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A study of Clinico-Etiological profile of Pancytopenia - Experience of tertiary care hospital in South India.

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Abstract

Background: Pancytopenia is common entity in clinical practise as a feature of myriad of conditions, some of which are life threatening. Since the cause of pancytopenia depends on various environmental factors. It is important to know clinico etiology of pancytopenia and therefore the present study was conducted for clinic etiological profile in tertiary care hospital in Hyderabad situated in southern zone of India.

Materials and Methods: The present observational study was conducted in tertiary care institute located in Hyderabad, Telangana state over a period of 1 year from June 2021 to June 2022 including 50 cases admitted of pancytopenia.

Results: The most common cause of pancytopenia was megaloblastic anemia (40%) followed by aplastic anemia and Myelodysplastic syndrome (10 %).

Conclusion: Study concludes Megaloblastic anaemia is the leading cause of pancytopenia. In most cases of pancytopenia, peripheral smear study provides inconclusive evidence, so bone marrow aspiration a safer invasive procedure was helpful to find out the etiological cause. So, in most cases, a comprehensive clinical, Haematological workup and bone marrowstudy of patients will usually helpful in evaluating the aetiology of pancytopenia. In addition, early recognition of underlying aetiology to be made, so that treatable causes are identified without any delay.

Keywords: Megaloblastic anemia, aplastic anemia, pancytopenia

Introduction

Pancytopenia is an important clinic -Haematological entity encountered in our day-to-day clinical practice characterized by decrease in all three cell lines. Pancytopenia itself is not a disease entity, but the triad of findings might result from a number of disease process ranging from benign conditions like infections, nutritional defeciencyto malignant neoplasms. [(1)] There are varying trends in clinical pattern, treatment modalities, and outcome. [(2)]It is a disorder in which all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number Pancytopenia has been defined as hemoglobin of less than 13.0g/dl for males, 12 g/ dl for non-pregnant females, leucocyte cunt of about less than 4000 cells / mm3, platelet count of about less than 1. 5 Lakhs / mm3. Pancytopenia could be result of decrease in in hematopouetic cell production as in aplastic anemia,trapping of normal cells in hypertrophied and overactive reticuloendothelial system as in hypersplenism, ineffective Hematopoiesis in megaloblastosis or replacement by abnormal or malignant tissue in bone marrow.[(3,4)]In India, the causes of pancytopenia are varied, so the present study has been undertaken to evaluate the various causes of Pancytopenia, thereby this data would be helpful in diagnostic and theraeupatic approach in patients with pancytopenia.

Materials and methods

The present prospective study was undertaken over 50 patients admitted with pancytopenia for period of 1 year from June 2021 to June 2022 at general medicine department in kamineni academy of medical sciences and research Centre, Hyderabad. All Patients after obtaining a detailed medical history and physical examination the following investigations are done Haemoglobin, Total count, differential count and Erythrocyte sedimentation rate (ESR), Platelet count. Peripheral smear study with reticulocyte count, Bone marrow smear study and trephine biopsy, other investigations as necessary such as; Serological study for HIV infection. Chest X- ray, USG abdomen and pelvis, Serum vitamin B12 assay and Serum Folic acid level

Inclusion criteria

Age >15 yrs, presence of all three of following Anaemia (Hemoglobin<13.0g/dl in males; 12.0 gm/dl in females), Leukopenia (total leukocyte count < 4000cells/ mm3), Platelet count < 1,50, 000 cells / mm3.

Exclusion criteria

Patients on cancer chemotherapy, on radiotherapy.

Results

A total of 50 patients who presented with pancytopenia were studied. They consisted of 26 males and 24 females with a male to female ratio of 1.1:1 shown in diagram 1. The age of patients ranged from 15 years to 80 years. among them age 20 patients are of age 15-30 years, 11 patients are from 51-60 years, remaining patients according to age group are shown in diagram 2.

Figure 1

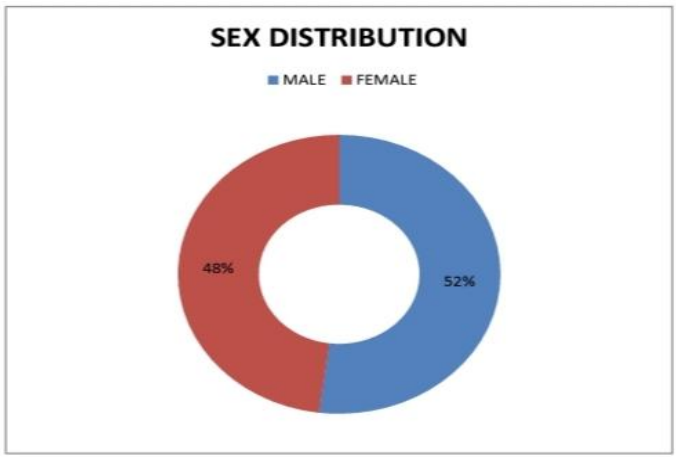
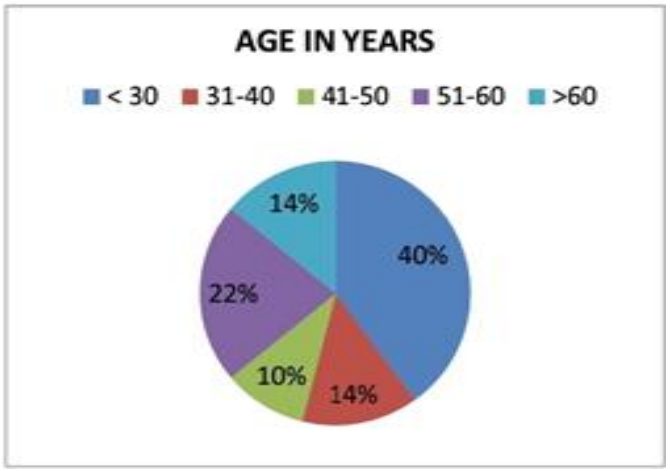


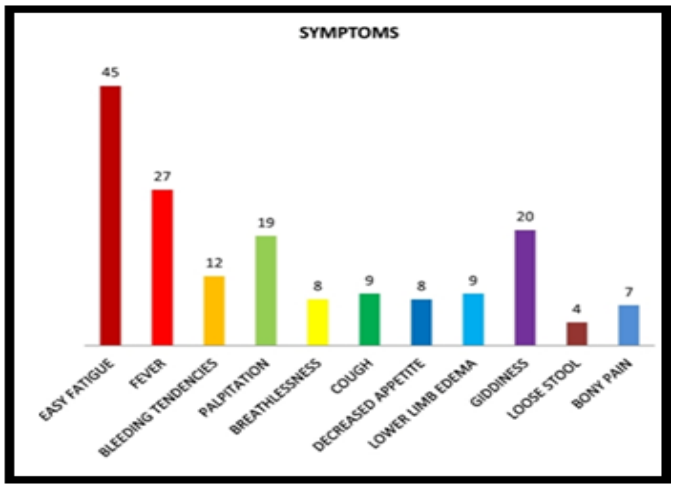
Figure 2



Presenting complaints and physical findings are shown in table 1 and diagram 3

The commonest mode of presentation was easy fatigue, other main symptoms are fever, giddiness, breathlessness, palpitations.

Figure 3: Presenting complaints in Pancytopenia



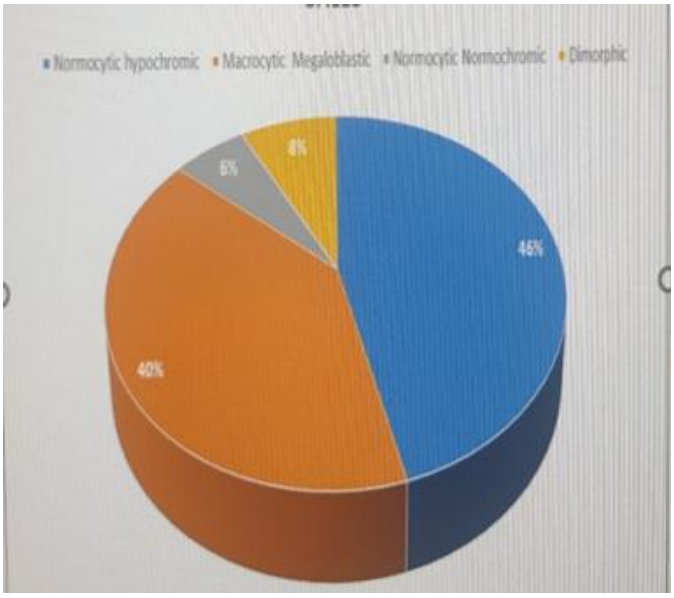
Pallor was present in all cases, followed by splenomegaly and hepatomegaly. Icterus,lymph a denopathy, pedal edema are other findings noted in various cases

Table 1: Physical findings in Pancytopenia

SIGNS	No of Patients	Percentage
PALLOR	50	100%
SPLENOMEGALY	20	40%
HEPATOMEGALY	6	12%
ICTERUS	6	12%
LYMPHADENOPATHY	10	20%
PEDAL EDEMA	9	18%
GLOSSITIS	7	14%
SYSTOLIC MURMUR	6	12%
KNUCKLE PIGMENTATION	5	10%

Predominant peripheral smear picture Majority (46%) of the patients had normocytichypochromic anemia, 40 % hadmacrocytic/ megaloblastic anemia, 6% had normocyticnormochromic anemia.,8 % had dimorphic anemia.pattern of peripheral smear picture is shown in diagram 4

Figure 4: Peripheral smear pattern in Pancytopenia



The causes of pancytopenia and case distribution are shown in diagram 5

Among pancytopenia causeswere megaloblastic anemia with 20 patients (40%), peripheral smear showing megaloblasts, bone marrow aspiration showed megaloblastic erythroid hyperplasia

Aplastic anemia with 5 patients (10%),Myelodysplastic syndrome with 5 patients (10%).

ALL (Acute lymphocytic leukemia) with 4 patients (8%), AML (acute myeloid leukemia) with 3 patients (6%) both ALL and AML cases have hypercellular bone marrow, erythroid and megakaryotic series were reduced. And all belong to age group of 15-30.

Sepsis with seen in 3 patients (10%) belonging to age group of 561-60 years, peripheral smear showing toxic granules and shift to left with few metamyelocytes

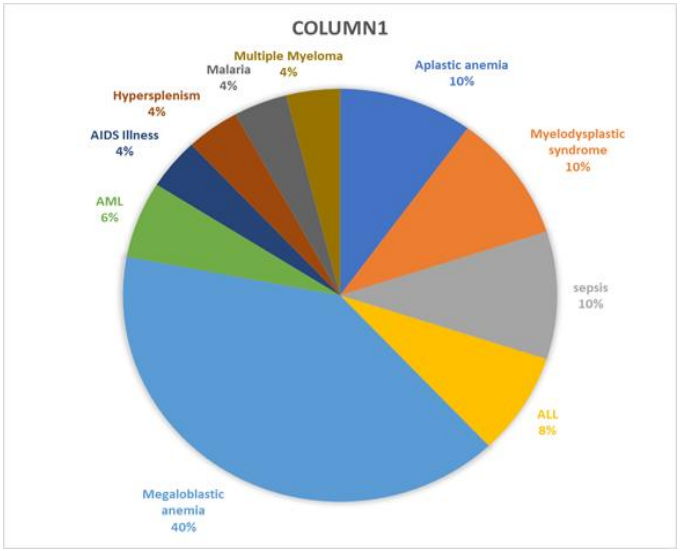
HIV AIDS with 2 patients (4%) with severe wasting and multiple opportunistic infections.

Hypersplenism with 2 patients (4%), Malarial infection with 2 patients (4%) with gametocytes of plasmodium falciparum were seen in peripheral smear, these 2 patients recovered after antimalarial treatment and Multiple myeloma with 2 patients (4%).

presented with weakness and bone tenderness.bone marrow showed abnormal proliferation of plasma cells, constituting >40% of marrow cells.

Megaloblastic anemia was the most common cause of pancytopenia followed by Aplastic anemia,Myelo dysplastic syndrome and Sepsis.

Figure 5: Etiology of Pancytopenia



Discussion

A total of 50 cases were studied. Age, sex wise incidence, presenting complaints, signs, peripheral smear blood picture, bone marrow aspiration smears and various etiology of pancytopenia were studied in all cases and observations were compared with various Indian and worldwide studies published in literature.

The age of patients ranged from 15 to 80 years with mean age being 44 years. Cytopenias were observed more in females (52%) than males (48%), with female to male(F:M) ratio 1.1: 1, different when compared with Gayathri and Rao etal[5] where male to female ratio 1.2: 1.

The most common presenting complaint in our study was easy fatigue (90%), followed by fever (54%) and

giddiness (40%). The most common physical finding was pallor seen in 100 % of patients followed by splenomegaly (40%) and lymphadenopathy (20%). These finding are similar to study done by Chandra H Guptaetal[6] in north Himalayan region of India.

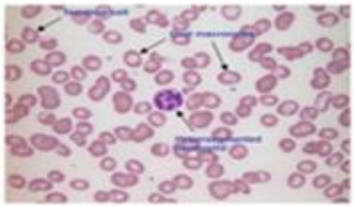
The presenting complaints are mainly attributed to Anemia and leucopenia. Thrombocytopenia was an uncommon cause of the patient presentation but can become major threat to underlying disease during the course of disorder.

In our study we found (46%) of the patients had normocytichypochromicanemia, 40 % hadmacrocytic/ megaloblastic anemia, 6% had normocyticnormochromic anemia, 8 % had dimorphic anemia. In our study it was found that hypersegmented neutrophils with anisopoikolocytosis is the predominant finding in megaloblastic anemia, other findings include macro ovalocytes.

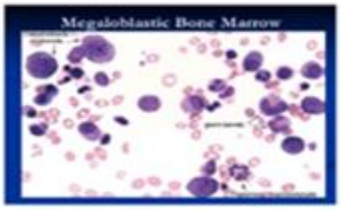
Hyper segmented neutrophils were noted in 40 % of cases in our study compared to 51.35 % in GayathriRaoetal, 84.9 % in Tilak V etal [7] study.

The commonest cause of pancytopenia, reported in various studies throughout the world has been Aplastic anemia. [4] This is in contrast with ourstudy, it was found Megaloblastic anemia is the most common cause of pancytopenia. The incidence was found to be 40% in our study group. Similar findings were observed in other studies conducted in India such as incidence of megaloblastic anemia was 74.04 % in Gayathri and Rao etal [5] incidence of 72% reported by Khunger JM etal[8]68% by Tilak V etal. [7] All these above studies have been done in India, and these stress the importance of megaloblastic anemia being the major cause of Pancytopenia.All cases of Megaloblastic anemia responded well to B12 and Folate supplementation

The next most common cause was found to be aplastic anemia and its incidence was found to be 10 %, MDS - 10%, Sepsis -10%. The incidence of aplastic anemia was found to be 10 % to 52% among pancyto panic patients in various studies, such as 14 % in studies by both Kumar R etal [9] and Khunger JM etal. A study conducted by Khungeretal reported incidence of MDS around 2%. sepsis was found in 6 % of cases in a study done by Praveen kumar Etal[10] in south India.



PERIPHERAL SMEAR OF MEGALOBLASTIC ANEMIA



BONE MARROW PICTURE OF MEGALOBLASTIC ANEMIA

Figure 6: Smear and bone marrow showing Macrocytic anemia with hypersegmented neutrophils

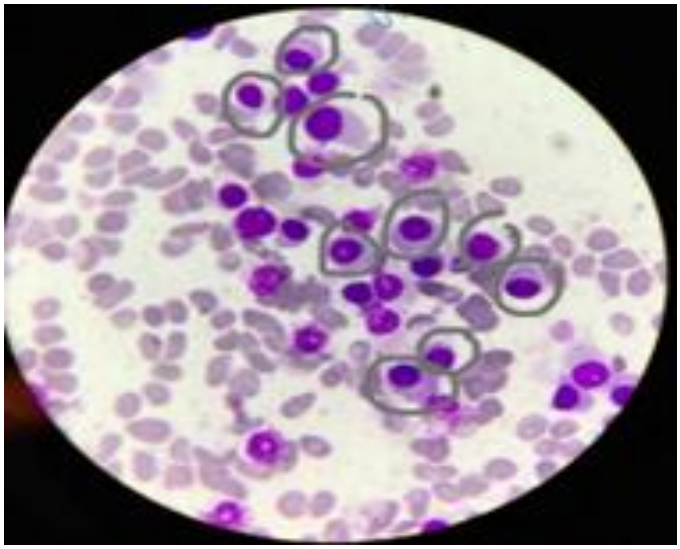


Figure 7: Peripheral smear showing plasma cells .

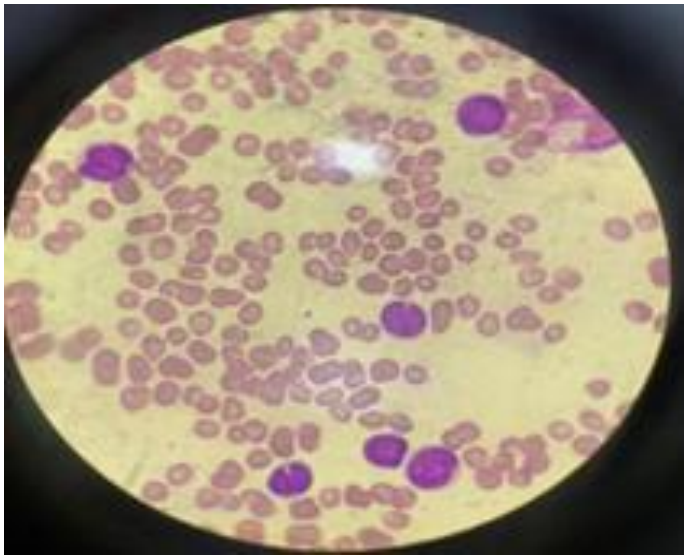


Figure 8: Peripheral smear showing blast cells in leukemia.

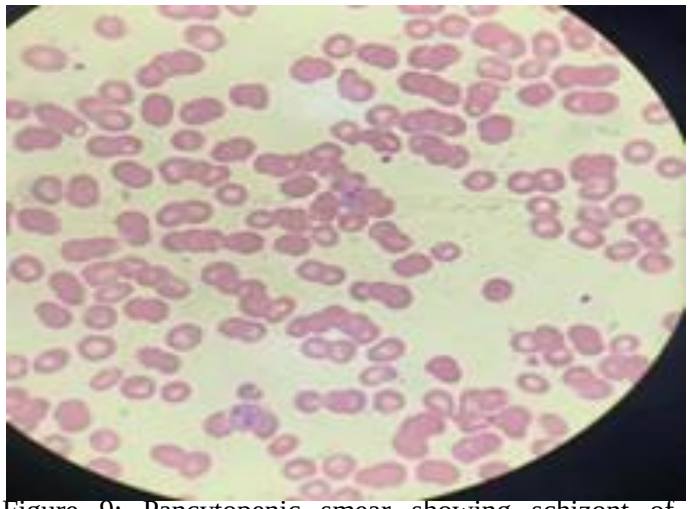


Figure 9: Pancytopenic smear showing schizont of plasmodium falciparum.

We encountered 7 cases having leukemia among them 4 cases having ALL and 3 cases having AML, the diagnosis was based on bone marrow aspiration study. Gayathrietal reported 3 cases of AML and 1 case of ALL out of 104 cases, Khodke k etal[11]

reported a single case of AML out of 50 cases of pancytopenia.

Other causes of pancytopenia and 4% are having AIDS illness, malaria, Hypersplenism, Multiple Myeloma. Tilak V etal who have reported an malaria incidence of 3.9 % and Kumar R etal who have reported an malaria incidence of 3 % of the total cases.

Khodke K etal reported an incidence of 4% of total cases having multiple myeloma, Khunger M etal reported incidence of 1 % of total cases having multiple myeloma. Pancytopenia was treatable in 60 % of patients, who fully recovered from cytopenia. Death occurred in 10 % of cases due to severe pancytopenia and overwhelming infections.

Table 2 Comparison of common causes of pancytopenia in various studies

Causes	*Khunger JM etal*	*Kumar R etal*	*Gayathri Rao et al*	*Present study*
Most common cause	Megaloblastic (72%)	Aplastic (29%)	Megaloblastic (74%)	Megaloblastic (40%)
Second common	Aplastic (14%)	Megaloblastic(22.8%)	Aplastic(18.3%)	Aplastic(10%) Sepsis(10%), MDS (10%)
Third common		Aleukemic leukemia (12.04%)	Sub leukemic leukemia (3.08%)	ALL (8%
Fourth common		Hypersplenism. 11.44 %	Malaria(2%)	AML (6%)

Conclusion

Study concludes Megaloblastic anaemia is the leading cause of pancytopenia.Pancytopenia was more commonly observed in young age groups than in older individuals.

Among the younger age groups, Megaloblastic anaemia was found to be the most common cause. In most cases of pancytopenia, peripheral smear study provides inconclusive evidence, so bone marrow aspiration a safer invasive procedure was helpful to find out the etiological cause. So, in most cases, a comprehensive clinical, haematological workup and bone marrow study of patients will usually helpful in evaluating the aetiology of pancytopenia.

In addition early recognition of underlying aetiology to be made, so that treatable causes are identified without any delay.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate consent forms. In the form the patients have given their consent for the images and other clinical information to be reported in the journal.

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