



Original Article

Clinico-hematological profile of pancytopenic adult patients in a tertiary care teaching hospital

Anil Jain^a, Ravinder Garg^a, Rupinderjeet Kaur^a, Sarita Nibhoria^b, Sumit Pal Singh Chawla^a, Sarabjot Kaur^a

^aDepartment of Medicine, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India, ^bDepartment of Pathology, Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab, India

ABSTRACT

Objective: The causes of pancytopenia vary in different populations depending on age, gender, nutrition, geographic location, standard of living, and exposure to certain infections and drugs. As the severity of pancytopenia and its underlying etiology determine the management and prognosis, identifying the correct etiology in a given case is crucial and helps in implementing timely and appropriate treatment. The objectives of this study were to study the clinical profile and hematological parameters of pancytopenic adults and to identify different etiologies of pancytopenia. This observational study was conducted in the Medicine department of a tertiary care teaching hospital. **Materials and Methods:** The study was conducted on 100 adult patients aged 18–65 years presenting with pancytopenia. All the participants were subjected to detailed clinical examination and relevant investigations including bone marrow (BM) examination. Categorical variables were presented in number and percentage (%). Qualitative variables were correlated using the Chi-square test. A $P < 0.05$ was considered statistically significant. **Results:** A female preponderance was observed, and the majority of patients were aged between 18 and 40 years. The most common clinical features were generalized weakness, fever, and pallor. Seventy-four percent of patients were vegetarians; 58% had vitamin B12 deficiency, 25% had folic acid deficiency and 19% had a deficiency of both. The most common cause of pancytopenia was megaloblastic anemia (MA) (37%), followed by dimorphic anemia (DA) (26%), aplastic anemia (AA) (20%), and hematological malignancies (11%). **Conclusion:** MA, DA, and AA are the most prevalent etiologies of pancytopenia. BM examination is of utmost importance in the definitive diagnosis of pancytopenia and is useful in initiating timely treatment as a significant number of causes of pancytopenia are potentially curable.

KEYWORDS: *Aplastic anemia, Bone marrow examination, Dimorphic anemia, Megaloblastic anemia, Pancytopenia*

Submission : 17-Jan-2021
Revision : 02-Feb-2021
Acceptance : 26-Mar-2021
Web Publication : 23-Aug-2021

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. Thus, it is not a disease entity by itself, but rather a triad of findings [1]. It is a striking feature of several disorders ranging from simple drug-induced bone marrow (BM) hypoplasia and megaloblastic anemia (MA) to fatal aplastic anemia (AA) and leukemias. It should be suspected clinically when a patient presents with pallor, prolonged fever, and a tendency to bleed. The etiology of pancytopenia varies in different populations depending on the differences in age composition, gender, nutritional status, geographical location, the standard of living, exposure to certain drugs/toxins, and infections.

The mechanism of the development of pancytopenia varies from a decrease in the hematopoietic cell production as in AA, sequestration of normal cells in the hypertrophied and overactive reticuloendothelial system as in hypersplenism, ineffective hematopoiesis in MA, or replacement by abnormal or malignant tissue in the BM [1,2].

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

***Address for correspondence:** Dr. Sumit Pal Singh Chawla, Department of Medicine, Guru Gobind Singh Medical College and Hospital, Sadiq Road, Faridkot - 151 203, Punjab, India.
E-mail: drsumitpsc@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Jain A, Garg R, Kaur R, Nibhoria S, Chawla SP, Kaur S. Clinico-hematological profile of pancytopenic adult patients in a tertiary care teaching hospital. *Tzu Chi Med J* 2022; 34(1): 95-101.

Access this article online	
Quick Response Code: 	Website: www.tcmjmed.com
	DOI: 10.4103/tcmj.tcmj_17_21

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 pancytopenic adults and to identify different etiologies of pancytopenia.

MATERIALS AND METHODS

This observational study, carried out in the department of Medicine of a tertiary care teaching hospital, enrolled 100 patients having pancytopenia attending the inpatient or outpatient departments, by non-probability consecutive sampling.

Inclusion criteria

Patients of either gender belonging to the age group of 18–65 years presenting with pancytopenia (i.e., hemoglobin <10 g/dL, total leukocyte count <4000/cc, and platelet count <1,50,000/cc) were included in the study.

Exclusion criteria

Patients who had received multiple blood/blood component transfusions within the previous 2 weeks, patients receiving erythropoietin and/or colony-stimulating factors, and patients who were too sick to undergo the proposed diagnostic workup were excluded from the study.

Data collection procedure

The study conformed to the Helsinki Declaration. Ethical approval for this study was provided by the Institutional Ethics Committee vide letter No. GGS/IEC/18/86 dated 20/02/2018. All the participants were explained about the purpose of the study and were ensured strict confidentiality. Written, 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. History of any previous treatment, intake of or exposure to potentially toxic chemicals, agents or drugs, radiation exposure, smoking status, alcohol intake, and other addictions, was also recorded. A detailed physical examination of every patient was done for pallor, jaundice, petechiae/purpura/ecchymoses, hepato-splenomegaly, lymphadenopathy, sternal tenderness, dermatological manifestations, and gum hypertrophy. Evidence of hypersplenism and primary malignancy was searched for, wherever necessary. Basic hematological investigations, routine investigations, ultrasound abdomen, and BM examination were performed in each case. Serum vitamin B12 (vit B12), folic acid (FA), and ferritin levels were also measured in each case. Peripheral blood film (PBF) 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 and May Grunwald Giemsa stain were used. Myeloperoxidase special stain, Sudan Black B, Periodic Acid–Schiff and Perl’s stain on aspirate smears, and Reticulin stain on biopsy were used, wherever indicated.

Data analysis

The data collected were entered into MS Excel spreadsheets and analysis was carried out using the Statistical Package for the Social Sciences (SPSS) for Windows, Version 21.0 (IBM SPSS, Chicago, IL). Categorical variables were presented in number and percentage (%). Qualitative variables were correlated using the Chi-square test. At 95% confidence interval, *P* <0.05 was considered statistically significant.

RESULTS

Table 1 shows the age distribution of male and female participants of the study. The study included 44 males and 56 females. The maximum number of participants belonged to the age group of 21–30 years (*n* = 28, 28%), followed by 31–40 years (*n* = 18, 18%), ≤20 years (*n* = 17, 17%), and >60 years (*n* = 16, 16%). The remaining participants were aged between 41 and 60 years. The most common presenting symptom of the study patients was a generalized weakness (seen in 68 patients), followed by fever (in 43), breathlessness (in 27), and easy fatigability (in 18). Other less common symptoms were abdominal pain (in 14), bleeding manifestation (in 9), loss of appetite (in 5), yellowish discoloration of eyes (in 5), rashes (in 3), and swelling of feet (in 3). On examination, all study patients were found to have pallor. Other signs observed were icterus (seen in 13 patients), pedal edema (in 7), alopecia (in 3), mouth ulcers (in 1), petechiae (in 1), ecchymoses (in 1), purpuric patches (in 1), gum hypertrophy (in 1), and bleeding gums (in 1). On interviewing for dietary habits, the majority of participants were vegetarians (*n* = 74, 74%) while the remaining 26 (26%) participants took a mixed diet. Seven patients were alcoholics, two consumed tobacco, another two were opium addicts and only one patient was a chronic smoker.

Table 2 summarizes the PBF findings of the study patients. The most common PBF finding was microcytic hypochromia with macrocytes, i.e., dimorphic picture (58%) followed by macrocytosis with hyper-segmented neutrophils, i.e., megaloblastic picture (18%) and microcytic hypochromia (15%). Atypical cells were observed in only two percent of patients.

In this study, 58 (58%) patients were found to have a deficiency of vit B12. FA deficiency was observed in 25 (25%) patients and 19 (19%) patients had a deficiency of both vit

Table 1: Age distribution of the study subjects

Age distribution in years	Gender		Total, <i>n</i> (%)	<i>P</i>
	Female (<i>n</i> =56), <i>n</i> (%)	Male (<i>n</i> =44), <i>n</i> (%)		
≤20	12 (70.59)	5 (29.41)	17 (100.00)	0.17*
21-30	19 (67.86)	9 (32.14)	28 (100.00)	
31-40	10 (55.56)	8 (44.44)	18 (100.00)	
41-50	3 (30.00)	7 (70.00)	10 (100.00)	
51-60	4 (36.36)	7 (63.64)	11 (100.00)	
>60	8 (50.00)	8 (50.00)	16 (100.00)	
Total	56 (56.00)	44 (44.00)	100 (100.00)	

*Chi-square test

B12 and FA. Low serum ferritin levels were observed in seven (7%) patients. Three (3%) patients had low serum levels of all three, i.e., vit B12, FA, and ferritin.

Ultrasound abdomen was done for all the participants and was found to be normal in the majority of participants ($n = 57$, 57%). Abnormal findings included splenomegaly, seen in 20 patients (20%), hepato-splenomegaly in 16 (16%), hepatomegaly in 5 (5%), hepato-splenomegaly with abdominal lymphadenopathy (1%), and splenomegaly with portal hypertension (1%) in one patient each.

On BM examination, the most common finding was MA, seen in 37 (37%) patients. Other frequent findings were dimorphic anemia (DA), observed in 26 patients (26%) and AA in 20 patients (20%). The less common findings were acute leukemia, plasma cell malignancy, myelodysplastic syndrome (MDS), lymphoproliferative disorder, chronic lymphoid leukemia (CLL), hematolymphoid malignancy, primary myelofibrosis, and metastases [Table 3]. Table 4 shows the distribution of various hematologic malignancies in the study patients.

Table 5 shows the association between PBF and BM examination findings in the study subjects. A statistically significant association was seen between PBF and BM examination findings ($P < 0.05$). Almost 92.31% of the patients with DA on BM examination also had a dimorphic picture on PBF (microcytic hypochromic with macrocytes). On the contrary, the dimorphic picture on PBF was seen in 50% of patients of AA, 43.24% of patients of MA, and 36.36% patients with malignancies. Approximately 43.24% of patients with MA on BM also had a megaloblastic picture (macrocytic with hypersegmented neutrophils) on PBF, while only 7.69% of patients of DA had a megaloblastic picture on PBF and none of the remaining pancytopenic patients had this picture. Atypical cells on PBF were seen in 18.18% of patients with malignancies and in none of the remaining pancytopenic patients.

All patients with low serum ferritin ($n = 7$) had DA on BM examination. Serum FA deficiency was observed in 10 out of 26 (38.46%) patients of DA, 13 out of 37 (35.14%) patients of MA, one out of 20 (5%) patients of AA, in none of the patients having hematologic malignancies and in one out of six (16.67%) patients having other findings on BM examination. Vit B12 deficiency was found in the majority (33 out of 37, 89.19%) of patients with MA. It was also observed in 20 out of 26 (76.92%) patients of DA, four out of 20 (20%) patients of AA, and in only one out of 11 (9.09%) patients having hematologic malignancies. A combined deficiency of vit B12 and FA was observed in eight (30.77%) patients of DA and 11 (29.73%) patients of MA. None of the patients having AA, hematologic malignancies, or other BM findings had combined deficiency of vit B12 and FA. Deficiency of vit B12 or FA or both was observed in 36 (97.30%) of 37 patients with MA in comparison to 29 (46.03%) of the remaining 63 pancytopenic patients. The deficiency of vit B12 or FA had a positive correlation with the diagnosis of MA on BM examination [$rpb = 0.519$, Table 6] in comparison to other etiologies of pancytopenia.

Table 2: Peripheral blood film findings in the study subjects

PBF	Frequency (%)
Macrocytic with hypersegmented neutrophils (megaloblastic picture)	18 (18.00)
Microcytic hypochromic	15 (15.00)
Microcytic hypochromic with atypical cells	2 (2.00)
Microcytic hypochromic with macrocytes (dimorphic picture)	58 (58.00)
Normocytic normochromic	7 (7.00)
Total	100 (100.00)

PBF: Peripheral blood film

Table 3: Bone marrow examination findings in the study subjects

BM examination findings	Frequency (%)
Megaloblastic anemia	37 (37.00)
Dimorphic anemia	26 (26.00)
Aplastic anemia	20 (20.00)
Acute leukemia	3 (3.00)
Plasma cell malignancy	3 (3.00)
Lymphoproliferative disorder	2 (2.00)
Lymphoid cells predominance	2 (2.00)
Myelodysplastic features	2 (2.00)
Chronic lymphoid leukemia	1 (1.00)
Hematolymphoid malignancy	1 (1.00)
Metastatic deposit possibly adenocarcinoma	1 (1.00)
Primary myelofibrosis	1 (1.00)
Micro normoblastic maturation	1 (1.00)
Total	100 (100.00)

BM: Bone marrow

Table 4: Distribution of different hematological malignancies in the study subjects

Hematological malignancies	Number of cases
Acute leukemia	3
Plasma cell malignancy	3
Lymphoproliferative disorder	2
Chronic lymphoid leukemia	1
Hematolymphoid malignancy	1
Metastatic deposit possibly adenocarcinoma	1
Total	11

Combined deficiency of vit B12 and ferritin was observed in four patients of DA (15.38%) and combined deficiency of all three, i.e., vit B12, FA, and ferritin were seen in three (11.54%) patients of DA. Deficiency of serum ferritin with vit B12 or FA deficiency was observed in 7 out of 26 patients (26.92%) of DA. Among the remaining 74 pancytopenic patients having BM diagnoses other than DA, none had combined deficiency of ferritin and vit B12 or FA. Thus, deficiency of ferritin and vit B12 or FA correlated positively [$rpb = 0.463$, Table 7] with the diagnosis of DA on BM examination as compared to other etiologies of pancytopenia.

Among patients with AA on BM exam ($n = 20$), two were found to have acquired immunodeficiency syndrome (AIDS) and were on antiretroviral therapy (ART). It was observed that one patient was a known cause of thyrotoxicosis on carbimazole while another patient gave a history of indigenous

Table 5: Association of peripheral blood film with bone marrow examination findings

PBF	BM examination					Total, n (%)	P
	AA (n=20),	DA (n=26),	Malignancies (n=11),	MA (n=37),	Others (n=6),		
	n (%)	n (%)	n (%)	n (%)	n (%)		
Macrocytic with hyper segmented neutrophils (megaloblastic picture)	0	2 (7.69)	0	16 (43.24)	0	18 (18.00)	<0.0001*
Microcytic hypochromic	8 (40.00)	0	4 (36.36)	1 (2.70)	2 (33.33)	15 (15.00)	
Microcytic hypochromic with atypical cells	0	0	2 (18.18)	0	0	2 (2.00)	
Microcytic hypochromic with macrocytes (dimorphic picture)	10 (50.00)	24 (92.31)	4 (36.36)	16 (43.24)	4 (66.67)	58 (58.00)	
Normocytic normochromic	2 (10.00)	0	1 (9.09)	4 (10.81)	0	7 (7.00)	
Total	20 (100.00)	26 (100.00)	11 (100.00)	37 (100.00)	6 (100.00)	100 (100)	

*Chi-square test. AA: Aplastic anemia, MA: Megaloblastic anemia, DA: Dimorphic anemia, PBF: Peripheral blood film

Table 6: Association of deficiency of vitamin B12 or folic acid with bone marrow examination

Deficiency of vitamin B12 or FA	BM examination		Total, n (%)	P
	MA, n (%)	Other diagnoses, n (%)		
Yes	36 (97.30)	29 (46.03)	65 (65.00)	<0.05*
No	1 (2.70)	34 (53.97)	35 (35.00)	
Total	37 (100.00)	63 (100.00)	100 (100.00)	

*Chi-square test. Point-biserial correlation coefficient (rpb)=0.519. FA: Folic acid, MA: Megaloblastic anemia, BM: Bone marrow

Table 7: Association of deficiency of ferritin and vitamin B12 or folic acid with bone marrow examination

Deficiency of ferritin and vitamin B12 or FA	BM examination		Total, n (%)	P
	DA, n (%)	Other diagnoses, n (%)		
Yes	7 (26.92)	0	7 (07.00)	<0.05*
No	19 (73.08)	74 (100.00)	93 (93.00)	
Total	26 (100.00)	74 (100.00)	100 (100.00)	

*Chi-square test. Point-biserial correlation coefficient (rpb)=0.463. FA: Folic acid, DA: Dimorphic anemia, BM: Bone marrow

medicine intake. These could be the possible etiologies or contributory factors to the causation of AA in these patients. Among patients who were diagnosed to have DA (n = 26), seven were chronic alcoholics, two had chronic hepatitis C while one had celiac disease; these could be the possible causes or contributing factors leading to DA in these patients. Out of 37 patients with MA, two were on antiepileptics (one each on phenytoin and valproate) and one was on antipsychotics (risperidone); which might have contributed to MA in these patients. Eight patients had diabetes mellitus and had variable etiologies of pancytopenia; four had AA, and the remaining four had MA, acute leukemia, lymphoproliferative disorder, and myelofibrosis.

DISCUSSION

The male-to-female ratio in the present study was 0.79:1, similar to the ratio in the study by Kulkarni *et al.* [4]. In contrast, many other studies on pancytopenia have shown male predominance [5-9].

The age of the patients ranged from 18 to 65 years, the most common age group being 21–30 years. Das Makheja *et al.* and Rehmani *et al.* also reported 21–30 years as the most common age group for the presentation of pancytopenia [8,10]. In other

studies, 12–30 and 21–40 years age groups were the most common age groups for presentation of pancytopenia [11,12]. On the contrary, Dasgupta *et al.* and Tariq *et al.* reported 41–50 years as the most common age group for cases with pancytopenia enrolled in their studies [3,13].

The most common presenting symptom of pancytopenia was a generalized weakness which is in concordance with other similar studies [6,9]. The next most common symptom was fever. The same was observed by Mansuri and Thekdi and Vaidya in their respective studies [6,9], while in the studies by Khodke *et al.* and Shafiq *et al.*, fever was the most common presenting complaint [11,14].

Another common symptom of pancytopenic patients was breathlessness which is observed in previous studies too [6,14]. Other presenting symptoms in this study were easy fatigability, abdominal pain, bleeding manifestations, loss of appetite, yellowish discoloration of eyes, rashes, swelling of feet, and swelling in the abdomen.

Pallor was universally seen in all the patients. Icterus was present in 13% of patients. Similar observations were made in other studies also [6,13]. Other signs were pedal edema, alopecia, petechiae, ecchymoses, purpuric patches, gum hypertrophy, and bleeding gums. Splenomegaly was present in 20% of patients; similar to the observation in other studies [8,9,12,13]. Hepatomegaly alone was found in 5% of patients only; a similar finding was reported in the previous studies done by Tariq *et al.*, Devi *et al.*, Rehmani *et al.* and Vaidya [8,9,12,13]. However, few other studies have reported a higher incidence of hepatomegaly [6,11,15]. Hepatosplenomegaly was seen in 16% of pancytopenic patients. Mansuri and Thekdi and Devi *et al.* also reported similar incidences of hepatosplenomegaly in their enrolled participants [6,12].

In this study, the majority (74%) of cases were vegetarians. Premkumar *et al.* also reported similar results [16]; however, most of the previous studies have not considered dietary habits. Of all patients, 58% were found to have vit B12 deficiency, and 25% of patients were FA deficient (Normal serum levels of vit B12 were taken as 180–971 pg/ml and those of FA were taken as >6 ng/ml). Combined vit B12 and FA deficiency were found in 19% of patients. Another study also reported that vit B12 deficiency was more common than FA deficiency and combined B12 and FA deficiency was present in 12.3% of patients [8]. Premkumar *et al.* found vit

B12 deficiency in 81% of their study patients, FA deficiency in 7%, and combined vit B12 and FA deficiency was found in only 3.5% of patients [16]. The majority of the studies did not get both serum vit B12 and FA levels. Serum ferritin levels were also measured in all the patients and low levels were found in 7% of patients. In another study, low serum ferritin levels were seen in 17.14% of patients [16].

In the present study, MA emerged as the most common cause of pancytopenia accounting for 37% of all cases, as also observed in recent similar studies [5,6,7,9,17]. The prevalence of MA in various other studies done on pancytopenia varies from 13.2% to 74% [4,8,10-15,18-22]. The diagnosis of MA in the present study was established by characteristic BM findings. Out of 37 patients of MA, two were on antiepileptics (one each on phenytoin and valproate) and another one was on antipsychotic (risperidone). Hence, these drugs might have contributed to the occurrence of MA in these patients.

Vit B12 deficiency was found among the majority (89.19%) of patients with MA, while FA deficiency was found in 35.14% of patients of MA. Combined vit B12 and FA deficiency were found in 29.73% of MA patients. The deficiency of vit B12 or FA correlated well with the diagnosis of MA on BM examination in comparison to other etiologies of pancytopenia. A similar study done by Aziz *et al.* reported that 77.77% of MA patients had vit B12 deficiency and 22.33% were deficient in FA [23]. In another study, vit B12 deficiency was found in 91% of MA patients and FA deficiency was found in 5% of MA patients [16].

The high prevalence of MA correlates with a high prevalence of nutritional, i.e., vit B12 and FA deficiencies [11]. These nutrients have a critical role in the synthesis of DNA. As a result, patients develop disordered RBC, WBC and platelet proliferation, which subsequently leads to pancytopenia and altered immune function [24]. MA is found to be an important cause of pancytopenia in various Indian studies because of the high prevalence of nutritional anemia in the Indian subcontinent [25]. A possible explanation for these nutritional deficiencies in our country could be the various chronic inflammatory disorders of the gut like chronic diarrheas, malabsorption, chronic alcoholism, *Helicobacter pylori* infection, poor nutrition, long-term use of certain drugs that interfere with vit B12 and FA metabolism, and absorption including antiepileptics, antipsychotics, methotrexate, anticancer drugs, etc.

The second-most common cause of pancytopenia in this study was DA (26%). Kulkarni *et al.* and Khan *et al.* reported prevalence of DA at 36% and 21%, respectively [4,7].

About 26.92% of patients of DA had a deficiency of ferritin and vit B12 or FA, while none of the remaining patients had a combined deficiency of ferritin and vit B12 or FA. Thus, deficiency of ferritin and vit B12 or FA correlated positively with the diagnosis of DA on BM examination as compared to other etiologies of pancytopenia. Of the 26 cases of DA, seven gave a history of alcoholism, two had chronic hepatitis C and one patient had celiac disease. Hence, the causes of DA

were thought to be nutritional deficiencies of iron, FA and vit B12, chronic alcoholism, and chronic hepatitis C. Alcohol is known to cause suppression of hematopoiesis, especially in severe alcoholism, and also lead to nutritional deficiencies of FA and other vitamins that play a role in the hematopoietic cell development [26].

The next most common cause of pancytopenia was AA, which accounted for 20% of all patients. This was comparable to the prevalence of AA in other similar studies (18%–21%) [12,15,20,27]. However, a higher incidence of AA was found in various other studies [5,9,21-23,27,28]. AA is characterized by failure of hemopoiesis manifested by pancytopenia and hypocellular BM. Most cases are acquired and immune-mediated but there are also inherited forms. Environmental triggers include drugs, viruses, and toxins but most cases are idiopathic [29]. In some cases, radiation, medical drugs, chemicals, and, viruses induce depletion of hematopoietic stem cells by direct toxicity; while immune diseases induce complex immune reactions leading to BM failure [30]. Out of 20 AA patients in this study, two had HIV/AIDS and were on ART. In other similar studies, HIV/AIDS was found to be a cause of pancytopenia [3,5,11,12,31]. Spivak *et al.* evaluated BM in AIDS patients and found a high incidence of myelofibrosis, pancytopenia, and alterations in marrow cellularity [32]. Hematological abnormalities are among the most common complications of HIV infection. These involve all the lineages of blood cells. The mechanisms include both quantitative and qualitative marrow defects. Immune cytopenias can occur directly due to HIV infection, whereas the effects of opportunistic infections, lymphomas, malignancy, and ART also play an important role [33].

Furthermore, in this study, one case gave a history of hyperthyroidism on carbimazole therapy and another case reported chronic indigenous medicine intake. On BM examination of both these cases, an AA picture was seen. Jain and Naniwadekar also reported 2 cases of thyrotoxicosis who were on carbimazole and presented with pancytopenia [31].

In this study, hematological malignancies accounted for 11% of cases of pancytopenia and included acute leukemia (3%), plasma cell malignancy (3%), lymphoproliferative disorder (2%), CLL (1%), hematomphoid malignancy (1%), and metastatic deposit in the BM (1%). Vaidya [9] also reported a similar prevalence of hematological malignancies, however, Jha *et al.* observed a higher percentage of hematological malignancies in their study [21]. The prevalence of acute leukemia contributing to pancytopenia in this study was comparable to previous similar studies [6,11,15,18,20]. A higher percentage of acute leukemia leading to pancytopenia was encountered in other studies [7,8,10,17,34] while few studies did not report any case of acute leukemia presenting with pancytopenia [4,22].

Plasma cell malignancy was found in 3% of pancytopenic patients; this observation was comparable to findings of similar studies done previously [3,9,11,13,17,20]. On the contrary, some studies reported a lower prevalence of plasma cell malignancy as a cause of pancytopenia [5,8,15,31].

Two cases of lymphoproliferative disorder (2%) were detected in this study as a cause of pancytopenia which was similar to the prevalence found in other studies [3,5,13,21]. Shafiq *et al.* reported a higher percentage of lymphoproliferative disorder (12%) as a cause of pancytopenia [14]. MDS was the underlying etiology of pancytopenia in 2% of cases. Similar prevalence was reported in several studies [4,8,11,17,18], while a higher prevalence of MDS leading to pancytopenia was noted in few other studies [5,13,14]. Other rare causes of pancytopenia in this study were primary myelofibrosis and metastatic disease.

CONCLUSIONS

Pancytopenia has multiple etiologies. MA, DA, and AA constitute the most common causes of pancytopenia among adults. Detailed clinical and hematological evaluation is essential for determining the underlying etiology of pancytopenia. PBF is a reasonable initial investigation for pancytopenia and can provide valuable clues to underlying etiology. BM examination is the gold standard investigation for a comprehensive evaluation of pancytopenia and guides further management of these cases. Vit B12 and FA deficiencies are quite common in adult pancytopenic patients and can be easily treated if diagnosed in time.

Strength of the study

Data regarding pancytopenia in the adult population are limited from the study region which prompted this study. This study highlighted the various clinical-hematologic parameters and etiologies of pancytopenia in adults. This study emphasized that identification of the underlying etiology of pancytopenia is critical for timely and appropriate treatment, as a significant number of cases of pancytopenia are potentially curable.

Limitations of the study

This was a single-center study with a small sample size.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- de Gruchy GC. Pancytopenia, aplastic anemia. In: Firkin F, Chesterman C, Penington D, Rush B, editors. *De Gruchy's Clinical Hematology in Medical Practice*. 5th ed. Berlin, Germany: Blackwell Science; 1989. p. 119-36.
- Williams DM. Pancytopenia, aplastic anemia and pure red cell anemia. In: Richard GL, Bithel TC, John F, John WA, John NL, editors. *Wintrobe's Clinical Hematology*. 10th ed. Philadelphia: Lea and Fabiger; 1998. p. 1449-89.
- Dasgupta A, Padma SK, Sajitha K, Shetty J. Etiological evaluation of pancytopenia in a tertiary care hospital. *Ann Pathol Lab Med* 2016;3:441-50.
- Kulkarni NS, Patil AS, Karchi SD. Study of pancytopenia in a tertiary care hospital in North Karnataka. *Int J Med Res Health Sci* 2017;6:61-7.
- Azaad MA, Li YP, Zhang QR, Wang HX. Detection of pancytopenia associated with clinical manifestation and their final diagnosis. *Open J Blood Dis* 2015;5:17-30.
- Mansuri B, Thekdi KP. A prospective study among cases of the pancytopenia on the basis of clinic-hematological analysis and bone marrow aspiration. *Int J Res Med Sci* 2017;5:3545-9.
- 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;5:946-9.
- Rehmani TH, Arif M, Haider S, Arif S, Ahmad R, Saeed M. Spectrum of pancytopenia: A tertiary care experience. *Prof Med J* 2016;23:620-6.
- Vaidya S. Evaluation of bone marrow in cases of pancytopenia in a tertiary care hospital. *J Pathol Nepal* 2015;5:691-5.
- Das Makheja K, Kumar Maheshwari B, 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;29:1108-11.
- Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. *J Indian Acad Clin Med* 2001;2:55-9.
- Devi PM, Laishram RS, Sharma PS, Singh AM, Singh MK, Singh YM. Clinico-hematological profile of pancytopenia in manipur. *Kuwait Med J* 2008;40:221-4.
- Tariq M, Khan N, Basri R, Amin S. Aetiology of pancytopenia. *Prof Med J* 2010;17:252-6.
- Shafiq M, Ayyub M, Noor A. Frequency of different causes of pancytopenia in a tertiary care hospital. *Pak Armed Forces Med J* 2014;64:559-63.
- Gayathri BN, Rao KS. Pancytopenia: A clinico hematological study. *J Lab Physicians* 2011;3:15-20.
- 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 center in north India. *Anemia* 2012;2012:707402.
- Sharma N, Bhatia PK, Kaul KK, Sharma S, Sharma M. A clinico-hematological study of pancytopenia: An experience of a tertiary care teaching hospital, Jammu, India. *Indian J Pathol Oncol* 2017;4:632-7.
- Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia – A clinico haematological study of 200 cases. *Indian J Pathol Microbiol* 2002;45:375-9.
- Tilak V, Jain R. Pancytopenia – A clinico-hematological analysis of 77 cases. *Indian J Pathol Microbiol* 1999;42:399-404.
- Sweta, Barik S, Chandoke RK, Verma AK. A prospective clinico-hematological study in 100 cases of pancytopenia in the capital city of India. *J Appl Hematol* 2014;5:45-50.
- Jha A, Sayami G, Adhikari RC, Panta AD, Jha R. Bone marrow examination in cases of pancytopenia. *J Nepal Med Assoc* 2008;47:12-7.
- Kumar R, Kalra SP, Kumar H, Anand AC, Madan H. Pancytopenia – A six year study. *J Assoc Physicians India* 2001;49:1078-81.
- Aziz T, Ali L, Ansari T, Liaquat HB, Shah S, Ara J. Pancytopenia: Megaloblastic anemia is still the commonest cause. *Pak J Med Sci* 2010;26:132-6.
- Trivette ET, Hoedebecke K, Berry-Cabán CS, Jacobs BR. Megaloblastic hematopoiesis in a 20 year old pregnant female. *Am J Case Rep* 2013;14:10-2.
- Desalphine M, Bagga PK, Gupta PK, Kataria AS. To evaluate the role of bone marrow aspiration and bone marrow biopsy in pancytopenia. *J Clin Diagn Res* 2014;8:FC11-5.
- Ballard HS. The hematological complications of alcoholism. *Alcohol Health Res World* 1997;21:42-52.
- Santra G, Das BK. A cross-sectional study of the clinical profile and aetiological spectrum of pancytopenia in a tertiary care centre. *Singapore Med J* 2010;51:806-12.
- Niazi M, Raziq F. The incidence of underlying pathology in pancytopenia. *J Postgrad Med Inst* 2004;18:76-9.
- Biswajit H, Pratim PP, Kumar ST, Shilpi S, Krishna GB, Aditi A. Aplastic anemia: A common hematological abnormality among peripheral

- pancytopenia. *N Am J Med Sci* 2012;4:384-8.
30. Găman A, Găman G, Bold A. Acquired aplastic anemia: Correlation between etiology, pathophysiology, bone marrow histology and prognosis factors. *Rom J Morphol Embryol* 2009;50:669-74.
 31. Jain A, Naniwadekar M. An etiological reappraisal of pancytopenia – Largest series reported to date from a single tertiary care teaching hospital. *BMC Hematol* 2013;13:10.
 32. Spivak JL, Bender BS, Quinn TC. Hematologic abnormalities in the acquired immune deficiency syndrome. *Am J Med* 1984;77:224-8.
 33. Kotwal J, Singh V, Kotwal A, Dutta V, Nair V. A study of haematological and bone marrow changes in symptomatic patients with human immune deficiency virus infection with special mention of functional iron deficiency, anaemia of critically ill and haemophagocytic lymphohistiocytosis. *Med J Armed Forces India* 2013;69:319-25.
 34. Safaei A, Shokripour M, Omidifar N. Bone marrow and karyotype findings of patients with pancytopenia in southern Iran. *Iran J Med Sci* 2014;39:333-40.