DOI: 10.7860/NJLM/2023/59789.2724

Original Article

Pathology Section

Bone Marrow Cellularity in Pancytopenia- A Paradigm of Underlying Pathology

ALOK KUMAR[1], PARINEETA SHELKE[2], PREETI RAJEEV DOSHI[3], AMIT NISAL[4], RAVINDRA NIMBARGI[5]

ABSTRACT

Introduction: Reduced numbers of all three types of peripheral blood cells characterise the hematologic condition known as pancytopenia. Practical distinction among various causes of pancytopenia is usually clear but some processes are so closely related that the diagnosis may get complicated and bone marrow examination aids in diagnosis of such cases.It is important to recognise marrow failure syndromes causing pancytopenia. Pancytopenia is a common finding, its explicit discussion is lacking even in major textbooks and has led many authors to highlight the spectrum of causes of pancytopenia.

Aim: To evaluate the various causes of pancytopenia and to evaluate clinical signs and symptoms, hematological parameters along with bone marrow cellularity and other morphological features on aspiration and trephine biopsy in patients presenting with pancytopenia.

Materials and Methods: In the present cross-sectional study for a period of 3.5 years from August 2018 to April 2022, a total 157 patients were included having pancytopenia in a tertiary care centre, Pune, Maharashtra, India. Clinical history was taken for all the cases of pancytopenia. The blood samples were collected for hematological analysis including hemogram and Peripheral Blood Smear (PBS) examination; also Bone Marrow (BM) samples were collected. Aspirates were stained with Leishman and Giemsa. Special stains like myeloperoxidase (MPO) and Periodic acid schiff stain (PAS) were used wherever required. Bone marrow biopsy was fixed in Bouin's fluid and processed and stained with Haematoxylin and eosin (H&E) and reticulin stain after decalcification. Results were analysed using Statistical Package for the Social Sciences (SPSS) software (version 26.0) and calculated as frequencies and percentages. P-value of <0.05 was considered significant.

Results: Out of 157 patients, majority (n=120) belonged to adult age group (18-86 years) (76.43%), with the mean age of 40.68±23.34 years. The male to female ratio was 1.34:1. Study showed megaloblastic anaemia encompassing majority of the causes of pancytopenia followed by acute leukemia, hypersplenism, hypocellular marrow, Hemophagocytic lymphohistiocytosis (HLH), myelodysplastic syndrome (MDS) and Aplastic anaemia. Out of 86 (54.78%) of total majority of hypercellular bone marrow patients, 51 (59.3%) had haemoglobin levels of <7 g/dL, while 45 (52.32%) hypercellular bone marrow patients had platelet count of <50000 cells/cumm. Patients with low TLC weresignificantly associated with hypo (p=0.0067) and hypercellular marrow (p=0.0291) compared to normocellular marrow. For reticulocyte count an increasing trend with low reticulocyte count was seen from normocellular (n=4, 6.9%) to hypocellular (n=12, 20.7%) to hypercellular (n=19, 32.8%) bone marrow,though it was not statistically significant.

Conclusion: It was concluded in the present study that megaloblastic anemia was the most common etiology of pancytopenia and the commonest clinical symptoms observed was fever.

Keywords: Bone marrow evaluation, Hemophagocyticlymphohistiocytosis, Megaloblastic anaemia, Pancytopenia

INTRODUCTION

In daily clinical work, pancytopenia is a frequent finding. There is a lack of red blood cells, white blood cells, and platelets in the blood. Symptoms include a haemoglobin level below 12 g/dL in women and 13 g/dL in men, platelet count below 150,000/mcL, and white blood cell count below 4000/ml (or absolute neutrophil count of less than 1800 per ml) [1,2].

The incidence of pancytopenia peaks in the third and fourth decades of life for both children and adults. According to the published data, the male to female ratio ranges from 1.4% to 2.6%. Myelodysplastic syndrome and multiple myeloma are more common in older patients, while acute leukemia and parvovirus B19 infection are more common in younger patients [3].

There are many potential causes of pancytopenia, and diagnosing the underlying condition can be difficult due to the breadth of possible causes. Pancytopenia, a mild impairment in marrow function, may not be noticed until times of stress or increased demand, [4]. Pancytopenia is a symptom of many different diseases, both hematopoietic and otherwise. There are a number of underlying mechanisms at play, including a decrease in hematopoietic cell production, the replacement of marrow with abnormal cells, the suppression of marrow growth and differentiation, ineffective hematopoiesis with cell death, defective cell formation that results in the removal of cells from circulation, antibody-mediated sequestration or destruction of cells, and the trapping of cells in a hypertrophied and overactive reticuloendothelial system [1,5,6].

Hypersplenism, infections, myelosuppression (cancer, chemotherapy, drug toxicity, or radiotherapy), and megaloblastic anaemia were found to be the most common causes in a 2013 study conducted in India [7]. Megaloblastic anaemia was found to be most common cause of pancytopenia followed by combined nutritional deficiency, aplastic anaemia, iron deficiency anaemia, acute leukaemia, Non-Hodgkin Lymphoma (NHL), Juvenile Myelomonocytic Leukaemia (JMML), Myelodysplastic Syndrome (MDS), Primary Myelofibrosis (PMF), and storage disorder in another study conducted in India in 2022 [8].

Megaloblastic anaemia was found to be the leading cause of anaemia in India, with aplastic anaemia coming in second [9].

As the principle site of haematopoiesis is BM, low blood counts necessitates the BM examination. Practical distinction among various causes of pancytopenia is usually clear but some processes are so closely related that the diagnosis may get complicated and BM examination aids in diagnosis of such cases. It is important to

recognise marrow failure syndromes causing pancytopenia in order to improve the prognosis of patients [10,11].

Although pancytopenia is a common finding, its explicit discussion is lacking even in major textbooks and has led many authors to highlight the spectrum of causes of pancytopenia. To better understand the causes of pancytopenia and develop tactics to address them, the current cross-sectional study was designed. The present study was carried out to evaluate the various causes of pancytopenia and to evaluate clinical signs and symptoms, hematological parameters along with BM cellularity and other morphological features on aspiration and trephine biopsy in patients presenting with pancytopenia.

MATERIALS AND METHODS

The present cross-sectionalstudy was done in Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune, Maharashtra, India from August 2018 to April 2022. Total 157 patients presenting with pancytopenia were recruited from a tertiary care hospital in western part of state of Maharashtra, India. The study was approved by the institutional ethics committee, BVDUMC/IEC/67.

Sample size calculation: The sample size was calculated to be 148 at 95% confidence interval and 8% of margin of error considering the prevalence of 43% [12]. We recruited additional 9 patients to make total of 157.

Inclusion criteria: All patients with pancytopenia were included in the study.

Exclusion criteria: Patients who received chemotherapy/ radiotherapyand dry tap were excluded from the study. Required clinical details were taken for all the cases.

Procedure

After informed consent was obtained from each participant included in the study, blood samples were collected in anticoagulated (K2 Ethylene Diamine Tetraacetic Acid (EDTA)) vacutainers for hemogram,the analysis of hemogram was carried out on fully automated analyser DXH 800 (Beckman Coulter) along with peripheral smear examination. Bone marrow aspiration was done from posterior superior iliac spine in all the patients with Salah needle, the aspirate was drawn with a 20-ml plastic syringe. Bone marrow smears were prepared immediately following aspiration. After being air dried these smears where stained withLeishman and Giemsa for morphological examination. Special stains like Iron stain, Myeloperoxidase (MPO) and Periodic acid Schiff (PAS) stains were used wherever necessary. Bone marrow biopsy was fixed in Bouin's fluid and processed & stained with H&E and reticulin stain after decalcification, and then BM aspiration smears and biopsy sections were interpreted after thorough microscopic examination. Anaemia was classified as mild, moderate or severe based on the concentrations of haemoglobin in the blood.

- Mild: >10.0 g/dL;
- Moderate: 7.1-9.9 g/dL;
- Severe anaemia: <7.0 g/dL [13].

STATISTICAL ANALYSIS

The data was analysed using SPSS software (version 26.0). The results of qualitative parameters were calculated as frequencies and percentages and compared between the groups using chi-square test. The continuous variables were calculated as mean±SD, and compared between the means using students 't' test. P-value of <0.05 was considered significant.

RESULTS

Total 157 patients with pancytopenia were included in the study. Out of 157 patients, 120 patients belonged to adult age group (18-86 years) (76.43%) with mean age of the patients was 40.68±23.34 years. There were 67 (42.68%) females and 90 (57.32%) were males as shown in [Table/Fig-1], with male: female ratio of 1.34:1.

	Gender			
	Females		Males	
Age group (years)	N	%	N	%
<18	14	37.8	23	62.2
≥18	53	44.2	67	55.8

[Table/Fig-1]: Distribution of patients according to age and gender.

The most common clinical symptoms observed were fever 49 (31.20%), followed by generalised weakness 41 (26.11%), pallor 32 (20.40%), bleeding 14 (8.9%) and others as shown in [Table/Fig-2].

Symptoms	Frequency (n)	Percentage (%)
Fever	49	31.20
Generalised weakness	41	26.11
Pallor	32	20.40
Bleeding manifestations	14	8.90
Portal hypertension	7	4.50
Chronic alcoholic	6	3.80
Nausea	4	2.50
Jaundice	3	1.90
Vomiting	2	1.30
Acute gastroenteritis	2	1.30

[Table/Fig-2]: Symptomatology of patients with pancytopenia.

Among the patients with pancytopenia, splenomegaly was predominant finding observed in 51 (32.5%) patients, followed by hepatomegaly in 31 (19.7%), hepatosplenomegaly in 16 (10.2%) [Table/Fig-3]. Out of total 157 patients, data of organomegaly for 3 patients was not available due to lack of clinical history.

	Frequency (n)	Percentage (%)
Hepatomegaly	31	19.7
Splenomegaly	51	32.5
Both	16	10.2
No organomegaly	56	35.7

[Table/Fig-3]: Observations of organomegalies in patients with pancytopenia.

Most common etiology reported was megaloblastic anaemia in 35 (22.29%), followed by acute leukemia in 29 (18.47%), hypersplenism and hypocellular marrow in 21 each (13.38% each), MDS 14 (8.92%), aplastic anaemia 04 (2.55%) and other etiologies in 09 (5.73%) patients. The distribution of etiologies as per BM analysis is shown in [Table/Fig-4].

Diagnosis	Frequency (n)	Percentage (%)
Megaloblastic anaemia	35	22.29
Acute leukemia	29	18.47
Hypersplenism	21	13.38
Hypocellular marrow	21	13.38
MDS	14	8.92
Lympho proliferative disorder	9	5.73
HLH	6	3.82
Myelofibrosis	5	3.18
Aplastic anaemia	4	2.55
Inadequate marrow	2	1.27
Plasmacell dyscrasia suggestive of plasma cell myeloma	2	1.27
Others	9	5.73
Total	157	100

[Table/Fig-4]: Distribution of pancytopenia patients as per etiology.
Others: Reactive marrow, Iron deficiency anaemia, Chronic myeloproliferative disorder

Most of the patients (n=88) had haemoglobin level of <7 g/dL, followed by level between 7-10 g/dl in 64 patients and there were only 5 patients with Hb level of >11 g/dL. Majority of the patients (n=113) had TLC values between 1000-3500/cu mm, 27 patients had value of ≤1000/cu mm and only 17 had TLC of ≥3500/cu mm. Similarly, only 20 patients had platelet level of >100000/cu mm, while rest had platelet level of <100000/cu mm. Out of 157 patients, the reticulocyte count was carried out in 58 patients. Out of these 58 patients, 35 patients showed reticulocyte count less than 0.5% while 8 patients had reticulocyte count more than 2.5%. The BM aspirate in the present study of pancytopenia showed normocellular in 28 (17.83%), hypocellular 43 (27.39%) and hypercellular in 86 (54.78%) patients. The findings are depicted in [Table/Fig-5].

Parameters	Categories	Frequency (n)	Percentage (%)
Haemoglobin (g/dL)	<7	88	56.1
	7.1 to 9.9	64	40.8
	>10	5	3.2
TLC (cells/cumm)	≤1000	27	17.20
	1000-3500	113	72.00
	≥3500	17	10.80
Platelet count (cells/cumm)	<50000	94	59.9
	50000-99000	43	27.4
	>100000	20	12.7
Reticulocyte count (%)	<0.5	35	60.3
	0.5-2.5	15	25.9
	>2.5	8	13.8
Bone marrow cellularity	Normocellular	28	17.83
	Hypocellular	43	27.39
	Hypercellular	86	54.78

[Table/Fig-5]: Hematological parameters and bone marrow cellularity findings in patients with pancytopenia..

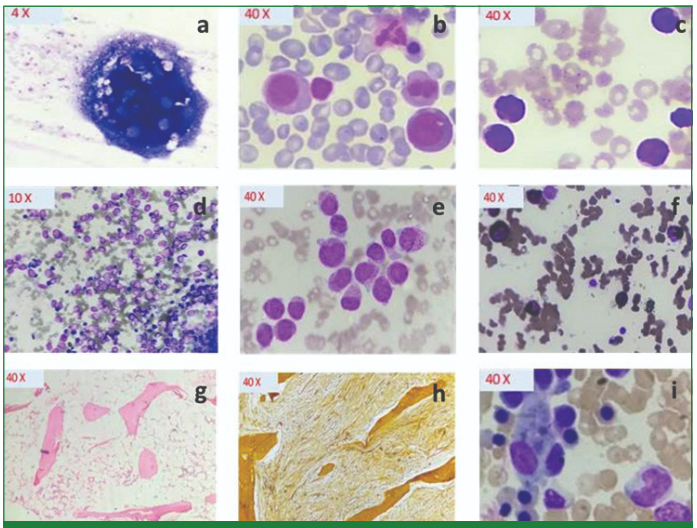
The numbers of patients based on levels of haematological parameters were distributed among the normocellular, hypocellular and hypercellular on BM aspiration. There was a significant p-value (p=0.0067, p=0.0291) for total leucocyte count in hypocellular and hypercellular marrow aspirate sample respectively. The distribution of patients according to haematological parameters among normocellular, hypocellular and hypercellular BM samples is shown in [Table/Fig-6].

		Normocellular		Hypocellular		Hypercellular	
		No	Yes	No	Yes	No	Yes
Hb level (g/dL)	<7	73	15	66	22	37	51
	7 to 10	52	12	45	19	31	33
	> 10	4	1	3	2	3	2
Total leucocyte count	≤1000	23	4	13	14*	18	9#
	>1000 to <3500	91	22	87	26	48	65
	≥ 3500 to <4000	15	2	14	3	5	12
Platelet count	<50000	76	18	63	31	49	45
	50000 to 99000	37	6	36	7	13	30
	100000 to 149000	16	4	15	5	9	11
Reticulocyte count	<0.5	31	4	23	12	16	19
	0.5 to 2.5	14	1	10	5	6	9
	>2.5	5	3	8	0	3	5

[Table/Fig-6]: Distribution of haematological parameters in patients with normocellular, hypocellular and hypercellularbone marrow.
TLC; hypocellular: p=0.0067; hypercellular: p=0.0291

The characteristic microscopic features of various causes of pancytopenia on BM examination are depicted in [Table/Fig-7]. The BM aspiration showed hypercellular marrow fragments with trilineagehematopoiesis in patients with hypersplenism [Table/Fig-7a]. In megaloblastic anaemia, BM aspiration showed megaloblastic erythroid hyperplasia. Megaloblasts had the characteristic feature of sieved nuclear chromatin, asynchronous nuclear maturation and bluish cytoplasm [Table/Fig-7b]. In present study acute lymphoid leukemia was seen in 15 patients which showed L1 type lymphoblasts showing high N:C ratio, fine chromatin, inconspicuous nucleoli and scanty amount of pale blue cytoplasm [Table/Fig-7c] while patients with acute myeloid leukaemia showed predominantly large blasts with high nucleus: cytoplasmic ratio, fine chromatin and 1-2 prominent nucleoli with moderate amount of pale blue cytoplasm in AML M1 [Table/Fig-7d] and abnormal promyelocytes/blasts showing lobulated reniform nuclei with moderate amount of granular cytoplasm in AML M3. These cells also showed auer rods at higher magnification on BM aspiration smears in AML M3 [Table/Fig-7e]. Out of 13 cases of Acute Myeloid Leukaemia, one case was diagnosed as AML M4 on BM morphology. Few of the blasts in this case showed strong MPO positivity while others were MPO negative on a special myeloperoxidase stain. [Table/Fig-7f]. In 1 patient the BM findings were only consistent with acute leukemia (AML-M0/ALL-L2) as only morphology and cytochemical stains were not adequate to classify it accurately and further immunophenotyping and cytogenetic studies were advised in this case.

The trephine biopsy in patients with aplastic anaemia showed characteristic hypocellular BM spaces with scattered lymphocytes on hematoxylin and eosin staining [Table/Fig-7g], while one case showed grade IV myelofibrosis on BM trephine biopsy stained with reticulin stain [Table/Fig-7h]. Six cases in this study showed increase in reticuloendothelial cell activity with increase in reticulum cells and evidences of hemophagocytosis on BM aspiration smears [Table/Fig-7i].



[Table/Fig-7]: Photomicrograph of Bone marrow aspiration smear a) Hypercellular marrow in a case of hypersplenism; b) Megaloblasts seen in case of megaloblastic anaemia; c) Blasts in ALL-L1; d) AML-M1; e) AML-M3; f) AML-M4: MPO positive in few of the blasts and negative in others; g) Hypocellular marrow spaces in a bone marrow biopsy of aplastic anaemia; h) Marrow showing grade IV myelofibrosis; i) Evidence of hemophagocytosis in a case of HLH

DISCUSSION

Bone marrow examination is an important investigation which aids to a diagnosis and for the treatment and its prognosis. Pancytopenia is a very common haematological finding with variable clinical symptoms and signs. The various investigations like complete blood count, biochemical test, reticulocytes count, BM aspiration and biopsy, cytochemical stains, immunophenotyping, cytogenetic and molecular studies are required for arriving to a definitive diagnosis. But the key investigation remains the BM examination in patients with pancytopenia which helps in arriving to the final diagnosis as well as guiding towards further investigation and deciding the management protocols.

The present study was carried out to evaluate various etiologies of pancytopenia and to study the morphology of BM in patients with pancytopenia. Among a total of 157 patients with pancytopenia, the mean age was 40.68±23.34 years. The incidence was reported to be more in patients with age ≥18 years i.e. adult age group, and there were more males (57.32%) affected than females (42.68%). Male to female ratio was 1.34: 1.0 to a study by an almost equal gender distribution among patients with pancytopenia. Different studies from central India are shown in [Table/Fig-8] cite references [9,14-18].

Study (Year)	N	Age range (years)	Male: Female ratio
Tilak V et al., [14] (1992)	104	2-80	1.2:1
Khodke K et al., [15] (2001)	50	3-69	1.3:1
Kumar R et al., [16] (2001)	166	12-73	2.1:1
Khunger JM et al., [9] (2002)	200	2-70	1.2:1
Ranaswamy M et al., [17] (2012)	100	11-80	1.6:1
Varma A et al., [18] (2018)	251	16-65	1.38:1
Present study	157	18-86	1.34:1

[Table/Fig-8]: Comparison of present study with other studies in respect to age range and gender.

In the present study, the most common clinical history observed was fever followed by generalised weakness, pallor, bleeding, portal hypertension, etc. These clinical findings were found similar in Rangaswamy M et al., [17] and Varma A et al., [18]. The most common sign was splenomegaly followed by hepatosplenomegaly and hepatomegaly, while there was no organomegaly in 35.7% of patients.

The haemoglobin level ranged between 2.1 to 10.7 g/dL, of which most had a haemoglobin level of <7 g/dL. The total leukocyte count ranged between 100 to 3900 cells/cumm with most of the patients having the TLC between >1000 to <3500 cells/cumm and platelet count range was between 9000 to 149000 cells/cumm with maximum patients having count of <50000 cells/cumm. In terms of all the above parameters, the results of Rangaswamy M et al., [17] Kavitha M et al., [19] and Sale SM et al., [20] were comparable to the current study.

The BM aspirate cellularity was classified into normocellular, hypercellular and hypocellular. Majority of the cases showed hypercellular marrow particles followed by hypocellular and normocellular in patients with pancytopenia.Similarly Gore CR et al., [21] had hypercellular BM particles as a more common finding. Rangaswamy M et al., [17] found a 75%, 14%, and 11% incidence of hypercellular, hypocellular, and normocellular BM, respectively. In patients with hypocellular and hypercellular BM particles, there was a significant difference in the 'p' value of TLC, while haemoglobin, platelet count and reticulocyte count did not show significant 'p' value. The various etiologies in these cases were megaloblastic anaemia(n=4), hypersplenism (n=4), acute leukemia (n=7), reactive BM with evidences of HLH (n= 3), HLH (n=2), normocellular marrow with features of iron deficiency with adequate megakaryocytes (n=3), MDS (n=3) and one case each of myelofibrosis and BM involvement by lymphroliferative disorder. These findings also suggests that normocellular marrow fragments also harbours the characteristic morphological features pertaining to the underlying pathology and therefore all the normocellular marrow particles and cellular trails should be thoroughly examined during BM examination.

The primary objective of the study was to find the causes of pancytopenia, of which the most common was megaloblastic anaemia, followed by acute leukaemia, hypersplenism, hypocellular marrow, MDS, lymphoproliferative disorder, HLH, myelofibrosis, aplastic anaemia, plasma cell dyscrasia and other causes.

According to Weinzierl EP et al., [22] in adults, hematologic neoplastic causes of pancytopenia were the most prevalent diagnoses, with the cases divided mostly between acute myeloid leukemia and myelodysplastic syndrome, with fewer numbers of cases of acute lymphoblastic leukemia, myeloproliferative neoplasms, and lymphomas. While as per Jain A et al., [23] the most common cause of pancytopenia was megaloblastic anaemia, followed by dimorphic anaemia, aplastic anaemia, and hematological malignancies.

A study from Jodhpur, Rajasthan reported acute leukemia to be the most common cause of pancytopenia, followed by megaloblastic anaemia, aplastic anaemia, hypersplenism, multiple myeloma, and myelodysplastic syndrome [24].

The commonest cause of pancytopenia according to Sindhiya CV et al., [8] was megaloblastic anaemia, followed by combined nutritional deficiency, aplastic anaemia, iron deficiency anaemia, normal and APL. According to Chandra H et al., [25] megaloblastic anaemia, aleukemic leukemia and hypoplastic/aplastic anaemia to be the commonest causes of pancytopenia. Comparison of present study with other studies with respect to etiologies of pancytopenia has been done in [Table/Fig-9] [9,14-17,22,23].

In this study acute lymphoid leukaemia was seen in 15 cases, out of which 1 patient had developed marrow fibrosis. There were 13 cases of acute myeloid leukaemia out of which 3 marrow aspirates showed features of myelodysplasia and probably developed from a dysplastic marrow.

In the Indian subcontinent, pancytopeniais are relatively common condition that receives insufficient attention. The underlying cause of pancytopeniais are usually identified through a comprehensive clinical and haematological examination of patients with the

	Present study	Tilak V et al., [14] (1992)	Khodke K et al., [15] (2001)	Kumar R et al., [16] (2001)	Khunger JM et al., [9] (2002)	Weinzierl EP et al., [22] (2013)	Jain A et al., [23] (2021)
Megaloblastic anaemia	35	53	22	37	144	-	63
Acute leukemia	29	1	1	20	10	47	4
Chronic lymphoid leukemia	-	-	-	-	-	2	1
Hypersplenism	21	-	-	19	4	-	-
Hypocellular marrow	21	-	-	-	-	-	-
MDS	14	-	1	6	4	55	2
Lymphoproliferative disorder	9	1	-	10	2	8	4
HLH	6	-	-	-	-	-	-
Myelofibrosis	5	1	-	2	2	1	1
Aplastic anaemia	4	6	7	49	28	-	20
Inadequate marrow	2	-	-	-	-	-	-
Plasma cell dyscrasia suggestive of plasma cell myeloma	2	1	2		2	4	3
Others	9	5	2	11	4	2	2

[Table/Fig-9]: Comparison of present study with other studies with respect to etiologies of pancytopenia.

condition. Pancytopenia, however, remains a diagnostic challenge for haematologists due to the wide rangeof etiologies.

Limitation(s)

One of the limitation of the present study was non-inclusion of dry tap/non-aspirable marrow samples where the aspiration smears were not available to study the morphology and it could be due to myelofibrosis or densely packed marrow cells. In such situations smears can be prepared from touch imprint smears of the BM trephine biopsy and the trephine biopsy which may prove helpful in arriving at the diagnosis or provides clues towards further investigations and treatment strategies.

CONCLUSION(S)

The present study concluded that the prevlence of pancytopenia was more in males as compared to females and megaloblastic anemia was the most common etiology of pancytopenia The current study suggests that, for the sake of diagnosis and therapy, it is essential to recognise the factors contributing to pancytopenia and their related BM morphology, especially in emergency situations like HLH where prompt detection is important. It is imperative to rule out megaloblastic anaemia as the cause of pancytopenia because it is the leading preventable cause of patient morbidity.

REFERENCES

[1] Das Makheja K, Kumar Maheshwari B, Arain S, Kumar S, Kumari S, Vikash, et al. The common causes leading to pancytopenia in patients presenting to tertiary care hospital. Pak J Med Sci. 2013;29(5):1108-11.
[2] Vargas-Carretero CJ, Fernandez-Vargas OE, Ron-Magaña AL, Padilla-Ortega JA, Ron-Guerrero CS, Barrera-Chairez E,et al. Etiology and clinico-hematological profile of pancytopenia: experience of a Mexican Tertiary Care Center and review of the literature. Hematology. 2019;24(1):399-04.
[3] Chiravuri S, De Jesus O. Pancytopenia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563146/
[4] Gnanaraj J, Parnes A, Francis CW, Go RS, Takemoto CM, Hashmi SK. Approach to pancytopenia: Diagnostic algorithm for clinical hematologists. Blood Rev. 2018;32(5):361-67.
[5] Shimamura A, Alter BP. Inherited aplastic anaemia syndrome. In: Greer JP, Foerster J, Rodgers GM, Paraskevas F, Gladet B, Arber DA, et al.editors , editors. Wintrobe's clinical hematology. Philadelphia: Lippincott Williams & Wilkins. 2008.117-361.
[6] Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. J Nepal Med Assoc. 2008;47:12-17.
[7] Jain A, Naniwadekar M. An etiological reappraisal of pancytopenia-largest series reported to date from a single tertiary care teaching hospital. BMC Hematol. 2013;13(1):10.
[8] Sindhiya CV, Hanagavadi S. Clinico-Haematological Study Of Pancytopenia- An Experience From Tertiary Care Hospital. Global Journal of Pathology & Laboratory Medicine. 2022; 1(4):64-74.
[9] Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia--a clinicohaematological study of 200 cases. Indian J PatholMicrobiol. 2002;45(3):375-79.
[10] Mudhumita JB, Zon LI. Hematopoiesis. Development. 2013;140(12):2463-67.
[11] Kar M, Ghosh A. Pancytopenia Journal, Indian Academy of Clinical Medicine. 2002;3:29-41.
[12] Barik SS, Chandoke RK, Verma AK. A prospective clinico-hematological study in 100 cases of pancytopenia in capital city of India. J ApplHematol. 2014;5:45-50.
[13] Kariyeva GK, Magtymova A, Sharman A. Anaemia 12 12.1 Introduction. 2002. Available from: https://dhsprogram.com/pubs/pdf/fr130/12chapter12.pdf.
[14] Tilak V, Jain R. Pancytopenia-A Clinco-hematologic analysis of 77 cases. Indian J PatholMicrobiol. 1992;42:399-04.
[15] Khodke K, Marwah S, Buxi G, Vadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. J Academy Clin Med. 2001;2:55-59.
[16] Kumar R, Kalra SP, Kumar H, Anand AC, Madan M. Pancytopenia-A six year study. J Assoc Physicians India. 2001;49:1079-81.
[17] Rangaswamy M, Nandini NM, Manjunath GV. Bone marrow examination in pancytopenia. Journal of the Indian Medical Association. 2012;110(8):560-62.
[18] Varma A, Lokwani P, Malukani K, Gupta S, Maheshwari P. Study of hematological profile of adults presenting with pancytopenia in a tertiary care hospital of central India. Medical Journal of Dr. DY Patil Vidyapeeth. 2018;11(6):512.
[19] Kavitha M, Yogalakshmi S. Evaluation of peripheral smear and bone marrow in patients presenting with pancytopenia. Journal of Evolution of Medical and Dental Sciences. 2018;7(29):3296-300.
[20] Sale SM, Mane VP, Pawar VR, Mohite SN, Dhaka V. Clinical correlation of pancytopenia with bone marrow study in a tertiary hospital. Indian J PatholOncol. 2016;3(2):247-54.
[21] Gore CR, Bardapurkar P, Paranjape S, Patel S, Karia K. Clinico-hematological evaluation of pancytopenic adults in a tertiary care. Indian J PatholOncol. 2018;2:391-97.
[22] Weinzierl EP, Arber DA. The differential diagnosis and bone marrow evaluation of new-onset pancytopenia. Am J ClinPathol. 2013;139(1):9-29.
[23] Jain A, Garg R, Kaur R, Nibhoria S, Chawla SPS, Kaur S, et al. Clinico-hematological profile of pancytopenic adult patients in a tertiary care teaching hospital. Tzu Chi Med J. 2021;34(1):95-01.
[24] Patel GR, Prajapati GR. Spectrum of Pancytopenia in Adults Attending a Clinical Hematology Department: A Four-Year Experience From a Tertiary Care Center of Western India. Cureus. 2022;14(5):e24933.
[25] Chandra H, Gupta AK, Nath UK, Singh N, Kumar U, Kishore S, et al. Clinico-hematological study of pancytopenia: A single-center experience from north Himalayan region of India. J Family Med Prim Care. 2019;8(12):3944-48.

PARTICULARS OF CONTRIBUTORS:

1. Postgraduate Student, Department of Pathology, Bharati Vidyapeeth (DTU) Medical College, Pune, Maharashtra, India.
2. Assistant Professor, Department of Pathology, Bharati Vidyapeeth (DTU) Medical College, Pune, Maharashtra, India.
3. Associate Professor, Department of Pathology, Bharati Vidyapeeth (DTU) Medical College, Pune, Maharashtra, India.
4. Associate Professor, Department of Pathology, Bharati Vidyapeeth (DTU) Medical College, Pune, Maharashtra, India.
5. Professor, Department of Pathology, Bharati Vidyapeeth (DTU) Medical College, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Preeti Rajeev Doshi,
Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune, Maharashtra, India.
E-mail: prdoshi22@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Aug 31, 2022
- Manual Googling: Oct 29, 2022
- iThenticate Software: Nov 03, 2022 (15%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Aug 22, 2022**
Date of Peer Review: **Sep 19, 2022**
Date of Acceptance: **Nov 04, 2022**
Date of Publishing: **Apr 01, 2023**