ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Etiology of pancytopenia with reference to bone marrow biopsy in a tertiary care hospital: A hospital-based study

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Submission: 08-06-2024 Revision: 29-07-2024 Publication: 01-09-2024

ABSTRACT

Background: Pancytopenia is a common hematological entity and a striking feature of many life-threatening illnesses. **Aims and Objectives:** The study was conducted to identify the etiology of pancytopenia. (i) To find out primary bone marrow (BM) causes of pancytopenia. (ii) To evaluate the spectrum of BM morphology in pancytopenia cases. **Materials and Methods:** This hospital-based observational study was conducted between June 2021 and May 2022 in a tertiary care hospital in Dibrugarh in all pancytopenia cases of age above 12 years and meeting the inclusion criteria. After taking written consent, detailed history, clinical examination, and baseline investigations were done followed by BM examination. **Results:** Mean age was 45.39 ± 15.49 years. Majority were males 41 (56.9%) and 31 (43.1%) were females. The most common cause of pancytopenia was Megaloblastic anemia (30.5%) cases, followed by aplastic anemia (18%) and myelodysplastic syndromes (16.7%). About 72 (100%) had pallor followed by weakness (86.1%), bleeding tendencies (70.8%), and fever (52.8%). **Conclusion:** The study underscores the critical role of BM biopsy in the diagnostic workup of pancytopenia. It confirms that BM biopsy is indispensable for identifying the diverse etiologies of pancytopenia and in implementing the appropriate therapy.

Key words: Pancytopenia; Bone marrow biopsy; Anemia; Hematology

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i9.67105

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Pancytopenia is one of the most common hematological conditions which manifest as a simultaneous decrease in all three formed blood elements – Red blood cells, white blood cells (WBCs), and platelets. The primary disorders of blood and blood-forming tissues can give rise to extremely varying clinical manifestations which may involve any of the organ systems and there are varying treatment modalities and outcome.[1]

The presenting features of thrombocytopenia are mainly mucocutaneous bleed, epistaxis, hematuria, and gastrointestinal bleed. Leucopenia manifests early as neutropenia which causes sore throat, chest, or soft-tissue infection. Anemia develops the slowest in pancytopenia cases.[2] Etiology of pancytopenia often varies by geographical distribution, age, gender, hereditary, and dietary factors. The severity of pancytopenia and the underlying pathology determines the management and prognosis of a disease, therefore a systematic approach to a patient with pancytopenia is fruitful.[3]

Bone marrow (BM) is a major site of hematopoiesis that supports the orderly proliferation, differentiation, and release of three cellular elements of blood. Various hematological disorders may arise from abnormality in one of the three lineages. BM aspirate along with

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trephine biopsy is often done to aid the diagnosis. BM biopsy can be used for the assessment of marrow activity and marrow cellularity in disorders like aplastic anemia.[4] Taking the above facts into consideration along with the important role of BM aspiration and BM biopsy in the diagnosis of pancytopenia, the present study on etiology of pancytopenia was conducted. Therefore, this study aims to identify the etiology of pancytopenia and to evaluate the spectrum of BM morphology in pancytopenia cases.

Aims and objectives

Aims

The study was conducted to identify the etiology of pancytopenia.

Objectives

The objectives of the study are as follows:

i. To find out primary BM causes of pancytopenia
ii. To evaluate the spectrum of BM morphology in pancytopenia cases.

MATERIALS AND METHODS

This hospital-based observational study was conducted in a hematology section, Department of Pathology, Assam Medical College and Hospital, Dibrugarh for a period of 1 year, from June 2021 to May 2022 among all the hematologically diagnosed new cases of pancytopenia admitted in Medicine ward, Assam Medical College and Hospital, Dibrugarh. Ethical clearance was obtained from the Institutional Ethics Committee (Human) of Assam Medical College and Hospital before the commencement of the study.

Sample size taken as all the patients fulfilling the following criteria: Inclusion criteria of hematologically diagnosed new cases of pancytopenia in patients of age 13 years old and above with the following findings: (a) Hemoglobin level <13.5 g/dL in males or <11.5 g/dL in females. (b) Leukocyte count is $<4\times10^9$/L. (c) Platelet count is $<100\times10^9$/L.[5,6] Those cases undergoing drug therapy for pancytopenia, chemotherapy, bleeding diathesis, osteomyelitis, pregnant women, and those who did not give consent were excluded from the study.

All the participants were explained about the purpose of the study and informed consent was taken from each of them. Relevant medical history was elicited including symptoms such as fever, lethargy, breathlessness, bone pains, night sweats, malaise, and weight loss. A detailed physical examination of every patient was done for pallor, jaundice, petechiae/purpura/ecchymoses, hepatosplenomegaly, lymphadenopathy, sternal tenderness, dermatological manifestations, and gum hypertrophy. Basic hematological investigations, routine investigations, and BM examination were performed in each case. Peripheral blood film was examined for the presence of anisopoikilocytosis, circulating erythroblasts, hypo or hypersegmented neutrophils, abnormally increased or decreased granulation in neutrophils, immature WBCs, and lymphocytosis. BM aspiration and trephine biopsy were carried out by standard methods. Stains such as Leishman stain, Giemsa stain, Hematoxylin, and Eosin stain were used. Myeloperoxidase special stain, Periodic Acid-Schiff, and Perl's stain on aspirate smears were used, wherever indicated.

The data collected were entered into MS Excel spreadsheets and analysis was carried out using the Statistical Package for the Social Sciences for Windows, Version 25.0. Categorical variables were presented in number and (%). The study population was described by using rates, proportions, mean and standard deviation. Data were presented as tables, bar diagrams, and pie diagrams wherever applicable.

RESULTS

The study participants consisted of 72 cases out of which 41 (56.9%) were males and 31 (43.1%) were females. Majority of the study participants belonged to the age group 51–60 years (25.0%). Overall mean age of the study participants was 45.39±15.49 years. The demographic characteristics are given in the table below (Table 1).

Out of 72 participants, 72 (100%) had pallor, followed by weakness (86.1%), bleeding tendencies (70.8%), and fever (52.8%). Most common peripheral blood smear (PBS) findings were anisocytosis (66.7%), followed by normocytic (43%) and macrocytic (33.3%) blood picture. Out of 72 participants, majority of the patients (66.7%) had hemoglobin level in the range of 6–10 g/dL. The mean hemoglobin level was 6.15 g/dL in megaloblastic anemia, 4.5 g/dL in aplastic anemia, 7.9 g/dL in myelodysplastic syndrome (MDS), and 6.5 g/dL in plasma cell myeloma. The mean thin layer chromatography was 2531.8 in megaloblastic anemia, 2030.8 in aplastic anemia, 2541.7 in MDS, and 2530 in plasma cell myeloma. The mean platelet count was 31818.2 in megaloblastic anemia, 18461.5 in aplastic anemia, 21000 in MDS, and 31200 in plasma cell myeloma. The most common causes of pancytopenia were found to be megaloblastic anemia (30.5%), followed by aplastic anemia (18%), MDS (16.7%), and plasma cell myeloma (15.3%) (Figure 1).

About 55.6% of the study participants had hypercellular BM, followed by normocellular (23.6%) and hypocellular BM (20.8%). About 41.7% of the study participants showed

erythroid hyperplasia and 30.5% showed megaloblastic maturation (Table 2). In the study population, normal iron stores were seen in 59.1% cases of megaloblastic anemia, 61.5% cases of aplastic anemia, 58.4% cases of MDS, 90.9% cases of plasma cell myeloma, and 66.7% cases of hypersplenism. The diagnostic accuracy was found to be more in the BM trephine biopsy (100%), followed by BM imprint cytology (94.4%) and BM aspiration cytology (87.5%).

Figure 2 shows Bone Marrow Biopsy with focal areas of cellularity and a solitary megakaryocyte in Aplastic anaemia. Whereas in Figure 3 shows bone marrow biopsy of a megaloblastic maturation having hypolobated megakaryocyte, quadrinucleate gigantoblast and erythroid precursor having nuclear budding.

DISCUSSION

In the present study, majority of the study participants were male (56.9%) and majority belonged to the age group 51–60 years (25.0%). Male: Female ratio was 1.32:1. Overall mean age of the study participants was 45.39±15.49 years. Vargas-Carretero et al., in their study in Mexico, observed that the mean age of pancytopenia was 49.4 years, with a slightly higher female incidence (53.2%).[7] Manzoor et al., in their study found that the most common age group of pancytopenia was 21–30 years (32%), followed by 11–20 years (20%), 31–40 years (18%), and 41–50 years (10%) and male: Female ratio was 1.63:1.[8] The most common age group of pancytopenia was found to be 51–60 years in this study in contrast to other studies where common age group was around 40 years.

In the present study, the most common causes of pancytopenia were found to be megaloblastic anemia (30.5%), followed by aplastic anemia (18%), MDS (16.7%), and plasma cell myeloma (15.3%). Agarwal et al., in Uttar Pradesh, India also found that the most common cause of pancytopenia was megaloblastic anemia (37.5%), followed by erythroid hyperplasia (20%) and aplastic anemia (10%).[9] Another study done by Islam et al., in tertiary care in Guwahati, Assam found that the most common cause of pancytopenia was megaloblastic anemia (28.2%) followed by Acute myeloid leukemia (22.1%).[6] The findings in this study are comparable to the above studies, which indicate that nutritional anemia is common in India.

The present study showed that 72 (100%) had pallor followed by weakness (86.1%), bleeding tendencies (70.8%), and fever (52.8%). Mangal and Sinha in their study in India also observed that pallor (80%) was the most

Table 1: Distribution of study participants according to gender and age group

Demographic characteristics	Frequency (%)
Gender	
Male	41 (56.9)
Female	31 (43.1)
Age group (years)	
13–20	3 (4.2)
21–30	11 (15.3)
31–40	14 (19.4)
41–50	15 (20.8)
51–60	18 (25.0)
61–70	9 (12.5)
71–80	2 (2.8)

Table 2: Bone marrow morphology in cases of pancytopenia (n=72)

Bone marrow morphology	Frequency	Percentage
Hypocellular	15	20.8
Normocellular	17	23.6
Hypercellular	40	55.6
Erythroid hyperplasia	30	41.7
Megaloblastic	22	30.5
Multiple myeloma	10	13.9
Acute leukemia	3	4.2
Bilineage dyspoiesis	14	19.4
Dyserythropoietic marrow	8	11.1

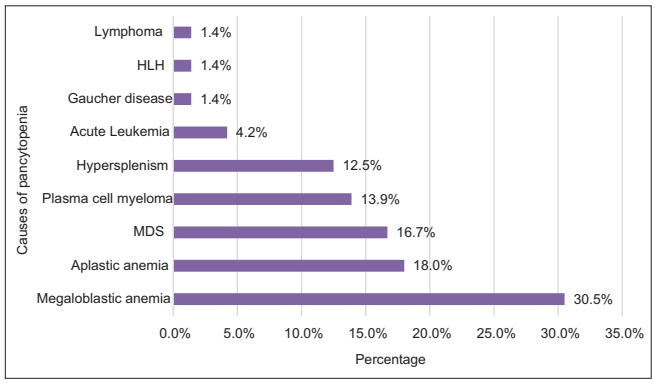

Figure 1: Classification of different causes of pancytopenia in the study participants

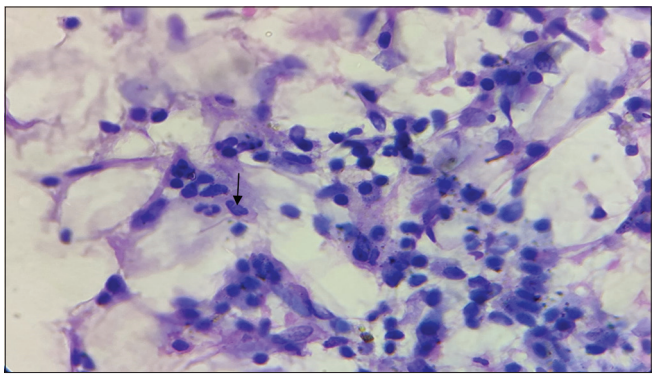

Figure 2: Trephine biopsy demonstrates focal areas of cellularity and a solitary megakaryocyte (↓) in aplastic anemia

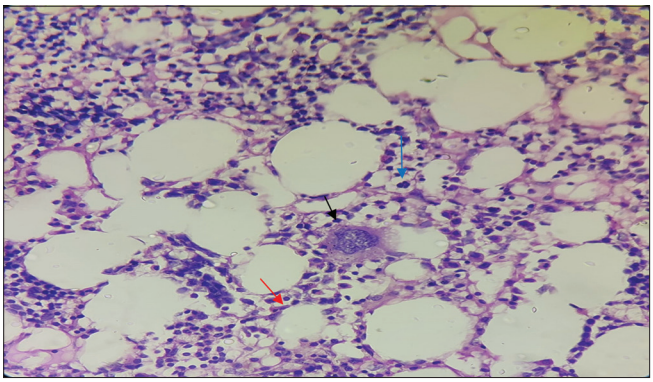

Figure 3: Trephine biopsy shows hypolobated megakaryocyte (↓) and quadrinucleate gigantoblast (↓) and erythroid precursor having nuclear budding (↓)

common clinical presentation, followed by splenomegaly (37%), lymphadenopathy (34.1%), hepatomegaly (24.2%), and icterus (23.1%).[1]

The most common PBS findings were anisocytosis (66.7%), followed by normocytic (43%) and macrocytic (33.3%) blood picture in the present study. Agarwal et al., in their study also observed that the most common PBS findings were anisocytosis (94%), macrocytic blood picture (45%), and hypersegmented neutrophils (30%).[9] Another study done by Sale et al., also found that anisopoikilocytosis (78%), macrocytic (55%), and hypersegmented neutrophils (30%) were the most common PBS findings.[10]

The present study showed that 55.6% of the study participants had hypercellular BM, followed by erythroid hyperplasia (41.7%) and megaloblastic maturation (30.5%). Ashalatha et al., also found that (40%) were erythroid hyperplasia, (27.1%) were normocellular, (11.4%) were hypocellular and (4.3%) were megaloblastic marrow.[11] Rohira and Meenai in their study found that the BM was hypercellular in (51%) of the cases, normocellular in (28%) and hypocellular in 20% of the cases.[12] Normal iron stores were most commonly in plasma cell myeloma (90.9%) followed by hypersplenism (66.7%) in the present study. While Prabhala et al., in their study found that the iron stores were increased in 61.2% of cases of megaloblastic anemia.[13]

Diagnostic accuracy was found to be more in the BM trephine biopsy (100%) in comparison to imprint and aspiration cytology in the present study. Similar findings were seen in a study done by Pant et al., and Taori et al., that the diagnostic accuracy was 100% in BM biopsy.[14,15] While Baskota et al., found that the diagnostic accuracy was highest in BM imprint cytology (92%), followed by BM trephine biopsy (89.9%) and BM aspiration cytology (87%).[16]

Limitations of the study

1. The number of patients included in the study may be relatively small, limiting the generalizability of the findings.
2. Data collected from a single tertiary care hospital may not be representative of other settings or regions, thus limiting external validity.
3. The study might not have considered all possible etiological factors of pancytopenia, focusing only on those detectable via bone marrow biopsy.
4. Interpretation of bone marrow biopsy results can be subjective and may vary among pathologists

CONCLUSION

The present study shows that megaloblastic anemia is one of the most common associated factor of pancytopenia although etiology of pancytopenia may vary according to geographical factors. Complete hematological investigations and BM examination in patients with pancytopenia are needed to rule out the causes of pancytopenia and planning for further management.

ACKNOWLEDGMENT

Due acknowledge to the Department of Pathology, AMCH, Dibrugarh, and all the study participants who have contributed in this study.

REFERENCES

1. Mangal S and Sinha SS. Complete clinicopathological profile and etiological spectrum of pancytopenia in adult patients attending a tertiary care referral center in Eastern India. Int J Acad Med. 2020;6(4):309-315.
   https://doi.org/10.4103/IJAM.IJAM_55_20
2. Garg AK, Agarwal AK and Sharma GD. Pancytopenia: Clinical approach. Chapter. 2017;95:450-454.
3. Abhange RS and Jadhav RP. A clinico-hematological evaluation of pancytopenia at government medical college and hospital, Latur: A 2-year observational study. Med J D Y Patil Vidyapeeth. 2021;14(3):292-296.
   https://doi.org/10.4103/mjdrdypu.mjdrdypu_333_19
4. Vala N and Shrinivasan C. Retrospective analysis of the bone marrow received at a tertiary care hospital-A study of 160 cases. Indian J Pathol Oncol. 2019;6(4):530-533.
   https://doi.org/10.18231/j.ijpo.2019.103
5. 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
6. Islam U, Valsaraj R and Goswami N. A clinical study of cytopenias with special reference to megaloblastic anaemia in a tertiary care centre. J Evid Based Med Healthc. 2016;3:3555-3560.
7. Vargas-Carretero CJ, Fernandez-Vargas OE, Ron-Magaña AL, Padilla-Ortega JA, Ron-Guerrero CS and Barrera-Chairez E. Etiology and clinico-hematological profile of pancytopenia:

Experience of a Mexican Tertiary Care Center and review of the literature. Hematology. 2019;24(1):399-404.

https://doi.org/10.1080/16078454.2019.1590961

8. Manzoor F, Karandikar MN and Nimbargi RC. Pancytopenia: A clinico-hematological study. Med J D Y Patil Univ. 2014;7(1): 25-28.

https://doi.org/10.4103/0975-2870.122763

9. Agarwal P, Shams A, Prakash P, Kumar H and Nigam A. Evaluation of pancytopenia in adults through haematological parameters and bone marrow studies. Indian J Pathol Oncol. 2018;5(4):548-543.

https://doi.org/10.18231/2394-6792.2018.0106

10. Sale SM, Mane VP, Pawar VR, Mohite SN and Dhaka V. Clinical correlation of pancytopenia with bone marrow study in a tertiary hospital. Indian J Pathol Oncol. 2016;3(2):247-254.

https://doi.org/10.5958/2394-6792.2016.00048.X

11. Ashalatha N, Netravathi P, Ragupathi A and Nagarajappa A. Hemogram and bone marrow morphology in cases of pancytopenia. Internet J Lab Med. 2010;4(2).

https://doi.org/10.5580/1684

12. Rohira N and Meenai FJ. A cross sectional study of clinical and aetiological profile of pancytopenia at a tertiary care hospital in Bhopal. Indian J Pathol Oncol. 2019;6(1):67-74.

https://doi.org/10.18231/2394-6792.2019.001

13. Prabhala S, Jayashankar E, Pavani B, Swamy M and RamamurtiT. Bone marrow examination in pancytopenia: A study of six years. J Evol Med Dent Sci. 2014;3(65):14189-14195.

https://doi.org/10.14260/jemds/2014/3900

14. Pant S, Dhingra H, Gupta A and Misra RK. Comparative analysis of bone marrow aspiration smears, touch imprints and trephine biopsy in haematological malignancies. Int J Contemp Med Res. 2020;7(6):F12-F16.

https://doi.org/10.21276/ijcmr.2020.7.6.33

15. Taori G, Ukey A and Bajaj P. Comparison of bone marrow aspiration cytology, touch imprint cytology and bone marrow biopsy for bone marrow evaluation at a tertiary health care institute. MVP J Med Sci. 2019;6(2):152-157.

https://doi.org/10.18311/mvpjms/2019/v6i2/22961

16. Baskota SU, Joshi AR and Singh SK. Bone marrow touch imprint smears as an adjunct to bone marrow aspiration smears in hematological disorders. J Pathol Nepal. 2015;5(9): 739-746.

https://doi.org/10.3126/jpn.v5i9.13783

Authors' Contribution:
AD- Literature survey, implementation of the study protocol, preparation of the manuscript, submission of article; **HE**- Concept, study design, clinical protocol, manuscript preparation, manuscript editing, and revision; **AB**- Study design, clinical protocol, manuscript preparation; **PR**- Statistical analysis, interpretation, and manuscript review; **AS**- Concept, design and manuscript revision; **MC**- Data collection, editing and manuscript revision.

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