Original Article

Clinicopathological study of splenomegaly in pediatric age group

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Abstract

The study is based on 100 cases in pediatric age group with splenomegaly carried out in the Government Medical College and Hospital, Aurangabad. The study group showed slight male predominance. Clinical grading of splenomegaly was done with conventional method. Majority of cases (87%) had either Grade I or II splenomegaly. Hackett's method for grading of splenomegaly was also employed. Majority of cases (70%) had Grade I or II splenomegaly. The most common presenting complaint was fever followed by pallor. The other complaints were lump in abdomen, history of bleeding, pain in abdomen and symptoms of general ill health. The associated clinical findings were hepatomegaly (85%) and lymphadenopathy (33%). Hematological evaluation including bone marrow examination revealed diagnosis in the majority of cases (62%). These tests are safe, easy to perform and cost effective investigations. Other investigations like histopathology, biochemistry, serology, radiology proved helpful in the diagnosis in 16% cases. Anemia including hemolytic anemia and hematological malignancies were the common etiologies (28%) in the causation of splenomegaly. The Grade I and Grade II splenomegaly was the most common. Hemolytic anemia was the most common anemia (53.6%) followed by megaloblastic anemia (21.4%). The hematological malignancies also encountered frequently (28%). The most common malignancy was acute lymphoblastic leukemia (46.4%) followed by chronic myeloid leukemia (17.8%). The infectious etiologies included malaria, hepatitis, dengue fever, enteric fever etc. Malaria was the most common among them (46.1%). Infiltrative diseases mainly encountered in Grade III (conventional) and Grade 5 (Hackett's method) splenomegaly.

Key Word: splenomegaly, pediatric age.

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INTRODUCTION

Spleen is the largest organ of lymphoreticular system. It is involved and enlarged in various hematologic, infectious, immunoregulatory and infiltrative diseases. Splenomegaly is the major manifestation when it is involved in systemic diseases. It is an important symptom as well as sign, helping in the diagnosis of disease. Splenomegaly, as a symptom or sign, can be evaluated with battery of investigations like hematology, biochemistry, cytology, histopathology, serology and radiology. Hematologic investigations play an important role in evaluation. An attempt is made to understand the clinicopathological associations of splenomegaly in children under the age of 12 years.

Present study was carried out in Government Medical College and Hospital, Aurangabad, which mainly receives patients from Marathwada region of Maharashtra. Present study brings out clinical presentations of patients with splenomegaly, various investigations and their clinicopathological correlation. We have tried to carry out most of the feasible investigations, ultimately to throw light on the wide spectrum of etiology of splenomegaly.

Extensive search for similar studies in literature has been made to compare the findings with different parts of world, so as to know the relative prevalence and the etiological variations in select group.

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MATERIALS AND METHODS

The present study comprises 100 cases of splenomegaly from the indoor patients of Government Medical College and Hospital, Aurangabad. These cases are diagnosed on the basis of hematological, biochemical, serological, cytological, histopathological and radiological criteria, whichever is necessary for the diagnosis. The grading of splenomegaly is done by conventional as well as Hackett's method. The conventional method divides splenomegaly into Grade I, II, III which

Grade I (Mild) - Splenic enlargement in between left costal margin upto midway between umbilicus and left costal margin.

Grade II (Moderate) -Enlargement upto umbilicus. Grade III (Severe) - Enlargement beyond umbilicus. Hackett's grades are from Grade 1 to Grade 5

Grade 0 -Spleen not palpable even on deep inspiration.

Grade 1- Spleen palpable below costal margin usually on deep inspiration.

Grade 2- Spleen palpable but not beyond horizontal line between costal margin and umbilicus measured in a line drawn vertically from left nipple.

Grade 3 - Spleen palpable more than halfway to umbilicus, but not below a line running horizontally through it.

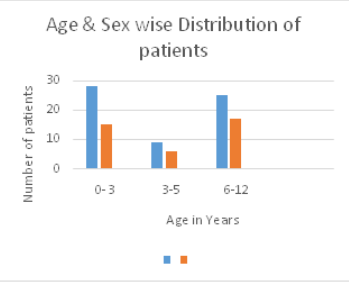
Grade 4- Spleen palpable below horizontal line drawn halfway between umbilicus and symphysis publis.

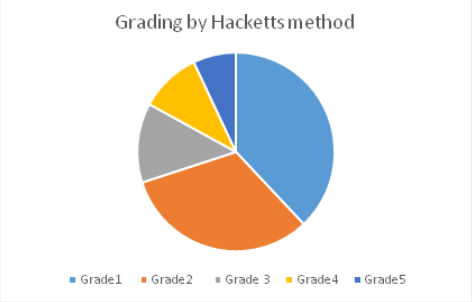
Grade 5- Spleen palpable and extending lower than in class IV.

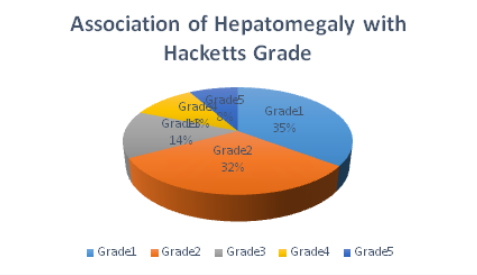
The hematological investigations include hemoglobin percentage, total leucocyte count, differential count, peripheral smear examination, platelet count, foetal fraction, sickling test, reticulocyte count. Bone marrow examination is done whenever necessary. Biochemical investigations are serum bilirubin, SGOT, SGPT, blood urea and serum creatinine. FNAC of spleen carried out whenever needed and also histopathology of lymph node, spleen or liver was studied as and when indicated.

OBSERVATIONS

This study comprises of 100 cases of splenomegaly in the children under 12 years of age which study included 62 male (62%) and 38 (38%) female patients with M:F ratio of 1.63:1. The study group showed male preponderance. There were 43 cases in the age group upto 3 years of which 28 cases were male and 15 were female with male to female ratio of 1.86:1. In the age group between 3 to 5 years, 9 were male and 6 were female with M:F ratio of 1.5:1. Twenty five male and 17 female cases were seen in the age group of 5-12 years with M:F ratio of 1.47:1. All the study groups showed slight male preponderance.







Clinical grading of splenomegaly was done with conventional method. Forty four cases presented with Grade I splenomegaly (44%), Grade II splenomegaly was observed in 43 (43%) cases, Grade III splenomegaly was in 13 (13%) cases.The majority of cases presented with Grade I and II splenomegaly. Grading of splenomegaly was also done with Hackett's method. Grade 1 splenomegaly was seen in 38 (38%) cases, grade 2 in 32 (32%). There was 13 (13%) which revealed Grade 3 splenomegaly, Grave 4 splenomegaly was observed in 10 (10%) cases and 7 (7%) cases presented with Grade 5 splenomegaly. Majority of cases (7%) had Grade 1 or 2 splenomegaly. Fever was the most common presenting complaint (80%), followed by pallor in 37%. Lump or distension of abdomen was observed in 31% cases, history of bleeding could be elicited in 23 (23%) cases. Pain in abdomen was present in 17 (17%), while cough was observed in 21% cases. The other presenting complaints were symptoms of general ill health i.e. fatigue, weakness in 12%, swelling in the neck in 9%, yellowish discoloration of eyes (Jaundice) in 8% and rash in 4% cases. Lymphadenopathy was observed in 33 patients of splenomegaly, 20 were male and 13 were female with male to female ratio of 1.53:1. The grade-wise association of cases with lymphadenopathy. Hepatomegaly was the most common associated finding with splenomegaly. In the study group, 85 patients had associated hepatomegaly with male to female ratio of 1.65:1.

The grade-wise association of cases with hepatomegaly was as follows Grade 1-30 cases , Grade 2 – 27 cases, Grade 3-12 cases, Grade 4- 09 cases , Grade 5 – o7 cases. Routine hematological investigations were done in all 100% patients. Bone marrow examination was done in 59% cases. Biochemical investigations were done in 35% cases. Serological investigations were performed in 13 cases. Test for Australia antigen (HbsAg) was done in 4, Widal test in 2, Direct Coomb's test in 2, IgG and IgM antibodies for Dengue in 2 and HIV in one case.

The other investigations done were fine needle aspiration cytology of spleen in 7 cases and histopathology in 7 cases. Histopathology included examination of spleen in one case, lymph node in 2 and liver biopsies in 4 cases. Radiological examination was carried out in 26 cases which included 22 ultrasonography and other in 4 cases. In the present study, 62% cases were diagnosed with hematological investigations, out of which 28 cases were diagnosed with routine hematological investigations and 34 with bone marrow examination.

Thirty-five cases were evaluated with biochemical investigations. In 2 cases diagnosis was positive. The positivity rate was 5.71%. Serological investigations were diagnostic in 4 out of 13 cases (30.76%). USG was diagnostic in 2 cases (9.09%), other radiological investigations were diagnostic in 2 cases out of 4 (50%). FNAC of spleen was done in 7 cases, which was helpful in diagnosis in 3 cases (42.9%). Histopathology of spleen was done in one case, which supported the diagnosis. Histopathology of lymph node was diagnostic in 50% cases. Liver biopsy was done in 4 cases, out of which 2 were diagnostic (50%). Twenty-three cases remained undiagnosed. Hemoglobin percentage was below 7 gm% in 38% cases in the present study. In 50% cases, it was found to be between 7 to 10 gm% and 10 gm% in 12 cases. Normocytic normochromic RBCs were observed in 32 cases. Mild hypochromia was present in 35 cases, 24 cases showed moderate hypochromia. Severe hypochromia was observed in 6 cases. WBC count – leucocytosis was present in 30 cases, 9 cases showed leucopenia. Peripheral smear suggestive of leukemia which was seen in 23 cases. Platelet count – thrombocytopenia was seen in 41% cases. Parasite – the peripheral smear showed presence of malarial parasites in 6 cases. Bone marrow examination was done in 34 cases, bone marrow aspirates showed normoblastic erythropoiesis in 18 cases (52.94%), two cases (5.88%) showed normoblastic erythropoiesis with erythroid hyperplasia. Micronormoblastic marrow was seen in 3 cases (8.82%). Six cases (17.64%) revealed megaloblastic erythropoiesis. Bone marrow suggestive of leukemia and lymphoma which was seen in 20 cases (58.82%). The diagnosis of aplastic or hypoplastic marrow was made in 4 cases (11.76%). Bone marrow revealed increased population of histiocytes in 2 cases (5.88%), one case (2.94%) showed normoblastic marrow with focal megakaryocytic hyperplasia. FNAC of spleen was carried out in 7 cases, in 3 cases (42.9%) the aspirate showed majority of lymphocytes. One case (14.2%), revealed myeloid metaplasia in the spleen. One case (14.2%) revealed the diagnosis of Gaucher's disease and one case (14.2%) splenic aspirate showed atypical lymphoid cells. In one case (14.2%), the diagnosis of lymphoma was made with aid of bone marrow examination. In one case of portal hypertension, histopathology of spleen was available which showed congestion of both red and white pulps of spleen. Lymph node biopsy was available in 2 cases. One case showed changes of reactive lymph node and other revealed Hodgkin's lymphoma. Histopathology of liver was examined in 4 cases, one case (25%) showed normal histology of liver. No specific pathology was seen. One case (25%) showed changes of fatty liver. Glycogen storage disorders was observed in 2 cases (50%). In the present study, in the diagnosed cases, anemia and hematological malignancies were the most common findings. The diagnosis of anemia was made in 28% cases, out of which hemolytic anemia was the most common (53.57%). The hematological malignancies included leukemia in 24% and lymphoma - leukemia in 4% cases. Infective etiology of splenomegaly was observed in 13% cases, in which malaria was common in 53.9% cases. Fibrocongestive splenomegaly was observed in 2% cases. Infiltrative disorders were observed in 3% cases. In this study it was noted that in anemia, Grade I and Grade II splenomegaly was frequently encountered. Grade II splenomegaly was present in hemolytic anemia. Hematological malignancies presented with Grade II and III splenomegaly. In malaria Grade I splenomegaly was observed. All the infiltrative diseases presented with Grade III splenomegaly. In anemia, Grade 1 splenomegaly was frequently observed. Hemolytic anemias presented with Grade 2 splenomegaly. Leukemia was present invariably in all grades, more in Grade 2. In malaria Grade 1 and 2 splenomegaly was observed. The other infective cases also had Grade 1 splenomegaly. All the infiltrative diseases had Grade 5 splenomegaly. In the present study, hemolytic anemia was the common anemia encountered with 15 cases (53.5%). In this, sickle cell anemia was present in 6 cases, 4 cases had leucoerythroblastic blood picture, one case had autoimmune hemolytic anemia. In 4 cases, exact typing of hemolytic anemia was not possible. Megaloblastic anemia was present in 6 cases (21.4%). Iron deficiency anemia was encountered in 3 cases

(10.7%), 4 cases had aplastic or hypo plastic anemia. Acute lymphoblastic leukemia (ALL) was the most common leukemia, accounting for 46.4% cases of leukemia. Lymphoma -leukemia was seen in 4 cases (14.2%), AML occurred with frequency of 10.7%. Chronic myeloid leukemia resembling adult type was encountered in 3 (10.7%) cases. Juvenile CML was observed in 2 (7.1%), 2 cases (7.1%) had sub leukemic leukemia and one case of ALL also had sickle cell anemia. In the present study, malaria was the most common (46.1%) infectious etiology in splenomegaly. The other causes were hepatitis (15.3%), dengue fever (15.3%), enteric fever (7.7%), tuberculosis (7.7%). In the present study, fibrocongestive splenomegaly was observed in 2 cases. Infiltrative diseases were encountered in 3 cases of which 2 male patients had glycogen storage disease and one female with Gaucher's disease. One case of osteopetrosis was observed.

DISCUSSION

The enlarged spleen is a frequent and important sign in clinical practice. It is generally observed by the clinician, in systemic examination. In few cases, it is described by the patient as lump in abdomen or distension of abdomen.

Splenomegaly requires multiple steps to identify the etiology. However in some cases, the exact cause of splenomegaly cannot be identified despite all diagnostic studies.

World-wide, splenomegaly is not uncommon, but clinical symptoms, signs and major aetiolgoical factors differ considerably, according to geographic distribution of disease. Tropical splenomegaly syndrome is more common in the tropical countries including India. As spleen is involved in many different types of disorders the study groups selected by different workers are also varied including all age groups,[1,2] paediatric age[3], college freshmen[4] etc. Some studies were based on the etiological factors in the causation of splenomegaly like malaria, tropical splenomegaly syndrome[5], hepatic pathology[6], AIDS[7], bacterial infections[8], lymphoma of spleen[9] and idiopathic[10] etc.

In the Indian scenario, studies on splenomegaly were mainly done in eastern states[1,11] where malaria and Kala azar were prevalent. x. The studies available were based on etiological factor like sickle cell anemia and gross splenomegaly.[12]

This study was undertaken with the aim of knowing various etiological factors that were prevalent in Marathwada region, as well as to study the role of routine, readily available, low cost investigations in the diagnosis. The study was carried out in 100 patients and group was selected as patients who have palpable spleen as a symptom or sign in paediatric age group.

All these patients were evaluated for etiology using multiple investigations, mainly haematological. Biochemical, serological, radiological, FNAC and histopathological investigations were carried out depending upon the case.

All the studies show male preponderance. The present study shows male to female ratio of 1.63:1, which was comparable with studies by Timite *et al* (1992)[3] and Nadir *et al* (2004)[2].

In the present study, the age group range was 3 months to 12 years, 58% children were below the age of 5 years and 42% cases were between the age of 5 to 12 years.

Timite *et al* (1992)[3], also noted slight more children below 5 years (54.4%). The results of present study were comparable with the study of Timite *et al* (1992)[3].

In the present study, grading of splenomegaly was done by both conventional and Hackett's methods. Majority of previous studies mention splenomegaly as mild, moderate or severe. No study was available for comparison in conventional method.

In study by Timite *et al* (1992)[3], majority of cases (61.8%) were in Hackett's grade II splenomegaly, followed by 14% in Hackett's Grade III, however, they does not mention exact number of cases in Grade I, IV and V.

In the present study, 38% cases in Grade 1, 32% in Grade 2 and 13% in grade 3 splenomegaly. Majority of cases (60%) were observed in Grade 1 and 2 splenomegaly.

Grading of splenomegaly was necessary as it gives some clue to the possible etiological factor and the necessary investigations to be done accordingly.

The presenting complaints of the patients with splenomegaly were fever, pallor, symptoms of general health like fatigue, weakness, history of bleeding and abdominal distension.

Choudhari R.N. (1957)[1] and Timite *et al* (1992)[51], noted fever and pallor most frequently. In the present study, fever was the most common complaint, accounting in 80% cases. Pallor was noted in 37% cases. Timite *et al* (1992)[3] noted it in 72%. These findings were not comparable with the present study.

The case of splenomegaly needs a battery of investigations to reach to the diagnosis. Table X shows the investigations done in 100 cases. Haematological investigatiosn played a major role in the diagnosis. 62% cases could be diagnosed on hematological basis.

Twenty-eight percent cases were diagnosed with routine haematological investigations. Bone marrow

examination was carried out in 59 cases in which 34 were diagnostic (57.6%).

Histopathological and cytological examination also revealed diagnosis in 42.8% cases. The other important investigations were biochemical, serological and radiological which were helpful in the diagnosis.

The association of hepatomegaly with splenomegaly is known. Timite *et al* (1992)[3], noted hepatomegaly in 33.5% cases. Nadir *et al* (2004)[2], noticed hepatomegaly in 59% cases.

In the present study, hepatomegaly was found in 85% cases, which is not comparable with other studies.

The disease, which had hepatosplenomegaly were leukemia, lymphoma, hemolytic anemia, portal hypertension, hepatitis, enteric fever, glycogen storage diseases and Gaucher's disease.

Timite *et al* (1994)[3], noticed associated lymphadenopathy in 7% cases, whereas Nadir *et al* (2004)[40] noted it in double i.e. 14%. In the present study, lymphadenopathy was associated in 33% cases, which is higher than previous studies. The disease which had associated lymphadenopathy was leukemia, lymphoma, tuberculosis and anemia in some cases.

In the present study 100 cases were evaluated with all possible investigations. In 77% cases diagnosis was possible remaining 23 cases (23%) were undiagnosed.

In the present study anemia (28%), and hematologic malignancies (28%) were found to be major etiological factors along with other infective, fibrocongestive infiltrative and miscellaneous causes.

Timite *et al* (1992)[3], found malaria (53%) as the commonest aetiolgoical factor in the tropics. They noticed sickle cell anemia (14%), thalassemia (2%) and infectious like salmonella infection in 15%, schistosomiasis in 9%, AIDS in 3%. They infrequently noticed malignancies.

Nadir *et al* (2004)[2], observed hemolytic anemia in 68.1%, ALL in 13.5%, Niemann-pick disease in 9% and Hodgkin's disease in 4.5%. They also noted causes of splenomegaly in adults and found megaloblastic anemia (13%), hemolytic anemia (13%), hematological malignancies (35%) and tropical splenomegaly (5%).

Anemia was found to be the common etiological factor in 28% cases (Refer Table - XVII). Diagnosis of anemia was done with routine haematological examination and bone marrow examination. The cause of splenomegaly in anemia is destruction of immature red cells in the spleen.

Iron deficiency anemia was found in 3 (10.7%), meglablastic anemia in 6 (21.4%). Hemolytic anemia was present in 15 (53.5%) cases.

Hemolytic anemia had grade 2 splenomegaly in majority of cases. Other anemias frequently had grade 1 splenomegaly. Megaloblastic anemia causes splenomegaly in rare cases (2%). The cause for megaloblastic anemia in these patients might be different as the diagnosis is based on hematological profile only. Choudhari R.N. (1967)[1], described that splenomegaly could be due to malnutrition as the cases had dimorphic anemia due to combined deficiency.

Hematological Malignancies accounted for 28% cases in the present study. Leukemia was diagnosed in 24 cases, lymphoma in one and lymphoma-leukemia in 3 cases. ALL was the most common leukemia (46.4%), adult type CML was seen in 3 (10.7%), juvenile CML in 2 (7.1%) cases. Hodgkin's lymphoma was found in one case. The diagnosis of lymphoma-leukemia was made in 3 cases. Along with leukemia, these cases had severe anemia and thrombocytopenia. Splenomegaly in these cases is due to infiltration and destruction of immature leucocytes in the spleen. Rajarajeshwari G. and Viswanathan J. (1980)[13], studied 100 cases of leukemia in children. In the study 28 cases had AML, 45 of ALL, 7cases of CML, 2 cases of erythroleukemia and one case of subacute leukemia. They noticed anemia and hepatosplenomegaly as frequent associations.

Malaria was found in 6 cases (6%), 5 cases had *P. falciparum* infestation and one of *P. vivax*. Majority of cases had Grade 1-2 splenomegaly. Splenomegaly in malaria was due to diffuse histiocytic proliferation. Spleen may not be enlarged to palpate in acute stage. Also parasitemia may not be present in cases of splenomegaly due to malaria. Choudhari R.N. (1957)[1], found that malaria and malnutrition play role in causation of splenomegaly. It may be possible that in some cases malarial infection remains latent and contribute to splenomegaly.

In the present study, infectious etiology other than malaria was found in 7 cases. The common etiologies were hepatitis (2), Dengue fever (2), enteric fever, tuberculosis and pyogenic meningitis in one case each. All these cases had grade 1-2 splenomegaly. Splenomegaly in these cases was due to cellular response of the spleen to circulating infectious agents and toxins.

The other infective etiologies described in the literature were infectious mononucleosis, brucellosis, toxoplasmosis, bacterial endocarditis, syphilis, Schistosomiasis and AIDS etc.

Infiltrative diseases were diagnosed in 3 cases, 2 had glycogen storage disease and one had Gaucher's disease. All had grade 5 splenomegaly.

One case of osteopetrosis was diagnosed on radiological basis. It had grade 2 splenomegaly. Fibrocongestive splenomegaly was found in 2 cases. Diagnosis was based on USG, serology and clinical basis. One specimen of splenectomy was available which showed congestion of

spleen. Comparable literature was not available, so exact comment cannot be made. Majority of cases (62%) were diagnosed with haematological investigations, other investigations supported the diagnosis.

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