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Diagnosis of Hematological and Non-Hematological Disorders Using Bone Marrow Aspiration and Trephine Biopsy(A Correlating Study).

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ABSTRACT

In today's era of advanced diagnostic procedures in the field of hematology, it is important to have proper diagnosis of various hematological and non-hematological disorders. It is the bone marrow examination that is considered an important valuable diagnostic tool, for evaluation and final diagnosis of various hematological and non-hematological disorders. This may directly or indirectly involve complete bone marrow analysis. Various indications for bone marrow examination include proper diagnosis, staging and therapeutic monitoring of different hematological disorders like disorders of hemopoiesis, leukopoiesis, lymphoproliferative disorders, myeloproliferatives disorders and plasma cell dyscrasias like multiple myeloma respectively. The non-hematological disorders include granulomatous disorders (tuberculosis and sarcoidosis), infection like AIDS as a cause of unexplained fever of unknown origin, parasitic infestations like malaria, leishmaniasis, histoplasmosis and various other disseminated fungal infections. It also includes certain storage diseases and metastatic secondary deposits from different malignancies respectively. A thorough bone marrow examination includes peripheral blood film (PBF), direct particle, buffy coat, bone marrow aspiration (BME) smears, BM trephine biopsy imprints and marrow volumetric data respectively. Other disorders like focal myeloma, lymphoma and marrow fibrosis can also be studied, but BM trephine biopsy is essential. To diagnose hematological and non-hematological disorders using BM aspiration and trephine biopsy was carried out. Study was conducted in the department of pathology MMIMS&R, (MMU) Mullana, Ambala (HR). Sixty cases were taken, during the period from June 2010 to Dec 2011. Both inclusion and exclusion criteria strictly followed. Clinical data, hematological investigations and BM analysis details were recorded and analyzed. Bone marrow aspiration included a study of wide spectrum of hematological and non-hematological disorders, but it has some limitations. In disorders like focal myeloma, lymphoma and marrow fibrosis, BM aspiration study alone fails to demonstrate disease processes. For these cases, BM trephine biopsy is essential. Hypocellular marrow, unexplained pancytopenias, leukoerythroblastic blood picture and marrow fibrosis are also strong indications for B M biopsy.

Keywords: Bone marrow aspiration, Trephine Biopsy, Hematological, PBF and MDS.

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INTRODUCTION

Present day, Bone marrow examination is considered a valuable diagnostic tool to evaluate hematological disorders. Various indications for bone marrow examination(BME) include proper diagnosis , staging and therapeutic monitoring of different hematological/non-hematological disorders like lymphoproliferative disorders, such as Chronic lymphocytic leukemia, Hodgkin's and non-Hodgkin's lymphoma, hairy cell leukemia, myeloproliferative disorders and plasma cell dyscrasias like multiple myeloma respectively [1]. Definitive diagnosis of several hematological diseases, such as leukemias, unexplained pancytopenias and other bone marrow disorders require BME (aspiration/or biopsy) [2]. B M is also studied for several other reasons including suspicion on underlying marrow disorders and associated additional Pathology [3]. A thorough B M morphological examination includes peripheral blood film (PBF), direct particle, buffy coat, BM aspiration smears, Trephine biopsy imprints for sections and marrow volumetric data respectively. Application of marrow analysis also includes non-hematological conditions like investigations of fever of unknown origin, especially in patients with AIDS, presence of microorganisms like tuberculosis, leishmaniasis, histoplasmosis and various other disseminated fungal infections. Diagnosis of **storage disorders** like Niemann-pick disease, Gaucher's disease, assessment of metastatic carcinomas and granulomatous diseases like Tuberculosis and sarcoidosis etc. The BM **aspirate** is the **sample of choice** to examine nucleated red cells of marrow (myeloid:erythroid ratio). At times, marrow aspirate may be diluted, dry tap, unsatisfactory or sometimes marrow involvement is focal eg. Granulomas, metastatic deposits, focal myeloma, Hodgkin's disease and associated fibrosis respectively. In these states, B M examination fails to demonstrate disease processes. In such areas, to arrive at a diagnosis, **marrow trephine biopsy** is **very essential**, which is carried out under local anaesthesia [4] by using **Jamshidi needle,** to improve procedure, size and quality of the specimen as compared to **core needle biopsy**.

In patients with **Hypocellular marrow**/or **fibrosis**, an aspirate will probably be inadequate or even impossible. So **complementary trephine biopsy** may show **architecture** of marrow and permits elaboration of abnormal distribution of cells, marrow granulomas , focal lymphoid infiltrates, Non-hematological neoplasms and unexplained pancytopenias /or leukoerythroblastic blood picture respectively, are strong indications for trephine biopsy[5]. Among various disorders, **nutritional anemia** is most common hematological disorder found on marrow examination, of which megaloblastic anaemia is commonest [6]. 25% of the world population is affected by iron deficiency, of which 32% are **pre-school children**. As such, there is no sole reliable biochemical indicator/marker, that is consistently diagnostic of iron deficiency, except **gold standard** bone marrow trephine aspirate [8]. The megaloblastic anaemia and other disorders in sequence are Hodgkin's disease, chronic myeloid leukemia, B-cell chronic lymphocytic leukemia or small lymphocytic lymphoma, Idiopathic/primary myelofibrosis (may be chronic), leukoerythroblastic blood picture, absence of Philadelphia chromosome and overt reticulin or collagenous fibrosis respectively in particular, in the bone marrow specimen. Parasitic infestations like visceral leishmaniasis ie, examination of Leishmania donovani bodies in marrow smear and another communal malaria in any forms (M. vivax, M. falciparum etc). **Secondary involvement** of marrow by malignant lymphomas, multiple myeloma, myelodysplastic syndrome, metastatic tumors, infections like toxoplasmosis and other **Opportunistic** infections in AIDS, granulomatous myelitis and lymphadenitis respectively.

Aim and Objective: To diagnose hematological and non-hematological disorders using bone marrow aspiration and Trephine biopsy.

METHODOLOGY

Study was conducted in the department of pathology Of MMIMS&R (MMU) Mullana Ambala (HR). **Sixty cases** were taken for study, during the period from June, 2010- Dec, 2011. Clinical data with reference to age, sex, socio-economic status, dietary habits, mode of onset, History of drug intake or exposure to toxic chemical agents, H/O bone pains, hepatosplenomegaly and lymphadenopathy respectively, were recorded. The following investigations were carried out in Clinical laboratory like Hb, TLC, DLC, Bleeding time, Clotting time, Platelets count, ESR, reticulocyte count and peripheral blood film (PBF) respectively. Bone marrow analysis was done in all cases using appropriate site (iliac crest, sternum and tibial tuberosity in infants and children). **Equipments;** included **Sahali's** apparatus, **Salah's** BM aspiration needle and **Jamshidi's** trephine biopsy needle, 5 ml and 20 ml disposable syringes, xylocaine (1%), glass slides, fixative- isopropyl alcohol, leishman's stain, Prussian blue stain and other antiseptic materials respectively. Patient's preparation was

done after explaining the procedure and written consent obtained. Both, Aspiration and Biopsy was done under aseptic precautions. Slides prepared, stained and examined by light Microscope.

Inclusion Criteria

The study subjects consisted of all patients undergoing bone marrow aspiration/ or biopsy, Irrespective of cause, age and sex.

Exclusion Criteria

Patients having bleeding/coagulation disorders, skin disorder (at site of examination), and anemia due to blood loss were excluded.

OBSERVATIONS AND DISCUSSION

A total of **sixty cases** presenting to the Department of Pathology, for bone marrow examination (BME) under evaluation, were included in the study. Based on their history, clinical features and various investigative parameters along with BME findings, the final diagnosis was made in all the cases. Megaloblastic anemia was found in 28.33% of cases, leukemias (acute and chronic) in 11.67% of cases. Among leukemias, (ALL) was commonest malignant hematological disorder. This was in concordance with study by Rahim et al [7]. Maximum number of cases were of nutritional anemias (40%), out of which, megaloblastic anemia contributed maximum number of cases (70.83%) followed by dimorphic anemia (29.17%). These findings also correlated with study findings by Rahim et al. From the pattern of age and sex-wise distribution of these anemias, it was evident that megaloblastic anemia was slightly more common in females (M:F=1:1.13) particularly in the reproductive age group. Moreover, most of these cases belonged to low socio-economic status (Khanduri et al) [9] Main cause of anemia was **dietary deficiency** in majority of cases, including two cases of chronic alcoholism. Majority of these patients were strict vegetarians and results showed that 87% of the patients with Cobalamine deficiency and 75% with folate deficiency were lactovegetarians. The peak incidence of megaloblastic anemia was in the age group of 10-30 years(48%) with female predominance (71%). Out of seventeen cases of megaloblastic anemia, 15% presented with pancytopenia, which was in concordance with study conducted by Gomer et al [10]. Another study by Khodke et al [11], carried out BM aspiration/biopsy in 50 patients having pancytopenia and study revealed that megaloblastic anemia was the **commonest association** (44%) of pancytopenia. (FIG 1-3). The age range was 3-69 years and maximum number of cases were found in younger age group of 12-30 years (40%). Another study by Gayathri et al [12] also studied 104 pancytopenic patients. In all cases of **dimorphic** anemia, history taking revealed, decreased intake of both **iron** and **folate** to be the cause of anemia. An overall **low calorie** intake was found in 30% of the population. The daily iron and folate intake levels were below the recommended levels. **Malnutrition** was found to be commonest cause of **dimorphic anemia in women** of reproductive age group. On bone marrow examination, a mixed picture was seen in all the cases, with presence of micronormoblasts, megaloblasts and normoblasts in different proportions (Fig-4-5).

There were six cases of **Aplastic** anemia. Patients mostly presented with weakness, fever and breathlessness. All the cases revealed **pancytopenia** in peripheral blood smears. Rehman et al [13], also studied 60 patients with Pancytopenia, over a period of two years. In the present study, B M aspiration resulted in a **dry tap** in all the six cases of Aplastic anemia. The diagnosis was made on BM biopsy that revealed overall decrease in hematopoietic tissue i.e. 90% replacement of normal marrow by fatty tissue with remaining interspersed normal hematopoietic tissue elements. Importantly, **megakaryocytes** were present (Fig-6). These findings were supported by Tichelli A et al [14], They concluded that bone marrow biopsy and histopathologic examination are necessary for definitive diagnosis of Aplastic anemia. The presence of megakaryocytes in BM specimens has a favorable prognostic significance. Their appearance is a reliable sign of disease improvement. Another set of three cases was diagnosed as **acute leukemias**, all being of Acute Lymphoblastic Leukemia (Fig-7-9). The age range varied from 6 to 17 years with M:F ratio of 2:1. Gum hypertrophy was observed in one case only, while hepatomegaly observed in all the cases. TLC was raised with DLC constituted mostly of lymphoblasts. The platelets were decreased in all the cases. In the study, marrow was hypercellular in all the cases with focal areas of infiltration by **blast cells,** while BM biopsy additionally showed increased **marrow fibrosis** also.

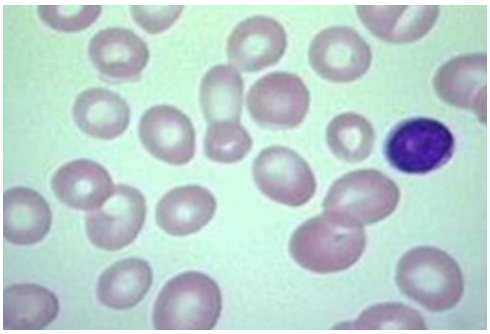
Among **Myeloproliferative disorders**, there were only two cases of Chronic Myeloid Leukemia(CML) and three cases of Idiopathic Myelofibrosis. Both the cases of CML showed a marked rise in TLC with DLC showing marked shift to left in the myeloid series with increased number of **myeloblasts** and **basophils**. Basophilia has been reported to indicate an accelerated phase of CML, heralding a poor prognosis. (Fig 10-12). Denburg et al [15] also studied 47 patients with chronic phase CML by basophil growth and differentiation assays. They reported that an increased **Basophil Growth Index** predicting death or progression to blast crisis in two years and was thus a poor prognostic marker. In a study by Khonglahet al [16], sixty patients with CML underwent bone marrow trephine biopsy at presentation. Five patients presented in **blast crisis**. Follow-up after few years revealed an increase in patients with blast crisis to 25%. This was statistically significant. These results further emphasized the importance of a BM biopsy in all the cases of CML, although, they can be diagnosed on PBF and BM aspiration, as it provides better prognostic information. Evaluation of **megakaryopoiesis**, **grading of fibrosis** and **localization of the blasts** are only possible on Trephine biopsy*. **Idiopathic Myelofibrosis (IMF)** showed a male predominance and all cases belonged to **elderly age** group. No aspirate could be obtained in patients with increased marrow fibrosis. B M biopsy showed a few areas of hypocellularity and an overall increased fibrosis of marrow. (Fig 13-14). It is also supported by study by Burh et al [17] & Ni H et al [18].

In a series of six cases of **Lymphoproliferative disorders** infiltrating bone marrow, there were two cases of Chronic Lymphocytic Leukemia (CLL), which were diagnosed and confirmed on bone marrow examination (Fig 15-17). Both the cases were elderly males. Our study proves that males are affected more often. There were two cases of **Non Hodgkin's Lymphoma (**NHL). Both patients clinically presented with anemia, weakness, significant weight loss, splenomegaly and generalized lymphadenopathy. Bone marrow aspiration revealed a dry tap in both the cases. So BM biopsy was mandatory to reach at the diagnosis. Fine needle aspiration of the lymph nodes also supported our diagnosis. (Fig 18-19). Other risk factors were low %age of blood neutrophils, high %age of blood lymphocytes, low absolute neutrophil count, low platelet count and high alkaline phosphatase respectively. Schmid C et al [19] studied BM biopsies in patients with lymphoproliferative disorders and found that a biopsy was mandatory for Histological confirmation, grading, staging and prognostication in all such cases. In present study, bone marrow biopsy showed diffuse involvement of marrow by lymphoma cells. In a study by Conlan MG [20], a high incidence of discordance was found between BM biopsy findings and lymph node biopsy findings (40%). Our study did not find any discordance in the diagnosis between bone marrow biopsy and lymph node biopsy. In a study by Lee et al [21], 156 patients with **non-Hodgkin's lymphoma** were evaluated for BM involvement as (35%). Most common patterns of involvement were **interstitial** and **diffuse** types (56% & 31%). Overall discordance between lymph node and BM biopsy histology was 18%. Of the two cases diagnosed as **Hodgkin's lymphoma** (HL) from BME, one was a case of primary Hodgkin's disease of BM in a 8 years old girl child (Fig-20). Jain A et al [22] also reported a similar case, where the patient presented with nonspecific symptoms of fever, weight loss and night sweats, with all investigations inconclusive of the disease. BM aspiration gave a diluted tap. Finally biopsy revealed small lymphocytes, neutrophils and eosinophils along with a few plasma cells and histiocytes. Occasional binucleate Reed Sternberg (RS) cells were also seen. Similarly, another case was clinically unsuspected case of Hodgkin's lymphoma diagnosed primarily on BME. The BM aspirate was normocellular with increase in lymphoid series of cells along with many atypical cells. Biopsy confirmed the presence of R S cells infiltrating the marrow. Our results were in concordance with the work by Kar A et al [23], who reported six cases during 5 yrs study, where diagnosis of Hodgkin's lymphoma was primarily made from BM trephine biopsy. As BM lacks **lymphatics infiltration** by Hodgkin's lymphoma, indicated vascular dissemination of disease (stage IV). If B M E is required in Hodgkin's lymphoma, a trephine biopsy is also essential, because even when the marrow is involved, it is rare for the neoplastic cells to be detected in an aspirate.

Of the five cases diagnosed with **MDS**, four were males with an age group between 30-71 years. Immature, dysplastic **micromegakaryocytes** were found in three out of five cases. Dysplastic changes were well documented in **Myelodysplastic syndrome,** but may also be observed in some non-MDS hematological disorders. (Fig 21-23) To study these dysplastic changes, Muhury M et al [24], conducted a prospective study of 144 BM aspirates, where thrombocytopenia was encountered. Various disorders associated with **dysplastic megakaryocytes** were idiopathic thrombocytopenic purpura, megaloblastic anemia, acute leukemias, myeloma, metastatic deposits and blast crisis of chronic myeloid leukemia. In such cases, diagnosis by BM aspiration alone is not conclusive. A bone marrow biopsy is required for the correct interpretation of the disease changes and for correct diagnosis. In our study of MDS, the blast cell counts ranged from 4-9%. The cases were categorized according to Mufti JG et al [25], for the proper diagnosis, classification and

prognostication of MDS. Bone marrow biopsy showed a hypercellular marrow with absence of **Abnormal Localization of Immature Precursors** (**ALIP**) in four out of five cases. Mangi et al [26], have shown ALIP to be of diagnostic and prognostic importance in cases of **refractory anemia**. The recognition of ALIP has been based exclusively on BM histological appearance. Its presence predisposes to early death due to transformation to acute leukemia. Estimation of **plasma cell infiltrates** in B M aspirates and B M biopsy is a standard method in the diagnosis and monitoring of **multiple myeloma** (MM). The two patients diagnosed with Multiple Myeloma clinically presented with fever, weakness and bone pains. Their Serum electrophoresis showed **M-spike**, favoring the diagnosis of multiple myeloma. (Fig -24) The percentage of plasma cells in the marrow aspirate was 35% and 44% respectively (figure-25-27). Stifter S et al [27], retrospectively studied the BM and biopsies of 59 multiple myeloma patients. The bone marrow biopsies consistently demonstrated greater plasma cell infiltration (50%) as compared to B M aspirates (29%). They inferred that estimation of plasma cell infiltrates in B M aspirates and B M biopsy is a standard method in the diagnosis and monitoring of multiple myeloma. In the present study, B M biopsy showed hypercellular sections with diffuse involvement of marrow by plasma cells in both the cases (Figure-27). Patients in advanced clinical stage ie, more than 50% plasma cells in the marrow, diffuse pattern of infiltration, high mitosis and increased fibrosis had a shorter median survival than patients with favorable features. So % age of **plasma cells in trephine biopsy** was found to be an **important prognostic factor** in multiple myeloma (Subramanian R et al) [28].

B M examination, by aspiration and/or trephine biopsy, is an important procedure in arriving at the diagnosis of **febrile illness of long-duration**. Four cases were diagnosed as **Tuberculous pathology**, as tuberculosis is endemic in India and always the first differential of a granulomatous pathology. The patients had fever of unknown origin, till they were diagnosed on bone marrow examination (Fig 28-30). Gupta V et al [29] studied 121 patients with pyrexia of unknown origin, over a period of eight years and similarly found granulomas in B M biopsy. Also, there was male predominance with a wide age range (2-81 years). Granulomas were rare on aspiration and may show only a few collections of epithelioid cells. Granulomas were present in 70% of bone marrow biopsies. Kinoshita M et al [30] confirmed that B M examination is must in diagnosing tuberculous pathology, especially military tuberculosis**. B M trephine biopsy is an important adjunct to aspiration** in arriving at an etiological diagnosis of patient with febrile illness of long-duration, and should be routinely performed in such cases. Five cases of **metastatic deposits** were found in elderly males. All the cases produced a dry tap on aspiration. This mandated performing of B M biopsy. (Fig 37-38) Our findings are in concordance with study by Humphrie JE et al [31], where they found metastatic deposits as the most frequent cause of dry tap followed by fibrosis, chronic myeloid leukemia and hairy cell leukemia respectively. Syed et al [32] and Xiao L et al also had studies supporting our findings of metastatic deposits in bone marrow.



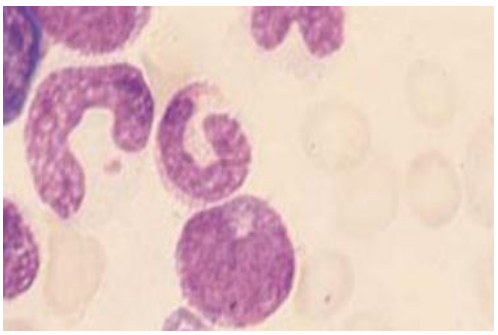


Figure 7: PBF: Macrocytic blood picture showing macro-ovalocytes (Leishman;1000X). Figure 8: BM aspirate, megaloblasticanaemia, showing megaloblastic erythropoiesis(thin arrow) and a giant metamyelocyte(thick arrow). (MGG;1000X).

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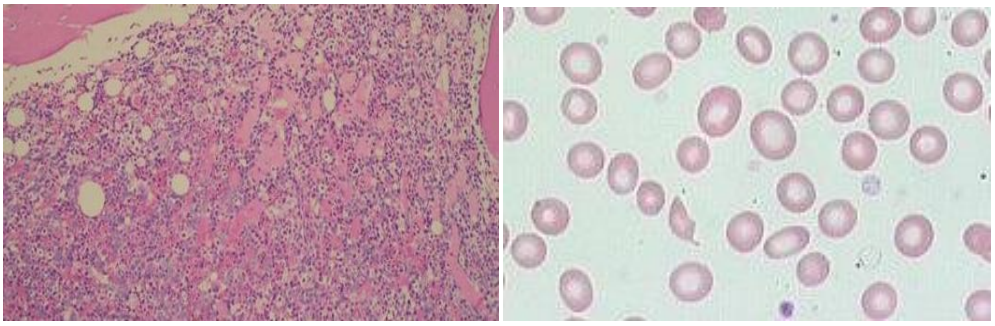

Figure 9: BM trephine biopsy section, megaloblastic anaemia, showing hypercellular marrow(H&E;100X). Figure 10: PBF : Dimorphic Anemia, showing macrocytes(thin arrow) and microcytes(thick arrow). (Leishman;1000X).

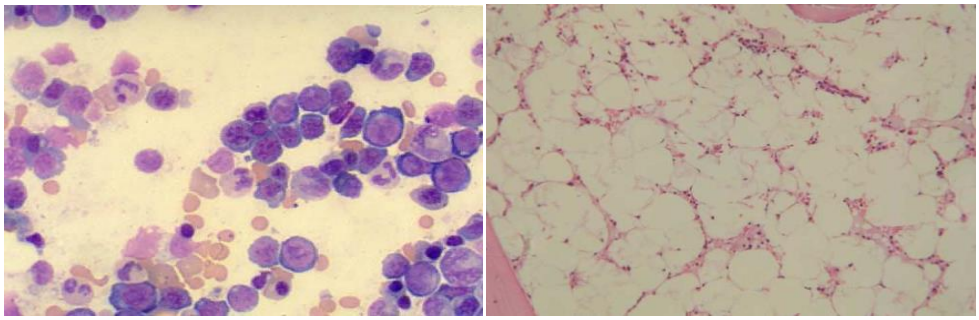

Figure 11: BM aspirate, Dimorphic anemia, showing micronormoblasts (thin arrow) with admixed megaloblasts(thick arrow)(MGG;400X. Figure 12: BM trephine biopsy section, aplastic anaemia, showing marked hypocellularity (H&E;400X).

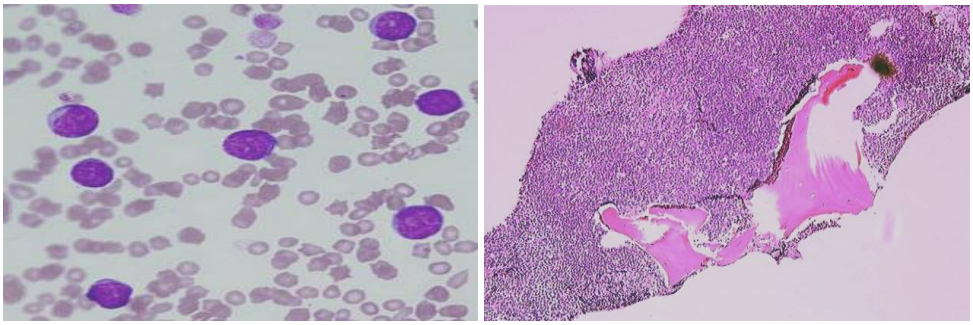

Figure 13: PBF, ALL showing a uniform population of small to medium sized blasts with a high nucleocytoplasmic ratio(arrow). (Leishman; 1000X). Figure 14: BM trephine biopsy section, ALL showing hypercellular marrow (H&E;100X)

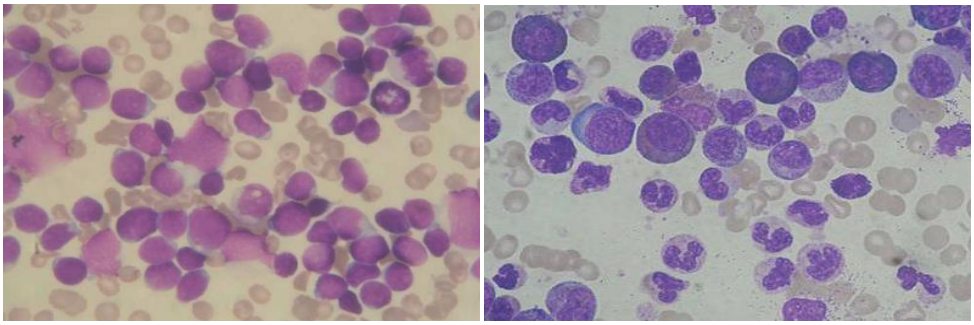

Figure 15: BM aspirate, ALL, showing uniform population of small and medium sized blasts(arrows) with a high nucleocytoplasmic ratio. (MGG;1000X). Figure 16: PBF ; CML, showing neutrophils, their precursors and one eosinophilic precursor(arrow). (Leishman;1000X).

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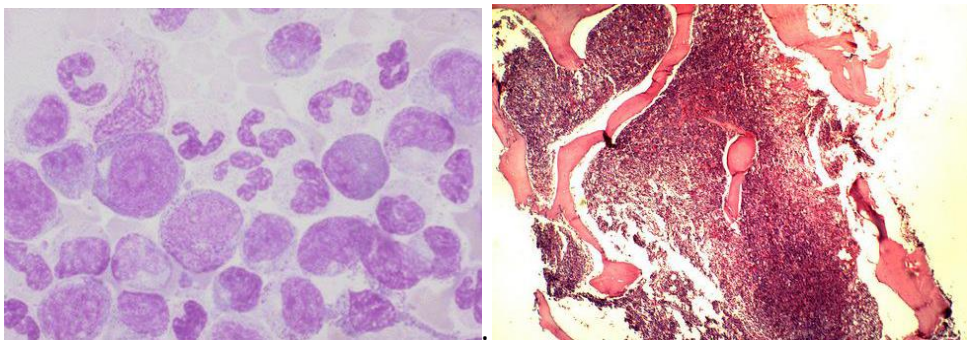

Figure 17: BM aspiration; CML, showing hyperplasia of all granulocytic lineages (MGG ;1000X). Figure 18: BM trephine biopsy section; CML, showing packed marrow with marked granulocytic hyperplasia (H&E;200X)

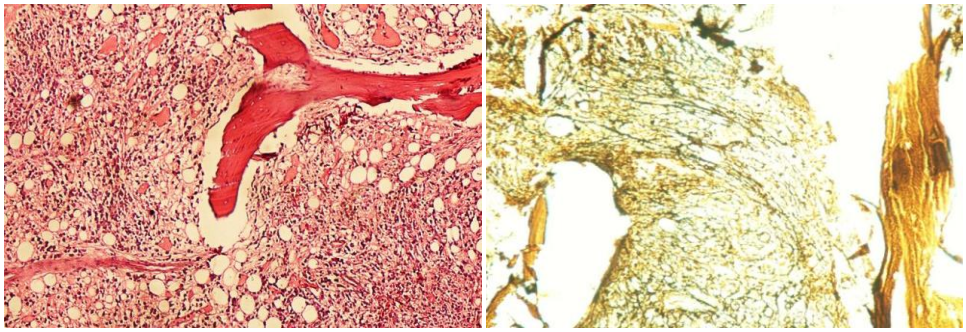

Figure 19: BM trephine biopsy section; idiopathic myelofibrosis (cellular phase), showing marked hypercellularity, with an increase in cells of all three haemopoietic cell lineages, and ectatic sinusoids. (H&E;400X). Figure 20: Bone marrow trephine biopsy section, Idiopathic myelofibrosis (cellular phase) (Gordon and Sweet reticulin stain;400X).

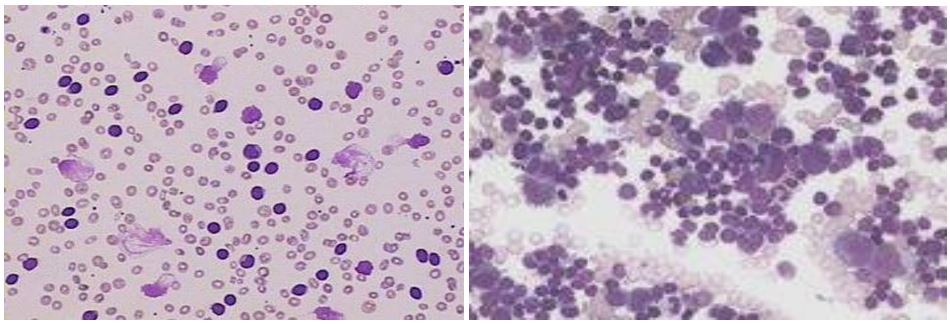

Figure 21: PBF in CLL, showing lymphoid cells (thin arrow) and smear cells(thick arrow) (Leishman;200X). Figure 22: BM aspirate, CLL, showing mature small lymphocytes(thin arrow) admixed with frequent very large cells with large nucleoli(thick arrow). (MGG; 400X).

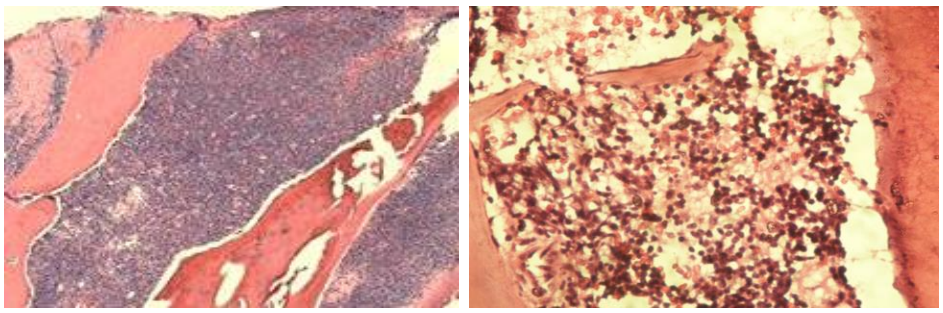

Figure 23: BM trephine biopsy section; CLL, hypercellular marrow and neoplastic small lymphocytes; diffuse involvement (H&E;200X) .Figure 24: BM trephine biopsy section, NHL, showing increased fibrosis(arrow) and diffuse infiltration by lymphoma cells(H&E;200X).

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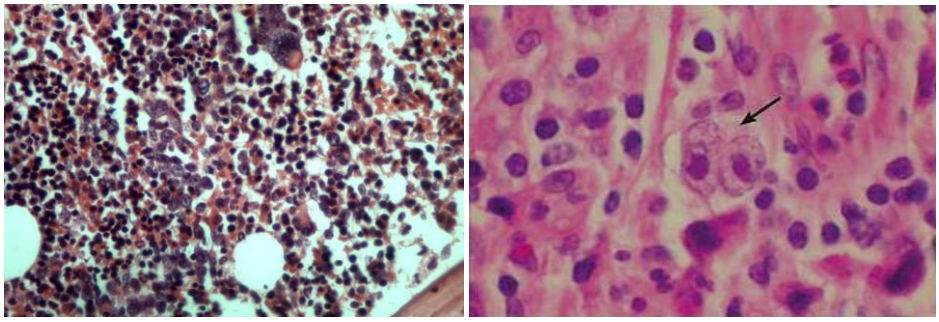

Figure 25: BM trephine biopsy section; NHL, showing diffuse infiltration by lymphoma cells(arrow) (H&E;400X). Figure 26: Bone marrow biopsy: A typical Reed Sternberg cell (arrow) characteristic of Hodgkin Lymphoma. The binucleate cell is surrounded by a mixed population of neutrophils, lymphocytes and plasma cells.(H&E;1000X)

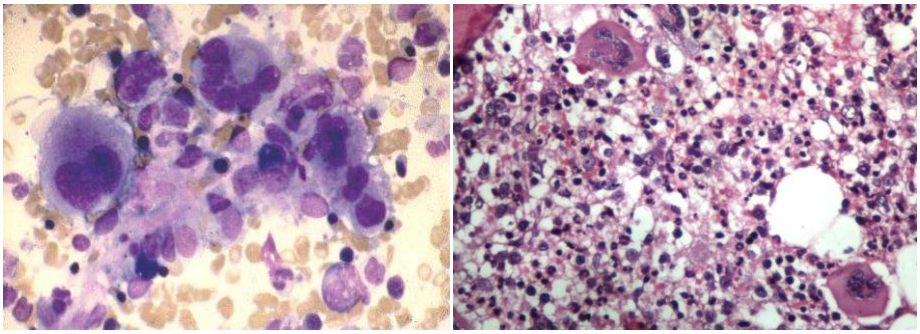

Figure 27: BM aspirate; MDS, showing dysplastic megakaryocytes (arrows) having variable size, nuclear lobe separation(MGG;1000X). Figure 28: Bone marrow biopsy: (MDS) ; dysmegakaryopoiesis(arrows) (H&E;400X).

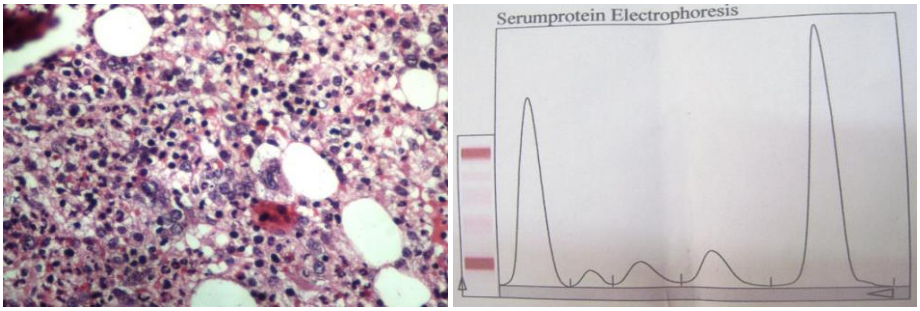

Figure 29: BM trephine biopsy section; MDS, showing increased numbers of blasts forming a small cluster (centre) (an abnormal localization of immature precursors or ALIP) (arrow). (H&E;400X) Figure 30: Serum Electrophoresis, multiple myeloma, showing M band spike.

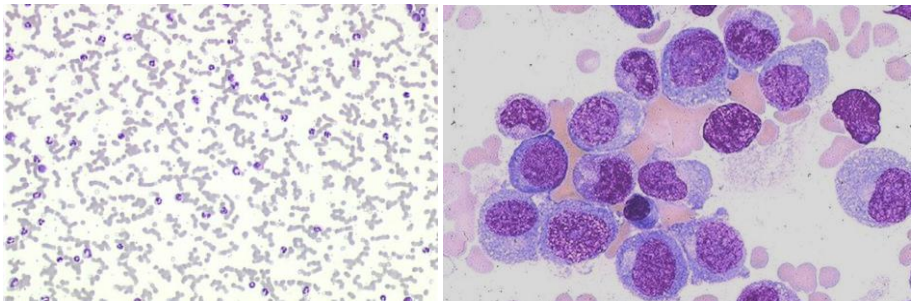

Figure 31: PBF, multiple myeloma; showing prominent rouleaux formation(arrows) (Leishman;200X) Figure 32: BM aspirate, multiple myeloma, showing a range of cells from a plasmablast(thin arrow) to mature plasma cells(thick arrow) (MGG;1000X)..

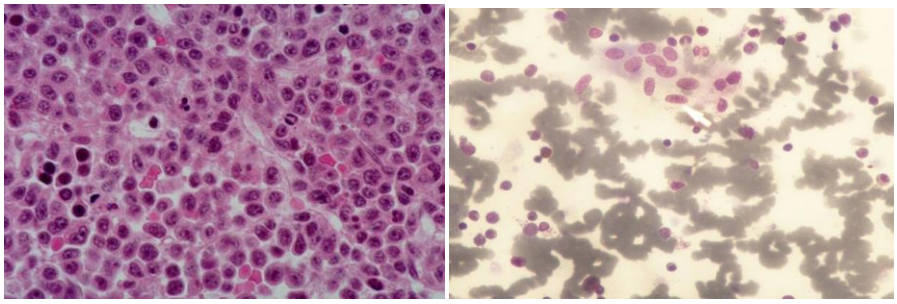

Figure 33: BM trephine biopsy section, multiple myeloma, showing interstitial infiltration of the marrow by plasma cells. (H&E;400X). Figure 34: BM aspirate, tuberculosis, showing collection of epithelioid cells(arrow) (MGG;1000X).

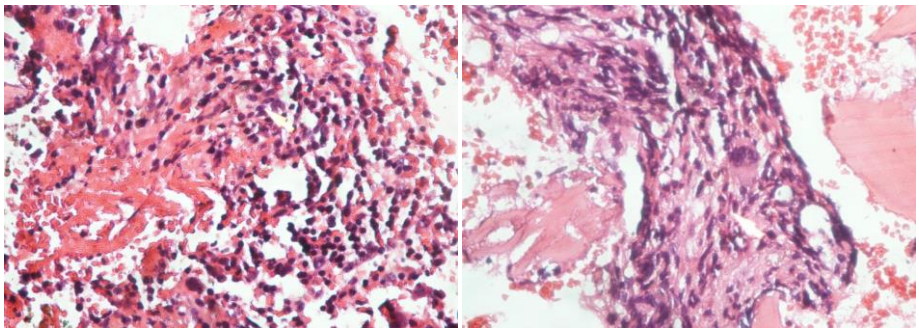

Figure 35: BM trephine biopsy section; Tuberculosis, showing Langhans giant cells(arrow) (H&E;400X). Figure 36:BM trephine biopsy section, tuberculosis, showing epithelioid cell clusters(arrows)(H&E;400X).

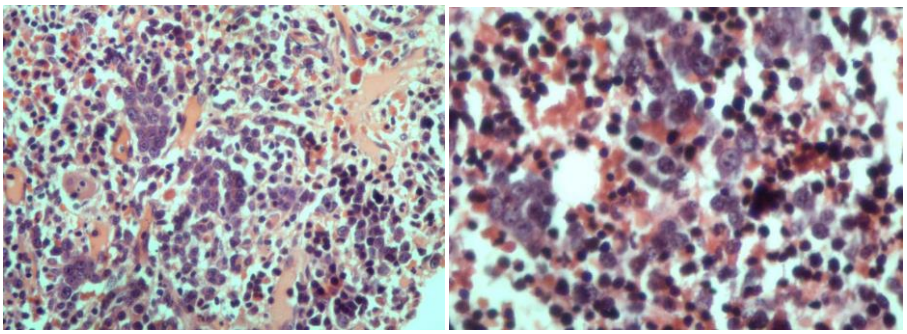

Figure 37: BM trephine biopsy section, showing osteoblastic activity (arrows) around the metastatic deposits (H&E;400X) Figure 38: BM trephine biopsy section, metastatic deposits(arrows) (H&E;1000X).

CONCLUSION

Among different **Anemias**, **megaloblastic** anemia was the **most prevalent anemia**, seen commonly in females of reproductive age group, especially in strict vegetarians followed by chronically alcoholic males. Acute lymphoblastic leukemia was most common acute leukemia followed by various **other hematological disorders** diagnosed in the order of frequency were, myelodysplastic syndromes, myeloproliferative lesions, lymphoproliferative disorders and plasma cell dyscrasias respectively. **Metastatic deposits** formed the bulk of non-hematological disorders followed closely by granulomatous diseases. Bone marrow aspiration along with biopsy performed in all the cases was enough to give confirmatory diagnosis. Features like ALIP (in MDS), patterns of involvement (in CLL & MM), extent of involvement (Acute leukemias), extent of fibrosis(in CML&IMF), were recognized on bone marrow biopsy and also gave useful prognostic information.There was diffuse involvement of BMin cases of lymphomas, tuberculosis and metastatic deposits respectively. So Bone marrow aspiration and biopsy are very essential investigative procedures that generally complement each other, in the workup of patients with various hematological and non-hematological disorders.

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