A study of Bone marrow aspirations and examination as a diagnostic tool in Hematological disorders

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ABSTRACT

In the present study 75 cases of blood disorders and bone marrow disorders occurring in pediatric patients, at the Guru Gobind Singh Hospital, were studied in, Department of Pathology, Shri M. P. Shah Medical College, Jamnagar from the year December 2001 to December 2003. Most numbers of patients were diagnosed with megaloblastic anaemia of these 63.6% were males and 36.3% were female patients. And majority of patients were in the age group of 1 month to 2 years of age in case of megaloblastic anaemia. The most common presenting symptom was fever, followed incidence by pallor and bleeding tendencies. The second most common abnormality detected in bone marrow smears of children was erythroid hyperplasia of varying degrees and it was followed in incidence by Gaucher's disease and dimorphic anaemia. In case of Gaucher's disease 60% were female and 40% were male patients and the common age of presentation of all these patients were in the age group of 1 year to YA years. Most common presenting symptom was found to be pallor and it was associated with hepatospelenomegaly.

Keywords: Bone marrow aspiration, Hematological disorders, Megaloblastic anaemia

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INTRODUCTION

Bone Marrow aspiration is at all times interesting and often affords a more complete picture of the reaction of the hemopoietic tissue than can be gained from the blood sample alone. And it yields crucial information in a number of conditions.[1] It is necessary that the hematologist must be conversant with the illness of the patient on a broad scale, because although certain diseases affect

primarily the blood and blood forming tissues, disorders of other organ systems result in alterations in the hemopoietic system.[1]

The symptoms of hematologic disorders are so varied and nonspecific that in themselves they may not suggest a hematologic problem. Likewise, physical examination may or may not direct attention to the hemopoietic system. The physical signs may be mainly those of CCF in some forms of anemia and nothing other than pallor when leukemia or aplastic anaemia is the underlying disorder. Study of the bone marrow is an indispensable adjunct to the study of diseases of the blood and may be the only way in which a correct diagnosis can be made.[2] Marrow can be obtained by needle aspiration, percutaneous trepine biopsy or surgical biopsy. If performed correctly bone marrow aspiration is simple and safe. It can be repeated many times and can be performed on outpatients; it seems to be safe in all circumstances, even when thrombocytopenic purpura is present.

Bone marrow aspiration smears are cheap to prepare rapidly stained with widely available routine and specialized techniques and are ready for examination in ten to twenty minutes and cause less pain and expense to the patients. They are even familiar to pathologists, hematologists, internists and pediatricians.[3] The evaluation of intracellular inclusions and maturation of erythroid precursors and the interpretation of Histo-chemical stains are usually more satisfactory in smears than in sections. Also the basophilic granulocytes and precursors are recognizable in Ramanowsky - stained smears easily. Sideroblasts and siderocytes are more often recognized in smears and as are the immature cells.[4]

Anaemia raise a different set of diagnostic possibility when found in children than when found in adults. Childhood anaemia is often caused by iron-deficiency, a hemoglobin abnormality, a red cell membrane disorder, or is self limited and of unknown etiology. The diagnosis can usually be made from the clinical presentation, complete blood count, reticulocyte count, examination of peripheral blood smear and other laboratory study of peripheral blood. But in some instances, however the etiology cannot be readily identified and further studies, including bone

marrow examination, becomes necessary.[5] study was done keeping in mind following objectives

AIMS AND OBJECTIVES:

- ✓ To study the bone marrow findings in various hematological disorders in children with the help of bone marrow aspiration smears.
- ✓ To gain important and diagnostic information about macrocytic anaemias other than megaloblastic anaemias, with the help of marrow picture in smears and thus to diagnose whether, it belongs to hemolytic anaemias, aplastic type of anaemias due to various causes and acute variety of Leukaemias.
- ✓ To establish the final diagnosis in case of megaloblastic anaemia in children.
- ✓ To diagnose lipid storage diseases, like Gaucher's disease and other forms of Lipoidosis in children through the study of bone marrow smears.
- ✓ To distinguish between primary and secondary thrombocytopenia with the help of marrow examination, in case of purpura and hemorrhagic diseases with low platelet count.
- ✓ To diagnose aleukemic Leukaemia in which abnormal cells are absent or too few for diagnosis in the peripheral blood and to confirm the diagnosis where peripheral smear is suggestive of Leukaemia.
- ✓ To look for secondary malignant cells found in bone marrow smears, as a cause of anaemia in children.
- ✓ To carry out bone marrow aspiration and examination in case of unexplained anaemia.

MATERIAL AND METHODS:

The patients selected for the present study were admitted in the Guru Gobind Singh Hospital, in Pediatric Department in Jamnagar having anaemia and few other hematological disorders. This study comprises of 75 patients in whom bone marrow aspiration was done. The procedure has been carried out at Guru Gobind Singh Hospital, Jamangar and all the cases were studied in the Department of Pathology, Shri M. P. Shah Medical College, Jamnagar during the period, December 2001 to December 2003.

In all cases patient's age, sex, clinical history other laboratory findings were recorded in proforma.

Bone Marrow Aspiration was done using standard method[3], The smears were stained by Leishman stain. The smears were mounted by DPX and observed and recorded. Others tests used for the present study were hemoglobin level, red blood cell count, white blood cell count, platelet count, peripheral , smear examination. Bone marrow examination was done of all smears and reported in terms of cellularity, M : E ratio, erythropoiesis, hemopoiesis, megakaryocytes, other associated features / findings and conclusion were drawn out and final diagnosis was established.

OBSERVATIONS & RESULTS

The present study comprises 75 cases of pediatric patients and the period of study was from December 2001 to December 2003.

1) Age: The distribution of patients according to age group is shown in table 1.

Table No 1: Patient age group distribution (Incidence)

Age in Years	No. of cases
0.1 -2	36 (48.00%)
>2-4	11 (14.70%)
>4-6	12(16.00%)
>6-8	12(16.00%)
>8-10	02 (02.70%)
> 10-12	02 (02.70%)
Total	75(100.0%)

The maximum age incidence was in 0.1-2 yrs. group (48%)

2) Sex: In case of sex incidence males (50.7%) and females (49.3%) were almost equally affected being slightly more in male.

3) **The distribution of patients according to presenting symptom is shown in Table no. 3.**

Table No. 3: Percentage of incidence of Presenting Symptoms

Sr. No.	Symptoms	No. of cases	Percentage
1	Fever	55	73.30%
2	Bleeding Tendency	28	37.30%
3	Pallor	25	33.30%
4	Breathtessness	20	26.70%
5	Anorexia	18	24.00%
6	Weakness	15	20.00%
7	Oedema	12	16.00%
8	Abdominal distension	09	12.00%
9	Epistaxis	08	10.70%
10	Lymphadenopathy	06	08.00%
11	Pica	05	06.70%

From above data was observed that fever was the most common presenting symptom in (73.3%) followed by bleeding tendency (37.3%) and pallor (33.3%).

4) **Signs in various hematological disorders depicted in Table No. 4**

Table No 4: Percentage of incidence of Presenting Sign

Sr. No	Sign	No. of cases	Percentage
1	Pallor of Mucous Membranes	IP	93.30%
2	Hepatomegaly	45	60.00%
3	Splenomegaly	22	29.30%
4	Petechiae	16	21.30%
5	Lymphadenopathy	10	13.30%
6	Ecchymosis	08	10.70%
7	Clubbing	03	04.00%
8	Jaundice	15	02.00%

Amongst the signs in various hematological disorders studied, pallor of mucous membranes was the most common (93.3%) followed by hepatomegaly (60%).

5) **The hemoglobin level:** (18.6%) patients had hemoglobin level less than 5 gm% and 81.3% of patients had hemoglobin ranging from 5.1 gm% to 9.3 gm%.

6) **Reticulocyte Count in various patients:** Most of patients 32 cases (42.70%) exhibited reticulocyte count between 1-2%, 25 cases (33.3%) had values less than 1% and 18 patients (24%) had reticulocyte count greater than 2%.

7) **Peripheral Smear Findings in terms of morphology of RBC:** More than half ss of the patients (56%) 42, had macrocytic hypochromic anaemia followed by (16%) 12 patients showing dimorphic picture. (4%) showed macrocytic hypochromic and (2.7%) showed normocytic normochromic. Remaining patients shared equal incidence of normocytic hypochromic and microcytic hypochromic (10.7%) of each.

The incidence of hypochromia was 77.3% normocytic RBC's were 13.3%, Microcytic were 10.7% and macrocytic were 60%.

8) **Distribution of patients according to site of aspiration of bone marrow is depicted in:** Bone marrow aspiration was carried out from posterior part of illiac crest in 40% of patients (30 patients) who were older children and from medial aspect of proximal part of Tibia in 44 patients (58.7%) and only one patient had bone marrow aspiration from sternum. Tibial aspiration was done in younger children.

9) **The bone marrow aspiration smears were examined and interpreted in terms of cellularity:** The bone marrow smears were hypercellular in 50 patients (66.70%) : and hypocellular in 19 patients (25.30%), normocellular in 6 patients (8.00%).

10) **The distribution of patients according to disease:** Among bone marrow aspiration smears studied in all patients the incidence of Megaloblastic anaemia was highest seen in 22 patients (29.30%) followed by erythroid hyperplasia, in 14 patients (18.70%). The incidence of Gaucher's disease, dimorphic anaemia, was found to be equal being in 5 patients of each (6.70%) and there were 4 patients with acute blastic leukemia (5.3%). There were single case of iron deficiency anaemia, juvenile CML, lymphoma metastasis and myelodysplastic syndrome. Again the incidence of

pancytopenia, thrombocytopenia, myeloid hyperplasia, red cell hypoplasia, idiopathic thrombocytopenic purpura, malaria parasite, was found to be equal with 2 patients of each (2.70%). 5 bone marrow smears were difficult to interpret because of poor material or heavy admixture with blood (6.70%).

11) **Age / Sex incidence in case of Megaloblastic anaemia**

Table No. 11-A: Age incidence of Megaloblastic anaemia.

No.	Age Groups	No. of cases	Percentage
1	1 month - 2 yrs.	15	68.10%
2	4-6 yrs.	05	22.70 %
3	6-8 yrs.	02	• 09.09%
	Total	22	100.0%

The maximum age incidence of megaloblastic anaemia was found in the age group of 1 month - 2yrs. No cases were found in age group of 2-4 yrs. Two cases were found in 6-8 yrs. of age.

Table No. 11- B: Sex incidence in case of Megaloblastic anaemia: The incidence of megaloblastic anaemia showed male preponderence being in 14 patients (63.60 %) and less in female, 8 patients (36.30%).

12) **Malignancies diagnosed by bone marrow aspiration:** Out of 75 patients 6 had malignant disorder. Out of it, 4 cases were of acute blastic leukemia, one case each of juvenile CML, and lymphoma metastasis were noted. All cases of acute blastic leukaemia were seen in females. Patient with Juvenile chronic myeloid leukemia was also female. Lymphoma metastasis was also seen in female. All malignant conditions diagnosed occurred in female.

13) **Morphologic incidence in case of Acute blastic leukemia:** In case of Acute blastic leukaemia, 2 patients showed L2 variety of ALL and 2 patients were diagnosed with undifferentiated myeloblastic type of leukaemia.

DISCUSSION

Bone marrow examination is an important diagnostic tool in hematology. Like any other laboratory procedure, it provides accurate, reproducible, rapidly available and

useful information. In the present study 75 cases of various blood disorders were studied with the help of bone marrow aspiration smears stained with Leishman's stain.

AGE:

Present study included patients of pediatric age group. Majority of cases were in the age range of 0.1-2 years (48%) followed by almost equal number of patients in the age group of 2-4 years, 4 -6 years and 6-8 years (16%). Minimum of patients were found in the age group of 8-10 eyars and 10-12 years (2.7%) (Vide Table-1).

Githanga et al[6] also carried out the study of bone marrow examination at a pediatric hospital, to look for common disorders diagnosed by bone marrow aspiration in children. He observed a total of 97 cases. He chose the age group from 3 months to 13 years of age from which majority of patients who came for bone marrow examination were in the age range of 6 years to 8 years compared to 3 months - 2 years of age in the present study.

Hasenbegovic et[7] al also carried out bone marrow punctures in 75 children in case of severe deficiency anaemia, but majority of cases were in the age range of 0-4 years of age. Mukiili et al[8] did prospective analysis of 620 bone marrow examinations in children in the age range of 6 months-15 years of age.

SEX: In the present study of 75 cases the male to female ratio (M : F ratio) was 0,50 : 0.49 (37 were female patients and 38 male patients). Majority of males were affected in the age range of 1 month-2 years. And majority of females were affected in the age range of 4-8 years of age.

Hasenbegovic et al [7] studied cytomorphologic findings in bone marrow punctures in 75 children and in his study also the male female ratio was almost equal like the present study i.e. 37 were male patients and 38 were female patients with M : F ratio of 0.49 : 0.50. Mukiibi et al [8] in his prospective analysis of bone marrow examination in 168 children found the Male: Female ratio of 1.1 : 1 in his study which is almost comparable to the present study. Showing almost equal incidence of affection by disease in both sexes.

INCIDENCE OF VARIOUS BLOOD DISORDERS:

The incidence of various blood disorders was derived. Megaloblastic

Anaemia (29.3%), Erythroid hyperplasia (21.3%), storage disorders (9.4%), malignant disorders (7.9%), cytopenias (5.4%), dimorphic anaemia (6.7%), idiopathic thrombocytopenic purpura (2.7%), myeloid hyperplasia (2.7%), red cell hypoplasia (2.7%, malarial parasite (4.0%), myelodysplasia (1.3%), hemolytic anaemia (5.3%), irondeficiency anaemia (1.3%).

Hasenbegovic et al [7] also in his study of cytomorphologic findings and diagnostic value of bone marrow punctures in children with Anaemia in 75 children could derive morphologic findings of bone marrow aspirate smears which showed features of dimorphic anaemia in (9.3%) patients, megaloblastic anaemia in (1.3%) patients (2.66%) with leukaemia.

Mukiibi et al [8] in his prospective analysis of 168 pediatric patients could arrive at the diagnosis of 3 important disorders Acute Leukaemia (22%), Hodgkin's and NonHodgkins Lymphoma (14.3%) and retinoblastoma (13.7%). In the present study the incidence of acute Leukaemia was (5.3%) and that of Lymphoma was (1.3%) which is comparatively very less.

Delacretaz et al[25] who simultaneously carried out bone marrow aspiration as well as biopsy in 200 patients noted the incidence of Lymphoma to be (26.5%), Myeloproliferative syndromes (17.5%), other hematological disorders such as cytopenia, anaemia, leukaemia (24%). In the present study incidence of myeloproliferative syndrome was only (1.3%) and other hematological disorders comprised (53.33%).

Sheikh et al[9] in his study of 80 patients with fever and splenomegaly, studied bone marrow aspiration smears of his patients to find that hematological malignancies were present in (23.75%) patients, megaloblastic changes were present in (15%) patients and malarial parasite in (40%) patients. In the present study the incidence of megaloblastic anaemia was high (29.3%) and malarial parasite in only (4.0%).

MEGALOBLASTIC ANAEMIA:

Total incidence of megaloblastic anaemia was found to be (29.3%) in the present study, diagnosed with the help of bone marrow aspiration in 75 cases.

Hasenbegovic et al[7] in his study also of 75 cases, found <

megaloblastic anaemia in only (1.3%) of patients. Sheikh et al [9] in his study of 80 patients, who underwent bone marrow aspiration, found megaloblastic anaemia in (15%) of patients. Tilak et al[10] in his study of 77 cases found megaloblastic anaemia in (68%) of cases.

ACUTE LEUKAEMIA:

In the present study in 75 children the incidence of Acute Leukaemia was found to be (5.3%) seen in only in 4 patients. Out of 4 patients, 2 were diagnosed with acute blastic leukaemia lymphoid L2 variety of ALL (50%). 2 were having undifferentiated myeloblastic variety (50%). Keleti et al[11] in his study of 270 cases found the incidence of acute leukaemia of L1 variety of ALL (53%) of patients and L2 variety (30%) of patients and L3 variety in only (1%) of patients. In case of AML the incidence of undifferentiated myeloblastic leukaemia was found to be only (5%). Viana et al[32] in his study of classification of ALL in children for the analysis of morphologic criteria found, out of 223 patients L'i variety of ALL in (84%) of patients, L2 variety in (11%) of patients and L3 in only (5%) of patients. Incidence of myeloblastic leukaemia was (40%) of patients. In his study children more than 7 years of age had an increased incidence of L2 type. In the present study also the patients diagnosed with L2 variety are above the range of 4-6 years of age.

AML LYMPHOMA:

In the present study the incidence of Lymphoma was found to be (1.3%) being seen only in one patient out of 75 pediatric marrow aspirations. Delacretaz et al[12] in his study of 200 patients could diagnose lymphoma in (26.5%) of patients and other myeloproliferative syndromes being (17.5%). Mukiibi et al[8] found (14.3%) of patients having lymphomas in his study of 168 pediatric patients. Githanga et al[6] in 97 bone marrow examinations in children found lymphoma in (10%) of total patients. In the present study of 75 cases, the efficacy of bone marrow aspiration to arrive at a final diagnosis or its usefulness for derivation of information which is clinically useful was found to be in (93.3%) of cases with only (6.7%) of cases with inconclusive reports either due to "dry tap" or scanty material obtained while aspiration of bone marrow.

Nanda et al[13] found the efficacy of bone marrow aspiration as an adjunct to the trephine biopsy in his 42 cases, comparing results obtained with aspiration with biopsy, found that in (88.6%) aspiration alone was sufficient in making the diagnosis, i.e. 372 cases out of 420 cases.

Hammerstrom J et al[29] found that bone marrow aspiration was helpful in arriving at a diagnosis in (53%) of cases. Engeset et al[14] carried out bone marrow aspirations in 2907 patients and found only (6.6%) of patients with "dry tap", And hence in his study also (93.4%) of cases were successfully diagnosed with the help of bone marrow aspiration only.

CONCLUSION & SUMMERY:

In the present study 75 cases of blood disorders and bone marrow disorders occurring in pediatric patients, at the Guru Gobind Singh Hospital, were studied in, Department of Pathology, Shri M. P. Shah Medical College, Jamnagar from the year December 2001 to December 2003. Most numbers of patients were diagnosed with megaloblastic anaemia of these 63.6% were males and 36.3% were female patients. And majority of patients were in the age group of 1 month to 2 years of age in case of megaloblastic anaemia.

The most common presenting symptom was fever, followed in incidence by pallor and bleeding tendencies. The second most common abnormality detected in bone marrow smears of children was erythroid hyperplasia of varying degrees and it was followed in incidence by Gaucher's disease and dimorphic anaemia. In case of Gaucher's disease 60% were female and 40% were male patients and the common age of presentation of all these patients were in the age group of 1 year to 2 years. Most common presenting symptom was found to be pallor and it was associated with hepatospelenomegaly.

Total incidence of malignancies diagnosed by bone marrow aspiration was 7.9%. Out of which 66.6% had Acute blastic leukaemia. 16.6% had Juvenile chronic myeloid leukaemia and 16.6% had lymphoma metastasis. All patients with acute blastic leukaemia were females. Surprisingly, even Juvenile CML and lymphoma metastasis occurred in female patients. So malignancies showed higher incidence in females.

Out of 75 patients 42.67% were having anaemia as the most common finding including all cases of megaloblastic anaemia, dimorphic anaemia, irondeficiency anaemia and hemolytic anaemia. And 57.33% of patients had disorders other than anaemia. When the bone marrow smears of all the patients were examined after doing Leishman's stain 66.70% of patients had hypercellular marrow, 25.30% had hypocellular marrow and only 6% of patients had normocellular marrow. Hypercellular marrow were most often associated with megaloblastic anaemia, or erythroid hyperplasia or myeloid hyperplasia and in some leukaemias.

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