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Research Article

CLINICO - HAEMATOLOGICAL PROFILE IN PANCYTOPENIA, A TERTIARY CARE CENTRE STUDY

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A R T I C L E I N F O

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A B S T R A C T

Background: Pancytopenia refers to a reduction in all three formed elements of the blood erythrocytes, leukocytes and platelets. Though It is not a disease entity, pancytopenia is a serious hematological problem. Many disease conditions can manifest as pancytopenia. The underlying cause of pancytopenia is diagnosed by bone marrow aspiration and biopsy.
Material & Method: A cross sectional study was done in the Department of Medicine, in a Tertiary care centre in central part of Kerala during a period of one year (1/1/2013 to 1/1/2014). 51 cases of pancytopenia patients admitted in the medicine department were studied. Clinical history, clinical examination, haematological investigations were analysed to make diagnosis. Study was approved by institutional ethical committee.
Results: Mean age at presentation was 50.2 yrs. 68% had fever as presenting complaint. 39.25 had hepatomegaly and 35% had splenomegaly.35.3% had macrocytic anemia in peripheral smear. 31.4% showed megaloblastic change in bone marrow. 25.4% had megaloblastic anemia.
Conclusion: Most common cause for pancytopenia was Megaloblastic anemia. It was prevalent in 51 – 70yrs age group.

INTRODUCTION

Pancytopenia refers to a reduction in all three formed elements of the blood erythrocytes, leukocytes and platelets. It is not a disease entity, but the triad of findings that may result from a number of disease processes (1).

Normal haematopoiesis occurs in bone marrow, within a specialised microenvironment where humoral factors play an important role. Pancytopenia is a serious hematological problem, the underlying cause of which is diagnosed by bone marrow aspiration and biopsy. Bone marrow examination is extremely helpful in evaluation of pancytopenia (2).

Evaluation of bone marrow failure was dated to 1888, when Paul Ehrlich described a young woman who died of a explosive short illness marked by severe anemia, bleeding and high fever. As a pathologist, Ehrlich was struck by the absence of nucleated RBCs and the fatty nature of the femoral marrow, opposite findings from the normal physiologic response to severe anemia and he inferred from the morphology, a mechanism of failed blood cell regeneration (3).Various diseases can manifest as pancytopenia

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Differential Diagnosis of Pancytopenia (4)

Table 1

A. Pancytopenia with hypocellular bone marrow	
1. Aplastic anaemia	
2. Hypoplastic MDS	
3. Aplastic crisis in hemolytic anemia	
4. Post chemotherapy	
5. Transfusion associated-GHVD	
B. Pancytopenia with cellular bone marrow	
Primary bone marrow disease	**Secondary to systemic disease**
1. Myelodysplasia	1. Vitamin B12, folate deficiency
2. Paroxysmal nocturnal hemoglobinuria	2. Hypersplenism
3. Myelofibrosis	3. Infection – Tuberculosis, leishmaniasis, brucellosis.
4. Aleukemic leukemia	4. Autoimmune diseases – Systemic lupus erythematosus, Sjogren syndrome, sarcoidosis.
5. Hairy cell leukemia	5. Storage diseases – Gaucher's disease, Nieman Pick's disease.
6. Bone marrow lymphoma	6. Metastatic tumors

The severity of pancytopenia and the underlying pathology determine the management and prognosis of the patients. In India, the causes of pancytopenia are not well defined. So the present study has been undertaken to evaluate the various causes of pancytopenia and to correlate the peripheral blood and bone marrow aspirate findings in arriving at a diagnosis.

Thereby, this data would help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

Aims of the Study

1. To study the clinical presentations in pancytopenia due to various causes.
2. To evaluate hematological parameters and arriving at a diagnosis.

MATERIALS AND METHOD

It was a cross sectional study. All cases of pancytopenia patients admitted in the Department of Medicine , in a tertiary care centre, in central part of Kerala during the period 1/1/2013 to 1/1/2014 were studied. 51 cases were studied.

Inclusion Criteria

Inclusion Criteria were Presence of all 3 of the Following

Hemoglobin, <10g/dl
Total leukocyte count <4,000 / µL
Platelet count, <100,000/ µL

Exclusion Criteria

Patients on chemotherapeutic drugs
Patients under the age of 13 years
Patients not giving informed consent

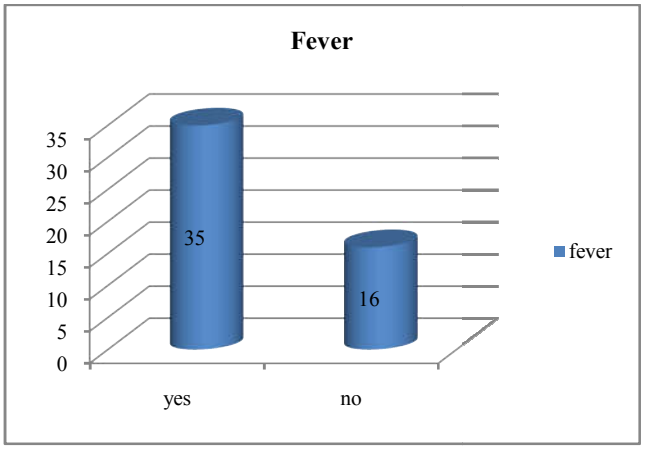
Clinical history, clinical examination findings and laboratory investigations of all 51 cases were obtained. Laboratory investigations included complete blood count, Vit B12 assay, peripheral smear study and bone marrow study. Study was approved by the ethical committee.

Statistical analysis was done using EPI INFO version 7 and SPSS version 16. Quantitative variables were reported as Means +/- SD and qualitative variables as percentage. Chi square test was used in analysis of risk factors.

OBSERVATIONS AND RESULTS

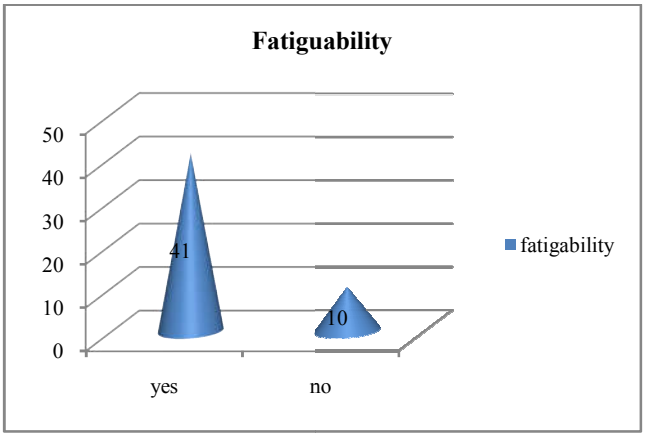
Of the 51 patients affected with pancytopenia, middle aged persons were predominantly involved. Maximum number of persons were in the age group of 51-70 yr (41.2%). Mean age was 50.6yrs. In the 51 cases studied, 27 cases (52.9%) were females & 24 cases (47.1%) were males.

Clinical History



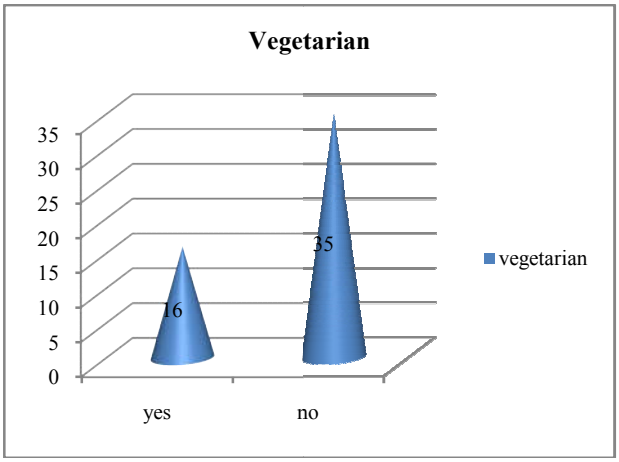
Picture 1

Of 51 patients, 68% were having fever as the predominant symptom.



Picture 2

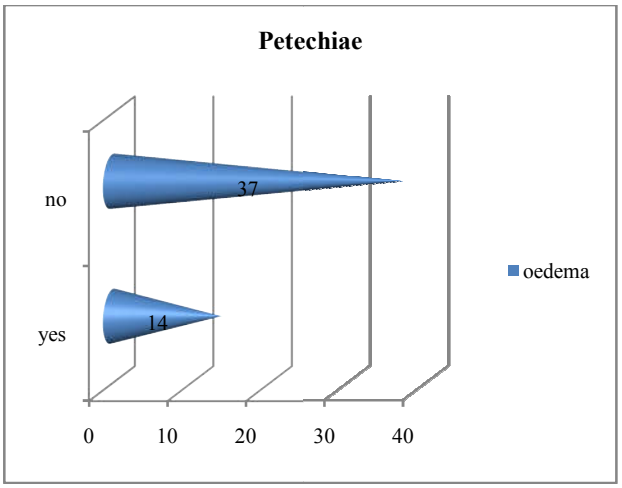
Out of 51 cases studied, 80% were having fatiguability.



Picture 3

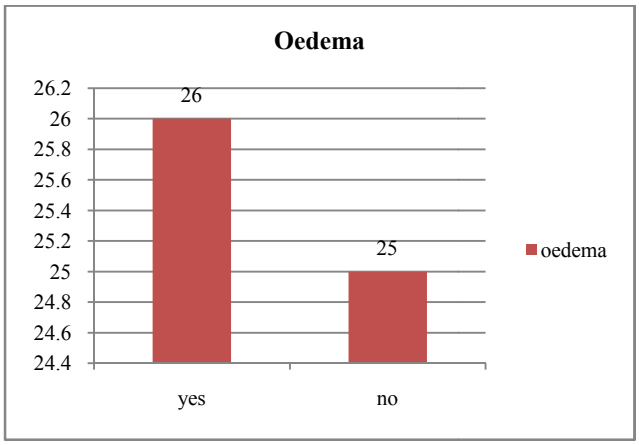
Non vegetarians contribute to 71% of pancytopenia patients.

Clinical Examination



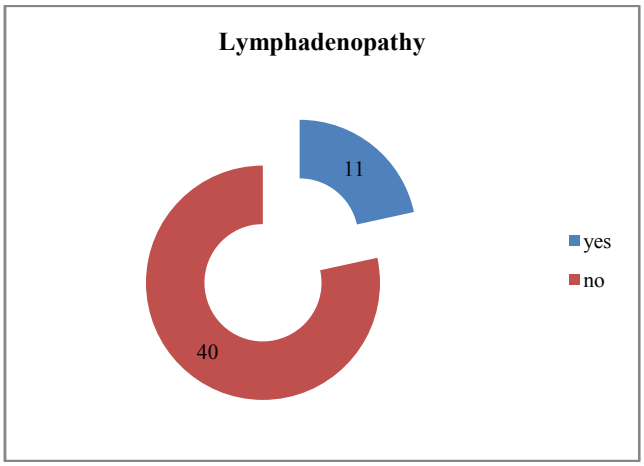
Picture 4

Of 51 patients, 27% were having petechiae as the presenting complaint.



Picture 5

Only 50% cases were having oedema as the presenting symptom.

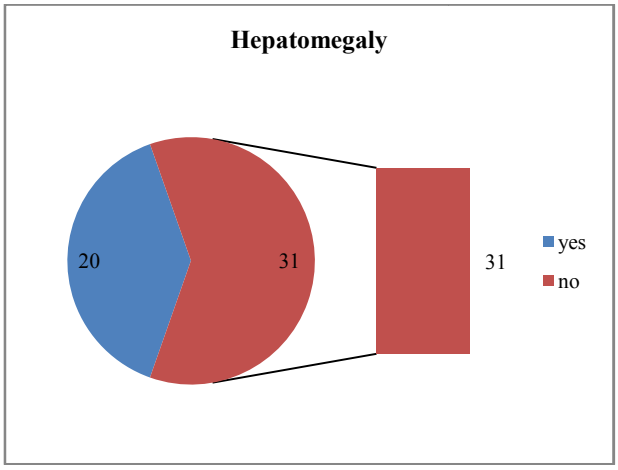


Picture 6

20% patients had lymphadenopathy.

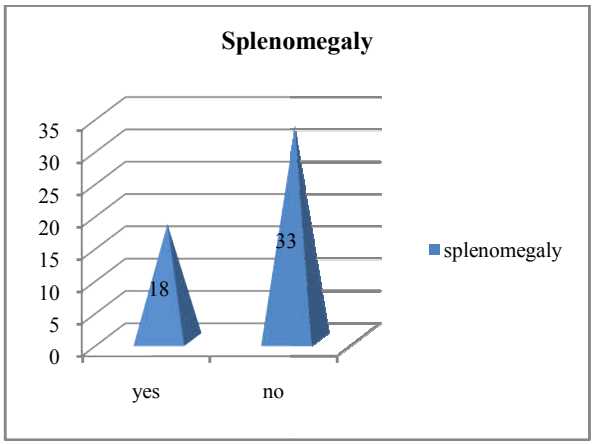
Of 51 patients with pancytopenia, 21.57% patients were having icterus.

Of 51 cases studied, 35% were having hyperpigmentation.



Picture 7

Of 51 patients, 20 (39.22%) patients were having hepatomegaly.



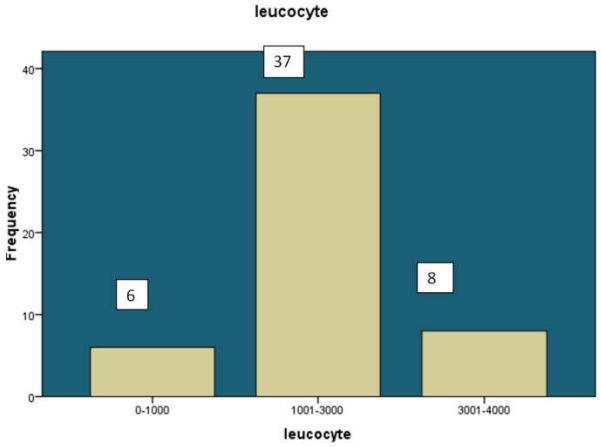
Picture 8

35% patients were having splenomegaly on examination.

Haematological Profile

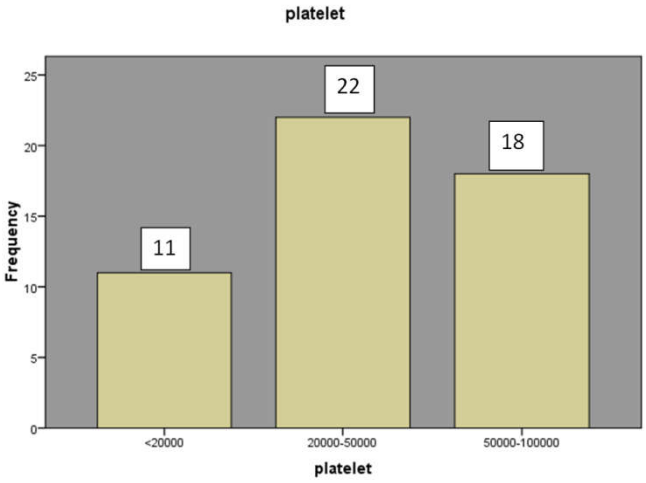
Table 2

Haemoglobin (gm/dl)	No. of Cases	Percentage (%)
<5	22	43.1
5-9	26	51
>9	3	5.9



Picture 9 – Total Wbc Count

72% patients had leucocye count in between 1000cells/cumm and 3000cells/cumm. Mean leucocyte count was 2106 +/- 771 cells / cumm



Picture 10 platelet count

Table 3

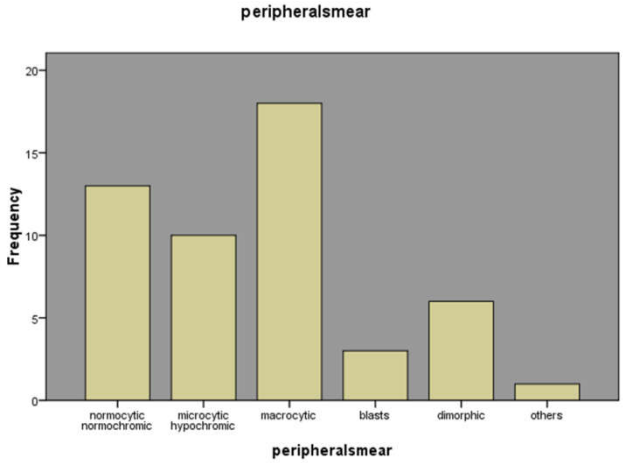
ESR	No. of Cases	Percentage
<40	6	11.8
40-80	22	43.1
>80	23	45.1

Table 4

MCV	No. of Cases	Percentage
<100	20	39.2
>100	31	60.8

60.8% cases had MCV >100 fl.

Hyper segmented neutrophils were found in around 29.41% patients with pancytopenia.



Picture 11 – Peripheral Smear Report

Macrocytic blood picture was found in around 35.3% of patients and normocytic normochromic picture in around 25.5% patients. Dimorphic blood picture was seen in around 11.8% patients.

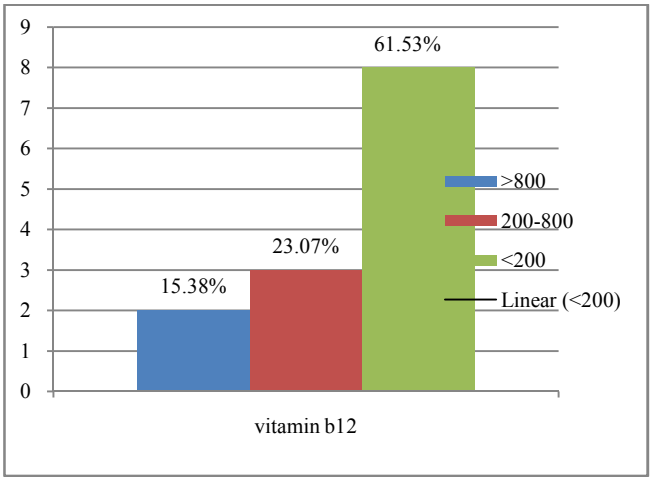
Table 5 Bone Marrow Examination

Bone marrow	No. of Cases	Percentage
Erythroid hyperplasia	12	23.5
Megaloblastic change	16	31.4
Hypoplastic	7	13.7
Leukaemia	4	7.8
Lymphoma	2	3.9
Dysplasia	8	15.7
Plasma cells	2	3.9

Megaloblastic change was the predominant bone marrow finding in patients with pancytopenia(31.4%) followed by erythroid hyperplasia(23.5%). Leukaemia was found in about 7.8% of patients.

Table 6

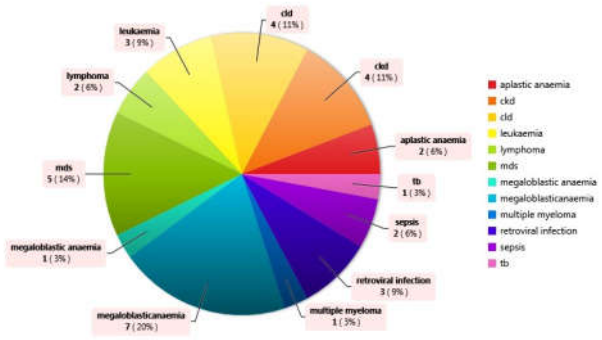
Diagnosis	frequency	percentage
Megaloblastic Anaemia	13	25.41%
Mds	8	15.7%
Cld	6	11.8%
Leukaemia	4	7.8%
Ckd	4	7.8%
Retroviral Infection	3	5.9%
Sepsis	3	5.9%
Tb	3	5.9%
Multiple Myeloma	2	3.9%
Lymphoma	2	3.9%
Aplastic Anemia	2	3.9%
SLE	1	2%



Picture 12 Vit B12 Assay

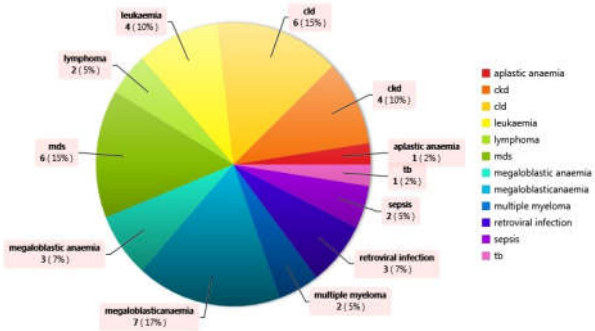
In patients with megaloblastic anaemia, vitamin b12 assay were done.It was found to be below <200pg/ml in about 61.53% patients and were found to be normal in about 23.07% and above normal in 15.38% patients.

Correlation of Clinical Features and Diagnosis



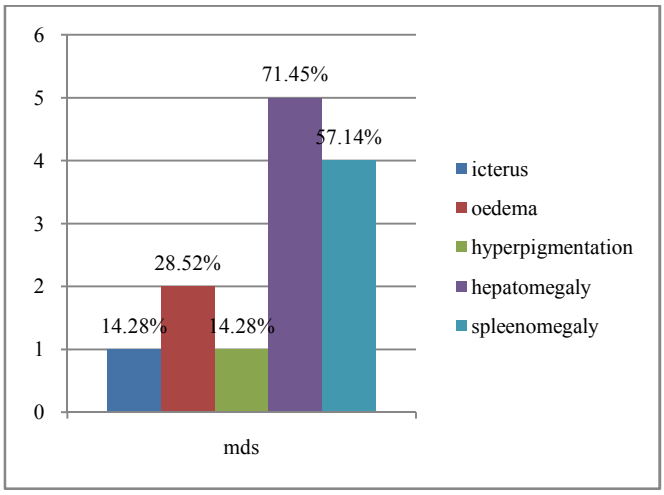
Picture 13

Out of 51 cases of pancytopenia, fever was present in 34 cases. Out of which, 8 cases of megaloblastic anaemia were having fever as a presenting complaint.



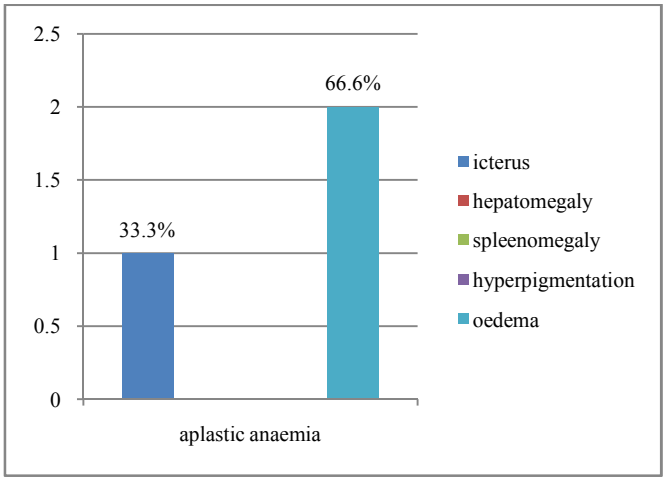
Picture 14

Out of 51 cases of pancytopenia, 41 cases were having fatiguability as a presenting complaint. Pallor was present in all 51 cases of pancytopenia. Bone tenderness was present in 2 out of 4 cases of leukemia.



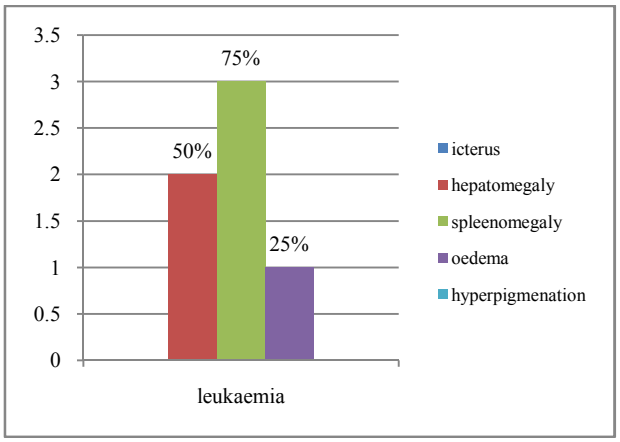
Picture 15 Mds And Clinical Features

In patients with MDS, hepatomegaly and splenomegaly were the predominant physical findings.



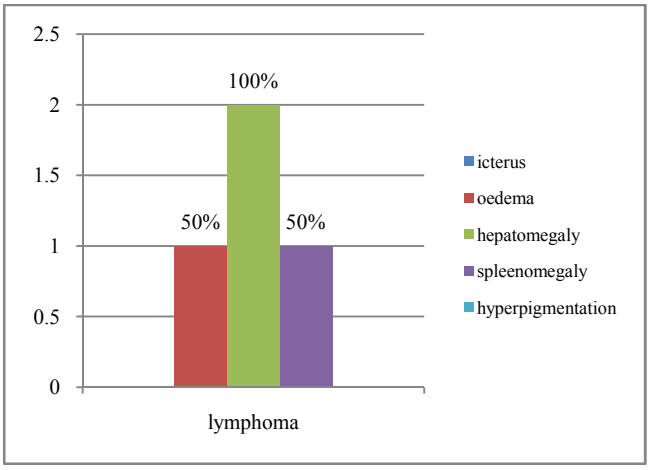
Picture 16 Aplastic Anemia

In patients with aplastic anaemia, splenomegaly and hepatomegaly were absent and oedema, pallor and icterus were the predominant features.



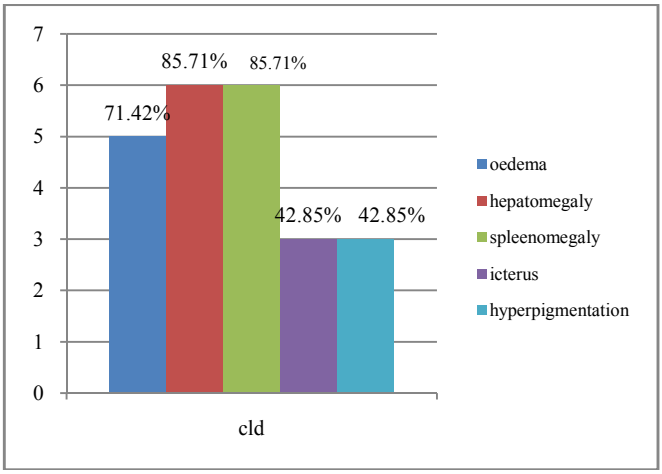
Picture 17 Leukemia

In patients with leukaemia, hepatomegaly and splenomegaly were predominantly present. Icterus and hyperpigmentation was absent.



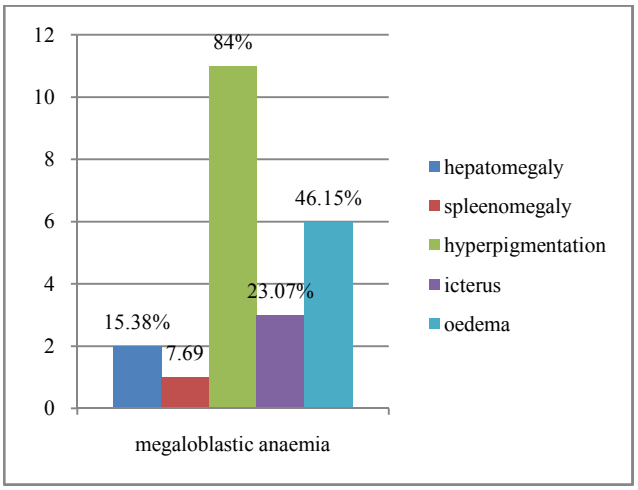
Picture 18 Lymphoma

In patients with lymphoma, hepatomegaly was the major physical finding followed by splenomegaly and oedema. Hyperpigmentation and icterus were not seen.



Picture 19 Chronic Liver Disease (Cld)

In CLD patients with hypersplenism, hepatomegaly and splenomegaly topped the list.(85%) followed by hyperpigmentation(71.42%).



Picture 20 Megaloblastic Anemia

In megaloblastic anaemia, hyperpigmentation was the main physical finding. Splenomegaly was found only in 8% of patients. In sex distribution pattern,major observation was

megaloblastic anaemia was 1.6 times more prevalent in females when compared to males.

DISCUSSION

Pancytopenia is an important hematological entity encountered in our day to day clinical practice. There are varying trends in its clinical pattern, treatment modalities, and outcome.

In this study 51 cases were studied of which 27 patients were females and 24 were males .Females outnumbered males by three while in other studies, done by Gayathri *et al* (5) showed a male predominance with male to female ratio of 1.2:1.

In the present study patients were predominantly in the age group of 51-70 years (41.2%). Mean age was 50years in the study population. According to another Indian study on pancytopenia, 65% of the patients were in the age group of<40years (6).

In the current study, percentage of patients presented with following presenting complaints fever, fatiguability, edema and bleeding were 68%, 80%, 50% and 27% respectively. Whereas asthenia (100%) and fever (28%) were the predominant symptoms in the study by Nafil h *et al* (7). In the study done by B N Gayathri *et al* most common presentation was generalized weakness; other main symptoms were dyspnea, fever and weight loss (5).

In this study100% patients were having pallor, 20% patients were having lymphadenopathy, icterus in 21%, splenomegaly in 35%, hepatomegaly in 39.55% and hyperpigmentation in 35%. So the most common findings were pallor, hepatomegaly and splenomegaly. In a study by Sarode *et al*, 46% had hepatomegaly, 34% had mild splenomegaly (8).While in the study by Gayathri *et al* the most common physical finding was pallor (100%), followed by splenomegaly (35.57%) and hepatomegaly (26.92%) (3).

Haemoglobin values were divided into 3 groups. Hb was 5-9gm% in 51% of cases, >9gm% in 5.9%. Mean haemoglobin was 5.88±1.74. Mean haemoglobin (Hb) was 5.6 +/- 1.7 g/dl in a study by Doshi D *et al* (9). In this study 72.5% of patients had leucocyte count in the range of 1001-3000 cells/mm^3. In the study by Nafil H *et al*, mean leucocyte count was around 2360/mm3 and range was 840-3360 cells /mm3 which was similar to present study (7). In this study, patients with platelet count in the range 20000-50000/mm^3 constituted 43.1% and 50000-100000 in 35.3%.. In the study by Doshi D e tal (9) mean platelet count was 52,250 +/- 24,213 and in the study by Nafil H *et al* (7) mean platelet count 66000/mm3 (range 3000 - 123 000/mm3).

In this study, 80% of patients had ESR value above 40mm/hr. In the study carried out by gayathri *et al* (5), ESR was elevated above 50 mm/hr in 78% of patients. In the present study, 31 patients were having MCV >100 out of which 13 had megaloblastic anaemia, out of 13 cases 61.53% had serum B12 levels <200 pg/ml. So 61% of patients with megaloblastic anemia had reduced Vitamin B12 assay. In the study by Doshi D *et al* (9) mean MCV value was 101.2 +/- 11 in patients with megaloblastic anaemia.

In a recent study, Sarode R etal have analysed 139 consecutive cases of nutritional megaloblastic anaemia over a period of four and a half years, vitamin B12 deficiency was detected in 76%, folate deficiency in 6.8%, combined B12 and folate deficiency in 8.8%; the remaining 7.8% had normal vitamin levels at presentation(8). Percentage of patients with megaloblastic anaemia who were having significant vitamin B12 deficiency in the current study was comparable to other studies.

In the present study, 35% of patients had a macrocytic blood picture, 25% patients had normocytic normochromic blood picture, 19.6% had microcytic hypochromic blood picture and 11.8% had dimorphic blood picture..In the study by Gayathri *et al* (5) the predominant blood picture was dimorphic anemia (37.5%), followed by macrocytic anemia (31.7%).

Bone marrow study in this study revealed megaloblatic changes in 31% patients, erythroid hyperplasia in 23.5% patients, dysplasia in 15.5% and hypoplastic changes in 13.7% of patients. Similar findings were observed in a study by Kumar R *et al* which showed hypercellularity with megaloblastic erythropoiesis as the commonest marrow finding (10).

In this study, hepatomegaly (71.45%) and splenomegaly (57%) were the predominant examination findings in patients with MDS. But according to literature hepatomegaly, splenomegaly, and lymphadenopathy are uncommon findings in MDS. (11,12)

In patients with aplastic anemia, hepatomegaly and splenomegaly were absent; oedema (66%) and icterus (33%) were the predominant findings. According to Biswajit *et al*, most common findings were fatiguability and pallor (13)
In patients with leukaemia, splenomegaly (75%) and hepatomegaly (50%) were the predominant examination findings. In patients with lymphoma, hepatomegaly (100%) splenomegaly (50%) and oedema were the predominant findings. This is in concordance with study conducted by Shahab *et al* (14).

In this study, Megaloblastic anaemia(25.41%) was the most common cause of pancytopenia followed by MDS(15.7%). Other causes were hypersplenism in CLD (11.8%), acute leukaemia (7.8%), CKD (7.8%).Retroviral infection, tuberculosis and sepsis contributed to about 5.9% each, followed by aplastic anemia, lymphoma, multiple myeloma contributing to 3.9% each. Sepsis was following malarial infection and pneumonia leading onto pancytopenia.
In a study by Santra G, Idiopathic aplastic anaemia (20.72 percent) was the commonest cause of pancytopenia, followed by hypersplenism due to chronic liver disease (11.71 percent) (15). Another study by Osama *et al*, also had megaloblastic anaemia as the leading cause of pancytopenia. (3)

Megaloblastic anemia was the most common cause of pancytopenia in this study. In another study from India which evaluated 77 cases of pancytopenia, also showed megaloblastic anemia as the most common cause of pancytopenia.(16).Incidence of megaloblastic anemia in this study was more in 51 to 70 yrs age roup. A study conducted on etiological causes of pancytopenia, also showed megaloblastic anemia more prevalent in < 65yrs age group (17).

According to present study, in megaloblastic anemia patients, hyperpigmentation was seen in 75%, oedema in 46% and splenomegaly in 8%. In 1963 Baker *et al* first described knuckle pigmentation as a manifestation of vitamin B12

deficiency, it was a predominant sign seen in patients with megaloblastic anaemia (18).

9 out of 15 vegetarians in this study population had megaloblastic anemia. Megaloblastic anemia showed significant correlation with vegetarian diet. Similar observations were present in study by Jignesh K *et al* (6).

CONCLUSION

The study conducetd on 51 patients with pancytopenia, showed fatiguability, fever, oedema as the predominant presentations. Pallor, oedema, hepatomegaly and splenomegaly were the predominant examination findings. Most common peripheral smear finding was macrocytic anemia. The study showed megaloblastic anemia as the most common cause of pancytopenia. It was more prevalent in 51 – 70 yrs age group and vegetarians.

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