Original Research Article

To evaluate the clinical and etiological profile of patients presenting with pancytopenia in Government Dharmapuri Medical College Hospital, Dharmapuri

P. S. Rani[1*], K. Sureshkumar[2]

[1]Associate Professor, [2]Assistant Professor
Department of Medicine, Govt. Dharmapuri Medical College, Tamil Nadu, India
[*]Corresponding author email: **Raniraja.1611@yahoo.co.in**

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Abstract

Introduction: The frequency of underlying pathology causing pancytopenia varies considerably depending upon various factors including geographic distribution and genetic disturbances. The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients with pancytopenia. The basic investigations in a suspected case of pancytopenia include Complete Blood Count with peripheral blood film and Reticulocyte count.
Aim: To evaluate the clinical and etiological profile of patients presenting with pancytopenia.
Materials and methods: A total of 65 patients were identified over a period of 12months were included in the study. Basic investigations were performed for each patient including Haemoglobin, Total leukocyte count, Platelet count, Reticulocyte count. Absolute values including packed cell volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated for every patient.
Results: 24.62% of patients had aplastic anemia. Of which 10 (62.5%) were male and 6 (37.5%) were female Mean age of patients with aplastic anemia is 33.43 yrs. Average Hb% of these patients are 4.78 gms%.56.25% of patients had thrombocytopenia < 100000 cells/chum Megaloblastic anaemia was more common in females (14) compared to males (11) in our study. While aplastic anemia is common in males (10) than females (6); both of which are statistically significant. Anisopoikilocytosis (92%) and hyper segmented neutrophils (92%) are the most common findings in peripheral smear of patients with megaloblastic anaemia. Hypersplenism, MDS, viral infections were

common in males; while acute leukaemia's, myelofibrosis were common in females. Both of which is statistically insignificant.

Conclusion: As much physicians should have a high index of suspicion for Vitamin B12 deficiency when dealing with patients presenting with symptoms of anemia such as pallor and weakness and/or diagnosed with pancytopenia on further workup. The finding of hyper segmented neutrophils in the peripheral smear will guide in the diagnosis of megaloblatic anemia.

Key words

Megaloblastic Anemia, Aplastic Anaemia, Splenomegaly, Pancytopenia.

Introduction

Cytopenia is a reduction in the number in any of the three types of peripheral blood cell. A reduction in all three types of cellular components is termed pancytopenia and this involves anaemia, leucopoenia, and thrombocytopenia. Initially, mild impairment in marrow function may go undetected and pancytopenia may become apparent only during times of stress or increased demand (e.g., bleeding or infection) [1]. As severity increases, the peripheral blood count decreases even in the steady state. Peripheral pancytopenia may be a manifestation of wide variety of diseases which can primarily or secondarily affect the bone marrow. The presenting symptoms are usually attributable to anaemia or thrombocytopenia. Red blood corpuscles survive much longer than platelets or neutrophils. Thus, anaemia develops slowly (unless there is significant bleeding) and the typical symptoms of tiredness, fatigue, puffiness of face, oedema, lassitude, and effort intolerance may not be striking in the initial phase [2]. The platelet count is first to be affected. Mucocutaneous bleeding is typical of thrombocytopenia with petechial haemorrhages in skin and mucous membranes (commonest being epistaxis, haematuria, GI bleeding, menorrhagia, and only rarely intracranial bleeding). The presence of spontaneous bleeding with platelet count $<20 \times 10^9$/l indicates severe marrow failure. Leukopenia is an uncommon of initial presentation, but can cause a more serious threat to the life in its subsequent course. Infections usually occur with commensal organisms of the skin or gastrointestinal tract. Early manifestation of neutropenia is often a sore throat or chest or soft tissue infection which typically shows incomplete response to antibiotics [3]. Unfortunately, patients with pancytopenia may develop overwhelming septicaemia without any focal sign of infection; the only clinical features being malaise and fever. Pancytopenia can be due to decrease in hemopoietic cell production in the bone marrow e.g. by infections, toxins, malignant cell infiltration or suppression or can have normocellular or even hypercellular marrow, without any abnormal cells, e.g. ineffective haematopoiesis and dysplasia, maturation arrest of all cell lines and peripheral sequestration of blood cells [4]. Bone marrow biopsy plays a significant role in understanding the aetiology of pancytopenia. Hence Bone marrow examination is indicated in all cases of pancytopenia. Pancytopenia is an important hospital clinic haematological entity encountered in our day-to-day clinical practice. There are varying trends in its pattern, treatment modalities, and outcome [5]. There are very few data about the clinical presentation, and the aetiology of pancytopenia in Indian patients. The aim of this study was to evaluate the clinical presentation and etiological spectrum of pancytopenias on the basis of bone marrow examination. Hence this study is designed to evaluate the presenting features and the causes of patients with pancytopenia [6].

Materials and methods

A total of 65 patients were identified over a period of 12 months (March 2016 – Feb 2017) according to the above criteria and were included in the study. In all patients, a detailed relevant history including the treatment history, history of

drug intake, radiation exposure. Meticulous clinical examination of every patient was done for pallor, jaundice, hepatomegaly, splenomegaly, sterna tenderness, and lymphadenopathy. Basic investigations were performed for each patient including Haemoglobin, Total leukocyte count, Platelet count, Reticulocyte count. Absolute values including packed cell volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were calculated for every patient, Chest radiograph and abdominal ultrasonography was done in selected patients. Peripheral smear examination, and Bone marrow examination was done in all patients and wherever required, a trephine biopsy were also performed.

Inclusion criteria: Patients admitted to general medical ward with Age > 18 years, Hb haemoglobin of less than 12 g per ld. in women and less than 13 g per ld. in men, WBC < 4000 cells/all Platelet count < 1, 50,000 /all

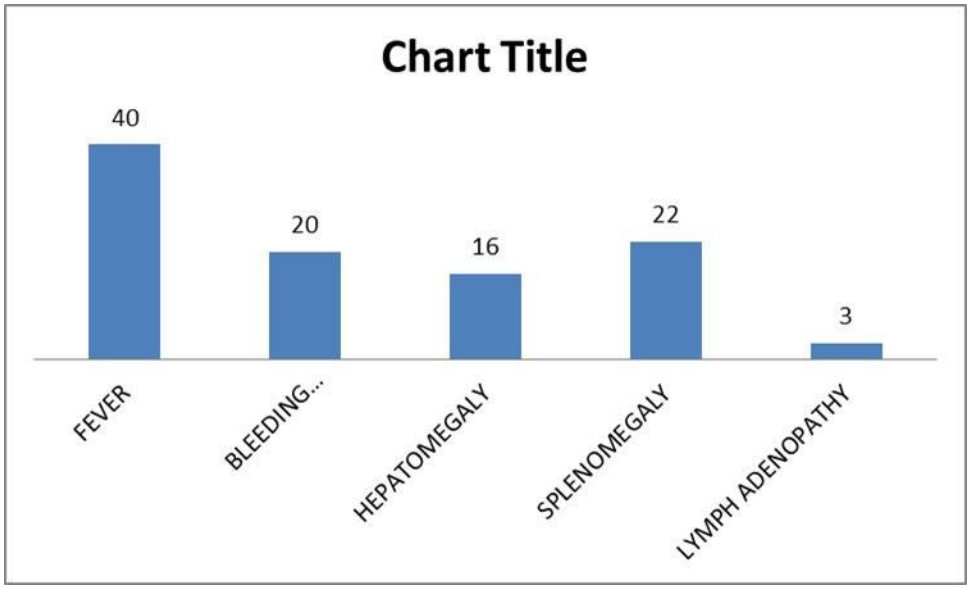
Exclusion criteria: Patients with a known haematological condition, Patients on cancer chemotherapy, Patients who received blood transfusion.

Statistical Analysis: Data analysis was done with use of SPSS, version 13. 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.

Results

30.77% of patients (20) had bleeding manifestations; and are found to have either aplastic anaemia or acute leukaemias. Liver was palpable in 16 (24.62%) of patients and was predominantly seen in patients with megaloblastic anaemia and leukaemia. Splenomegaly was found in 22 patients (33.85%); found in all cases of hypersplenism, and in few cases of megaloblastic anaemia, MDS, and myelofibrosis. Lymphadenopathy was found only in 3 (4.62%) cases of acute leukaemia (**Chart – 1, 2**).

Chart – 1: Clinical feature of patients according to various etiologies.



Anisopoikilocytosis (92%) and hyper segmented neutrophils (92%) are the most common findings in peripheral smear of patients with megaloblastic anaemia (**Chart – 3**).

Pallor was present in all cases. The other features were fever (48%), icterus (12%), hepatomegaly (28%), and splenomegaly (24%) as per **Chart – 4**.

8 patients (12.31%) with thrombocytopenia were diagnosed to have hypersplenism of which 6 are male and 2 are female patients. Out of 8 patients 2(25%) had Extra Hepatic Portal Obstruction, while the remaining 6 (75%) had Cirrhosis of liver leading to hypersplenism (**Chart – 5**).

Chart – 2: Distributions of various etiologies of pancytopenia.

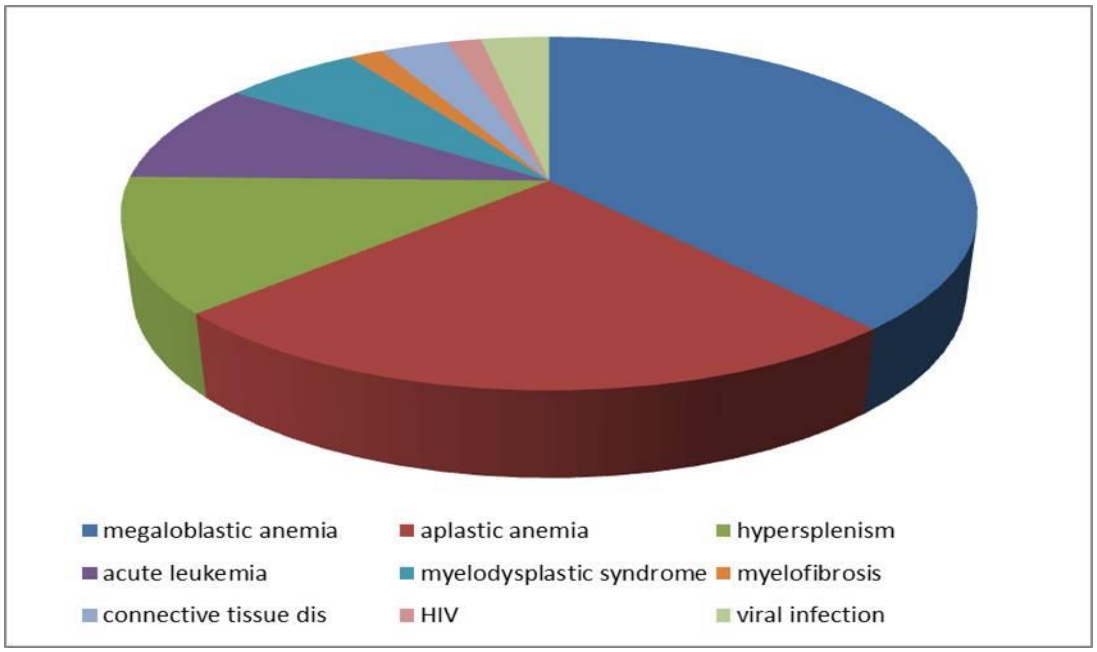
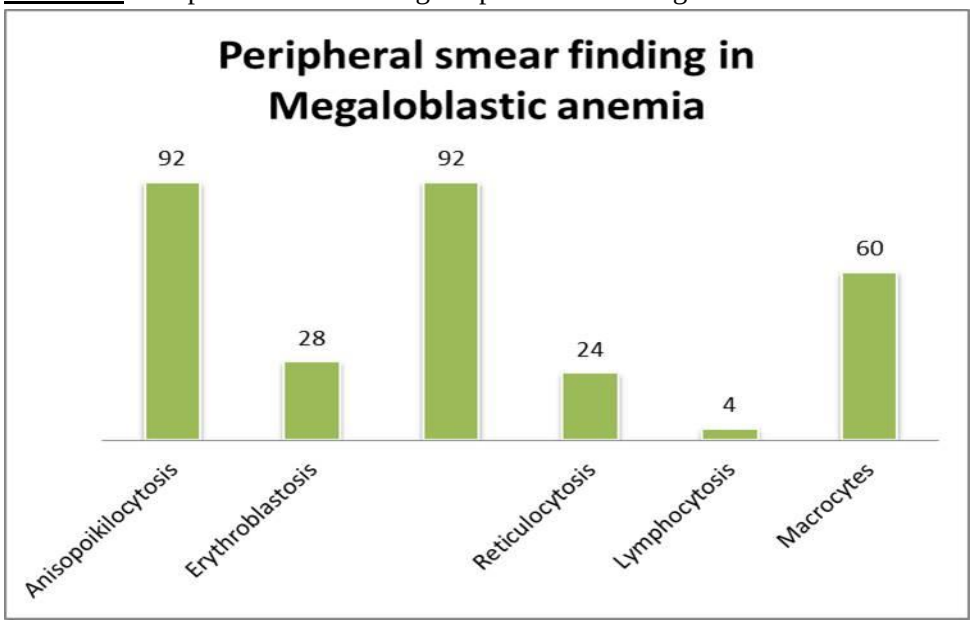


Chart – 3: Peripheral smear findings in patients with megaloblastic anemia.



Discussion

Our study population included 65 patients distributed across various age groups ranging from 14 years to 60 years of these patients 30 were females and 35 were males. Among these patients, males are common in younger age group (< 30 years), while females are more common in old age (> 40 years). In our study, pallor was the most common presentation (100%) with which patients presented to the physicians. Similar results have been reported in previous studies [6, 7]. The other clinical features were fever (46.4%), bleeding manifestation (30.77%), splenomegaly (33.85%),

hepatomegaly (24.62%) and lymphadenopathy (4.62%). The frequency of other clinical features was variable and different from those of other studies possibly due to the broad spectrum of etiologies or disorders behind Pancytopenia. Aniospoikilocytosis and hyper segmented neutrophils are the most common (92%) finding in peripheral smear of patients with pancytopenia. Anisocytosis is also seen in patients with erythroblasts are seen in patients with megaloblastic anaemia and myelofibrosis. Circulating WBC blasts were seen in patients with acute leukaemia and MDS [8]. Lymphocytosis was found in viral infections and megaloblastic anaemia. The most common cause of pancytopenia in our study was megaloblastic anemia (38.46%), followed by aplastic anaemia (24.62%), hypersplenism (12.31%). The other causes are acute leukaemia's (9.23%), Myelodysplastic syndrome (6.15%), collagen vascular disorder (3.08%), viral infection (3.08%), HIV (1.54%), and myelofibrosis (1.54%). This finding correlates with study done by Tilak, et al. [6], but the incidence of megaloblastic anemia is high in their study (77%) and the incidence of aplastic anaemia is low (7.7%). This low incidence of megaloblastic anemia in our study is in contrast with Das, et al. in 2002 [9]. In the West, pancytopenia has become less common in patients with megaloblastic anemia, as only 13.7% of cases were reported in a study done in New York. The incidence of megaloblastic anemia is 38.46% of all pancytopenia patients. This finding correlated with studies done by Kumar, et al. [10] in 1999 in whose incidence for the same is 37%. All the above studies done in India stresses the importance of megaloblastic anaemia as the major cause of pancytopenia in India. The high prevalence of nutritional anaemia's in India has been cited for the increased frequency of megaloblastic anaemia [6]. It is a rapidly correctable disorder and should be promptly identified and treated. Aplastic anaemia (24.62%) was the next most common cause of pancytopenia in our study, while in other similar studies it varied from 38% to 41%. As compared with other studies like tender et al the incidence (7.7%) is comparatively high. One study have reported Avery high incidence of aplastic anaemia (70%). Hypersplenism accounts for 12.31% of cases with pancytopenia in our study [10]. Chronic liver disease is the most common disease associated with hypersplenism in our study followed by extra hepatic portal obstruction. This is in contrast with earlier studies where they found the predominant cause of hypersplenism as chronic malaria and kala azar [11]. But since these studies were done more than a decade ago, the better diagnosis and treatment of malaria and kala azar leading to a decreased incidence of these in conditions and in our study Acute leukemia was found to be the fourth most common cause (9.23%) of Pancytopenia in our study which is similar to a study conducted by Savage et al who observed that the most common cause of pancytopenia was megaloblastic anemia followed by aplastic anaemia, acute leukaemia, AIDS and hypersplenism, and another study by Kumar who reported the causes of pancytopenia in order of frequency as Aplastic Anaemia at 29.5%, megaloblastic anaemia at 22%, Leukemic Leukaemia or lymphoma (18%) and hypersplenism at 11.4%.Of the 6 patients with acute leukemias, 4 had acute myeloid leukemia, and 2 had acute lymphatic leukaemia [12].

Conclusion

Megaloblastic anaemia is still the most common cause of pancytopenia in our setting. This probably indicates the poor nutritional status of the general population in our community. All patients with pancytopenia should be sought for megaloblsatic anaemia as it is a potentially treatable condition. The finding of hyper segmented neutrophils in the peripheral smear will guide in the diagnosis of megaloblatic anaemia .Hypersplenism is an important cause of pancytopenia in our setting. Hypersplenism should be sought as the cause of pancytopenia in patients with chronic liver disease especially alcoholics. Myelodysplastic syndrome is a common cause of pancytopenia in the elderly population. Pancytopenia should be evaluated

aggressively as significant number of patients has malignant condition in which early and aggressive treatment is warranted. Peripheral smear and bone marrow examination would help in identifying the aetiology of pancytopenia in almost all patients. Bone marrow examination is necessary in the evaluation of patients with pancytopenia. Failure to evaluate pancytopenia with these investigations could lead to delayed diagnosis of potentially treatable conditions [13].

Chart – 4: Clinical features of patients with megaloblastic anemia.

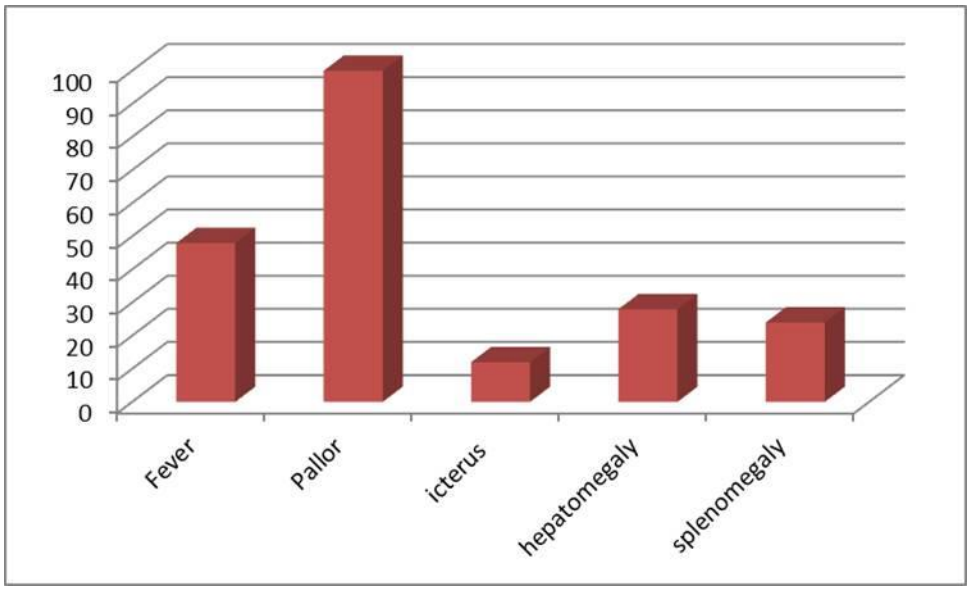
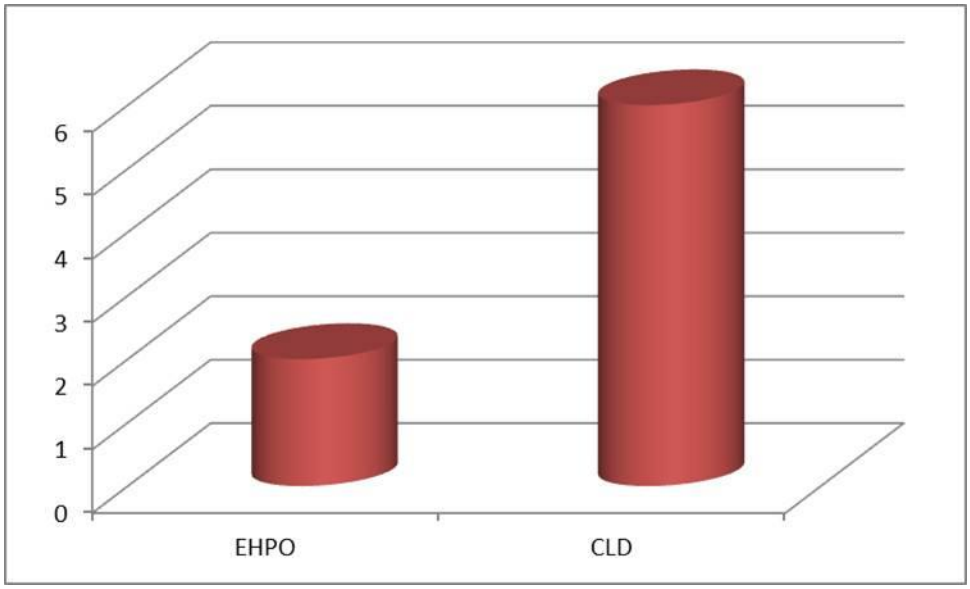


Chart – 5: Various etiologies of hypersplenism.



References

1. Imbert, et al. Adult patients presenting with pancytopenia. Hematology pathology, 1989; 3(4): 159-167.
2. Kumar R, Kalra SP, Kumar H, Anand AC, Madan M. Pancytopenia-A six year study. JAPI, 2001; 49: 1079-81.
3. R Sarode, et al. Pancytopenia in nutritional megaloblastic anemia. Trop Geogr Med., 1989; 41(4): 331-6.
4. Babu SY. Clinico-Haematological study of pancytopenia. Dissertation submitted to the Faculty of medicine, Kuvempu University, M.D (Path) 1998.

5. Khunger JM, Arculselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia-A Clinico-haematological study of 200 cases. Indian J Pathol Microbiol., 2002; 45(3): 375-379.
6. Tilak V, Jain R. Pancytopenia-A Clinco-hematologic analysis of 77 cases. Indian J Pathol Microbiol., 1992; 42(4): 399-404.
7. Panderson J, et al. Simultaneous deficiency of iron and vit b12-dimorphic anemia. Saxena R, Pati HP, Mahapatra M. De Gruchy's Clinical Hematology in Medical Practice. 6th Adapted Edition. London: Blackwell Science; 2013.p. 106-19.
8. Khunger JM, Arulselvi S, Sharma U, Ranga S, Talib VH. Pancytopenia a clinicohaematological study of 200 cases. Indian J Pathol Microbiol., 2002; 45: 375–379.
9. Das Makheja K, Kumar Maheshwari B, Arain S, KumarS, Kumari S, Vikash. The common causes leading to pancytopenia in patients presenting to tertiary care hospital. Pak J Med Sci., 2013; 29: 1108-11.
10. Kumar R, Kalra SP, Kumar H, Anand AC, Madan H. Pancytopenia a six year study. J Assoc Physicians India, 2001; 49: 1078–1081.
11. Gayathri BN, Rao KS. Pancytopenia: A clinico hematological study. J Lab Physicians, 2011; 3: 15-20.
12. 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.
13. 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: 90-5.