Section: Pathology

Original Research Article

A DESCRIPTIVE STUDY OF BONE MARROW INFILTRATIVE LESIONS PRESENTING AS MYELOPHTHISIC ANEMIA ADMITTED IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Myelophthisic anemia is a normocytic normochromic anemia that occurs when normal marrow space is infiltrated and replaced by non-hematopoietic or abnormal cell. Causes include acute leukemias, myeloproliferative disorders, plasma cell myeloma, metastasis, storage disorders and granulomas. **Aims:** To study the cause of anemia with or without bicytopenia or pancytopenia or leucoerythroblastic blood picture.

Material and Methods: Present study is retrospective evaluated 40 patients by fufilling the inclusion and exclsion criteria. Bone marrow studies were performed in the patients who presented with anemia as an isolated parameter or with pancytopenia or leukoerythroblastic blood picture on peripheral smear. Retrospective studies were done by collecting the slides of confirmed and already diagnosed cases.

Results: Out of 40 cases, 32 cases (80%) were diagnosed as hematological disorders, and 8 cases (20%) were diagnosed as non-hematological disorders. Out of 40 cases presenting as myelophthisic anemia, 35 cases (87.5%) were neoplastic, and 5 (12.5%) cases were non-neoplastic.

Conclusion: Bone marrow aspiration and trephine biopsy are commonly used investigations for the study of marrow infiltrations that present as myelophthisic anemia on peripheral smear. Bone marrow studies guide towards diagnosis in patients with anemia or pancytopenia and not responding to treatment. However, genetic studies are required for molecular diagnosis, targeted therapy and prognosis.

Key Words: myelophthisic anemia, hematological disorders, leukoerythroblast, leukemia.

INTRODUCTION

Myelophthisic anemia is caused by massive marrow infiltration with abnormal cells or tissue components like blasts of leukemia, plasma cells of myeloma, involvement of bone marrow by fibrosis, metastasis, infections, and metabolic (storage) diseases. Anemia is normocytic normochromic and mild to moderate. Total leucocyte count is normal, low, or raised. Platelets may be normal or reduced. Peripheral smear may show isolated anemia or with pancytopenia or with leucoerythroblastic picture. The term leuco-erythroblastic blood picture is used to describe the presence of immature myeloid and nucleated red cells in the peripheral blood. Decreased functional hematopoietic tissue due to bone marrow infiltration

is the leading cause of anemia. Myelopthisis is observed more frequently in countries where access to medical care is difficult, and diseases are allowed to progress to advanced stages.

The clinical manifestations of myelophthisic anemia depend on the underlying disease and severity of the condition. Bone marrow studies are necessary for definitive diagnosis. Radioisotope scanning and magnetic resonance imaging are other investigations, but they are less sensitive than bone marrow studies.[1,2]

Bone marrow was first obtained from patients for diagnostic purposes during the first decade of the twentieth century, but it was not until the introduction of sterna aspiration in the late 1920s that this became an essential diagnostic procedure. All bone marrow aspirates and needle biopsies require informed consent and performed under strict aseptic conditions. Bone marrow aspiration causes only mild discomfort to the patient. A standard Romanowsky-type staining method should be employed for routine morphologic analysis. As with peripheral smears, well-controlled staining protocols are essential for accurate morphological evaluation.

A trephine biopsy causes moderate discomfort, and in an apprehensive patient, sedation can be useful. In addition to at least one level stained with hematoxylin and eosin, many laboratories perform additional stains on the bone marrow sections, either routinely or as on need basis. Complications of bone marrow biopsy and aspiration are rare, especially when performed by experienced practitioners. The most common complications are localized bleeding or infection.[3,4] Hence this study cause of anemia with or without bicytopenia/ pancytopenia / leukoerythroblastic blood picture.

MATERIAL AND METHODS

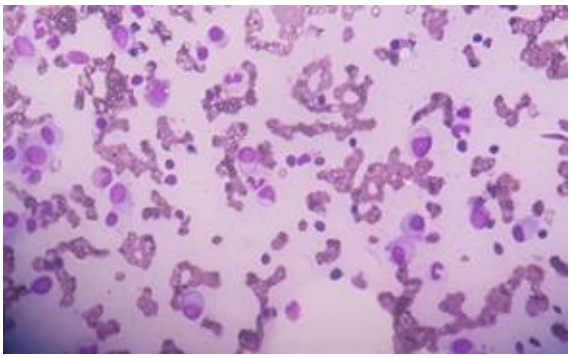
It is a Retrospective and prospective study was done medical college and general hospital, Nellore, after taking ethical approval from the ethical review committee of Narayana medical college, Nellore. The study includes data for three years from May 2015 to April 2018. Retrospective studies are done by collecting the slides of confirmed and already diagnosed cases. This study includes 40 patients. Patient details, presenting complaints, and other hematological and biochemical findings were documented. Each patient was given a hematology identification number.

Inclusion Criteria: Patients who presented with anemia as an isolated parameter or with pancytopenia or leukoerythroblastic blood picture that is not responding to treatment.

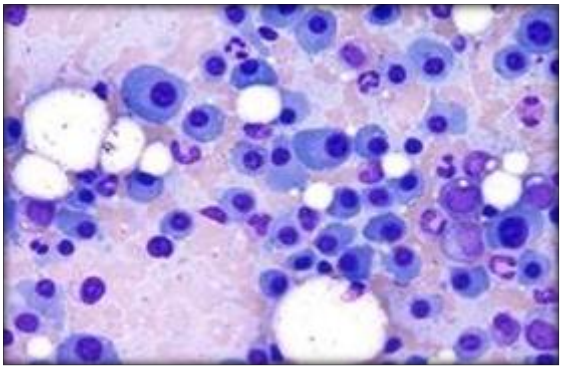
Exclusion Criteria: Uncooperative patients, inadequate marrow aspirates and hemorrhagic marrow aspirates.

Peripheral smears are stained using commercially available RANKEM Leishman's stain solution following standard protocols.

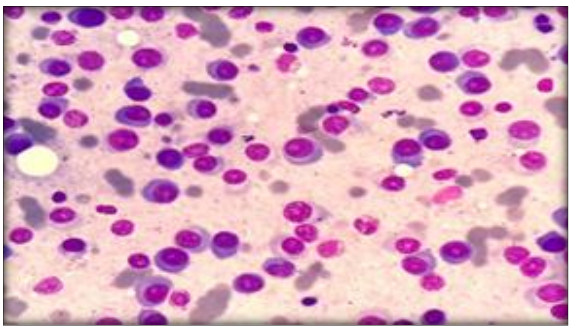
RESULTS



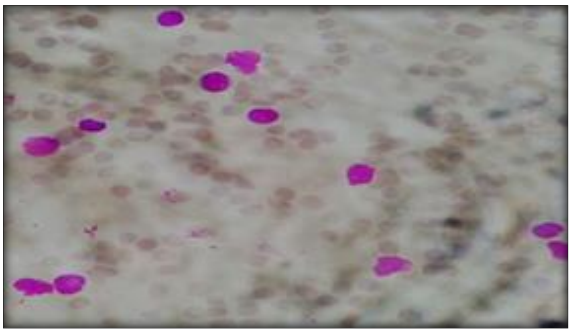
Bone marrow aspirate smear - Plasma cell myeloma (Leishmans X 100)



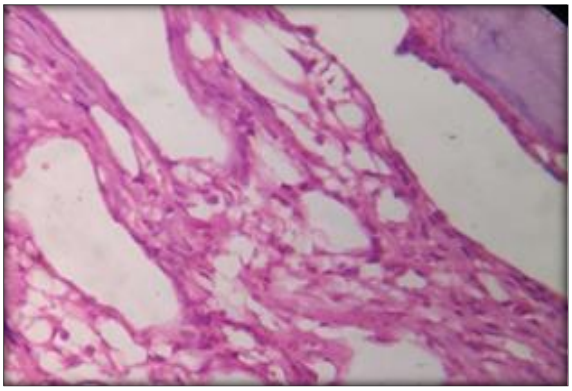
Bone marrow aspirate smear - Plasma cell myeloma (Giemsa X 400)



Bone marrow aspirate smear - Plasma cell myeloma (Leishmans X400)



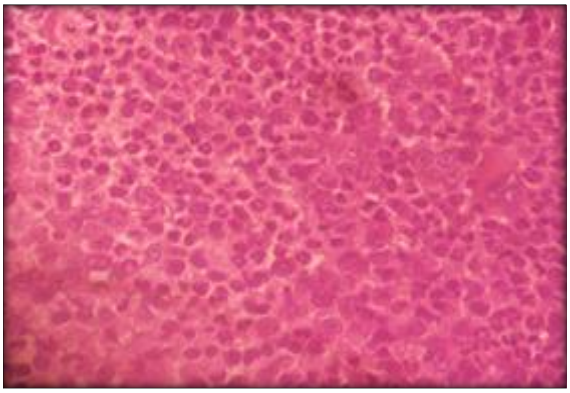
Peripheral smear – Chronic lymphocytic leukemia (Leishmans X400)



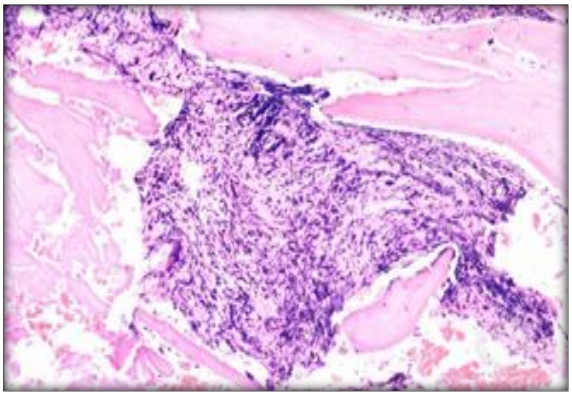
Bone marrow biopsy section – Myelofibrosis (H&E X 400)

Bone marrow biopsy section – Chronic myeloid leukemia (H&E X 400)

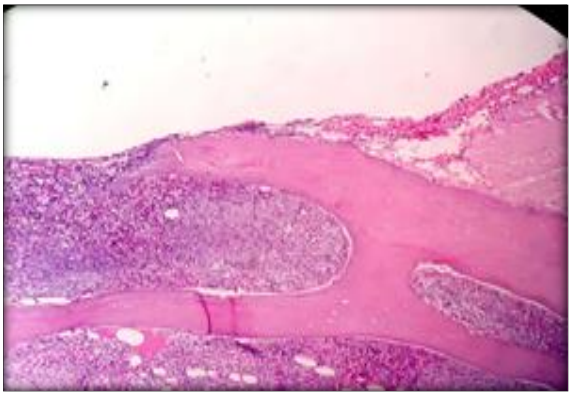
Bone marrow biopsy section – Myelofibrosis (Reticulin X 400)



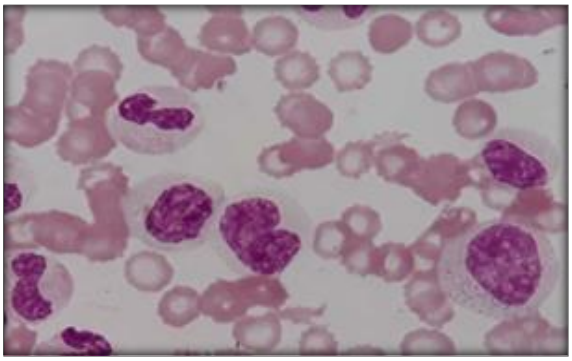
Bone marrow biopsy section – Chronic myeloid leukemia (MPO X 400)



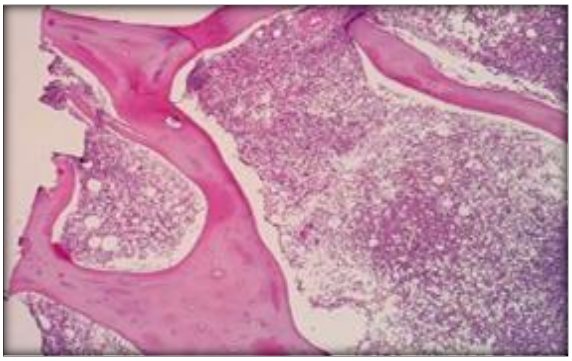
Bone marrow biopsy section – Myelofibrosis (H&E X 100)



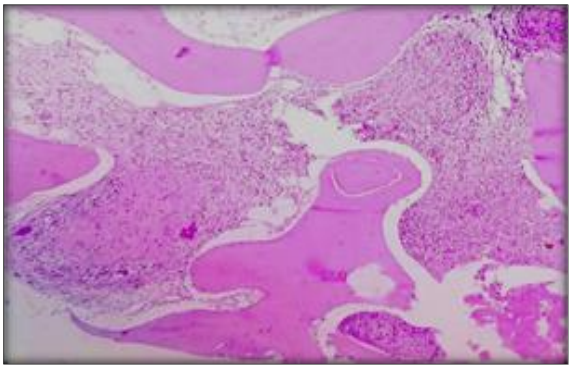
Bone marrow biopsy section – Non- Hodgkin's lymphoma (H&E X 400)



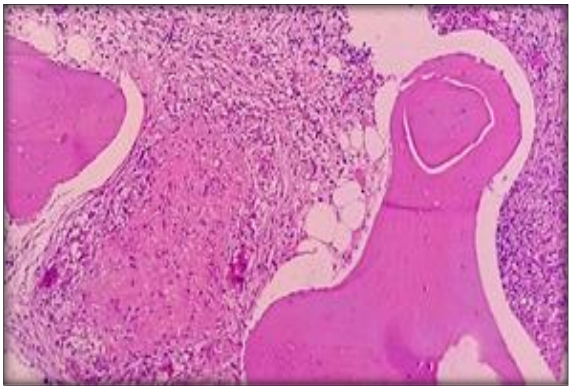
Peripheral smear – Chronic myeloid leukemia (Leishmans X 1000)



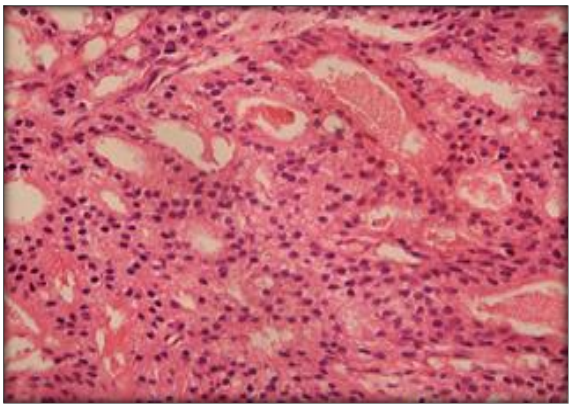
Bone marrow biopsy section – Non- Hodgkin's lymphoma (H&E X 400)



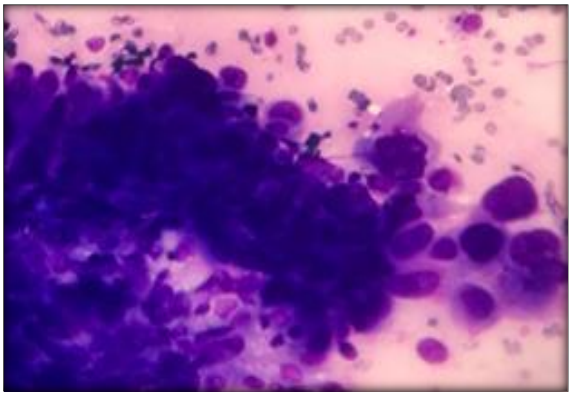
Bone marrow biopsy section – Granuloma (H&E X 100)



Bone marrow biopsy section – Granuloma(H&E X 400)



Bone marrow aspiration smear- Metastatic deposits (Giemsa X 400)



Bone marrow biopsy – Metastatic adenocarcinoma (H&E X 400)

The present study included 40 cases of Myelophthisic anemia that were diagnosed on peripheral smear and bone marrow examination retrospectively and prospectively at Narayana Medical College, Nellore. The age group of the patients in this study ranges from 7 years to 75 years. The maximum number of cases is seen in the fourth and fifth decades, followed by the sixth decade.

Out of 40 cases evaluated, 27(67.50%) were males, and 13(32.55%) were females (Table 2), which showed male predominance. Out of 40 cases presenting as myelophthisic anemia, 35 cases (87.5%) were neoplastic, and 5 (12.5%) cases were non-neoplastic showing neoplastic etiology to be more common than non-neoplastic etiology. Out of 40 cases, 32 cases (80%) were diagnosed as hematological disorders, and 8 cases (20%) were diagnosed as non-hematological disorder. Out of 40 cases, 9 cases were Acute leukemia (22.50%). [Table 1]

On peripheral smear, out of 40 cases, 17 cases (42.50%) presented as anemia as an isolated parameter, 7 cases (17.5%) presented with bicytopenia, 11 cases (27.50%) presented with pancytopenia and 4 cases(10%) presented with leucoerythroblastic picture. Out of 9 acute leukemia cases, 4 cases (66.66%) were seen in age group between 41 to 60 years, 3 cases (44.44%) were seen in the age group between 0 to 20 years, 2 cases(22.22%) were seen between 21 to 40 years. [Table 2]

Out of 9 cases of Acute leukemia in our study, 5 cases(55.55%) were seen in males, and 4 cases(44.44%) were seen in females. Out of 9 cases of acute leukemia, 3 cases (33.33%) were acute lymphoblastic leukemia, and 6 cases(66.66%) were acute myeloid leukemia. AML cases were confirmed by using a myeloperoxidase stain. Out of 9 cases of acute leukemia, 1 case (11.11%) showed anemia as an isolated parameter, 4 cases (44.44%) showed bicytopenia, and 4 cases(44.44%) showed pancytopenia blood picture on peripheral smear. Out of 6 cases, plasma cell myeloma in our study 3 cases (50%) were seen in age group between 41 to 60 years and 3 cases were seen in the age group above 60years. [Table 3]

Out of 6 cases of plasma cell myeloma, 3 cases (50%) were seen in males, 3 cases(50%) were seen in females. Out of 6 cases of plasma cell myeloma, 4 cases(66.66%) presented as anemia, 1 case (16.66%) presented as bicytopenia, 1 case (16.66%) presented as pancytopenia on peripheral smear. Out of 9 cases of myeloproliferative disorder, 4 cases(44.44%) were seen in age group between 30-50 years, 3 cases (33.33%) were seen in age group between 51 -70 years, 2 (22.22) cases were seen in the age group above 70 years. [Table 5]

Out of 9 cases of Myeloproliferative neoplasms, 6 cases (66.66%) were seen in males, and 3 cases (33.33%) were seen in females. Out of 9 cases of myeloproliferative disorder, 5 cases (55.55%) presented as anemia, 2 cases (22.22%) presented as bicytopenia, and 2 cases (22.22%) presented as pancytopenia on the peripheral smear. Out of 9 cases

of myeloproliferative disorders, 4 cases (44.44%) were chronic myeloid leukemia, and 5 cases (55.55%) were myelofibrosis. [Table 6]

Out of 9 cases of myeloproliferative disorders, 4 cases of bone marrow aspirate smears are hypercellular, in 1 case aspirate smear was hypocellular, and in 4 cases it was dry tap. [Table 18]

Out of 40 cases in the present study,5 cases (12.5%) were diagnosed as Non- Hodgkin's lymphoma. All the 5 cases of Non -Hodgkins lymphoma were seen in males in the present study

Out of 40 cases in the present study,3 cases (7.5%) were diagnosed as chronic lymphocytic leukemia. All the 3 cases were seen in males and the age group above 50 years. Out of 40 cases in the present study, 3 cases (7.5%) were diagnosed as metastatic adenocarcinoma. All the 3 cases were seen in males in the age group above 70 years. Out of 40 cases in the present study, 4 cases (10%) were diagnosed as granulomas Out of 4 cases, 2 cases were seen in males, and 1 case was seen in females . Out of 40 cases in the present study, 1 case (2.5%) was diagnosed as a storage disorder in an 11 years old male patient. [Table 7]

Table 1: Distribution of cases in Myelophthisic anemia

Age group	Number of cases	Percentage
0-20 years	5	12.5%
21-40 years	6	15%
41-60 years	20	50%
>60 years	9	22.5%
Sex wise distribution		
Males	27	67.50%
Females	13	32.55%
Neoplastic/ non- Neoplastic		
Neoplastic	35	87.5%
Non neoplastic	05	12.5%
Causes of Myelophthisic anemia		
Haematological	32	80%
Non-haematological	08	20%

Table 2: Various diagnostic entities presenting as Myelophthisic anemia

Diagnosis	Number of cases	Percentage
Acute leukemia	9	22.50%
Non-Hodgkins lymphoma	5	12.50%
Chronic lymphocytic leukemia	3	7.50%
Chronic myeloid leukemia	4	10%
Myelofibrosis	5	12.50%
Plasma cell myeloma	6	15%
Metastasis	3	7.50%
Granulomas	4	10%
Storage disorder	1	2.5%
Total	40	100%
Peripheral smear findings		
Anemia	18	45%
Bicytopenia	7	17.5%
Pancytopenia	11	27.50%
Leukoerythroblastic picture	4	10%
Total	40	100%

Table 3: Distribution of Acute leukemia

Age group distribution	Number of cases	Percentage
0-20 years	3	66.66%
21-40years	2	22.22%
41-60years	4	44.44%
Total	9	100%
Sex		
Males	5	55.55%
Females	4	44.44%
Morphological diagnosis		
Acute myeloid leukemia	6	66.66%
Acute lymphoblastic leukemia	3	33.33%
Peripheral smear		
Anemia	1	11.11%
Bicytopenia	4	44.44%
Pancytopenia	4	44.44%
Total	9	100%

Table 4: Distribution of Plasma cell myeloma cases

Age group	Cases	Percentage
41-60years	3	50%
>60years	3	50%
Total	6	100%
Gender		
Males	3	50%
Females	3	50%
Peripheral smear findings		
Anemia	4	66.66%
Bicytopenia	1	16.66%
Pancytopenia	1	16.66%

Table 5: Distribution of Myeloproliferative disorders

Age group	Cases	Percentage
30-50 years	4	44.44%
51-70 years	3	33.33%
>70 years	2	22.22%
Total	9	100%
Sex		
Males	6	66.66%
Females	3	33.33%
Peripheral smear findings		
Anemia	5	55.55%
Bicytopenia	2	22.22%
Leukoerythroblastic picture	2	22.22%

Table 6: Incidence of different categories of Myeloproliferative disorders

Myeloproliferative disorder	Cases	Percentage
Chronic myeloid leukemia	4	44.44%
Myelofibrosis	5	55.55%
Total	9	100%

Table 7: Cellularity in the bone marrow aspiration in Myeloproliferative neoplasms

Bone marrow aspiration	Number of Cases	Percentage
Hypercellular	4	44.44%
Hypocellular	1	11.11%
Dry tap	4	44.44%
Total	9	100%

DISCUSSION

Myelophthisis is a form of bone marrow failure due to the replacement of hemopoietic tissue by abnormal cells. Decreased hemopoietic precursors may result in anemia as an isolated parameter or bicytopenia or pancytopenia. Peripheral smear may show leucoerythroblastic picture showing nucleated RBCs on smear. Bone marrow studies are useful in the diagnosis and prognosis of conditions that present as myelophthisic anemia. Accurate diagnosis of marrow infiltrative lesions presenting as myelophthisic anemia helps not only in treatment of disease but also in staging of certain diseases. In the present study peripheral smears, bone marrow aspirates, trephine biopsy sections were analyzed in patients not responding to treatment for anemia or thrombocytopenia.

The age group of the patients in this study ranges from 7 years to 75 years. The maximum number of the cases are seen in the fourth and fifth decades followed by the sixth decade. The present study was compared with other bone marrow studies like Shubha et al,[6] study and Shastry et al,[5] study In Shubha et al,[6] study, the maximum number of bone marrow cases were studied in the age group between 21 to 40 years, i.e., second and third decades which did not correlate with the present study. In shastry et al,[5] study, the maximum number of bone marrow cases were studied in the age group between 21 to 40 years, i.e., second and third decades which did not correlate with the present study

Out of 40 cases evaluated 27(67.50%) were males, and 13(32.55%) were females which showed male predominance in the present study. In Shubha et al,[6] study, the maximum number of bone marrow evaluations was performed in males compared to females. In Shastry et al,[5] study the distribution of cases among males and females was equal. In Manjit kaur et al,[7] study, out of 50 bone marrow aspirations and biopsies, 31 cases (62%) were males, and 19 cases (38%) were female which showed male predominance. The present study was correlated with Shubha et al,[6] study and Manjit kaur et al,[7] study. The present study was not correlated with Shastry et al,[5] study

In the present study hematological lesions (80%) are more than non-hematological lesions (20%). The present study was correlated well with Sreelakshmi et al,[8] Study. Out of 40 cases in the present study, 35

cases (87.50%) were neoplastic, and 05 cases (12.50%)were non-neoplastic. The present study was correlated with Sreelakshmi et al,[8] study, which showed predominance of neoplastic conditions.

Out of 40 cases in the present study, 9 cases were acute leukemia (22.50%), 5 cases were lymphoproliferative disease (12.50%), 3 cases were chronic lymphocytic leukemia (7.50%), 4 cases were chronic myeloid leukemia (10%), 5 cases were myelofibrosis (12.5%), 6 cases were plasma cell myeloma (15%), 3 cases were metastasis (7.5%), 4 cases were granulomas (10%), 1 case was storage disorder (2.5%). A maximum number of cases were acute leukemias (22.5%) in the present study. Various diagnostic entities in the present study were compared with diagnostic entities in other bone marrow studies The present study was compared with Burkett et al,[9] study and Nitin gupta et al,[10] study. In Nitin gupta et al,[10] study, out of 40 cases studied, 20 cases(50%) were acute leukemias. In Nitin gupta et al,[10] study, the maximum number of cases were acute leukemia which correlated with the present study. In Burkett et al,[9] study maximum cases were chronic myeloid leukemia 10 cases (21.3%) which were not correlated with the present study.

In the present study maximum number of cases18 (45%) presented as anemia as an isolated parameter on peripheral smear. In Ruchita et al. study and Ahmet Dirican et al. study the maximum number of cases presented as bicytopenia on peripheral smear. [Table 8]

Out of 40 cases in the present study, 9 cases were diagnosed as acute leukemias. Out of 9 cases, maximum number of cases were between the age group 41 to 60 years. The present study was compared with Priya Subashchandrabose study in which the maximum number of cases of acute leukemia was seen between age group 41 to 60 years which correlated with the present study. [Table 9]

In the present study, the maximum number of acute leukemia cases were seen in males (55.55%) which correlated with Priya subash chandrabose et al,[13] study maximum number of cases of acute leukemia were seen in males

In the present study Out of 9 cases of Acute leukemia 6 cases (66.66%) were Acute myeloid leukemia and 3 cases(33.33%) were Acute lymphoblastic leukemia. In Priya Subashchandrabose et al,[13] study the maximum number of cases were Acute myeloid leukemia than other types of Acute leukemia. The present study was correlated with Priya Subashchandrabose et al,[13] study

Age group range of plasma cell myeloma cases in our study is 45 – 75 years which is 42- 90 years in Sanja Stifter et al,[14] study Out of 6 cases of plasma cell myeloma in the present study 3 cases (50%) were diagnosed in the age group between 41 to 60 years and 3 cases (50%) were diagnosed in the age group above 60 years. In Sreelakshmi et al,[8] study, out of 19 cases presented as bone marrow infiltrative lesions, 4 cases were diagnosed as plasma cell myeloma. Maximum number of cases (3 out of 4 cases) were seen in the age group above 60 years which did not correlate with present study. [Table 10]

In the present study, the sex distribution of plasma cell myeloma is equal among both the sexes. In Sanja stifter et al,[14] study, out of 59 cases, 26 cases (44%) were seen in males, and 33 cases(56%) were seen in females which showed female predominance. In Sreelakshmi et al[8] study all the four cases, diagnosed as plasma cell myeloma, were seen in females. Sex distribution of plasma cell myeloma in present study was not correlated with Sanja stifter et al,[14] study and Sreelakshmi et al,[8] study

Out of 9 cases of Myeloproliferative neoplasms in the present study 4 cases were diagnosed as Chronic myeloid leukemia and 5 cases were diagnosed as Myelofibrosis. In Nitin Gupta et al. study 4cases were diagnosed as chronic myeloid leukemia, and 2 cases were diagnosed as myelofibrosis. The present study was not correlated with Nithin gupta et al,[10] study

Out of 9 cases of myeloproliferative neoplasms in the present study,4 cases (44.44%) were hypercellular, 1 case(11.11%) was hypocellular, and in 4 cases (44.44%) it was dry tap on bone marrow aspirate smears. our study was compared with Manjit Kaur et al. study. In Manjit kaur et al,[7] study, 50 bone marrow cases were studied out of which 6 cases were myeloproliferative neoplasms.

Out of 6 cases of myeloproliferative neoplasms. In Manjit kaur et al,[7] study was 1 case (16.67%) was hypercellular, 2 cases (33.33%) showed dry tap, and 3 cases (50%) showed bloody tap on peripheral smear. Maximum number of cases of myeloproliferative neoplasms in the present study showed hypercellularity and dry tap on peripheral smear which was not correlated with Manjit Kaur et al,[7] study, in which maximum number of cases of myeloproliferative neoplasm showed bloody tap on bone marrow aspiration.

Out of 40 cases in the present study, 3 cases (7.50%) were Chronic lymphocytic leukemia. In Nithin Gupta et al,[10] Study, 2 cases (5%) out of 40 cases were diagnosed as Chronic lymphocytic leukemia. Out of 40 cases in the present study, 4 cases were diagnosed as granulomatous lesions in bone marrow biopsy sections. In sreelakshmi et al,[8] Study 1 case (5.26%) out of 19 cases was diagnosed as Granulomatous lesion in bone marrow biopsy sections. Out of 40 cases in the present study, 5 cases (12.5%) were diagnosed as Non-Hodgkins lymphomas. In Nitin Gupta et al,[10] study, 3 cases(7.5%) out of 40 cases were lymphomas. Out of 40 cases in the present study, 3 cases (7.5%) were diagnosed as metastatic adenocarcinomas with primary diagnosed as prostatic adenocarcinoma. In Fahir Ozkalemkas et al,[15] Study, 3 cases out of forty cases were Metastatic adenocarcinomas with primary diagnosed as prostatic adenocarcinoma. [Table 11]

Table 8: Various diagnostic entities in the present study with other studies

Diagnosis	Present	Burkett et al[9]	Nitin gupta et al[10]
Acute leukaemia	9(22.50%)	4(8.5%)	20(50%)
Non hodgkins lymphoma	5(12.50%)	6(12.8%)	03(7.5%)
Chronic lymphocytic leukaemia	3(7.50%)	4(8.5%)	02(5%)
Chronic myeloid leukaemia	4(10%)	10(21.3%)	04(10%)
Myelofibrosis	5(12.5%)	6(12.8%)	02(5%)
Plasma cell myeloma	6(15%)	4(8.5%)	04(10%)
Metastasis	3(7.5%)	8(17%)	-
Others	5(12.5%)	5(10.6%)	05(12.5%)
Total cases	40	47	40

Table 9: Peripheral smear findings of the present study in comparison with other studies

Peripheral smear	Number of cases	Ruchita Tyagi et al[11]	Ahmet Dirican et al[12]
Anaemia	18(45%)	4	12
Bicytopenia	7(17.5%)	11	18
Pancytopenia	11(27.5%)	1	7
Leukoerythroblastic picture	4(10%)	10	-
Others	-	11	18

Table 10: Comparison age group-wise distribution of acute leukemia cases with other studies

Age-group distribution	Present study	Priya subhachandrabose et al [13]
0-20 years	3(66.66%)	30(30%)
21-40years	2(22.225)	14(14%)
41-60years	4(44.44%)	38(38%)
>60 years	-	18(18%)
Sex		
Males	5(55.55%)	56(56%)
Females	4(44.44%)	44(44%)
Morphological diagnosis		
Acute myeloid leukaemia	6(66.66%)	22(61.11%)
Acute lymphoblastic leukaemia	3(33.33%)	12(33.33%)
Others (acute leukaemia unclassified)	-	2(5.55%)

Table 11: Comparison of age group-wise distribution of plasma cell myeloma with other studies

Age group	Present study	Sreelakshmi et al[8]. study
41-60 years	03 (50%)	01(25%)
>60 years	03(50%)	03(75%)
Sex		
Males	3(50%)	4(100%)
Females	3(50%)	-

CONCLUSION

All the cases presenting as anemia or bicytopenia, or pancytopenia on peripheral smear and not responding to treatment should be investigated for marrow infiltration. Bone marrow aspiration and trephine biopsy are commonly used investigations for the study of marrow infiltrations that present as Myelophthisic anemia. In addition to appropriate diagnosis, bone marrow studies are helpful grading prognosis and staging of certain bone marrow infiltrative diseases. Bone marrow aspiration and biopsy techniques are inexpensive but causes mild pain and discomfort to the patient. This can be overcome by adequate anesthesia and analgesia.

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