

# Importance of bone marrow examination in cases of pancytopenia: A morphological study in a tertiary care center



Deepshikha Verma<sup>1</sup>, Ranjan Yadav<sup>2</sup>, Rajnikant Ahirwar<sup>3</sup>, Pratibha Meena<sup>4</sup>

<sup>1,2</sup>Senior Resident, <sup>3,4</sup>Assistant Professor, Atal Bihari Vajpayee Government Medical College, Vidisha, Madhya Pradesh, India

Submission: 14-01-2024

Revision: 03-03-2024

Publication: 01-04-2024

## ABSTRACT

**Background:** Anemia, leukopenia, and thrombocytopenia are all combined as pancytopenia. It could be a symptom of many diseases that directly or indirectly impact the bone marrow. The cause of pancytopenia, however, differs depending on the location. An essential step in determining the cause of pancytopenia is bone marrow aspiration (BMA). **Aims and Objectives:** This study aimed to determine the causes of pancytopenia and the morphology of the bone marrow in pancytopenia patients. **Materials and Methods:** This study was carried out over a year in the pathology department of a tertiary care facility in central India. Patients taking chemotherapy or radiation therapy were excluded from the study. **Inclusion Criteria:** Cases with hemoglobin <10 g/dL, total leukocyte count <4000/mm<sup>3</sup>, and platelet count <100,000/mm<sup>3</sup> were included in this study. The patient's posterior iliac crest was used for BMA. The Leishman stain was used to color BMA smears for microscopy. **Results:** This study comprised 51 cases of pancytopenia, with acute leukemia and megaloblastic anemia accounting for the majority (11 cases each out of 51), followed by dimorphic anemia (10/51), hypocellular marrow (9/51). The clinical symptom of generalized weakness and pallor was present in all instances (100%) and was followed by fatigability (72%) and dyspnea (48%). The last two least frequent symptoms, lymphadenopathy, and hepatomegaly, were also present in many patients. A significant proportion of pancytopenia individuals experienced lymphadenopathy and hepatomegaly, which were the last two least prevalent appearances. **Conclusion:** In most cases, bone marrow aspiration in pancytopenia patients aids in determining the underlying reason. Understanding the illness process, planning future research, and managing cytopenia patients can all benefit from it.

**Key words:** Bone marrow aspiration; Pancytopenia; Thrombocytopenia

### Access this article online

**Website:**

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v15i4.61870

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2024 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

## INTRODUCTION

Blood is “the fountain of life and the principal seat of the soul,” according to Sir William Harvey. Our blood is sown in the marrow of our bones.<sup>1</sup> Analyzing the bone marrow is crucial to understanding and treating various hematological illnesses. Anemia, leukopenia, and thrombocytopenia all occur simultaneously in pancytopenia. When an adult's hemoglobin level is <10 g/dL, leukocyte count is <4×10<sup>9</sup>/L, and platelet count is <100×10<sup>9</sup>/L, it is considered pancytopenia.<sup>2</sup> Pancytopenia is not a distinct disease but a pathological sign of several diseases that

directly or indirectly impact the bone marrow. Infections, toxins, the invasion of malignant cells, chemotherapy, and radiotherapy are the common causes. Pancytopenia, however, may result from peripheral blood cell apoptosis, as in cases of hypersplenism. Anemia, leukopenia, and thrombocytopenia can all cause a variety of clinical symptoms in pancytopenia patients. The care and prognosis of the patients depend on the degree of pancytopenia and the underlying condition.<sup>3</sup> The current study aimed to assess the function of bone marrow aspiration in pancytopenia cases.

### Address for Correspondence:

Dr. Deepshikha Verma, Shrimangalam, Pooranpura Main Road, Vidisha-464001, Madhya Pradesh, India. **Mobile:** +91-8989870460.

**E-mail:** deepshikhaverma705@gmail.com

## Aims and objectives

The present study was conducted to study the importance of bone marrow in patients with pancytopenia in a tertiary care center in the Madhya Pradesh state of India. It was also intended to study if these causes showed any variation from other studies done in different regions of India.

## MATERIALS AND METHODS

From January 2019 to June 2020, a hospital-based prospective observational study was conducted. Patients, where bone marrow aspiration, is not indicated and non-co-operative patients were excluded from this study. All cases of thrombocytopenia initially diagnosed on a hematology analyzer (Hb 10 g/dL, total leukocyte count 4000/cumm, and platelet counts 1,00,000/L) and subsequently confirmed by peripheral smear were taken up for the study. A signed consent was acquired for each instance. All required clinical data were gathered. A bone marrow aspiration was performed in each case using only aseptic methods. The bone marrow aspiration smears were then stained with Leishman stain, inspected by accepted best practices, and the results were recorded.

Fresh blood was prepared for a peripheral smear after a new 4 mL sample was taken and placed in an EDTA vial. The slide was filled with Leishman's stain and left for 2 min. This made it possible to fix the peripheral blood film in methyl alcohol. The process was repeated after adding twice as much buffered water dropwise to the slide and mixing for 5 min. The slide was cleaned in water for a few seconds, air-dried, and inspected through an oil immersion lens.<sup>4-6</sup>

Following all aseptic procedures, bone marrow was aspirated from the sternum or posterior superior iliac spine. Lignocaine (2–5 mL) was administered as a local anesthetic to lessen discomfort. The location was punctured with a bone marrow aspiration needle after 2–3 min. One or two mL of bone marrow were aspirated after the stellate was removed and the needle was connected. From the material that was aspirated, smears were taken, air dried, and stained with Leishman's stain in the same way as peripheral blood films were analyzed.<sup>4-6</sup>

The ethical committee of the institution approved the study.

## OBSERVATION AND RESULTS

In the hematology division of the Department of Pathology, a total of 51 cases of pancytopenia underwent bone marrow examination during the study period.

A very wide range of hematological illnesses can affect both children and adults. A bone marrow analysis is a useful test to

make the final diagnosis. It is among the most frequent and generally highly safe invasive procedures regularly carried out in hospitals. An invasive operation can be performed even in cases of severe pancytopenia. The procedure is frequently used to evaluate unexplained cytopenia, diagnose storage problems, and stage leukemias and other malignancies.

Aplastic anaemia, chronic myeloid leukaemia, parvovirus infection, acute leukaemia, and megaloblastic anaemia were all present in this study's 51 pancytopenia cases, with acute leukaemia and megaloblastic anaemia making up the majority (11 cases each out of 51), followed by dimorphic anaemia (10/51), hypocellular marrow (9/51), reactive to infection (5/51), granulomatous disease (2 cases), and reactive to infection which is shown in Table 1. The clinical symptom of generalized weakness and pallor was present in all instances (100%) and was followed by fatiguability (72%) and dyspnea (48%). The last two least frequent symptoms, lymphadenopathy and hepatomegaly, were also present in many patients. A sizable number of pancytopenia individuals experienced lymphadenopathy and hepatomegaly, which were the last two least prevalent appearances.

Males were more likely to experience pancytopenia (66.67%) than females (33.33%) throughout a wide range of ages. Ten instances of megaloblastic anemia were found in boys who were 57% pancytopenic.

Bone marrow cellularity was elevated in all pancytopenia cases brought on by leukemias, megaloblastic anemia, and dimorphic anemia, while it was lowered in pancytopenia cases brought on by aplastic anemia. The M/E ratio was reversed in all cases of megaloblastic and dimorphic anemia, although it was elevated in cases of AML and normal in cases of aplastic anemia. The M/E ratio was difficult to determine in acute lymphoblastic leukemia (ALL) cases.

## DISCUSSION

Pancytopenia is characteristic of several serious and life-threatening disorders. The pattern of disorders, leading to pancytopenia may differ amongst demographic groups due to differences in age, nutritional status, and infection prevalence. In India, the root causes of pancytopenia are poorly known. Only adults are involved in the vast majority of reported cases.<sup>7,8</sup> In this investigation, acute leukemia and megaloblastic anemia were the most frequent causes of pancytopenia. Fifty instances were included in the current investigation. The cases ranged in age from 1 to 85, with a mean age of 43.59. 2:1 was the male-to-female ratio. Khunger et al. studied 200 patients with a male-to-female ratio of 1.2:1 and ages ranging from 2 to 70 years.<sup>9</sup> The male: female ratio in the 334 instances included by Khan et al. was 1.2:1.<sup>10</sup>

The most frequent causes of pancytopenia in the current study were acute leukemia and megaloblastic anemia, each accounting for 21.56%. Erythroid hyperplasia with sieve-like chromatin in the erythroblasts was a defining feature of megaloblastic anemia. Megaloblastic anemia, which accounted for 68% of pancytopenia in a related study by Tilak et al., was the most frequent cause of the condition.<sup>3</sup> In research by Khodke et al., megaloblastic anemia was the most frequent cause of pancytopenia, accounting for 44% of cases.<sup>11</sup> In research by Gayathri and Rao, 74.04% of the participants had megaloblastic anemia.<sup>12</sup>

Megaloblastic anemia may be caused by a diet deficient in cobalamin and folate, increased needs during growth and pregnancy, and usage of acid-suppressing medications in a developing nation like India.<sup>13</sup> Geography, socioeconomic level, diet, and religion are additional variables that may have a role in the development of megaloblastic anemia. CBC results such as MCV, MCH, and MCHC were not consistently associated with bone marrow morphology in patients with megaloblastic anemia. The presence of megaloblasts, dyserythropoietic characteristics, increased marrow cellularity with a decreased M/E ratio, megaloblast presence, and a giant myeloid precursor were found to be diagnostic features of megaloblastic anemia in the current study, as well as in previous studies.<sup>13</sup>

In the current investigation, acute leukemia and megaloblastic anemia were the most frequent causes of pancytopenia. Pancytopenia-associated ALL and AML cases were found in bone marrow smears with more than 20 lymphoblasts and myeloblasts, respectively. Peripheral blood smears from these patients showed pancytopenia with infrequent blasts present. The outcomes for ALL matched those mentioned by Sohn et al.,<sup>14</sup> The patient was referred to a higher level of care since leukemia cytochemistry was unavailable at the facility.

A positive bone marrow examination was found in 94.11% of pancytopenia patients. In studies undertaken by Imbert et al.,<sup>15</sup> Parajuli and Tuladhar,<sup>16</sup> and Pathak et al.,<sup>17</sup> the diagnostic value of morphological examination of bone marrow in cases of pancytopenia was 55%, 84.26%, and 76.5%, respectively.

The significant discrepancy in pancytopenia causes is occurrence across various research published from India and other nations might be ascribed to methodological variations; the population's genetic variations, nutritional state, frequency of infectious diseases, and exposure to different myelotoxic substances all play a role in the diagnosis criteria selection process.

Even though the haematological markers frequently exhibited significant overlap and were vague in many

**Table 1: Bone marrow aspiration findings in the present study in cases of pancytopenia**

S. No.	Bone marrow findings	No. of cases	Percentage
1	Acute leukemia	11	21.56
2	Megaloblastic anemia	11	21.56
3	Dimorphic anemia	10	19.6
4	Hypocellular marrow	9	17.64
5	Reactive to infection	5	9.8
6	Granulomatous disease	2	3.9
7	Parvovirus infection	1	1.9
8	Aplastic anemia	1	1.9
9	Chronic myeloid leukemia	1	1.9
	Total	51 cases	100

cases, they provide diagnostic guidance for assessing pancytopenia cases. The outcomes are nearly identical to those of Singhal et al.<sup>18</sup> and Kumar et al.<sup>19</sup>

In our analysis, the most common causes of pancytopenia were acute leukemia, which can be treated more effectively if recognized early, and dimorphic anemia, which can be treated with minimal expense if diagnosed appropriately.

Bone marrow examination is an important diagnostic tool for treating hematological problems. Bone marrow aspiration is a fairly easy and safe procedure that can be repeated as needed and performed in outpatients.

#### Limitations of the study

As a tertiary care center in the state capital, it serves the typical population that surrounds it, typically urban, suburban, and near-peripheral. However, there is a large perimeter that remains unscreened in this study. Furthermore, because the sample size in this study was relatively small, the results may differ in a larger study group. Further morphological and quantitative abnormalities discovered by our investigation should not be regarded as conclusive and should be evaluated with a large study group and patient follow-ups. Finally, the COVID-19 pandemic hampered the study due to a limited inflow of patients during the study period.

#### CONCLUSION

The present study shows that physical findings, complete blood count, and peripheral blood smear examination provide valuable information in the workup of pancytopenic patients. Bone marrow examination is an important diagnostic tool in hematology which helps to evaluate various causes of pancytopenia. A frequent hematological condition seen in clinical practice is pancytopenia. The present study concluded that pancytopenia was more prevalent in males and younger age groups. Leading causes of pancytopenia in our study found was acute leukemia which on early diagnosis

can get better treatment followed by megaloblastic anemia which can be treated with minimum expenditure when diagnosed correctly. Most patients had adequate medication and follow-up, which addressed the nutritional deficiency of folic acid and Vitamin B12, the most frequent causes of megaloblastic anemia. This is because nutritional anemia, a more common cause of pancytopenia in our study cohort, is more common.

Ours is a small study group, resulting a lack of statistical power, therefore further studies with large cohort preferably multicentric, are needed along with proper follow-up to explore the role of bone marrow examination in patients of pancytopenia along with its correlation with morphological details.

## ACKNOWLEDGMENT

The authors acknowledge the support received from the Hematology Unit, GMC Bhopal, and the technicians of the Hematology Laboratory, GMC Bhopal.

## REFERENCES

- Perkins SL, editor. Wintrobe's. Examination of blood and bone marrow. In: Clinical Haematology. 10<sup>th</sup> ed. Maryland: Williams and Wilkins; 1999. p. 23-32.
- Gupta V, Tripathi S, Tilak V and Bhatia BD. A study of clinical-haematological profiles of pancytopenia in children. Trop Doct. 2008;38(4):241-243.  
<https://doi.org/10.1258/td.2008.070422>
- Tilak V and Jain R. Pancytopenia-a clinical-hematologic analysis of 77 cases. Indian J Pathol Microbiol. 1999;42(4):399-404.
- Riley RS, Hogan TF, Pavot DR, Forysthe R, Massey D, Smith E, et al. A pathologist's perspective on bone marrow aspiration and biopsy: I. Performing a bone marrow examination. J Clin Lab. 2004;18(2):70-90.  
<https://doi.org/10.1002/jcla.20008>
- Bain BJ and Lewis SM. Basic haematological techniques. In: Dacie JV and Lewis SM, editors. Practical Haematology. 7<sup>th</sup> ed. Edinburgh, Churchill Livingstone; 1991. p. 54-59.
- Singh T. Normal Hematopoiesis and Evaluation of Bone Marrow and Peripheral Blood Films, Atlas and Text of Hematology. 4<sup>th</sup> ed., Vol. 1. New Delhi: Jaypee Brothers; 2018. p. 35-41.
- Kumar R, Kabra SP, Kumar H, Anand AC and Madan H. Pancytopenia - a six year study. J Assoc Phys India. 2001;49:1078-1081.
- Varma N and Dash S. A reappraisal of underlying pathology in adult patients presenting with pancytopenia. Trop Geogr Med. 1992;44:322-327.
- Khunger JM, Arulselvi S, Sharma U, Ranga S and Talib VH. Pancytopenia-a clinico haematological study of 200 cases. Indian J Pathol Microbiol. 2002;45(3):375-379.
- Khan SP, Geelani S, Khan FP, Ali N, Akhter S, Shah S, et al. Evaluation of pancytopenia on bone marrow aspiration- study at a tertiary care center in Kashmir valley, India. Int J Adv Med. 2018;5:946-949.  
<https://doi.org/10.18203/2349-3933.ijam20183125>
- Khodke K, Marwah S, Buxi G, Yadav RB and Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Indian Acad Clin Med. 2001;2:55-59.
- Gayathri BN and Rao KS. Pancytopenia: A clinico hematological study. J Lab Physicians. 2011;3(1):15-20.  
<https://doi.org/10.4103/0974-2727.78555>
- Khanduri U and Sharma A. Causative and prevalence of megaloblastic anemia. Natl Med J India. 2007;20(4):172-175.
- Sohn SK, Suh JS, Lee J and Lee KB. Pancytopenic prodrome(pre-ALL) of acute lymphoblastic leukemia in adults: Possible pathogenesis. Korean J Intern Med. 1998;13(1):64-67.  
<https://doi.org/10.3904/kjim.1998.13.1.64>
- Imbert M, Scoazec JY, Mary JY, Jouzult H, Rochant H and Sultan C. Adult patients presenting with Pancytopenia. Hematol Pathol. 1989;3(4):159-167.
- Parajuli S and Tuladhar A. Correlation of bone marrow aspiration and biopsy findings in diagnosing hematological disorders - a study of 89 cases. J Pathol Nepal. 2014;4:534-538.  
<https://doi.org/10.3126/jpn.v4i7.10294>
- Pathak R, Jha A and Sayami G. Evaluation of bone marrow in patients with pancytopenia. J Pathol Nepal. 2012;2:265-271.  
<https://doi.org/10.3126/jpn.v2i4.6875>
- Singhal N, Gupta N and Kulhari S. Evaluation of bone marrow examination in cases of pancytopenia in tertiary health center in North-West Rajasthan. Int J Contemp Med Res. 2019;6(3):C1-C4.  
<https://doi.org/10.21276/ijcmr.2019.6.3.40>
- Kumar P, Chandra K, Singh T, Mishra A, Singh SK and Mishra AK. Morphological evaluation and clinical correlation of bone marrow aspiration cytology at tertiary care centre. Int J Health Clin Res. 2021;4(12):120-123.

### Authors Contribution:

**DV**- Literature survey, prepared the first draft of manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation, and submission of the article; **RY**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **RA**- Design of study, statistical analysis and interpretation, co-ordination, and manuscript revision; **PM**- Design of study, statistical analysis, and interpretation, co-ordination, and manuscript revision.

### Work attributed to:

Department of Pathology, Atal Bihari Vajpayee Government Medical College, Vidisha, Madhya Pradesh, India.

### Orcid ID:

Dr. Deepshikha Verma - <https://orcid.org/0000-0003-1516-0077>  
 Dr. Ranjan Yadav - <https://orcid.org/0009-0007-5026-517X>  
 Dr. Rajnikant Ahirwar - <https://orcid.org/0000-0003-3593-4367>  
 Dr. Pratibha Meena - <https://orcid.org/0009-0005-2988-1424>

**Source of Support:** Nil, **Conflicts of Interest:** None declared.