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Diagnostic spectrum of Bone Marrow Aspiration in Evaluation of Haematological and Non-hematological disorders

One Year Study in a Tertiary Care Hospital at Vadodara, India

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Abstract:
Introduction: Peripheral smeargives much crucial diagnostic information in hematology though in many hematological and non- haematological diseases, bone marrow is required for definitive diagnosis. Bone marrow aspiration is one of the important investigations for diagnosis of pancytopenia, anemia or other hematological and non-hematological disorders.

Aims and objective: The aim of this study is to know prevalence of various hematological disorders and to correlate findings of peripheral smear bone marrow aspiration and bone marrow biopsy.

Materials and methods: Total 63 cases were taken for bone marrow examination. Bone marrow aspiration was performed under aseptic precautions. Slides were prepared and stained with Leishman's stain and Giemsa stain and Prussian blue stain for Iron.

Result: A total of 63 cases were included in this study. The age ranged from 11 months to 67 years. Males were 28 (44%) and females were 35(56%). In this study pancytopenia was the most common indication followed by anemia, suspected malignancy and thrombocytopenia.

Conclusion: In this study, the commonest cause of pancytopenia was Megaloblastic Anemia followed by Aplastic Anemia. No infectious entity in bone marrow aspiration was observed like tuberculosis, Leishmaniasis or Kala azar except one case of Parvovirus Infection and one granulomatous inflammation.

Key Words: ***Granulomatous inflammation ,Pancytopenia, Parvovirus B19.***

I. Introduction:

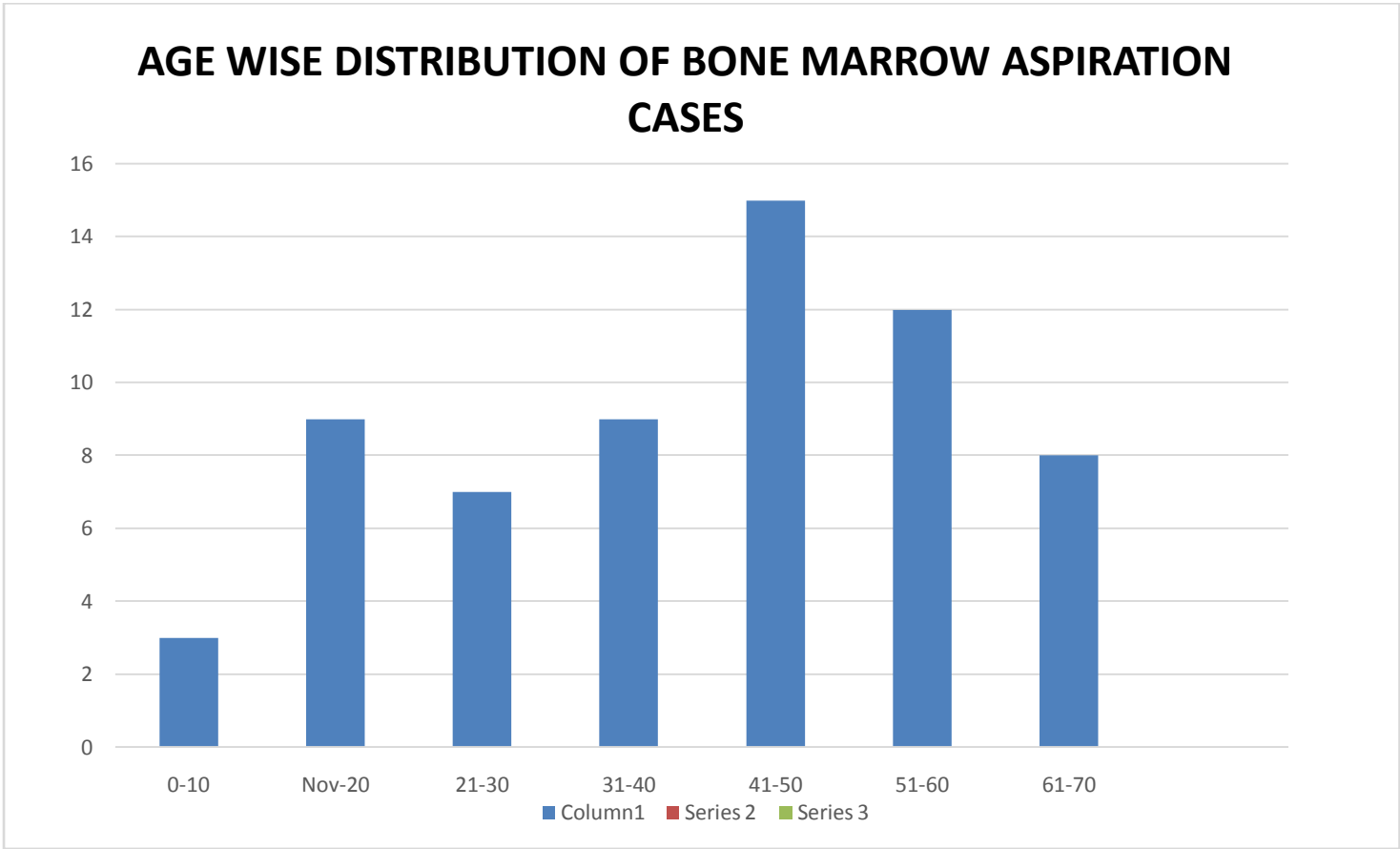
Bone marrow aspiration and biopsy is useful in the diagnosis of both haematological and non-haematological disorders. Bone marrow aspiration is procedure where bone marrow is obtained through a needle aspiration for diagnostic evaluations. [1][2][3] Bone marrow aspiration specimens are useful in further diagnostic assays including cyto chemical/special staining, immune phenotyping[1][2][3] cytogenetic analysis and molecular studies.

It may be useful in establishing the diagnosis of storage diseases and metastatic non-haemopoietic malignancies or when a leucoerythroblastic peripheral blood picture is present. Deviations from the normal may be qualitative with abnormal cell morphology or quantitative with [4] aplasia, hypoplasia or hyperplasia .

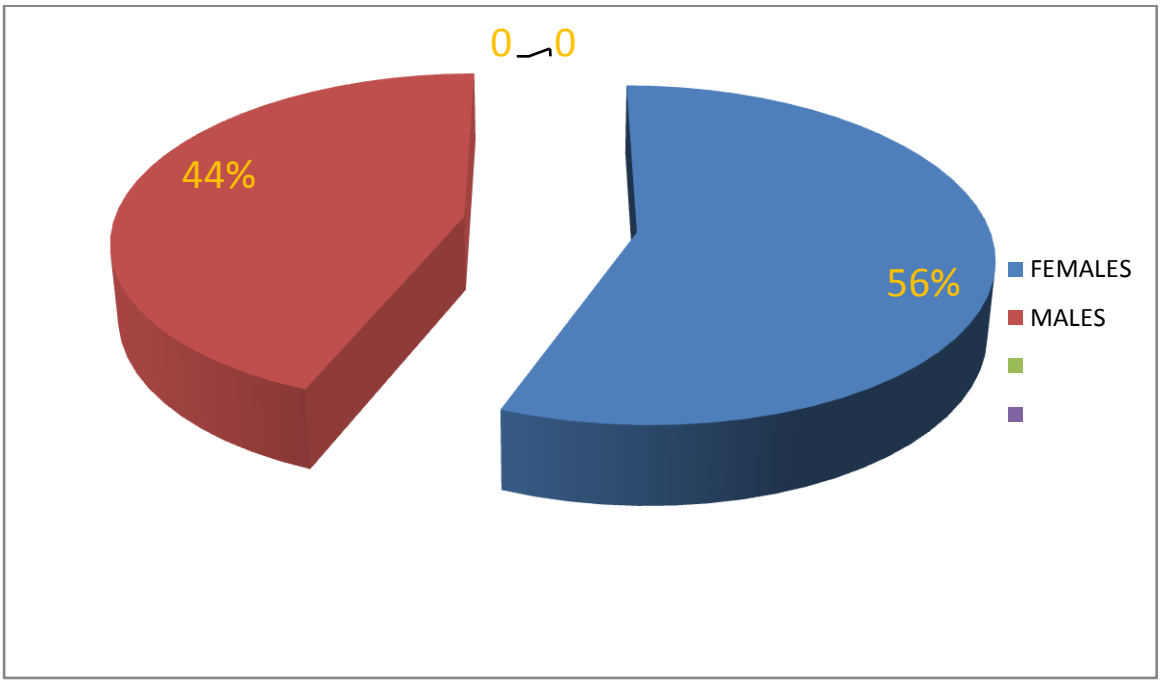
II. Materials and methods

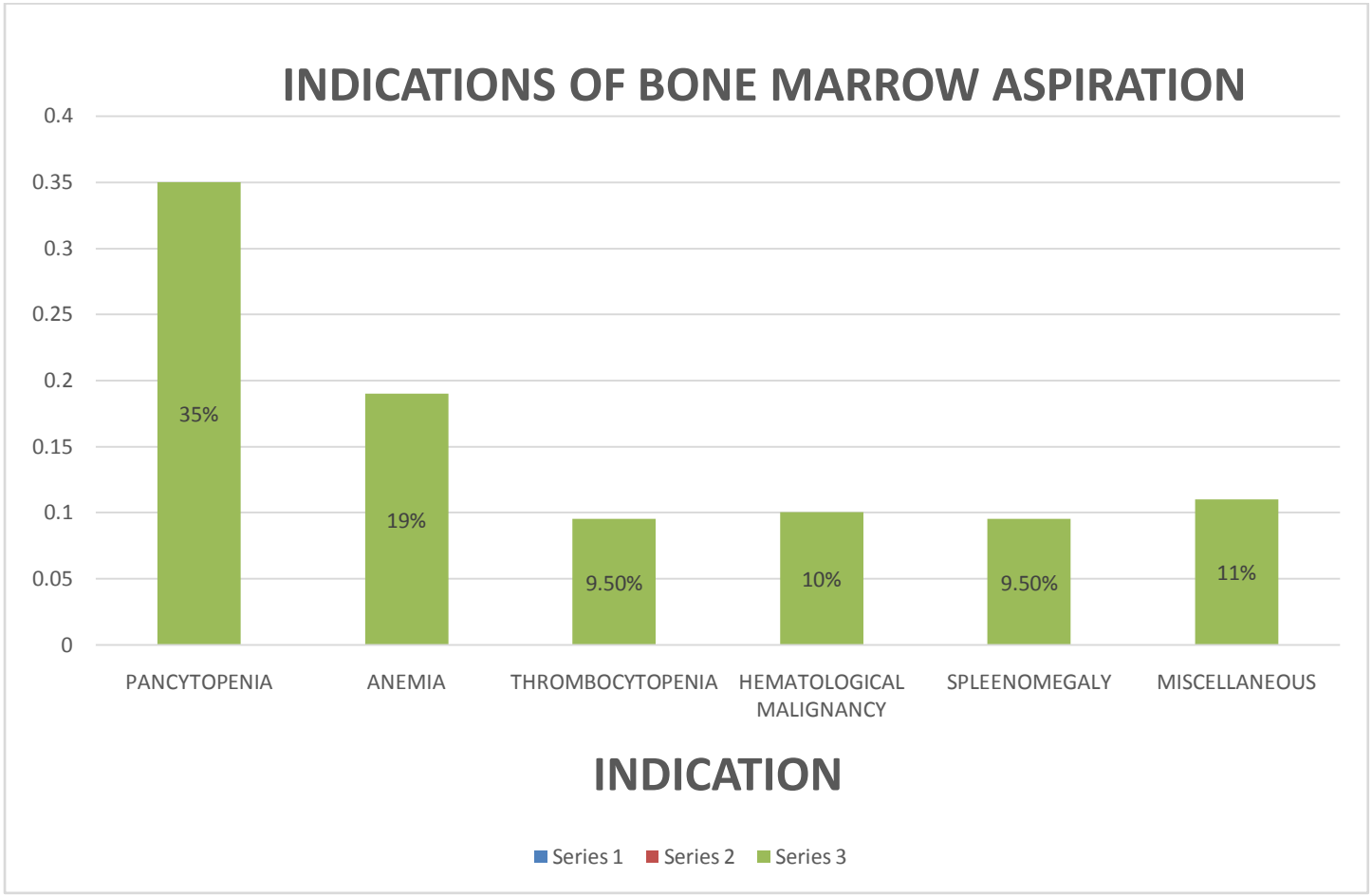
We evaluated a total number of 63 cases from January 2019 to December 2019 in the Central Laboratory, Department of Pathology, Baroda Medical College and S.S.G.Hospital. Bone marrow aspiration was performed only in those patients who were advised to do so by their clinicians. Patients were of different age groups, both genders. Bone marrow aspiration was done under aseptic condition . The Bone marrow aspiration material was collected and smears were prepared by wedge-slides were stained with Leishman's stain and Giemsa stain and where needed, special stains like Sudan Black was used. To evaluate iron stores in the bone marrow, Prussian Blue stain was used.[5]Posterior superior iliac crest was the site of choice for Bone marrow aspiration in all the patients. Records regarding the patient detailed information, consent, clinical history, physical examination, clinical indication for the procedure and all laboratory test findings including peripheral smear reports were recorded. All slides were examined by the consultant pathologist and the data were analyzed.[6]

III. Results

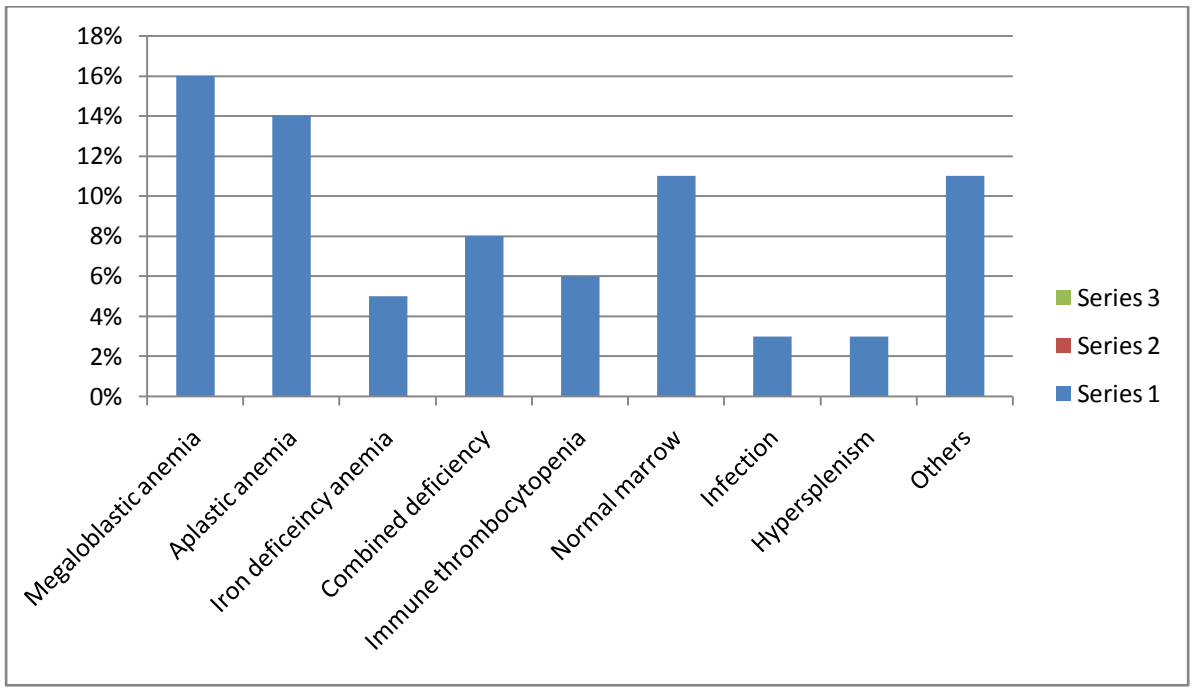


Sex Wise Distribution Of Bone Marrow Aspiration Cases

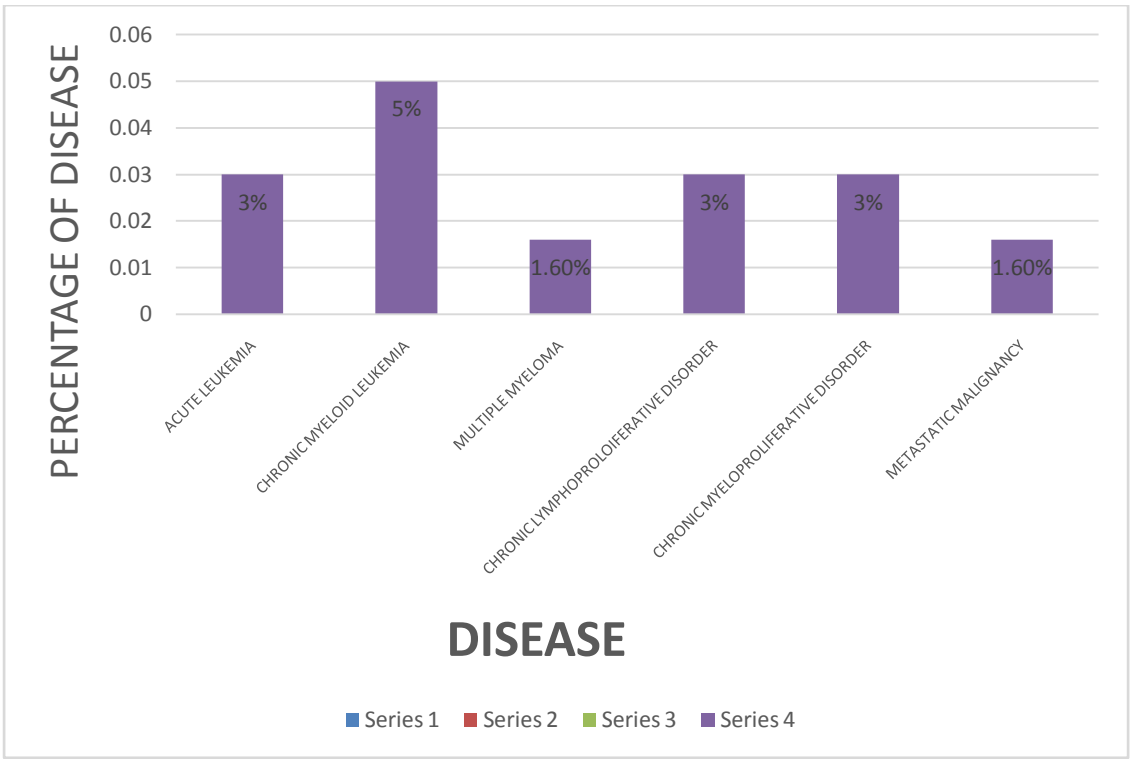

0_0
44%
56%
FEMALES
MALES


INDICATIONS OF BONE MARROW ASPIRATION
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
35%
19%
9.50%
10%
9.50%
11%
PANCYTOPENIA
ANEMIA
THROMBOCYTOPENIA
HEMATOLOGICAL MALIGNANCY
SPLEENOMEGALY
MISCELLANEOUS
INDICATION
Series 1
Series 2
Series 3

Spectrum of non-malignanathematological conditions



Spectrum of Malignant hematological conditions



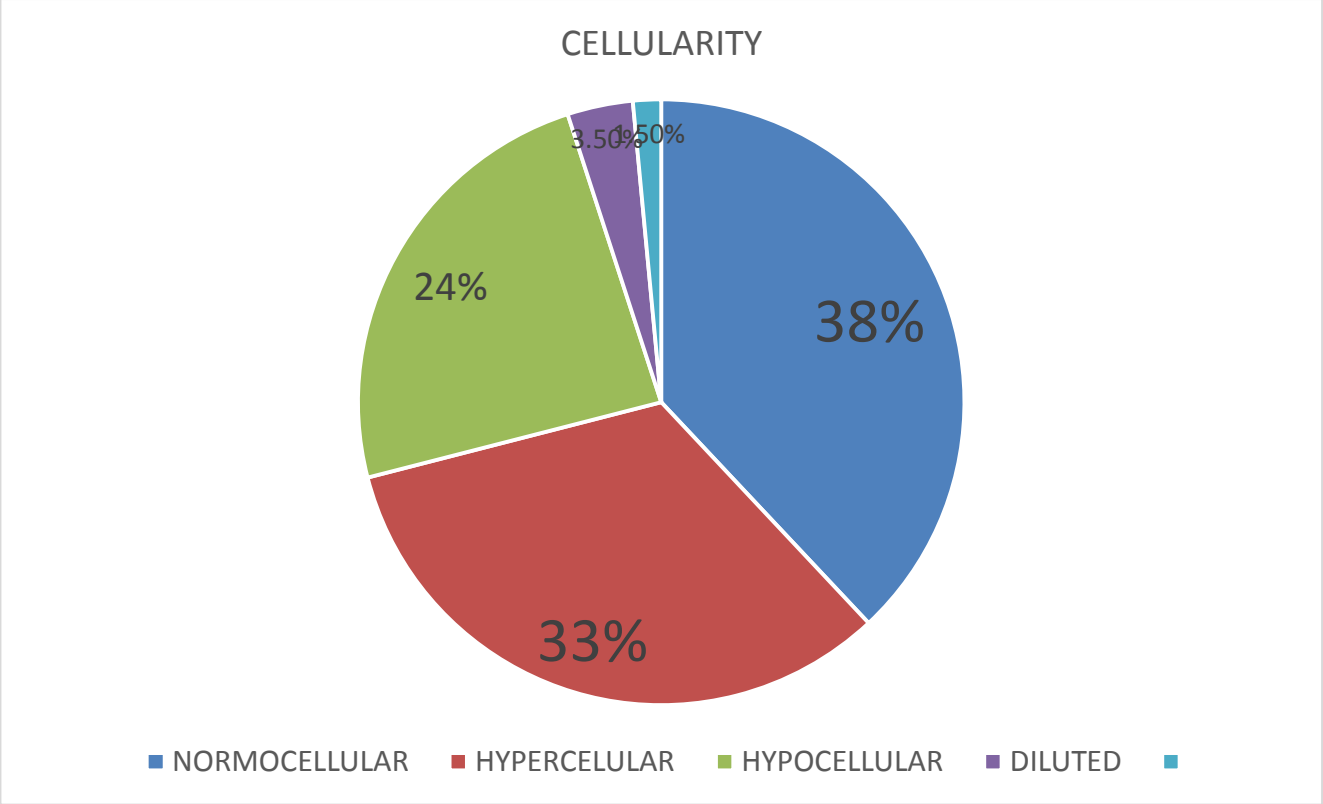
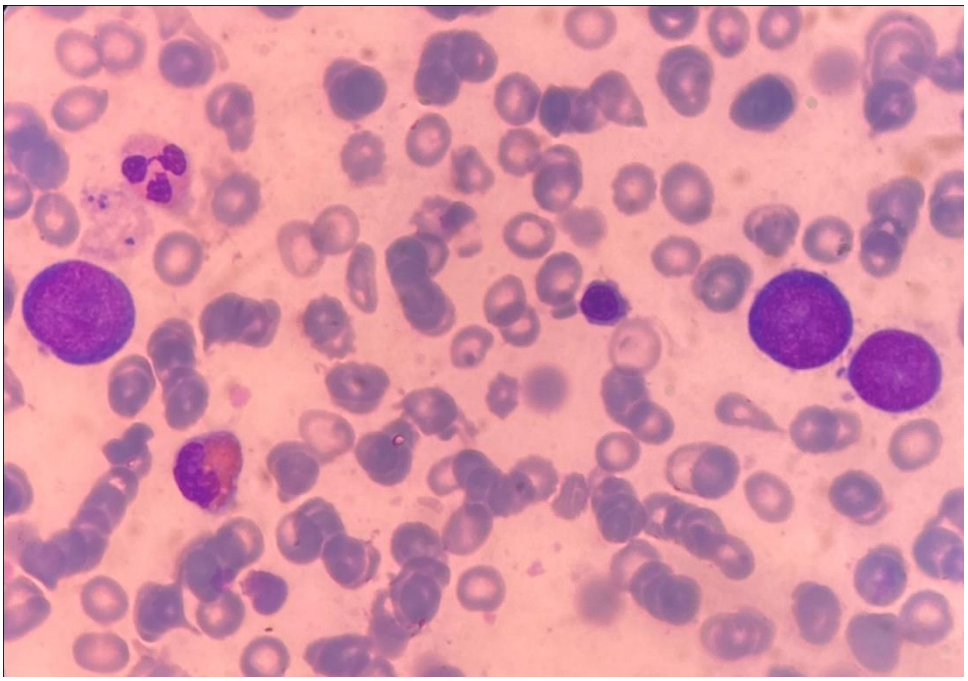


Figure 1:



A total of 63 cases underwent bone marrow examination from January 2019 to December 2019 were included in this study. Out of that 63, 28 (44%) were males and 35(56%) were females.The ratio of male to female was (1:1.25). The age of patients in this project were ranged between 11 months to 67 years with mean age of 41 years.(Chart 1 and chart 2)

The indications for bone marrow examination were based on the clinical findings and or complete blood pictures. In this study, the main indications for examination of bone marrow were Pancytopenia22 cases(35%) followed by Anaemia 12cases (19%), Malignancy 10cases(16%), Thrombocytopenia and splenomegaly each comprising 6 cases(9.5% each) and others include fever under investigation 5 cases(8%), and fracture neck femur in case of avascular necrosis of Hip joint 1 case and Drug induced Bone Marrow suppression 1 case.(Chart 3)

Various haematological disorders were encountered in this study as the result of bone marrow examination. The most frequent diagnosis was Megaloblastic Anaemia 10 cases(16%). Overall, there were 9 cases(14%) of Aplastic anemia, 3 cases of Iron Deficiency Anaemia (5%), 5 cases of Combined Megaloblastic and Iron Deficiency Anaemia(8%), 4 cases of Immune Thrombocytopenia(6%), 2 cases of infection out of which one was of Parvovirus Infection (Figure 1) and another was Granulomatous Infection in case of HIV infected person(3%), 2 cases were reported as hypersplenism(3%). Among all the cases, 7 were reported as normal marrow(11%) .Others include a case of Auto Immune Haemolytic Anaemia, Drug Induced Thrombocytopenia, Avascular Necrosis Refractory Anaemia, Hemophagocytic syndrome one for each .There was one case in which patient presented with abdominal pain , hepatomegaly and spleenomegaly .Bone marrow aspiration showed hypercellular marrow while bone marrow biopsy showed primary myelofibrosis.One more case presented with pancytopenia in which findings suggested hypercellular marrow with reduced megakaryosis and erythroid hyperplasia possibly due to anemia of pregnancy. (Total 7cases- 11%) (Chart 4)

Total 11cases of malignant haematological disorderswere reported, out of which there were3 cases of Chronic Myeloid Leukaemia(5%), 2 cases of Chronic Lymphoproliferative disorder(3%) , 2 cases of Chronic Myeloproliferative Disorder(3%) ,a case of Multiple Myeloma, Acute Lymphoblastic Leukemia, Acute Myeloid Leukemia and Metastatic Epithelial Malignancy one for each .

Majority of the marrows received were Normocellular (24 cases), followed by Hyper cellular (21 cases) and hypo cellular (15 cases), for age. There were also a case of dry tap and 2 cases of Diluted Marrow. (Chart 5)

IV. Discussion

The bone marrow is one of the body's largest organs, constituting 4.5% of the total body weight and weighs 3375 g in an average 75 kg individual. [7] It is the principal site of hematopoiesis. The hematopoietic bone marrow is organized around the vasculature of the bone cavity. Its main function is to supply mature hematopoietic cells for circulating blood in a steady state as well as to respond to increased physiological or pathological demands. BMA is a cytologic preparation of bone marrow cells obtained by aspiration of marrow and a smear of the cells. It is used to diagnose, confirm, and/or stage hematologic malignancies. It helps to evaluate cytopenia, thrombocytosis, leukocytosis, anemias, and iron status. It is also a diagnostic tool in non-haematological disorders such as storage disorders and systemic infections. The spectrum of haematological disorders is very wide. It is an ambulatory procedure performed under local anesthesia with minimal morbidity. It is a safe and useful test in reaching the final diagnosis. The common indications for BME include unexplained cytopenia, leukocytosis due to suspected leukaemias, leuko erythroblastic picture raising suspicion of BM infiltration, treatment monitoring and staging of some malignancies, unexplained splenomegaly, pyrexia of unknown origin and assessment of iron stores. Haematological disorders, both benign and malignant comprise a major health problem. They have a high mortality and morbidity. Both men and women get affected at any age. Early diagnosis and prompt treatment can save the patient if managed timely. Hence, Bone marrow examination remains a crucial test in the diagnosis of both haematological and non haematologicalmalignancies, when the routine peripheral blood and other laboratory tests are not conclusive of a diagnosis. The present study determines the indications and the spectrum of disorders diagnosed by BMA cytology examination. Total 63 cases of Bone Marrow aspiration were included in this study out of which two cases were of diluted marrow and one was a dry tap.

In this study, the patients undergoing bone marrow examination ranged from 11 months to 67 years of age. The M: F ratio was 1:1.25. Most of the studies show a slight male predominance which is compared in Table 1

Table 1

Comparison of age and sex with various studies

Study name	Age range	M: F ratio
Kumar K et al [8]	2 9 days to 75 years	1.02 : 1
Pudasaini S et al [9]	3 9 months to 75 years	1.1 : 1
Gilotra M et al [10]	4 1.5 years to 88 years	1.2 :1
Thiyagarajan P5 [11]	8 years to 90 years	1.3 :1
Sterling Hospital Vadodara [12]	2 years to 80 years	1.25 : 1
Present Study	11 months to 67 years	1: 1.25

In this study the most frequent indication of bone marrow examination was pancytopenia(35%), followed by Anaemia(19%) and Malignancy (10%). Other indications included thrombocytopenia, splenomegaly and fever. Similarly, by Pudasaini et al [9] in 2012 in Nepal,Bashawari[13] in 2002 at Saudi Arabia and study in tertiary care center, Rajkot [6] showed pancytopenia as most common indication. While studies like Kumar et al [8] reported anaemia (34.4%) to be the most common indication, Aljadeyeh et al [14] reported anaemia (22.4%) as the most common indication of marrow examination.

Pancytopenia is apparently a very sinister finding, but in our study the most common diagnosis was Megaloblastic Anaemia (16% cases) followed by Aplastic Anaemia (14% cases) as the cause of Pancytopenia. It was same as study done by Gayathri and Rao [15] in 2011 in India as well as a study done at Rajkot [6]in which Megaloblastic Anaemia was the most common cause of pancytopenia and was the most common finding in BMA (22.5%cases) . Aplastic anaemia which may be congenital or acquired, is the result of failure of normal hemopoietic cells of the bone marrow which results in decreased production of all types of blood cells (RBCs, WBCs platelets). Aplastic anaemia is more common in male than the female[16] In this study the number of affected males was double to that of females. In a study conducted in Karachi, out of 144 patients of aplastic anaemia, 108 were male and only 38 were female[17]. Aplastic anaemia is more common in developing countries than in developed countries.[18]It was the second most common anaemia (11.9% of all cases) in a study [19]. In the study of Atla et al, 19% cases had aplastic anaemia [19]. Some other studies had lower incidence of the disease. It was seen in only 5.3% cases in a study done by Pudasaini et al .[9] The frequency was even lower in a study carried out in Jordan by Momani et al; only one case was found in that study [21]. Although aplastic anaemia is an autoimmune disease, its incidence is equal in both sexes .[22]

In this study Anaemia was the second commonest indication of BMA .The most common cause of anaemia was Aplastic Anaemia (13%) then Megaloblastic Anaemia (7 Cases-11%), followed by Combined Iron deficiency and Megaloblastic Anaemia (5 cases) 3 cases of Iron deficiency Anaemia , 1 case of Hemolytic Anaemia. .However ,In a study done by Ahmed et al[23]in 2011 inRavalpindi, 23.8% of cases were diagnosed as iron deficiency anaemia. Although the most common anaemia in our country is due to iron deficiency, there is no need of BMA for diagnosis and management. Hence, the prevalence of dimorphic and pure megaloblastic anaemia is a higher side in the study. Thus, bone marrow examination could be used effectively in most cases to determine the cause of anaemia.

Immune Thrombocytopenic Purpura (ITP) is an autoimmune disease. Like all autoimmune diseases, ITP is more common in women. In our study, total 4 cases(6%) were of ITP, among which 2 were females and 2 were males. In study of Nepal.[19] the female to male ratio was 1.6:1. The proportion of ITP cases in two studies from Nepal [9][24]found it to be 9.33% and 10.5%. International studies have shown the proportion to be 6.21%, 14.5% and 5%. [23][25][26]

In this study, Non neoplastic diseases were 85%, while malignant cases 15%. Study of Nepal [19] suggested Non-neoplastic diseases consisting of 81.1% and neoplastic diseases consisting of 18.9% . In one study from Nepal, the incidence of neoplastic diseases was 19.3%.[9] In our study, Leukemia was the most common malignancy. Out of that 11 cases, most common was Chronic Myeloid Leukemia (3 cases), followed by Acute Myeloid Leukemia , and Acute Lymphoblastic Leukemia one-one case each and like that Chronic Myeloproliferative disorder(CMPD) and Chronic Lymphoproliferative Disorder(CLPD) accounts for 2 cases one-one for each. In a Rajkot study [6] Acute Myeloid Leukemia was most common malignant disorder accounting for 4.1%case.Similarly, , Acute Myeloid Leukemia was the most common disorder in one more study conducted by Atla BL et al [20] in 2015 in India, Multiple myeloma was found to be the second-most common malignant disease (2.5%) which is close to the data (3.5%) in one study [9] In one more study at the Rajkot Tertiary care Hospital.,[6] Multiple Myeloma was second most common malignancy accounting for 2.9%.In a study by Ranabhat S et al in 2017 in Nepal, [19] Multiple Myeloma constituted 13.3%. In our study, Multiple Myeloma accounted only one case(1.6%).

In this study, metastatic deposits were found in one case(1.6%). In study at the Rajkot Tertiary care Hospital [6] metastasis were seen in 1.4% cases, Adewoyin AS et al [27]in 2014 in India in their study had seen marrow carcinomatosis in 7.9% cases. In our study Normal marrow findings were seen in 3 cases(4.5%) while in a study conducted at Rajkot tertiary care Hospital normal marrow was found in 6.8%cases [6], in a study of Atla et al it was 3.8% ,[20] in a study by Pudasaini et al [9] in 2012 at Nepal it was 10.5%.

V. Conclusion:

Bone marrow aspiration cytology is a minimal invasive, safe , relatively cheap technique which can diagnose many haematological and non-haematological diseases that can be confirmed by more advanced investigations, serological, biochemical or molecular. However, bone marrow sample cannot be obtained (dry tap) in a proportion of cases. In such cases, a bone marrow biopsy needs to be performed.

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