Original Article

Bone-marrow spectrum in a tertiary care hospital: Clinical indications, peripheral smear correlation and diagnostic value

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ABSTRACT

Aim: The aim was to identify the indications for a bone-marrow aspiration study, to correlate between peripheral blood smear findings and those of bone-marrow aspiration; and to assess the diagnostic value of bone-marrow aspiration examination. **Settings and Design:** A retrospective study was done on patients referred for bone-marrow aspiration in a tertiary care hospital for a period of about 3 years. **Materials and Methods:** Stained bone-marrow aspirate smears were examined. Records regarding the clinical indication for the procedure, peripheral blood smear reports, blood counts and significant findings on bone-marrow aspiration examination were retrieved. The role of bone-marrow aspiration in the diagnosis of hematological and nonhematological disorders was reviewed in the study. **Results:** Of a total of 153 cases, 24 (15.68%) were from the pediatric age group and 129 (84.32%) were adults. Male:female ratio was 1.3:1. The indications were anemia for evaluation (33%), evaluation of pancytopenia (26%), suspicion of malignancy (17%), fever (10%) and thrombocytopenia (3%). Bone-marrow aspiration yielded a diagnosis of hematological malignancy in a total of 11 cases. However, peripheral blood smear examination was able to pick up only seven of these cases. Furthermore, one case of metastatic deposits was seen in a case of carcinoma of unknown primary. The bone-marrow findings correlated with the peripheral blood smear findings in 54 (43.2%) out of 125 of the total cases. **Conclusion:** This study shows that bone-marrow aspiration is a valuable diagnostic tool and aids in diagnoses and etiology of various hematological findings such as anemia and pancytopenia.

Keywords: Anemia, bone-marrow, pancytopenia

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Introduction

Anemia is very commonly encountered in developing countries.[1] Among the adult population in rural India, anemia is prevalent among 50% of the women, and 44.3% of the men.[2]

Bone-marrow aspiration is requested in various conditions including anemia, pancytopenia, and suspected cases of malignancies. Often, samples are inadequate on aspiration, and a biopsy needs to be performed simultaneously.[3]

This study was conducted to identify the indications for a bone-marrow aspiration study, to correlate between peripheral blood smear and bone-marrow aspiration findings. It aims to assess the diagnostic value of bone-marrow aspiration examination.

Materials and Methods

A retrospective study was done on patients referred for bone-marrow aspiration in a tertiary care hospital: Sri R. L. Jalappa Hospital and Research Centre, Kolar; from January 2010 to April 2013: A period of little over 3 years. The bone-marrow aspirates were all obtained by access from the posterior superior iliac spine. The material was collected in sodium citrate, and smears were prepared by the wedge spread method. Staining was done using Leishman's stain. Records regarding the clinical indication for the procedure, peripheral blood smear reports, blood counts, and significant findings on bone-marrow aspiration examination were retrieved. The role of bone-marrow aspiration in the diagnosis of hematological and nonhematological disorders was reviewed in the study.

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Results

Of a total of 153 cases, 24 (15.68%) were from the pediatric age group (defined as those below or equal to 18 years of age), and 129 (84.32%) were adults. The age groups varied from 8 to 90 years. The male:female ratio was 1.3:1.

Clinical indications for bone-marrow aspiration

The most common indication was anemia for evaluation (33%), followed closely by evaluation of pancytopenia (26%). The other indications included the malignancy (17%), fever (10%), and thrombocytopenia (3%) [Graph 1].

Material acquired was inadequate for interpretation or was obscured by blood and blood elements in 18% of the cases, that is, 28 out of 153 cases. These cases were excluded from the study. Hence, the sample size was reduced to 125 patients.

The distribution of cases based on the final impression obtained after bone-marrow aspiration was as follows: 48 showed dimorphic maturation, 20 showed normal maturation, 12 showed micronormoblastc maturation, 11 showed hematological malignancies, two cases of idiopathic thrombocytopenic purpura were diagnosed, and a case of secondary from carcinoma of unknown primary was found [Figure 1].

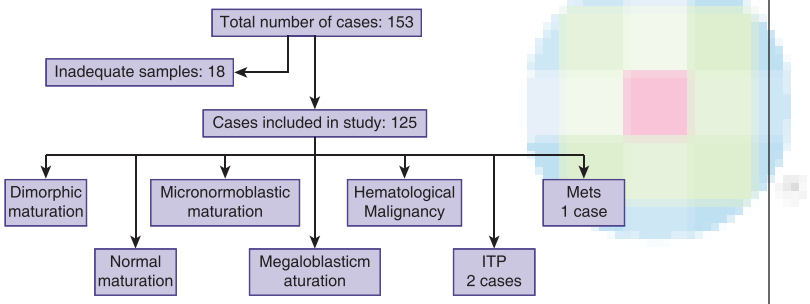
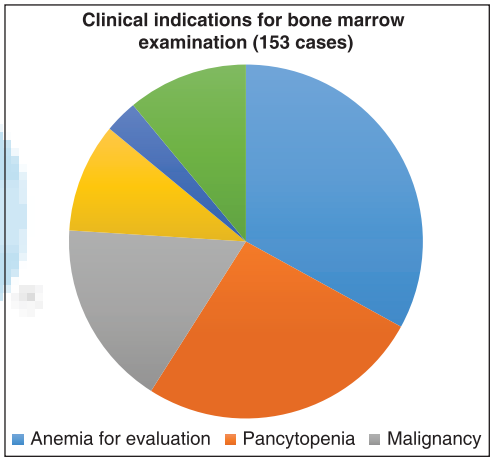


Figure 1: Distribution of cases based on bone-marrow aspiration findings: 48 showed dimorphic maturation, 20 showed normal maturation, 12 showed micronormoblastc maturation, 11 showed hematological malignancies, 2 cases of idiopathic thrombocytopenic purpura were diagnosed, and a case of secondary (Mets) from carcinoma of unknown primary was found

Bone-marrow aspiration was able to yield a diagnosis of hematological malignancy in a total of 11 cases. However, peripheral blood smear examination was able to pick up only seven of these cases [Table 1].

Furthermore, one case of adenocarcinomatous deposits was seen in a case of carcinoma of unknown primary.

Comparison of the bone-marrow aspirate findings with that of the peripheral blood smear showed the following findings: In cases reported as dimorphic anemia on peripheral blood smear (44), dimorphic maturation was confirmed in 56% of the cases. One case of malignancy was identified and diagnosed as multiple myeloma [Graph 2].



Graph 1: The most common indication was anemia for evaluation (33%), followed closely by evaluation of pancytopenia (26%). The other indications included the malignancy (17%), fever (10%), and thrombocytopenia (3%)

Table 1: Distribution of cases diagnosed as various malignancies on bone-marrow aspiration

Age	Sex	Clinical indication	Peripheral blood smear	Bone-marrow diagnosis
37	Female	Fever for evaluation	CML	CML
80	Male	? Lymphoma	CLL	CLL
50	Male	Fever for evaluation	Acute leukemia	Acute leukemia
26	Female	? CML	CML	CML
23	Male	Pancytopenia for evaluation	Pancytopenia	APML
65	Male	AML	AML	AML
26	Male	Anemia	Pancytopenia	ALL
65	Female	MM	Normocytic normochromic picture	MM
50	Female	CML	CML	CML
65	Female	? MM	Dimorphic anemia	MM
65	Male	CMML	CMML	CMML
64	Male	? Metastasis	Normocytic normochromic picture	Mets-adenocarcinoma

CML: Chronic myeloid leukemia, CLL: Chronic lymphocytic leukemia, AML: Acute myeloid leukemia, APML: Acute promyelocytic leukemia, MM: multiple myeloma, ALL: Acute lymphoblastic leukemia, CMML: Chronic myelomonocytic leukemia

In cases of pancytopenia (38), two of the patients were diagnosed with a malignancy. Acute lymphoid leukemia and acute myeloid leukemia were the diagnoses [Graph 3].

In cases with microcytic hypochromic blood picture (26), 25% showed micronormoblastic maturation, an equal number (25%) showing dimorphic maturation, followed by megaloblastic maturation (20%) and normoblastic maturation (20%). The distribution of the cellularity was as follows: 40% were hypercellular, 30% were normocellular, 20% hypocellular.

Assessment of normocytic normochromic blood picture was as follows: Of the 17 cases, three (18%) showed dimorphic maturation, two (11.7%) were diagnosed with malignancy, the marrow diagnoses being as follows: Multiple myeloma and adenocarcinomatous metastatic deposit. The remaining nine cases were consistent with peripheral blood smear findings and showed a normal maturation pattern. Six (36%) were normocellular, four (24%) were hypercellular.

Of the seven cases diagnosed as leukemia on peripheral blood smear, all seven were confirmed for malignancy on bone-marrow examination. Three cases of chronic myeloid leukemia, two cases of chronic lymphocytic leukemia, and two cases of acute myeloid leukemia were confirmed, respectively.

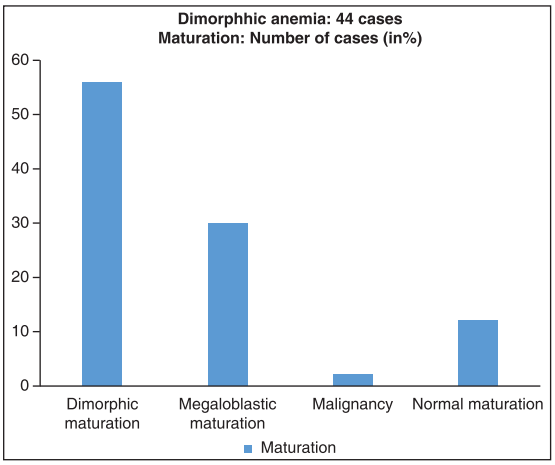
Idiopathic thrombocytopenia was diagnosed in two out of four cases evaluated for thrombocytopenia.

Dyserythropoietic changes such as nuclear budding, multinuclearity, Howell–Jolly bodies, basophilic stippling, and cytoplasmic vacuolation were seen in 20 cases. Of these, 55% were seen in cases of dimorphic maturation and 35% in the megaloblastic maturation.

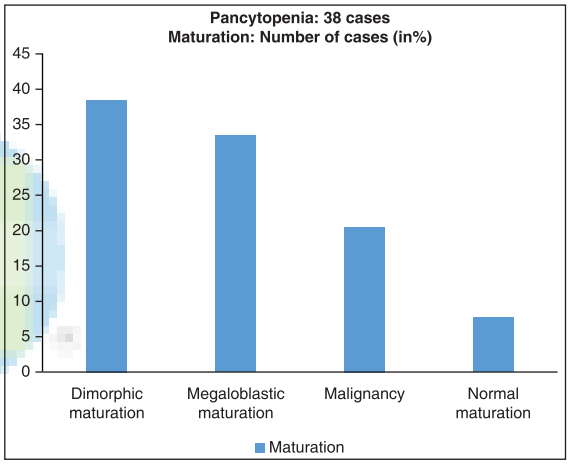
Diagnostic value for various clinical indications is as follows: Clinically, anemia was suspected in 47 cases. In all cases, an etiological diagnosis was made following bone-marrow examination [Graph 4].

Twelve patients were clinically suspected to have hematological malignancy. Bone-marrow examination confirmed the diagnosis in seven of these cases (58%) [Graph 5].

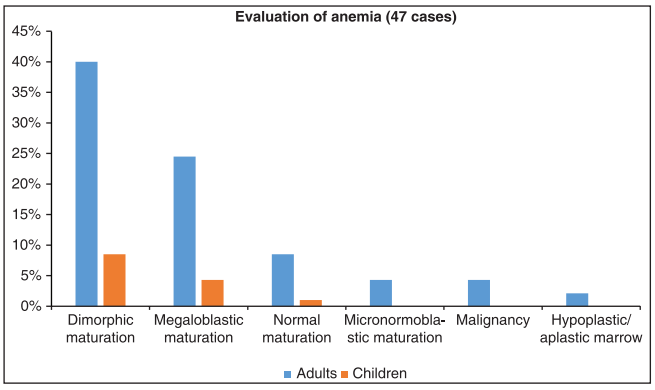
One patient clinically suspected to have carcinoma of an unknown primary, showed adenocarcinomatous deposits in the marrow.



Graph 2: Maturation pattern in patients with dimorphic blood picture: Dimorphic maturation confirmed in 56% of the cases, 30% of the cases showed megaloblastic maturation, 12% showed normal maturation, one case showed evidence of multiple myeloma



Graph 3: Maturation patterns in patients with pancytopenia: 38.5% showed dimorphic maturation, 33.4% showed the megaloblastic maturation, 20.5% showed evidence of malignancy, 7.7% revealed a normal study



Graph 4: Bone-marrow aspirate findings of clinical cases of anemia. Dimorphic maturation seen in 48.5% of patients (40% A, 8.5% P); megaloblastic picture seen in 31.9% of the patients (24.5% A, 7.4% P); Normal maturation seen in 9% of patients (8% A, 1% P). (A: Adults, P: Pediatric population)

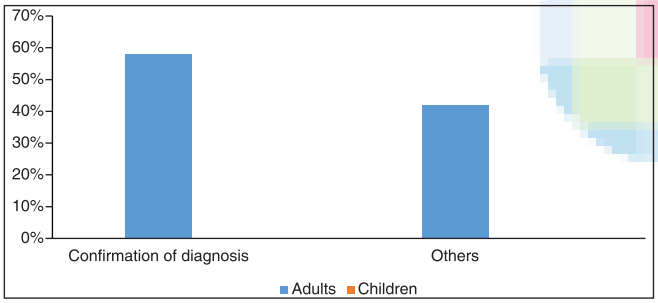
In patients with clinical evaluation of fever (16), bone-marrow examination was diagnostic in two cases (12.5%), where malignancy was detected and were diagnosed as chronic myeloid leukemia and acute myeloid leukemia, respectively.

Discussion

Bone-marrow is one of the most widely distributed organs of the body. It is the principle site of hematopoiesis. A bone-marrow aspirate is used to diagnose, confirm, and/or stage hematologic malignancies. It helps to evaluate cytopenias, thrombocytosis, leukocytosis, anemias, and iron status. It is also a diagnostic tool in nonhematological disorders such as storage disorders and systemic infections. It is an ambulatory procedure performed under local anesthesia with reduced morbidity.

Comparison of age and sex distribution in different studies [Table 2]. The range was comparable to our study which ranged from 8 to 90 years. The procedure was performed more on adults, and there was a slight predominance among the males (1.3:1).

The most common clinical indications for a bone-marrow aspiration according to this study were anemia (33%), followed by pancytopenia (26%). Most common indications for bone-marrow aspiration among adults are pancytopenia for evaluation and anemia for evaluation among children. A study conducted by Mirzai *et al*.,[8] on 1154 cases showed pancytopenia for evaluation to be the most common indication. Another study by Bashawri[9] on a total of 1813 cases showed that evaluation of acute leukemias and staging of lymphomas were the most common indications (22.2% and 15.2%, respectively). This discrepancy can be explained by the higher incidence of unexplained anemias among the people in rural areas in our study.



Graph 5: Clinically suspected cases of malignancy: Diagnosis was confirmed in 58% cases (7 out of 12 cases)

Table 2: Comparison of age and sex distribution in different studies (out of 153 cases)

Study	Study age group (years)	Pediatric: Adult cases	Overall male:female ratio
Current study	8-90	1:5.38	1.3:1
Egesie *et al*.[4]	3-80	1:3.20	1.5:1
Gayathri and Rao[5]	2-80	1:2.36	1.2:1
Kibria *et al*.[6]	3.5-80	1:3.32	1.69:1
Jha *et al*.[7]	1-79	1:2.52	1.5:1

Evaluation of etiology of pancytopenia: Comparison with studies conducted: [Table 3].

According to a study conducted by Gayathri and Rao[5] the most common cause of pancytopenia was megaloblastic anemia (74%). Jha *et al*.,[7] and Kumar *et al*.,[3] showed aplastic anemia ([29%] and [29.5%]) to be the most common cause. It has been established that a deficiency of Vitamin B12 leads to ineffective hematopoiesis, which can lead to cell lysis, and hence the presenting feature of pancytopenia.

The high prevalence of dimorphic maturation is explained by the occurrence of nutritional deficiencies in rural areas. Nutritional deficiencies of both iron and folate commonly occur together, more commonly in pregnant women. Iron deficiency occurring concurrently with megaloblastic anemia has been reported in many areas. In some instances, the megaloblastosis may be intermediate in degree but may become more marked after administration of iron, and some cases of severe dimorphic anemia do not respond initially to iron therapy, probably owing to concomitant severe folate and occasionally Vitamin B12 deficiency.[10]

It may seem paradoxical that leukemias can present with peripheral pancytopenias. However, many patients present in fibrotic and postproliferative stage of the disease. The fibrotic stage often presents with anemia and thrombocytopenia due to accompanying splenomegaly. The white blood cell count, on the other hand, can be low, normal or elevated. As fibrosis becomes more severe, the patients' cytopenias worsen.[11] In this study, two cases that showed pancytopenia on peripheral smear examination, revealed hematological malignancy on bone-marrow aspiration.

Table 3: Evaluation of pancytopenia: Comparison with other studies

Present study cases: 38 (%)	Gayathri and Rao[5] cases: 104 (%)	Jha *et al*.[7] cases: 148 (%)	Kumar *et al*.[3] cases: 163 (%)
Dimorphic anemia (38.4)	Megaloblastic anemia (74)	Hypoplastic anemia (29)	Aplastic anemia (29.5)
Megaloblastic anemia (33.4)	Aplastic anemia (18)	Mealoblastic anemia (24)	Megaloblastic anemia (22)
Hematological malignancies (20.5)		Hematological malignancy (22)	Leukemia/lymphoma (18)

Types of anemias in malignancies can be divided into three types: Hypoproliferative anemias, hemolytic anemias, and anemia due to blood loss.

Uncomplicated hypoproliferative anemias are the most common form of anemias in malignancies and are due to: Impaired mobilization of reticuloendothelial iron, ineffective erythropoiesis, and reduced survival of erythrocytes.

Occult malignancies are the most common causes of anemia of chronic disease in adults. Marrow reveals normal to increased iron stores with normal erythroid precursors. It is associated with normocytic normochromic blood picture with normal red blood cell indices.

Conclusion

Clinical indications for a bone-marrow examination in this study are evaluation of anemia, evaluation of pancytopenia, and suspicion for malignancy.

It was also found that the bone-marrow findings correlated with the peripheral blood smear findings in 54 (43.2%) out of 125 of the total cases.

Highest diagnostic yield was obtained in cases of evaluation of anemia: 100% of the cases were aided by bone-marrow aspiration. In cases of clinically suspected malignancies, 58% of the cases were confirmed. In four cases, malignancy was confirmed by bone-marrow examination alone.

In conclusion, this study shows that bone-marrow aspiration is a valuable diagnostic tool and aids in the confirmation of diagnoses as well as explaining the cause for various hematological findings such as anemia and pancytopenia.

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