Section: Pathology

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A CLINICO - HAEMATOLOGICAL APPROACH TO PANCYTOPENIA - A STUDY FROM TERTIARY CARE HOSPITAL

Itha.Muni Bhavani[1], Katta Ramya[1], Kolla. Sireesha[1], Pentakota Tulyasri[2], Aparna Chinnam[3], Bora. Sreedhar[4]

[1]*Assistant Professor, Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India*
[2]*Undergraduate student, Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India.*
[3]*Professor, Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India.*
[4]*Professor and Head, Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India.*

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Corresponding Author:
Dr. Pentakota Tulyasri,
Undergraduate student, Department of Pathology, Guntur Medical College, Guntur, Andhra Pradesh, India.
Email: pvt12102019@gmail.com

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ABSTRACT

Background: Pancytopenia is a condition causing a decrease in blood cell count in erythrocytes, leukocytes, and platelets. It is a significant challenge in clinical practice due to its underlying causes, including malignant and non-malignant conditions. Common causes include Aplastic anemia(AA), Myelo-dysplastic syndromes(MDS), Acute Myeloid Leukemia(AML), Megaloblastic anemia, Paroxysmal Nocturnal Hemoglobinuria(PNH), Lymphoproliferative disorders, Infections, and Autoimmune conditions, Drug/Treatment induced. It is common in resource-limited settings like India, where infectious diseases, nutritional deficiencies, and genetic blood disorders are more prevalent. Present study provides a comprehensive clinico-haematological approach to evaluate pancytopenia, aiming to improve patient outcomes by systematically assessing, timely recognising and managing the underlying cause. This study aims to analyse the aetiology and frequency of pancytopenia, which can range from nonspecific symptoms like fatigue to severe manifestations like bleeding and organ dysfunction. It also outlines the clinico-haematological evaluation of patients, including detailed medical history and targeted laboratory investigations, to determine the underlying cause.

Materials and Methods: The present observational, cross-sectional study was conducted in 50 pancytopenia patients in department of pathology over a period of two months at Guntur medical college, Guntur, Andhra Pradesh.

Results: This study aimed to explore the causes, demographic characteristics, and clinical features of pancytopenia among 50 participants. The most common cause of pancytopenia is observed as infectious fevers (20%), especially Dengue fever, followed by each 8 cases of Liver abnormalities (most Chronic Liver Disease), Bone marrow abnormality (Bone marrow abnormalities include, 4 cases of aplastic anemia, 2 cases of Beta thalassemia minor and each 1 case (2%) of AML, MDS respectively) and Acute febrile illness. Pregnancy related Pancytopenia of 5 cases (10%) are observed. Also, each 3 cases (6%) of nutritional deficiency (B12 and folic acid deficiency anemia), autoimmune disorders associated conditions (each one case of RA, SLE, Splenomegaly with hypersplenism) and miscellaneous conditions (each one case of cardiac abnormalities, hip injuries and stroke). Hematological parameters revealed severe pancytopenia, with a mean hemoglobin level of 5.61 g/dL, a mean white blood cell count of 2.73 × 10^9/L, and platelets averaging 49.64 × 10^9/L, highlighting the severity of the condition. Demographically, the study found a fairly equal distribution of males (52%) and females (48%), with the majority of participants being from rural areas (58%) and lower socio-economic backgrounds. Age was distributed across various groups, with the mean age being 37.4 years. Educational levels were low, with 50% of participants being illiterate, suggesting the need for better health education in such communities.

Conclusion: The present study emphasises the multifactorial nature of pancytopenia with infectious fevers, liver abnormalities, and bone marrow disorders emerging as the most common aetiologies, Easy fatigability, bleeding tendencies, and fever were the most common clinical presentations; pallor was a common physical finding. Laboratory findings highlighted the haematological impact by showing significant decreases in haemoglobin, WBCs, and platelets. Depending on the underlying condition, bone marrow findings could present as a combination of hypocellular and hypercellular presentations. Rural, socioeconomically disadvantaged people with low levels of education made up the majority of the impacted population. The majority of participants were actively receiving treatment in spite of these obstacles. The findings highlight the need for targeted healthcare interventions and public health initiatives to reduce the burden of pancytopenia.
Keywords: Pancytopenia, Bone marrow, Anaemia, HPLC, Thalassemia.

INTRODUCTION

Pancytopenia is a condition in which there is decreased count of blood cells in all the three major cell lineages.[1] It is a clinical condition characterized by a simultaneous reduction in the levels of all three major blood cell lineages - erythrocytes, leukocytes, and platelets - presents a significant challenge in clinical practice.[2] It can arise from a diverse range of underlying causes, including malignant disorders that disrupt normal blood cell production, such as hematologic malignancies, as well as non-malignant conditions that suppress or impair the bone marrow's ability to generate blood cells, like aplastic anemia.[3] This haematological anomaly can result from a variety of underlying pathology thus poses a significant diagnostic challenge. The differential diagnosis of pancytopenia is expansive, encompassing a wide range of hematological, oncological, infectious, and systemic disorders. Common causes include, acquired aplastic anemia, myelodysplastic syndromes, acute myeloid leukemia, megaloblastic anemia, paroxysmal nocturnal hemoglobinuria, lymphoproliferative disorders, infections (e.g., viral hepatitis, HIV, tuberculosis), and autoimmune conditions (e.g., Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA).).[1,3]

Pancytopenia is a frequent finding in clinical practice, particularly in resource-limited settings like India where infectious diseases, nutritional deficiencies, and genetic blood disorders are more prevalent.[4] Possessing a significant diagnostic dilemma for healthcare providers due to the wide array of potential underlying causes. Accurate identification of the etiology is crucial for guiding appropriate treatment and improving patient outcome.[5] The initial evaluation of pancytopenia should begin with a thorough review of the patient's medical history and a comprehensive physical examination, as these can provide valuable insights into the underlying cause.[6] Clinicians must also consider the potential impact of various treatment strategies, as some interventions, such as certain cancer therapies, can contribute to the development of pancytopenia.[7]

The key aspects of the clinico-haematological approach to pancytopenia includes.[4,8]

- Eliciting a detailed medical history along with evaluation of physical findings to identify potential contributing factors and associated factors.
- Obtaining a complete blood count and peripheral blood smear to characterize the type and degree of cytopenia.
- Evaluating bone marrow aspiration, bone marrow biopsy findings to determine the underlying pathological processes wherever necessary.
- Correlating clinical presentation and laboratory data to formulate a differential diagnosis.

Pancytopenia is a common hematological disorder encountered in medical practice, especially in developing countries like India with commonest cause being nutritional deficiencies.[9] it has a diverse etiology and requires a systematic clinico-haematological approach for accurate diagnosis and appropriate management, the high prevalence of conditions like nutritional deficiencies, infections, and genetic blood disorders in India makes the study of pancytopenia particularly relevant in this geographical context.[10] Pancytopenia can have a significant impact on an individual's health and quality of life. The decreased production of blood cells can lead to a heightened risk of life-threatening complications, such as severe infections, uncontrolled bleeding, and end-organ damage due to poor oxygen delivery. Prompt diagnosis and management are crucial to prevent these complications and improve patient outcome.[11]

In resource-constrained settings, particularly in India, the evaluation of pancytopenia can be hindered by the limited availability of diagnostic modalities, such as bone marrow aspiration and biopsy. However, a thorough clinical history, physical examination, and basic laboratory investigations can still yield valuable insights into the underlying cause.[12] In such scenarios, a prioritized approach focusing on the most common etiologies and tailoring the diagnostic workup accordingly can help optimize the utilization of available resources.[12] Thus, careful history-taking, physical examination, and laboratory investigations are essential in determining the

etiology and accurate diagnosis and prompt management of pancytopenia are crucial, as it can be a manifestation of a wide range of underlying disorders, including hematological malignancies, aplastic anemia, and other bone marrow failure syndrome.[5]

This study aims to provide a comprehensive evaluation of pancytopenia, integrating clinical and haematological findings. In resource – limited settings, the clinico-haematological approach can assist clinicians in systematically evaluating pancytopenia, leading to accurate diagnoses and improved patient outcomes by facilitating timely identification and management of the underlying cause.

Aims and objectives:

The aim of this study is

- To analyse the aetiology and their frequentness in pancytopenia.

Discuss the common underlying aetiologies and associated clinical presentation of pancytopenia, which can range from nonspecific symptoms such as fatigue, weakness, and increased susceptibility to infections, to more severe manifestations like bleeding and organ dysfunction.

- To evaluate the patients with pancytopenia.

Outline the clinico-haematological evaluation of pancytopenia, encompassing a detailed medical history and targeted laboratory investigations, including complete blood count, peripheral blood smear, and bone marrow assessment and High-Performance Liquid Chromatography HPLC, to determine the underlying causes.

MATERIALS AND METHODS

The study was conducted after obtaining informed consent from the participants and also approval from the institutional ethics committee. (Application no. GMC/IEC/012/2024)

Type of study: Observational study.

Study Design: Observational, cross-sectional study.

Study setting: Study conducted in the Department of Pathology in Guntur medical college and Hospital, Guntur, Andhra Pradesh.

Sample size, Study population and study period: The study population consists of 50 patients presented with pancytopenia, attending to the tertiary care hospital in a period of two consecutive months from September 2024 to October 2024.

Pancytopenia will be defined as a reduction in all three major blood cell lines:

- Haemoglobin <10 g/dL
- Leukocyte count < 4000 cells/mm³
- Platelet count < 100,000/mm³[10] .

Selection criteria:

Inclusion Criteria:

- Patients of all ages and genders presenting with pancytopenia.
- Patients who provide informed consent for invasive procedures like bone marrow aspiration or bone marrow biopsy.
- Assent along with parental consent for patients below 18yrs of age.

Exclusion Criteria:

- Patients who are not willing to participate in the study.
- Patients with incomplete medical records.
- Patients with transient pancytopenia due to acute infections and drug-induced causes that resolve without intervention.

Data collection procedures and proposed intervention:

1. Patient Recruitment and Consent:

Patients meeting the inclusion criteria were identified and approached for participation. Informed consent was obtained from all participants (and from parents/guardians in the case of minors).

2. Clinical Evaluation:

A semi-structured demographic questionnaire related to the study was prepared. Data regarding complete detailed history and examinations was obtained from the patient records.

3. Laboratory Investigations and Interventions:

- All the data related to the laboratory investigations like peripheral smears were collected from the patient records.
- Bone marrow aspiration, bone marrow biopsy and High-Performance Liquid Chromatography HPLC was conducted wherever necessary and the data was obtained from the patients records.

Study instruments:

EDTA Anti -coagulated whole blood is used for Blood counts and HPLC.

- **Laboratory Instruments:** Fully Automated haematology analyser- Aspen 3200, 3-part analyser are used for blood counts; Magnus microscope MX-21iLED was used for peripheral smear examinations. Staining used is Leishman stain.
- **Bone Marrow Biopsy Instruments:** Bone marrow aspiration (Salah bone marrow aspiration needle) and biopsy needles (Jamshidi needle). the smears are stained using Leishman stain.
- **High Performance Liquid Chromatography HPLC:** BIO RAD D10 haemoglobin testing system is used for analysis.

Data Analysis: The data collected was entered into the MS Excel spreadsheet and analysed using SPSS version 28 (statistical package for social sciences). The data is presented in the form of tables, percentages, proportions, chi-square test and p value.

RESULTS

During the two months study period from September 2024 to October 2024, a total of 50 patients were presented with pancytopenia, the following were the results.

Age distribution among participants is 22% each, in the age groups of 21-30, 31-40 and 41-50. Remaining 10% of patients were in the age group of 11 - 20 years and 8 % of 71 -80 years of age. Age groups of 51-60

and 61 -70 are of 6% each. Only 4% cases were of 0-5 years depicted in table 1. The mean age of pancytopenia was observed as 37 - 38 years of age, with the maximum age recorded of 78 years while 1 year being the minimum age.

Out of 50 participants, 26(52%) are males while the others 24(48%) are females shown in [Table 1].

The residency of most of the participants is found to be rural (58%) while the remaining are from urban (42%) residency shown in [Table 1].

Occupational status among study population was distributed as follows 45% of participants are dependents while 35% of participants were on daily wages and the remaining 20% participants are standard income.

Highest level of education among the participants is shown in [Table 1], showing that majority of them were illiterates (50%) while the remaining were intermediate (22%), high school (14%), graduates (10%) and middle school (4%).

Among 50 participants the socio-economic status is of lower class among 40% of the people, 4% are of upper class, remaining 56% cases belongs to middle class as depicted in [Table 1].

The marital status among 50 participants of pancytopenia were married in 86% and unmarried in 14% of people as depicted in [Table 1].

Family history of similar complaints were observed in 16% of people in first degree relatives, while in 2% in both degree relatives and absent in 82% of remaining cases as shown in [Table 1].

Dietary habits showing 20%of the cases were vegetarians while others 80% have mixed diet.

The duration of illness among the participants is as shown in the [Table 1], which depicts that most common duration of presenting illness is 1 week with 10 cases (20%) followed by 2 months of 8 cases (16%). Out of 50 cases, 7(14%), 6(12%),5(10%) and 4(8%) cases show of duration of illness 10 days, 1month, 2 weeks and 5 days respectively. Each 3 cases (6%) of show duration of illness 6 months and 4 months and each 1 case (2%) of 2 days, 15 days, 3 days and 3 months.

Treatment status of the participants is depicted in the [Table 1]. Out of 50 cases 46 cases (92%) were currently undergoing treatment, while other 8% were not receiving treatment.

Table 1: Demographic and medical history particulars of patients with pancytopenia

patients Age distribution (in years)	0 - 5	2	4%
	6-10	nil	nil
	11- 20	5	10%
	21 - 30	11	22%
	31 - 40	11	22%
	41 - 50	11	22%
	51 - 60	3	6%
	61 - 70	3	6%
	71 - 80	4	8%
Gender	Female	24	52%
	Male	26	48%
Residency	Rural	29	58%
	Urban	21	42%
Occupational status	Dependents		45%
	Daily wages		35%
	Salary/ standard income		20%
Highest level of education	postgraduate	0	0%
	Graduate	5	10%
	Intermediate	11	22%
	High school	7	14%
	Middle school	2	4%
	Primary school	0	0%
	Illiterate	25	50%
Socio economic status	Upper class	2	4%
	Upper middle class	2	4%
	Middle class	12	24%
	Lower middle class	14	28%
	Lower class	20	40%
Marital status	Married	43	86%
	Unmarried	7	14%
Family history of similar complaints	Absent	41	82%
	Present in first degree relatives	8	16%
	Present in second degree relatives	1	2%
Dietary habits	Mixed	40	80%
	Vegetarian	10	20%
Duration of illness	1 week	10	20%
	2months	8	16%
	10 days	7	14%
	1 month	6	12%
	2 weeks	5	10%
	5 days	4	8%
	6 months, 4 months	Each 3	Each 6%

	2 days, 15 days, 3 days, 3 months	Each 1	Each 2%
Any treatment given or undergoing	No	4	8%
	Yes	46	92%

The following were considered as the causes of pancytopenia as depicted in [Table 1]

Table 2: categorization of conditions presenting with pancytopenia

Bone marrow abnormalities	Aplastic anemia	4	8%	8	16 %
	Acute myeloid leukemia AML	1	2%		
	Myelo Dysplastic Syndrome MDS	1	2%		
	Beta thalassemia trait	2	8%		
Pregnancy associated conditions (Preeclampsia, HELLP syndrome, infections like HIV, nutritional cause)	G3A2 with fever	1	2%	5	10 %
	P3L2D1	1	2%		
	G2P1L1	1	2%		
	G2P1L1 with CLD	1	2%		
	G3A2, RVD+	1	2%		
Nutritional deficiency	Vit B12, folic acid deficiency	3	6%	3	6%
Autoimmune disorders	SLE	1	2%	3	6%
	splenomegaly and Hypersplenism	1	2%		
	Rheumatoid Arthritis	1	2%		
Infectious fevers	Dengue	7	14 %	10	20 %
	Malaria	1	2%		
	HBV	2	4%		
Acute febrile illnesses		8	12 %	8	16 %
GI abnormalities	Upper GI bleed	1	2%	2	4%
	Pancreatitis	1	2%		
Liver abnormalities	Chronic liver disease	6	12 %	8	16 %
	Viral hepatitis	1	2%		
	Cholelithiasis	1	2%		
Miscellaneous	Hip fracture (Blood loss)	1	2%	3	6%
	Stroke with fever	1	2%		
	Cardiac abnormalities	1	2%		

Categorization of conditions presenting with pancytopenia is depicted in [Table 2].

The most common cause of pancytopenia is observed as infectious fevers (20%), especially Dengue fever, followed by each 8 cases of Liver abnormalities (most common was chronic Liver Disease), Bone marrow abnormality (Bone marrow abnormalities include, 4 cases of aplastic anemia, 2 cases of Beta thalassemia minor and each 1 case (2%) of AML, MDS respectively) and Acute febrile illness. Pregnancy related Pancytopenia of 5 cases (10%) are observed. Also, each 3 cases (6%) of nutritional deficiency (B12 and folic acid deficiency anemia), autoimmune disorder associated conditions (each one case of RA, SLE, Splenomegaly with hypersplenism) and miscellaneous conditions (each one case of cardiac abnormalities, hip injuries and stroke).

High Performance Liquid Chromatography HPLC was performed in four cases out of overall 50 cases. Two pancytopenia cases were diagnosed as thalassemia carrier, remaining cases normal HPLC study.

First case: A 5-year-old male child came with history of fever with anemia and organomegaly (hepato-splenomegaly) with history of blood transfusion 3 years back and no history of parent's consanguinity. Blood investigation reveals Hb 2.2 g/dl, WBC count 3800 cells /cumm, and Platelet count 1.2 lakhs /cumm with altered red cell indices, peripheral smear shows microcytic hypochromic RBCs with anisopoikilocytosis and occasional target cells. Patient advised for High Performance Liquid Chromatography HPLC. On HPLC, HbA0 87.0%, HbA2 4.4%, HbA1c 2.4%, HbF less than 0.8% and the patient was diagnosed with Thalassemia carrier (HPLC no.71).

Second case: A Fifteen-year-old female child brought to the hospital with complaint of anemia and easy faigibility. There is no history of previous blood transfusion, jaundice, organomegaly and no history of parent's consanguinity. Her blood investigation reveals Hb 4.1 g/dl, WBC counts 2640 cells /cumm, and Platelet count 1 lakh /cumm with altered red cell indices, peripheral smear shows microcytic hypochromic RBCs, nucleated RBCs 20cells/100wbc with anisopoikilocytosis and occasional target cells. Patient advised for HPLC. On HPLC HbA0 83.8%, HbA2 3.9%, HbA1c 2.4%, HbF less than 0.8%, and the patient was diagnosed with Thalassemia carrier (HPLC No. 254).

The clinical presentation of pancytopenia among participants is as follows as depicted in table 3. Easy fatigability has been the most common clinical presentation 38 cases (76%), while bleeding manifestations accounted for 25 cases (50%). Fever is present in 18 cases (36%). Difficulty in breathing and loss of appetite was complained by 6 participants (12%).

Table 3: clinical presentation of pancytopenia

Clinical presentation	No. Of cases	% of cases
Easy fatigability	38	76%
Bleeding manifestations	25	50%
Fever	18	36%
Breathing difficulty &loss of appetite	6	12%

The physical findings of pancytopenia are represented in table 4. Pallor is present in all the cases 100%, pedal edema is present in 17 cases (34%). 12 cases (24%) have petechia spots, while icterus and hepatomegaly are observed in 10 case each (20% each). Splenomegaly in 9 cases (18%), periorbital edema 8 cases (16%) and lymphadenopathy in 4 cases (8%) are observed.

Table 4: physical findings in pancytopenia

Physical sign	No. Of cases	% of cases
Petechia spots	12	24%
Lymphadenopathy	4	8%
Periorbital edema	8	16%
Icterus	10	20%
Hepatomegaly	10	20%
Splenomegaly	9	18%
Pedal edema	17	34%
Pallor	50	100%

The peripheral smear findings were indicated in [Table 5].

Table 8

Causes	No. of cases	Aniso-poikilocytosis	Immature wbc	Hyper segmented neutrophils	Activated lymphocytes	Lymphocytosis	Immature RBC	Increased reticulocytes
Megaloblastic anemia	3	present	present	present	absent	present	absent	present
Hypersplenism	1	present	absent	absent	absent	absent	absent	absent
Aplastic anemia	4	present	absent	absent	present	absent	absent	absent
Dengue fever	6	present	absent	absent	present	present	absent	absent
Systemic lupus erythematous	1	present	present	absent	absent	present	absent	absent
Myelodysplastic syndrome	1	present	absent	absent	absent	absent	absent	absent
Acute myeloid leukemia	1	present	absent	absent	absent	absent	absent	absent
Beta thalassemia	2	Present Basophilic stippling	absent	absent	absent	absent	present	present

Out of 50 cases, 39 cases do not require bone marrow study, while in remaining 11 cases bone marrow studies were conducted. The following results were obtained as in [Table 6].

Table 6: bone marrow study in pancytopenia

Disease	No. of cases underwent bone marrow aspiration	Bone marrow study result	% of cases
Aplastic anemia	4	Hypocellular	36.36%
AML	1	Hypercellular	9.09%
Megaloblastic anemia /nutritional	3	Hypercellular	27.27%
MDS	1	Hypercellular	9.09%
SLE	1	Hypocellular	9.09%
Beta thalassemia carrier	1	Hypercellular	9.09%

The Bone marrow study indicates that 5 out of 11 cases have hypocellular marrow whereas 6 cases have hypercellular marrow.

The parameters of Haemoglobin, WBC, platelets were depicted in the [Table 7].

Mean haemoglobin: 5.61±2.11 g/dl
Mean total WBC count: 2.73±1.2710⁹/L
Mean platelet count: 49.64±28.14 10⁹/L

Table 7: parameters of Hb, WBC, platelets

	Mean	SD	Minimum	Maximum
Hb (g/dl)	5.61	2.11	1.74	9.8
WBC (10^9/L)	2.73	1.27	0.5	8.5
Platelets (10^9/L)	49.64	28.14	10	99

There is no significant association between bone marrow findings and peripheral smear findings [11] as shown in [Table 8], X2 (1, N = 11) = 1.06, p = .30.

Table 8: Association between bone marrow findings and peripheral smear.

Bone marrow / peripheral smear	Hypercellular	Hypocellular	Row Totals
Microcytic + Normocyctic	3 (3.82) [0.18]	4 (3.18) [0.21]	7
Macrocytic	3 (2.18) [0.31]	1 (1.82) [0.37]	4
Column Totals	6	5	11(Grand Total)

The chi-square statistic is 1.0607. The p-value is .303052, The result is not significant at $p < .05$.

DISCUSSION

The present study analysed the clinical and haematological profiles of 50 patients diagnosed with pancytopenia. The most common causes of pancytopenia in this study were infectious fevers (20%), followed by liver abnormalities (16%), bone marrow abnormalities and acute febrile illnesses (16%). Pregnancy-related pancytopenia (10%), while nutritional deficiencies and miscellaneous conditions contributed to 6% of cases. The findings reflect a broad spectrum of underlying causes, including haematological disorders, infections, and systemic conditions. The etiological distribution observed in this study is consistent with those reported in various other studies.

The most frequently observed causes of pancytopenia in this study were infectious fevers (20%), particularly dengue fever, and liver abnormalities (16%), these results align with findings from other studies such as Gayathri and Rao et al,[2] and Das Makheja et al,[8] where infectious and liver-related causes were prominent. Infectious causes of pancytopenia, particularly dengue fever, have been widely documented as significant contributors to bone marrow suppression, leading to pancytopenia. Liver-related pancytopenia is often linked to chronic liver diseases such as cirrhosis, which can impair bone marrow function due to hypersplenism or portal hypertension.

In contrast, megaloblastic anemia, a nutritional deficiency, was reported as a significant cause of pancytopenia in several studies, such as those by Manzoor et al,[9] and Chandra et al,[10] but it was less prominent in the present study (6%). This difference may reflect regional variations in dietary habits or access to healthcare resources, such as vitamin supplementation.

The study also found that autoimmune disorders, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), contributed 6% of cases. These findings corroborate other studies, such as those by Yokuş and Gedik study,[6] where autoimmune diseases were frequently implicated in pancytopenia.

Clinical Presentation and Physical Findings

The clinical presentation in this study was dominated by easy fatigability (76%) and bleeding manifestations (50%), which is in line with previous research. For instance, in a study by Jain et al,[11] weakness and pallor were the most common presenting symptoms. The presence of bleeding manifestations such as petechiae, ecchymosis, and mucosal bleeding, seen in 50% of the participants, further supports the clinical importance of bone marrow suppression in pancytopenia.

Physical findings such as pallor (100%), pedal edema (34%), and splenomegaly (18%) were also common. The high incidence of pallor is consistent with most studies, where it is typically observed due to anemia associated with pancytopenia. Splenomegaly is a feature that is often seen in cases of hypersplenism due to liver abnormalities or hematological malignancies.

Peripheral Smear and Hematological Findings

The peripheral smear findings in this study showed anisopoikilocytosis and hyper-segmented neutrophils in cases of megaloblastic anemia with iron deficiency, similar to the findings of Manzoor et al,[9] and Makheja et al.[8] Immature white blood cells and activated lymphocytes were observed in cases of dengue fever and systemic lupus erythematosus (SLE), which is consistent with immune-mediated bone marrow suppression seen in these conditions.

Hematological parameters in this study revealed a mean hemoglobin level of 5.61 g/dL, a mean WBC count of 2.73 x 10^9/L, and a mean platelet count of 49.64 x 10^9/L. These findings indicate significant bone marrow suppression, with low hemoglobin levels indicating anemia, low WBC count suggesting leukopenia, and low platelet count pointing to thrombocytopenia. Similar findings were observed in studies by Bhushan et al.12 and Vargas-Carretero et al.7, where pancytopenia was characterized by low counts across all three blood cell lines.

Peripheral smear findings:

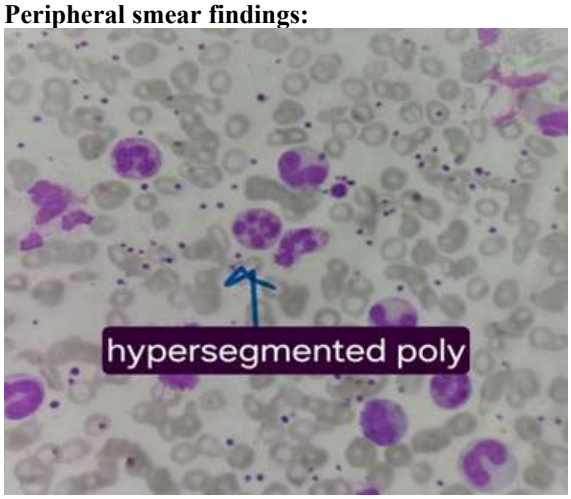

Image 1: Pancytopenia patient peripheral smear showing hyper-segmented neutrophils, a case of megaloblastic anaemia.

Hyper-segmented polymorphs observed in peripheral smear of Megaloblastic anemia as seen in [Image 1].

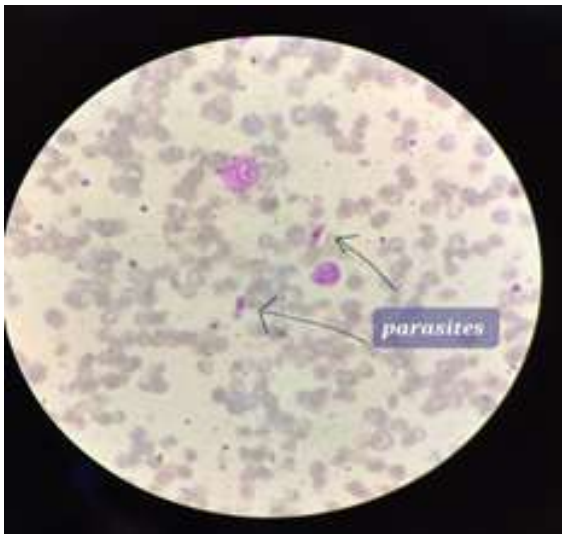

Image 2: Pancytopenia patient peripheral smear showing plasmodium falciparum parasites, a case of malaria.

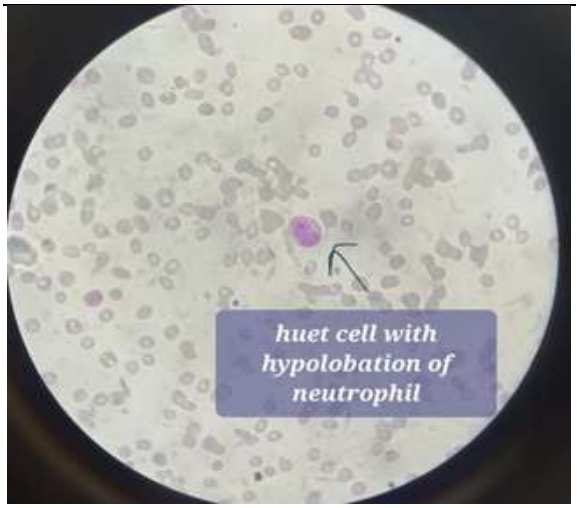

Image 3: Pancytopenia patient peripheral smear showing Huet cells, a case of Myelodysplastic syndrome.

Plasmodium falciparum parasites can be observed in peripheral smear of a patient with malaria as seen in [Image 2].

Pseudo pelger-huetanomaly, Huet cells with hypolobation of neutrophils are observed in a case of MDS as seen in [Image 3].

Bone marrow findings: Bone marrow findings show hypocellular, hypercellular marrows according to the disease.

Demographic and Socioeconomic Characteristics

The age distribution of participants in this study showed a peak in the 21-30, 31-40, 41-50 years age group, with a mean age of 37.4 years. This is consistent with studies such as those by Chandra et al.10 and Makheja et al.8, where pancytopenia was predominantly observed in adults, particularly in those aged between 30 and 50 years. The gender distribution was relatively balanced, with 52% males and 48% females, similar to findings from various studies such as those by Gayathri and Rao et al.3, who reported a male predominance.

Most participants (58%) were from rural areas, reflecting the socioeconomic status and access to healthcare, which may influence the diagnosis and management of pancytopenia. A majority of the participants (40%) belonged to the lower socioeconomic class, which is often associated with inadequate nutrition, limited access to healthcare, and higher prevalence of infections, all of which contribute to the development of pancytopenia.

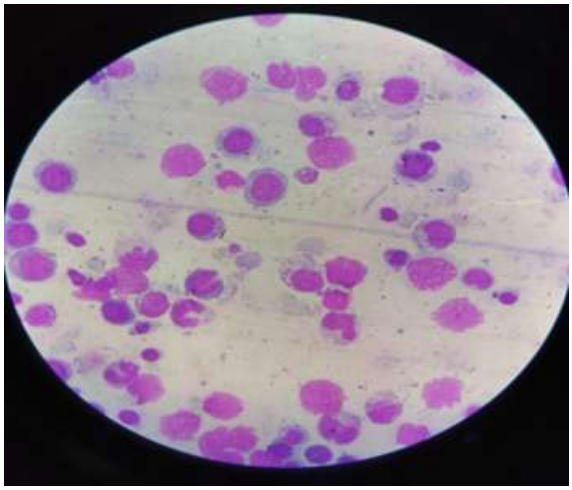

Image 4: Megaloblastic anaemia bone marrow picture

Treatment and Prognosis: Most of the participants (92%) were receiving treatment at the time of the study, highlighting the importance of early intervention in managing pancytopenia. The treatment approaches were likely based on the underlying etiology, including supportive care, nutritional supplementation, antibiotics for infections, and specific therapies such as immunosuppressive therapy for autoimmune condition.

Strengths and limitations: Strength of our study is that we have conducted study with a sample size of 50 within a duration of 2 months. The limitations of

our study is sample size and duration of our study was not adequate and this study was conducted only in one hospital in South India which hinders the generalisability. And more-over the diagnostic testing methods are not well improved with infrastructural limitations.

Comparison of various studies on pancytopenia

Study Reference	Sample Size	Mean Age (Years)	Gender Ratio (M:F)	Most Common Cause(s)	Other Significant Causes	Common Presentations
Gayathri & Rao (2011),[2]	104	41	Male Predominance	Megaloblastic anemia (74%)	Aplastic anemia (18%)	Pallor, splenomegaly, fever
Das Makheja et al. (2013),[8]	62	37.76 ± 16.38	1.38:1	Megaloblastic anemia (41.9%)	AML (27.4%), aplastic anemia	Fever, generalized weakness
Manzoor et al. (2014),[9]	50	Not Specified	Male Predominance	Megaloblastic anemia (56%)	Aplastic anemia (14%), sepsis	Pallor, splenomegaly
Yokuş & Gedik (2016),[6]	137	63.52 ± 21.32	1:1	Vitamin B12 deficiency (17%), liver disease	Malignancy (13%), MDS (13%)	Fatigue, pallor, Spleenomegaly
Vargas-Carretero et al,[7] (2019)	109	49.4	1:1.14	Megaloblastic anemia, MDS	AML, ALL	Anemia, bleeding, Weakness
Chandra et al,[10] (2019)	68	35 (median)	1.19:1	Megaloblastic anemia	Aleukemic leukemia, VL	Hepatosplenomegaly, pallor
Jain et al,[11] (2021)	100	18–40	Female Predominance	Megaloblastic anemia (37%), dimorphic anemia	Aplastic anemia (20%)	Weakness, pallor, fever
Bhushan et al. (2022),[12]	73	46.97	1.2:1	Megaloblastic anemia, Aplastic anemia	Infections,	Fatigue, rash, splenomegaly
Qasim et al. (2022),[4]	119	59	1:1.08	Infections, Megaloblastic anemia	AML, aplastic anemia	Pallor, weakness, hepatomegaly
Current Study (2024)	50	37.4 ± 16.9	1.08:1	Infectious fevers (20%)	Liver disease, Bone marrow abnormalities, acute febrile illness (16%),	Weakness, fever, pallor

Summary: A Cross-sectional study was conducted after obtaining approval from the institutional ethics committee and informed consent was taken from the participants. This study aimed to explore the causes, demographic characteristics, and clinical features of pancytopenia among 50 participants.

The most common cause of pancytopenia is observed as infectious fevers (20%), especially Dengue fever, followed by each 8 cases of Liver abnormalities (most Chronic Liver Disease), Bone marrow abnormality (Bone marrow abnormalities include, 4 cases of aplastic anemia, 2 cases of Beta thalassemia minor and each 1 case (2%) of AML, MDS respectively) and Acute febrile illness. Pregnancy related Pancytopenia of 5 cases (10%) are observed. Also, each 3 cases (6%) of nutritional deficiency (B12 and folic acid deficiency anemia), autoimmune disorders associated conditions (each one case of RA, SLE, Splenomegaly with hypersplenism) and miscellaneous conditions (each one case of cardiac abnormalities, hip injuries and stroke).

Hematological parameters revealed severe pancytopenia, with a mean hemoglobin level of 5.61 g/dL, a mean white blood cell count of 2.73 × 10⁹/L, and platelets averaging 49.64 × 10⁹/L, highlighting the severity of the condition.

The study had a similar gender split (52% male, 48% female), with 58% rural and 40% low-income participants. The mean age was 37.4 years across groups. The 50% illiteracy rate suggests that such communities need better health education.

Early intervention was common, with 92% of participants receiving treatment, but 8% did not, likely due to access issues. The findings highlight the need for targeted public health education, healthcare interventions and public health initiatives to reduce the burden of pancytopenia.

CONCLUSION

The study highlights the multifactorial nature of pancytopenia, with infectious fevers, liver abnormalities, bone marrow disorders are emerging as the most common etiologies. Clinical presentations predominantly included easy fatigability, bleeding tendencies, and fever, with pallor being a universal physical finding. Laboratory results reflected severe reductions in hemoglobin, WBCs, and platelets, underscoring the hematological impact. Bone marrow findings varied, with a mix of hypocellular and hypercellular presentations depending on the underlying condition.

The affected population primarily comprised rural, socioeconomically disadvantaged individuals, with limited educational attainment. Despite these challenges, most participants were actively undergoing treatment. These findings emphasize the need for timely diagnosis and management, with particular focus on addressing treatable causes such as infections and nutritional deficiencies.

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