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MORPHOLOGICAL FEATURES OF BONE MARROW ASPIRATES IN VARIOUS TYPES OF CYTOPENIA(S) AT SAIDU TEACHING HOSPITAL, SWAT

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ABSTRACT

OBJECTIVES: To find and document clinico-hematological features of bone marrow aspirates in patients presenting with various forms of cytopenia(s) at Saidu Teaching Hospitals Swat.

STUDY DESIGN: Descriptive study.

PLACE AND DURATION OF STUDY: This study was carried out over a period of one year (1st January 2013 to 31st December 2013) at Pathology department, Saidu Medical College, Saidu Sharif, Swat.

METHODS AND MATERIALS: Total 200 patients of both genders and all age groups with cytopenias referred from Saidu Teaching Hospital for bone marrow cytology were included for bone marrow aspiration and assessment.

RESULTS: Two hundred patients underwent bone marrow sampling procedure. Patient's age ranged from 6 months to 90 years. There were 56% male and 44% female at the ratio of 1.5:1. The most common non malignant hematological condition was megaloblastic anemia 28%, mixed nutritional deficiency anemia 16%, hypoplasia 8%, hemolytic anemia 7%, iron deficiency anemia was present in 6% cases, visceral leishmaniasis 4%, thrombocytopenia due to any cause (immune thrombocytopenic purpura (ITP)) 2%, anemia of chronic illness was present in 2% cases, malaria and sepsis leading to cytopenia were 1% each. Malignant neoplasms in our study were 50 cases (25%), which were comprised of; ALL 10%, AML 5%, CML 4%, MDS 3%, multiple myeloma 1.5% and lymphoproliferative disorders in 1% cases.

CONCLUSION: This study showed the pattern of morphological features on bone marrow aspiration, which was found to be different from pattern seen in European and Middle East regions and similar to that found in Asian subcontinent.

KEY WORDS: Cytopenias, pancytopenia, bicytopenia, anemia, thrombocytopenia, megaloblastic anemia, acute leukemia, myelodysplastic syndrome.

INTRODUCTION

Cytopenia(s) means reduction in number of any cellular elements of blood and it may involve any cellular component of blood. It can be a decrease in hemoglobin concentration for age, sex and geographical distribution (anemia) or decrease in total leukocyte count (leukopenia) or thrombocytopenia.[1,2,3,4] Table 1 shows normal reference ranges of the haematological parameters. In clinical settings we can have decrease in formed elements of blood independently or in different combination as monocytopenia (anemia, thrombocytopenia or leucopenia), bicytopenia and pancytopenia. The global prevalence of anemia according to WHO (data collected during 1993-2005) is 24.8%[4]. However in Pakistan anemia prevalence is 45% and it is attributed mainly to iron deficiency.[5] The overall prevalence of thrombocytopenia in USA is about 5.1% [6,7] Ikram N et.al reported 5.7% prevalence of ITP in Pakistan[8]. Amongst 87.5% cytopenic children in Pakistan, bicytopenia accounts for 45%, while pancytopenia constitutes 42.5%.[9] However

pancytopenia prevalance is 3.57% according to Memon S et.al. 2007.[10] Sharif M et.al documented 62.9% bicytopenia and 37.1% pancytopenia cases in their study[11]. Among 57.7% cytopenic peadiatric patients in India, bicytopenia accounts for 40%, while pancytopenia contributes 17.7%.[2] In USA 9.5% new cases of malignant hematological disorders are diagnosed each year among the total cancers, where Leukemia accounts for 30.4% and lymphomas contribute 55.6%.[12] In Pakistan the incidence is 23.6% for leukemias and 15.1% for lymphomas.[13]There is a wide spectrum of pathological events which can lead to various combinations of cytopenias. These may be directly involving bone marrow or indirectly affecting the bone marrow cytology due to replacement of normal hematopoietic stem cells by abnormal cells either originating within the bone marrow or migrating from other sites.

Table 1[14] Reference ranges of Haematological Parameters

	Children	Male (adult)	Female (adult)
HB	12.5-13.0 g/dl	13.5-16.5 g/dl	12.0-15.0 g/dl
TLC	4.0-10.0 x 10^9/l	4.0-10.0 x 10^9 /l	4.0-10.0 x 10^9 /l
PLATELET COUNT	170- 450 x 10^9/l	280 ± 130 × 10^9/l	280 ± 130 × 10^9/l

METHOD AND MATERIALS

This was a prospective descriptive study carried out over period of one year (1st January 2013 to 31st December 2013) at Pathology department, Saidu Medical College, Saidu Sharif, Swat. Permission from the hospital ethics committee was taken to conduct the study. Total of 200 patients of both genders with cytopenias referred from Saidu Teaching Hospital for bone marrow cytology were included in this study while those not consenting to participate in study or not willing for bone marrow biopsy were excluded. Non-probability consecutive sampling technique was used. Informed written consent was taken from all patients for participation in the study. The patients were assessed by adequate history (including history of drugs, radiation exposure, travel history and exact address of stay in the last 10 years), thorough physical examination and investigations such as full blood counts, peripheral smear, differential leucocytes counts, red cell indices, bone marrow aspirate/biopsy. About 3 ml of venous blood was taken in EDTA vacutainer, then by automated analyzer counts were obtained, blood smears were made manually fixed with methanol, stained with Geimsa stain and examined under multi-head microscope. After obtaining bone marrow samples, smears were made immediately, fixed and stained by Geimsa / special stains following methods recommended internationally[15]. Other investigations like liver function tests, renal function tests, lactate dehydrogenase levels, serum ferritin assays and protein electrophoresis were only done where required. Data was recorded and documented in proforma and frequency distribution of various variables was analyzed with SPSS version 16.

RESULTS

Two hundred patients were included in the study that underwent bone marrow sampling procedure, in which male to female ratio in our study was 1.5:1. Table no 2 shows frequency distribution.

Table- 2 Gender Distribution

	Frequency	Percent (%)
Male	112	56.0
Female	88	44.0
Total	200	100.0

Age Patients of all ages were included in the study and age ranged from 6 months to 90 years. Frequency distribution of various age groups is shown in table 3

Table-3 Frequency Table of age distribution

	Frequency	Percentage
<=10.00	56	28.0
10.01 – 30.00	72	36.0
30.01 – 50.00	28	14.0
50.01 – 70.00	36	18.0
70.01+	08	04.0
Total	200	100.0

Spectrum of Diseases on the basis of Bone Marrow Morphology

The bone marrow findings of cytopenic patients were categorized as non malignant hematological causes and malignant hematological causes. Frequency distribution in accordance with age and gender is shown in table 4. Which shows that in adult population megaloblastic anemia was frequent finding while in children acute leukemia was frequent. The conditions which were only prevalent in adults were multiple myeloma, MDS, chronic myeloid leukemia and malaria. The condition found only in children was Lymphoproliferative disorders (lymphomas). Unlike other studies AML was found only in adult population and not even a single case encountered among children.

Table- 4 Bone marrow evaluation showing percentages distribution of various diagnosis [presenting with cytopenias of varying types] (n=200)

Cytopenias	Frequency	Percent (%)	Adults 17-90yrs		Children 6month-16.99yrs	
Non-Malignant causes	**150**	**75%**	**M**	**F**	**M**	**F**
hemolytic anemia	14	07.0	05	03	03	03
megaloblastic anemia	56	28.0	24	20	06	06
iron def. anemia	10	05.0	01	03	03	03
mixed nut. def. anemia	32	16.0	07	08	08	09
anemia of chronic illness	4	02.0	04	00	00	00
Hypoplasia	16	08.0	03	03	04	06
Malaria	3	01.5	02	01	00	00
visceral leishmaniasis	8	04.0	00	02	03	03
thrombocytopenia	4	02.0	00	02	02	00
Sepsis	3	01.5	00	01	02	00
Malignant causes	**50**	**25%**				
AML	10	05.0	04	06	00	00
ALL	20	10.0	04	00	10	06
CML	8	04.0	06	02	00	00
MDS	6	03.0	04	02	00	00
Lymphoproliferative disorders(lymphoma)	2	01.0	00	00	01	01
multiple myeloma	4	02.0	02	02	00	00
Total	**200**	**100.0**	**66**	**55**	**42**	**37**

DISCUSSION

Bone marrow cytology is very important for confirmation of many hematological as well as non-hematological disorders that result in bone marrow suppression. Assessment of bone marrow is done in the light of clinical features, peripheral smear findings and other investigations/ biochemical assays. It is safe to perform bone marrow aspirate/biopsy to reach final diagnosis. In our study 200 cases were recorded over a period of 1 year and age ranged from 6 months to 90 years. M:F ratio was 1.5:1 and the indications for bone marrow sampling were bicytopenias (42.0%), pancytopenia (38.0%), anemia (18%), and thrombocytopenia (2%). The most common pathology detected was megaloblastic anemia (28%) followed by mixed type of nutritional deficiency anemias (16%). Acute lymphoblastic leukemia was the 3rd most common bone marrow diagnosis (10%). Bone marrow hypoplasia (8%), hemolytic anemia (7%), iron deficiency anemia and acute myeloid leukemia (5% each) followed. Visceral leishmaniasis and chronic myeloid leukemia were (4% each). Other less frequent findings were myelodysplastic syndrome (3%), thrombocytopenia (2%), multiple myeloma (2%), anemia of chronic illnesses (2%), malaria (1.5%), sepsis (1.5%), and Lymphoproliferative disorders (1%). However a study conducted in France by Imbert et. al[16] reported malignant myeloid disorders 42% followed by malignant lymphoid disorders 18% and hypoplasia (aplastic anemia) 10% cases as the causes of pancytopenia, the study population was adults and different ethnic and socioeconomic group also other cytopenias such as anemia only and bicytopenia were not considered in this study. In study done in Saudi Arabia acute lymphoblastic leukemia 242 (13.3%), immune thrombocytopenia 123 (6.8%), acute myeloblastic leukemia 80 (4.4%), hypersplenism 79 (4.4%), chronic granulocytic leukemia 73 (4.0%), megaloblastic anemia 66 (3.6%), bone marrow positive for lymphomatous infiltration 63 (3.5%), chronic lymphocytic leukemia 40 (2.2%), and multiple myeloma 32 (1.8%) were common diagnosis encountered[17]. Saudi Arab is

Middle Eastern country and due to ethnic as well as nutritional and socioeconomic differences, the findings were different. Nepal is also southern Asian country as Pakistan. In Nepali study similar data was obtained, the common indications were pancytopenia 50% of cases, bicytopenia 36% cases and thrombocytopenia in 14% cases[18]. The sample size was 57cases and age ranged from 9 months to 75 years and male to female ratio was 1:1.1. The most common bone marrow diagnosis were erythroid hyperplasia 21 %, megaloblastic anemia 12.3%, infections 12.3%, acute leukemia 12.3%, ITP 10.5%, iron deficiency anemia 7% cases, hypoplasia 5.3%, MDS and multiple myeloma 3.5% each and leishmaniasis 1.8%. Amongst acute leukemias 10.5% were AML type and 1.8% ALL type. As erythroid hyperplasia can occur in megaloblastic anemia, hemolytic anemia and iron deficiency anemia so this study was also in correspondence with our findings. The overall spectrum, of bone marrow cytology in study done in a hospital at Faridpur India, was AML 27.69%, mixed nutritional deficiency anemia 24.87%, hypoplasia 10.74%, ALL 9.04%, MDS 7.91%, ITP 6.21%, leishmaniasis 2.82%, multiple myeloma 1.69%. Total numbers of patients in this study were 177 and study was done over a period of two and a half years. Age ranged from 3.5 years to 80 years. Male to female ratio was 1.6:1[19]. In another study done in India total numbers of patients were 120 cases and the duration of study was over two and half years. Age ranged from 0-18 years and male to female ratio was 1.7:1. The most common diagnosis was anemia 61.66%, infections 11.66%, leukemias and ITP 8.33% both and other causes. Among the anemias the most common type was dimorphic (mixed nutritional deficiencies) 60.81%, iron deficiency anemia 13.51%, hemolytic anemia 12.16%, hypoplastic anemia 9.45% and megaloblastic anemia 9.45%. Infectious causes of cytopenia were non-specific in 42.9%, malaria 28.6%, Kala-azar (leishmaniasis) 21.4% and hemophagocytic syndrome 7.1%. Among the malignant disorders (8.33%) ALL constituted 80% (8 cases) and AML 20% (2 cases)[20]. The differences noted in these two studies were because of the differences in age groups, ethnicity and environment. Our data was found to resemble with data from Abbottabad, and Rawalpindi, Pakistan [8,21], India[20], Nepal[18] and Singapore[22] but study done in private hospital at Bangladesh[19] showed slight difference in incidence of their common diagnosis. As the study was done in a private hospital so the population under study was slightly different on the basis of socioeconomic status. Our data was also different from that of Middle Eastern countries and European countries.

CONCLUSION

The morphological spectrum of bone marrow in our study was found to correspond with data recorded in other Asian countries; in which most common finding was nutritional deficiency anemias but was different from European countries where malignant causes were more frequent. Possibly because of differences in ethnicity, socioeconomic status, environment and lifestyle which need further study to exactly evaluate the causative agents.

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