Role of bone marrow aspiration in hematological disorders

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ABSTRACT

Background

Bone marrow aspiration is a safe procedure with a high degree of accuracy in the diagnosis of hematological disorders. This study was done to analyze the causes, spectrum of hematological disorders and interpret the bone marrow findings.

Method

This was a retrospective study of bone marrow aspiration (BMA) and biopsies done on 94 patients who were referred for bone marrow examination to the Department of Pathology of Grande International Hospital in the last 5 years. Cases were analyzed in detail regarding the clinical examination and other investigations.

Result

BMA from 94 patients were analyzed. 63 cases were male. The age of the patient ranged from 8 months to 85 years. The highest number of cases (44 cases, 46.08%) were in the age group of >45 years. PUO (42 cases, 44.68%) followed by pancytopenia (13 cases,13.82%) was the most common indication for BMA. Megaloblastic anemia (3 cases, 23.07%) and aplastic anemia (3 cases, 23.07%) was the most common cause of pancytopenia. Erythroid hyperplasia (23 cases, 24.46%) was the most common finding in BMA. Multiple myeloma (6 cases, 6.38%) followed by Acute Leukemia (5 cases, 5.31%) was the most common malignancy with AML (3 cases, 60%) more than ALL (2 cases, 40%).

Conclusion

Although bone marrow examination is an invasive procedure this is well tolerated by patients. The examination helps in many cases to arrive at a final diagnosis within a short period.

Keywords: **Bone marrow aspiration (BMA), Pyrexia of unknown origin (PUO), Pancytopenia, Megaloblastic Anemia, Leukemia**

Introduction

Bone marrow aspiration is performed primarily for morphological evaluation, although they can also be used for immunophenotypic, cytogenetic, molecular genetics, and other specialized studies[1]. It can be performed both in the inpatient and outpatient settings for the diagnosis of a multitude of hematologic disorders. It has a high degree of accuracy with a low complication rate[2].

Clinical history, complete blood count, peripheral blood smear, and other laboratory investigations are required before bone marrow examination[3]. Bone marrow aspiration and biopsy are complementary to each other[4]. Nutritional

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Received: 8 December 2021
Accepted: 21 December 2022

anemias, acute leukemias, myelodysplasia, myeloma, and parasitic infestations can all be diagnosed with bone marrow aspiration (BMA) only. However, granulomatous diseases, myelofibrosis, bone marrow secondaries, lymphoma infiltration, storage disorders, marrow aplasia, and myeloproliferative neoplasm are better illustrated in trephine biopsy. Individual cell morphology can be assessed by bone marrow aspiration. The biopsy is important in determining the architectural pattern and distribution[5,6].

This study was carried out to find out the causes of hematological disorders, their spectrum, and interpret the BMA findings.

Material and Methods

This was a retrospective study done in the Department of Pathology of Grande International Hospital. A total of 94 cases that were diagnosed in the past five years were included in this study. BMA and biopsy reports of the patients were retrieved from the record file in the department. Peripheral Blood Smear(PBS) along with necessary hematological and clinical parameters were also noted from the record file.

The procedure was done under local anesthesia (Injection of 2% xylocaine). The posterior superior iliac spine (PSIS) was the most common site used for the procedure followed by the anterior superior iliac spine (ASIS). For aspiration, we used Salah 16 G needle and for biopsy, we used Jamshidi needle. Aspirate slides were checked macroscopically for the presence of particles and a 2 cm biopsy was considered adequate on gross examination.

Giemsa stained slides were examined in the available cases for bone marrow aspirate and Hematoxylin and Eosin-stained (H&E) slides were examined for biopsy. Aspirates of inadequate material or dry tap were excluded from the study. Then data were manually collected and subsequently analyzed.

Results

A total number of 94 patients were included in this study aged 8 months to 85years. 63 (67.02%) were males and 31 (32.97%) were females with (M:F= 2.03:1). The maximum number of patients (44 cases, 46.08%) with hematological disorders who underwent BMA were in the age group of>45 years. Table 1 shows the age distribution of the patients.

Table 1: Age distribution of the patients

Age groups	Male (n)	Female (n)	No of cases (%)
<15	16	8	24(25.53%)
15-30	8	9	17(18.08%)
31-45	5	4	9(9.57%)
>45	34	10	44(46.80%)
Total	63	31	94(100%)

The most common indication for bone marrow aspiration was pyrexia of unknown origin (42 cases, 44.68%), pancytopenia (13 cases,13.82%) followed by anemia (10 cases, 10.63%). These findings are illustrated in table 2.

Table 2: Indications of BMA

Clinical diagnosis	No of cases (%)
PUO	42(44.68%)
Pancytopenia	13(13.82%)
Anemia	10(10.63%)
Multiple myeloma	7(7.44%)
Lymphoma	7(7.44%)
RCC	2(2.12%)
CKD	2(2.12%)
Eosinophilia	2(2.12%)
Bicytopenia	1(1.06%)
Thrombocytopenia	1(1.06%)
Leukemia	1(1.06%)
Leukopenia	1(1.06%)
Drug reaction with Steven Johnson Syndrome (SJS)	1(1.06%)
Polycythemia vera	1(1.06%)
Generalized lymphadenopathy	1(1.06%)
Infectious mononucleosis	1(1.06%)
Generalized body weakness	1(1.06%)
Total	**94(100%)**

Among PUO, bone marrow findings showed (14 cases, 33.33%) normocellular marrow, (7 cases, 16.66%) erythroid hyperplasia, (7 cases, 16.66%) reactive plasmacytosis, (5 cases, 11.9%) myeloid hyperplasia, (4 cases, 9.52%) eosinophilia, (2 cases, 4.76%) MDS, (1 case, 2.38%) AML-M3, (1 case, 2.38%) myeloproliferative neoplasm-primary myelofibrosis and (1 case, 2.38%) plasma cell neoplasm-multiple myeloma. These findings are illustrated in Table 3.

Table 3: BMA findings in Pyrexia of Unknown Origin (PUO)

BMA findings	No of cases (%)
Normocellular marrow	14 (33.33%)
Erythroid hyperplasia	7(16.66%)
Reactive plasmacytosis	7(16.66%)
Myeloid hyperplasia	5(11.9%)
Eosinophilia	4(9.52%)
Myelodysplastic syndrome (MDS)	2(4.76%)
Acute promyelocytic leukemia	1(2.38%)
Myeloproliferative neoplasm-Primary myelofibrosis	1(2.38%)
Plasma cell neoplasm- multiple myeloma	1(2.38%)
Total	**42 (100%)**

Among pancytopenia, bone marrow findings revealed megaloblastic anemia (3 cases, 23.07%), aplastic anemia (3 cases, 23.07%), myeloid hyperplasia (2 cases, 15.38%), reactive plasmacytosis (2 cases, 15.38%), primary myelofibrosis (1 case, 7.69%), AML (1 case, 7.69%) and erythroid hyperplasia (1 case, 7.69%). These findings are illustrated in Table 4.

Table 4: Causes of Pancytopenia in BMA

BMA Findings	No of cases (%)
Megaloblastic anemia	3(23.07%)
Aplastic anemia	3(23.07%)
Myeloid hyperplasia	2(15.38%)
Reactive plasmacytosis	2(15.38%)
Acute Myelogenous Leukemia(AML)	1(7.69%)
Primary myelofibrosis	1(7.69%)
Erythroid hyperplasia	1(7.69%)
Total	**13 (100%)**

Bone marrow was hypercellular in (47 cases, 50%), normocellular in (42 cases, 44.68%), and hypocellular in (5 cases, 5.31%). These findings are illustrated in Table 5.

Table 5: Cellularity in BMA

Cellularity	No of cases (%)
Hypercellular marrow	47(50%)
Normocellular marrow	42(44.68%)
Hypocellular marrow	5(5.31%)
Total	**94(100%)**

Table 6: Bone marrow aspiration findings

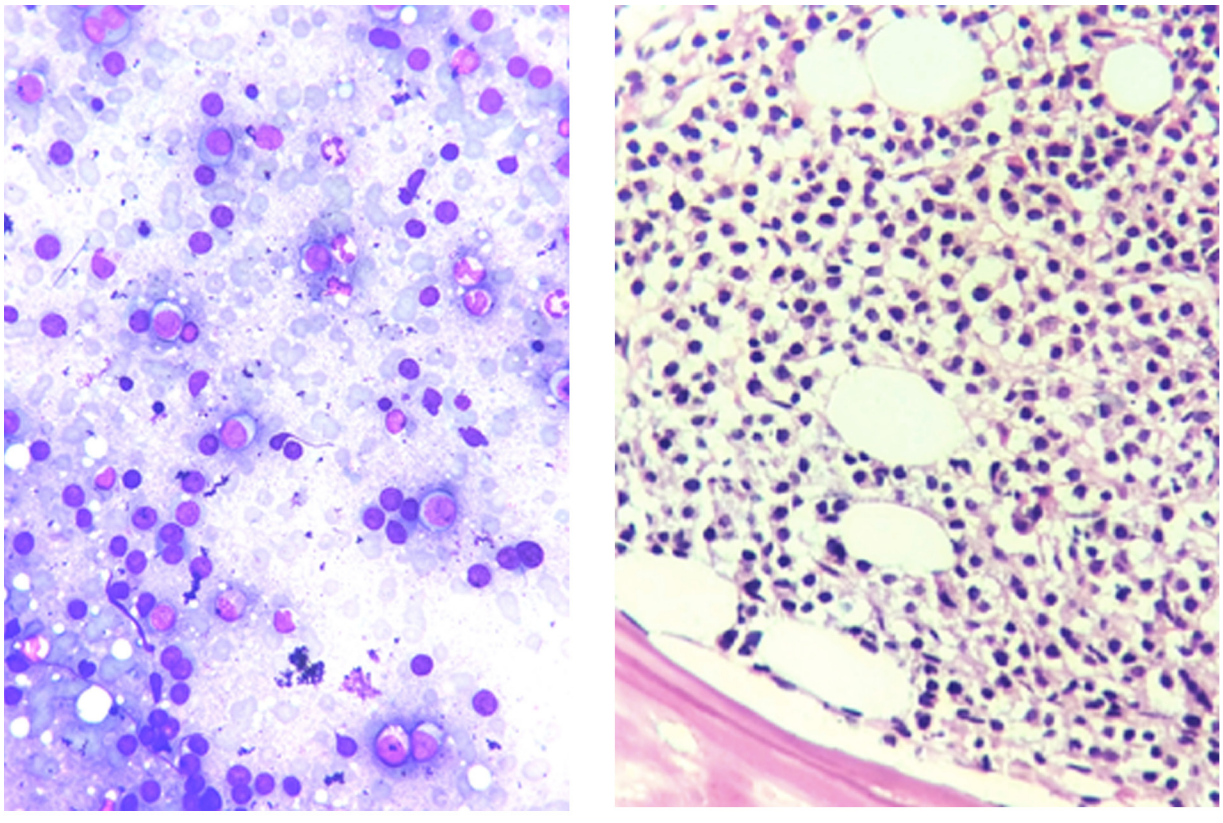
BMA findings	No of cases (%)
Erythroid hyperplasia	23(24.46%)
Normocellular marrow	21(22.34%)
Reactive plasmacytosis	10(10.63%)
Myeloid hyperplasia	8(8.51%)
Plasma cell neoplasm-multiple myeloma	6(6.38%)
Bonemarrow Eosinophilia	6(6.38%)
Acute Leukemia	5(5.31%)
Megaloblastic anemia	3(3.19%)
Aplastic anemia	3(3.19%)
Idiopathic thrombocytopenic purpura (ITP)	2(2.12%)
Myelodysplastic Syndrome (MDS)	2(2.12%)
Chronic Myelogenous Leukemia (CML) accelerated phase	1(1.06%)
Metastatic tumor	1(1.06%)
Myeloproliferative neoplasm-Primary myelofibrosis	1(1.06%)
Micronormoblastic precursors	1(1.06%)
Non-Hodgkin's Lymphoma (NHL)	1(1.06%)
Total	**94(100%)**

Bone marrow examination findings are illustrated in Table 6. Erythroid hyperplasia (23 cases, 24.46%) was the most common finding in our study. In these cases, there were no other significant findings. Out of 23 cases of erythroid hyperplasia, (3 cases,13.03%) showed micro-normoblasts, and (4 cases, 17.39%) showed megaloblastic changes.

Among the other cases, normal marrow were (21 cases, 22.34%), reactive plasmacytosis were (10 cases, 10.63%), and myeloid hyperplasia were (8 cases, 8.51%) followed by bone marrow eosinophilia (6 cases, 6.38%).

Megaloblastic anemia (3 cases, 3.19%) and aplastic anemia (3 cases, 3.19%) were the most common anemia. Megaloblastic anemia showed megaloblastic maturation in erythroid precursors. In all cases of aplastic anemia and hypoplastic anemia, the marrow was hypocellular and all 3 lineages of cells were suppressed. Micronormoblast precursors were observed in (1 case, 1.06%) of suspected iron deficiency anemia.

Plasma cell neoplasm (Multiple myeloma) was the most common malignancy (6 cases, 6.38%).



(1a) (1b)

Figure 1: a, b- Plasma cell neoplasm-Multiple Myeloma. Plasma cells some with binucleated and immature forms (1a. BMA Giemsa stain and 1b. BMB H &E stain 40X)

(Figure 1a & 1b) One case was of recurrent multiple myeloma. The clinical, biochemical, and radiological correlation was advised in all these cases of multiple myeloma. Serum protein electrophoresis was done in (3 cases, 50%) cases that showed M spikes.

Acute Leukemia was diagnosed in (5 cases, 5.31%). Out of this, (3 cases, 60%) were AML, and (2 cases, 40%) were ALL. (Figure 2) One of the AML was diagnosed as AML-M3 type. Flow cytometry was advised in all these cases for further typing of leukemia. One of the ALL was further diagnosed as T-ALL in flow cytometry.

CML accelerated phase was diagnosed in (1 case, 1.06%). Myeloproliferative neoplasm- primary myelofibrosis was diagnosed in (1 case, 1.06%) because bone marrow biopsy revealed fibrosis and immature precursors.

Myelodysplastic syndrome (MDS) was diagnosed in (2 cases, 2.12%) cases. One was diagnosed as MDS –RAEB (Refractory anemia with excess blasts) and the other as Childhood MDS. Both cases showed increased erythroid series of cells with dyserythropoiesis.

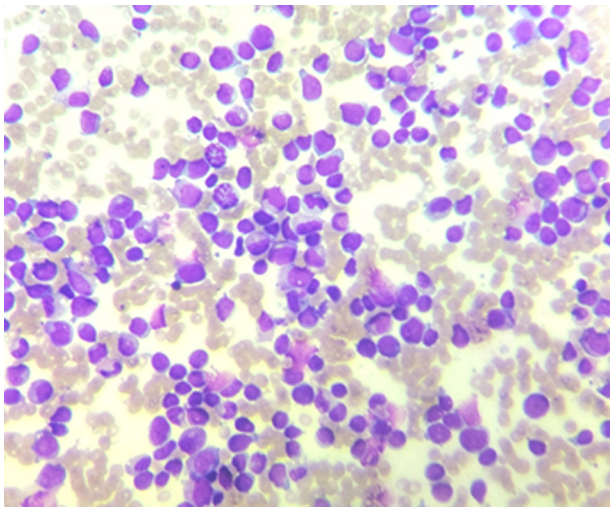


Figure2. Acute Leukemia. Blast cells with a high nuclear-cytoplasmic ratio. (Giemsa stain, 40X)

Idiopathic thrombocytopenic purpura (ITP was diagnosed in (1 case, 1.06%) case in which bone marrow aspiration revealed increased megakaryocytes with hypo-lobation and immature forms.

Metastatic tumor with differential diagnosis as lymphoma and poorly differentiated carcinoma was given in (1 case, 1.06%). Further immunohistochemistry was recommended.

Non-Hodgkin's Lymphoma (NHL) was diagnosed in (1 case, 1.06%) case.

Discussion

The spectrum of hematological disorders is relatively different in the developing world than the developed countries. BMA is a safe and useful investigation for final diagnosis [7].

In our study, the most common age group undergoing BMA was >45 years. In a study done by Pudasaini et al, the majority of the patients were from the age group 31-45 years[8]. In our study age of the patient ranged from 8 months to 85 years. 63 (67.02%) were males and 31(32.97%) were females with (M: F=2.03:1). Age and sex distribution were compared with other studies as shown in Table 7.

Table 7: Comparison of age and sex distribution in different studies.

Study	Age (years)	M:F
Kibria et al[7]	3.5-80	1:0.59
Pudasaini et al[8]	0.75-75	1:1.1
Rao et al[9]	2-80	1.2:1
Niazi et al[10]	1-75	1.7:1
Jha et al[11]	1-79	1.5:1
This study	0.66-85	2.03:1

In this study bone marrow was hypercellular in 47(50%), normocellular in 42(44.68%), and hypocellular in 5(5.31%). This finding was similar to the study done by Bashir et al.[19].

PUO (44.68%) was the most common indication followed by pancytopenia (13.82%). In contrast to our study, pancytopenia was the commonest indication in a study done by Ahmed et al.[12]. Pancytopenia was the third common indication (11.9%) in a study done by Bashawri et al.[13].

Among PUO, bone marrow findings showed (14 cases, 33.33%) normocellular marrow, (7 cases, 16.66%) erythroid hyperplasia, (7 cases, 16.66%) reactive plasmacytosis and (5 cases, 11.9%) myeloid hyperplasia, (4 cases, 9.52%) bone marrow eosinophilia, (2 cases, 4.76%) MDS, (1 case, 2.38%) AML-M3, (1 case, 2.38%) myeloproliferative neoplasm-primary myelofibrosis and (1 case, 2.38%) plasma cell neoplasm-multiple myeloma.

In contrast, a study done by Jha et al showed reactive myeloid hyperplasia (44%) followed by neoplastic conditions (19.25%) and erythroid hyperplasia with megaloblastic changes (7.01%) as the common findings in PUO14.

Among pancytopenia, bone marrow findings revealed megaloblastic anemia (3 cases, 23.07%) and aplastic anemia (3 cases, 23.07%). This finding is similar to various other studies illustrated in table 8.

Erythroid hyperplasia was seen in (23 cases, 24.46%) cases. A similar finding was seen in a study done by Pudasainiet al.[8] (21%) and Jha et al.[11] (19.6%).

Table 8: Common causes of pancytopenia in different studies.

Study	Country	Year	No. of cases	Commonest cause (%)	Second common cause (%)
Khungern et al.[15]	India	2002	100	Megaloblastic anemia (44%)	Aplastic anemia (14%)
Niazi et al10	Pakistan	2004	89	Aplastic anemia (38.27%)	Megaloblastic anemia (24.7%)
Pathak et al.[16]	Nepal	2010	102	Aplastic anemia (42.15%)	Hematological malignancy (19.4%)
Hirachand et al.[17]	Nepal	2013	52	Aplastic anemia (50%)	Megaloblastic anemia (34.61%)
Vaidya et al.[18]	Nepal	2015	83	Megaloblastic anemia (34.95%)	Aplastic anemia (31.33%)
This study	Nepal	2021	13	Megaloblastic anemia (23.07%)	Aplastic anemia (23.07%)

Normocellular marrow was observed in (21 cases, 22.34%) followed by Reactive plasmacytosis (10 cases, 10.63%) in this study which is a little bit similar to the study done by Bashir et al[19] with normocellular marrow (12.2%) and reactive plasmacytosis (12%).

In this study myeloid hyperplasia was seen in (8 cases, 8.51%). A study done by Bhagat et al.[20] showed myeloid hyperplasia in 18% of cases.

Megaloblastic anemia (3 cases, 3.19%) and aplastic anemia (3 cases, 3.19%) were more common than iron deficiency anemia (1 case, 1.06%) in this study. These findings were similar to the study done by Khungernet al[15] and Vaidya et al.[18]. The increased incidence of megaloblastic anemia reflects the higher incidence of nutritional deficiency anemia in our country. Iron deficiency anemia was observed in (1 case, 1.06%). In contrast to this, 7% and 23% cases were iron deficiency anemia in the study done by Pudasainiet al[8] and Ahmad et al.[12].

ITP was seen in (1 case, 1.06%). Other studies showed ITP in 5% and 6.21% respectively.[7,12] The low incidence of ITP may be attributed to a fewer number of pediatric cases in our study.

In this study plasma cell neoplasm (Multiple myeloma) was the most common malignancy (6 cases, 6.38%) compared to Laishramet al[21], Kibria et al[7], and Upadhyaya-Baskota et al.[22] who showed 20.5%, 9.04%, and 9.4% respectively.

Acute Leukemia was seen in (5 cases, 5.31%). Out of this, (3 cases, 60%) were AML, and (2 cases, 40%) cases were ALL. Similarly, other studies showed acute leukemia as the commonest hematological malignancy and AML more common than ALL.[7,11,23]

Myelodysplastic syndrome (MDS) was diagnosed in (2 cases, 2.12%). Other studies showed the incidence of MDS ranging from 2% to 7.9%[7,10,11,13].

Other malignancies in our study were CML accelerated phase (1 case, 1.06%), myeloproliferative neoplasm- primary myelofibrosis (1 case, 1.06%), Non-Hodgkin's Lymphoma (NHL) (1 case, 1.06%) and metastatic tumor (1 case, 1.06%). A similar study done by Shastry et al24 showed 1 (0.9%) cases of CML, 1 (0.9%) cases of Myelofibrosis, and 1 (0.9%) case of metastatic deposits.

Conclusion

Although BMA and biopsy are uncomfortable procedures for the patient and should only be done when there is a clear clinical indication, it is a valuable approach for diagnosing a variety of hematological disorders.

References

1. Bain BJ. Bone marrow trephine biopsy. Journal of clinical pathology. 2001;54(10):737-42.
2. Bain BJ. Morbidity associated with bone marrow aspiration and trephine biopsy-a review of UK data for 2004. Haematologica. 2006;91(9):1293-4.
3. Brown DC, Gatter KC. The bone marrow trephine biopsy: a review of normal histology. Histopathology. 1993;22(5):411-22.
4. Krause JR. An appraisal of the value of the bone marrow biopsy in the assessment of proliferative lesions of the bone marrow. Histopathology. 1983;7(5):627-44.
5. Sola MC, Rimsza LM, Christensen RD. A bone marrow biopsy technique suitable for use in neonates. British journal of hematology. 1999;107(2):458-60.
6. Brynes RK, McKenna RW, Sundberg RD. Bone marrow aspiration and trephine biopsy: an approach to a thorough study. American journal of clinical pathology. 1978;70(5):753-9.
7. Kibria SG, Islam MD, Chowdhury AS, Ali MY, Haque MR, Mustanzid SM, Ali SY. Prevalence of hematological disorder: a bone marrow study of 177 cases in a private hospital at Faridpur. Faridpur Medical College Journal. 2010;5(1):11-3.
8. 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;2(4):309-12.
9. Rao KS. Pancytopenia: a clinico hematological study. Journal of laboratory physicians. 2011;3(1):15-20.
10. Niazi M. The incidence of underlying pathology in pancytopenia-an experience of 89 cases. Journal of Postgraduate Medical Institute (Peshawar-Pakistan). 2004;18(1).
11. Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc. 2008;47(169):12-7.

12. Ahmad SQ. Utility of bone marrow examination in a secondary care hospital. Journal of Rawalpindi Medical College. 2011;15(1):40-1.

13. Bashawri LA. Bone marrow examination. Indications and diagnostic value. Saudi medical journal. 2002;23(2):191-6.

14. Jha A, Sarda R. Value of bone marrow examination in pyrexia of unknown origin. Journal of Pathology of Nepal. 2013;3(6): 447-51.

15. Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia--a clinicohaematological study of 200 cases. Indian journal of pathology & microbiology. 2002;45(3):375-9.

16. Pathak R, Jha A, Sayami G. Evaluation of bone marrow in patients with pancytopenia. Journal of pathology of Nepal. 2012;2(4):265-71.

17. Hirachand S, Singh R, Lama S. Frequency of causes of pancytopenia in a private hospital in Kathmandu. Health Renaissance. 2013;11(2):134-7.

18. Vaidya S. Evaluation of bone marrow in cases of pancytopenia in a tertiary care hospital. Journal of Pathology of Nepal. 2015;5(9): 691-5.

19. Bashir N, Musharaf B, Reshi R, Jeelani T, Rafiq D, Angmo D. Bone marrow profile in hematological disorders: an experience from a tertiary care center.International Journal of Advances in Medicine. 2018;5(3):608-13

20. Bhagat R, Jandial R, Kumar V. Different Causes of Pyrexia of Unknown Origin on Bone Marrow Examination--An Institutional Experience. Journal of Evolution of Medical and Dental Sciences. 2020;9(8):492-6.

21. Laishram S, Shimray R, Sharma AB, Pukhrambam G, Singh AM, Sharma LD. Neoplastic lesions in the bone marrow: a 10-year study in a teaching hospital. JIACM. 2008;9(3):175-8.

22. Baskota SU, Joshi AR, Singh SK. Bone marrow touch imprint smears as an adjunct to bone marrow aspiration smears in hematological disorders. Journal of Pathology of Nepal. 2015;5(9):739-46.

23. Egesie OJ, Joseph DE, Egesie UG, Ewuga OJ. Epidemiology of anemia necessitating bone marrow aspiration cytology in Jos. Nigerian Medical Journal. 2009;50(3):61.

24. Shastry SM, Kolte SS. Spectrum of hematological disorders observed in one-hundred and ten consecutive bone marrow aspirations and biopsies. Medical Journal of Dr. DY Patil University. 2012;5(2):118.