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Research Article

STUDY OF PANCYTOPENIA IN RURAL AREA

Dr. Punjala Manisha Goud[1], Dr. Devonoori Sagarika[2], Dr. P. Chatuurya Kalanidhi[3*]

[1,2]Senior Resident, SVS Medical College, Mahbubnagar
[3*]Senior Resident, Govt Medical College, Nalgonda

A R T I C L E I N F O

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A B S T R A C T

Pancytopenia [1-3] is a common clinico-hematological entity encountered in day-to-day clinical practice. Pancytopenia refers to a disorder in which all three elements of the blood (RBCs, WBCs and Platelets) are lower in counts than normal. Thus, it is not a disease entity by itself, but rather a triad of findings. It is a primarily or secondarily affecting bone marrow manifesting and lead to various hematological derangements, which is reflected in the peripheral blood smear as pancytopenia.

Objectives:

- To study the incidence and evaluate the etiological causes of pancytopenia in patient from age group 18 to 70 years.
- To study their clinico-haematological profile

Materials & Methods: A cross sectional study was taken up among fifty patients with a hematological diagnosis of pancytopenia during the period, August 2020 to August 2022, in the Department of Pathology, SVS Medical College and hospital, Mahabubnagar. Patients between age group 18-60 with hematological evidence of pancytopenia were included in the study. Two ml of anticoagulated blood was collected for complete hemogram. The peripheral smear was studied after staining with Leishman's stain. Bone marrow aspiration was done to establish the etiological diagnosis. **Results:** Hypercellular bone marrow was observed in 38 patients and it was normo- cellular in 7 patients. Most common etiology noted was megaloblastic anemia (48.9%), followed by nutritional anemia (22.2%), hypersplenism (13.3%), leukemia (6.7%), myelodysplastic syndromes (2.2%) and others (6.6%). Normocellular marrow was seen in (8%) megaloblastic anemia, (4%) hypersplenism and 2% in nutritional anemia. **Conclusion:** The most common cause of pancytopenia is megaloblastic anemia followed by nutritional anemia.

INTRODUCTION

Pancytopenia[1-3] is a common clinico-hematological entity encountered in day-to-day clinical practice. Pancytopenia refers to a disorder in which all three elements of the blood (RBCs, WBCs and Platelets) are lower in counts than normal. Thus, it is not a disease entity by itself, but rather a triad of findings. It is a primarily or secondarily affecting bone marrow manifesting and lead to various hematological derangements, which is reflected in the peripheral blood smear as pancytopenia. There are varying trends in its etiology, clinical pattern, treatment modalities, and outcome in different studies.

Pancytopenia is defined as hemoglobin<12 gm%, WBCs count < 4 × 109 /L and platelet count <100 × 109 /L. Anemia defined as mild (Hb 9-12 gm %), moderate (Hb 5-9 gm %), severe (Hb 3,000/ mm3), moderate (WBCs 1,000-3,000/mm3) and severe (WBCs 50,000/mm3), moderate (platelet count 20,000-50,000/ mm3) and severe as (platelet count < 20,000/mm3).

Most of the time pancytopenia is insidious in onset. The presenting symptoms are usually anemia and thrombocytopenia, Leukopenia is an uncommon cause of initial presentation. There are many factor encompassing geographic distribution and genetic disturbances which cause pancytopenia according to various studies.

To understand the etiology of pancytopenia bone marrow biopsy plays a significant role. In some other selected cases radiological, biochemical and microbiological investigations are useful. The severity of pancytopenia and underlying etiology determine management and prognosis. Thus identification of correct cause will help in treatment. This study is therefore aimed to identify the frequent causes of pancytopenia in patients belonging to a rural area.

Objectives

- To study the incidence and evaluate the etiological causes of pancytopenia in patient from age group 18 to 70 years.
- To study their clinico-haematological profile

Corresponding author:* **Dr. P. Chatuurya Kalanidhi
Senior Resident, Govt Medical College, Nalgonda

MATERIALS & METHODS

A cross sectional study was taken up among fifty patients with a hematological diagnosis of pancytopenia during the period, August 2020 to August 2022, in the Department of Pathology, SVS Medical College and hospital, Mahabubnagar.

Inclusion criteria: Patients between Age group 18-60 with hematological evidence of pancytopenia.

Exclusion criteria: Patients with below 18 years and above 60 years with pancytopenia. Patients not ammendable for follow up are excluded.

The data was collected in the pre tested semi structured questionnaire demographic parameters, clinical features, presenting complaints, examination findings and lab investigations. Two ml of anticoagulated blood was collected for complete hemogram. The peripheral smear was studied after staining with Leishman's stain.

Special stains-Periodic acid Schiff reagent stain, Myeloperoxidase, Sudan black and Perls' stains were used wherever indicated. Further all the patients underwent bone marrow aspiration to establish the etiological diagnosis.

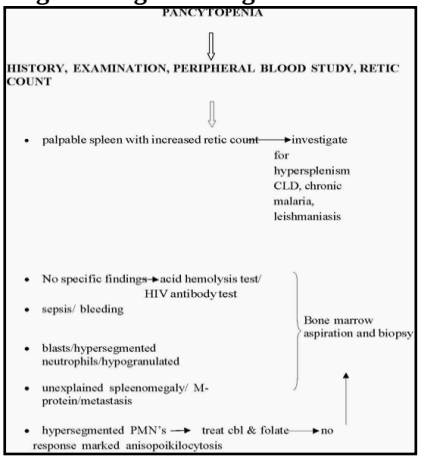
Bone marrow aspiration

This was done in all the patients to identify the etiology. An informed consent was obtained. A Jamshidi needle was used to aspirate material from the Posterior iliac crest in adults. Local anaesthetic infilitration was done after administering a test dose. Sterile precautions were observed. The needle and the stillette were placed in position and the cap was closed. After piercing the skin and subcutaneous tissue, the periosteum and cortex were pierced with a drilling action. Once in the marrow cavity, the stillette was removed and 0.2-0.3 ml of marrow fluid was aspirated with a sterile disposable 10 ml syringe. The aspirate was transferred to a set of slides and smeared. The needle was withdrawn and a tincture benzoin seal applied. Slides were stained with Leishman's stain. In case of failure, bone marrow aspirations were done at different sites.

Reticulocytes

The Reticulocytes have biconcave discoid shape. The staining of the reticulocyte cytoplasm has a characteristic feature similar to that of orthochromatic erythroblasts. Over a course of few days, the reticulocytes lose their mitochondria and ribosomes and finally gets evoked into mature erythrocytes

Figure showing the diagnostic algorithm of Pancytopenia



Data entry and analysis

Data was entered using Microsoft excel and analysed using Epi info 7.2.1.0. Descriptive and inferential statistical analysis were used in the present study. Results on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Student t-test is used to compare inter group variation for continuous variables. Chi square test is used to compare inter group variation for categorical variables.

RESULTS

Fifty patients with a hematological diagnosis of pancytopenia were studied during the period, august 2020 to august 2022, in the Department of Pathology, SVS Medical College and hospital, Mahabubnagar.

Age & Gender distribution

Age group (years)	Female	Male	Total	Percentage
18-20	1	3	4	8
21-30	2	6	8	16
31-40	2	8	9	19
41-50	2	12	15	29
51-60	5	7	12	24
61-70	0	3	3	6
Total	12	38	50	100

Most of the patients were in the age group of 41-60 years (53%) and least occurrence was seen in the age group of 61-70 years (6%). The sex distribution of pancytopenia showed a male preponderance. The male to female ratio was 2.1:1.

Symptoms

Symptoms	No. of cases	Percentage
Generalised weakness	42	86
Fever	21	39
Bleeding	2	66
Pain abdomen	24	46
Abdominal distension	40	81
Fever with rashes	5	10

Table showing the ranges of Hb, WBC and platelets of study population

Parameter	Sub group	No. of cases	Percentage
Hemoglobin	1 to 3	4	8
	3.1 to 5	11	22
	5.1 to 7	26	52
	7.1 to 10	09	18
WBC count	500-1000	4	8
	1100-2000	12	24
	2100-3000	14	28
	3100-4000	20	40
Platelet count	4000-25000	4	8
	26000-50000	8	16
	51000-75000	18	36
	76000-100000	10	20
	101000-150000	10	20
Reticulocyte count	0.1-2	44	88
	2.1-4	3	6

	4.1 - 6	1	2
	6.1-8	1	2
	8.1-20	1	2
Cellularity of bone marrow	Hypercellular	44	88
	Hypocellular	4	8
	Normocellular	6	12

The present study focuses on hypercellular bone marrow and normocellular and its causes.

Pancytopenia with hypercellular and normocellular marrow

Etiology	Total no. of cases		Hypercellular		Normocellular	
Etiology	Frequency	%	Frequency	%	Frequency	%
Megaloblastic anemia	22	100	19	81.8	4	18.2
Nutritional anemia	10	100	8	80	1	10
Hypersplenism	5	100	4	66.7	2	33.3
Leukemia	4	100	3	100	0	0
Myelodysplastic syndrome	1	100	1	100	0	0
Dengue	2	100	2	100	0	0
Hemolyticanemia	1	100	1	100	0	0

Hypercellular bone marrow was observed in 38 patients and it was normo- cellular in 7 patients. Most common etiology noted was megaloblastic anemia (48.9%), followed by nutritional anemia (22.2%), hypersplenism (13.3%), leukemia (6.7%), myelodysplastic syndromes (2.2%) and others (6.6%). Normocellular marrow was seen in (8%) megaloblastic anemia, (4%) hypersplenism and 2% in nutritional anemia.

Megaloblastic anemia

Megaloblastic anemia was seen to occur in the age group ranging from 21-70 years. Majority of the patients were seen in the age group of 31-50 years (63.6%). There were male preponderance and the male to female ratio was 2.4:1.

Table showing ranges of Hb, WBC and platelets of study population

Parameter	Sub group	No. of cases	Percentage
Hemoglobin	1 to 3	4	16.6
	3.1 to 5	4	16.6
	5.1 to 7	10	41.6
	7.1 to 10	6	25
WBC count	500-1000	4	8
	1100-2000	2	7.6
	2100-3000	4	15.2
	3100-4000	10	38.4
Platelet count	4000-25000	2	8.3
	26000-50000	4	16.6
	51000-75000	10	13.3
	76000-100000	10	13.3
	101000-150000	2	8.3
Reticulocyte count	0.1-2	12	60
	2.1-4	4	20
	4.1 - 6	2	10
	6.1-8	2	10
	8.1-20	0	0

Peripheral Smear Findings

Macroovalocytosis with a considerable degree of anisopoikilocytosis were the main features. Mean corpuscular volume was more than 100 fl in (57.5%) of patients. Dimorphic blood picture was seen in 10 patients (30%).
Hyper segmented neutrophils were seen in most of the patients. Basophilic stippling and cabot rings were present. Platelets were reduced in number in all the cases.

Bone marrow findings

The bone marrow was hypercellular with a reduction of fat cells in most of the patients (81.8%). Four patients (18.2%) had a normocellular marrow. Erythroid hyperplasia with megaloblastic maturation and reversal of M: E ratio was seen in all the patients. Megakaryopoiesis was normal in 63.6%, decreased in 18.2% and increased in 18.2% of patients.

Nutritional anemia

Total numbers of patients were 10.

Age (years)	Female	Male	Total no. of cases	Percentage
18-20	2	2	4	40
21-30	0	0	0	0
31-40	0	4	4	40
41-50	0	0	0	0
51-60	0	2	2	20
61-70	0	0	0	0
Total	2	8	10	100

Table showing ranges of Hb, WBC and platelets of study population

Parameter	Sub group	No. of cases	Percentage
Hemoglobin	1 to 3	2	20
	3.1 to 5	4	40
	5.1 to 7	3	30
	7.1 to 10	1	10
WBC count	500-1000	1	10
	1100-2000	0	0
	2100-3000	4	40
	3100-4000	5	50
Platelet count	4000-25000	4	40
	26000-50000	3	30
	51000-75000	2	20
	76000-100000	0	0
	101000-150000	1	10
Reticulocyte count	0.1-2	4	40
	2.1-4	2	20
	4.1 - 6	2	20
	6.1-8	2	20
	8.1-20	0	0

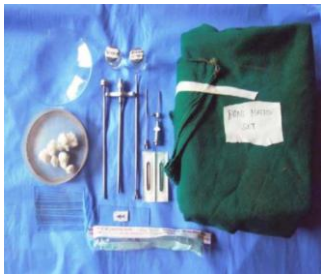
Peripheral smear findings

Most of the patients had normocytic normolchronic anemia. In two patients had microcytic hypochromic anemia, MCV was in the range of 65.6-108fl. MCHC was in the range of 26-34.7% and MCH was in the range of 18-38.9 pg.

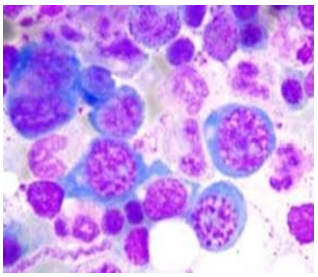
Bone marrow aspiration findings

Nine patients (90%) had hypercellular marrow with a reversal of M:E ratio. Erythroid hyperplasia along with both megaloblastic and micronormoblastic maturation was observed in all the patients. Leucopoiesis was normal. Megakaryocytes were either normal or increased. Only two patients had decreased megakaryopoiesis.

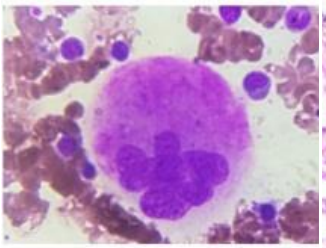
Images of smears



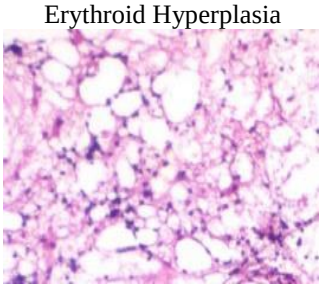
Bone marrow aspiration set



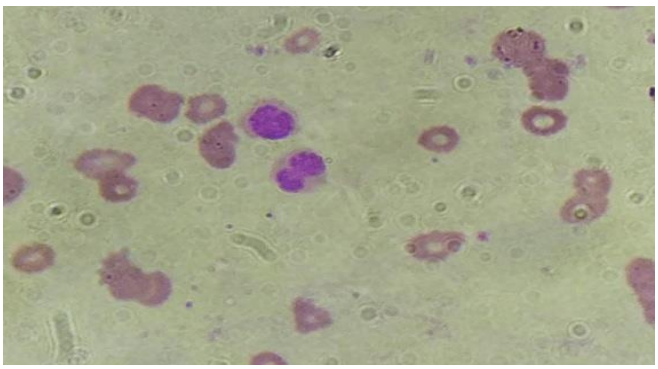
Erythroid Hyperplasia



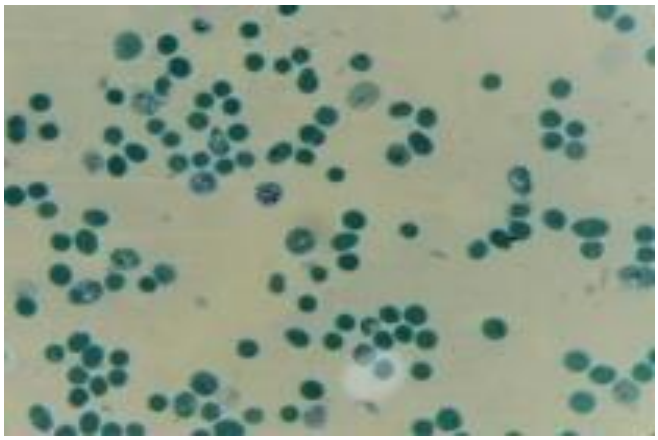
Megaloblasts



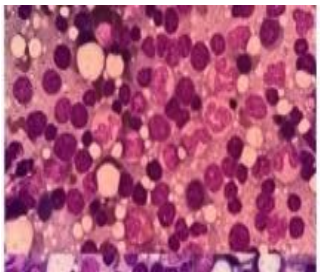
Aplastic anemia



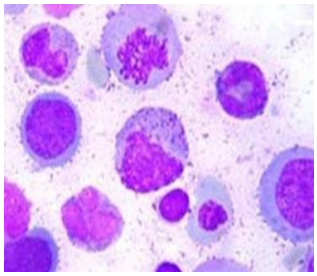
Microcytic Hypochromic picture



Reticulocytes



Erythroid hyperplasia



Mega oblasts with mitosis

DISCUSSION

In the present study, megaloblastic anemia (48.9%) was the commonest cause of pancytopenia, followed by nutritional anemia (22.2%), hypersplenism(13.3%), aplastic anemia (10%), malignant diseases (5%), myelodys plastic syndromes (0.6%) and others (4%). Others included uncommon causes like Dengue fever (2%) and Hemolytic anemia (2%). Tilak V, Jain R [4] (1998) found megaloblastic anemia (68%) to be the commonest cause of pancytopenia followed by a plastic anaemia (7.7%). Kumar *et al*. [5] found hypo plastic anemia (29.5%) to be the commonest cause followed by megaloblastic anemia. Jha A *et al*. (2008)[6] found hypo plastic bone marrow (29%) followed by megaloblastic anemia (23.64%) as the common causes.

Megaloblastic Anemia Associated With Pancytopenia

Megaloblastic anemia is common in India. This seems to reflect the higher prevalence of nutritional anemia in Indian subjects.

Age and sex distribution

In the study of pancytopenia cases by Jha *et al*., the age range was 10-79years (31 years). There was a male preponderance and male to female ratio was1.5:1. In the study by Kumar *et al*.[5] the ages ranged from 14-73 years (39.5%).There was a female preponderance and the male to female ratio was 2:1. In the present study, age ranged from 18-70 years. Majority of the patients were in the age group of 31-50 years (62%). There was a male preponderance and the male to female ratio was 2.4:1.

Peripheral Smear

The principal hematologic manifestations are, varying degrees of anemia, leucopenia, thrombocytopenia, anisopoikilocytosis, macroovalocytosis andhyper- segmented neutrophils. In the study by Tilak *et al*.[4] 51/53 cases showedanisocytosis, 45/53 cases showed hypersegmented neutrophils, 13/53 showed circulating erythroblasts. Reticulocytes were seen in 5/53 and relative lymphocytosis was seen in 7/53 cases. In the present study, macroovalocytes with considerable degree of anisopoikilocytosis were the main features in all the cases. MCV was more than100 fl in 57.5% of cases and dimorphic blood picture was seen in 30% of cases (10 patients). Hyper segmented neutrophils were seen in most of the patients.

Bone Marrow

Bone marrow is usually hypercellular with predominantly megaloblastic erythropoiesis. Giant band forms, metamyelocytes and giant megakaryocytes are also seen. In the present study, the bone marrow was hypercellular with

reduction off at cells in most of the patients (81.8%). Four patients (18.2%) had normocellular marrow. Erythroid hyperplasia with megaloblastic maturation was seen in all the patients.

NUTRITIONAL ANEMIA (MIXED)

Nutritional anemia as a common etiological factor causing pancytopenia iswell recognised and established. The nutritional deficiency of either B12 or folate results in megaloblastic anemia. Other causes include mixed deficiency anemia (microcytes and macrocytic). In the present study, mixed deficiency was seen in 22.2% of patients. This percentage is much lower than expected because 60-80% of world population is affected by iron deficiency anemia which is the most common preventable nutritional deficiency in the world. The possible explanation is that, majority of the cases present with anemia rather than pancytopenia and are diagnosed on smear examination and treated as outpatients. The age ranged in the present study from 18-60 years. There was amale preponderance and male to female ratio was 2.3:1. Most of the patients had dimorphic anemia. Two patients had macrocytic and hypochromic anemia. Bone marrow was hypercellular. Erythroid hyperplasia with both megaloblastic andmicro normoblastic maturation was observed in all the patients. Leucopoiesis was normal. Megakaryopoeisis was either normal or increased.

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Conflicts of Interest: none.

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