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Original research article

Evaluation of Pancytopenia – A Clinico-Hematological Study in A Tertiary Care Hospital in Bihar

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Abstract

Background: Pancytopenia is defined as reduction of all the three formed elements of blood below the normal reference level. It is an important clinical haematological entity encountered in our day-to-day clinical practise. It may be a presentation of wide variety of disorder, which primarily or secondarily affect the bone marrow. This study was under taken to find out the various causes of pancytopenia by bone marrow examination.

Material and Method: The study was carried out over a period of 2 year and 6 months, from May 2019 to October 2021. Total 100 patient who had pancytopenia were included in the study. Based on clinical findings, complete blood count and peripheral blood smear examination, bone marrow aspiration and biopsy were carried out. All the aspirate smear were stain with Leishman stain and trephine biopsies were stained with hematoxylin and eosin.

Result: Total 100 cases of pancytopenia were included in study, out of which 63 were male and 37 were female. Most of the patient were in the age group of 3-20 year. Based on the clinical findings bone marrow aspiration and biopsy, the commonest cause of pancytopenia was megaloblastic anemia (52%) followed by aplastic anemia (28%), acute leukemia (8%), myelodysplastic syndrome (MDS) (3%), osseous neoplasm (2%), metastatic deposite (2%), haemolytic anemia (2%), renal bone disease 1%, multiple myeloma (1%) and kalazar (1%).

Conclusion: Bone marrow aspiration and trephine biopsy along with physical examination and other haematological investigation is essential in diagnosis of cases of pancytopenia.

Introduction

Pancytopenia is a common hematological problem, which creates a diagnostic dilemma in our day to day clinical practise.(1) It is defined as reduction of all the three cellular elements of blood below the normal reference,(ie, RBC, WBC and Platelet) in peripheral blood.(2) As the bone marrow is the site for hematopoiesis in body, any condition affecting the marrow will lead to pancytopenia. This may be due to ineffective red cell production, decreased cell production, increased utilization of cells and increased destruction without an adequately matching compensatory increase in the cell production (3). The cause of pancytopenia may be thus lies in the bone marrow, periphery or both.

Pancytopenia is not a disease itself; it is a triad of findings which result from either Primary or Secondary disease of bone marrow. [4] Etiology of pancytopenia varies from drug induced bone marrow hypoplasia, Vit B-12 deficiency, infection, congenital bone marrow failure, marrow space occupying lesion to leukemia. [5]It varies in different population depending on the climate, prevalence of infection, nutritional status and differences in age groups. [6] Hence bone marrow examination is extremely useful in evaluation of pancytopenia. [7]

Pancytopenia patient present with symptoms like fatigue and weakness due to anemia, increased susceptibility to infection due to leucopenia and excessive bleeding due to thrombocytopenia. [8] Study aimed to identify the etiology and bone marrow morphology of pancytopenia patients.

Materials and methods:

Study design: A retrospective observational study of 2 year and 6 months conducted at a tertiary care centre in Bihar.

Duration of study: May 2019 to October 2021(2 year and 6 month).

Study Population: All patients coming to Hematology department with relevant clinical features and hematological findings suggestive of pancytopenia.

Place of study: Department of Hematology, IGIMS Patna.

Inclusion criteria:
All patients presenting with relevant clinical features and hematological findings suggestive of pancytopenia going for bone marrow examination with;
Hemoglobin<9 g/dL
Total leukocyte count (TLC)<4,000/ μL;
Platelet count<100,000/ μL

Exclusion criteria:
1. All cases who have already been diagnosed with pancytopenia.
2. Patients who have recently received blood transfusion or on prior chemotherapy /radiotherapy.

Sample collection and parameters estimation: The required quantity of venous blood was collected in EDTA vials. The collected blood was analysed by using fully automated analyser, SIEMENS ADVIA 2120i having 6 parts from which CBC was estimated and subsequently peripheral blood smears was prepared and stained with Leishman's stain. Subsequently Bone marrow aspiration and biopsy was done and slides stained with Leishman's stain and trephine biopsies were stained with hematoxylin and eosin was evaluated.

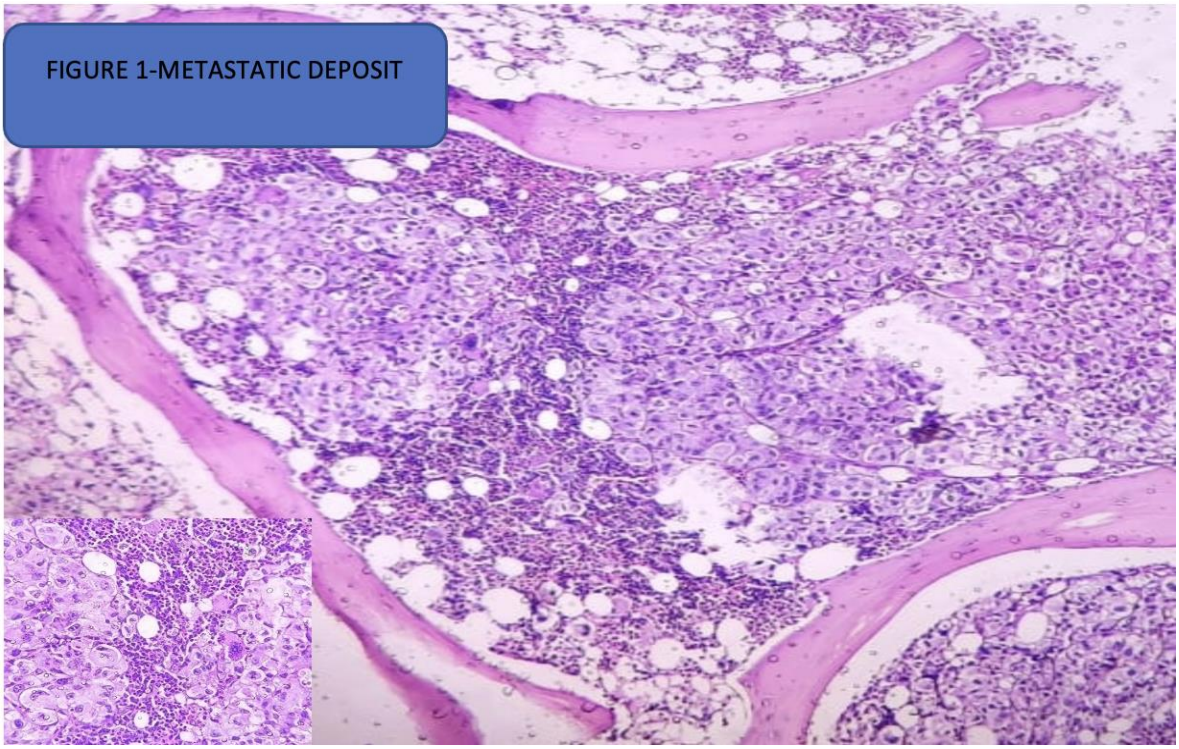
Result:
Total 100 patient of pancytopenia fulfilling the inclusion criteria and undergoing bone marrow aspiration and biopsy were included in study. Age ranged from 3 year to 82 years. Majority of patient were in age group of 3 to 20 year. Out of 100, 63 were male and 37 were female. The male to female ratio was 1.7:1.

The commonest presenting complaint was generalised weakness in 68 % followed by fever in 45 %. Other presenting complaints were fatigue, breathlessness and icterus. Pallor was present in almost all cases. Bleeding manifestation like epistaxis, gum bleeding and petechial rashes were seen in 18 % cases. Spleenomegaly was seen in 30 % cases and hepatomegaly was seen in 22 % cases. Lymphadenopathy was seen in 15 % cases.

Table 1: Clinical presentation of pancytopenia

Clinical finding	Percentage
Pallor	100
Weakness	68
Fever	45
Splenomegaly	30
Hepatomegaly	22
Pain abdomen	25
Bleeding	18
Dyspnea	18
Weight loss	18
Lymphadenopathy	15
Icterus	12
Bone pain	08
Others(Decrease apetite, diarrhoea, vomiting)	15

The commonest cause of pancytopenia was megaloblastic anemia and was seen in 52% cases, followed by aplastic anemia 28%, acute leukemia 8%, myelodysplastic syndrome 3% and metastatic deposite 2%. Other causes include osseous neoplasm 2%, haemolytic anemia 2%, renal bone disease 1%, multiple myeloma 1% and kalazar 1%.



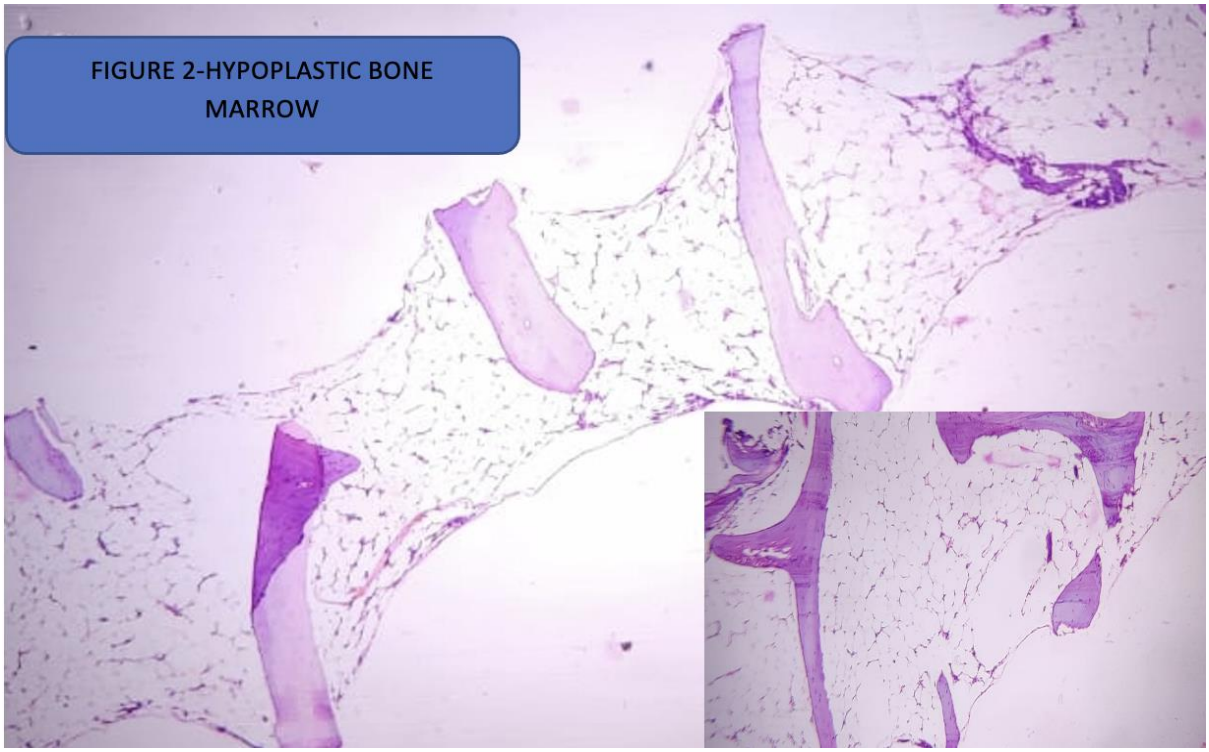


FIGURE 2-HYPOPLASTIC BONE MARROW

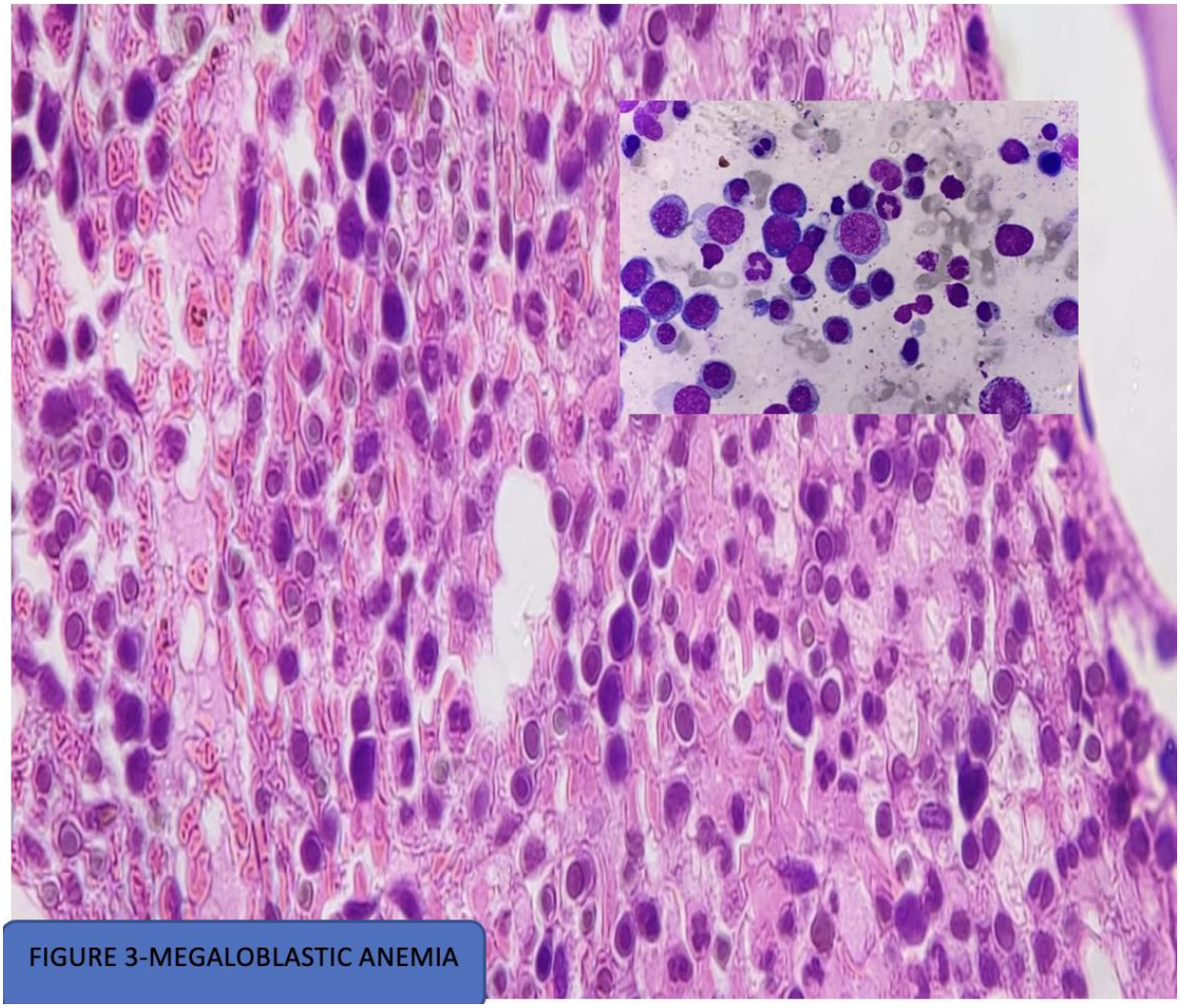


FIGURE 3-MEGALOBLASTIC ANEMIA

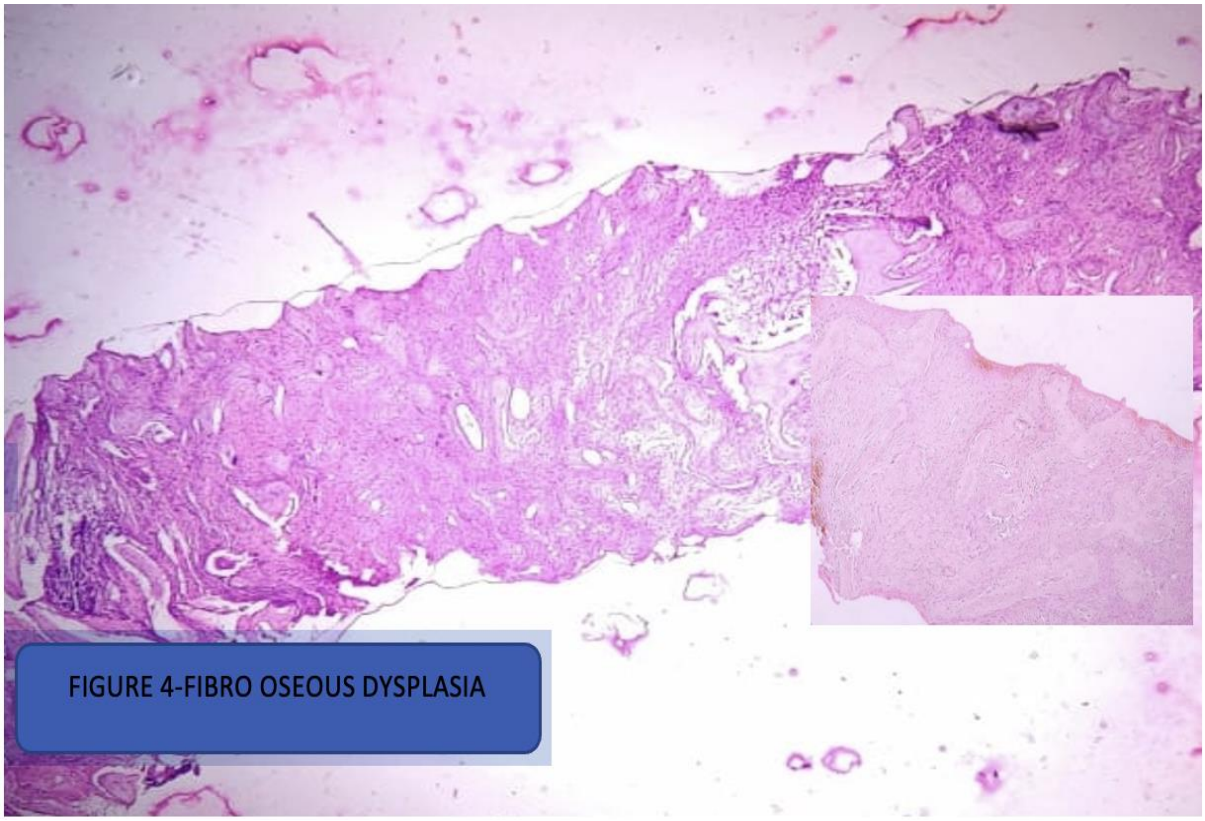


FIGURE 4-FIBRO OSEOUS DYSPLASIA

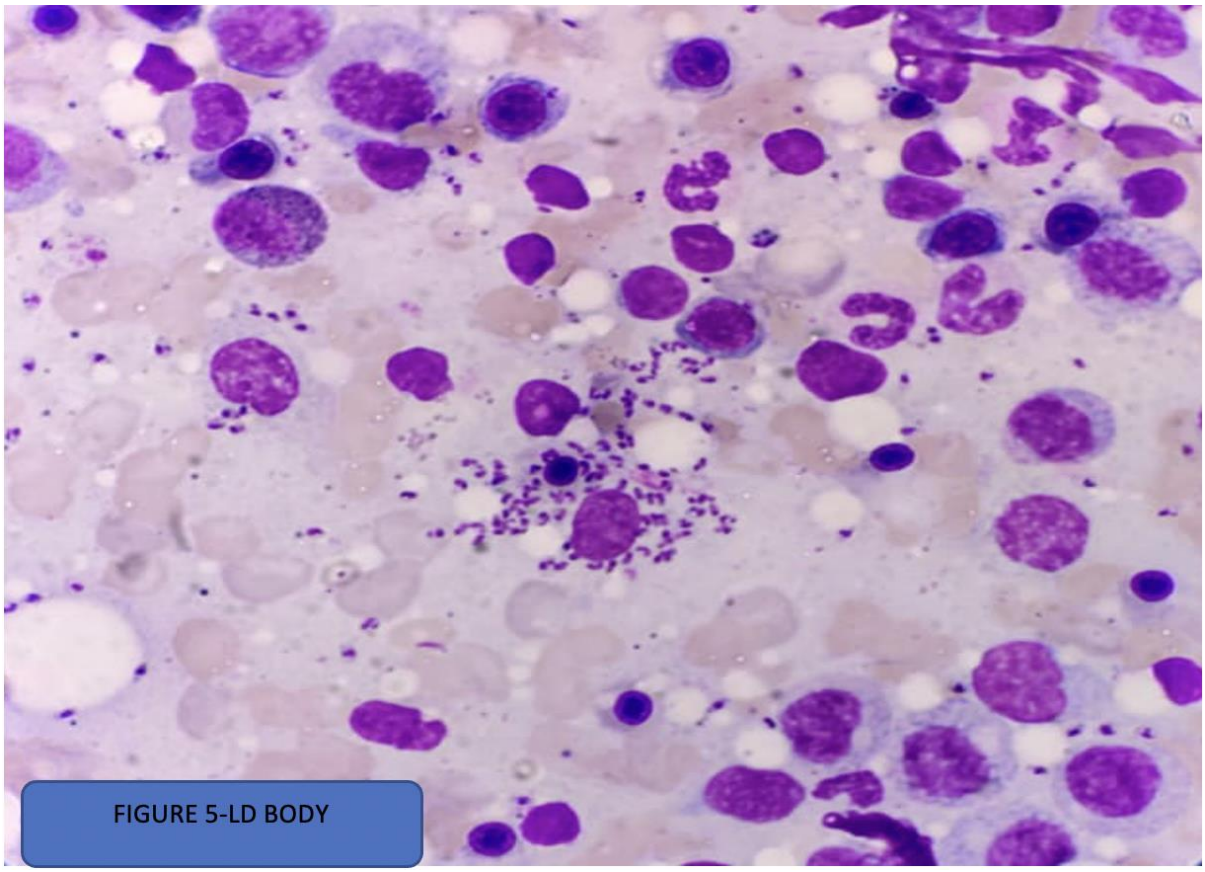


FIGURE 5-LD BODY

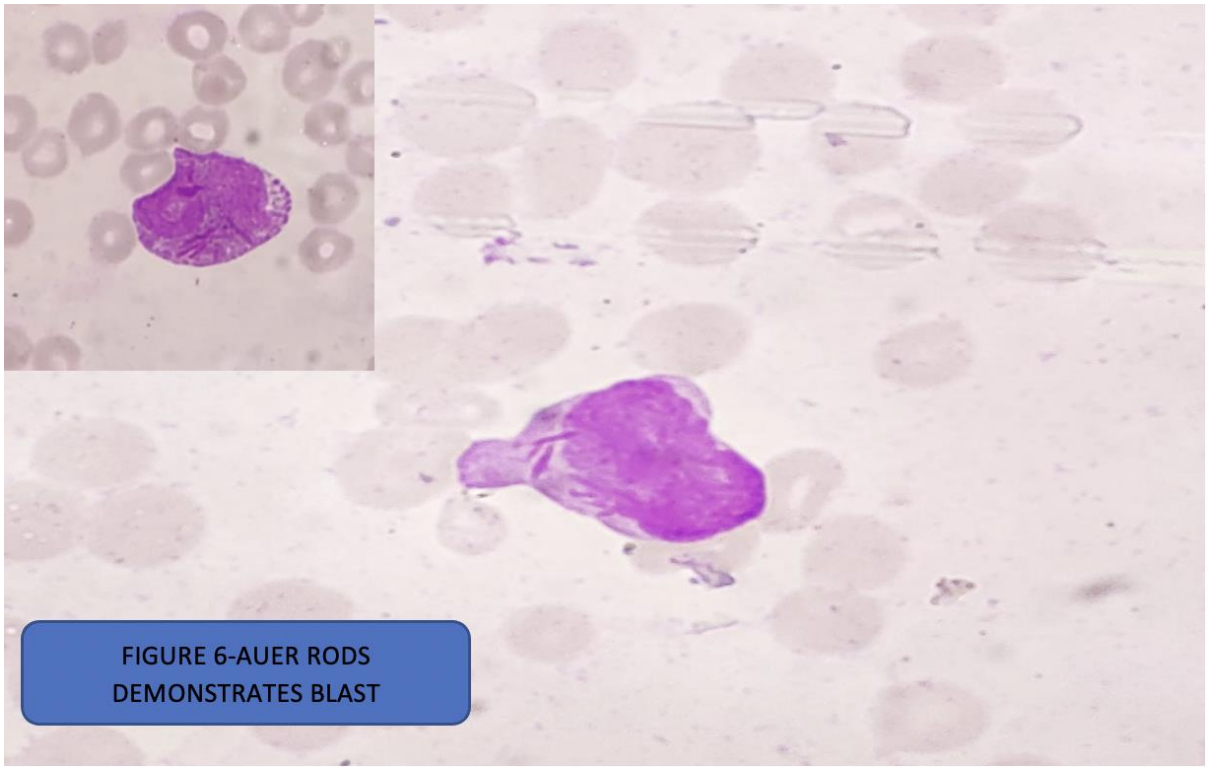


Table 2: ETIOLOGY OF PANCYTOPENIA IN VARIOUS STUDIES

Study	Country	Year	No of cases	Commonest cause	Second commonest
1.International agranulocytosis and aplastic anemia group	Israel & Europe	1987	319	Hypoplastic anemia (52.7%)	Myelodysplastic syndrome (4.5%)
2.Hossain M. et al[12]	Bangladesh	1992	50	Aplastic anemia	Chronic malaria and Kalaazar
3. Tilak V and Jain R[14]	India	1998	77	Megaloblastic anemia (68%)	Aplastic anemia (7.7%)
4. Khodkeel a[9]	India			Megaloblastic anaemia (44%)	Aplastic anemia (14%)
5.Khunger et al	India	2001	200	Megaloblastic anemia (72%)	Aplastic anemia (14%)
6. Gayathri etal[5]	India	2007	104	Megaloblastic anemia (74.04%)	Aplastic anemia (19%)
7. Aziz etal[16]	Pakistan	2007	88	Megaloblastic anemia (40.90%)	Aplastic anemia (31.88%)
8. Jha et al[15]	Nepal	2008	148	Hypoplastic Anemia (29.5%)	Megaloblastic anemia (23.64%)
9. Jigneashetal	India	2009	100	Megaloblastic anemia (45%)	

10. Gayathri BN et al[5]	India	2011	104	Megaloblastic anemia (74.04)	Aplastic anemia (18.26)
11. Kumar DB et al[13]	India	2012	48	Hypoplastic marrow (33.33)	Normoblastic erythroid hyperplasia (27.08)
12. Makhejia DK et al	Pakistan	2013	62	Megaloblastic anemia	AML
13. Chandra K et al	India	2014	83	Megaloblastic anemia	Acute leukemia
14. Vaidya S et al	Nepal	2015	83	Megaloblastic anemia	Aplastic anemia
15. Jella R et al[10]	India	2016	56	Megaloblastic anemia	Aplastic anemia
16. Shah P et al[11]	India	2017	40	Megaloblastic anemia	Aplastic anemia
17. Present study	India	2022	100	Megaloblastic anemia	Aplastic anemia

Discussion:

In the present study megaloblastic anemia was the commonest cause of pancytopenia. This constitutes 52% of total cases of pancytopenia. Findings are similar to other studies. Tilak and Khodke et al in which megaloblastic anemia was the commonest cause of pancytopenia. [9]Jella R et al (2016) in their study of 56 cases of pancytopenia concluded megaloblastic anemia (42.9%) as the most common cause followed by aplastic anemia (23.2%), malaria and rheumatoid arthrirtis each 7.1%. Other causes being hematological malignancies, liver disease, DIC, septicemia, dengue, tuberculosis. [10]Shah P et al (2017) studied 40 cases of pancytopenia out of which commonest cause was megaloblastic anemia (35%) followed by aplastic anemia (32.5%). Other causes included acute leukemia, myelodysplastic syndrome (MDS) and round cell tumor.[11]However these findings are in sharp contrast with various studies worldwide. Hossain MA et al observed aplastic anemia was the commonest cause of pancytopenia. [12]Kumar DB et al (2012) conducted a study on 48 cases of pancytopenia. The commonest cause of pancytopenia was hypoplastic marrow (33.33%), followed by normoblastic erythroid hyperplasia (27.08%), megaloblastic marrow (18.75%), and myelodysplastic syndrome (8.33%). [13]This may be due to high prevalence of nutritional anemia and severe malnutrition in Indian population. Our result was comparable to study done by BN Gayatri and Kadam where the most common cause of pancytopenia is megaloblastic anemia (74.04%), followed by aplastic anemia (18.26%). [5]Occurrence of megaloblastic anemia was 72% and 68% in studies done by Khunger et al and Tilak et al. [14]All the above studies have been carried out in India and they have shown the importance of megaloblastic anemia being the major cause of pancytopenia.

Aplastic / Hypoplastic anemia is another frequent cause of pancytopenia in present study (28%). Jha et al and Pathak et al have aplastic anemia as commonest cause of pancytopenia. [15] Aplastic anemia is relatively common and is seen in both children and adult. Although the majority of cases are idiopathic, this disease can be caused by multiple etiologies including drugs, chemicals, radiation, viruses, anorexia and even pregnancy. Although the exact mechanism is unknown, idiopathic aplastic anemia is thought to be the result from an attack of

effector T lymphocyte on hematopoietic stem cell, resulting in bone marrow failure and peripheral pancytopenia.

Paroxysmal nocturnal hemoglobinuria demonstrate a peculiar relationship with aplastic anemia. Patient who presents with paroxysmal nocturnal hemoglobinuria clones can eventually progress to aplastic anemia and patient with aplastic anemia can develop PNH clones.

Acute leukemia was found to be the third most common cause of pancytopenia. Study show 8% cases of pancytopenia was diagnosed as acute leukemia, which is similar to study done by Aziz et al (10%). [16]Immature cell can be seen in peripheral blood smear, however, bone marrow examination establishes the diagnosis.
Myelodysplastic syndrome(MDS) was diagnosed as cause of pancytopenia in 3% cases, however International agranulocytosis and Aplastic anemia group diagnosed it as second most common cause of pancytopenia.
Metastatic deposites of prostate and lung seen in 2% cases.Deposite of NHL is seen in 1 case. In present study 2 patient of haemolytic anemia present with pancytopenia. Osama et al in their study found 2% cases of pancytopenia with haemolytic anemia. Renal bone disease was diagnosed in bone marrow biopsy in 1 case. Multiple myeloma and kalazar was found in 1 case of each.

Conclusion:
Pancytopenia is a common entity in clinical practise and should be evaluated completely. However, it has received inadequate attention in the Indian subcontinents. The present study concludes that detailed physical examination, haematological investigation along with bone marrow aspiration and trephine biopsy are useful to diagnosed causes of pancytopenia. These are also useful in planning further investigation and proper treatment.

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