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Bone Marrow Aspiration Cytology in Diagnosing Hematological Disorder in a Tertiary Care Center

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ABSTRACT

Introduction: Bone marrow aspiration is a safe, simple and minimally invasive procedure used for evaluation of hematological disorder. It is useful when diagnosis from the first line investigations are inconclusive.

Objectives: To compare the clinical findings and bone marrow aspiration cytology findings

Methodology: This is a prospective hospital based cross sectional study carried out in Birat Medical College. Simple random consecutive sampling was done in patients that underwent bone marrow aspiration from December15th 2021 to June 14th 2022.

Dry tap, patient under treatment and inadequate material were excluded from the study. After informed consent, BMA was done from the right or left posterior superior iliac crest using local anesthesia. Smeared slides were stained by Wright stain and was examined by two pathologists. Special stain was not done. Ethical clearance was taken from Institutional Review Committee (IRC). Data collected was then tabulated by using Microsoft Excel sheet and SPSS

Results: A total of 106 patients were included in this study with majority aged > 45 years (50.9%). The commonest indications for bone marrow aspiration was anemia under evaluation (35.9%) followed by pancytopenia under evaluation (22%). The most common diagnosis identified by bone marrow aspiration was mixed nutritional deficiency anemia (21.7%).In patients evaluated for pancytopenia six were diagnosed with hematological malignancy.

Conclusion: Nutritional deficiency anemia, commonly indicated for bone marrow aspiration, was the most common cause diagnosed by bone marrow aspiration. Bone marrow aspiration is important to arrive at diagnosis especially in patients with anemia and pancytopenia.

INTRODUCTION

Bone marrow is one of the largest body organ constituting 4.5% of total body weight.[1] It is principal site of hematopoiesis. There are numerous sites of hematopoiesis at birth but these become restricted to axial skeletons specially the anterior, posterior superior iliac crest and sternum. Bone marrow aspiration (BMA) is a safe and relatively simple minimal invasive procedure.[2] Posterior superior iliac crest is typically selected for sampling due patients comfort and safety.[3] Representative spongy bone marrow is obtained by BMA needle. It is an important tool for evaluation of hematological as well as non-hematological pathology. Spectrum of hematological disorder varies in developing as well as developed countries. Anemia is a common hematological disorder worldwide which can be diagnosed by few simple basic investigations like complete blood count, peripheral smear and biochemical tests like Iron profile, serum vitamin

levels. [2] However, sometimes due to unusual presentations, without BMA the diagnosis is usually not confirmatory. [4] Similarly, as pancytopenia is a tricky manifestation of multiple etiological factors, it may be useful to identify the etiology. [5] Patients with leukemia present with blast cell in peripheral blood smear, but sometimes they may present as aleukemic leukemia or subleukemic leukemia, thus BMA is required for diagnosis of these cases as well as for morphological classification of leukemia. Thus when diagnosis from the first line investigations and other biochemical and radiological tests are inconclusive, BMA cytology is useful.

In BMA particles are obtained for microscopic morphological evaluation, its cellularity and differential count. It is useful for staging, prognostication as well as therapeutic response in some disorders. [2] It is useful to evaluate and diagnose anemia, reactive marrow and malignancies along with focal lesions such as granulomatous as well as metastatic infiltration. [6] Not only cytology, material obtained from bone marrow aspiration can be used for ancillary tests such as immunophenotyping (flow cyotometry and immunocytochemistry), cytogenetics (karyotyping), microbiological culture and molecular assessment.[7]

Many studies have highlighted the importance of bone marrow aspiration to evaluate the etiology especially in patients with pancytopenia. [4,8–10] Few studies have measured the contribution of bone marrow to diagnosis and treatment especially in critically ill patients.[11,12] Few studies have studied the indications and diagnostic value of bone marrow aspiration.[13] Hence despite being highly informative, there are only sparse literature in this clinical settings on its indications and diagnostic utility. Thus this study was conducted to compare clinical findings and BMA cytology that ultimately helps in diagnosis for the better management of the patients

METHODOLOGY

This is a prospective hospital based cross sectional study carried out in the department of Pathology, Birat Medical College, Biratnagar, Nepal. Simple random sampling was done. Consecutive sampling was done where all patients that underwent bone marrow aspiration from December15th 2021 to June 14th 2022 were included in the study.

Exclusion criteria: Patients who were already diagnosed and are under treatment, patients with dry tap and inadequate material were excluded from the study. Patient's detail history as well as clinical findings were documented. Patients were informed about the procedure and written consent was taken. Under aseptic condition and using local anesthesia (2% lignocaine), BMA was done from the right or left posterior superior iliac crest in lateral or prone position. Material aspirated was smeared in two to three glass slides and residual material was kept in EDTA vial. Prepared slides were stained by Wright stain and was examined by two pathologists. Ethical clearance was taken from Institutional Review Committee (IRC) of Birat Medical College. Data collected was then tabulated by using Microsoft Excel sheet and SPSS.

RESULT

A total of 106 patients were included in this study aged between 1 to 85 years with mean age of 48yrs. The majority of the patients were aged > 45 years (50.9%). Among these 63 (59.4%) were female and 43 (0.6%) were male. (Table 1)

Table 1: Age and sex distribution of bone marrow aspiration cases.

Age group(yrs)	Male	Female	Total N (%)
<15	4	3	7(6.6)
15-30	6	4	11(10.4)
31-45	10	24	34(32.1)
>45	23	31	54(50.9)
Total	43	63	106(100%)

The commonest indications for bone marrow aspiration was anemia under evaluation (35.9%) followed by pancytopenia under evaluation (22%). Other indications of bone marrow aspiration were fever under evaluation, suspected leukemia, lymphoma, eosinophilia? cause etc. (Table2)

Table 2: Indications of bone marrow aspiration

Indications of bone marrow		Number (%)
Anemia under evaluation		38(35.9)
Pancytopenia under evaluation		22(20.8)
Fever under evaluation		10(9.4)
Hematological malignancy	Suspected Leukemia	9 (8.5)
	Suspected lymphoma	4(3.8)
Suspected mixed nutritional deficiency anemia		5(4.7)
Suspected ITP		6(5.7)
Eosinophilia? Cause		6(5.7)
Suspected hemolytic anemia		3(2.8)
Unexplained splenomegaly		1(0.9)
Suspected metastasis		2(1.8)
Total		106 (100)

Most common disease diagnosed by bone marrow aspiration was nutritional deficiency anemia majority of which were of mixed type (21.7%) followed by micronormoblastic (16.9%) and megaloblastic anemia (10.4%). (Table 3)

Table 3: Disease diagnosed by bone marrow aspiration cytology.

Bone marrow diagnosis		Number (%)
Nutritional deficiency anemia	Micronormoblastic	18(16.9)
	Megaloblastic	11(10.4)
	Mixed	23 (21.7)
Hypoplastic marrow	Hypoplastic marrow	4(3.8)

Hematological malignancy	ALL	2(1.9)
	CLL	1(0.9)
	AML	6(5.7)
	CML	4(3.8)
	Plasma cell neoplasm	2(1.9)
Megakaryocytic hyperplasia	?ITPs	6(5.7)
	? CML	1(0.9)
Others	Eosinophilia	6(5.7)
	Erythroid hyperplasia	6(5.7)
	? MDS	1(0.9)
	Hemophagocytic syndrome	1(0.9)
	Metastasis	1(0.9)
Infection	Visceral Leshmaniasis	2(1.9)
Normal	Normal	11(10.4)
Total		106(100)

15 cases were diagnosed with hematological malignancy, most common being AML. One patient had M6 variant of AML (figure 1) which was confirmed on flowcytometry.

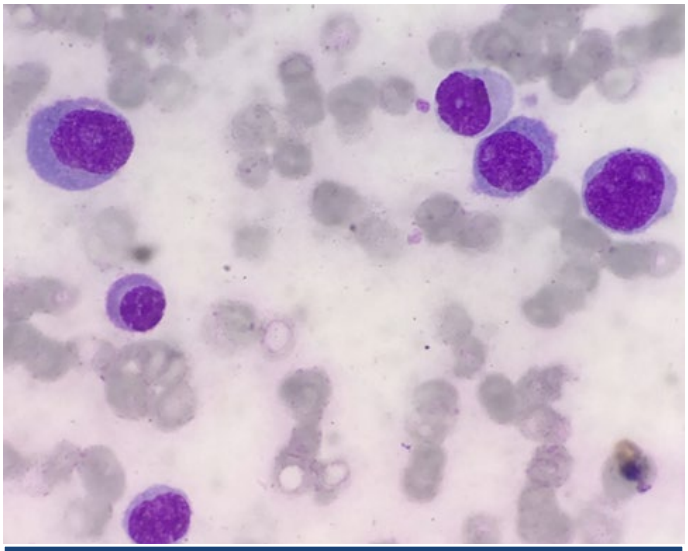

Fig 1: Erythroblasts in bone marrow in patient with AML. Wright stain (100X)

Infective pathology had normocellular marrow. Clusters of LD bodies were seen in both the cases. (Figure 2). One case of hemophagocytic syndrome was found. One case was suspected to have MDS as dysplasia was seen in >10% of erythroid as well as myeloid series. This patient was recommended for vitamin B 12, folic acid assay as well as cytogenetics analysis. One patient had metastatic small round blue cell tumor in bone marrow (Figure 3)

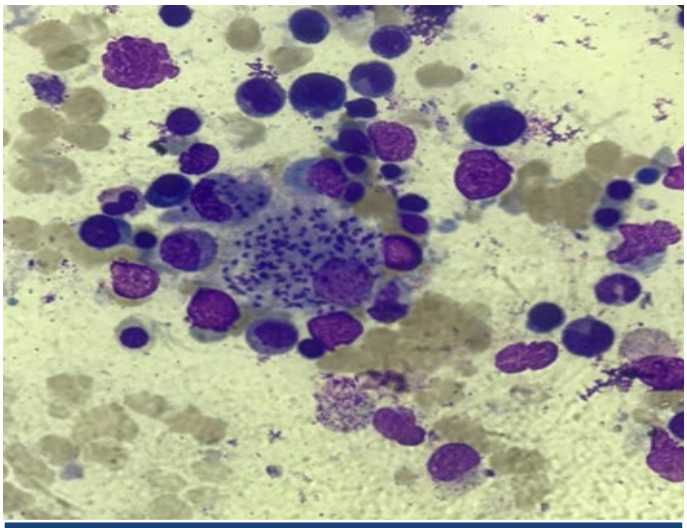

Fig 2: LD bodies seen in bone marrow aspiration. (Wright stain 100X)

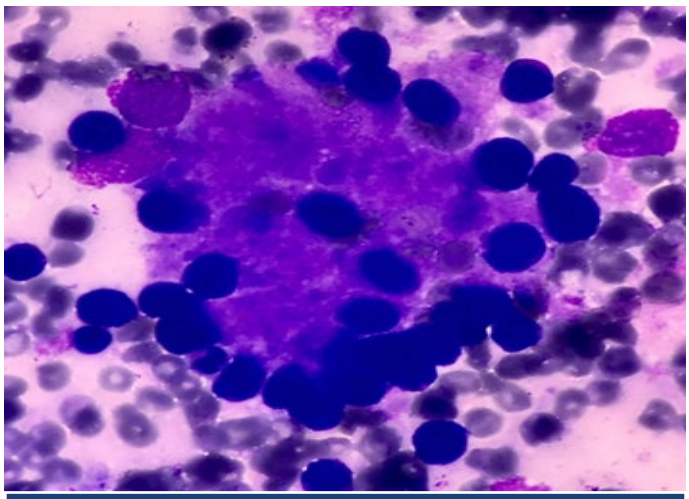

Fig 3: Metastatic small round blue cell tumor (Wright stain 100X)

Table 4: Comparison of bone marrow aspiration diagnosis with clinical findings.

Clinical Findings	Bone marrow diagnosis
Anemia under evaluation (38)	Micronormoblastic anemia (16)
	Mixed nutritional deficiency anemia (13)
	Megaloblastic (6)
	Bone marrow plasmacytosis (2)
	Erythroid hyperplasia (1)

Pancytopenia under evaluation (22)	Mixed nutritional deficiency anemia (6)
	Megaloblastic anemia (5)
	AML (4)
	Hypoplastic marrow (3)
	ALL (2)
	? MDS (1)
	Hemophagocytic syndrome (1)
Fever under evaluation (10)	Normal marrow (8)
	Visceral leshmaniasis (2)
Suspected Leukemia (9)	CML (4)
	AML (2)
	Hypoplastic marrow (1)
	Megakaryocytic hyperplasia (1)
	Normal (1)
Suspected mixed nutritional deficiency anemia(5)	Mixed nutritional deficiency anemia (4)
	Micronormoblastic anemia (1)
Suspected ITP (6)	Megakaryocytic hyperplasia? ITP
Suspected lymphoma (4)	Micronormoblastic (1)
	Normal (2)
	CLL (1)
Eosinophilia ? cause (6)	Bone marrow eosinophilia
Suspected hemolytic anemia (3)	Erythroid hyperplasia (3)
Unexplained splenomegaly (1)	Erythroid hyperplasia (1)
Suspected metastasis (2)	Metastatic small round blue cell tumor (1)
	Erythroid hyperplasia (1)

Most of the cases evaluated for anemia under evaluation showed anemia (92.1 %). However two cases showed bone marrow plasmacytosis with differential of multiple myeloma. Bone marrow aspirationwas helpful in patients evaluated for pancytopenia. In six patients, pancytopenia was caused due to hematological malignancy. Four cases were diagnosed as AML and two as ALL. One patient was suspected to have Myelodysplastic syndrome.

Only two cases of visceral Leshmaniasis was seen in patients evaluated for fever. Rest showed normal active marrow. In patients with clinically suspected leukemia, six patients were diagnosed with hematological malignancy by BMA while one patient each had normal active marrow and hypoplastic marrow respectively.

DISCUSSION

Bone marrow is the principal site of hematopoiesis. The hematopoetic bone marrow is organized around the vasculature of bone cavity where its main function is to supply mature circulating hematopoetic cells continuously. It responds according to the physiological and pathological demands. As there are myriads of hematological disorders aspiration cytology of bone marrow helps in diagnosing many different disease conditions.

In our study BMA of 106 patients aged between one to 85 years were evaluated. Most of the patients were aged more than 45 years (50.9%). In contrary to this other studies had undergone BMA in lesser age group, Pudasaini et al (31-45years) and Niazi et al (1-30years).[4,8] This variation in study population shows that BMA can be used for diagnostic utility irrespective of any age.

The commonest indication of bone marrow aspiration was anemia. Similarly in the study done by Dapus et al, Tripathy et al, Marwah et al and Thiyagarajan et al anemia was the commonest indications. [9–12] This shows anemia to be common presentation in any disease. In contrary, pancytopenia was the most commonest indication in the study done by Pudasaini et al and Bashawri et al.[4,13] This could be due to difference in predominant age group evaluated. Around 20.8% of patients with clinical indication of pancytopenia underwent BMA.

Anemia was the most common disease diagnosed by BMA (49.1%) , higher than (22.7%) in study by Parajuli and Tuladhar. [14] Among these mixed nutritional deficiency anemia was the most common diagnosis made by bone marrow aspiration in patients who presented clinically with pancytopenia. Studies by Niazi et al, Jha et al, Pudasaini et al showed megaloblastic anemia as the commonest BMA diagnosis. [4,15] Study by Marwah et al and Gayathri et al also showed pancytopenia as the commonest presentation in patients with mixed nutritional deficiency anemia. [11,16] These findings suggests increasing incidence of nutritional deficiency anemia in our country and its varying presentation thus BMA could be used effectively as one of the method to determine the cause of anemia. Microcytic hypochromic anemia mainly iron deficiency anemia is the most common nutritional deficiency anemia worldwide. [7] However comparatively lesser patients were diagnosed in bone marrow because most of the cases can simply be diagnosed on peripheral blood and biochemical findings.

In Fifteen patients (14.2%) hematological malignancy was diagnosed by BMA. Similar findings were seen in study by Ranabhat et al, Pudasaini et al.[4,7] Acute Myeloid leukemia was the most commonly diagnosed hematological malignancy. Other studies by Egessie et al, Kibria et al Gayathri et al and Jha et al showed similar findings. [2,15–17] Out of 15 cases diagnosed as hematological malignancy by BMA , six patients presented with pancytopenia. Similar results were seen in study done by Marwah et al.[11] This showed the importance of BMA to diagnose hematological malignancy in patients who present with pancytopenia and where the cause of pancytopenia cannot be identified clinically and other investigations. One patient (0.9%) with pancytopenia was suspected to have Myelodysplastic syndrome with recommendations of other tests which could not be followed. Two patients (1.9%) presenting with anemia was diagnosed to have plasma cell neoplasm in BMA. Other studies showed plasma cell neoplasm in BMA in about 0.9-4.1%. [9,14,20,21] Out of nine suspected leukemia, two patients were diagnosed as acute leukemia, where on bone marrow aspiration morphologic classification of AML M2 and AML M6

was made with further recommendation of flowcytometry. This highlights the importance of BMA not only in diagnosis but for the morphological sub-classification as well.

Hypoplastic marrow was seen in 4(3.8%) cases, most of which presented with pancytopenia. Similar findings were seen in study by Pudasaini et al.[4] In contrary more number of patients were diagnosed to have hypoplastic marrow in study done by Gayatri and Rao, Jha et al Marwah et la (19%, 29% and 14% respectively). [11,15,16] The difference could be due to the additional bone marrow biopsy along with BMA done in these study which is more sensitive to diagnose hypoplastic as well as aplastic marrow. Diagnosis in our study was however based only in BMA and BM biopsy was not done. All patients with dry tap were excluded from the study. Hence it highlights the importance of requirement of BM biopsy simultaneously to diagnose hypoplastic and aplastic marrow.

Six patients (5.7%) with suspected ITP showed megakaryocytic hyperplasia, similar to study done by Pudasaini et al.[4] Out of 10 patient evaluated for fever, two had visceral Leishmaniasis while other two showed normal marrow. Similar findings was seen in study by Santra et al and Pudasaini et al. [4,18] Higher incidence (14%) was seen in study by Marwah et al. [11]

CONCLUSION

Commonest indication for bone marrow aspiration is for evaluation of anemia and pancytopenia. Nutritional deficiency anemia was the most common cause of anemia diagnosed by bone marrow aspiration. Nutritional deficiency anemia was also seen along with hematological malignancy in patients who presented with pancytopenia. Hence Bone marrow aspiration is important to arrive at diagnosis especially in patients with anemia and pancytopenia

RECOMMENDATION

Bone marrow aspiration is a very simple, minimally invasive procedure that can be used as a diagnostic tool in many patients where first line investigations like hematological and biochemical findings are inconclusive. Hence we should equip the hospital, train the staffs accordingly.

LIMITATION OF STUDY

Bone marrow biopsy would be an additional investigation to arrive in diagnosis especially in cases of dry tap and acute leukemias. In our study Bone marrow biopsy was not done. Flowcytometry was not done which limited us to further categorize and confirm leukemia. Special stains in bone marrow aspiration was not done which limited us to comment about the iron status and also to categorize leukemia.

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CONFLICT OF INTEREST None

FINANCIAL DISCLOSURES None

REFERENCES

1. 1.Gohil M, Rathod K. Bone Marrow Aspiration Cytology Study in a Tertiary Care Center, Gujarat, India. 2018;5(10). DOI: 10.17354/ijss/2018/3
2. Egesie OJ, Joseph DE, Egesie UG, Ewuga OJ. Epidemiology of Anaemia Necesitating Bone Marrow Aspiration Cytology in Jos. Niger Med J. 2009;50(3):61-3. DOI:10.4314/nmj.v50i3.54437
3. Rindy LJ, Chambers AR. Bone Marrow Aspiration And Biopsy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 May 31]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK559232/
4. Pudasaini S, Prasad KBR, Rauniyar SK, Shrestha R, Gautam K, Pathak R, et al. Interpretation of bone marrow aspiration in hematological disorder. J Pathol Nepal. 2012 Sep 25;2(4):309-12. DOI: 10.3126/jpn.v2i4.6885
5. Chiravuri S, De Jesus O. Pancytopenia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 May 24]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK563146/
6. Kaur M, Singh Rana AP, Kapoor S, Puri A. Diagnostic Value of Bone Marrow Aspiration and Biopsy in Routine Hematology Practice. J Clin Diagn Res JCDR. 2014 Aug;8(8):FC13-6. DOI:10.7860/JCDR/2014/9823.4760 PMID:25302200 PMCID:PMC4190721
7. Ranabhat S, Maharjan S, Tiwari M, Bhandari A, Osti B. Bone marrow aspiration cytology in the diagnosis of hematologic and non-hematologic diseases in a multi-specialty hospital in Nepal. Int J Res Med Sci. 2017 Mar;5(3):922-6. DOI: 10.18203/2320-6012.ijrms20170637
8. Vijay N, Ramana P. Diagnostic utility of bone marrow aspiration in pancytopenia. IAIM. 2018;5(9):1-6. ISSN: 2394-0034 (O)
9. Gayathri BN, Rao KS. Pancytopenia: a clinico hematological study. J Lab Physicians. 2011 Jan;3(1):15-20. DOI: 10.4103/0974-2727.78555 PMID:21701657 PMCID:PMC3118050
10. Pathak R, Jha A, Sayami G. Evaluation of bone marrow in patients with pancytopenia. J Pathol Nepal. 2012 Sep 28;2. DOI: 10.3126/jpn.v2i4.6875

11. Calvet L, Pereira B, Sapin AF, Mareynat G, Lautrette A, Souweine B. Contribution to diagnosis and treatment of bone marrow aspirate results in critically ill patients undergoing bone marrow aspiration: a retrospective study of 193 consecutive patients. J Intensive Care. 2017 Dec 4;5(1):67.
DOI: 10.1186/s40560-017-0263-7
PMID:29225888 PMCID:PMC5715543

12. Thiolliere F, Serre-Sapin AF, Reignier J, Benedit M, Constantin JM, Lebert C, et al. Epidemiology and outcome of thrombocytopenic patients in the intensive care unit: results of a prospective multicenter study. Intensive Care Med. 2013 Aug;39(8):1460-8.
DOI: 10.1007/s00134-013-2963-3
PMID:23740274

13. Bashawri LA. Bone marrow examination. Indications and diagnostic value. Saudi Med J. 2002 Feb;23(2):191-6. ISSN: 0379-5284

14. Niazi M, Raziq F i. The incidence of underlying Pathology in Pancytopenia - An experience of 89 cases. J Postgrad Med Inst. 2004 Sep;18(1). ISSN: 1811-9387

15. Dapus DO, James D. Diagnostic Outcome of bone marrow aspiration in a new centre in Nigeria. Glob Adv Res J Med Med Sci. 2012 Aug;1(7):166-71. ISSN: 2315-5159

16. Tripathy S, Dudani S. Comparative Evaluation of Simultaneous Bone Marrow Aspiration and Trephine Biopsy - Experience From Routine Hematology Practice. In 2013 [cited 2023 Jan 5]. Available from: https://www.semanticscholar.org/paper/Comparative-Evaluation-of-Simultaneous-Bone-Marrow-Tripathy-Dudani/fbf8bef418f11d1da45a4a4637b6a0c076dc3247

17. Marwah N, Bhutani N, Sunita Singh, Kalra R, Gupta M, Sen R. The spectrum of haematological disorders from bone marrow aspiration cytology in a tertiary care centre. Int J Curr Res. 2017 Jan;9(01):44938-41. ISSN: 0975-833X

18. Thiyagarajan P, Suresh TN, Anjanappa R, Kumar MLH. Bone-marrow spectrum in a tertiary care hospital: Clinical indications, peripheral smear correlation and diagnostic value. Med J Dr Patil Univ. 2015 Jul 1;8(4):490.
DOI: 10.4103/0975-2870.160793

19. Parajuli S, Tuladhar A. Correlation of bone marrow aspiration and biopsy findings in diagnosing hematological disorders- a study of 89 cases. J Pathol Nepal. 2014 Apr 25;4(7):534-8.
DOI: 10.3126/jpn.v4i7.10294

20. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone Marrow Examination in Cases of Pancytopenia. J Nepal Med Assoc. 2008 Jan 1;47(169).
DOI: 10.31729/jnma.209

21. Kibria SG, Islam MDU, Chowdhury A, Ali MY, Haque MR, Mustanzid SM, 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(1):11-3.
DOI: 10.3329/fmcj.v5i1.6806

22. Santra G, Das BK. A cross-sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre. Singapore Med J. 2010 Oct;51(10):806-12.
PMID: 21103817