



Study of Clinical and Hematological Profile of Patients with Pancytopenia in a Teaching Hospital

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Abstract: Background: In our daily work, pancytopenia—the simultaneous presence of leucopenia, thrombocytopenia, and anemia—is a prevalent clinical condition. Adult pancytopenia is described as having a hemoglobin level of less than 13.5 g/dl in men and 11.5 g/dl in women, a leucocyte count of less than $4 \times 10^9 /L$, and a platelet count of less than $150 \times 10^9 /L$. Anemia or thrombocytopenia are typically the cause of the presenting symptoms. **Materials & methods:** A prospective cross-sectional research on 120 instances of pancytopenia was conducted at the general medicine department at Mamata Academy of Medical Sciences, Bachupally, over the course of two years, from May 2022 to May 2023. **Results:** Malaria accounted for 22.5% (27/120) of pancytopenia cases, with vitamin B12 deficient anemia accounting for 49.1% (59/120). 10.8% (13/120) of cases were Dengue. Aplastic anemia (6.6%), multiple myeloma, AML (2.5%), and anemia from chronic illness were less prevalent causes. 3.3% for MDS and 0.8% for myelofibrosis. CLD with hepatitis B, aleukemic leukemia (0.8%), and splenomegaly (15%). 5.8% (or 7/120) of the patients had normocytic hypochromic anemia, 18.3% (or 22/120) had microcytic hypochromic anemia, 69.1% (or 83/120) had macrocytic anemia, and 6.6% (8/120) had microcytic hypochromic anemia. **Conclusion:** Pancytopenia is a frequent hematological issue that arises in clinical settings. Patients who exhibit unexplained anemia, a protracted fever, and a bleeding tendency should be suspected of having pancytopenia based on clinical grounds. The current study comes to the conclusion that comprehensive primary hematological investigations and bone marrow aspiration in cytopenic patients are useful in planning further investigations and managing cytopenic patients as well as in understanding the disease process and diagnosing or ruling out the causes of cytopenia. Severe pancytopenia can serve as a prognostic signal and has a substantial correlation with the clinical outcome.

Key Words: Adults, Bone marrow, Dimorphic anemia, Megaloblastic anemia, Pancytopenia

INTRODUCTION

A hematologic disorder called pancytopenia is defined by a reduction in all three peripheral blood cell lineages. fewer than 12 g/dL of hemoglobin in women and 13 g/dL in males, fewer than 150,000 platelets per mL, and less than 4000 leukocytes per milliliter (or an absolute neutrophil count of less than 1800 per milliliter) are the characteristics that define it. [1–2] But the primary factors influencing these limits include age, gender, color, and different clinical situations.

Peripheral pancytopenia is the simultaneous occurrence of anemia, leucopenia, and thrombocytopenia due to a drop in all three main blood components to levels below their lower normal range. According to Reddy RJP et al.'s study on dengue fever in India, thrombocytopenia is the most typical manifestation and the aetiology of pancytopenia in viral and

dengue fever epidemics. As a result, it is actually a trio of observations rather than a single illness entity. Finding the proper etiopathology in a particular instance is important because it aids in the implementation of prompt and suitable therapy, since the severity of pancytopenia and the underlying pathology dictate the care and prognosis of these individuals [4].

When evaluating pan cytopenic patients, a thorough clinical history, a careful physical examination, and baseline hematological investigations provide invaluable information. These details aid in the systematic planning of additional investigations to diagnose and determine the cause, preventing needless tests that not only increase treatment costs but can occasionally cause delays in diagnosis and treatment [5].

Many variables, including age, gender, diet, geographic

distribution, standard of living, exposure to cytotoxic medications or toxins, infections, and genetic and mutation profiles, might influence the genesis of pancytopenia in distinct populations. Research from both northern and southern India has demonstrated that megaloblastic anemia is the most prevalent cause of pancytopenia, whereas research from western India found that hypersplenism and infections were the most common underlying illnesses [6, 7].

Similar research from eastern India on the pathogenesis of pancytopenia revealed that megaloblastic anemia, then aplastic anemia, was the most prevalent cause of pancytopenia [8]. Research carried out in Nepal found that the most prevalent cause of pancytopenia was hypoplastic anemia [9]. However, in Europe and Israel, neoplastic illnesses and radiation have been found to be the most prevalent causes of pancytopenia [11, 12]. Research conducted in Korea found that acute myeloid leukemia (AML) was the most common cause of pancytopenia. Myelodysplastic syndrome (MDS) was shown to be the most prevalent cause of pancytopenia in Mexican research, with megaloblastic anemia coming in second [13].

Aim of the study:

To study Clinical, Hematological profile of patients with pancytopenia.

Its objectives:

- To investigate the range of clinical manifestations in pancytopenia patients.
- Analyze the etiology of pancytopenia in various individuals and establish a connection between the cause and the clinical manifestation.
- Investigating the relationship between a patient's hematological profile and the etiology of pancytopenia as well as its clinical manifestation

MATERIALS AND METHODS

Study design: Prospective cross-sectional study.

Study period: Duration of 2 years i.e., from may2022 to May 2023.

Place of study: Mamata Academy of Medical Sciences, Bachupally

Sample size: 120 cases.

The Institutional Ethics Committee granted approval for the project.

All of the study's patients had given their written, informed consent.

Inclusion criteria:

- Patients who are open to taking part in the research.
- Age group ranges above 18 years to 60 years.
- Patients having pancytopenia.
- Haemoglobin levels are less than 13.3 g/dl in males or 11.5 g/dl in females.
- Total leukocyte counts less than $4 \times 10^9 /L$.
- Platelet count less than $150 \times 10^9 /L$.

Exclusion criteria:

- Patients not willing to participate in the study.
- Age less than 18 years.
- Pregnant women.
- Patients receiving chemotherapy for malignant neoplasm.

INCLUSION CRITERIA FOR DIAGNOSING AS PANCYTOPENIA

- Haemoglobin levels are less than 13.3 g/dl in males or 11.5 g/dl in females.
- Total leukocyte counts less than $4 \times 10^9 /L$.
- Platelets count less than $150 \times 10^9 /L$

METHOD OF COLLECTION OF DATA

The research included patients with pancytopenia who were hospitalized to the Department of Medicine's wards and who attended the General Medicine OPD. The cases were chosen at random. The patients received an explanation of the research protocols. A complete clinical history was obtained, covering the patient's age, gender, prior medical history, current ailment, family history, and personal history, including any drug or alcohol use or smoking.

Proforma also included a history that may have shown prior pancytopenia, aplastic anemia, hereditary bone marrow failure syndrome, recurrent early fetal loss, cancer, liver illness, metabolic problems, or connective tissue condition.

A comprehensive physical assessment was used to examine the patients.

INVESTIGATIONS

The investigation was done in central lab and department of pathology, biochemistry and microbiology of the hospital.

1.Complete blood count (CBC):

- From each of the study's patients, a 2-milliliter blood sample was taken and placed in EDTA vials.
- On a Siemens Coulter 5-part differential haematology analyzer, CBC counts were conducted. Every day, three levels of commercial quality control samples (Siemens Coulter) were conducted to verify the accuracy of the haematology analyzer. Performance was also assessed by producing a Levey-Jennings chart and using Westgard rules with two standard deviation limits.
- The complete and differential leucocyte count (CBC), red cell indices, total and differential leucocyte count, platelet count, and anemia, leucopenia, and thrombocytopenia were graded.

2.Peripheral smear examination:

- Peripheral smear was stained by Leishman stain and examined in detail.

3.Reticulocyte count:

- Reticulocyte count was estimated on Supravital stain (methylene blue)

4. Hematology slides were reported by Pathologist and observed for

Clinical diagnosis	No. of cases	Percentage
Vitamin B12 deficiency anemia	59	49.1
Dengue	13	10.8
Malaria	27	22.5
Aplastic anemia	8	6.6
Acute leukemia	3	2.5
MDS	4	3.3
Myelofibrosis	1	0.8
CLD with splenomegaly	3	15
Hepatitis B	1	0.8
Aeukemic leukemia	1	0.8
Total	120	99.9%

- RBC-Anis poikilocytosis, nucleated RBCs and morphological type of anemia.
- WBC- Hyper-segmented neutrophils, toxic granulation, relative lymphocytosis and immature cells/ blasts.
- Platelets- Adequacy.
- Screened for hemiparasites.

Bone marrow aspiration

Carried out following patient education about the operation and acquisition of written permission

Statistical data analysis:

- All of the demographic, biochemical, and haematological parameters were noted, and the observations and outcomes were tallied according to the following criteria: gender, age group, physical signs, bleeding manifestations, aetiology, bone marrow findings, and essential haematological parameters.
- Software version IBM SPSS 20.0 was utilized for data analysis.
- Data analysis - ANOVA test was applied for significance.

RESULTS

The majority in the current research, including 36.6% (44/120) of those aged 18 to 30, were followed by those aged 31 to 40, who made up 21.6% (26/120) and those aged 41 to 50, who made up 20% (24/120) and 14.1% (17/120). 7.5% in 61-70 years and 51-60 years (9/120)

When compared to females in the current study, men accounted for 50.8% (61/120) of the total and 49.1% (59/120) of the female participants.

In this research, 39.1% (47/120) of the patients had fever, and 33.3% (40/120) had generalized weakness. 21.6% (26/120) had a fever with chills and rigors, 2.5% (3/120) had abdominal distension, and 3.3% (4/120) had SLE.

Pallor was seen in 43.3% (52/120) patients in the current research, Pallor+ Splenomegaly in 31.6% (38/120) cases, Splenomegaly in 20% (24/120) cases, and Hepatomegaly in 5% (6/120) instances.

Table 1: Distribution of Cases Based on Clinical Diagnosis

According to the current study, vitamin B12 deficiency anemia, or 49.1% (59/1200) of cases of pancytopenia, was the most prevalent cause, followed by malaria (22.5%) (27/120). 10.8% (13/120) of cases were Dengue. Aplastic anemia (6.6%), multiple myeloma, AML (2.5%), and anemia from chronic illness were less prevalent causes. 3.3% for MDS and 0.8% for myelofibrosis. Hepatitis B, leukemia (0.8%), and CLD with splenomegaly (15%).

In the current study, 37.5% (45/120) of the patients had < 6 g/dl hb, 55.8% (67/120) had 6-8.9%, and 6.6% (8/120) had 9-11 g/dl.

In the current study, 5.8% (or 7/120) of the patients had normocytic hypochromic anemia, 18.3% (or 22/120) had microcytic hypochromic anemia, 69.1% (or 83/120) had macrocytic anemia, and 6.6% (or 8/120) had microcytic hypochromic anemia.

Within the current investigation, 2000–4000 cells/cumm were seen in 66.6% (80/120) of the cases, 1000–2000 cells/cumm in 23.3% (28/120) of the cases, and <1000 cells/cumm in 10% (12/120) of the cases.

In the current study, 37.5% of patients (45/120) had mild thrombocytopenia, 30.8% had moderate thrombocytopenia, and 31.6% had severe thrombocytopenia.

Table 2: Correlation of Clinical diagnosis and Hb% distribution

CLINICAL DIAGNOSIS	Hb %		Total	χ^2 value (DF=2)	p ^a value
	< 6g/dl	≥6g/dl			
Vitamin B12 deficiency anemia	23	36	59	0.1652	0.9207
Infectious etiology	14	26	40		
Others	8	13	21		
Total	45	75	120		

a Chi-square test (p<0.05 is significant)

Hemoglobin distribution among cases

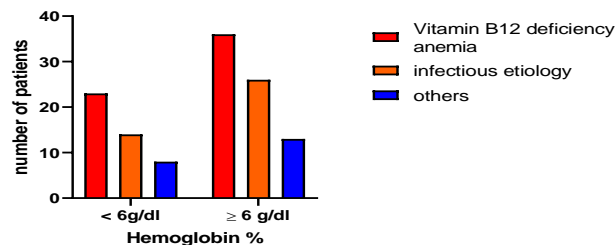


Table 3: Correlation of Clinical diagnosis and Peripheral smear impression

CLINICAL DIAGNOSIS	Peripheral smear impression				Total	χ^2 value (DF=4)	p ^a value
	Microcytic	Macrocytic	Normocytic	Dimorphic			
Vitamin B12 deficiency anemia	7	41	5	6	59	35.88	<0.0001 ***
Infectious etiology	11	10	17	2	40		
Others	5	16	0	0	21		
Total	23	67	22	8	120		

a Chi-square test (p<0.05 is significant)

a Chi-square test (p<0.05 is significant)

With a p value of 0.001, the correlation between the clinical diagnosis and the peripheral smear impression is statistically significant

Peripheral smear and Vit B12 Levels among cases

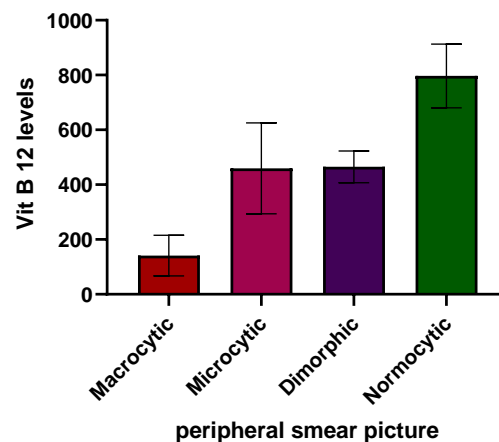


Table 5: Clinical correlation of Clinical diagnosis and WBC Count distribution.

CLINICAL DIAGNOSIS	WBC Count/mm ³		Total	χ^2 value (DF=2)	p ^a value
	<2000	2001-4000			
Vitamin B12 deficiency anemia	16	43	59	3.004	0.227
Infectious etiology	14	26	40		
Others	10	11	21		
Total					

a Chi-square test (p<0.05 is significant)

There is no statistical significance Correlation between Clinical diagnosis and WBC with p value 0.227.

Peripheral smear finding among cases

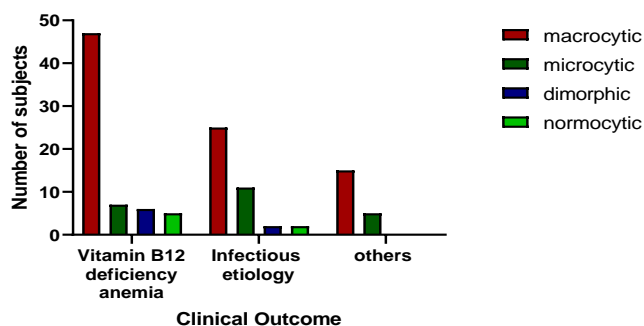


Table 4: Brown-Forsythe ANOVA test

Peripheral smear findings	No. of cases	Vitamin B12 Mean \pm SD	P value ^b
Normocytic Hypochromic anemia	22	797.0 \pm 116.3	<0.0001 ****
Microcytic hypochromic anemia	23	459.6 \pm 165.9	
Macrocytic anemia	67	141.4 \pm 73.91	
Dimorphic anemia	8	465.0 \pm 57.82	
Total	120		

^b Brown-Forsythe ANOVA test

Table 5: Clinical correlation of Clinical diagnosis and WBC Count distribution

WBC count distribution among cases

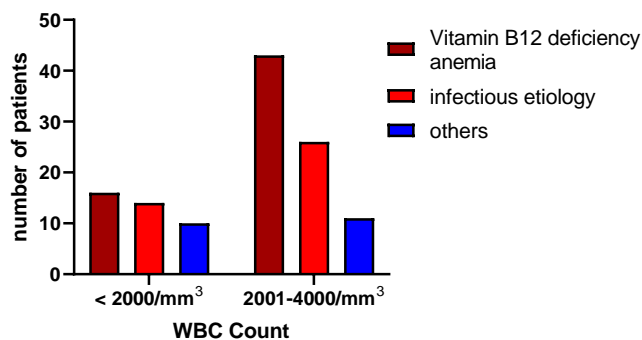


Table 6: Distribution of Cases Based On Platelet Count and Clinical Diagnosis

CLINICAL DIAGNOSIS	Platelet Count/mm ³			Total	χ^2 value (DF=4)	p ^a value
	<20000	20001-50000	50001- \geq 1 lakh			
Vitamin B12 deficiency anemia	15	21	23	59	12.68	0.0129
Infectious etiology	20	6	14	40		
Others	3	10	8	21		
Total						

a Chi-square test (p<0.05 is significant)

There is Statistical significance Correlation between Clinical

diagnosis and Platelets with p value 0.01.

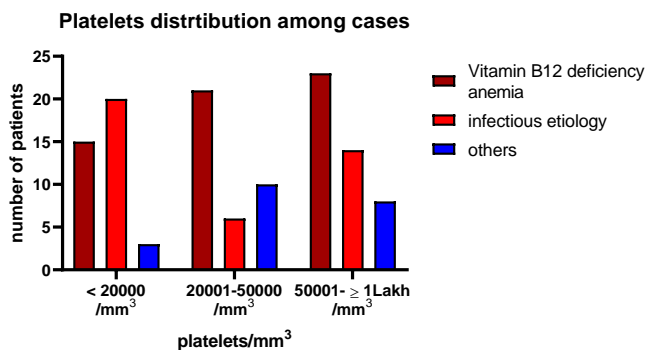


Table 7: Distribution of Cases Based on Bone Marrow Aspiration Diagnosis.

Bone marrow Diagnosis	No. of cases	Percentage
Aplastic anemia	6	5
Megaloblastic anemia	30	2.5
MDS	4	3.3
Infective etiology	7	5.8
NOT DONE	73	60.8
Total	120	99.9

In the current study, 5.8% of patients had an infectious origin, 2.5% had megaloblastic anemia, 3.3% had MDS, and 5% had bone marrow aplastic anemia.

DISCUSSION

Comparative studies related to Age sex distribution

The majority in the current study, including 36.6% (44/120) of those aged 18 to 30, were followed in frequency by those aged 31 to 40, who made up 21.6% (26/120), by those aged 41 to 50, who made up 20% (24/120), by those aged 51 to 60, who made up 14.1% (17/120), and by those aged 61 to 70, who made up 7.5% (9/120).

Charusheela et al¹⁴ study, mean age was 41yrs. The age range of 31 to 40 years old accounted for the greatest number of cases (25%). The age group of 21–30 years old came in second (22.9%), while the least impacted age group was those over 70. There were 32.1% female patients and 67.9% male patients, for a male to female ratio of 2.1:1.

Pooja Agarwal¹⁵ et al study most of the patients were in the age group 18–40 years and maximum cases were in the age group 20–29 years (23.75%). The lowest incidence (2.5%) was seen in 70–80 years. The oldest patient was seventy-eight years old, while the youngest was eighteen. The majority of megaloblastic anemia patients (53.3%) belonged to the 18–29 age range. The study's age distribution revealed that in this region, pancytopenia patients often present at a younger age. There were twenty-seven females and fifty-three men, indicating a male predominance. The ratio of men to women was 1.94:1.

In Gaythri et al¹⁶ study the most typical presenting style was broad weakness; dyspnea, fever, and weight loss were the other primary symptoms. In every case, pallor was seen. Megaloblastic anemia was associated with splenomegaly and

hepatomegaly, then sub leukemic leukemia and malaria. Multiple myeloma patients had skeletal discomfort. In cases of lymphoblast-type sub leukemic leukemia, lymphadenopathy was seen.

In Shreyansh et al¹⁸ study A widespread weakness was the most frequent style of presentation, occurring in 79 (92.9%) of the patients.

In Dr Reddy RJP et al (3) study addition to the usual symptoms of fever (90, 95.7%) and myalgia (80, 85.1%) observed in Dengue fever patients, stomach discomfort is observed in 44 (46.8%) of the patients.

The following symptoms were also prominent: palpitations, giddiness, fever, dyspnea, and fatigability. A common observation among all the patients was pallor. There were 23.5% and 21.1% of individuals with splenomegaly and hepatomegaly, respectively. Additional physical findings included ascites, clubbing, skin abnormalities, edema, and jaundice.

Comparative studies related to Distribution of clinical signs associated with pancytopenia

Pallor was seen in 43.3% (52/120) patients in the current research, Pallor+ Splenomegaly in 31.6% (38/120) cases, Splenomegaly in 20% (24/120) cases, and Hepatomegaly in 5% (6/120) instances.

Charusheela et al¹⁴ Physical examination revealed splenomegaly in 20% of cases, hepatomegaly in 10%, and lymphadenopathy in 3.6% of cases.

Comparative studies related to clinical Diagnosis

According to the current study, vitamin B12 deficiency anemia, or 49.1% (59/120) of cases of pancytopenia, was the most prevalent cause, followed by malaria (22.5%) (27/120). 10.8% (13/120) of cases were Dengue. Aplastic anemia (6.6%), multiple myeloma, AML (2.5%), and anemia from chronic illness were less prevalent causes. 3.3% for MDS and 0.8% for myelofibrosis. Hepatitis B, leukemia (0.8%), and CLD with splenomegaly (15%).

Dr Reddy RJP et al [3] in India showed that Pancytopenia 42 (46%) and thrombocytopenia 84 (89.36%) are reported as two prevalent presentations in viral fevers during the Dengue and viral fever outbreak of 2014–2015.

In Charusheela et al¹⁴ study, Dimorphic anemia was the most frequent cause of pancytopenia (49.3%). Megaloblastic anemia came in second place (35%). Aplastic anemia, multiple myeloma, ALL, and anemia from chronic illness were less frequent causes.

In Shreyansh et al¹⁸ study, In 51.8% of instances, combined/dual deficiency anemia was the most prevalent cause of pancytopenia; in 31.8% of cases, megaloblastic anemia was the reason. There were around 8.2% of myelodysplastic syndrome cases, 3.5% of iron deficiency anemia patients, and 3.5% of normal bone marrow cases.

Comparative studies related to Hemoglobin

In the current study, 37.5% (45/120) of the patients had < 6 g/dl hb, 55.8% (67/120) had 6-8.9%, and 6.6% (8/120) had 9-11 g/dl.

In Pooja Agarwal et al¹⁵ study the hemoglobin values ranged from 1.4 to 10.8 g/dl. The majority of patients (58.75%) had hemoglobin levels between 4 and 7 g/dl, with 23.75% having levels between 1-4 g/dl. The hemoglobin levels of 13.75% of patients were between 7 and 10 g/dl. Hb levels exceeding 10 g/dl were seen in only 3.75% of patients.

Geetika et al (19) stated that the most prevalent manifestation in acute critically sick and chronic infection cases is reduced hemoglobin (<10g/dl), which is seen in 85 (85%) of patients; in 44 (44%) of these cases, hemoglobin is <4g/dl.

Comparative studies related to Peripheral blood smear findings

In the current investigation, 5.8% (or 7/120) of the patients had normocytic hypochromic anemia, 18.3% (or 22/120) had microcytic hypochromic anemia, 69.1% (or 83/120) had macrocytic anemia, and 6.6% (or 8/120) had macrocytic anemia.

In Pooja Agarwal et al¹⁵ study the range of the leucocyte count was 500–1,73,000 cells/mm³. TLC values for the majority of patients (42%) ranged from 1000 to 2499 cells/mm³. TLC values of 2500–4000 cells/mm³ were seen in 24% of individuals. Values over 4000 cells/mm³ were present in 33% of individuals. A one instance received TLC.

In Gaythri et al¹⁶ study Dimorphic anemia (37.5%) and macrocytic anemia (31.7%) were the most common blood types; a peripheral smear revealed macro-ovalocytes with hyper segmented neutrophils.

In Shreyansh et al study¹⁸ A single case of malaria constituting 1.2% total was also detected. Each patient had a thorough peripheral smear examination. A noteworthy discovery (p value=0.001) in megaloblastic anemia and mixed deficiency anemia was anis poikilocytosis. The majority of cases of combined deficiency anemia showed blood images that were dimorphic. In the majority of cases of megaloblastic anemia, macrocytic RBCs were followed by dimorphic RBCs. Cases of myelodysplastic syndrome exhibited dimorphic RBC shape after normocytic normochromic morphology. RBCs in malaria cases with normal bone marrow are normocytic normochromic.

Bone marrow aspirate and biopsy findings

In the current study, 5.8% of patients had an infectious origin, 2.5% had megaloblastic anemia, 3.3% had MDS, and 5% had bone marrow aplastic anemia.

In Yasmeen et al¹⁷ study the majority of bone marrow aspiration results (27%), were found to have megaloblastic anemia; this was followed by megaloblastic anemia (15.6%), acute leukemia (13%), mixed deficiency anemias (9.3%), and malaria (rarely observed in just 2 individuals).

Shreyansh et al¹⁸ study Bone marrow aspiration was performed

on all the 85 patients. Three patients had hypercellular marrow, whereas seven cases had hypocellular marrow. The marrow in the remaining instances was normocellular. The most noteworthy discovery (p value = 0.0005) in combined deficiency anemia was erythroid hyperplasia, which was followed by megaloblastic anemia and myelodysplastic syndrome. Myelodysplastic syndrome, combined deficiency anemia, megaloblastic anemia, and one instance of iron deficiency anemia have all been linked to dysgranulopoiesis, which includes gigantic metamyelocytes. Thirteen instances of combination deficiency anemia, megaloblastic anemia, myelodysplastic syndrome, and one case of malaria and iron deficiency anemia all showed dysmegakaryopoiesis, including hypolobated and hyperlobated variants. In one case, malarial parasites were found. In two cases, trephine biopsy was carried out.

A study by Geetika et al^[19] concluded that Macrocytic normochromic anemia is a cause of pancytopenia in individuals with acute critical and chronic illnesses. Patients' mortality and morbidity are decreased by early diagnosis. Pancytopenia can have a wide range of causes, from easily treated illnesses to catastrophic, life-threatening conditions. Therefore, it's critical to assess these individuals in order to give them the right care.

CONCLUSION

Pancytopenia is a frequent hematological issue that arises in clinical settings. Patients who exhibit unexplained anemia, a protracted fever, and a bleeding tendency should be suspected of having pancytopenia based on clinical grounds. The current study comes to the conclusion that comprehensive primary hematological investigations and bone marrow aspiration in cytopenic patients are useful in planning further investigations and managing cytopenic patients as well as in understanding the disease process and diagnosing or ruling out the causes of cytopenia.

Severe pancytopenia can serve as a prognostic signal and has a substantial correlation with the clinical outcome. When a patient presents with non-specific symptoms such as pallor and widespread weakness, a bone marrow examination can be a crucial diagnostic tool in determining the cause of pancytopenia. The most frequent causes of pancytopenia were megaloblastic anemia and malaria.

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