Section: Pathology

Original Research Article

CLINICO-HAEMATOLOGICAL EVALUATION OF PANCYTOPENIA AT TERTIARY CARE CENTRE

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Abstract

Background: Pancytopenia refers to a reduction in all the three formed elements of blood, i.e., red blood cells (RBCs), white blood cells (WBCs), and platelets leading to the simultaneous presence of anemia, leukopenia, and thrombocytopenia respectively. The features of pancytopenia are variable. It may present with non-specific symptoms like generalized weakness, fever, weight loss or specific features according to its affected lineage like bleeding diathesis as gum bleeding, specific symptoms like generalized weakness, fever, weight loss or specific features according to its affected lineage like bleeding diathesis as gum bleeding, petechiae, purpura, hemarthrosis, recurrent infection, dyspnoea on exertion, palpitation, and edema. This study was undertaken to study the clinical profile and hematological parameters of pancytopenia. **Materials and Methods:** The present study was conducted in the Department of Pathology, Pt. J.N.M. Medical College & associated Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh. It was an Observational Cross-Sectional Descriptive type study. A detailed relevant history was taken and done general examination. Complete blood count, Peripheral smear examination, Reticulocyte count, Bone marrow aspiration examination, Solubility test for hemoglobin S, Estimation of Serum Iron Concentration and Vitamin B12 ESSAY were done and all data was collected for statistical analysis. **Result:** In the present study, 100 cases of pancytopenia were included. Out of which the study population age ranges from 01-80 years with a maximum number of cases (22%) belonging to 11-20 years of age group, followed by 41-50 years (17%), 1-10 years (16%), 31-40 years(13%), 21-30 years and 51-60 years (11%), 61-70 years (9%) and the mean age of the study population was 32.245 ± 20.419 years. In the present study, the most common etiology of pancytopenia was megaloblastic anemia seen in 17% of cases followed by acute leukemia (14%), iron deficiency anemia (10%), hypersplenism (8%), sickle cell anemia (7%), chronic liver disease (6%), dimorphic anemia, dengue, and HIV was observed in 3% cases respectively, sepsis and malaria seen in 2% of cases respectively. **Conclusion:** Pancytopenia is not a disease entity itself but it is a manifestation of diverse hematological and systemic disorders. It is usually suspected when a patient presents with unexplained prolonged anemia, prolonged fever, and a tendency to bleed. Through this study, we conclude that the cases of pancytopenia require both routine investigations and a panel of special investigations for determining the exact etiology complemented and correlated with detailed clinical history and physical examination.

INTRODUCTION

Pancytopenia refers to a reduction in all the three formed elements of blood, i.e., red blood cells (RBCs), white blood cells (WBCs), and platelets leading to the simultaneous presence of anemia, leukopenia, and thrombocytopenia respectively. It is not a disease entity by itself, but rather a triad of Anemia {Red blood cell count <4.3x106/µL (Male) or <3.53x106/µL(Female)}, Leukopenia {Total white cell count <4000 /µL} and Thrombocytopenia {Platelet count <150000 /µL}.[1] Pancytopenia is

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usually insidious in onset. In most cases, the etiology can be determined from consideration of the clinical features, biochemical, microbiological, radiological, and examination of the bone marrow aspirate and trephine biopsy. It is a striking feature of several disorders ranging from simple drug-induced bone marrow hypoplasia and megaloblastic anemia to fatal aplastic anemia and leukemias. It should be suspected clinically when a patient presents with fatigue, prolonged unexplained fever, and repeated infection.[2] The features of pancytopenia are variable. It may present with non-specific symptoms like generalized weakness, fever, weight loss or specific features according to its affected lineage like bleeding diathesis as gum bleeding, petechiae, purpura, hemarthrosis, recurrent infection, dyspnoea on exertion, palpitation, and edema. The majority of causes of pancytopenia are curable with early diagnosis and treatment. However, in some cases, where cure is not possible, early diagnosis and implementation of supportive treatment will improve quality of life by reducing morbidity and mortality.[3] As the severity of pancytopenia and its underlying etiology determine its treatment and prognosis, identifying the correct etiology in a given case is crucial and helps in implementing timely and appropriate treatment. This study was undertaken to study the clinical profile and hematological parameters of pancytopenia.

MATERIALS AND METHODS

The present study was conducted in the Department of Pathology, Pt. J.N.M. Medical College & associated Dr. B.R.A.M. Hospital, Raipur, Chhattisgarh. It was an Observational Cross-Sectional Descriptive type study. All cases of Pancytopenia and fulfilled the following criteria [1] were included in the study.

Anemia: RBC count- <4.5x106/µL(Male) or <3.53x106/µL(Female)

Leukopenia: Total white cell count <4000 / µL

Thrombocytopenia: Platelet count <150000 / µL

Patients on chemotherapy & radiotherapy and who had received blood transfusions recently were excluded from the study. A detailed relevant history was taken and done general examination. Complete blood count, Peripheral smear examination, Reticulocyte count, Bone marrow aspiration examination, Solubility test for hemoglobin S, Estimation of Serum Iron Concentration and Vitamin B12 ASSAY were done and all data was collected for statistical analysis.

RESULTS

In the present study, 100 cases of pancytopenia were included.

Out of which the study population age ranges from 01-80 years with a maximum number of cases (22%) belonging to 11-20 years of age group, followed by 41-50 years (17%), 1-10 years (16%), 31-40 years(13%), 21-30 years and 51-60 years (11%), 61-70 years (9%) and the mean age of the study population was 32.245 ± 20.419 years.

In the present study, out of 100 patients 52% of the patients were female and 48% of the patients were male, indicating slight female preponderance in present study with male to female ratio was 1:1.08 [Table 1].

In the present study, Pallor was universally present in almost all cases (99%), followed by splenomegaly (28%), hepatomegaly (26%), icterus (22%), pedal edema (18%), petechiae (17%), lymphadenopathy (14%), Purpuric spot (11%), sternal tenderness and gum hypertrophy both are seen in 2% patients [Table 2].

In the present study, hemoglobin level ranges from 1.1 – 11 gm%. The majority of patients were having severe anemia with hemoglobin value of less than 7gm/dl (58%), followed by moderate anemia with a hemoglobin value 7-9 gm/dl (25%) and 17% of patients were having to mild anemia with hemoglobin value 9-11 gm/dl. The mean hemoglobin value of the study population was 6.406 ± 2.5 gm/dl.

In the present study, out of 100 cases, the majority of the cases (40%) were having total leukocyte count of less than 2000 cells/ mm3 followed by 31% of patients belonging to 3001 – 4000 cells/ mm3 and 29% of patients were having total leukocyte count 2001 – 3000 cells/ mm3. The mean leukocyte count of the study population was 2357.5 ± 1038 cells/ mm3 [Table 3].

In the present study, majority of the cases were found to have severe thrombocytopenia (56%) where platelet count was less than 50000/µl followed by 31% of patients were having moderate thrombocytopenia where platelet count was 50001 – 100000/µl and 13% patients were having mild thrombocytopenia where platelet count was 100001 – 150000/µl.The mean platelet count was 51366 ± 38823 cells/ µl.

In the present study majority of the cases had corrected reticulocyte count below <0.5% observed in 54 cases, followed by 26 patients having 0.5-1%, 18 cases having 1-1.5% , 2 cases were having 1.5-2 %.

The mean corrected reticulocyte count was 0.595±0.414%.

In the present study most of the patients were having normocytic normochromic RBCs (46%), followed by 25% patients having microcytic hypochromic RBCs, 17% patients were having macrocytic normochromic RBCs and 12% patients had dimorphic blood picture in the peripheral smear. In the present study few cases had toxic granulation (20%), followed by hypersegmented neutrophils seen in 15% of cases.

In the present study, the most common bone marrow finding was erythroid hyperplasia found in about 22% of cases of pancytopenia followed by acute leukemia found in about 17% of cases, megaloblastic maturation was seen in 12% of cases, and micro-

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normoblastic maturation and reactive bone marrow was observed in 7.5% cases respectively [Table 4].

In the present study, the most common etiology of pancytopenia was megaloblastic anemia seen in 17% of cases followed by acute leukemia (14%), iron deficiency anemia (10%), hypersplenism (8%), sickle cell anemia (7%), chronic liver disease (6%), dimorphic anemia, dengue, and HIV was observed in 3% cases respectively, sepsis and malaria seen in 2% of cases respectively, systemic lupus erythematosus, enteric fever, and drug-induced pancytopenia was observed in 1%, of cases respectively.

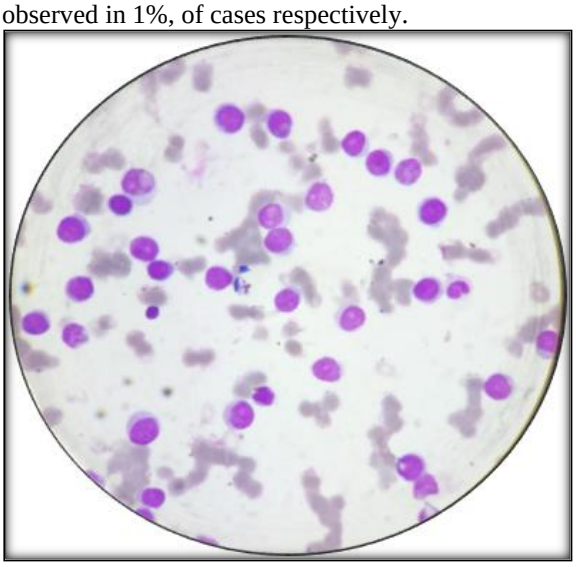

Figure 1: Photomicrograph of bone marrow aspiration showing blast >80% seen in Acute Leukemia(Leishman's stain 1000x)

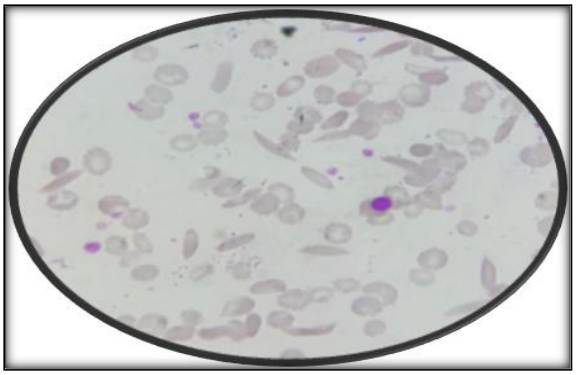

Figure 2: Photomicrograph of peripheral smear showing sickle-shaped RBCs with nucleated RBCs. (Leishman's stain 1000x)

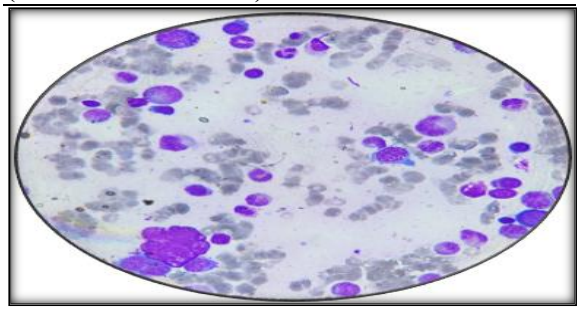

Figure 3: Photomicrograph of bone marrow aspiration showing megaloblast with royal blue cytoplasm and sieve-like chromatin and dyserythropoiesis seen in megaloblastic anemia (Leishman's stain 1000x)

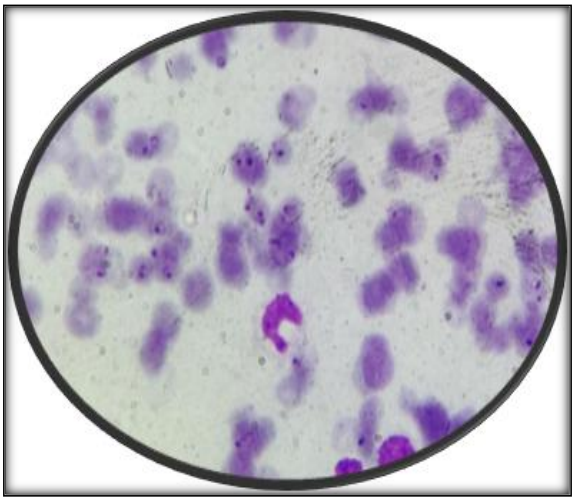

Figure 4: Photomicrograph of peripheral smear showing ring forms inside the RBCs seen in infestation with P. Falciparum.(Leishman stain 1000x)

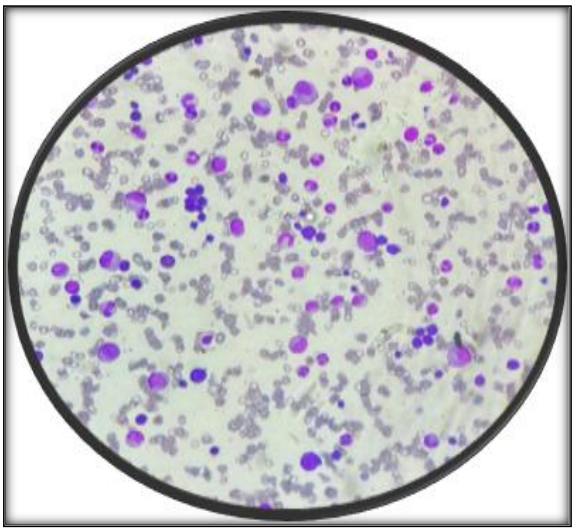

Figure 5: Photomicrograph of bone marrow aspiration smear showing micro-normoblastic maturation seen in iron deficiency anemia. (Leishman stain 400x)

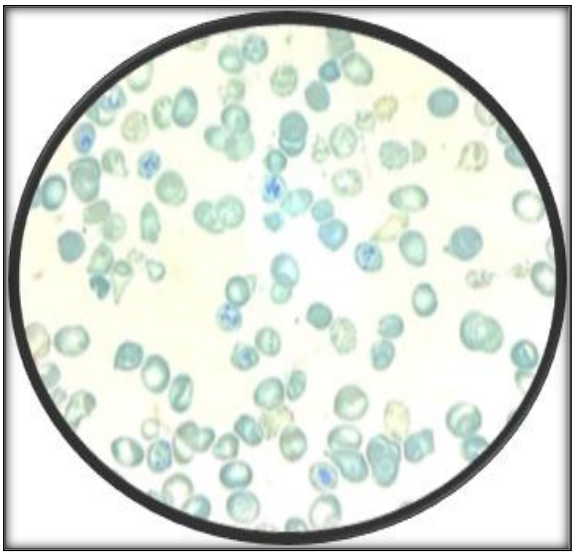

Figure 6: Photomicrograph showing Reticulocytes with blue reticulum (Arrow) in supra vital staining (New methylene blue stain 1000x)

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Table 1: Sex-wise distribution of the study population (n=100).

Sex	Patient (numbers)	Patient (%)
Male	48	48 %
Female	52	52%
Total	100	100 %

Table 2: Signs among the study population (n=100).

Sign	Patient (numbers)	Patient (%)
Pallor	99	99%
Icterus	22	22%
Pedal edema	18	18%
Splenomegaly	28	28%
Hepatomegaly	26	26%
Petechiae	17	17%
Purpuric spots	11	11%
Lymphadenopathy	14	14%
Sternal tenderness	02	02%
Gum hypertrophy	02	02%

Table 3: Total leukocyte counts among the study population (n=100).

Leukocyte count (cells/mm3)	Patient (numbers)	Patient (%)
<2000	40	40%
2001-3000	29	29%
3001-4000	31	31%
TOTAL	100	100%

Table 4: Bone marrow aspiration findings in case of pancytopenia (n=41).

Bone marrow findings	Number of cases	Percentage
Erythroid hyperplasia	09	22%
Hyperplastic with megaloblastic maturation	05	12%
Micro-normoblastic maturation	03	7.5%
Acute Leukemia	07	17%
Reactive bone marrow	03	7.5%
Inconclusive	14	34%
Total	41	100%

Table 5: Comparison of peak age of presentation in pancytopenia in various studies.

S. No.	Authors	Year Of Study	No. Of Cases	Age Range Years	Peak Age Incidence
1	Anjana Sharma, et al,[7]	2016	132	2.5 – 76 years	11-20 years (23.4%)
2.	Arun P. Bakshi, et al,[6]	2018	100	2 – 71 years	11-20 (28%)
3.	Anil Jain, et al,[8]	2021	100	18-65 years	21-30 years (28%)
4.	Swati Handralmath, et al,[4]	2023	60	1-80 years	21-30 years (32%)
5.	Present study	2024	100	1 - 80 years	11-20 years (22%)

Table 6: Comparison of the most common causes of pancytopenia among various studies.

S. NO.	Authors	Year of Study	Commonest cause	2nd common cause
1.	Harish Chandra, et al,[24]	2019	Megaloblastic anemia (25%)	Aleukemic leukemia (19%)
2.	Shreyanshu Sahay, et al,[26]	2018	Combined deficiency (51.8%)	Megaloblastic anemia (31.8%)
3.	Majed Momin, et al,[5]	2018	Megaloblastic anemia (34%)	Acute leukemia(14%)
4.	Suhas S. Gajbhiye, et al,[25]	2022	Aplastic anemia (36%)	Megaloblastic anemia (22%)
5.	Present study	2024	Megaloblastic anemia (17%)	Acute leukemia (14%)

DISCUSSION

Pancytopenia is a common clinical presentation encountered in daily clinical practices. Pancytopenia is suspected when a patient presents with features of anemia (generalized weakness, fatigue, breathlessness), prolonged fever, and bleeding tendency some sometimes it can be an incidental finding too.

In the present study, total of 100 cases of pancytopenia were studied. The study population was evaluated by taking clinical history, physical examination finding, study of hematological parameters, and bone marrow aspiration finding. On the basis of all the relevant investigation probable etiology of pancytopenia was studied.

There are many studies on pancytopenia and the causes are varied for areas of study, methods of study, habits of individuals, drug history, and infections. The observation of the present study was compared and correlated with recent published literature on these relevant parameters.

In the present study, the participating patient's ages ranged from 1 to 80 years, which were in concordance with the findings of Swati Handralmath, et al,[4] (2023) where age ranged from 1-80 years, Majed Momin, et al,[5] (2018) where cases age

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ranging from 2-85 years, and Arun P. Bakshi, et al,[6] (2018) with age group belonging to 2-71 years.

However, the study conducted by Anil Jain, et al,[2] (2022) showed dis-concordance in the age group of patients ranging from 18-65 years. The present study found that the maximum number of cases belonged to the 11-20 years age group (22%), followed by the 41-50 years age group (17%). This was in concordance with the findings of Arun P Bakshi, et al,[6] (2018) and Anjana Sharma, et al,[7] (2016) where the maximum number of cases belonged to the 11-20 years age group at 28% and 23.4% respectively. However, in the study conducted by Anil Jain, et al,[8] (2022) and Swati Handralmath, et al,[4] (2023) the maximum number of cases belonged to the age group 21-30 years, Majed Momin, et al,[5] (2018) the maximum number of cases belonged to the age group 55-65 years, Which was in discordance with the present study [Table 5].

In the present study, a total of 100 cases were included out of which 52 were female and 48 were male. Slight female preponderance was observed in the present study and the male: female ratio was 1:1.08 which was in concordance with the study conducted by Swati Handralmath, et al,[4] (2023) Pradeep Kumar Nagaich, et al,[9] (2021) V Chandrashekhar, et al,[10] (2021) Kulkarni Naveen, et al,[11] (2017) Purna Chandra Karua, et al,[12] (2020) Subhangi V Deshpande, et al,[13] (2019) were male: female ratio was1:1.07, 1:1.06, 1:1.06, 1:1.09, 1:1.08 and 1:1.10 consecutively. Other studies conducted by Anil Jain, et al,[8] (2022) Roopali J, et al,[14] (2019) Deepti Grover, et al,[15] (2018) Vandana, et al,[16] (2012) and Soma Yadav, et al,[17] (2013) observed female preponderance in their studies but the male-female ratio was different from the present study.However, in studies conducted by Anjana Sharma, et al,[7] (2016) and Lakhey Talwar, et al,[18] (2012) male preponderance was observed, and the male: female ratio was 1.5:1 and 2.6:1, which was discordant with the present study.

In the present study the most common physical sign observed in patients was pallor (99%) due to anemia followed by splenomegaly observed in 28% of patients it is in concordance with study of Arun P. Bakshi, et al,[6] (2018) were pallor found in 100% patient and splenomegaly seen in 33%, and also study conducted by Savith A, et al,[19] (2015) found pallor in 100% patient and splenomegaly in 20% patients. The study conducted by Srishtidhar Mangal, et al,[20] (2020) observed pallor in 80.2% and splenomegaly in 34% patients, Shubhangi V Deshpande, et al,[13] (2019) observed pallor in 78.7% and splenomegaly in 30.69% patients, Pooja Agrawal, et al,[21] (2018) observed pallor in 100% and splenomegaly in 43.75% patients, Majed Momin, et al,[5] (2018) observed pallor in 100% and splenomegaly in 56.66% patients, Mallik, et al,[22] (2016) observed pallor in 97.9% and splenomegaly in 41.9% patients, Chandan, et al,[23] (2017) observed pallor in 96.45% and splenomegaly in 34.04 % patients, in their observations most common presenting sign was pallor followed by splenomegaly which was similar to the present study but frequency of findings is different from the present study.

In the present study majority of cases were under the severe thrombocytopenia category, and the platelet count was <50,000 cells/cumm (56%). This is in concordance with the study of Pooja Agarwal, et al,[21] (2018), who observed platelet levels < 50,000 cells/cumm in maximum patients (57%). Another study conducted by Pradeep Kumar Nagaich, et al,[9] (2021) also observed platelet count <50,000 cell/cumm in maximum cases (43.7%) but the frequency was different from the present study. However, the studies of Srishtidhar Mangal, et al,[20] (2020) and V Chandrashekhar, et al,[10] (2021) observed in their studies the platelet level was <25,000 and <20,000 cell/cmm in maximum cases 48% and 48% respectively.

In the present study, normocytic normochromic blood picture was the most common peripheral smear finding observed in 46% of patients, which was in concordance with the study conducted by Pradeep Kumar Nagaich, et al,[9] (2021) where the most common RBC morphology in peripheral smear was normocytic normochromic observed in 28.1% of cases. However, the studies conducted by Pooja Agarwal, et al,[21] (2018) and Majed Momin, et al,[5] (2018) observed macrocytic normochromic and dimorphic RBCs in peripheral smears in their studies which were discordance with the present study.

In the present study, the most common cause of pancytopenia, was megaloblastic anemia (17%), it was also a common cause in studies conducted by Harish Chandra, et al. (2019) [24] and Majed Momin, et al,[5] (2018) [Table 6]. However, the studies conducted by Suhas S. Gajbhiye, et al,[25] (2022) observed aplastic anemia was the most common etiology of pancytopenia and Shreyanshu Sahay, et al,[26] (2018) observed combined deficiency anemia was the most common cause of pancytopenia in their studies which was discordance with the present study.In the present study, the 2nd most common cause of pancytopenia was Acute leukemia which was observed in 14% of cases, which was concordance with studies conducted by Majed Momin, et al,[5] (2018) and Harish Chandra, et al,[24] (2019) they also observed acute leukemia was 2nd most common cause of pancytopenia in their studies.

CONCLUSION

Pancytopenia is not a disease entity itself but it is a manifestation of diverse hematological and systemic disorders. It is usually suspected when a patient presents with unexplained prolonged anemia, prolonged fever, and a tendency to bleed. The etiologies of pancytopenia show diversification and vary according to age, gender, nutritional status, and geographical area. Detailed clinical history, physical examination, and hematological investigations including CBC and PS are preliminary for diagnosing

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pancytopenia. In determining, the varied etiologies of pancytopenia apart from CBC and PS special investigation like bone marrow aspiration or biopsy, Vit. B12 level, Folate level, and Serum Iron Profile are required. Chhatisgarh is a belt of Sickle Cell Disorders so screening is routinely done for same. Through this study, we conclude that the cases of pancytopenia require both routine investigations and a panel of special investigations for determining the exact etiology complemented and correlated with detailed clinical history and physical examination.

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