Original Research Article

A study of clinical and etiological profiles of patients presenting with Pancytopenia in NRI General Hospital

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Abstract

Introduction: Pancytopenia is characterized by a decrease in the red blood cells, white blood cells along with the platelet count below the normal levels. It can be due to a number of pathologic mechanisms, depending on the geographic location. Early diagnosis and treatment are crucial in the management of pancytopenia. There are very few studies regarding the clinic-pathological profile of such patients.

Materials and methods: A cross-sectional study was undertaken at NRI General Hospital, Chinakakani. All eligible participants more than 13 years of age were included. Data collection was done from August 2016 to August 2018. A thorough history taking along with clinical examination and laboratory investigations were performed among the study population. Data was analyzed using SPSS version 13.

Results: The most common finding suggestive of etiology was megaloblastic anemia at 38.4%, which was more common among females. Aplastic anemia was the second most common finding at 24.6%. Other diagnoses included hypersplenism, myelodysplastic syndrome and acute leukemia. Fever and pallor were the most common presenting symptoms. Blood examinations demonstrated anisopoikilocytosis, hypersegmented neutrophils, erythroblasts, macrocytes and reticulocytes, which were found in differing proportions in the various etiological diagnoses.

Conclusion: It is noteworthy that megaloblastic anemia, a reversible condition, is common in India compared to the higher occurrence of aplastic anemia and myelodysplastic syndrome in developed

nations. Clinical alertness and suspicion can assure early diagnoses and treatment can prevent complications and reduce the burden. The need for more standard management protocols is immediate.

Key words

Pancytopenia, Anemia, Megaloblastic, Aplastic.

Introduction

Pancytopenia is characterized by a decrease in the three blood elements (red blood cells, white blood cells and platelets) below the normal. Pancytopenia in adults is characterized by a triad of findings – a) hemoglobin less than 13.5 g/dL in males and less than 11.5 g/dL in females, b) total leucocyte count less than 4000/mm^3, and c) platelet count less than 150000/mm^3 [1].

It is a relatively less explored, but important clinic-hematological entity and not a disease which may occur due to a number of pathogenetic mechanisms. It may occur due to damage or suppression of pluripotent stem cells or committed progenitor cells. Pluripotent cell damage is less common while most cytotoxic drugs used in malignancies exert their action on the committed progenitor cells [2]. Pancytopenia may be associated with a hypocellular bone marrow, hypercellular marrow or bone marrow infiltration. Pancytopenia with a hypocellular bone marrow may be caused by aplastic anemia, drugs, viruses, radiation, toxins, autoimmune disease, malignancies, PNH etcetera. In cases of pancytopenia with hypercellular bone marrow, the causative factors may be hypersplenism, megaloblastic anemia, myelodysplastic syndrome, infections such as HIV and TB etcetera. Malignancies, granulomas and fibrosis are causes of pancytopenia with bone marrow infiltration. The etiology of pancytopenia differs from one geographical area to another. The common causes identified in developing countries are megaloblastic anemia, infection, drugs, hypersplenism and aplastic anemia. Megaloblastic anemia has been reported as the case of pancytopenia at a rate between 38% and 72% in local studies in the country, suggesting that it should be promptly evaluated for [3]. The severity of the condition and the underlying pathogenesis decide the management and prognosis of the patients [4].

Usually patients with pancytopenia present symptoms attributable to anemia and thrombocytopenia [5]. The most common clinical manifestations are fever, fatigue, dizziness, weight loss, anorexia, night sweats, pallor, bleeding, splenomegaly, hepatomegaly and lymphadenopathy [3, 6]. There is a wide disparity between clinical pictures gleaned from different studies. Detailed complete blood count with peripheral film and reticulotcyte count is the basic investigation to be done. Bone marrow examination using biopsy is extremely useful in the evaluation of pancytopenia, as it enables complete picturization of the marrow architecture and the distribution of any abnormalities in the form of infiltrates and focal lesions [3]. Trephine biopsy may be needed in some cases.

The management of pancytopenia is mostly supportive. Prevention of infection is absolutely crucial. The lack of established protocols for assessment and the overwhelming number of possible differential diagnoses complicates the management of the condition. The present study attempts to add to the limited literature available on the clinical and etiological profile of patients presenting with pancytopenia.

Materials and methods

The present study was a cross-sectional study conducted among patients admitted in the general medical wards at the NRI General Hospital, Chinakakani. All patients aged more than 13 years, with hemoglobin less than 12 g/dL in women and less than 13 g/dL in men, WBC count less than 4000 cells/μL and platelet count

less than 150000/μL were included in the study. Patients with a known hematological condition, those on cancer chemotherapy and who had received blood transfusion were excluded from the study. The study was conducted over a period of 2 years from August of 2016 to August of 2018.

After acquiring informed consent from all eligible subjects, a detailed relevant history was obtained including the dietary history, treatment history, intake of alcohol and drugs and radiation exposure. This was followed by a clinical examination of the patients for pallor, fever, bleeding tendencies, jaundice, hepatomegaly, splenomegaly, sternal tenderness and lymphadenopathy.

Basic investigations were performed for each subject. The panel consisted of Hemoglobin, total leucocyte count, platelet count, reticulocyte count and liver function tests. Values such as packed cell volume (PCV), Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were calculated for every patient. Viral markers (HBsAg, Anti HCV, HIV) were done in all patients. Chest radiograph and abdominal ultrasonography were done for all patients. Peripheral smear examination and Bone marrow examination were done in all patients and wherever required, a trephine biopsy was also performed. Vit. B12 levels, serum folate levels, upper and lower gastrointestinal endoscopy were done in selected patients. Also thyroid profile is done in selected patients. Necessary clearances from the Institutional Ethics Committee were obtained before starting data collection.

Data was analyzed using SPSS version 21. Descriptive statistics were used to calculate the frequency, mean, and standard deviation. To examine the linear trend of the proportions, trend chi-square was used and to find the test of association chi-square was computed. We declare that there was no conflict of interest and that no financial support was used.

Results

Among the study population, 35 (53.85%) participants were male remaining 30 (46.15%) participants were female. Among male participants, 6 (17.14%) participants were aged below 21 years, 10 (28.57%) participants were aged between 21 to 30 years, 9 (25.61%) participants were aged between 31 to 40 years, 5 (14.28%) participants were aged between 41 to 50 years and above 50 years age group for each. Among female participants, 2 (6.67%) participants were aged below 21 years, 5 (16.67) participants were aged between 21 to 30 years, 7 (23.33%) participants were aged between 31 to 40 years, 9 (30%) participants were aged between 41 to 50 years and 7 (23.33%) participants were aged above 50 years age. Among the male participants, majority of 31.42% participants had megaloblastic anemia, followed by Aplastic anemia, hypersplen1sm and myelodysplastic syndrome was 28.57%, 17.14% and 8.57% respectively. Among the female participants, majority of 46.67% participants had megaloblastic anemia, followed by Hypersplenism and Acute leukemia was 20% and 13.33% respectively (**Table - 1**).

Among the people with fever, majority of 35% participants had aplastic anemia, followed by, megaloblastic anemia and acute leukemia was 35% and 15% respectively. Among the people with pallor, majority of 39.06% participants had megaloblastic anemia, followed by Aplastic anemia, hypersplenism and myelodysplastic syndrome 25%, 12.5% and 9.38% respectively (**Table – 2**).

Among the people with Anisopokilocytosis, majority of 79.31% participants had megaloblastic anemia and 13.79% participants had aplastic anemia. Among the people with Erythroblasts all of them 100% had megaloblastic anemia. Among the people with hyper segmented neutrophils, all of them 100% participants had megaloblastic anemia. Among the people with Immature WBC, all of them 100% participants had acute leukemia. Among

the people with Lymphocytosis was 100% participants had megaloblastic anemia. Among the people with Reticulocytosis, majority of 60% participants had megaloblastic anemia and 40% participants had hypersplenism. Among the people with macrocytes, majority of 93.75% participants had megaloblastic anemia and 6.25% participants had Aplastic anemia (**Table - 3**).

Table - 1: Age and gender distribution of study population (N=65).

Parameter	**Males**	**Females**
Gender	35 (53.85%)	30 (46.15%)
Age Group		
Below 21	6 (17.14%)	2 (6.67%)
21-30	10 (28.57%)	5 (16.67)
31-40	9 (25.61%)	7 (23.33%)
41-50	5 (14.28%)	9 (30%)
Above 50	5 (14.28%)	7 (23.33%)
Diagnosis		
Megaloblastic anemia	11 (31.42%)	14 (46.67%)
Aplastic anemia	10 (28.57%)	6 (20%)
Hypersplen1sm	6 (17.14%)	2 (6.67%)
Myelodysplastic syndrome	3 (8.57%)	1 (3.33%)
Acute leukemia	2 (5.71%)	4 (13.33%)
Viral infection	2 (5.71%)	0 (0%)
HIV infection	1 (2.85%)	0 (0%)
Myelofibrosis	0 (0%)	1 (3.33%)
Connective tissue disorder	0 (0%)	2 (6.67%)

Table - 2: Clinical features of patients according to various etiologies.

Diagnosis	**Fever**	**Pallor**	**Icterus**	**Bleeding**	**Hepato megaly**	**Spleeno megaly**	**Lymph adenopathy**
Megaloblastic anemia (N=25)	12 (48%)	25 (100%)	3 (12%)	0 (0%)	7 (28%)	7 (28%)	0 (0%)
Aplasticanemia (N=16)	14 (87.5%)	16 (100%)	2 (12.5%)	12 (75%)	1 (6.25%)	1 (6.25%)	0 (0%)
Hypersplenism (N=8)	2 (25%)	8 (100%)	6 (75%)	4 (50%)	1 (12.5%)	8 (100%)	0 (0%)
Acute leukemia (N=6)	6 (100%)	6 (100%)	0 (0%)	4 (66.67%)	4 (66.67%)	3 (50%)	3 (50%)
Myelodysplastic syndrome (N=4)	1 (25%)	4 (100%)	2 (50%)	1 (25%)	0 (0%)	2 (50%)	0 (0%)
Myelofibrosis (N=1)	0 (0%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)	0 (0%)
Connective tissue disorders (N=2)	2 (100%)	2 (100%)	1 (50%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)
HIV related (N=1)	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infection induced (N=2)	2 (100%)	1 (50%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)
TOTAL	40	64	15	22	15	23	3

Table - 3: Peripheral smear findings according to various diagnosis.

Diagnosis	Anisopoikilocytosis	Erythroblasts	Hypersegmented neutrophils	Immature WBC	Lymphocytosis	Reticulocytosis	Macrocytes	Microcytic, hypochromic RBCs
Megaloblastic anemia (N=25)	23 (92%)	7 (28%)	23 (92%)	0 (0%)	1 (4%)	6 (24%)	15 (60%)	(0%)
Aplasticanemia (N=16)	4 (25%)	(0%)	(0%)	(0%)	(0%)	(0%)	1 (6.25%)	9 (56.25%)
Hypersplenism (N=8)	(0%)	(0%)	(0%)	(0%)	(0%)	4 (50%)	(0%)	8 (100%)
Acute leukemia (N=6)	(0%)	(0%)	(0%)	6 (100%)	(0%)	(0%)	(0%)	1 (16.67%)
Myelodysplastic syndrome (N=4)	1 (25%)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	3 (75%)
Myelofibrosis (N=1)	1 (100%)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	1 (100%)
Connective tissue disorders (N=2)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	2 (100%)
HIV related (N=1)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	1 (100%)
Infection induced (N=2)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	(0%)	1 (50%)

Discussion

A total of 65 subjects were included in the study. The proportion of males (53.85%) was slightly higher than the proportion of females (46.15%). This is similar to the study by Makheja, et al. [3] (2013) were 58% of those with pancytopenia were males and 42% were females. The highest incidence of pancytopenia was found among those 21 to 30 years old and 31 to 40 years old with regards to men. While among women, pancytopenia was most common among 41 to 50 years followed by 21 to 30 years and above 50 years of age.

The most common diagnosis made as to the etiology of pancytopenia was megaloblastic anemia among both genders (31.42% among males and 46.67% among females). The combined prevalence was 38.4%. This is similar to the study by Doshi, et al. [1] (2013) where the most common cause of pancytopenia was megaloblastic anemia found among 45% of the study population. Gayathri and Rao, et al. [7] (2011) report a much higher prevalence of megaloblastic anemia (74.04%). Makheja, et al. [3] (2013) report that 41.9% of pancytopenia cases were due to megaloblastic anemia. Similarly, Khodke, et al. [8] (2001), Tilak and Jain, et al. [9] (1999) also report megaloblastic anemia to be the most common cause of pancytopenia. This increased prevalence of megaloblastic anemia is more commonly reported among developing countries due to the increased incidence of malnutrition and vitamin deficiencies. Hence in countries such as India, megaloblastic anemia is one of the reversible

etiologies of pancytopenia. In our study, the higher prevalence of megaloblastic anemia among females also is indicative of the fact that females are at an increased risk of micronutrient deficiencies (1989) [10]. Aplastic anemia was the second most common etiology (28.57% among males and 20% among females). The combined prevalence was 24.6%. In the study by Doshi, et al. [1] (2013), aplastic anemia was less common (3%). Other causes were hypersplenism, myelodysplastic syndrome and acute leukemia. Hypersplenism was more commonly reported among men since the etiology is mostly alcoholic leading to complications such as portal hypertension and cirrhosis of liver. Etiologies such as viral infections and HIV were exclusively diagnosed among men while myelofibrosis and connective tissue disorders were exclusively diagnosed among women.

With regards to the clinical features of patients, fever and pallor were the most common symptoms. This is in concordance with the study by Doshi, et al. [1] (2013), where fever and pallor were the most common presenting clinical features. Fever commonly occurs due to the release of pyrogens and pro-inflammatory cytokines. Symptoms such as icterus, bleeding, hepatomegaly, splenomegaly and lymphadenopathy were less common.

When peripheral smear examination was performed among the patients, anisopoikilocytosis, hypersegmented neutrophils, erythroblasts, macrocytes and reticulocytes were the most common findings among those with megaloblastic anemia. This is similar to the study by Doshi, et al. [1] (2013) where macrocytes and hypersegmented neutrophils were the common peripheral smear findings in pancytopenia. They also report that the presence of megaloblasts indicate the early stages of megaloblastosis. Those with aplastic anemia had anisopoikilocytosis, macrocytes and microcytic, hypochromic RBCs. Hypersplenism was characterized by reticulocytosis and microcytic hypochromic RBCs. Immature RBCs and microcytic hypochromic RBCs were found among those with acute leukemia. Anisopoikilocytosis and microcytic hypochromic RBCs were characteristic among those with myelodysplastic syndrome and myelofibrosis. Microcytic hypochromic RBCs were found among those with connective tissue disorders and infection induced pancytopenia.

Conclusion

The etiological profile of pancytopenia is variable among different countries. Conditions such as aplastic anemia, myelofibrosis and myelodysplastic syndrome are more common among the developed nations. In contrast, among developing countries such as India, reversible causes such as megaloblastic anemia are more common, especially among females. A complete history taking, assessing the clinical features such as fever, pallor along with performing a complete hemogram including a peripheral smear is essential for the diagnosis of pancytopenia. The rare causes such as Myelodysplastic syndrome, connective tissue disorders, HIV infection and aplastic anemia also have to be kept in mind after excluding the most common causes [5]. Early diagnosis and treatment can prevent complications; reduce mortality and morbidity especially in reversible conditions such as megaloblastic anemia. Hence further studies are recommended to be undertaken for developing diagnostic algorithms for assessing patients presenting with pancytopenia and for further treatment modalities.

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