

SPECTRUM OF DISORDERS ON BONE MARROW EXAMINATION – PHYSICIAN’S PERSPECTIVE

1)Lakshmi priya Kalidindi - lakshmpriya.20593@gmail.com

2)Arun kumar Bathena - arun_kumar5233@yahoo.com

3)Mahendra kumar Kalappan - mahindran1985@gmail.com

4)Jagadeesan Mohanan - drjagadeesan@gmail.com

5)Gnanadeepan Thirugnanam - ttdeepu27@gmail.com

6)Yogalakshmi Eswaran - kiruba.yoga@gmail.com

ABSTRACT :

INTRODUCTION: Haematological disorders are one of the most common disorders encountered by physician ranging from anaemias to malignancies having wide range of presentations. Pancytopenia having various aetiologies poses a diagnostic challenge. Bone marrow aspiration and biopsy has a key role in diagnosis and treatment of haematological disorders and various systemic illnesses like pyrexia of unknown aetiology where the underlying aetiology is not obvious. The present study was undertaken to analyse the spectrum of bone marrow aspiration and biopsy findings in various haematological and systemic illnesses.

MATERIALS AND METHODS: This is a retrospective and prospective study. Fifty patients were included in whom bone marrow aspiration and biopsy was done for various disorders. Patients with bleeding disorders and patients whose diagnosis was confirmed by clinical profile and initiated on treatment were excluded from the study.

RESULTS: The common indications of bone marrow examination in our study are Pancytopenia followed by anemia, leukemia and multiple myeloma.

Out of 50 cases, 2 cases were excluded from analysis due to inadequate sample. Of the remaining 48 cases – 4 were normocellular (8.4%), 22 cases (45.8%) are of hematological malignancies, 20 (41.7%) were non-malignant hematological disorders, 2 cases (4%) are of non-hematologic disorder.

Among 50 cases 33 (66%) cases were diagnosed on basis of clinical profile and bonemarrow examination was just to strengthen the diagnosis, 15 (30%) cases were diagnosed only on bone marrow examination and the remaining 2 (4%) cases required further work-up.

CONCLUSION: Bone marrow aspiration is an invasive and useful technique which can diagnose and confirm many haematological and non-hematologic diseases accurately. The clinical profile alone cannot be sufficient at times for diagnosis of certain disorders and leaves physicians in a dilemma. This study emphasizes the need for Bone marrow examination in guiding the physicians for early detection of various underlying conditions and thereby modifying the outcome of disease.

Keywords : Bonemarrow, Hematology, Pancytopenia

INTRODUCTION

Hematological disorders are very common in all age groups. The commonest disorders of blood being anemia worldwide especially in developing countries (1). Bone marrow examination being invasive and indispensable procedure to find out the accurate diagnosis, it also gives enlightenment for unexplained cytopenias and leukemia (2). Megaloblastic anaemia and acute myeloid leukemia are the most commonly encountered non-malignant and malignant conditions respectively (3, 4). Bone marrow cellularity, architecture and the stages of maturation of different type of blood cells can be analysed by bone marrow examination (5). Hemo-parasites, infiltrates and storage diseases can be diagnosed by examining bone marrow (6). Though bone marrow examination is invasive it is associated with minimal or no risk and can be done safely in thrombocytopenia (2). Bone marrow examination is confirmatory even though the diagnosis is done by clinical examination. So, the present study was undertaken to analyse the spectrum of bone marrow aspiration and biopsy findings in various haematological and systemic illnesses.

MATERIALS AND METHODS

This is a retrospective and prospective study. Fifty patients were included in whom bone marrow aspiration and biopsy was done for various disorders. Patients with bleeding disorders and patients whose diagnosis was confirmed by clinical profile and initiated on treatment were excluded from the study. A thorough physical and systemic examination was conducted and all the clinical data was collected on the study proforma. Data was expressed in percentage.

RESULTS

The common indications of bone marrow examination in our study are Pancytopenia followed by anemia, leukemia and multiple myeloma. The other indications were bicytopenia, thrombocytopenia, polycythemia, pancytosis, pyrexia of unknown origin.

Out of 50 cases, 2 cases were excluded from analysis due to inconclusive report, either due to improper technique or inadequate sampling. Of the remaining 48 cases – 4 were normal (8.4%), 22 cases (45.8%) are of hematological malignancies, 20 (41.7%) were non-malignant hematological disorders and 2 cases (4%) are of non-hematologic disorder.

Among hematological malignancies multiple myeloma is found to be most common which is present in 5 cases (22.7%), followed by acute myeloid leukemia in 5 (22.7%), Chronic lymphocytic leukemia in 3 (13.6%), Plasmacytoma in 2 (9%), Polycythemia vera in 2 (9%), Myelodysplastic syndromes in 2 (9%), Chronic myeloid leukemia in 2 (9%) and essential thrombocythemia in 1(4.5%).

Out of 20 non-malignant hematological disorders; 13 cases are of erythroid hyperplasia (65%), 4 are of hypoplastic marrow (20%), 2 were Megaloblastic anemia (10%), one case (5%) is of Idiopathic thrombocytopenic purpura.

A total of 13 bone marrow aspirations showed erythroid hyperplasia in a normocellular or hypercellular marrow which was the commonest finding in our study. The bone marrow aspiration of these cases showed normoblastic erythropoiesis in 42.8%, dimorphic in 21.4%, megaloblastic in 21.4%, micronormoblast in 14.4%.

16 cases in the study were found to have pancytopenia out of which one remain undiagnosed. Commonest cause of pancytopenia was acute myeloid leukemia followed by multiple myeloma and hypoplastic anemia (Table – 2). The other causes were Megaloblastic anemia and Myelodysplastic syndromes.

One case is diagnosed to be mixed connective tissue disease with Monoclonal Gammopathy of Undetermined significance (MGUS) based on clinical findings, ANA profile and bone marrow examination. Clinically muscle tenderness with skin thickening, Raynaud's phenomenon was present. Anti U1 RNP antibodies were positive. Serum protein electrophoresis showed M spike. Bone marrow examination showed hypocellular marrow with evidence of plasmacytosis (plasma cells – 9%).

One case was evaluated for Pyrexia of unknown origin which is diagnosed to be Kikuchi disease with brucellosis. Bone marrow examination in this case was found to be normocellular and required further work up. Axillary lymph node biopsy was done suggestive of kikuchi disease and Ig M for brucella was positive.

Among 50 cases 33 (66%) cases were diagnosed on basis of clinical profile and bonemarrow examination was just to strengthen the diagnosis, 15 (30%) cases were diagnosed based on bonemarrow examination and the remaining 2 (4%) cases required further work-up. (fig-1)

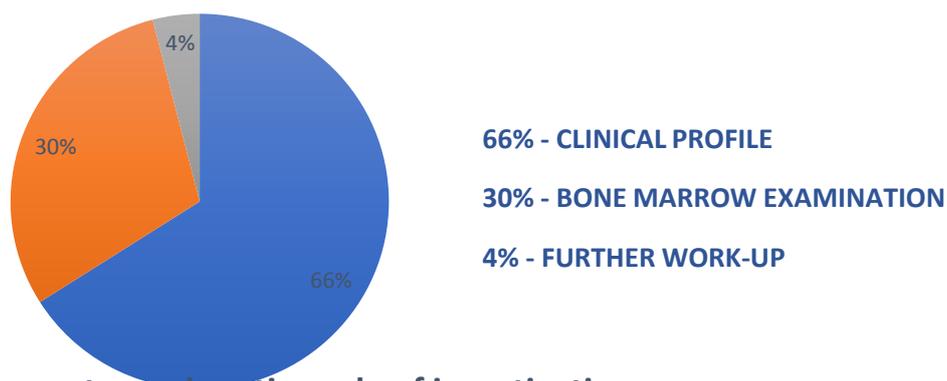
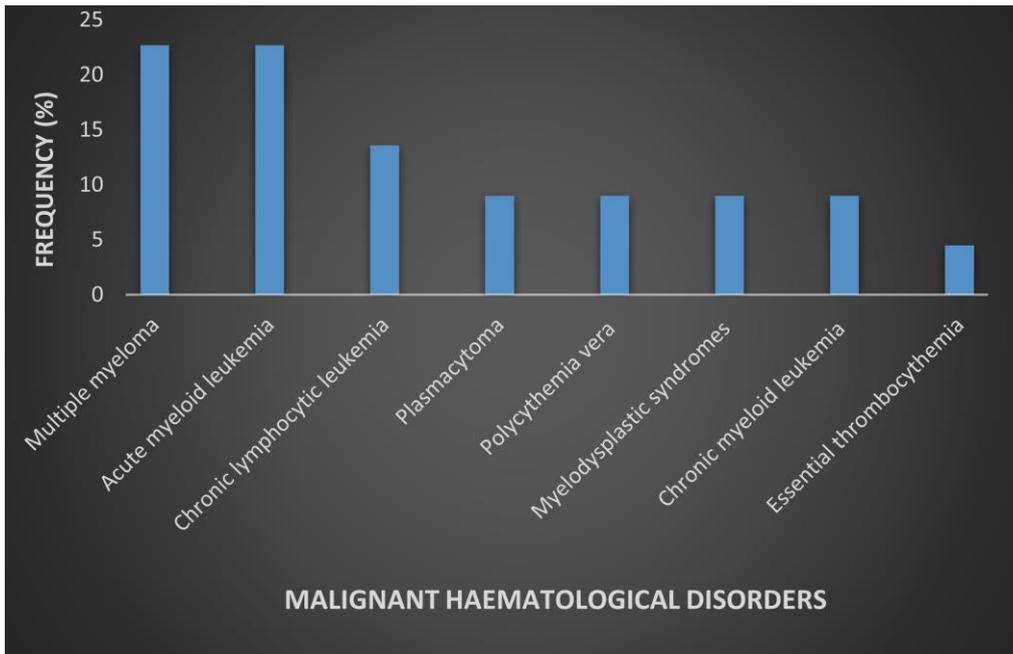
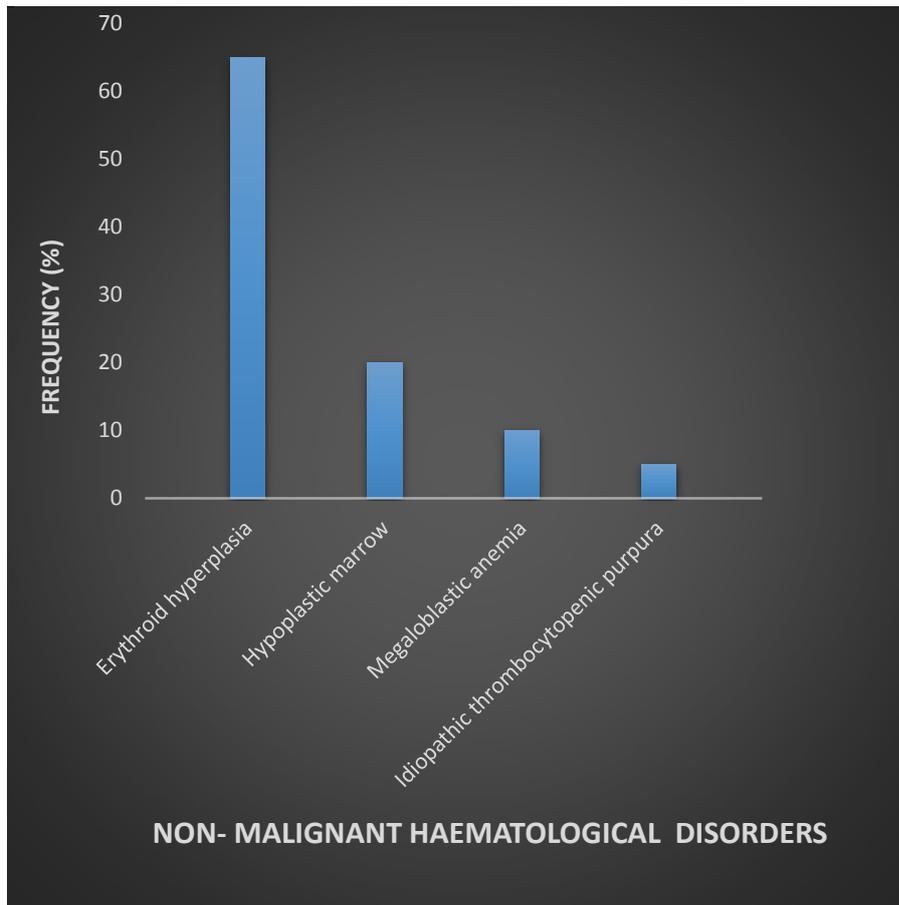


Fig.1 : Percentages denoting role of investigations

Frequency of malignant hematological disorders based on bone marrow aspiration and biopsy



Frequency of non-malignant hematological disorders based on bone marrow aspiration and biopsy



BONE MARROW EXAMINATION FINDINGS

DIAGNOSIS	NUMBER OF CASES (%)	NO: OF CASES WITH FINDINGS SAME AS CLINICAL DIAGNOSIS	NO: OF CASES DIAGNOSED ONLY ON BONE MARROW
Erythroid hyperplasia	13 (26)	8	5
Multiple myeloma	5 (10)	4	1
Acute myeloid leukemia	5 (10)	3	2
Hypoplastic marrow	4 (8)	2	2
Normocellular marrow	4 (8)	4	
Chronic lymphocytic leukemia	3 (6)	2	1
Polycythemia vera	2 (4)	2	
Plasmacytoma	2 (4)	1	1
Megaloblastic anemia	2 (4)	2	
Myelodysplastic syndromes	2 (4)	1	1
Chronic myeloid leukemia	2 (4)	1	1
Idiopathic thrombocytopenic purpura	1 (2)	1	
Essential thrombocythemia	1 (2)	1	
MGUS with MCTD	1 (2)	1	
Pyrexia of unknown origin	1 (2)		1
Inconclusive	2 (4)		

Total	50 (100)	33	15
--------------	-----------------	-----------	-----------

CAUSES OF PANCYTOPENIA BASED ON BONE MARROW ASPIRATION AND BIOPSY

DIAGNOSIS	TOTAL NUMBER OF CASES	PERCENTAGE (%)
Acute myeloid leukemia	5	31.3
Multiple myeloma	3	18.7
Hypoplastic anemia	3	18.7
Megaloblastic anemia	2	12.5
Myelodysplastic syndromes	2	12.5
Undiagnosed	1	6.3
Total	16	100

DISCUSSION

In this study, out of 48 cases, 4 were normal (8.4%), 22 cases (45.8%) are of hematological malignancies, 21 (43.7%) were non-malignant hematological disorders and 2 cases (2%) are of non-hematologic disorders. Past studies have shown similar findings of around 40.79% of non-malignant conditions and malignant conditions were 49.34% (7).

The common indications of bone marrow examination in our study are Pancytopenia followed by anemia, leukemia and multiple myeloma. Ahmad SQ et.al, reported that pancytopenia was the commonest indication for bone marrow examination (8). Our study also showed similar findings in which 33.3% subjects had pancytopenia findings. Megaloblastic anaemia accounted for 12.5% of subjects in pancytopenia category. Memon S et.al, also noticed that 13.04% of the subjects had megaloblastic anaemia (9).

Among hematological malignancies multiple myeloma and acute myeloid leukemia were found to be most common which are present in 5 cases each (22.7%). Hematological malignancies like multiple myeloma requires serum protein electrophoresis for diagnosis in addition to bonemarrow examination. Our study is in accordance with the study done by

Kibria SG et.al, wherein they have found that acute myeloid leukemia occupies the top position (2). We have observed chronic lymphocytic leukemia in 3 cases (13.6%), plasmacytoma in 2 subjects (9%), Polycythemia vera in 2 cases (9%), Myelodysplastic syndromes in 2 (9%), Chronic myeloid leukemia in 2 (9%) and essential thrombocythemia in 1 subject (4.5%).

A total of 13 bone marrow aspirations showed erythroid hyperplasia, normocellular or hypercellular marrow which was the commonest finding in our study. The bone marrow aspiration of these cases showed normoblastic erythropoiesis in 42.8%, dimorphic in 21.4%, megaloblastic in 21.4%, micronormoblast in 14.4%.

So, it was observed that among overall 48 subjects around 27% had erythroid hyperplasia. Pudasaini S et.al, had reported similar findings that erythroid hyperplasia was noticed in 21% of cases (10). Hypoplastic marrow was seen in 8% of total cases and 19% of cases in non-malignant category. According to Nigam RK et.al, around 9% of the cases had hypoplastic marrow which is in accordance with our study.

Idiopathic thrombocytopenic purpura is seen in 2% of our overall cases, where in past studies reported higher percentage of cases (12). Routine bonemarrow examination in patients with Idiopathic thrombocytopenic purpura is not necessary, provided a thorough clinical assessment is done and peripheral blood smear examination reveals no abnormalities. Around 4% had megaloblastic anemia wherein Anita et.al, noticed megaloblastic anemia in only 2% of the cases (13). This minute variations in the overall percentage may be due to the variation in size, population and region of this study when compared to past studies.

Pyrexia of Unknown origin still remains a diagnostic challenge and bone marrow examination has a crucial role in its evaluation. Yield of diagnosis is increased if it is combined with other diagnostic modalities like fluorodeoxyglucose-positron emission tomography scan (FDG-PET), lymphnode biopsy.

CONCLUSION

Bone marrow aspiration is an invasive and useful technique which can diagnose and confirm many haematological and non-hematologic diseases accurately. The common findings of bone marrow examination in this study are Pancytopenia followed by anemia, leukemia and multiple myeloma. The clinical profile alone cannot be sufficient at times for diagnosis of certain disorders and leaves physicians in a dilemma.. This study emphasizes the need for Bone marrow examination in guiding the physicians for early detection of various underlying conditions and thereby modifying the outcome of disease.

References

1. Egesie OJ, Joseph DE, Egesie UG, Ewuga OJ. Epidemiology of anemia necessitating bone marrow aspiration cytology in Jos. Niger Med J. 2009;50:61-1

2. Kibria SG, Islam MDU, Chowdhury ASMJ et al. Prevalence Of Hematological Disorder: A Bone Marrow Study of 177 Cases In A Private Hospital At Faridpur. Faridpur Med. Coll. J. 2010;5:11-3.
3. Dapus DO, Damen JG. Diagnostic outcome of bone marrow aspiration in a new centre in Nigeria. Global Adv Res J Medicine and Med Sci 2012; 1:161-71.
4. Lowenberg B, Downing JR, Burnett A. Acute myeloid leukemia. New Eng J Med 1999; 341:1051-62.
5. Rahim F, Ahmad I, Islam S, Hussain M, Khattak TA, Bano Q. Spectrum of hematological disorders in children observed in 424 consecutive bone marrow aspirations/biopsies. Pak J Med Sci 2005; 21:433-6.
6. Bain BJ. Bone marrow aspiration. J Clin Pathol 2001; 54:657-63.
7. Chowdhury MR, Rashid MH, Begum A. Diagnostic role of bone marrow examination in detecting haematological and nonhaematological disorders. Medicine today. 2019 Feb 20;31(1):15-8.
8. Ahmad SQ, Khan OU, Zafar N. Utility of Bone Marrow Examination in a Secondary Care Hospital JRMC 2011;15:40-1
9. Memon S, Shaikh S, Nizamani MA. Etiological spectrum of pancytopenia based on bone marrow examination in children. J Coll Physicians Surg Pak. 2008 Mar 1;18(3):163-7.
10. Pudasaini S, Prasad KB, Rauniyar SK, Shrestha R, Gautam K, Pathak R, Koirala S, Manandhar U, Shrestha B. Interpretation of bone marrow aspiration in hematological disorder. Journal of Pathology of Nepal. 2012 Sep 25;2(4):309-12.
11. Nigam RK, Malik R, Kothari S, Gour D, Shrivastava A, Balani S, Ahirwar R, Jain R. Spectrum of diseases diagnosed by bone marrow examination in central india. Journal of evolution of medical and dental sciences. 2014 jan 13;3(2):326-38.
12. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone Marrow Examination in Cases of Pancytopenia. JIACM 2001;2:55-9
13. Anita Tahlan, Cherry Bansal, AnshuPalta, Sandeep Chauhan. "Spectrum and analysis of bone marrow findings in anemic cases". Indian J Med Science, 2008; 62(8):336-339.