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"Clinico Hematological study in cases of pancytopenia"

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ABSTRACT

BACKGROUND: Pancytopenia is a common clinical presentation seen in pateints attending general OPD.

OBJECTIVE: To study and assess the haematological and bone marrow findings in various cases of pancytopenia.

MATERIAL & METHODS: Study Design: prospective analytical study.**Study area:** The study was conducted in the haematology section of Department of Pathology of Jawaharlal Nehru Medical College; Sawangi (M). **Study Period:** 1st July 2014 to 31st July 2016. **Study population:** patients attending outdoor and indoor department of AVBRH.**Sample size:** Total 53 cases were subjected for clinical and hematological study.

RESULTS: In the present study in females, pancytopenia was common in the age group of 21-30 years, in males **,** pancytopenia was common in the age group of 11-20 years. The commonest finding in the present study was Megaloblastic anemia in 28 cases i.e. (52.8%), followed by Acute leukemia in 11 i.e. (20.8%) followed by Normoblastic erythroid hyperplasia in 6 cases i.e. (11.3%) , followed by Aplastic anemia in 5 cases i.e. (9.4%) other causes were Mixed nutritional anemia, Multiple myeloma and Non-Hodgkin's lymphoma all had 1(1.9%) case each.

CONCLUSION: The study showed Megaloblastic anemia was a common hematological abnormality among peripheral pancytopenia in our region. Most patients were between 21-30 years of age group presenting with Generalized weakness, fever, bleeding and edema. Male to female ratio was 1:1.12.

Key words: Pancytopenia, Megaloblastic anemia

INTRODUCTION:

Pancytopenia is defined as the reduction in all 3 formed elements of blood RBCs, WBCs, & platelets below the normal limit. The term was used almost synonymously for aplastic anaemia, it being the major cause of pancytopenia in the western countries.[1] Aplastic anemia is a life-threatening bone marrow failure disorder, if untreated, is associated with very high mortality. The incidence of Aplastic anemia is higher in Asia than in the West. It appears to be 2 to 3 fold more common in Asia than in Europe.[2] The etiology of pancytopenia varies ranging from the

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transient marrow viral suppression to marrow infiltration by life threatening malignancies.

Etiological spectrum in children ranges from common condition like Iron deficiency anemia to relatively rare congenital disorders like Fanconi anaemia. It is relatively different in the developing countries from the developed ones. Primary or genetic causes include Dyskeratosis congenita, Shwachman Diamond syndrome, and Amegakaryocytic thrombocytopenia. Acquired causes can be idiopathic or secondary to exposure to radiation, drugs and chemicals (chemotherapy, chloramphenicol, sulfa group, antiepileptic, gold etc.), viral infection (Cytomegalovirus, Epstein-Barr, Hepatitis B or C, Human immunodeficiency virus etc.), Autoimmune, Paroxysmal nocturnal hemoglobinuria and Marrow replacement disorders (Leukemia, Myelodysplasia, Myelofibrosis).[5] Frequency may vary from 0.8%, 1% and1.2%, 6 to 12.6%. [6] Megaloblastic anemia and infections such as enteric fever, malaria, kala-azar and bacterial infections can be common causes of pancytopenia in the developing countries. Nutritional Megaloblastic anemia is also one of the leading causes of pancytopenia in younger children.[7]

Most common non-malignant cause of acquired pancytopenia is Aplastic anemia followed by Megaloblastic anemia. Among the malignant causes, Acute leukemia is the most common. Pancytopenia caused by marrow replacement is seen to occur in leukemia. Non-malignant conditions are Immune Thrombocytopenic Purpura (ITP), Megaloblastic anemia, marrow hypocellularity and Visceral Leishmaniasis.

Careful examination of peripheral blood smear for Red blood cell (RBC), Leucocyte, Platelet count and morphology is important. A Reticulocyte count should be done to assess erythropoietic activity. Bone marrow examination should include bone marrow aspiration along with biopsy wherever indicated. Marrow should be carefully examined for morphology and cellularity.

Bone marrow examination is a simple and safe invasive procedure, which causes a moderate discomfort and can be performed easily. Its greatest utility is for investigating and it is an important diagnostic modality for evaluating the causes of pancytopenia.[9]

In India, the causes of pancytopenia are not well defined, so the present study has been undertaken to evaluate, the various causes and to correlate the peripheral blood findings with bone marrow aspirate.[11, 12]

Thereby, this data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia. Treatment and prognosis of patients with pancytopenia are governed by the cause and severity of the underlying disease.[11]

OBJECTIVES: To study and assess the haematological and bone marrow findings in various causes of pancytopenia in our region.and their correlation with age and sex.

MATERIAL & METHODS:

- **Study Design:** prospective analytical study.
- **Study area:** The study was conducted in the haematology section of Department of Pathology of Jawaharlal Nehru Medical College; Sawangi (M).

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- **Study Period:** 2 yrs.
- **Study population:** patients attending outdoor and indoor department of AVBRH.
- **Sample size:** Total 53 cases were subjected for clinical and hematological study.
- **Inclusion criteria:** Patients of all age group and sex presenting with pancytopenia.
- **Exclusion criteria:** Patients having Pancytopenia due to the effect of chemotherapy, radiotherapy and immunosuppresants were excluded.

Diagnostic criteria for Pancytopenia:-[17]

i) Hemoglobin less than 10 gms/dl,

ii) Total leucocyte count <3500/cumm,

iii) Platelet count less than 1, 00,000/cumm.

Complete history was taken and physical examination was performed. For hematological study, blood samples were collected in Ethylene diamine tetra acetic acid (EDTA) anticoagulant. CBC was carried out using Automated Hematology Analyser (three part) **(Sysmex) KX-21**(Transasia). Hematological parameters considered in this study were Hemoglobin, Total leucocyte count, Platelet count and Red cell mass. Peripheral smears were stained using Leishman's stain for all the cases and examined in detail. Informed consent was taken from all patients prior to enrollment in the study. Bone marrow aspiration was then carried out under all aseptic precautions and slides were stained with Leishman's stain.

OBSERVATIONS & RESULTS

Graph 1:- Age and sex distribution of 53 cases of pancytopenia

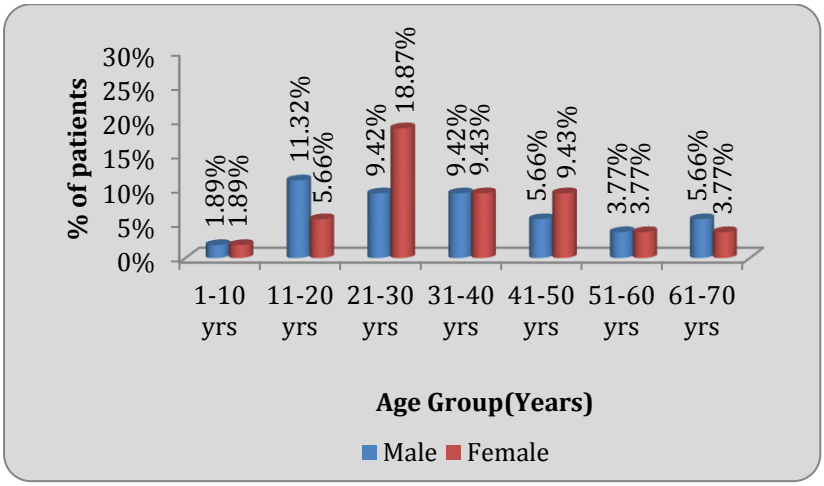

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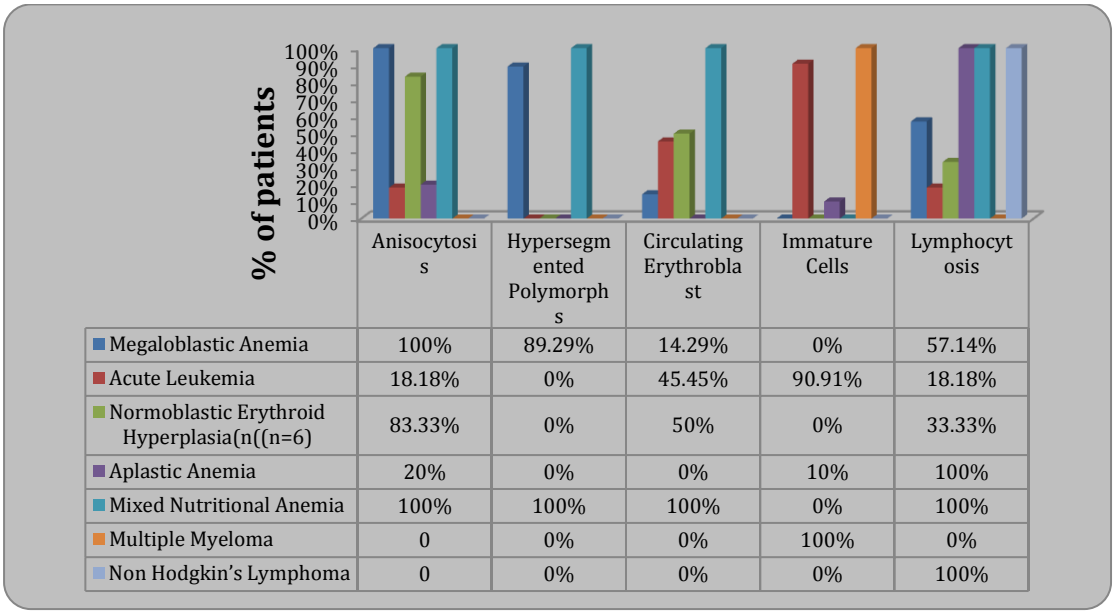
Table 1:-Total no. of diagnosed cases of pancytopenia

Diagnosis	No of Cases (n=53)	Percentage%
Megaloblastic Anemia	28	52.8%
Acute Leukemia (AML)	11	20.8%
Normoblastic Erythroid Hyperplasia	06	11.32%
Aplastic Anemia	05	9.4%
Mixed Nutritional Anemia	01	1.9%
Multiple Myeloma	01	1.9%
Non Hodgkin's Lymphoma	01	1.9%

Graph 2:- Peripheral Blood findings in 53 cases of Pancytopenia



	Anisocytosis	Hypersegmented Polymorphs	Circulating Erythroblast	Immature Cells	Lymphocytosis
Megaloblastic Anemia	100%	89.29%	14.29%	0%	57.14%
Acute Leukemia	18.18%	0%	45.45%	90.91%	18.18%
Normoblastic Erythroid Hyperplasia(n((n=6)	83.33%	0%	50%	0%	33.33%
Aplastic Anemia	20%	0%	0%	10%	100%
Mixed Nutritional Anemia	100%	100%	100%	0%	100%
Multiple Myeloma	0	0%	0%	100%	0%
Non Hodgkin's Lymphoma	0	0%	0%	0%	100%

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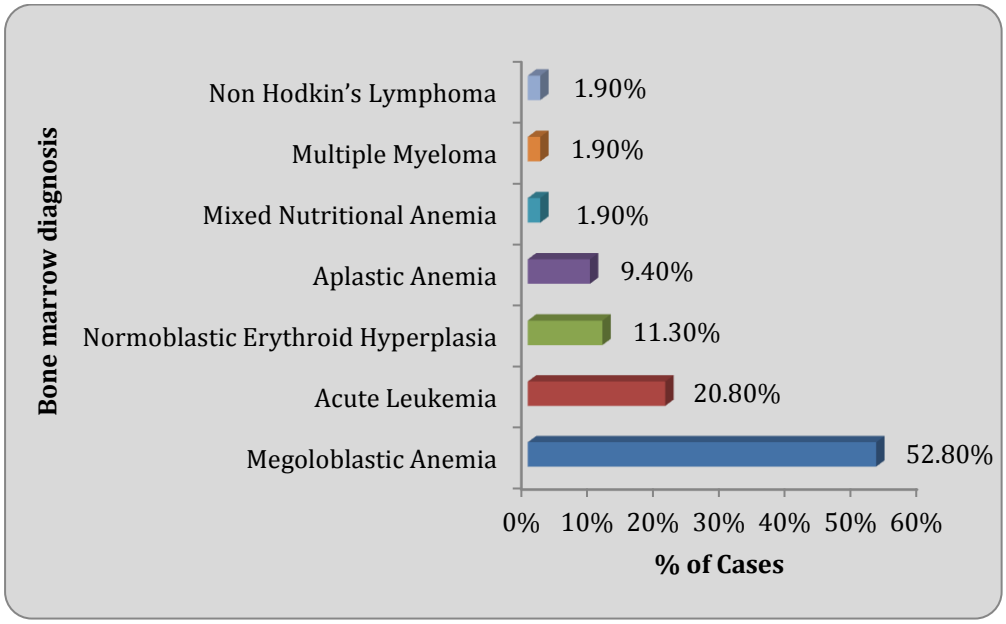
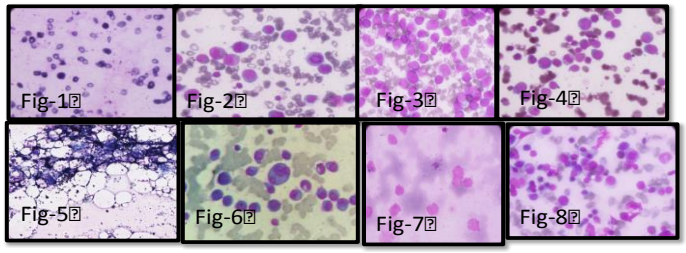
Graph 3:- Bone marrow diagnosis in 53 cases of Pancytopenia





All (Leishman's stain) (1oo×)
Fig 1 - *PBS showing decreased red cell mass*
Fig 2 - BMA showing megaloblast having sieve like chromatin in Megaloblastic anemia
Fig 3 - BMA showing Myeloblasts in Acute myeloid leukemia
Fig 4 - BMA showing hypercellular marrow with Erythroid hyperplasia
Fig 5 - BMA showing increased fat spaces with trapped lymphocytes and plasma cells in Aplastic anemia
Fig 6 - BMA showing predominant population of plasma cells in Multiple Myeloma
Fig 7 - *BMA showing deposits of Lymphoma cells in Non Hodgkin's lymphoma*
Fig 8 - *BMA showing Micronormoblast and Megaloblast in Mixed nutritional anemia*

DISCUSSION

Examination of the bone marrow is a key element in diagnosing many haematological and non-haematological disorders.

Pancytopenia can result from failure of production of hematopoietic progenitors, their destruction, or replacement of the bone marrow by tumor

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or fibrosis. Although selective cytopenias are important clinical entities, pancytopenia is a loss of all marrow elements. Careful examination of peripheral blood smear for red blood cell, leucocyte and platelet morphology and counts are important.

In the present study there was a female preponderance (52.83%) with a male to female ratio of 1:1.12. Present study correlated well with the findings of **Kumar et al (2012)** [9] **Aziz et al (2010)** [10] and **Agarwal et al (2015)**[11] they found females to be commonly affected in their study.

Studies like **Jha et al (2008)**[12]**, Memon et al (2008)**[5]**, Gayathri et al (2011)**[13] showed male predominance, this was in contrast with the present study as probably , females are the undernourished strata of the society in a developing country hence, commonly affected.

In the present study highest number of patients i.e**.** 15 (28.30%) belonged to the age group of 21-30 years followed by 10 patients **(**18.87%) in the age group of 31-40 years. Present study has similar findings and is in close proximity with the studies done by **Agarwal et al (2015)**[11] **and Pathak et al (2012).**[14]

In the present study, out of total 53 cases the commonest cause was found to be Megaloblastic anemia in 28 cases i.e. (52.8%) second common was found to be Acute leukemia in 11 cases i.e. (20.8%) followed by Normoblastic erythroid hyperplasia in 6 cases i.e. (11.3%), followed by Aplastic anemia in 5 cases i.e. (9.4%).

Megaloblastic anemia was the commonest cause that was observed in 52.8% (28/53) in the present study hence, the present study is in concordance with the findings of Makheja et al (2013)[15] who also found the commonest cause to be Megaloblastic anemia i.e. 41.9%, followed by Acute leukemia 27.4%, and Aplastic anaemia 19.4%.

Increased incidence of Megaloblastic anemia in the study was probably due to high prevalence of nutritional anemia in the non-industrialized world. In the present study isolated megaloblastic anemia was the most common cause. Megaloblastic anemia is a group of disorder characterized by the presence of distinctive morphologic appearances of the developing red cell in the bone marrow. The commonest cause of megaloblastic anemia is folate and cobalamine deficiency and rarely by genetic or acquired abnormalities affecting the metabolism of the vitamin or because of defect in DNA synthesis not related to cobalamine or folate. Diagnosis of megaloblastosis in this study was established by bone marrow diagnosis.

Although it was in sharp contrast with the study of Jha et al (2008)[12] **who found Aplastic anemia to be the commonest cause , this could be because ,** the reported incidence of Aplastic anemia varies considerably between countries e.g. from 0.7 to 4.1 per million per year . Incidence is lower in Europe and North America than in various other parts of the world e.g. Asia.

Variation in the frequency of disorders causing pancytopenia has been ascribed to differences in methodology, stringency of diagnostic criteria, geographic area, period of observations, genetic differences, and varying exposure to cytotoxic agents.

In the present study**,** Anisocytosis was present in 40 (75.5%) of cases, followed by Relative lymphocytosis in 27(50.94%) followed by Hypersegmented

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polymorphs in 26 (49.05%), of cases circulating erythroblast in 13 (24.52%) cases, Immature cells in 12 (22.64%).

The present study is in concordance with the findings of **Gupta et al (2016)**[16], and **Khodke et al (2001).**[17]

CONCLUSION

Bone marrow examination is an important tool in the diagnosis and early initiation of treatment in vulnerable pancytopenic patients. Aspiration coupled with trephine biopsy can diagnose majority but not all the cases of pancytopenia.

Aspiration is fairly safe procedure with minimal discomfort to the patient and useful in the differential diagnosis of cytopenias.

In conclusion, pancytopenia is a common entity. However, it has received inadequate attention in the Indian subcontinent. In our country main cause of pancytopenia being fortunately Megaloblastic anemia which responds very well to treatment if diagnosed correctly in time.

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