

# Clinicohematological study of pancytopenia in a tertiary care hospital of Rohilkhand region – An observational study

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**Introduction:** Reduction of all three formed elements of blood (erythrocytes, leukocytes, and platelets) below the normal reference range. The incidence of various hematological disorders causing pancytopenia differs according to geographical distribution and genetic predisposition. Therefore, it is not a disease entity but a triad that may result from a number of disease processes – primarily or secondary involving the bone marrow. The management and prognosis of pancytopenia rely on the primary etiology. Therefore, the correct finding of etiology in a given case is primary for appropriate course of treatment. **Materials and Methods:** The present observational study was conducted in tertiary care Centre Rohilkhand Medical College and Hospital (RMCH) situated in Uttar Pradesh state of India over a period of 1 year in COVID-19 pandemic crisis. November 2019 till October 2020 including all the diagnosed cases of pancytopenia. **Results:** Most common cause of pancytopenia was megaloblastic anemia (60.8%), followed by aplastic anemia (23.5%), multiple myeloma (5.9%), leukemia (5.9%), and dimorphic anemia and metastatic bone marrow (2%). **Conclusion:** Pancytopenia is regularly encountered hematological complication in clinical practice. If patients with undiagnosed cause of anemia, prolonged weakness and fever and tendency to bleed then diagnosis can be suspected for pancytopenia and a complete laboratory investigation should be carried out. Clinical findings, complete blood count and bone marrow examination can help out in sequencing the diagnosis. Peripheral blood smear assessment help in evaluating the most probable cause of anemia while bone marrow examination help in definitive diagnosis.

**KEY WORDS:** Aplastic anemia, leukemia, megaloblastic anemia, pancytopenia

## INTRODUCTION

Pancytopenia is an exigent clinical hematological entity encountered in day-to-day clinical practice. This is define as simultaneous presence of anemia (<13.5 g/dL [male] or 12 g/dL [female]), leukopenia (white blood cell <4000/ $\mu$ L), and thrombocytopenia (platelets <140,000/ $\mu$ L), that is, reduction of

all three formed elements of blood (erythrocytes, leukocytes, and platelets) below the normal reference range.<sup>[1]</sup>

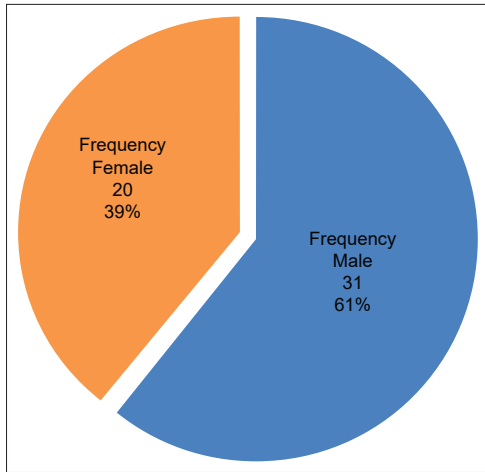
Therefore, it is not a disease entity but a triad that may result from a number of disease processes — primarily or secondary involving the bone marrow.

There is slight male predominance with male and female ratio of 1.2:1, the peak age of pancytopenia is in between 11 and 20 (36.7%), and second peak in 21–31 years (21.6%) Fig 1.<sup>[2]</sup>

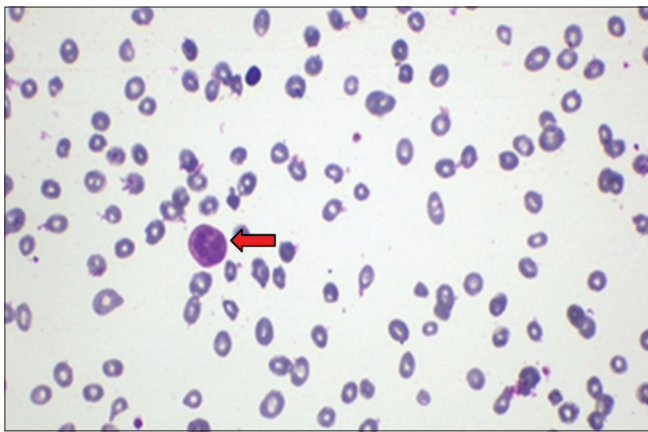
The marrow is usually hypocellular in cases of pancytopenia caused by primary production defects. Cytopenia develop from ineffective hematopoiesis, increased peripheral utilization or destruction of cells, and bone marrow invasive processes

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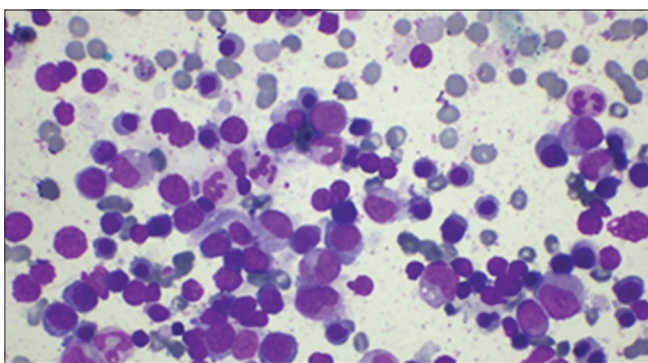
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**Figure 1:** Bone marrow biopsy correlation with gender



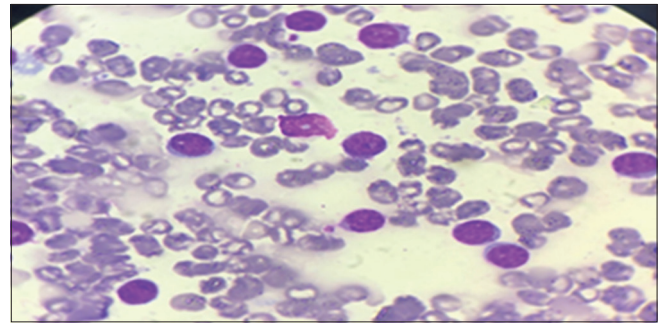
**Figure 2:** Peripheral blood smear showing macrocytes along with hyper segmented neutrophil ( $\times 400$  Leishman)



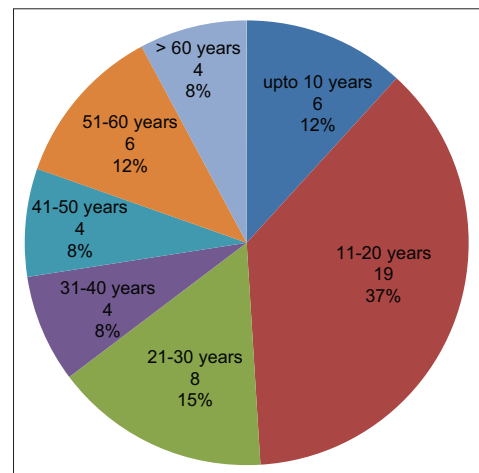
**Figure 3:** Bone marrow aspiration showing hypercellular marrow with megaloblast ( $\times 1000$  Leishman Giemsa)

are usually associated with a normocellular or hyper cellular marrow.<sup>[3]</sup>

Therefore, peripheral and examination bone marrow involve crucial evaluations of hematological diseases to predict a definitive result. As shown in Figures 2 and 3 peripheral and bone aspiration correlation to diagnosed case of Megaloblastic anemia Stress the importance of systematic and diligent examination of hematological parameter to provide definitive diagnosis is obligatory.<sup>[4]</sup> Diagnostic values acquired from hemogram and



**Figure 4:** Bone marrow aspiration showing acute leukemia blast with punched out nuclei ( $\times 1000$  Leishman Giemsa)



**Chart 1:** Incidence of pancytopenia in different age groups

**Table 1:** Incidence of pancytopenia in different age groups

Age intervals	Frequency	Percent
up to 10 years	6	11.8
11–20 years	19	37.3
21–30 years	8	15.7
31–40 years	4	7.8
41–50 years	4	7.8
51–60 years	6	11.8
>60 years	4	7.8
Total	51	100

examination bone marrow are important in early diagnosis of disorder that leads to better prognosis in majority of cases.

Chart 1 and Table 1 shows most common age group affected was 11 to 20 years. The management and prognosis of pancytopenia rely on the primary etiology. Therefore, the correct finding of etiology in a given case is primary for appropriate course of treatment.

Unfortunately, pancytopenia is a relatively common but “inadequate attention entity” in Indian subcontinent. Pancytopenia causes widespread effects on the whole body by causing to have oxygen deficiency as well as complication with immune functions.<sup>[5]</sup>

**Table 2:** Correlation of bone marrow biopsy finding with age

Age intervals	Bone marrow biopsy									
	Aplastic anemia		Leukemia		Megaloblastic anemia		Multiple myeloma		Others	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Upto 10 years	2	16.7	1	33.3	3	10.0	0	0.0	0	0.0
11–20 years	4	33.3	2	66.7	12	40.0	0	0.0	1	33.3
21–30 years	1	8.3	0	0.0	6	20.0	0	0.0	1	33.3
31–40 years	2	16.7	0	0.0	2	6.7	0	0.0	0	0.0
41–50 years	0	0.0	0	0.0	3	10.0	0	0.0	1	33.3
51–60 years	3	25.0	0	0.0	1	3.3	2	66.7	0	0.0
>60 years	0	0.0	0	0.0	3	10.0	1	33.3	0	0.0

Applied  $\chi^2$  test for significance.  $P=0.237$ ; NS

**Table 3:** correlation of bone marrow biopsy finding with gender.

Gender	Frequency	Percent
Male	31	60.8
Female	20	39.2
Total	51	100

Early discovery of various causes of pancytopenia is very critical and requires elicit clinical examination and investigations such as complete blood count (CBC), peripheral smear (PS) and examination bone marrow as marrow cellularity and composition in cases of pancytopenia differ in relationship to underlying pathologic conditions [Table 2]. The marrow is usually hypocellular in cases of pancytopenia caused by primary production defects. As gender correlation in this study show male preponderance as shown in above table 3.<sup>[6]</sup>

### Statistical Analysis

The entire data were incorporated in Microsoft Excel sheet, using Statistical Package for the Social Sciences version 22.0 the analysis was prepared. To assess the association between these parameters, like hood ratio test and Chi-square test were used.

### Objectives

The objectives of the study were to observe disease spectrum producing pancytopenia based on clinic-hematological and/or bone marrow studies.

## MATERIALS AND METHODS

It is a retrospective study done in pandemic phase that was carried out over a period of 1 year in the department of pathology of tertiary care center Ethical committee RMCH approval was obtained to conduct this study.

All patients referred to central clinical laboratory of hospital for routine CBC PS examination from the outpatient and inpatients

department were screened for pancytopenia and a total of 51 cases were selected on the criteria defined by (N. S. Young)<sup>[7]</sup> as follows:

- Hemoglobin: males' <13.5 mg/dl or females 12 mg/dl
- Total leucocyte count  $4 \times 10^9/L$
- Platelet below  $150 \times 10^9/L$ .<sup>[8]</sup>

History including age, sex. History of symptoms, bone pains, fever, night sweats, malaise, weight loss, and pruritus was taken. A detailed attentive physical examination of every patient was done for pallor, jaundice, hepatosplenomegaly, lymphadenopathy, and petechial rash. Evidence of hypersplenism and primary malignancy was searched for whenever necessary.

Basic hematological investigation such as CBC, reticulocyte count, and PS examination was performed in each cases.

Blood counts were done by semi-automated electronic cell counter (Sysmex -Transasia [1000 i] Biomedicals) and were again rechecked manually during PS examination.

Bone marrow aspiration and trephine biopsy were done each and every diagnosed case of pancytopenia from anterior superior iliac spine using standard methods.

Whenever indicated other investigations performed included erythrocyte sedimentation rate, urine, and liver and renal function test – ELISA for HIV, Hepatitis B and C viruses, the suspected underlying pathology and the provisional diagnosis were workup.

## RESULTS

In our study, total number of patients is 51 who were clinically diagnosed as pancytopenia. They were studied during a course of 1 year that is from September 2019 to August 2020, so called the pandemic Era, at RMCH. Following results were recorded and analyzed.

The commonest age group affected was 11–20 years of age group that is 37% and the least common age group of concern

**Table 4: Bone marrow biopsy correlation with gender**

Gender	Bone Marrow Biopsy									
	Aplastic anemia		Leukemia		Megaloblastic anemia		Multiple myeloma		Others	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Male	10	83.3	3	100.0	13	43.3	2	66.7	3	100.0
Female	2	16.7	0	0.0	17	56.7	1	33.3	0	0.0

Applied  $\chi^2$  test for significance.  $P=0.036$ ; consider significant

**Table 5: Incidence of bone marrow aspiration finding in pancytopenia cases**

Bone marrow aspiration	Frequency	Percent
Aplastic anemia	12	23.5
Dimorphic anemia	1	2.0
Erythroid hyperplasia with megaloblastic changes	31	60.8
Leukemia	3	5.9
Metastatic bone marrow	1	2.0
Multiple myeloma	3	5.9
Total	51	100.0

was two parameters that is 31–40 years (8%) and more than 60 years that was also (8%). The study population consists of 51 study subjects aged between 2 and 80 years with a mean age of  $29.14 \pm 19.91$  years. Majority of the patients were between 11 and 20 years of age (37.3%), while 15.7% were 21–30 years and remaining were >30 years and  $\leq 10$  years of age.

Table 4 explains sex ratio in our study population showed that male's proportion was higher than females, that is, 60.8% and 39.2%, respectively.

Above table 5 shows the association of bone marrow biopsy and their age groups distribution. Its showed similar age among the groups ( $P = 0.237$ ), that is, did not differ significantly.

The above comparisons concluded that the association between bone marrow biopsy according to their gender distribution, the frequency (%) of males was higher than females. Comparing the sex proportions (M/F) of each groups of bone marrow biopsy,  $\chi^2$  test revealed significant correlation proportions of males and females ( $P = 0.036$ ).

In this study, in bone marrow aspiration was done in all 51 patients maximum number patient have erythroid hyperplasia with megaloblastic anemia 60.8% hemodilution 9% hypoplastic marrow that is aplastic anemia 23.5% leukemic and multiple myeloma cases of 5.9%, and least with 2% metastatic marrow and dimorphic anemia cases.

Applied  $\chi^2$  test for significance.  $P \leq 0.001$ ; consider highly significant. Statistically a significant correlation was found in association between bone marrow biopsy and its aspiration ( $P \leq 0.001$ ) [Table 5].

## DISCUSSION

Pancytopenia not a disease but an exemplification of different ailments that lead to depletion of the cellular module derive in anemia, thrombocytopenia, and leukopenia in the peripheral blood. It is a state that is very often observed in clinical practice; nevertheless, there are very few studies performed to point out the etiology of pancytopenia.<sup>[9]</sup>

Barik *et al.*<sup>[10]</sup> age groups 2–80 years and Jain and Naniwadekar.<sup>[11]</sup> did their studies on same age groups of patients of pancytopenia. In contrast, many studies were done but it has an exclusion criteria of age more than 18 years as example is Yadav *et al.*<sup>[12]</sup>

Age distribution in our study was divided in up to 10 years, from 11 to 20 years, 21 to 30 years, 31 to 40 years, 41 to 50 years, 51 to 60 years, and last be more than 60 years. The most common age group affected was 11–20 years 37.3% that is first to second decade of life was found be affected mostly in this study. Accordance to this study various study undertaken Deshalphine *et al.*,<sup>[13]</sup> Singh *et al.*,<sup>[14]</sup> and Arshad *et al.*,<sup>[15]</sup> has similar results of affecting first and second decade of life affected. Other concordance studies were also seen given by Reddy and Rao,<sup>[16]</sup> Varma *et al.*<sup>[17]</sup>

In this present study, there is a slight male preponderance was scrutinized as total no of males with pancytopenia were 31 (60.8%) including adults and children and number of females were 20 (39.2%) so the ratio male is to female with  $n = 51$  will 1.5:1. Various similar studies were seen having male predominance Sahay *et al.*,<sup>[18]</sup> Kavitha and Yogalakshmi,<sup>[19]</sup> and Zeeshan *et al.*<sup>[20]</sup> all of these study showed similar result but many contradictory studies were also observed by Deshpande *et al.*<sup>[21]</sup> with ratio M: F having 1:1.2 and other one was by Geetanjali and Das<sup>[22]</sup> M: F 1:1.25.

In our study p value 0.036 considered significant in accordance with 10 males and 2 females having aplastic anemia with 83.3% in total no of males where as 16.7% 3 male pancytopenia patients presenting with significance value of 100% whereas 13 males and 17 females megaloblastic anemia patients with 43.3% and 56.7%. Multiple myeloma with a significance of 2 males as 66.7% and females with 33.3% value are considered as significant. Similar studies were done Deshalphine *et al.*<sup>[13]</sup> in this study it observed female are predominately affected in megaloblastic anemia with maximum number of cases.

In this present study as table 6 shows, megaloblastic anemia is the most common cause of pancytopenia erythroid hyperplasia

**Table 6: Bone marrow aspiration and bone biopsy correlation**

Bone marrow aspiration	Bone marrow biopsy					Total (%)
	Aplastic anemia (%)	Leukemia (%)	Megaloblastic anemia (%)	Multiple myeloma (%)	Others (%)	
Aplastic anemia	12	0	0	0	0	12
	100.0	0.0	0.0	0.0	0.0	23.5
Dimorphic anemia	0	0	0	0	1	1
	0.0	0.0	0.0	0.0	33.3	2.0
Erythroid hyperplasia with megaloblastic changes	0	0	30	0	1	31
	0.0	0.0	100.0	0.0	33.3	60.8
Multiple myeloma	0	0	0	3	0	3
	0.0	0.0	0.0	100.0	0.0	5.9
Leukemia	0	3	0	0	0	3
	0.0	100.0	0.0	0.0	0.0	5.9
Metastatic bone marrow	0	0	0	0	1	1
	0.0	0.0	0.0	0.0	33.3	2.0
Total	12	3	30	3	3	51
	100.0	100.0	100.0	100.0	100.0	100.0

megaloblastic anemia (60.8%), followed by aplastic anemia (23.5%), multiple myeloma (5.9%), leukemia two cases of acute leukemias and one case of chronic myeloid leukemia (5.9%), dimorphic anemia (2%), metastatic bone marrow (2%), and malaria (2%) [Figure 4].

Various similar results studies as Arshad *et al.*<sup>[15]</sup> a 2-year cross-sectional study having megaloblastic anemia 49.33% aplastic anemia 16% multiple myeloma 4% chronic myelocytic leukemia 1.33% all 8% cases.

Dhooria *et al.*<sup>[23]</sup> total 100 case in which 66% megaloblastic anemia aplastic anemia 18% malaria 6% acute myeloid leukemia 2% case. Shwetha *et al.*<sup>[24]</sup> showed megaloblastic anemia 68% hypoplastic marrow 14% acute myeloid leukemia 4.7% acute lymphoid leukemia 3.4% multiple myeloma 1.4% and also with 4.7% of normal marrow. Disconcordance seen in study done by Javalgi and Dombale<sup>[9]</sup> 106 cases most common cause was megaloblastic anemia and second most common was iron deficiency anemia.

## CONCLUSION

Pancytopenia is regularly encountered hematological complication in clinical practice. If patients with undiagnosed cause of anemia, prolonged weakness and fever and tendency to bleed then diagnosis can be suspected for pancytopenia and a complete laboratory investigation should be carried out.

Clinical findings, CBC, and bone marrow examination can help out in sequencing the diagnosis.

Peripheral blood smear assessment help in evaluating the most probable cause of anemia while bone marrow examination help in definitive diagnosis.

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