignancies 14%. There were 2% patients found with enlarged spleen due to tuberculosis, remaining 4% comprised 1% each of enteric fever, infective endocarditis, CCF and SLE. Among the patients of hematological malignancies there were 9% patients of leukemia, 4% of lymphoma and 1% of myelofibrosis. As to the 9% leukemic patients, 4% suffered from Chronic Myeloid Leukemia, 3% from Acute Myeloid Leukemia and 2% from Chronic Lymphocytic Leukemia. Most common associated clinical sign was anemia demonstrated in 77% of patients.

CONCLUSIONS: Chronic liver disease is the most common that leads to splenomegaly in population studied. Malaria and hematological malignancies appear to be the major contributors for splenomegaly. Finding of enlarge spleen needs clinical work up to reach the correct diagnosis.

KEYWORDS: Splenomegaly. Chronic liver disease. Malaria. Hematological malignancies.

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INTRODUCTION

Spleen is usually not palpable in healthy people, it often become palpable due to some underlying disease.¹ Splenomegaly may occur because of mild illness but may be because of hematological malignancies². The prevalence of splenomegaly is varied and increases significantly among selected populations, such as in HIV patients (up to 66%), or in patients of schistosomiasis.³ It has also been noted that spleen may be palpable without any abnormality. It occurs in persons with low diaphragm (e.g. Emphysema) or with widely spread ribs². According to a study 3% of

healthy students and 12% of normal postpartum women had splenomegaly³.

When the spleen grows in size, it filters large number of blood cells and platelets leading to cytopenia (hypersplenism).⁴ This may have its consequences, e.g. anemia, frequent infections and bleeding disorders. Hypersplenism may present without splenomegaly and vice versa.⁴

Evaluation of etiology of splenomegaly is also stressed in developed countries as its presence may be an indicator of hematological malignancies⁵ Our study is focused on finding out causes of

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splenomegaly in adult patients at a tertiary care hospital and to observe frequency of various causes which may lead to splenomegaly, comparing hematological versus non hematological causes of splenomegaly. We have also assessed clinical finding associated with splenomegaly including anemia, fever, jaundice, hepatomegaly and lymphadenopathy.

Objectives

The objective of this study was to evaluate the causes of splenomegaly in adult patients presented at Liaquat University of Medical and Health Sciences Jamshoro/ Hyderabad.

MATERIAL AND METHODS

This descriptive case series study was conducted at Medical unit-III, Liaquat University Hospital Jamshoro from 1st March 2007 to 31st August 2007 over the period of six months. 100 Male and Female patients older than 13 years of age and admitted in ward with clinically enlarged spleen were selected by non probability convenient sampling. Patients below 13 years of age were excluded from the study.

After getting informed consent, all patients were evaluated by history, examination & laboratory investigations. Data obtained included: age, gender, signs & symptoms relevant to causes of splenomegaly including anemia, jaundice, fever, generalized edema, cough, dyspnea, wasting skin rash, bleeding, lymphadenopathy, hepatomegaly and ascites. Patients with chronic liver diseases like chronic hepatitis B and C, compensated and decompensated cirrhosis were grouped together. Investigations performed included Blood CP, ESR, Urine analysis, Urea, Creatinine, HBsAg & Anti-HCV and U/S abdomen. Chest radiograph Prothrombin time, reticulocyte count, LFT's, RA Factor, ANA, Blood culture, Bone marrow examination, lymph node biopsy & echocardiography etc. were performed where needed for evaluation. Splenomegaly was classified as moderate if the spleen enlargement is between 11-20cm and massive if the largest dimension is greater than 20 cm. All information was recorded on proforma.

The data was analyzed by using SPSS version 16.0 software program.

RESULTS

Among 100 patients selected, 60% were male. The age of patients ranged between 14 to 75 years with mean age of $43 \pm SD 16.5$ years. Frequency of splenomegaly in different age groups is shown in figure no 1. The frequency of splenomegaly was higher among individuals within age group 51-75 years. Figure 2 showed various causes of splenomegaly found in our study along-with the percentage of each cause.

Among the patients of hematological malignancies there were 9% patients of leukemia, 4% patients of lymphoma and 1% of myelofibrosis. As to the 9% leukemic patients, 4% suffered from Chronic Myeloid Leukemia, 3% from Acute Myeloid Leukemia and 2% from Chronic Lymphocytic Leukemia. Stratification of etiology of splenomegaly with regards to age and sex is shown in Figure 3 & 4 respectively. Other clinical signs like Anemia and Fever etc. are shown in Table I. Anemia was most frequently found associated sign with splenomegaly, demonstrated in 77% of patients. Massive splenomegaly (>20 cm) was found in 8 patients. Commonest cause of massive splenomegaly in this was Chronic Myeloid Leukemia (n=4), followed by Tropical splenomegaly(n=3) syndrome. We found massive splenomegaly in 1 patient having Chronic liver disease.

FIGURE I:

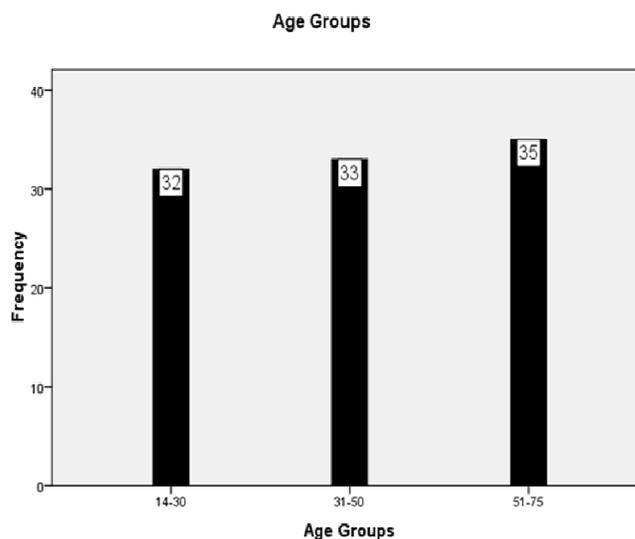


FIGURE II:

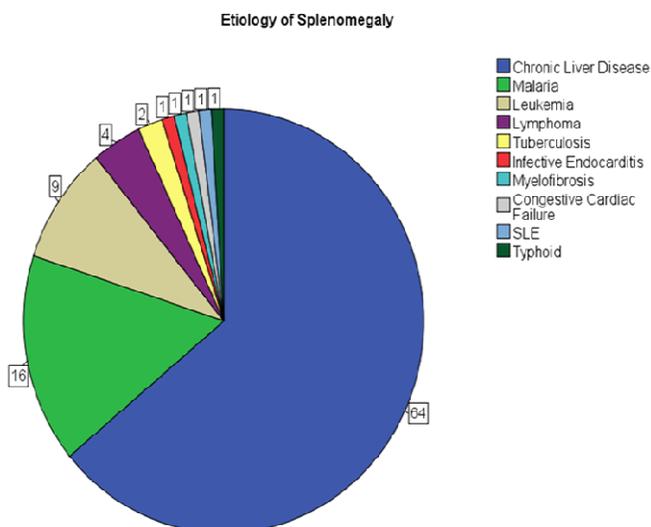


TABLE I: OTHER CHARACTERISTICS OF PATIENTS WITH SPLENOMEGALY

Total No. of Patients	Fever	Jaundice	Lymphadenopathy	Anemia	Hepatomegaly
100	26	23	8	77	19
Frequency	26%	23%	8%	77%	19%

FIGURE III:

Stratification of Etiology of Splenomegaly via Age Groups

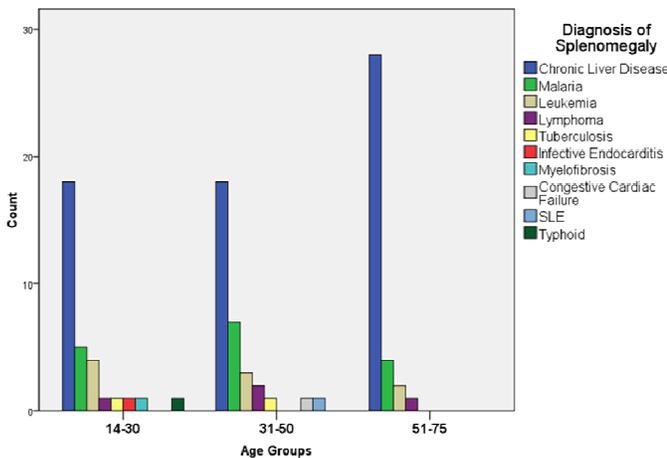
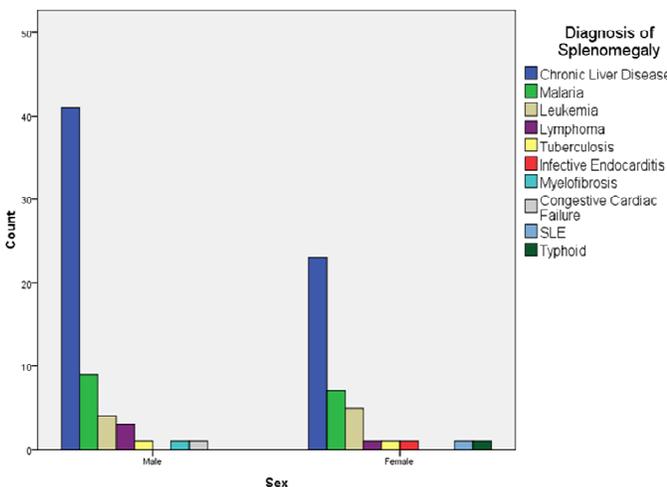


FIGURE IV:

Stratification of Etiology of Splenomegaly via Sex



DISCUSSION

This study was carried out at a tertiary care hospital from 1st March 2007 to 31st August 2007.

Spleen is often involved as a secondary process to diseases in other body tissues especially in hematological malignancies. Primary diseases of spleen are uncommon while massive enlargement of spleen carries a greater risk of rupture with mild physical trauma⁶.

In our study majority of patients were male i.e. 60% although no sex predilection was found for

splenomegaly but Tropical splenomegaly syndrome (or hyperactive malarial syndrome) has a female-to-male incidence ratio of 2:1.²

In a study conducted at Combined Military Hospital Attack in Pakistan, for splenomegaly Male to female ratio was 4:1⁷. In another study slight male preponderance was found i.e. 53% male while 47% were female.⁸

As far as the age of the patients is concerned, it ranges from 14 to 75 years in our study as such no age limit is exception for splenomegaly as also shown in various other studies.^{2,7,8} Among causes of splenomegaly most frequent cause found in our study was chronic liver disease which accounted for 64%. This includes patients with decompensated cirrhosis, compensated cirrhosis and chronic hepatitis B and C. This finding is comparable to result of a local study conducted at Mayo Hospital Lahore, in which 69% of patients had splenomegaly due to chronic liver disease.⁸ Different frequencies may reflect the variability of etiology of splenomegaly in different regions.⁵ In the study conducted at Attack CMH hospital authors found malaria as most frequent cause for splenomegaly while hepatitis /cirrhosis accounted for only for 9.4% of cases.⁷ Likewise, a study in India, indicated that Malaria was the most frequent cause of splenomegaly though the patients with ascites were exclude.⁹ This picture may be explained by the fact that Cirrhosis is a very common ailment in Pakistan, mainly caused by hepatitis B and C, whose prevalence is very high here.¹⁰ The incidence of cirrhosis varied worldwide and depended also upon the frequency of hepatitis B & C in the particular country.¹¹ Chronic Hepatitis B and C affect a large segment of populations; 350 to 400 million people suffered from Hepatitis B globally, resulting in 1 million deaths. 130–170 million people suffered from Hepatitis C all over the world, majority of them from developing nations.¹² In Pakistan prevalence of hepatitis B and C is 4% and 6% respectively¹⁰ but some other studies showed it is much higher than this.^{12,13} In Pakistan burden of HCV related chronic liver disease has increased. Previous studies showed that among CLD patients 16.6% were anti-HCV positive while recent data showed nearly 60–70% patients with CLD were positive for anti-HCV¹⁴. Seroprevalence of hepatitis C is different in different parts of Pakistan and varying from 2.2% to 13.5% during the last 5 years. It may reflect the standard of medical practice in these areas, awareness and

availability of Hepatitis B vaccine and other factors like re-use of syringes or sharing of razors etc. The highest seroprevalence of hepatitis C is reported from Lahore 13.5%, Jamshoro and Mardan 9%.¹⁵ The incidence of splenomegaly in cirrhotic patients varies from 36% to 92%.¹⁶ In a study on cirrhotic patients conducted at Peshawar by Khan et al reported splenomegaly in 36% patients.¹⁵ In another study splenomegaly was reported in 72.6% of patients of chronic hepatitis B and or C.¹⁷ Spleen is relatively less enlarged in patients with alcoholic cirrhosis as compared to other forms of cirrhosis.¹⁶

In our study second most frequent cause of splenomegaly was malaria, found in 16% of patients. This may reflect the situation of the casual disease in our region. According to WHO 300 to 500 million clinical cases of Malaria occurs annually causing death of about 1.5 to 2.7 million people. A large number of cases belonged to tropical regions.¹⁸ Pakistan comes in moderately endemic area and about 1.5 million cases occurred annually.¹⁹ In our study malaria was the second most frequent cause of splenomegaly but situation may be different in other parts of the country. In India Sundaresen et. al found Malaria as the commonest cause of massive splenomegaly.⁹

The basic mechanism behind this massive splenomegaly is Immune system activation. In response to repeated malarial infection Cytotoxic IgM suppressor lymphocyte (CD8+) antibodies are produced, which inhibit suppressor T cells with resultant uninhibited B cell production of IgM. The Reticuloendothelial system activation results in hyperplasia and manifest as progressive and enormous enlargement of the spleen.²⁰

In another study conducted in Ghana the most common causes of splenomegaly were hyper-reactive malaria splenomegaly (HMS, 41%), B-lympho proliferative disorders (22%), and chronic myeloid leukemia (8%). In 23% of patients authors were unable to find specific cause.²¹

In another study conducted in India by Dabadghao, authors found that 49% of cases were due to inflammatory causes, in which malaria was the most frequent other causes included dengue infection, enteric fever, hepatitis B and C, HIV and tuberculosis etc. Other causes were congestive, neoplastic and hyperplastic.¹

The third most common cause of splenomegaly in our study was hematological malignancies, including both leukemia, lymphoma and myelofibrosis. It constituted 14% of the total patients, including 9% of leukemia, 4% of lymphoma and 1% of myelofibrosis. Out of 9% patients of leukemia, 4% suffered from Chronic Myeloid Leukemia, 3% from Acute Myeloid Leukemia and 2% from Chronic Lymphocytic Leukemia. In the study con-

ducted at Attock frequency of hematological malignancies were 16.2%.⁷ In the study conducted by Hus-sainet. al at Mayo Hospital Lahore, authors found that 11% patients had splenomegaly due to hematological malignancies.⁸ Ali et. al while searching for the hematological causes of splenomegaly found that 37% of adults suffered due to hematological malignancies.²²

These malignancies are also an important cause of massive splenomegaly.²¹ In a retrospective analysis conducted in U.S.A. authors found that hematological malignancies were the most common cause of splenomegaly, specially lymphoma, followed by liver disease, infections and congestive splenomegaly.⁶

In our study 2% patients were found with enlarged spleen due to tuberculosis, 1% because of enteric fever, while in another local study Nadeem A. et al. found 2-1% patients with spleen enlargement due to tuberculosis and 10.4% due to enteric fever.⁷

Our remaining 3% patients comprised 1% each of infective endocarditis, Congestive Cardiac Failure and systemic lupus erythematosus, not entirely different but lesser than reported in other studies.⁸

Patients with disseminated TB may have splenic involvement, but splenic TB is rarely the main feature in patients with disseminated TB. Although splenomegaly due to the splenic TB found in immune competent patients too but more frequently found in immune compromised patients, e.g. HIV positive patients.²³

Splenomegaly due to Systemic lupus erythematosus was found in one patient in our study. It is a recognized feature of SLE. According to a study focusing on Hematological and clinical abnormalities in patients of systemic lupus erythematosus authors found that 65.8% had splenomegaly.²⁴

As to the clinical features Anemia was most frequently found clinical sign, present in 77% of patients. This number was higher than the number of anemic patients in the study of Dabadghao conducted in India. They found 61 patients of splenomegaly with anemia, including 49 patients with moderate to severe anemia.¹ Fever, Jaundice, Hepatomegaly and Lymphadenopathy were evident in 26%, 23%, 19% and 8% patients respectively in our study. Whereas in previously mentioned study, these authors found Fever in 48 % and Hepatomegaly in 73%.¹

In another recent study in India, authors found that 98% of patients of splenomegaly suffered from anemia. They also detected enlargement of liver in 36% of patients and lymphadenopathy in 14% of patients.²⁵ Regarding associated clinical features a local study assessed that Fever was present in 61% of patients of splenomegaly, Hepatomegaly was present in 37.5% patients, 21% patients were found anemic and Jaundice was detected in 4% of patients.⁷

As to the patients with massive splenomegaly 4 out of 8 patients suffered from Chronic Myeloid Leukemia, 3 patients from Tropical splenomegaly syndrome and 1 patient from cirrhosis. This is again comparable to the study of Nadeem et al who found 4 patients with spleen greater than 10 cm among them 2 patients suffered from hematological malignancies, 1 from tropical splenomegaly and 1 from Hepatitis / cirrhosis.⁷ In a study conducted in India authors found 5 out of 6 patients with massively enlarged spleen suffered from hematological malignancies.²⁵

Our study was focused on splenomegaly, occurs because of various diseases, etiology varied with geographical area under study and importance lies in recognition of the causal diseases. This study uncovered that chronic liver diseases were most common cause of splenomegaly at this tertiary care hospital catering to interior of Sindh, while most of the studies showed Malaria as a most common cause of splenomegaly.^{7,9} We did not find any patient with glycogen storage diseases. This signifies the imminent need for control of Hepatitis B and C along with other infectious diseases like malaria, enteric fever and tuberculosis. This study would be helpful for the community, in creating awareness by revealing common reason for splenomegaly which would guide the physician/doctor to focus on common etiology of splenomegaly rather than the rear ones.

Limitation of the study

The study was conducted on hospitalized patients of single center therefore results may not be generalized.

CONCLUSIONS

No age is exception for splenomegaly. Male and female both are affected with male predominance. Most common cause of splenomegaly found in our study was chronic liver disease. This is due to alarming situation of Hepatitis B & C in our country. Other important cause of splenomegaly was malaria so bulk of the causes of splenic enlargement was due to the infectious disease and points towards vigorous attempts for their proper control or eradication.

Hematological malignancies stand out of third highest in causes of splenomegaly in this study and presence of this sign should alert the physician to find out the actual disease.

Most common associated clinical sign with splenomegaly is anemia.

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AUTHOR AFFILIATION:

Dr. Mona Humaira (*Corresponding author*)
Assistant Professor of Medicine
Liaquat University of Medical & Health Sciences
(LUMHS), Jamshoro, Sindh-Pakistan.
Email: monaahmed2810@gmail.com

Dr. Atif Ahmed
Medical Officer
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Asadullah Memon
MBBS Student
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Sohail Ahmed Siddique
Medical Officer
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Pir Abdul Hayee
Post Graduate Trainee
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Mohammad Hanif Ghani
Professor of Medicine
LUMHS, Jamshoro, Sindh-Pakistan.

Dr. Rafi Ghouri
Professor of Medicine
LUMHS, Jamshoro, Sindh-Pakistan.