The Common Causes Leading to Pancytopenia in Patients Presenting in Hospital of Central India

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ABSTRACT

Introduction: Pancytopenia is an important and common clinico-hematological entity encountered in day-to-day clinical practice. This study is aimed to identify the frequent causes in patients presenting to Gandhi medical college and hamidia hospital bhopal with pancytopenia.

Material and methods: This prospective observational study was done in the Department of Medicine, Gandhi Medical college and Hamidia hospital, Bhopal from November 2014 to October 2015 after taking ethical clearance from ethical committee and informed consent was taken from the patients before participating. All participants underwent a detailed clinical examination and baseline investigations followed by Bone marrow examination.

Result: Out of 70 patients 41 were male and 29 were female. Maegaloblastic anemia was the commonest cause that was observed in 41.4% cases followed by aplastic anaemia (22.9%), hypersplenism(15.7%) and leukaemia (14.2%). Together these four causes accounted for 94.3% cases. Rare causes were infections, myeloproliferative disease and SLE.

Conclusion: This study concluded that most common causes of pancytopenia is megaloblastic anemia followed by aplastic anaemia, hypersplenism and leukaemia. Rare causes were infections, myeloproliferative disease and SLE. Bone marrow examination is a single useful investigation which reveals the underlying causes in patients with pancytopenia.

Keywords: The Common Causes Leading to Pancytopenia in Patients Presenting in Hospital of Central India

INTRODUCTION

Pancytopenia is a common clinico-hematological entity encountered in day-to-day clinical practice. Pancytopenia refers to a disorder in which all three elements of the blood (RBCs, WBCs and Platelets) are lower in counts than normal. Thus, it is not a disease entity by itself, but rather a triad of findings. It is a primarily or secondarily affecting bone marrow manifesting and lead to various hematological derangements, which is reflected in the peripheral blood smear as pancytopenia. There are varying trends in its etiology, clinical pattern, treatment modalities, and outcome in different studies.[1]

Pancytopenia is defined as hemoglobin < 12 gm%, WBCs count < 4 × 10^9/L and platelet count < 100 × 10^9/L. Anemia defined as mild (Hb 9–12 gm%), moderate (Hb 5-9 gm%), severe (Hb <5 gm%). Leucopenia defined as mild if (WBCs >3,000/mm3), moderate (WBCs 1,000-3,000/mm3) and severe (WBCs <1,000/mm3). And thrombocytopenia defined as mild (platelet count >50,000/mm3), moderate (platelet count 20,000-50,000/mm3) and severe as (platelet count < 20,000/mm3).[2]

Most of the time pancytopenia is insidious in onset. The presenting symptoms are usually anemia and thrombocytopenia, Leukopenia is an uncommon cause of initial presentation. There are many factors encompassing geographic distribution and genetic disturbances which cause pancytopenia according to various studies.[3] To understand the etiology of pancytopenia bone marrow biopsy plays a significant role. In some other selected cases radiological, biochemical and microbiological investigations are useful. The severity of pancytopenia and underlying etiology determine management and prognosis. Thus identification of correct cause will help in treatment.[4,5] This study is therefore aimed to identify the frequent causes of pancytopenia in patients presenting to a tertiary centre of central India with pancytopenia.

MATERIAL AND METHODS

This prospective observational study was done in patients who presented in the Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal between November 2014 to October 2015 after taking ethical clearance from ethical committee. Total number of 70 cases of pancytopenia were included after taking informed consent. Sample size calculated on bases of result (effect size) according to previous published studies. All participants underwent a detailed history, clinical examination and investigations which included CBC with RBC indices and peripheral smear, LFT, RFT, USG abdomen and Bone marrow examination.

Inclusion criteria

All patients >13yrs presenting in medicine OPD or ward with pancytopenia.

Exclusion criteria

1. Patients age <13 yrs.
2. Patients on cancer chemotherapy/ radiotherapy.
3. Patient with mono and bicytopenia.

STATISTICAL ANALYSIS

All study data was entered in Microsoft excel before statically analysed and result are shown as tables and chart format. P value ≤0.05 was considered to be statistically significant. Chi square test was used to find the significance.

RESULT

Out of 70 patients, 49 (70%) were less than 40 years and 21 (30%) were more than 40years. Male to female ratio was 1.41:1 (table-1).

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Most common presentation were fever and weakness. Other common symptoms were bleeding, weight loss, bodyache, breathlessness, reduced appetite and Vomiting.

Most common physical findings were pallor, splenomegaly, hepatomegaly and icterus. Less common findings were sternal tenderness, lymphadenopathy and hematuria

In this study, Megaloblastic anaemia was most common cause of pancytopenia followed by aplastic anaemia, hypersplenism and leukaemia. Together these four causes accounted for 94.3% cases. Other causes were infections like enteric fever, malarial fever, myeloproliferative disease and SLE.

Age wise distribution revealed that in patients less than 40, most common causes were megaloblastic anemia and aplastic anemia followed by leukemia, hypersplenism, autoimmunity and infection. In patients more than 40 years the most common case was again megaloblastic anemia but followed by hypersplenism, aplastic anemia, leukemia and infection (Figure - 1).

Gender wise distribution revealed that in males most common causes were megaloblastic anemia and aplastic anemia followed by leukemia, hypersplenism and infection. Whereas in females most common causes were megaloblastic anemia but followed by hypersplenism, leukemia, aplastic anemia, autoimmuninity and infection (Figure-2).

Bleeding was presenting symptom in 10 cases. In patients presenting with bleeding 5 had aplastic anemia, 2 had megaloblastic anemia 2 had AML and 1 hyperslenism. Splenomegaly was seen in 45cases. In patients with splenomegaly common causes were megaloblastic anemia (51.1%), hypersplenism (17.8%), acute leukemia (15.6%).

Bone marrow was hypercellular in 50 cases, hypocellular in 17cases and normocellular in 3 cases. Among the hypocellular marrow, aplastic anemia was the diagnosis in 16 cases. One case had hypocellular marrow secondary to infection.

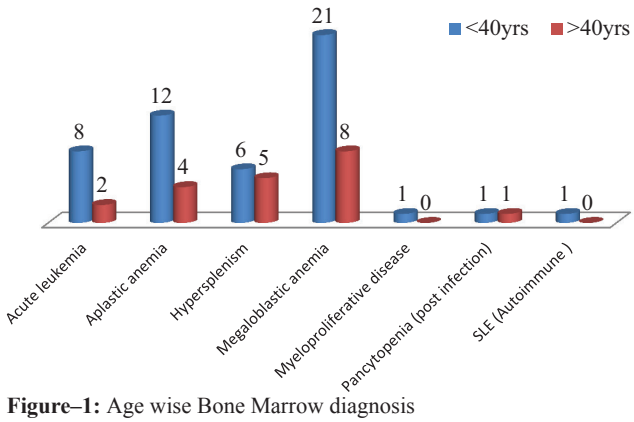
In our study, out of 70 patients, 29 (41.4%) patients diagnosed as megaloblastic anemia, 16 (22.9%) patients diagnosed as aplastic anemia (significant P value in males), 11 (15.7%) patients diagnosed as hypersplenism, 09 (12.9%) patients diagnosed as AML, 02 (2.4%) patients diagnosed as Pancytopenia secondary to infection, 01 (1.4%) patient diagnosed as ALL,01 (1.4%) patient diagnosed as Myeloproliferative disease and 01 (1.4%) patient diagnosed as SLE [Autoimmune] (table-2).

Sex	No of patients	Percent
Female	29	41.4
Male	41	58.6
Total	70	100.0

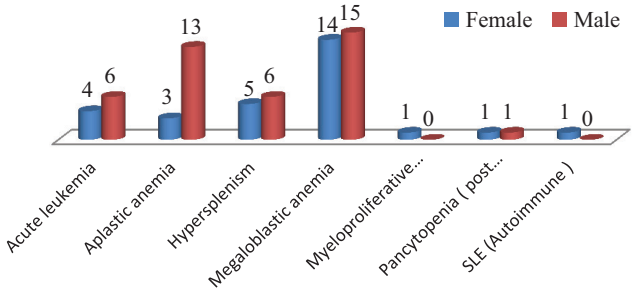
Table-1: Gender wise distribution of patients

DISCUSSION

Pancytopenia is a common manifestation of varied disease



Figure–1: Age wise Bone Marrow diagnosis



Figure–2: Gender wise Bone Marrow diagnosis

Bone marrow Final diagnosis	Sex		Total	p value, compared between Male and females
	Female	Male		
ALL	0	1	1	0.39
	0.0%	2.4%	1.4%	
Acute myeloid leukaemia	4	5	9	0.84
	13.8%	12.2%	12.9%	
Aplastic anaemia	3	13	16	0.036 [significantly more in males]
	10.3%	31.7%	22.9%	
Hypersplenism	5	6	11	0.76
	17.2%	14.6%	15.7%	
Megaloblastic anaemia	14	15	29	0.32
	48.3%	36.6%	41.4%	
Myeloproliferative disease	1	0	1	0.23
	3.4%	0.0%	1.4%	
Pancytopenia secondary to infection	1	1	2	0.81
	0.0%	2.4%	2.4%	
SLE [Autoimmune]	1	0	1	0.23
	3.4%	0.0%	1.4%	
Total	29	41	70	
	100.0%	100.0%	100.0%	

Table-2: Causes of pancytopenia on basis of Bone Marrow Cytology.

entities. Etiological evaluation of pancytopenia using easily available and less invasive diagnostic techniques is therefore important. Pancytopenia can be either due to reduction in haematopoietic cell production in the bone marrow as in aplastic anemia or due to infections, toxins, alcohol, chemotherapy, radiotherapy, malignant cells infiltration and parasitic infestation or due to increased cells destruction either in bone marrow itself or in spleen[6] as in hypersplenism, autoimmune, infection etc.[7] Age and gender distribution of patients in our study was consistent with the finding in other studies.

Vitamin deficiency patients (approx 80) induce pancytopenia were admitted per year and these vitamin deficiency common in underdevelop countries, which is responsible for megaloblastic anemia.[8] A Clinico Hematological Study done by B N Gayathri and Kadam et al, 104 pancytopenic patients clinically evaluated. In this study most common cause for pancytopenia was megaloblastic anemia (74.04%) followed by aplastic anemia (18.26%).[9]

Megaloblastic anemia was commonest cause of pancytopenia in this study. Most other studies had reported aplastic anemia as a common cause. This seems to reflect the higher prevalence of nutritional deficiency in India. Other common causes were aplastic anemia, hypersplenism and hematological malignancies. Uncommon etiological factor like Dengue, Malaria, SLE were identified in this study.

Megaloblastic anemia: Megaloblastic anemia is a group of disorder characterized by defective nuclear maturation caused by impaired DNA synthesis.

This was the most common cause of pancytopenia in the present study. There was slight male preponderance with male to female ratio of 1.07:1. It was more common in younger age group. Majority of patients had macrocytic and hypochromic anemia. Hypersegmented neutrophils presented in more than 50% cases. Bone marrow was hypercellular with megaloblastic erythropoeisis and giant metamyelocytes. Megakaryocytes were normal.

Many studies in the past especially from Indian subcontinent have shown megaloblastic anemia to be a common cause of pancytopenia in this region. A study was conducted in department of hematology and transfusion medicine, govt. medical college and hospital, Chandigarh for over period of 32 month. The most common cause of pancytopenia was megaloblastic anemia.[10] Rizwaan azz qaazi Ayesha massood conducted study of 100 consecutive patients with laboratory incidence of pancytopenia, collected systematically over a period of 14 month beginning from december1999. The final diagnosis was based on bone marrow examination findings and the most common cause was megaloblastic anemia(28%).[11] The department of pathology, Dr RML hospital New Delhi conducted a study over a period of six month, during this period the total cases were250 in which BME done. In this study also commonest cause of pancytopenia was megaloblastic anemia which was seen in 22 out of 50 patients(44%).[12] Other study which was conducted over a period of one year in department of Hematology, Sufdarjung hospital medical college, New Delhi to ascertain the percentage of occurrence and causes of pancytopenia and bone marrow examination were done in most of the cases (200 out of 250). The most common cause of pancytopenia was Megaloblastic anaemia (72%).[13]

Aplastic anemia - Aplastic anemia is defined as the failure of bone marrow to produce blood cells. The hallmarks of the disease are pancytopenia and a hypocellular bone marrow.

This was the next common cause of pancytopenia in this study. There was significant male preponderance with male to female ratio of 4.3:1. It was more common in younger age group (< 20 yrs) Majority of patients had normocytic normochromic anemia. Some showed macrocytosis. There was relative lymphocytosis in most.Bone marrow was hypocellular with increase in fat. Lymphocytes and plasma cell were prominent.

During January 1971-June 1975 Retief FP, Heyns AD examined 195 pancytopenic patients, common cause of bone marrow failure were aplastic anemia in 67.7% followed by hypersplenism and severe infection.[14]

Hypersplenism: hypersplenism is an overactive spleen. If spleen is overactive, it remove the blood cells too early and too quickly. There are many condition in which spleenomegaly occure and it lead to hypersplenism with pancytopenia. Such pancytopenia develop due to premature destruction of RBCs and hemolysis.[15,16] This was the next common cause of pancytopenia in this study. Male to female ratio was 1.2:1 (male preponderance) it was more common in age group of >40 yrs age group. Majority of patients had normocytic normochromic anemia. Bone marrow was hypercellular with reversal of M:E ratio.

Green D et al. presented a case of Gaucher disease with hypersplenism and pancytopenia in 1971.[17] In 1989 Johnson HA et al. in a review of 391 cases of splenectomies perfomed over 16 yrs observed that pancytopenia and hemolytic complications of disease processes were the commonest indication for splenectomy.[18] In 2005 Gamal Abdul Hamid, Safa A. R. Shukry studied prospective descriptive study that included all patients with pancytopenia admitted to or attending the Hematology-Oncology Department in Al-Gamhouria Teaching Hospital, Aden and most common causes of pancytopenia were malaria and hypersplenism (> 45%), followed by megaloblastic anemia (14.7%), and aplastic anemia and acute leukemia in 13.3%.[19]

Leukemias: Hematopoietic neoplasms can present with pancytopenia in both children and adults, and acute leukemias are among the most common of these.This was the fourth common cause of pancytopenia in this study. More common in younger males. Majority of patients had normocytic normochromic anemia. Immature cells including myeloblast were seen in almost all cases. Bone marrow was hypercellular with blast >20%.

Infections and autoimmune disease: Typhoid and malaria were infections identified. Bone marrow was hypercellular in malaria but hypocellular in enteric fever. One patient had classical SLE with positive ANA. Bone marrow was hypercellular.

Infections cause bone marrow necrosis and bone marrow suppression along with increased peripheral destruction due to persistent congestive splenomegaly.[20] R sood, S roy, P kaushik (1996) studied case of enteric fever with pancytopenia and reported that haematophagocytosis is commonly associated with severe infection like typhoid.[21] Nevin uzuner, Ahmet et al. (2002) reported typhoid fever with pancytopenia. According to this study in patients with salmonellosis, pancytopenia mostly due to histocytic hyperplasia in bone marrow, with marked

phagocytosis of platelets, leukocytes and RBCs.[22]

Autoimmune diseases are another cause of new onset pancytopenia, such as systemic lupus erythematosus (SLE). These patients present with new-onset pancytopenia, which can have multiple etiologic factors. Approximately 57% to 78% of SLE patients develop anemia, because of a combination of anemia of chronic disease, autoimmune hemolytic anemia, microangiopathic hemolytic anemia and renal insufficiency.[23,24]

CONCLUS ION

Megaloblastic Anemia is most common cause of pancytopenia. While other causes are aplastic anemia, hypersplenism, leukaemia, infections. In India poor eating habits, poverty, poor quality of foods, lack of education and self avoidance of necessary foods may be causes of nutritional deficiency which leading to megaloblastic anemia. Bone marrow examination is single useful investigation which reveal the underlying causes and prognosis in patients with pancytopenia. Megaloblastic anemia is either cause can be prevented by improving the nutritional status of our population.

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