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A Bone Marrow Aspiration Study in Evaluation of Severe Anemia in Adults

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Anemia is a global health challenge and is the most significant health problem encountered in the developing countries especially in India. According to the World Health Organisation (WHO), 1.62 million !! billion people per year are affected globally with anemia which constitutes 24.8% of the world population. To evaluate the clinical presenting features and the basic haematological parameters in adult patients with severe anemia, the morphological alterations of Bone marrow aspirates in these patients were studied. To correlate these morphological alterations of Bone marrow aspirates with the clinical and the basic haematological parameters in severe anemia.

Keywords: Anemia; bone marrow; haematological.

1. INTRODUCTION

Anemia is a global health challenge and is the most significant health problem encountered in the developing countries especially in India. According to the World Health Organisation (WHO), 1.62 million !!! people per year are affected globally with anemia which constitutes 24.8% of the world population [1]. It is also a common haematological problem in the

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geriatric age group and its incidence increases with increasing age [2]. The third National Health and Nutrition Examination Survey (NHANES-III) of United States revealed prevalence of anemia as 42% in women and 30% in men belonging to the age group of 15–59 years, 10.2% women and 11% men in adults >65 years [3]. The etiology of severe anaemia in adults is multi-factorial, the most common cause being Nutritional deficiencies and other causes include Anemia of Chronic disease and Haematological malignancies [4].

Bone marrow examination is a useful, safe and cost effective invasive procedure in the evaluation of severe anemia. To understand the cause and effect of severe anemia , it is essential to look into the bone marrow for specific changes. For example, the diagnosis, classification and prognostication of MDS, is based on the peripheral blood film and Bone Marrow morphology of the patient. Hence Bone Marrow Morphology remains the cornerstone and most often the gold standard in disease diagnosis and is an important tool that complements cytogenetic finings for prognostic discrimination [5].

Though iron deficiency anemia is the commonest anemia in our country relatively few Indian studies are avalaible describing the etiopathogenesis and bone marrow morphology changes in severe anemia in adults. Our present study was designed as a prospective descriptive study of the haematological parameters and bone marrow morphology in patients with severe anemia.

2. MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology, Sree Balaji Medical College & Hospital under due approvals of the Institutional Research and Ethics Committee. Patients were sourced from the Department of General Medicine over a period of 18 months from April 2015 to September 2016.

Adult patients of age 18 years and more, who are presenting with severe anemia, fulfilling the WHO criteria of severe anemia (Hemoglobin < 8 gms/dl) and who consented for bone marrow examination were included in the study.

The patients were excluded as per the following Exclusion Criteria: (1) Patients with a history of recent transfusion (2) Patients who have undergone major surgical procedure in the past 3months. (3) Acute and Terminally ill patients. (4) Pregnant women.

Sixty five patients who satisfied our selection criteria were selected for the study. A detailed clinical interview was undertaken and all details regarding age, gender, presenting complaints, past history, history of exposure to chemicals or drugs, dietary habits, co-morbid conditions, were recorded. A detailed clinical examination and standardized set of lab investigations were done for all these patients. Complete Blood Count, Basic Clinical Chemistry, Liver Function Tests, Reticulocyte Count and Peripheral smear study were done. Radiological investigations such as roentgenogram, sonographic studies, CT scans and MRI were performed based on clinical needs. Some patients were given an endoscopic analysis of the upper and lower GIT as clinically required.

All the patients who were selected for the study were advised a bone marrow aspiration study as per standard clinical protocols of our hospital. Bone marrow was aspirated from the sternum or the posterior superior iliac crest, using a Salah needle. Aspirates were used to make 8- 10 smears. The smears were air-dried, fixed in methanol and stained with Leishman's stain as per standard protocol. One smear was stained for Pearl's stain for iron stores. The Bone marrow samples were examined and the findings were recorded in a standard format. The smears were assessed for (1)Degree of Cellularity -graded as hypocellular, normocellular or hypercellular (2) Relative distribution of erythroid, myeloid, and lymphoid cells (3) Morphological abnormalities of the erythroid, granulocytic, and megakaryocytic series (4) Presence of other cells. Iron stores were determined by Gale Grading method. [0-No iron granules,1-small granules in reticulum cells only under oil immersion,2-few granules visible with low power,3-Numerous small granules in all marrow particles,4-large granules in small clumps,5- Dense large clumps of granules.6-Very large deposits]

Grade 0:iron deficiency (7 BM particles)
Grade 1-3:normal iron stores
Grade 4-6:Increased iron stores.
The findings were recorded.

3. RESULTS

A 25 year old male from North East came presented with jaundice, massive

hepatosplenomegaly and had history of repeated transfusion. His Hb was 3.9 g%, RBC-5.8 million/cu.mm,WBC-6.6 X10^3 mm^3, Platelet was adequate.MCV was found to be 49 fl. Retic count was found to be 8%. RDW -12.6%. RBC count was increased and morphology showed mild anisocytosis and poikilocytosis with microcytic hypochromic cells with good number of target cells and nucleated rbcs (Fig. 5). Bone marrow was hypercellular with erythroid hyperplasia (Fig. 6). Iron stores were increased. Hb Elecrtrophoresis confirmed presence of HbE disease.

4. DISCUSSION

A cause for severe anemia needs to be determined in each patient as the etiology is often multifactorial. Bone marrow examination is required for the diagnosis and management of severe anemia. In the present study we analyzed the clinical, hematological parameters and the bone marrow aspiration findings in adult patients with severe anemia.

Iron deficiency anemia (IDA) is often associated with chronic blood loss resulting from gastrointestinal bleeding. In our study Upper and lower GI endoscopy done in 19 patients, detected lesions in 63% of patients in our study and malignancy in 3 patients (15.8%) and normal in 21% of the patients. Z. Fireman et al. [6] reported 24 out of 43 (55.8%) IDA patients having gastrointestinal lesions. They found erosive gastritis in 12 (27.9%), erosive duodenitis in 4 (9.3%), erosive

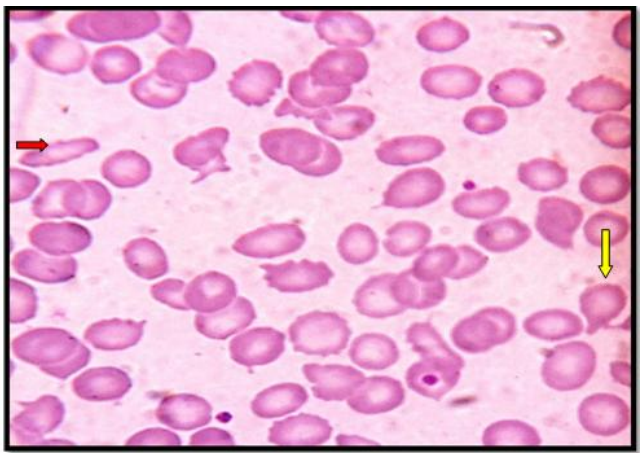

Fig. 1. Photomicrograph of a peripheral blood smear showing microcytic hypochromic RBCs with marked anisopoikilocytosis with pencil shaped cells(➢) and tear drop cells($)as in Iron Deficiency Anemia. *(Leishman 1000 X)*

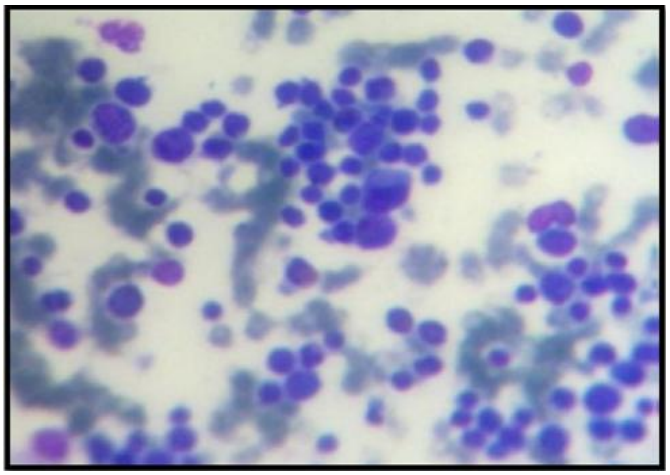

Fig. 2. Photomicrograph showing bone marrow smear with erythroid hyperplasia with micronormoblastic maturation.(*Leishman 400 X)*

esophagitis in 3 (7.0%), active duodenal ulcer in 1 (2.3%) , adenocarcinoma of the right colon in 2 (4.6%) and 1 case had (2.3%) had segmental colitis (Crohn's disease).

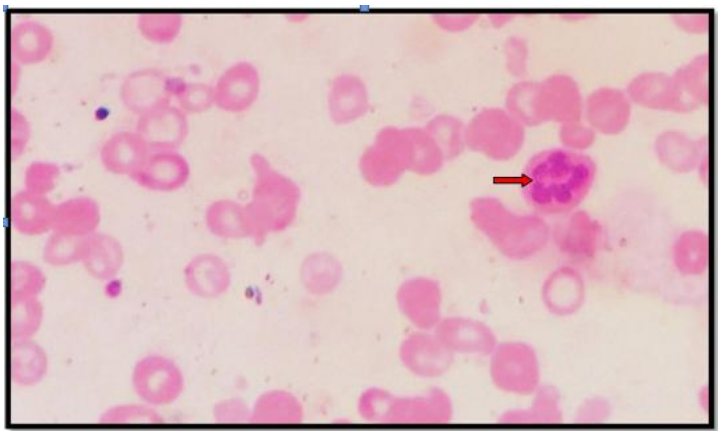

Fig. 3. Photomicrograph of a peripheral smear showing hypersegmentation of the neutrophil (<,6 lobes) in Megaloblastic anemia. (*Leishman 1000 X)*

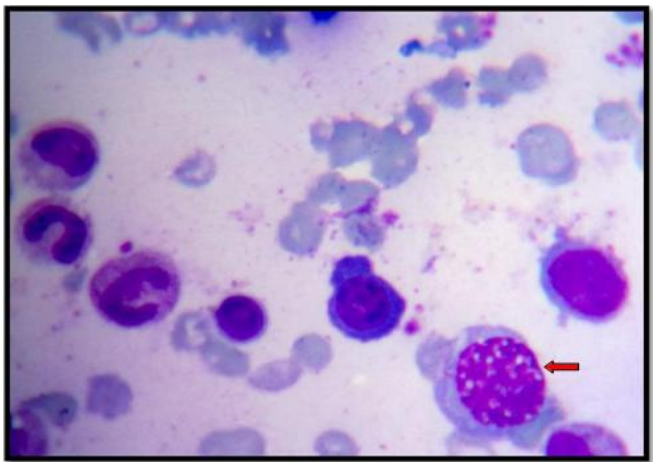

Fig. 4. Photomicrograph of a bone marrow smear showing megaloblast (sieve like chromatin, >) in Megaloblastic anemia *(Leishman 1000 X)*

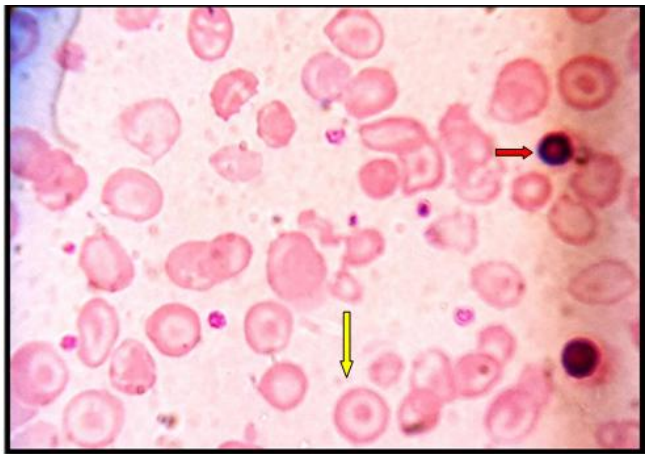

Fig. 5. Photomicrograph of a peripheral smear showing target cells ($) and nucleated red blood cells(<) in hemolytic anemia *(Leishman 1000 X)*

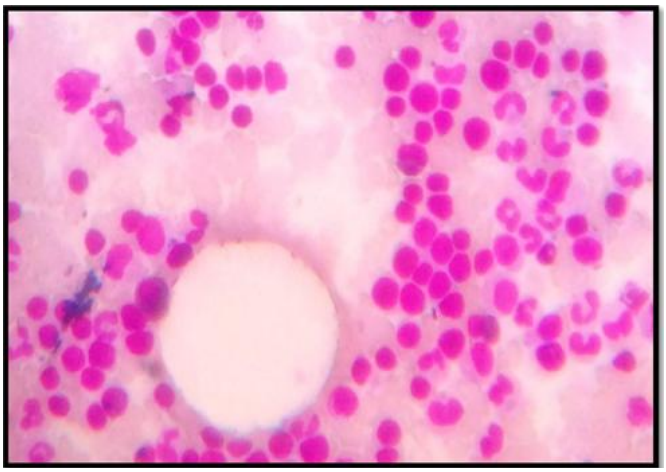

Fig. 6. Photomicrograph showing bone marrow smear with erythroid hyperplasia in hemolytic anemia. (*Leishman 400 X)*

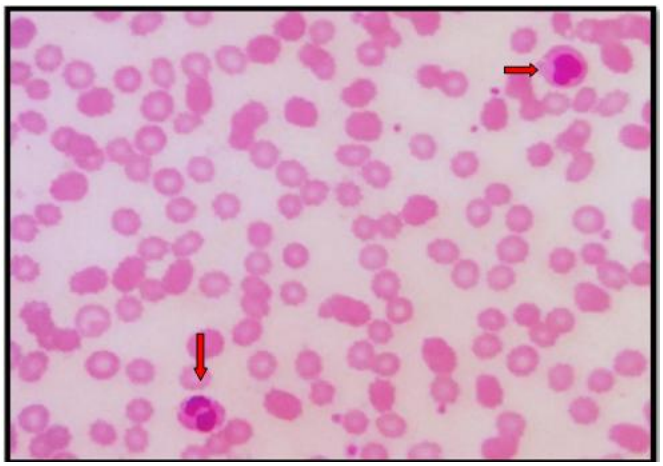

Fig. 7. Photomicrograph of a peripheral smear showing pseudo- Pelger-Huet cells ($) in a case of MDS.*(Leishman 400 X)*

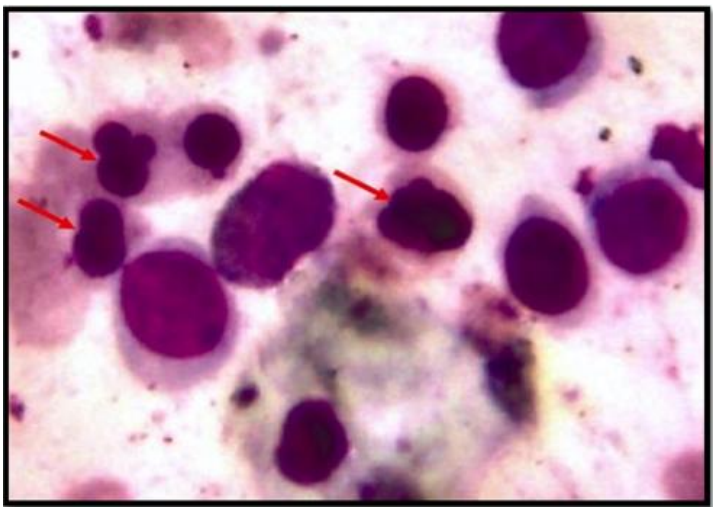

Fig. 8. Photomicrograph of a bone marrow smear showing Dyserythropoiesis $. *(Leishman 1000 X)*

Anemia of Chronic Disease(AOCD) most often presents as reactive marrow with normoblastic maturation in patients with severe anemia . In our study reactive marrow was found in 7 cases (10.7%), 85.7% occurring in age group 40-60 years and 14.2% in >60 years. In the present study, the co-morbid illnesses associated in this group of patients were Liver disease, Renal disease, GI or Genitourinary bleed and Tuberculosis. Momani et al., 72 ??observed AOCD common in 36-65 years age group (17.5%) among 200 cases. In the present study, AOCD presented as normocytic normochromic blood film in 57.1% and microcytic hypochromic anemia in 28.5% and macrocytic anemia in 14.2%. Elis et al. [6] found 93% of reactive marrow with normocytic normochromic blood film (n=38).

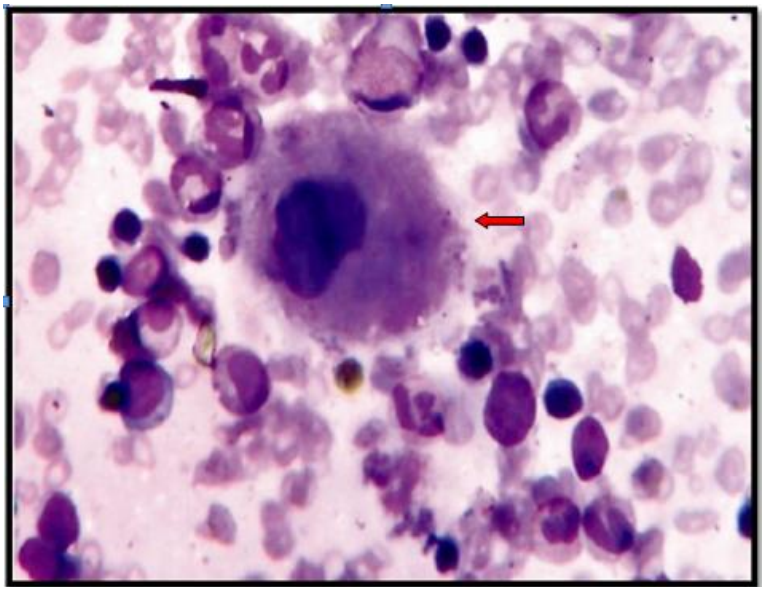

Fig. 9. Photomicrograph of a bone marrow smear showing a Hypolobated Megakaryocyte(➢).(Leishman 1000 X)➢

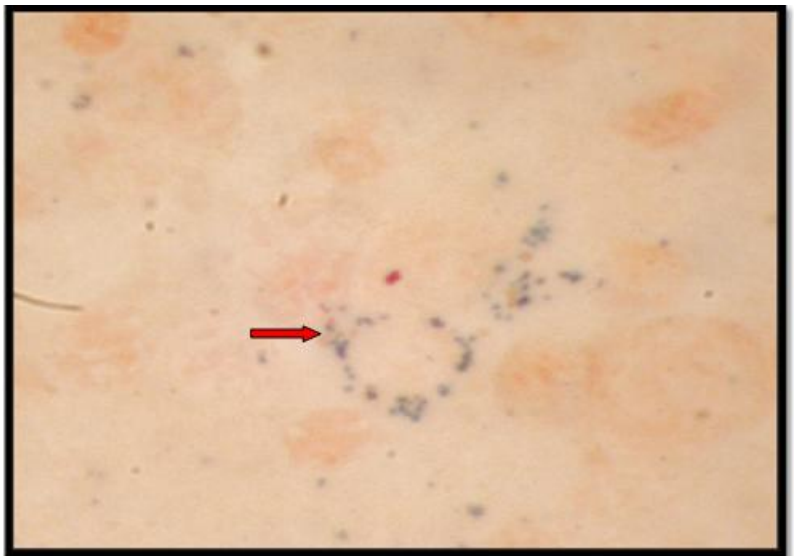

Fig. 10. Photomicrograph of a bone marrow smear showing ring sideroblast.(➢)(Pearl 1000 X)

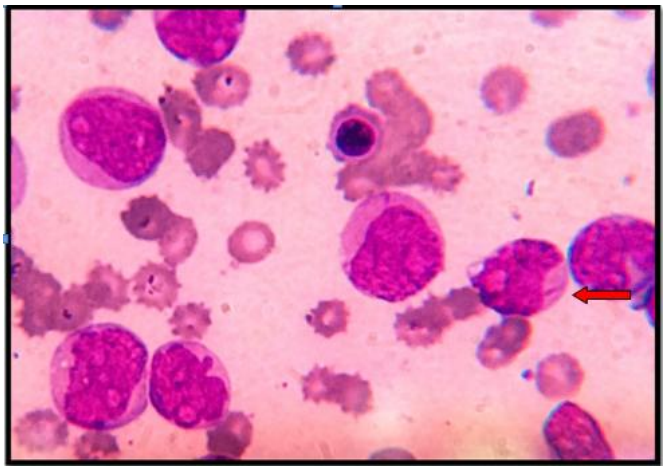

Fig. 11. Photomicrograph of a bone marrow smear showing myeloblasts with Auer rods in a case of AML.(➢) (Leishman 1000 X)

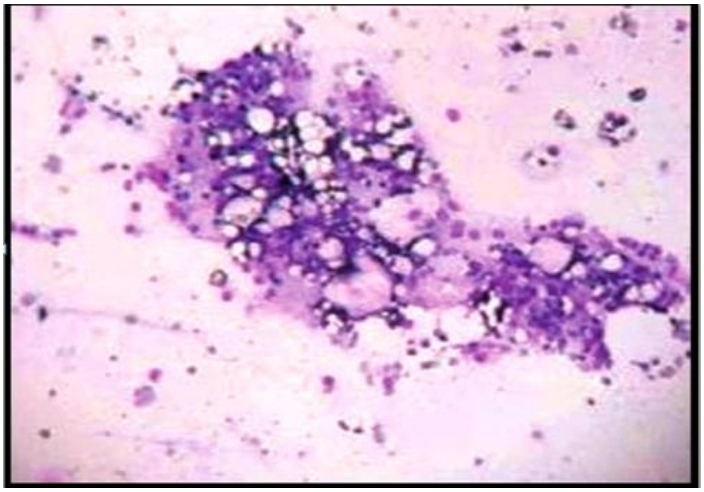

Fig. 12. Photomicrograph showing hypo≺cellular bone marrow smear.(Leishman 40 X)

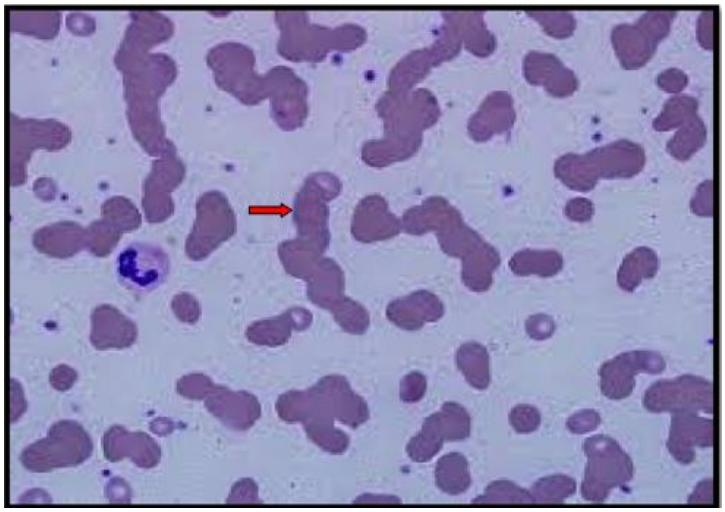

Fig. 13. Photomicrograph of a peripheral smear showing rouleux formation of the red blood cells in a case of Multiple Myeloma(≺).(Leishman 400 X)

In the present study, Megaloblastic anemia was observed in 18.5% of patients. This is similar to that shown by Pudasini et al. [7] who had shown a 12.3%(among 57 cases) of patients with Megaloblastic anemia. However Al-Ghazaly et al. 98 and Tahlan et al. [8] showed a high prevalence of 57% (among 78 cases) and 87% Megaloblastic anemia in their studies. It was common in age group >40 years in the present study. Khandhuri et al.,99 found it common in age group 10-30 years(48%) among 175 cases. In our study Macrocytic anemia was present in 41.6% of patients. Vineetha et al.,100 had shown a percentage of 34.8% macrocytic anemia among 60 adults with megaloblastic anemia. In our study, Pancytopenia was present in 50% of patients with Megaloblastic anemia. This is relatively correlates !! /consistent with Khandhuri et al. [9] reported pancytopenia in 62% but Kumar et al. [10] have shown a 20.3% of pancytopenia with megaloblastic anemia.

In the present study, Dual B12/ iron deficiency accounted for 16.9% of patients. This is similar to the observations of Athar et al. [11] (12.5%), but Tahlan et al., 69 ((is this mistakenly repeated to 69%)) showed higher percentage of 69% in their study. In our study, the common age group was above 60 years and Dimorphic blood film was present in 63.6%, Athar et al., has showed 84.4% of dimorphic peripheral smear report in dual deficiency and common in age group 21-30 years [9].

Malignant hematological disorders comprised 23% cases in the present study. Acute myeloid leukemia accounted for 6% of cases in our study. However Halim et al. [8] in their study have shown a higher 40.4% occurrence of Leukaemias in severly anaemic patients. Multiple myeloma accounted for 4.6% in our study. Tahlan et al., showed occurrence as 7% [9]. Lymphoma infiltration of the bone marrow was present in 1.5% in the present study. In a large European Cancer Anemia Survey (ECAS), enrolling 2360 lymphoma and myeloma patients, showed that 52.5% were anaemic,73% severe anemia after 6 month follow up due to chemotherapy [8]. In our study MDS was present in 4.6%. Malcovati et al. [9] has showed that severe anemia occurs in 10% of MDS cases due to severe bone marrow fibrosis. Hypoplastic anemia accounted for 4.6% in oue study, but Halim et al. [12] showed 29%. Bone marrow biopsy was essential to find the etiology of hypocellularity. Metastasis of unknown primary occured in 1.5%. Kaur et al. [13] have showed that 77.7% patients are anaemic with secondaries in the bone marrow. Further workup was essential to confirm the primary tumor. Hemoglopinopathy (Hb E) occurred in 1.5% in our study. In a study by Chopra et al. [7] analysed anemic patients and found abnormal hemoglobin pattern in 25%, Hb E was found in 0.8% in their study [14-25].

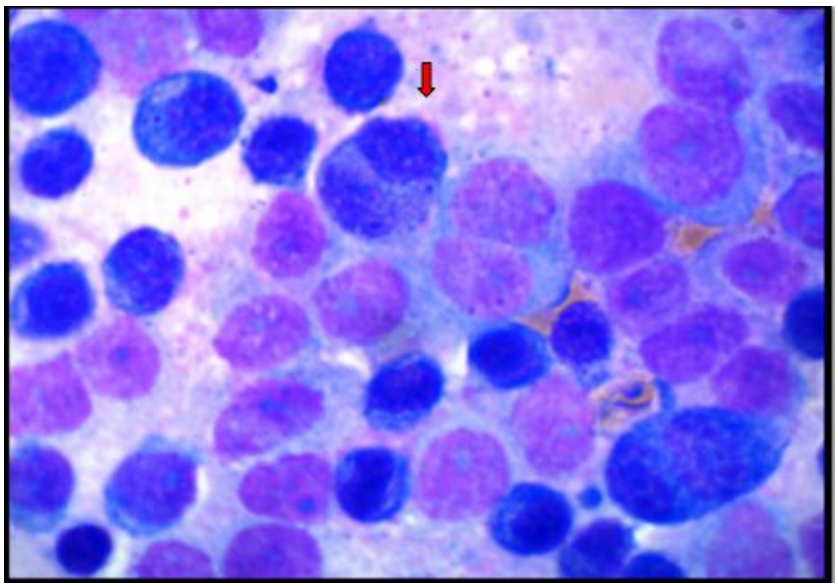

Fig. 14. Photomicrograph of a bone marrow smear showing plasma cells in a case of Multiple Myeloma. (Leishman 1000 X)

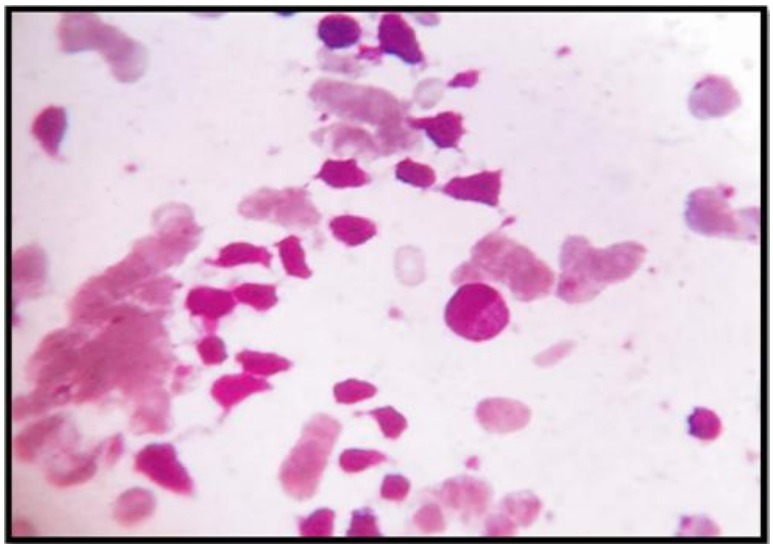

Fig. 15. Photomicrograph of a bone marrow smear showing leukemic infiltration of NHL. *(Leishman 400 X)*

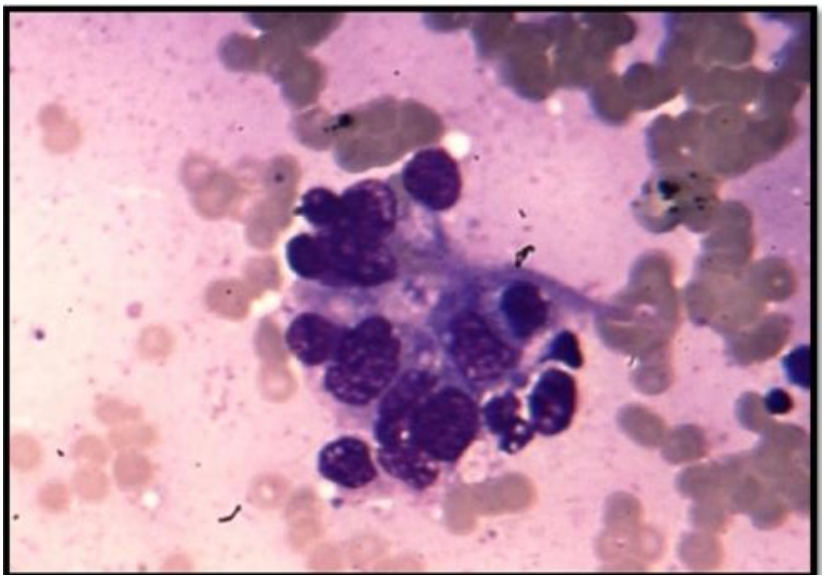

Fig. 16. Photomicrograph of a bone marrow smear showing cluster of pleomorphic non-hematopoietic cells in a case of metastasis to the bone. (***Leishman 1000 X)***

5. CONCLUSION

Severe anemia is more common in the elderly with female predominance. Fatigue and breathlessness were the common presentation. Nutritional anemia is the most common etiology and malignant disorders constitute 10.7% with predominant haematological malignancies.

Adult patients with severe anemia should always be evaluated for an underlying cause. Hence a Bone marrow examination which aids in identifying various haematological disorders, is necessary in all the cases of severe anemia for management.

CONSENT

Informed written consent was taken and preserved by the author.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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