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RESEARCH ARTICLE
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SPECTRUM OF VARIOUS HEMATOLOGICAL DISORDERS INVOLVING BONE MARROW

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Abstract:
Background: Hematological disorders are the major global public health problems affecting both developing and developed countries with severe consequences for human health as well as socio-economic development. These occur at all stages of the life cycle but are more prevalent in the pregnant women and young children. **Objective:** To find out spectrum of various hematological disorders involving bone marrow. **Methods:** The present study was conducted on fifty patients in department of pathology L.L.R.M Medical College, Meerut referred from outpatient & inpatient Department of Medicine and Pediatrics, SVBP Hospital, attached to L.L.R.M Medical College Meerut. The study was done from March 2018 to June 2019 in patients with symptoms viz., pallor, fever, bleeding manifestations, body aches and pains, hepatosplenomegaly and lymphadenopathy. **Result:** Of the 50 cases studied, maximum numbers of cases were of Megaloblastic anemia in 24% followed by20% in Normoblastic anemia, 4% in aplastic anemia and each cases of hemolytic anemia & refractory anemia. In all cases of leukemia 18% cases of chronic leukemia, 16%casesof acute leukemia and observed. In lymphoma, 4% cases Non-Hodgkin's lymphoma & 2% case Hodgkin's lymphoma were observed. In present study one case of each Multiple myeloma, Myelofibrosis, Leishmaniasis, Idiopathic thrombocytopenic Purpura was seen. Bone marrow aspiration and biopsy was done in all the cases. A dry tap on aspiration was obtained in cases of myelofibrosis, aplastic anemia and single case of chronic myeloid leukemia. Bone marrow biopsy was found to be more informative as compared to aspiration in cases of myelofibrosis, aplastic anemia and lymphoma.
Conclusion: Bone marrow aspiration as well as biopsy allowed the evaluation of the hematopoietic cellularity. Hypercellular bone marrow was observed in 37 cases. Hypocellular bone marrow was seen in 2 cases of aplastic anemia and one case of myelofibrosis. In all cases of anemia diagnosis was made by bone marrow aspiration as well as by biopsy

Keywords: Bone marrow aspiration, hematological disorders, bone marrow

INTRODUCTION:

Bone marrow aspiration (BMA) is a simple, reliable and rapid method of marrow evaluation. Trephine biopsy provides more comprehensive information regarding the marrow cellularity, architectural patterns and overall hematopoiesis. But biopsy is a painful procedure and its processing takes at least 48–72 hours. So, to perform trephine biopsies in all patients may not be cost effective in terms of clinician and laboratory personnel time, efforts and patient discomfort. Few studies have analyzed the diagnostic accuracy of bone marrow aspirate in comparison with trephine biopsy. The indication for biopsy has widened to include many conditions in hematology, in internal medicine, and in oncology. In hematology, a marrow biopsy is indicated in the differential diagnosis of cytopenias and for a more precise prognostic classification of the myeloproliferative and lymphoproliferative disorders. A bone biopsy is also valuable in the research into basic problems related to immunology, mesenchymal, vascular, hematopoietic and osteogenic tissues and their regulatory mechanism[1,2].

In spite of the impressive advances in the area of molecular pathology, bone marrow morphology remains the diagnostic cornerstone to identify the various subtypes of myeloid neoplasms[2]. Morphological examination of the bone marrow requires both bone marrow aspirate and bone marrow trephine biopsy. Immunohistochemistry of bone marrow biopsy with markers in paraffin-embedded tissues represents a powerful diagnostic tool; its results can be easily correlated with those obtained by other techniques such as flow cytometry and genetic analysis, and above all, the clinical findings. Particular emphasis is being given to the correct identification of cases of myeloid neoplasms associated with myelofibrosis and for which the bone marrow biopsy represents the only available diagnostic mean. Moreover, the often low cellular yield of the bone marrow aspirate in these cases may also be insufficient to obtain adequate cytogenetic information[3]. Such cases include two subtypes of acute myeloid leukemia which typically cause diagnostic difficulties: acute megakaryoblastic leukemia and acute panmyelosis with myelofibrosis (acute myelosclerosis). Acute myeloid leukemia with multilineage dysplasia, therapy-related myelodysplastic syndrome/ therapy-relatedacute myeloid leukemia. The value of bone marrow biopsy in this group of disorders is generally well established. Acute myeloblastic leukemia had increased marrow reticulin at the time of initial presentation[4].

Bone marrow involvement has a different prognostic meaning for each lymphoma type for example, favouring for immunocytic, indifferent for lymphocytic and unfavourable for centrocytic or centroblastic.

Finally, the important group of the myelodysplastic/ myeloproliferative disorders can only be accurately categorized by a careful multiparametric approach in which the bone marrow biopsy exerts a pivotal role[4].

Material and Methods:

The present study was conducted in department of pathology, LLRM Medical College, Meerut and included patients with various hematological conditions, attending the Out Patient Departments and in patient Departments of Pediatrics and Medicine of SVBP Hospital attached to LLRM Medical College, Meerut, over a period of one year i.e. from March 2018 to May 2019.

A detailed clinical history, physical examination and laboratory examination of all the cases was done.

Peripheral Blood Examination-

Blood was collected in EDTA (ethylenediaminetetra-acetate) vial from anticubital fossa and peripheral blood smears were prepared and stained with May-Grunwald-Giemsa (MGG) and Leishman stains.

The following investigations will be done using automated cell counter-

1. Hemoglobin estimation
2. PCV, RBC count and absolute values.
3. Total leukocyte count (TLC).

4. Platelet count (PC).
5. Erythrocyte Sedimentation Rate(ESR) by Westergren‟smethod.
6. Reticulocyte Count(RC)by Supravital Stain(Newmethyleneblue)
7. General blood picture (GBP) including Differential leukocyte count. For pancytopenia, Inclusion criteria will be :(According to WHO) Hemoglobin-<9gm/dl, Total leukocyte count (TLC)-<4,000/microlitre, Platelet count- < 100,000 /microlitre.

Bone marrow aspiration and Trephine Biopsy:
It was done preferably from posterior superior iliac spine, however depending on clinical evaluation of patients. It was done from anterior superior iliac spine, sternum, tibia as well as by modified Jamshidi needle using standard method (Dacie and Lewis 2012).

BONE MARROW ASPIRATION AND BIOPSY PROCEDURE:
The patient was placed in right or left lateral position with knees drawn up towards his chest and back comfortably flexed. The posterior superior iliac spine was be located (at the level of S1 - S2) and with the use of sterile technique the skin was prepared with antiseptic and draped. Then the skin, subcutaneous tissue and periosteum were infiltrated with local anaesthesia (Xylocaine 2%), one small 3 mm skin incision was made with 11 no scalpel blade. Modified Jamshidi needle with the stylet and handle in place was advanced through the incision.
The entrance into the marrow cavity was detected as a decrease in resistance. The needle was advanced for 4-5 mm. Stylet was removed and aspiration was done by a well fitted 20 ml syringe locked on to the proximal portion of needle. Smears were prepared from the marrow material aspirated into the syringe.
After taking the marrow for smears, the modified Jamshidi needle was advanced gently with clockwise and anticlockwise motion until adequate marrow was obtained in bore of the needle. Thereafter the needle was drawn back 2-3 mm and with less pressure, its tip was directed at a slightly different angle. Then the needle was further advanced for 2-3 mm ensuring that the specimen was severed before withdrawing the needle. The needle was then rotated along the axis with quick full twists several times to the right and to the left and slowly removed with alternating rotator motions. The marrow specimen was removed with the probe after introducing it through the distal cutting end. This prevents crushing of tissue.
For touch imprint preparation, the fresh bone marrow core was gently rolled between two slides. The imprints were wet and cellular at first but as the surface dries, it eventually becomes less cellular. At this point the core was placed in 10 % formal saline and sent for processing.

POST PROCEDURE CARE:
The edge of the wound was pressed together with adhesive tape. Asingle stitch was applied in some cases where needed. The patient was instructed to lie on his back for 15-20 minutes or longer if the patient had low platelet count. The patients with bleeding tendency or other complications were carefully observed for a longer period of time. Analgesics are seldom necessary after the procedure.
Bone marrow aspiration smears and touch imprint smears were stained with May-Grunwald-Giemsa and Leishman‟s stains. (Dacie and Lewis 2012).
Bone marrow trephine biopsy was stained with Hematoxylin and Eosin. and reticulin stain whenever necessary.

Results:
Maximum number of cases were of Anemia26/50(52%) followed by Leukemia 17/50 (34%), Lymphoma 5/50(10%), Multiple myeloma 1/50(2%), Myelofibrosis 1/50(2%), Leishmaniasis 1/50(2%) and Idiopathic thrombocytopenic purpura 1/50(2%).
Among the cases of Anemia, most common was Megaloblastic anemia 12/26 (46.15%) followed by Normoblastic anemia 10/26(38.46%), Aplastic anemia/hypoplatic 2/26(7.69%), Hemolytic anemia 1/26(3.84%), Refractory anemia 1/26 (3.84).

Among the cases of leukemia, most common was chronic leukemia 09/50(18%) followed by acute leukemia 8/50(16%). In chronic leukemia, most common case was chronic myeloid leukemia 7/9(77.22%), and in acute leukemia, most common was acute myeloid leukemia 5/8(62.50%).

Age groups of patient varied from 1th to 7th decade. Out of 50 cases, 27 (54%) were females and 23(46%) males with female to male ratio of 1.17:1.
Among all the cases, maximum number of cases were found in third decade of life, 15 cases (30%), followed by 10 cases (20%) in fourth decade, 7 cases (14%) in second decade, 6 cases (12%) each in fifth decade and first decade and 3 cases(6%) each in sixth and seventh decade of life.

TABLE1: PRESENTING SYMPTOMS OF TOTAL 50 CASES

S.N	Diagnosis	No. of cases	Weakness	Fever	Palpitation	Breath lessness
1	MA	12	6	2	2	2
2	NA	10	4	2	2	2
3	AA	2	2	2	2	-
4	HA	1	1	-	1	-
5	RA	1	1	1	-	-
6	ALL	3	2	1	-	-
7	AML	5	5	1	1	1
8	CLL	2	6	3	-	-
9	CML	7	5	2	1	1
10	HL	1	1	1	-	-
11	NHL	2	2	2	-	-
12	MM	1	1	1	-	-
13	MF	1	1	-	1	-
14	LS	1	1	-	1	-
15	ITP	1	1	-	1	1
	TOTAL	**50**				

Out of 50 patients evaluated, weakness was observed in 39/50(78%), fever in 18/50(36%), palpitations in 12/50(24%) and breathlessness in 7/50(14%) cases

Out of 50 cases, pallor was observed in 38/50 (76%) followed by splenomegaly in 19/50(38%), hepatomegaly in 18/50 (36%), dyspnoea in 12/50 (24%), sternal tenderness in 8/50 (16%) and lymphadenopathy in 6/50 (12%),
A hemoglobin level of 13-15 gm% percent in males, 12-14% gm. percent in females and 11–16% gm percent in children were taken as normal.
Mild degree of anemia was observed in 5/26(19.23%) cases of anemia, 3/8(37.5%) cases of acute leukemia, 3/9(33.3%) cases of chronic leukemia, 1/1(100%) case of multiple myeloma, and 1/3(33.33%) cases of lymphoma.
Moderate degree of anemia was noted in 16/26(61.53%) cases of anemia, 4/8(50%) cases of acute leukemia, 5/9(55.55%) cases of chronic leukemia, 2/3(66.66%) cases of lymphoma and 1/1(100%) cases of myelolfibrosis and leishmaniasis each.
Severe anemia was seen in 5/26(19.23%) cases of anemia, 2/17(11.76%) cases of leukemia and 1/1(100%) case of ITP.
Out of 26 cases of anemia the most common type was normocytic hypochromic 7/26(29.92%) followed by macrocytic normochromic 7/26(26.92%), dimorphic picture 5/26(19.23%), normocytic normochromic 4/26(15.38%) and microcytic hypochromic 3/26(11.53%).
12/17(70.58%) cases of leukemia were normocytic normochromic and 5/17(29.41%) cases normocytic hypochromic. 3/3(100%) cases of lymphoma were normocytic normochromic. Single cases of MM, MF, ITP and Leishmaniasis showed normocytic normochromic blood picture.
Total leucocyte count of 4000-11000/cumm was taken as normal. Out of 26 cases of anemia

14/26(53.84%) cases showed normal TLC, while 12/26(46.15%) cases had leucopenia. 17/17(100%) cases of leukemia and 3/3(100%) lymphoma had leukocytosis. Normal TLC was seen in MM, MF, & ITP while single case of Leishmaniasis showed leucopenia.
E.S.R was normal in 8 /26 (30.76%) cases of anemia while increased in 18/26 (69.23%) cases. 10/17(58.28%) cases of leukemia showed normal ESR while 7/17(41.71%) cases showed increased ESR. All cases of 3/3(100%) lymphoma showed normal ESR and each case of Multiple Myeloma, Myelofibrosis, Leishmaniasis and ITP showed increased ESR.
Normal differential count was taken as: polymorphs 40-70%,
Lymphocytes 20-40%, Eosinophils 2-6%, Monocyte 2-8% and Basophils0-1%.
Neutrophilia in7/9(77.77%) cases of chronic leukemia followed by 5/8(62.5%) cases of acute leukemia while normal in 2/3(75%) cases of lymphoma**.**
Neutropenia was noted in 2/9(22.22%) cases of chronic leukemia and 3/8(37.50%) cases of acute leukemia.

Lymphopenia was observed in 7/9(77.77%) cases of leukemia and 3/8(60%) cases of acute leukemia. Lymphocytosis was observed in 3/8(60%) case of acute leukemia and 2/9(22.22%) cases of chronic leukemia.

Eosinophilia was noted in majority of the cases of chronic leukemia. Basophilia was observed in 7(100%) cases of chronic myeloid leukemi Myeloblasts were observed in 5 (100%)cases of acute myeloid leukemia.

Promyeloblast, myelocytes, metamyelocytes and band forms were noted in all 7/7(100%) cases of chronic myeloid leukemia. 2/7(28.57%) cases of chronic myeloid leukemia were in blast crisis with 21 % and 28% blasts respectively. Atypical lymphoid cells were noted in all 3/3(100%) cases of lymphoma.

Polymorphs were found to be increased in 4/26(15.38%) cases of anemia. Polymorphs were decreased in 4/26 cases of anemia, single case of leishmaniasis and ITP. Polymorphs were normal in 18/26(69.23%) cases of anemia and single case of MM, and MF each. Lymphocytes were found to be increased in 2/26(7%) cases of anemia, and 1/1 case of (100%) ITP and Leishmaniasis each. Lymphocytes were found to be normal in 22/26(84.46%) cases of anemia and single case of MM and MF. Eosinophils were normalinall 50/50 (100%) cases. Monocytes were observed normal in single case of each MM, MF, Leishmnaiasis and ITP. Monocytes were increased in 4/26(15.38) cases of anemia.

The platelet count and the reticulocyte count in the present 50 patients suffering from various hematologic disorders.
Platelet count of 1.5 to 4 lacs per cmm was taken as normal. Platelet count which was found to be decreased in 2/10(20%) cases of Normoblastic anemia, 9/12(75%) cases of Megaloblastic anemia and 2/2(100%) case of Aplastic anemia, 8/8(100%) cases of acute leukemia, 1 (11%) of chronicleukemia,2/3(66.66%)cases of lymphomaand single case each of MF, Leshmaniasis and ITP. Platelet count was increased in5/9 (55.55%) cases of chronic leukemia .Normal platelet count was observed in 12/26(46.15) cases of anemia, 3/9(33.33%) cases of chronic leukemia, 1/3(33.33%) case of lymphoma and single case of MM.

Reticulocyte count of 0.2 to 2% was taken as normal. Reticulocyte count was increased in 1/10(10%) case of Normoblastic anemia, and single case each of Hemolytic Anemia and Leishmaniasis.

TABLE 2: BONE MARROW ASPIRATION IN CASES OTHER THAN LEUKEMIA AND LYMPHOMA (N=30)

BONE MARROW ASPIRATIO N	MA	NA	AA	HA	RA	MM	MF	LS	ITP
Cellularity									
Normocellular	2	3	–	–	–	–	–	01	01
Hypercellular	10	7	–	01	01	01	–	–	–
Hypocellular	–	–	02	–	–	–	1	–	–
Erythroid Series							–		
Normal	–	–	–	–	–	01		01	01
Hypoplasia	–	–	02	–	–	–	01	–	–
Hyperplasia									
• Normobla stic	–	10	–	01	01	–		–	–
• Megalobla stic	12	–	–	–	–	–	–	–	–
Myeloid Series							–		
Normal	-	10	–	-	-	01		01	01
Hypoplasia	12	–	02	01	01	–	1	–	–
Hyperplasia	–	–	–	–	–				
Megakaryocytes							–		
Normal	08	10	–	01	01	01		01	–
Increased	–	–	–	–	–	–	–	–	01
Decreased	04	–	02	–	–	–	01	–	–
Lymphocytes			02					01	
Plasmacells						01		01	
LD Bodies	–	–	–	–	–	–	–	01	–
Total(30)	**12**	**10**	**02**	**01**	**01**	**01**	**01**	**01**	**01**

TABLE 3: BONE MARROW BIOPSY IN CASES OTHER THAN LEUKEMIA AND LYMPHOMAN (N=30)

BONE MARROW BIOPSY	ANEMIA					MM	MF	LS	ITP
	MA	NA	AA	HA	RA				
Cellularity									
Normocellular	02	3	–	–	–	–	–	-	01
Hypocellular	–	–	02	–	–	–	01	–	–
Hypercellular	10	7	–	01	01	01	–	01	–
Acellular	–	–	–	–	–	–	–	–	–
ErythroidSeries									
Normal	–	–	–	–	–	01	–	01	01
Hypoplasia	–	–	02	–	–	–	01	–	–
Hyperplasia									
• Normoblastic	–	10	–	01	01	–	–	–	–
• Megaloblastic	12	–	–	–	–	–	–	–	–
Myeloid Series									
Normal	-	10	–	-	-	01	–	01	01
Hypoplasia	12	–	02	01	01	–	01	–	–
Hyperplasia	–	–	–	–	–				
Lymphocytes	–	–	02	–	–	–	–	–	–
PlasmaCells	–	–	–	–	–	01	–	01	–

Megakaryocytes									
Normal	08	10	–	01	01	01	–	01	–
Increased	–	–	–	–	–	–	01	–	01
Decreased	04	–	02	–	–	–	–	–	–
LD BODIES								01	
Total (30)	**12**	**10**	**02**	**01**	**01**	**01**	**01**	**01**	**01**

The bone marrow aspiration and biopsy were done in all the 50 cases presenting with various hematological disorders.

Anemia:

Out of 12 cases of megaloblastic anemia, bone marrow aspiration revealed hypercellular marrow in 10/12(83.33%) cases and 2/12(16.66%) cases were normocellular. 12/12(100%) cases revealed megaloblastic type of erythroid hyperplasia. Myeloid series was hypoplastic in 12/12(100%) cases while megakaryocytes were decreased in 4/12(33.33%) cases. Biopsy showed megaloblasts with large pale vesicular often lobated nucleus. Most of the nuclei contained prominent nucleoli and relatively solid acidophilic cytoplasm.

Out of 10 cases of normoblastic anemia, 7/10(70%) cases were hypercellular on aspiration and 3/10(30%) cases normocellular. Myeloid: erythroid ratio varied from 2.5:1 to 1:3. Myeloid series was normal in all 10 cases. Erythroid series was normoblastic and megakaryocytes were normal in all 10 cases. Biopsy confirmed the findings of aspiration in all cases.

In both cases of aplastic anemia, aspiration was hypocellular with replacement of marrow by fat and infiltration of lymphocytes and plasma cell. Biopsy confirmed the findings.

Single case, each of hemolytic anemia and refractory anemia showed hyper cellular bone marrow, hypo plastic myeloid series, normoblastic hyperplasia of erythroid series and normal megakaryocytes both on aspiration and biopsy.

Leukemia:

All 8/8(100%) cases of acute leukemia and 9 (100%) cases of chronic leukemia revealed hypercellular bone marrow on aspiration. Leukemic cells were diffusely scattered throughout the smears. Erythroid hypoplasia was noted in all 8/8(100%) cases of acute leukemia and 9/9(100%) case of chronic leukemia. Decreased megkaryocytes were seen in 6/8(75%) cases of acute leukemia and 3(33.33%) cases of chronic leukemia. Bone marrow biopsy confirmed the findings of aspiration.

Cellularity was increased in all the cases of chronic leukemia. Myeloid series showed increased number of myelocytes and metamyelocytes in all cases. Increased number of myeloblasts 21% and 28% were seen due to blast crisis. Three 3/9(33.33%) cases showed increase number of lymphocytes. Erythroid series were hypocellular in all 9/9(100%) cases, megakaryocytes were normal in 5/9(55.55%) cases, increased in 1/9(11.11%) case and decreased in 3/9(33.33%) cases. Megakaryocytes were smaller in size and uni or binucleated forms of megakaryocyte swere seen in one case. Biopsy findings were almost similar to aspiration in all cases. In the other case of CML with blast crisis, cellularity was variable from hypercellular to complete absence of hematopoietic tissue and replacement by firbrous tissue. Which was further confirmed by reticulin stain

Lymphoma:

In all cases of lymphoma, aspiration was normocellular with normal myeloid,erythroid andmegakaryocytic series.There was marked increase in number of lymphocytes and lymphoblasts in Hodgkins lymphoma and Reed- Sternberg cells were seen on biopsy. In both cases of Non-Hodgkin's lymphoma the cells had monomorphic appearance. Trephine biopsy shows nodular, paratrabecular infiltration by atypical lymphoid cells in a patient of small lymphocytic lymphom The findings of bone marrow biopsy were almost similar to those of aspiration.

Multiple Myeloma:
The findings of aspiration and biopsy were essentially similar. Single case of MM reported showed hypercellular bone marrow. The cells of myeloid, erythroid and megakaryocytic series were normal. Plasma cells were increased in the case. Both mature and immature both types of myeloma cells were seen. Immature forms were large cells with basophilic cytoplasm, eccentric nucleus, prominent nucleoli & lacked perinuclear hoff, Russell body& flame cells were noted.

Myelofibrosis:
Single case of myelofibrosis, bone marrow aspiration showed dry tap. This case revealed hypocellular bone marrow aspritaion preparation with hypoplasia of myeloid and erythroid series. Megakaryocytes were absent. Biopsy also showed almost similar findings with replacement of marrow elements by fibrous tissue. There was proliferation of megakaryocytes which were seen in clusters. At places, osteosclerosis was seen.

Leishmaniasis:
Single case of leishmaniasis showed normocellular picture with normal myeloid, erythroid and megakaryocytic series. Plasma cells were increased (10%) Macrophages with L.D. bodies were noted. Biopsy confirmed the findings of aspriration.

Idiopathic Thrombocytopenic Purpura:
Single case of ITP in Bone marrow aspiration revealed hypercelluar marrow with normal myeloid and erythroid series. Megakaryocytes were increased in number but they were not surrounded by platelets. Biopsy confirmed the findings.

Discussion:
In this study, positive correlation was seen between bone marrow aspiration and biopsy. In majority of the cases and in cases where diagnosis was not possible by aspiration, it was confirmed by bone marrow biopsy. According to Verma et al[5] (1993) and Nanda et al[6] (2002), there was good correlation between bone marrow aspiration and biopsy, and bone marrow biopsy is better in cases where diagnosis by aspiration alone was not possible.
In present study 47/50(94%) cases were diagnosed by aspiration while 3/50(6%) cases were not diagnosed by aspiration which were further confirmed by biopsy. Concordance rate between bone marrow aspiration and biopsy was found to be 94%.

Megaloblastic Anemia:
Bone marrow was found to be hypercellular in (83.33%) cases and normocellular in (16.66%) cases in aspiration as well as biopsy. Tevatia et al (2016)[7]also observed hypercelluar marrow in aspiration.

Normo blastic Anemia:
In present study bone marrow was found to be hypercellular in (70%) cases on aspiration as well as biopsy. Myeloid series and megakaryocytes were normal in all the cases. Most of the cases responded well to iron therapy. These findings were in accordance with Davidson et al[8].

Aplasticanemia/Hypoplasticanemia:
In present study aspiration showed hypocellular marrow. Biopsy also showed hypocellular bone marrow with hypoplasia of myeloid and erythroid precursor and increased number of lymphocytes in both cases. Tevatia et al[7] (2016) observed hypocellular marrow in aplastic anemia. Megakaryocytes were also decreased in these cases. Biopsy showed lymphocytes and few plasma cells. Bartl et al[9] (1982) found lymphoid nodulesin 8% of biopsies.

Acute Leukemia:

In this study, (62.50%) cases were of acute myeloid leukemia and (37.50%) cases of acute lymphoblastic leukemia. In both cases, bone marrow was hypercellular, the cells had features of myeloblasts in myeloblastic leukemia and that of lymphoblasts in lymphoblastic leukemia. The cells of erythroid series were decreased in all cases megakaryocytes were normal in (64.70%) cases and decreased in (29.41%) cases. In AML most common type was AML-M3. These findings are in accordance with Pudasaini S et al (2012)[10].

CHRONIC LEUKEMIA:

In present study (77.77%) cases of chronic myeloid leukemia and (22.22%) cases of chronic lymphocytic leukemia were reported. In both cases, bone marrow was hypercellular. In chronic myeloid leukemia, predominant cells were myelocytes, metamyelocytes and band forms while in chronic myeloid leukemia with blast crisis, predominant cells were myeloblasts. Hematopoeitic system WHO (2017) mentioned that immature cells were in form of myeloblast, promyelocytes myelocytes, metamyelocytes and band forms in CML.

In chronic lymphocytic leukemia, maturelymphocytes and smudge cells were observed. Erythroid series was hypoplastic in all the cases. Bartl et al (1993) and Thiele et al (2000) observed decreased erythropoiesis in CML cases. Megakaryocytes were normal in (64.70%0 cases, increased in (11.11%) cases with unilobed or bilobed forms[11]. In CLL, mature lymphocytes were seen with normal megakaryocytes in (100%) cases. Studies on erythroid precursors have demonstrated an ineffective erythropoiesis and maturation arrest in a large series of patients with myeloid leukemia.

Diagnosis of chronic myeloid leukemia with blast crisis was made with peripheral blood smear and bone marrow aspiration, this was in line with Wintrobe et al (2013) while at variance with Islam et al (1980). Islam studied 15 patients of CML with blast crisis by means of serial bone marrow biopsy specimens. Results were compared with peripheral blood smear and bone marrow aspirates.[12] Bone marrow aspirates were either dry tap or yielded an aparticulate sample. Diagnosis of blast transformation was made from core biopsy[11].

In this study, bone marrow content of reticulin was increased. ManjulaP et al (2016) observed that increased fibrosis and reticulin stain was done for grading of fibrosis. Diffuse thick fibres without collagenization (Grade-2) were seen[13]. Findings were in accordance with those of Gralnick et al (1971) who also found increased reticulin.

Tefferi (2000)[13] observed that reticulin framework (the glycoprotein coating of stromal cell strands) of the marrow can be observed after subjecting the marrow to silver staining techniques such as, the Gomori‟s reticulin technique[14].

LYMPHOMA:

In present study 33.33% Hodgkins‟s lymphoma and 66.66% Non Hodgkin‟s lymphoma were noted. In both the cases bone marrow aspiration and biopsy was done. In 100% cases of NHL, diffuse as well as nodular pattern of marrow involvement was seen. Goyaletal (2014)[15]observed that in NHL marrow infiltration is in the form of paratrabecular , nodular, interstial, or diffuse patterns.

In HL marrow showed infiltration by RS cells. Goyal et al (2014) stated that large binucleate cells with moderate amount of cytoplasm, vesicular nuclei and prominent eosinophilic nucleolus (classical Reed Sternberg cells) and monomorphic cells were seen in Hodgkin‟s lymphoma. Bartl et al (1982)[9] found bone marrow involvement in (14%) cases when Reed Sternberg cells or mononuclear Hodgkin‟s cells or both were found in appropriate morphological settings.

Nanda et al (2002) observed that in cases of marrow involvement by lymphoma, the final diagnosis could be made only after examining bilateral trephine biopsies. Normal bone marrow had favourable prognosis and those with leukemoid reaction had worst prognosis. Hypocellular bone marrow showed unfavourable course. Patients with mixed inflammatory and exudative reaction had good prognosis.[16]

MULTIPLEMYELOMA:
Single case of multiple myeloma was encountered in this study. It presented with pancytopenia. According to Harrison et al (2018), pancytopenia could occur in cases of multiple myeloma. In this case, positive Bence jones proteins in urine and osteolytic bone lesion were seen. Bone marrow was hypercellular with presence of (35%) to (70%) myeloma cells[17]. This constitutes one of the main diagnostic criteria for multiple myeloma (WHO 2017 (revised).

Idiopathic Thrombocytopenic Purpura:
Single case of ITP showed hypercellular marrow with normal myeloid and erythroid series. Megakaryocytes were increased in number with no platelet formation. These findings are in accordance with Tevatia et al (2016)[18].

Myelofibrosis:
Single case of myelefibrosis was encountered in the present study. Bone marrow aspiration was unsuccessful in this case. Tefferi (2000) observed that bone marrow of patients with myelofibrosis is not easily aspirated.
In this case biopsy showed diffusely fibrotic marrow with decrease in cells of myeloid and erythroid series. Megakaryocytes were increased in number. Manjula P et al (2016) also observed increased fibrosis. Reticulin was 2+fibrosis of bone marrow today is regarded as secondary to a large number of diseases that may afflict the hematopoietic tissue[19]. These include myeloproliferative and lymphoproliferative disorders as well as metastatic neoplasia[20].
In fibrotic marrow (areas of myeloproliferative disorders), abnormal deposition of platelets and accumulation of necrotic megakaryocytes have been observed Momani A et al (2012)[21]
Myelofibrosis due to other causes differs in appearance. Fibrosis associated with CML may be almost indistinguishable from that of acute myeloid metaplasia, although some authors Harrison et al (2018) and Davidsons et al (2014) claim that proliferation in CML is monomorphic and that in acute myeloid metaplasia is trilinear[22].

Leishmaniasis:
There was a single case of leishmaniasis. In this case, bone marrow was normocellular with normoblastic erythroid series, normal myeloid series and normal megakaryocytes. Plasma cells were increased in number and both intracellular and extracellular L.D. bodies were present. Splenic puncture was also positive. Plasmacytosis in infectious disease has been observed by Gobaldon et al (2002) & Idris M, Farid J et al (2018)[23].

Conclusion:
Bone marrow aspiration as well as biopsy allowed the evaluation of the hematopoietic cellularity. Hypercellular bone marrow was observed in 37 cases. Hypocellular bone marrow was seen in 2 cases of aplastic anemia and one case of myelofibrosis .In all cases of anemia diagnosis was made by bone marrow aspiration as well as by biopsy. However, localization of foci of erythropoiesis was better evaluated by trephine biopsy. Normal erythropoiesis occurred in per sinusoidal foci. In erythroid hyperplasia there was increase inactivity and number of foci. The hyperplasia was normoblastic in 10 cases and megaloblastic in 12 cases. Localization of foci of leucopoiesis was also better evaluated by biopsy. Normal leucopoiesis was found close to the endosteum, whereas pathological leucopoiesis is followed the capillaries in addition to maintaining the endosteal site.

In cases of chronic myeloid leukemia, there was diffuse proliferation of cells of myeloid series. In acute leukemia, whole of the marrow was replaced by blast cells producing a packed marrow pattern. In case of Hodgkin's lymphoma and Non- Hodgkin's lymphoma, bone marrow was diffusely involved.

Evaluation of marrow fibrosis was done on examination of bone marrow biopsy only. Fibrosis was observed in single case of Myelofibrosis and one case of chronic myeloid leukemia, in single case of Myelofibrosis, whole of the marrow was replaced by fibrous tissue and single case of aplastic anemia.

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