Journal of Advances in Medicine and Medical Research

33(7): 26-32, 2021; Article no.JAMMR.64657
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Etiological and Clinical Spectrum of Pancytopenia Based on Peripheral Blood Smear and Bone Marrow Examination: A Cross-sectional Study

Vipin Porwal[1*], Rajesh Deshpande[1] and Rohit Modi[1]

[1]Department of Medicine, R.D. Gardi Medical College Ujjain, Madhya Pradesh, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author VP designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors RD and RM managed the analyses of the study. Author RM managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i730871
Editor(s):
(1) Dr. Mohamed Essa, Sultan Qaboos University, Oman.
Reviewers:
(1) Deniz Akyol, Ege University, Turkey.
(2) Deijanira Albuquerque, Federal University of Mato Grosso, Brazil.
Complete Peer review History: http://www.sdiarticle4.com/review-history/64657

Original Research Article

Received 25 November 2020
Accepted 29 January 2021
Published 29 March 2021

ABSTRACT

Aims: Pancytopenia is a common clinic-haematological problem suspected in patients with anaemia, prolonged fever, and a bleeding tendency. This study was performed to find the prevalence of pancytopenia and to determine the common causes of pancytopenia.
Study Design: Cross-sectional observational study.
Place and Duration of Study: department of general medicine at R. D. Gardi Medical College, Ujjain, India between November 2017 toAugust 2019.
Methodology: The study was conducted among patients with pancytopenia during a two-year period. The etiological pattern was assessed through routine blood tests to determine their clinical features, peripheral blood pictures, and bone marrow morphologies.
Results: Out of 100 patients with pancytopenia, the majority (64.0%) were men. A total of 34 patients were aged between the 21 and 30 years and 28 were aged between 31 and 40 years. Generalized weakness was the most common (88%) presentation and the most common clinical finding was pallor (94.0%), followed by splenomegaly (40.0%) and hepatomegaly (30.0%).

**Corresponding author: E-mail: porwal.diab@gmail.com;*

Megaloblastic anaemia was the most common cause of pancytopenia that was observed in 58 patients, followed by aplastic anaemia (n=12), cirrhosis of the liver (n=8), leukaemia (n=6), dengue, myelodysplastic syndrome, and malaria (n=4 each), paroxysmal nocturnal haemoglobinuria and acquired immunodeficiency syndrome (n=2 each). A total of 28.0% patients had normocellular bone marrow and 72.0% had cellular marrow.
Conclusion: Megaloblastic anaemia was the most common aetiology of pancytopenia.

Keywords: Pancytopenia; peripheral blood smear; bone marrow examination; cross-sectional study.

1. INTRODUCTION

Pancytopenia is characterized by a reduction of all three cellular elements including red, white blood cells, and platelets of peripheral blood, leading to anaemia, leukopenia and thrombocytopenia [1]. It is most often observed in patients with bone marrow infiltration, anticancer chemotherapy, hypersplenism, systemic diseases, and HIV infection [2]. The manifestations of pancytopenia depend on the severity of anaemia, leukopenia, and thrombocytopenia [3].

The incidence of pancytopenia can result either from the failure of production of multiple hematopoietic progenitor cells, malignant cell infiltration, immune-mediated bone marrow failure, ineffective haematopoiesis, and dysplasia, or peripheral sequestration of blood cells altered by immune mechanism [4]. Sheehan's syndrome and filariasis are some rare causes of megaloblastic anaemia [3].

The presenting symptoms of pancytopenia are mild progressive weakness, fatigue, dyspnoea, increased tendency to infection, bleeding, haemorrhage from skin, nose, or gums, and cardiac symptoms, due to thrombocytopenia. Thrombocytopenia can cause excessive mucosal bruising and bleeding. The aetiology of pancytopenia varies with geographical distribution, genetic condition, and mutations.

Initially, mild pancytopenia in bone marrow may not be detected but it may become more apparent during the stress period [5]. Peripheral pancytopenia requires sequential analysis of a bone marrow biopsy and bone marrow aspirate for assessment of cellularity and morphology. Bone marrow aspiration and trephine biopsy are important in the assessment of aetiology of pancytopenia. It can be easily performed during the presence of severe thrombocytopenia with no risk of bleeding. Diagnosis of unexplained cytopenia and malignant are generally performed using bone marrow aspiration. Furthermore, it is preferred for the evaluation and staging of a neoplasm. Trephine biopsies are usually taken for evaluation of hypoplasia or aplasia on aspiration.

There is a need to document the common aetiologies and clinical characteristics of pancytopenia in patients attending healthcare care centres. Thus, this cross-sectional study was performed to find the prevalence of pancytopenia and to determine the common causes of pancytopenia.

2. MATERIALS AND METHODS

2.1 Study Design

This was a cross-sectional observational study conducted among patients with pancytopenia presenting to the department of general medicine at R. D. Gardi Medical College, Ujjain, India between November 2017 and August 2019.

2.2 Inclusion and Exclusion Criteria

Patients of either sex, aged 15 years or older and newly detected pancytopenia were included in this study. Patients receiving chemotherapy or radiotherapy and aged <15 years and were excluded from the study.

2.3 Laboratory Investigations

Routine blood tests performed included complete hemogram with thin peripheral smear, red blood cell indices, reticulocyte count, serum bilirubin total, alanine transaminase, aspartate transaminase, total serum proteins, albumin and globulin levels, serum electrolytes, blood urea, serum creatinine, random blood sugar, hepatitis B surface antigen, hepatitis C virus, human immunodeficiency virus infection, chest X-ray, and ultrasonography of abdomen. Bone marrow aspiration was done as per indication.

2.4 End Points

Primary endpoint was to determine the common aetiology and clinical features of patients with pancytopenia. Secondary endpoints were to determine the age and sex distribution in young patients diagnosed with pancytopenia.

2.5 Statistical Analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 23.0 Continuous variables were summarized with descriptive statistics, including categorical variables were presented as frequency and percentages

3. RESULTS AND DISCUSSION

In this study, 100 patients were included in this study, of which 64 (64.0%) were men and 36 (36.0%) were women (men to women ratio 1.8:1). Most of the patients were between the 21 to 30 age group which included a total of 34 patients (34.0%). There were 28 (28.0%) patients in the age group of 31 to 40 years, 20 (20.0%) patients from the age group of 41 to 50 years, and 10 (10.0%) patients from the age group of 51 to 60 years. The least patients were in the age group of 15 to 20 years which included 8 (8.0%) patients.

The most common clinical feature in this study was pallor (94.0%), followed by splenomegaly (40.0%). Hepatomegaly (30.0%), lymphadenopathy (16.0%), purpura (16.0%), and oedema (12.0%) were also noted. Recorded signs and symptoms of patients were generalized weakness (88.0%), bleeding (34.0%), fever (30.0%), and dyspnoea (28.0%).

The etiological break up was according to the following order: megaloblastic anaemia (n = 58; 58.0%), aplastic anaemia (n = 12; 12%), cirrhosis of liver (n = 8; 8.0%), leukaemia (n = 6; 6.0%), dengue (n = 4; 4.0%), myelodysplastic syndrome (n = 4; 4.0%), malaria (n = 4; 4.0%), paroxysmal nocturnal haemoglobinuria (n = 2; 2.0%), acquired immunodeficiency syndrome (n = 2; 2.0%). The predominant blood picture was megaloblastic anaemia followed by erythroid hyperplasia and aplastic anaemia (Fig. 1).

The haematological parameters revealed that anaemia was severe (Hb, 0-3) in 2.0%, moderate (Hb, 3-6) in 24.0%, and mild in 74.0% of the cases. Out of 100 patients, 60.0% of the patients had mild leukopenia, while 28.0% and 12.0% had moderate and severe leukopenia, respectively. The platelet count of <0.5 lakhs/cmm was observed in 24 patients, <1.0 lakhs/cmm in 26 patients and <1.5 in 60 patients. The bone marrow study showed that 28.0% of the patients had normocellular bone marrow and 72.0% had cellular marrow (including hypercellular [60.0%] and hypocellular [12.0%]). The clinical manifestations based on the aetiology of pancytopenia are presented in Table 1.

3.1 Discussion

This retrospective study assessed the clinical profile and aetiological spectrum of pancytopenia event in Indian settings. The majority of the present study population was from the age group 21 to 30 years with men preponderance. Etiological factors of pancytopenia were recorded as megaloblastic anaemia, aplastic anaemia, hypersplenism, infection, myelodysplastic syndrome, and HIV. In this study, the most common general physical finding was pallor which included 94.0% of patients. Total 28.0% of the patients had normocellular bone marrow and 72.0% had cellular marrow.

In the present study, the majority of the cases were in the age group 21 to 30 years which is similar to the study of Chandan RH, et al. with reported 40% cases in the same age group [6]. Another study conducted in both rural and urban communities of eastern India reported the prevalence of pancytopenia and it was found to be prevalent in the younger age group (14 to 45 years) [7]. However, another study conducted by Yokuş O, et al showed that incidence of pancytopenia was directly proportional with increasing age and the majority of patients diagnosed with pancytopenia were in the age group of ≥65 years [n=92; 67%] [8].

In the present study, the men to women ratio was found to be 1.8:1. These results are considered alongside the research of Dasgupta S, et al in which 248 patients with pancytopenia were studied and men preponderance was observed with men to women ratio of 1.7:1 [9]. This is similar to the study conducted in India by Shah, et al. therein 53.9% of their pancytopenic patients were men and 46.2% were women [10]. Similarly, Chandra H, et al also observed a men predominance in their series [11]. Few studies reported that pancytopenia is more in women than men [7,12]. However, the men preponderance was observed in this study which

agrees with previous studies. This wide variation in the distribution of prevalence among men and women is possibly due to men are more exposed to agricultural insecticides and pesticides, or industrial toxins, or radiation likewise women also perform jobs in different sectors surrounding chemicals and environment in urban areas therefore both of them are exposed to toxins [7,12]. The exact cause of this sex variation is not clearly understood.

In the present study, pallor to be a common presentation by 94.0% of the patients, followed by splenomegaly in 40.0%, hepatomegaly in 30.0%, lymphadenopathy, and purpura each in 16.0% patients, and oedema in 12.0% of patients with pancytopenia. Sharma A, et al showed similar observations in terms of clinical features. In which, pallor was present collectively in almost all the patients (96.9%) [13] Pallor, splenomegaly, hepatomegaly, and icterus was observed in the majority of patients in a study of Dubey TN, et al. These were followed by sternal tenderness, lymphadenopathy and haematuria [14]. Current evidence highlighted similar results in the case of clinical features [13]. Another noteworthy study in Indian literature reported fever as the most common presenting symptom in 40.0% of patients which is higher than that reported by the present study (40.0% vs. 30.0%). Petechial haemorrhages were present in 5.0% of patients [10].

Previous literature revealed that megaloblastic anaemia as the most common cause of pancytopenia whereas aplastic anaemia is the second most common aetiology of pancytopenia. A study by Dasgupta S, et al. had reported that aplastic anaemia was the most common cause of pancytopenia followed by leishmaniasis, hypersplenism, tuberculosis, connective tissue disorders [9]. In another study from India that had evaluated the etiological causes of pancytopenia in 83 patients, megaloblastic anaemia was reported to be the most common cause (33.8%), whereas megaloblastic anaemia (20.97%), leishmaniasis (13.7%), hypersplenism (13.7%), tuberculosis (4.84%), and other connective tissue disorders (2.42%) were the rare causes [9]. Sharma A, et al observed splenomegaly (31.0%) and hepatomegaly (23.9%) in 132 cases of pancytopenia which is comparable to the present study [13]. In another study that had reported vitamin B_{12} deficiency to be the most common cause. Megaloblastic anaemia was the most common cause of pancytopenia in patients accounting for 58%. These results are in line with a study conducted by Gandhi P, et al in 2016 in India [15]. It emphasized that megaloblastic anaemia can be correlated with nutritional deficiency.

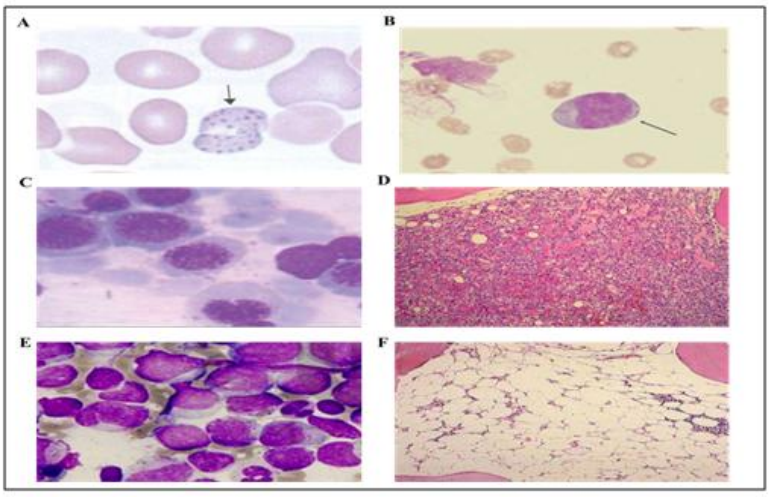

Fig. 1. Peripheral blood smear and bone marrow aspirate smear examination

(A) Bone marrow aspirate showing aperipheral smear showing basophilic stippling in case of megaloblastic anemia (Field's stain, ×100 XS). (B) Peripheral blood smear showing myeloblast with Auer rod in case of Acute Myeloid Leukemia (Field's stain, ×100 XS). (C) Bone marrow aspiration showing markedly erythroid hyperplasia with megaloblastic erythropoiesis (Field's stain, ×100 XS) (D) Bone marrow aspirate showing with hypercellularity in case of megaloblastic anemia (lower power, HandE). (E) Bone marrow aspiration showing myeloblasts in AML-M2 (Field's stain 100xs). (F) Bone marrow biopsy showing hypocellularity with replacement of hemopoietic tissue by fat in case of aplastic anemia (low power, HandE)

Table 1. Clinical and etiological presentation of patients with pancytopenia

Parameters	Number of patients (N=100)
Sex	
Men	64 (64.0)
Women	36 (36.0)
Age group (years)	
15 - 20	8 (8.0)
21 - 30	34 (34.0)
31 - 40	28 (28.0)
41 - 50	20 (20.0)
51 – 60	10 (10.0)
Chief complaints	
Generalized weakness	88 (88.0)
Bleeding	34 (34.0)
Fever	30 (30.0)
Dyspnoea	28 (28.0)
Clinical findings	
Pallor	94 (94.0)
Splenomegaly	40 (40.0)
Hepatomegaly	30 (30.0)
Lymphadenopathy	16 (16.0)
Purpura	16 (16.0)
Oedema	12 (12.0)
Aetiologies	
Megaloblastic anaemia	58 (58.0)
Aplastic anaemia	12 (12.0)
Cirrhosis of liver	8 (8.0)
Leukaemia	6 (6.0)
Dengue	4 (4.0)
Myelodysplastic syndrome	4 (4.0)
Malaria	4 (4.0)
Paroxysmal nocturnal haemoglobinuria	2 (2.0)
Acquired immunodeficiency syndrome	2 (2.0)
Haemoglobin (g/dL)	
0-≤3	2 (2.0)
>3-≤6	24 (24.0)
>6-9	74 (74.0)
Total leukocyte count (per cmm)	
1000-≤2000	12 (12.0)
>2000-≤3000	28 (28.0)
>3000-4000	60 (60.0)
Platelet count (lakhs/cmm)	
0-0. ≤5	24 (24.0)
>0.5-≤1.0	26 (26.0)
>1.0-1.5	50 (50.0)
Peripheral blood smear	-
Macrocytic	76 (76.0)
Normocytic normochromic	14 (14.0)
Dimorphic	6 (6.0)
Microcytic hypochromic	4 (4.0)
Cellularity of bone marrow	
Normocellular	28 (28.0)
Hypercellular	60 (60.0)
Hypocellular	12 (12.0)

Data shown as n (%)

Bone marrow biopsy amongst the patients with pancytopenia revealed the patients had normocellular bone marrow and cellular marrow which was comparable to other studies. In the previous prospective study, a bone marrow examination was performed in 101 patients [13]. They reported normocellular marrow in 24% of patients and hypercellular marrow smears in of 61% of patients which is comparatively lower than the observation by the present study in which normo-and hypercellular marrow was observed in 88.0% cases [13]. The higher number of cellular marrow smears in the present study is likely to be because of the higher cases of megaloblastic anaemia than aplastic anaemia cases [16].

An important limitation of the present study is that it is a cross-sectional observational study, which was performed in a single centre. Therefore, the exact causes of pancytopenia prevalent in the region may not have been predicted in the study. Thus, further larger studies are required to understand the exact causes of pancytopenia.

4. CONCLUSION

Megaloblastic anaemia was the most common aetiology among patients with pancytopenia. This study helps to understand age, sex distribution among patients with pancytopenia. Proper diagnosis of pancytopenia in an earlier phase may be life-saving

CONSENT

All authors declare that written informed consent was obtained from each participant before participation in the study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

This study was conducted in accordance with the ethical principles that are consistent with the declaration of helsinki, international conference on harmonization good clinical. The study protocol was approved by ethics committee prior to commencement of the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Vargas-Carretero CJ, Fernandez-Vargas OE, Ron-Magaña AL, Padilla-Ortega JA, Ron-Guerrero CS, 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.
DOI: 10.1080/16078454.2019.1590961
PMID: 30890036.
2. Premkumar M, Gupta N, Singh T, Velpandian T. Cobalamin and folic Acid status in relation to the etiopathogenesis of pancytopenia in adults at a tertiary care centre in north India. Anemia. 2012; 707402.
DOI: 10.1155/2012/707402
3. Suryaresmi BS, Abraham L, Mathew A, Raj JM. The etiological spectrum of pancytopenia diagnosed from blood smears examined in the pathology department of a rural tertiary care centre in South India. Int J Med Sci Public Health 2018;7(2):126-131.
4. Yadav BS, Varma A, Kiyawat P. Clinical profile of pancytopenia: A tertiary care experience. Int J Bioassays 2015;4(01): 3673-3677.
5. Makheja KD, Maheshwari BK, Arain S, Kumar S, Kumari S, Vikash. The common causes leading to pancytopenia in patients presenting to tertiary care hospital. Pak J Med Sci. 2013;29(5):1108-1111.
DOI:http://dx.doi.org/10.12669/pjms.295.3458
6. Chandan RH, Giriyan SS. Role of bone marrow aspiration and biopsy in elaborating the diagnosis of pancytopenia. Trop J Path Micro. 2018;4(2):144-149.
DOI: 10.17511/jopm.2018.i2.04
7. Bijaya M, Reetu S, Satish P. Changing trends in etiology of pancytopenia-our experience. Arch Gen Intern Med. 2017; 1(4):1-6.
8. Yokuş O, Gedik H. Etiological causes of pancytopenia: A report of 137 cases. Avicenna J Med. 2016;6(4):109-112.
DOI:10.4103/2231-0770.191447
9. Dasgupta S, Mandal PK, Chakrabarti S. Etiology of pancytopenia: An observation

from a referral medical institution of eastern region of India. J Lab Physicians. 2015;7(2):90-5.
DOI:10.4103/0974-2727.163136
PMID: 26417158.
PMCID: PMC4559635.

10. Shah P, Patel R, Gamit B, Gheewala S. Bone marrow examination in cases of pancytopenia. Int J Res Med Sci. 2017; 5(4):1494-1498.
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20171253
11. Chandra H, Gupta AK, Nath UK, Singh N, Kumar U, Kishore S. Clinico-hematological study of pancytopenia: A single-center experience from north Himalayan region of India. J Family Med Prim Care. 2019; 8(12):3944-3948.
DOI: 10.4103/jfmpc.jfmpc_539_19
12. El-Hagrasy HA, Hassanein N, Ahmed AME. Clinico- pathological study of pancytopenia in adult cases at a tertiary hospital in Saudi Arabia. AL-AZHAR Assiut Medical Journal 2015;13(3):209-217.
13. Sharma A, Ravindranath M, Bhalla M. Pancytopenia- A Clinicopathological Analysis of 132 Cases. Int J Med Res Re 2016;4(8):1376-1386.
14. Dubey TN, Nigotia P, Saxena R. The common causes leading to pancytopenia in patients presenting in hospital of central India. Int J Contemp Med Res. 2016; 3(10):3027-3030.
15. Gandhi PB, Shankar T, Pasha MA, Gour M. Etiological and clinical spectrum of pancytopenia based on bone marrow examination and case records: A retrospective study Annals of Applied Bio-Sciences. 2016;3(1):A27-32.
16. Imbert M, Scoazec JY, Mary Jy, Jeuzult H, Rochant H, Sultan C. Adult patients presenting with pancytopenia. A reappraisal of underlying pathology and diagnostic procedures in 213 cases. Haemotol Pathol 1989;3(4):159-167.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/64657