

## Research Article

# Study of bone marrow: dyserythropoiesis for etiological evaluation of anemia

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## ABSTRACT

**Background:** Bone Marrow Aspiration plays a major role in the diagnosis of various hematological disorders which are very frequent in various age groups. The aim of this study was to analyze the causes of haematological disorders, and to interpret the bone marrow aspiration findings with various dyserythropoietic changes in it.

**Methods:** This was a study carried out in the department of Pathology of Shri M P Shah Govt. Medical college over a period of two years from June 2008 to June 2010. Bone marrow examination of 100 cases of suspected haematological disorders was carried out. All details of the patients were recorded in the department of pathology.

**Results:** Out of 100 cases of bone marrow aspiration, erythroid hyperplasia and megaloblastic changes were commonest findings and Megaloblastic anemia was most common diagnosis given on bone marrow examination. Other dyserythropoietic changes were erythroidhypoplasia, micronormoblasts, dimorphic erythropoiesis, megaloblastoid changes and other like – cytoplasmic bleb, multinucleation, nuclear bridging.

**Conclusions:** The sincere blood film examination and keen morphological evaluation of erythroid series for dyserythropoiesis and leukopoiesis and megakaryopoiesis in bone marrow aspiration smear - supported with other investigation can navigate to etiological factors of anaemia and other haematological disorders.

**Keywords:** Dyserythropoiesis, Bone marrow aspiration and examination

## INTRODUCTION

The history of bone marrow examination dates back to 1908, when the first biopsy was accomplished. In the first few decades thereafter the reports were based on smears of bone marrow aspiration. The importance of histological sections and touch preparations of marrow in comparison with bone marrow smears was revealed in 1933.<sup>1</sup>

Bone marrow aspiration is useful in making out better individual cell morphology. Whereas biopsy is useful in bone marrow architectural pattern and distribution.<sup>2</sup>

Bone marrow aspiration always give important information of reaction of hemopoietic tissue in various condition in addition to findings of blood sample as the bone marrow can be affected by both hematological and non hematological disorders.

Marrow can be obtained by needle aspiration, percutaneous trephine biopsy or surgical biopsy. If performed correctly bone marrow aspiration of 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 thrombolytic purpura is present. Bone marrow aspirations 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 causes less pain to and expense to the patients. They are even familiar to pathologist, haematologists, internists and paediatricians.<sup>3</sup>

The evaluation of maturation of erythroid precursors & intracellular inclusions and the interpretation of histochemical stains are usually more satisfactory in smears than in sections. Also the basophilic granulocytes and precursors are recognizable in Romanowsky – stained smears easily. Sideroblasts and siderocytes are more often recognized in smears and as are the immature cells.<sup>4</sup>

Dyserythropoiesis refers to ineffective, morphologically abnormal erythropoiesis. Abnormal proportion of erythroid precursors in the bone marrow with morphologic features indicating aberrant proliferation of differentiation defines dyserythropoiesis. Common cause of dyserythropoiesis include homozygous beta –thalassemia, megaloblastic anemia, iron deficiency anemia, sideroblastic anemia, AML, hairy cell leukemia, MDS, chronic myeloproliferative disorders, aplastic anemia, etc.<sup>5</sup>

When erythropoiesis alone is affected, as dyserythropoiesis, it describes the situation where there is a qualitative abnormality of the bone marrow (dysplasia) resulting in inefficient hemopoiesis with intramedullary death of at least some cells which have failed to mature.<sup>6</sup>

The aim and objectives of the study were,

- To study the bone marrow findings in various haematology disorders to evaluate dyserythropoiesis with the help of bone marrow aspiration smear.
- To study Morphological variations in erythroid series with support of PS examination, reticulocyte count & other investigation to clarify the etiological aspect of anemia.
- To gain important information about dyserythropoiesis in various anaemia & to diagnose it.
- To carry out bone marrow aspiration & examination to evaluate dyserythropoiesis in unexplained anemia, leukemia & pyrexia of unknown origin (PUO).

## METHODS

The patients selected for the present study were admitted in the Guru Gobind Singh Government hospital in Jamnagar having anemia and few other hematological diseases. The procedure has been carried out at Guru Gobind Singh Government hospital, Jamnagar and all the cases were studied in the department of pathology, Shri M.P. Shah Govt. Medical College.

In all cases patient's age, sex, clinical history other laboratory findings were recorded like complete blood count, reticulocyte count, examination of peripheral blood etc.

For bone marrow aspiration a needle with strong, wide base, short bevelled with stillete and adjustable guard was used. Sternum, Anterior superior iliac spine, Posterior iliac crest are site of choice for aspiration while Medial aspect of tibia – preferred in the children under the age of one year.

## Procedure

The procedure was performed in a sterile manner. Local anaesthesia was infiltrated & the needle was introduced in the bony cavity & fitting syringe was attached. Strong but brief suction was applied to with draw 0.2 ml of bone marrow tissue. Immediately aspirated material was placed on a glass slide & smears were prepared. Allow it to dry and then fixed it with methanol. The smears were stained by leishman's stain. The smears were mounted by DPX and observed and recorded others tests used for the present study were hemoglobin level, complete blood count and peripheral smear examination. Bone marrow examination was done of all smears and final reports were prepared.

## RESULTS

Bone marrow films were examined and reported in a systemic manner for cellularity, M: E ratio, a differential count performed and morphology of various lineage and finally findings interpreted in the light of the clinical and hematological features and other laboratory findings.

In present study 53 male and 47 females were included. Bone marrow aspiration was carried out from posterior part of iliac crest in maximum 50 % patients, in 25 % patients from anterior part of iliac crest, in 24 % patients from medial aspect of proximal part of tibia and in 1 % from sternum. The bone marrow smears were normocellular in 49 cases, hypercellular in 32 cases and hypocellular in 19 cases.

From data It was observed that was the most common presenting symptom is fever (71%) followed by weakness (32%) and easy fatigability. Clinically signs in various hematological disorders studied, pallor was the most common (43%) followed by Hepatomegaly (35%).

Cases were arranged according to age group in Table: 1. The incidence of findings of bone marrow examination concluded and incorporated in study: Megaloblastic anemia (17%), normal bone marrow (14%). Iron deficiency anemia (10%), Dimorphic anemia (9%), Hemolytic anemia (8%), Idiopathic thrombocytopenic purpura (5%), Erythroid hyperplasia (5%), Myeloid leukemia (4%), Infections (4%), Acute blastic leukemia (3%), Lymphoma infiltration (3%), Marrow hypoplasia (3%), Myeloid hyperplasia (2%), Multiple myeloma (2). Secondaries in bone marrow Bone marrow (2%), Marrow hyperplasia (1), Myelodysplasia (1%), Gaucher's disease (1%), Aplastic anemia (1%), Congenital dyserythropoietic anemia (1%), Leishmaniasis (1%),

Myelosuppression (1%), Granulomatous infection (1%), Eosinophilia(1%).

Among bone marrow aspiration maximum number of disorder diagnosed was megaloblastic anemia. In the present study various morphological changes of erythropoiesis observed were arranged in Table 2.

**Table 1: Age group distribution of study.**

Age in Years	No of Cases
0-10	53
11-20	26
21-30	4
31-40	4
41-50	4
51-60	8
61-70	1
Total	100

**Table 2: Various morphological changes observed in erythropoiesis.**

Various Morphological Changes	No of Cases (%)
1 Erythroid hyperplasia	39
2 Megaloblastic changes	17
3 Erythroid hypoplasia	12
4 Micronormoblasts	10
5 Dimorphic erythropoiesis	9
6 Megaloblastoid changes	4
7 Other - like cytoplasmic bleb, multinucleation, nuclear bridging	1

## DISCUSSION

Sir William Harvey described blood as “the fountain of life and the primary seat of the soul. The marrow of our bones is the seedbed of our blood”.<sup>7</sup>

Bone-marrow is one of the most widely distributed organs of the body. It is the principle site of hematopoiesis. So a careful examination of the blood elements is primary step towards assessment of hematopoiesis and final diagnosis.

The spectrum of hematological disorders is very wide. Bone marrow examination is safe and a useful test in reaching the final diagnosis.<sup>8</sup>

### *Dyserythropoiesis*<sup>9</sup>

Erythropoiesis may be impaired due to variety of causes, acting primarily on the bone marrow or involving other biological process which may influence erythropoiesis ,these would include defects of stem cells with

consequent abnormalities in the development of hemopoietic line(s), as well as altered environmental states within the bone marrow impair the orderly proliferation & maturation of erythroid precursors cells.

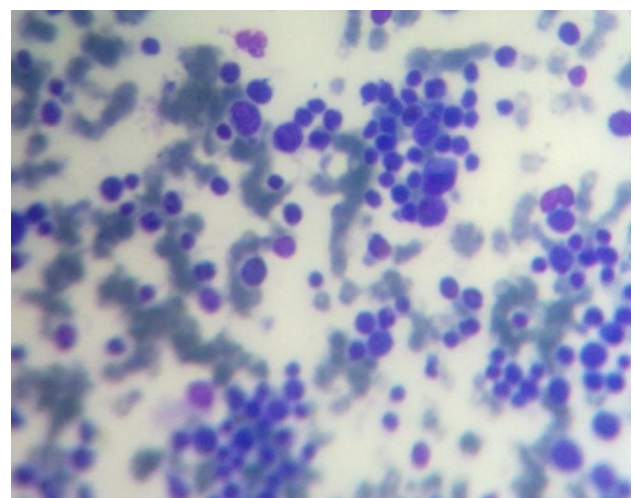
This state of disturbed erythropoiesis in the bone marrow, irrespective of cause may be described as “dyserythropoiesis”.

Morphological changes in dyserythropoietic states involve both the nucleus & cytoplasm of erythroblasts. Asynchrony of growth & maturation of the nucleus & the cytoplasm constitute the outstanding feature at all stages of development of these cells. The nuclear abnormalities include mitotic aberration, nuclear lobulation and fragmentation associated with karyorrhexis and pyknosis, binuclearity and multinuclearity, internuclear bridging and in some special instances,chromatin changes leading to megaloblastosis.

Cytoplasmic abnormalities consist of variable changes which include persistent cytoplasmic basophilia with or without stippling or vacuolation, cytoplasmic bridge and excessive iron deposition in the lysosome or mitochondria.

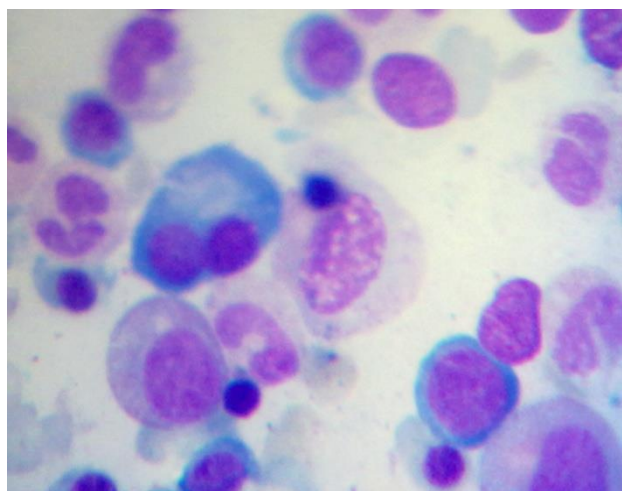
Grace f D’ Costa and their colleague study spectrum of pediatric marrow trephine biopsy in 0 - 18 yrs of age group & correlated with bone marrow aspiration and peripheral smear finding.<sup>10</sup> Out of the 74 cases of anaemias, the bone marrow was hypercellular with evidence of erythroid hyperplasia in- 30% cases & erythroid hypoplasia in only 9.45% cases.

In our study we studied all 100 cases for erythroid cellularity. In 39 cases we found erythroid hyperplasia (Figure 1) while 12 cases shows hypoplasia. Out of 100 cases 46 cases diagnosed as anemia. Out of 46 cases, 31 cases show erythroid hyperplasia while 1 cases shows hypoplasia.

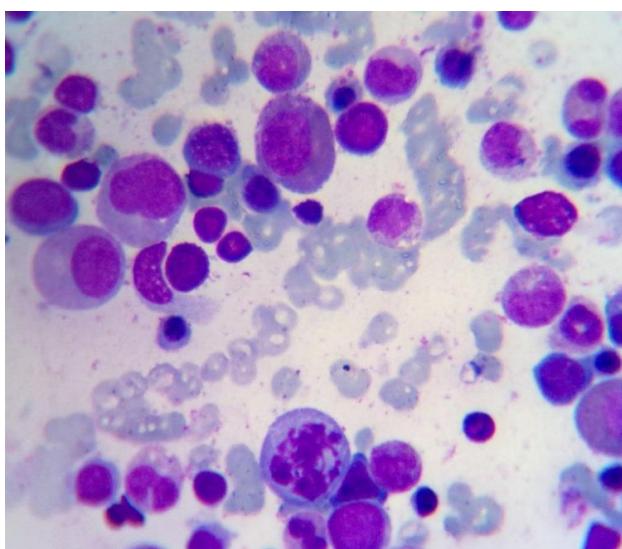


**Figure 1: Erythroid hyperplasia.**

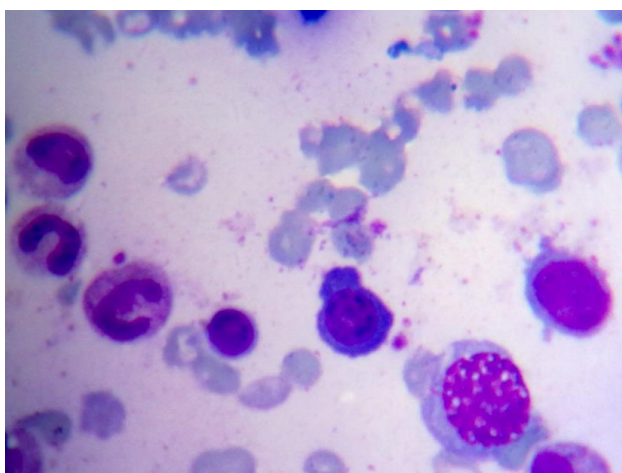




**Figure 2: Binucleation seen in megaloblastic anemia.**



**Figure 3: Nuclear irregularity observed in megaloblastic anemia.**



**Figure 4: Seive like nucleus observed in megaloblastic anemia.**

Out of 46 cases of anemia, megaloblastic changes (Figure 2, Figure 3, Figure 4) seen in 17 cases. Grace F D'costa & their colleague found megaloblastic change in 3 cases out of 74 cases.<sup>10</sup> In present study dimorphic anemia manifesting as micronormoblastic and megaloblastic change seen in 9 cases out of 46 cases while it was observed in 45 cases out of 74 cases of studied by Grace F D'costa and their colleague. In our study micronormoblastic maturation seen in 10 cases out of 46 cases, in study of Grace f D'costa<sup>10</sup> and colleague found micronormoblastic maturation seen in 10 cases out of 74 cases. Other change like cytoplasmic blebs, multinucleation & nuclear bridging & giant erythroblast in seen in single case of congenital dyserythropoietic anemia out 46 cases of anemia.

Rajan et al,<sup>11</sup> studied correlation 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. 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. 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.

In our study 8 cases out of 46 cases of anemia diagnosed as hemolytic anemia which shows erythroid hyperplasia (Figure 1). In study of Grace F D'costa<sup>10</sup> and their colleague found 9 cases of out of total 74 case of anemia which shows erythroid hyperplasia on marrow examination. In present study aplastic marrow change seen in single case while Grace f D 'costa and colleague in their study found aplastic / hypoplastic change in 7 cases.

Tahlan et al,<sup>12</sup> studied spectrum and analysis of bone marrow findings in anemic cases. Retrospective analysis of all cases of anemia with subsequent bone marrow examination in 3.5 years. Bone marrow examinations of 742 non pediatric (>15 yrs) patients were done. Malignant hematological disorders comprised 133 (18.0%). Non malignant disorders formed the major

group 609 cases (82.0%). Dyserythropoiesis was observed in 74.3% with adequate iron stores and 69.4% cases with low iron stores.

Dhingra et al,<sup>13</sup> studied morphological findings in bonemarrow biopsy and aspirate smears of visceral kala azar findings. Total 18 patients diagnosed either on bone marrow biopsy or biopsy from year 2000 to 2006 were reviewed. Erythroid hyperplasia with myeloid erythroid ratio ranging from 2 : 1 to 1: 4 were seen in four cases, three of them showed megaloblastic erythroid reaction with open nuclear chromatin and asynchronous nucleocytoplasmic maturation. In the present study bone marrow aspiration findings in a single case is normocellular, with normal M/E ratio with megaloblastic erythroid reaction.

Tripathi et al,<sup>14</sup> study of bone marrow abnormalities in patients with HIV disease. Seventy four (74) patients with HIV / AIDS included in the study. Majority of patients (72.9%) had AIDS. Bone marrow was normocellular in 78.95% of non-AIDS and 74.55% of AIDS, hypocellular in 5.26% of non-AIDS and 7.27% of AIDS, hypercellular in 15.79% of non-AIDS and 18.18% of AIDS patients. Important dysplastic changes observed in granulocytic series were cytoplasmic vacuolations (60%), nuclear dysmorphism (30%), monocytoid cells(1%) and others (1%), in erythroid series were irregular nuclear outline and basophilic stippling(66.67%), megaloblastoid changes (33.33%); in megakaryocytic series were hypolobulation (100%). In the present study bone marrow aspiration findings in a single HIV patient shows apparently normal marrow.

## CONCLUSION

Bone marrow aspirations turn out to be a simple and safe investigation can be repeated and can even be carried out in our patients rapidly and is ready for examination only in few minutes. The sincere blood film examination and keen morphological evaluation of erythroid series for dyserythropoiesis in bone marrow aspiration smear - supported with other investigation can navigate to etiological factors of anaemia and other haematological disorders.

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