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Spectrum of Malignant and Non-Malignant Hematological Disorders in a Tertiary Care Centre

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ABSTRACT

Objective: To analyze the spectrum of malignant and non-malignant hematological disorders in our setup.

Patients and Methods: This cross-sectional study was done in the Department of Pathology, Khyber Teaching Hospital, Peshawar, from 1st January -2016 to 30th December-2016. A total 352 patients underwent bone marrow biopsy during study period. About 15 patients had inadequate aspirate samples that were unfit for opinion. So these were excluded from the study. The remaining of 337 patients were included in the study. All patients of both sexes and all ages were included in the study. Bone marrow aspiration and biopsy was done, the slides were stained, examined and diagnosis was recorded. Data was analyzed by SPSS version 16 and results were drawn accordingly.

Results: Among total 337 patients, there were 185 (55%) male and 152 (45%) females. Male to female ratio was 1.2:1. The median age of participants was 26 years and range was 9 months -72 years, (mean age was 36±17.8 years). Regarding pattern of hematological illnesses, commonest non-malignant disorder was Megaloblastic anemia. Among malignant hematological illnesses, frequent disorder was Acute Lymphoblastic Leukemia.

Conclusion: Megaloblastic anemia, Hemolytic anemia, and Aplastic anemia are common non-malignant hematological disorders in our setup. Acute Lymphoblastic Leukemia, Acute Myeloid Leukemia and Multiple Myeloma are common malignant hematological disorders in our set up.

Key words: Acute leukemia, Anemia; Bone marrow biopsy, Megaloblastic anemia; Multiple myeloma.

Author`s Contribution

[1] Conception, synthesis, planning of research and manuscript writing

[2,3] Interpretation and discussion Data analysis, Interpretation, manuscript writing and Active participation in data collection

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Introduction

Hematological disorders are quite common in general poplation.[1] These disorders range from simple conditions like iron deficiency anemia to life threatening conditions like carcinomas involving bone marrow.[1-6] Most of the hematological disorders present with vague symptoms.[6] Thus, they create a diagnostic problem for the clinicians.[1,6] Such cases need the bone marrow examination to reach the final diagnosis and help clinician decide further management.[1,6] Relevant medical history, clinical examination, and review of already performed laboratory investigations is necessary before performing the bone marrow biopsy.[1,7] Interpretation of bone marrow aspirate findings is carried out in the light of patient's history, examination and laboratory findings; and final diagnosis is made accordingly .[2]

Megaloblastic anemia, Leukemia, Aplastic anemia, Idiopathic thrombocytopenia purpura are commonly seen hematological disorders.[1,6] In Megaloblastic anemia, there is low hemoglobin level and raised Mean cell volume of above 100 fl.[1] The most common cause of Megaloblastic

anemia is nutritional deficiency of Vitamin B-12 and folate.[1,8,9] In Idiopathic thrombocytopenic purpura, there is an autoimmune destruction of platelets in the spleen.[1] The platelet count is low but bone marrow megakaryocytes are increased in such patients.[1,3] Patients with fever, pallor, and enlarged liver or spleen usually have some underlying malignancies like leukemia.[1] Leukemia is common hematological malignant disorder in children and bone marrow examination is necessary for making its diagnosis. [6]

Worldwide, the commonest non-malignant hematological disorders are iron deficiency anemia while commonest malignancies are Acute lymphoblastic leukemia in children and Acute myeloid leukemia in adults. However, the pattern of hematological disorders is different in the western countries and the developing world.[6] So, the data regarding pattern of hematological disorders in the developed countries may not be representative of our population. This study was conducted with the aim to determine the pattern of hematological disorders in our setup.

Patients and Methods

This Cross-sectional study was performed at the Department of Pathology, Khyber Teaching Hospital, Peshawar, from 1st January 2016 to 31st December 2016. Sample size was calculated by using the sample size formula:

$$n = \frac{z^2 \times p\,(1-p)}{d^2}$$

where: z (level of confidence) =1.96; p (prevalence of megaloblastic anemia) = 16.6% [1,] d (precision)= 0.05; sample size turned out to be 213.

We inducted 337 patients through non probability purposive sampling technique to further strengthen the data. Patients of all ages and both sexes, for them bone marrow biopsy was advised by their consultants were included in the study. Patients whose bone marrow samples were inadequate and final diagnosis could not be reached were excluded from the study. Demographic data of patients was noted. Bone marrow aspiration was done. Slides were stained and examined under microscope. Mean and standard deviation were calculated for quantitative variables e.g. age. Frequencies and percentages were calculated for qualitative variables like diagnosis and gender. Data was analyzed using SPSS version 16.

Results

Among total of 337 samples, 185 (55%) were males and 151 (45%) were female patients. The median age of participants were 26 years, ranging from 9 months to 72 years (mean age 36 years ±17.8 SD). The bone marrow aspiration/biopsy showed the commonest hematological malignancy was Acute Lymphoblastic Leukemia, that was seen in 31 (9%) patients, followed by Acute Myeloid Leukemia, which was seen in 26 (7.7%) cases. Multiple myeloma and mononuclear infiltration was seen in 17 (5%) patients each. Chronic Lymphocytic Leukemia was seen in 10 (2.9%) cases. (Table 1)

Table 1: malignant hematological disorders in study participants (n=109)

Malignant disorders (n=109)	n (%)	Gender	
		Male n(%)	Female n(%)
Acute Lymphoblastic Leukemia	31(9.1)	18(5)	13(4.1)
Acute Myeloid Leukemia	26(7.7)	12(3.5)	14(4.2)
Multiple myeloma	17(5)	15(4.4)	2(0.6)
Mononuclear infiltration	17(5)	14(4)	3(1)
Chronic Lymphocytic Leukemia	10(2.9)	6(1.8)	4(1.1)
Chronic Myeloid Leukemia	8(2.4)	5(1.5)	3(0.9)

The commonest non-malignant hematological disorder was megaloblastic anemia, seen in 37(10%) cases, followed by Hemolytic anemia and Aplastic anemia which was seen in 20(5.9%) and 18(5.3%)cases respectively. Anemia of chronic disorder was seen in 16(4.7%) cases. Idiopathic Thrombocytopenic Purpura was seen in 12 (3.6%) patients. Iron deficiency anemia was seen in 11 (3.3%) patients. Mixed deficiency anemia in 9 (2.7%),

Myelodysplasia in 6 (1.7%), Malaria in 5(1.5%), and Niemann Pick in 4 (1.2%) patients. Gaucher disease and Visceral Leishmania was seen in 2 (0.6%) patients each.

Table 2: Pattern of non-malignant hematological disorders in study participants (n=228)

Non-malignant Disorders (n=228)	n (%)	Gender	
		Male n(%)	Female n(%)
Megaloblastic anemia	37(10.9)	21(6.2)	16(4.7)
Excessive Peripheral Destruction	32(9.4)	25(7.3)	7(2.1)
Normocellular marrow	31(9.1)	17(5)	14(4.1)
Hemolytic anemia	20(5.9)	8(2.4)	12(3.5)
Aplastic anemia	18(5.3)	8(2.4)	10(3)
Anemia of chronic disorder	16(4.7)	7(2)	9(2.7)
Idiopathic Thrombocytopenic Purpura	12(3.6)	5(1.5)	7(2.1)
Iron deficiency anemia	11(3.3)	5(1.5)	6(1.8)
Mixed deficiency anemia	9(2.7)	7(2)	2(0.7)
Myelodysplastic syndrome	6(1.7)	4(1.2)	2(0.5)
Polycythemia vera	6(1.7)	4(1.2)	2(0.6)
Essential Thrombocythemia	5(1.5)	2(0.6)	3(0.9)
Myelofibrosis	5(1.5)	2(0.6)	3(0.9)
Hypereosinophilic syndrome	5(1.5)	3(0.9)	2(0.6)
Malaria	5(1.5)	2(0.6)	3(0.9)
Nieman pick disease	4(1.2)	1(0.3)	3(0.9)
Gaucher disease	2(0.6)	1(0.3)	1(0.3)
Visceral leshmeniasis	2(0.6)	2(0.6)	-
Chediak hegashi syndrome	1(0.3)	1(0.3)	-
Hemophagocytic Lymphohistiocytosis	1(0.3)	1(0.3)	-

Histiocytic lymphohistiocytosis and Chediak Hegashi syndrome was seen in 1 (0.3%) patients each. (Table 2).

Discussion

The spectrum of hematological disorders is very wide, ranging from anemias to leukemias.[10,11] Bone marrow aspiration and biopsy are very helpful in diagnosing the hematological disorders.[6] It not only helps in giving final diagnosis but also helps the clinicians to decide which further tests should be performed.[1] In certain cases, patient cannot be managed further until bone marrow report gives conclusive diagnosis.[1,2]

Interpretation of bone marrow findings is tailored to the patient's clinical history, clinical examination and other laboratory results in order to make final diagnosis.

In the present study, the commonest non-malignant hematological disorder was Megaloblastic anemia, which was seen in 37 (10.9%) patients. Similar findings are presented by Shasri SM from india, in which Megaloblastic anemia was the commonest anemia found in 59% patients.[10] Similar findings were reported in local studies done by Rahim F and Anjum.[11,12] Megaloblastic anemia was commonest disorder in studies done by Gautam R and Atla BL[13,14] In another local study done by Munir and colleagues, Megaloblastic anemia was seen in 16.6% of patients.[1] In another study done by Shiddappa, Megaloblastic anemia was present in 27% of the patients.[15] These values are high as compared to the present study. In another study done by Khan A, megaloblastic anemia was present in 14.6% of the cases.[6] This figure is somewhat close to the one in the present study. In addition to poor dietary meat intake, factors like chronic diarrhea, worm infestations, and malnutrition are responsible for causing vitamin B12 deficiency in our setup.[6]

The diagnosis of Excessive peripheral destruction was made in 32 (9.4%) patients. Excessive Peripheral Destruction of hematopoietic cells is often due to enlarged spleen, causing removal of cells from circulation at a much faster rate.[16] In a local study done by Munir and collegues, excessive peripheral destruction was seen in 3.2% of the patients.[1] In a study done in King Fahad Hospital Saudi Arabia, 4.4% of the patients were diagnosed as having excessive peripheral destruction.[17] Normal bone marrow was seen in 31 (9.1%) cases. In a

study done by Addo and collegues in Ghana, about 8.75% of the patients had a normal bone marrow.[2] In a study done by Anjum et al in Abottabad, about 8.3% patients had normal bone marrow.[11] This is quite close to the figure in the present study. In another study by Atla BL, about 16.8% patients had normal marrow.[14]

Hemolytic anemia was seen in 20 (5.9%) cases in the present study). In a study done by Munir and collegues in Peshawar, about 10.8% patients showed hemolytic anemia.[1] This is much higher than that reported in the present study. Atla BL found a higher prevalence of about 46% in his study.[14] In Hemolytic anemia, there is increased red blood cell destruction and bone marrow fails to form new red blood cells at the same rate. [1] In order to know the cause of hemolysis, investigations like G6PD level, osmotic fragility test, and Coomb's test are done.[1] Aplastic anemia was seen in 18 (5.3%) cases in the present study. Atla BL showed the prevalence of 19% in his study which is much higher than the present study.[14] Aplastic anemia may be congenital or acquired.[1,18] Failure of the bone marrow causes decreased production of blood cells.[18] Such patients present with pallor, fever and bruises all over the body.[6] Viral infections and drugs are common causes of acquired Aplastic anemia.[19] Hepatitis is a common cause of Aplastic anemia in our society.[19]

Anemia of chronic disorder was seen in 16 (4.7%) cases in the present study. Treating the underlying chronic disease would cure the anemia in such cases.[19,20] Idiopathic Thrombocytopenic Purpura (ITP) was seen in 12 (3.6%) cases in the present study. It was common in females. In one study done by Munir and colleagues, ITP was seen in 16.6% of patients.[1] This is much higher than that reported in the present study. Similar findings were presented by other local and international studies.[3,6,21,22] Patients with ITP present with epistaxis and bruises all over body and a trial of corticosteroids usually improve the condition.[23] Iron deficiency anemia (IDA) was seen in 11 (3.35%) cases. It was common in females (Table.1). Microcytic hypochromic red blood cells with absent bone marrow iron stores is suggestive of iron deficiency anemia.[24,25] In a study conducted in Peshawar, about 5.7% patients referred for bone marrow biopsy, had iron deficiency anemia.[1] This figure is somewhat close to the present study. In another study done by Khan A., about 7.6% patients had iron deficiency anemia[6]. Similar data was presented in a study of Ikram N. from Islamabad. [26] Commonest cause of iron deficiency anemia is worm infestations and nutritional deficiency of iron. [1]

Myelofibrosis was seen in 5 (1.5%) cases. In a study done by Munir and colleagues, myelofibrosis was seen in only 0.6% of the patients[1]. In a study conducted in Ghana, myelofibrosis was present in 2.5% of the patients.[2] This figure is somewhat close to that in the present study. Visceral leishmaniasis was diagnosed in 2 (0.6%) cases by bone marrow aspirate examination. Higher incidence of 6.6% was reported in two local studies.[5,6] In a study done in Peshawar, only 0.5% patients had visceral leishmaniasis .[1] In a similar study done by Niazi M at Lady Reading Hospital Peshawar, only 0.2% patients had visceral leishmaniasis.[27] This is in accordance with the present study. Patients suspected of having visceral leishmaniasis present with pallor, fever and visceromegaly.[28] Bone marrow examination establishes final diagnosis in such cases. [28]

In the present study, the commonest malignant hematological disorder was Acute Lymphoblastic Leukemia (ALL), which was seen in 31 (9.1%) cases. Similar findings were reported in a local study done by Rahim F in which ALL was the commonest hematological disorder.[12] Acute Myeloid Leukemia (AML) was seen in 26 (6.6%) cases in the present study. Thus, it was second commonest leukemic disorder next to ALL in the present study. Similar findings are presented by Anjum in his study in which ALL is the commonest malignancy followed by AML.[11] Similar results are reported in another studies done in Peshawar.[1,5,29] In a study done by Shastry in India, AML was the commonest leukemia seen in about 3.6% cases.[10] ALL is the commonest malignant disorder of childhood.[6] Multiple myelomas was seen in 17(5%) cases in the present study. So it was common malignancy next to acute leukemias. Similar findings were presented by Anjum in a study from Abbottabad in which 10% patients had multiple myeloma and was common next to acute leukemias. [11]

Mononuclear infiltration was seen in 17 (5%) cases. In a study done in Peshawar, only 2% patients had metastatic cells in the bone marrow.[1] In a study done in india by Atla BL, about 4% patients showed infiltration in bone marrow.[14] Spread of tumor cells to the bone marrow

points to poor prognosis of the disease.[30] Chronic lymphocytic leukemia (CLL) was seen in 10 (2.9%) cases. In a study done in Ghana, about 10% patients had CLL.[2] Atla BL has shown incidence of 2.9% in his study which is same as in the present study.[14].

Conclusion

Megaloblastic Anemia was the commonest non-malignant hematological disorders in our setup. Acute Lymphoblastic Leukemia was the most common malignant hematological disorders, followed by Acute Myeloid Leukemia. Proper education and awareness of population regarding the causation, prevention and treatment of these diseases may improve health of community and reduce morbidity.

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