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Study of Pancytopenia in a Tertiary Care Hospital in North Karnataka

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ABSTRACT

Introduction: *Pancytopenia refers to the combination of anaemia, leukopenia and thrombocytopenia. Causes may be due to bone marrow failure, bone marrow infiltration, ineffective haematopoiesis or peripheral pooling/ destruction. A bone marrow aspirate is usually required to establish the diagnosis. Aetiologies of pancytopenia vary from one geographical region to other. Aim: Study of pancytopenia in patients admitted to a tertiary care hospital in north Karnataka.* ***Methods:*** *This study was conducted at SNMC and HSK, Bagalkot. This study was prospective, observational undertaken for 6-month period between July 2016-January 2017. History, physical examination, and primary blood investigations were done in all patients. Selected patients were evaluated with bone marrow examination.* ***Materials:*** *A total of 69 human subjects were enrolled. A thorough history, clinical examination and blood investigations were carried out.* ***Results:*** *Dimorphic anaemia is common than megaloblastic anaemia. Among those subjected for bone marrow megaloblastic anaemia was commoner than dual deficiency bone marrow. Other causes of pancytopenia were malaria, dengue, enteric fever, and less common causes included sepsis, MDS, TB, HIV, SLE.* ***Conclusion:*** *Nutritional anaemia is commonest cause for pancytopenia. This may be due to megaloblastic anaemia or deficiency of iron/vitamin B_{12}/folate combined.*

Keywords: Pancytopenia, megaloblastic, dimorphic anaemia, infections

INTRODUCTION

Pancytopenia refers to combination of anaemia, leukopenia and thrombocytopenia [1]. WHO definition of anaemia is haemoglobin of less than 13 g/dl in males and 12 g/dl in females [2]. Leukopenia refers to WBC count of less than 4×10^9/L whereas platelet count of less than 150×10^9/L is referred to as thrombocytopenia [3]. Pancytopenia may be caused by bone marrow failure, bone marrow infiltration, ineffective haematopoiesis or peripheral pooling/destruction [1]. However, aetiology of pancytopenia varies from one geographical region to another. Common aetiologies in developing countries like India being megaloblastic anaemia, infection, drugs, hypersplenism and aplastic anaemia. The presenting symptoms are often attributable to anaemia or thrombocytopenia. Leukopenia is an uncommon cause of initial presentation [4,5]. The purpose of this study is to evaluate pancytopenia clinically and investigate accordingly.

Objectives

1) To study the clinical profile of patients with pancytopenia.

2) To find out the aetiology of pancytopenia in northern Karnataka.

3) To identify the specific causes of pancytopenia where bone marrow examination is required.

MATERIALS AND METHODS

Setting

This study is undertaken at S Nijalingappa medical college and HSK hospital, Bagalkot in the department of general medicine. The time of study was between July 2016 to January 2017.

Design

The study design was prospective, observational, non-comparative, non-randomized, analytical.

Participants

Patients more than 15 years of age were included in the study. The study included 69 human subjects fulfilling inclusion and exclusion criteria. The subjects received appropriate specific treatment including blood and blood products.

Study size

Sixty-nine patients admitted in department of general medicine were taken up for study considering inclusion and exclusion criteria mentioned below. All patients were evaluated with thorough history, examinations and blood investigations, bone marrow examination was done in relevant patients where diagnosis was not reached or who did not show any improvement with treatment in the hospital.

Ethical approval

The approval was given by independent ethics committee and written consent from patients was taken.

Method of collection of data

Inclusion criteria: Patients more than 15 years and patients newly detected pancytopenia were included in the study.

Exclusion criteria: Patients receiving chemotherapy and patients receiving radiotherapy were excluded from the study.

In all patients, a detailed history was taken. Complete physical examination was done with emphasis on lymphadenopathy, hepatosplenomegaly, gum hypertrophy and sternal tenderness. Routine blood tests performed included complete hemogram, liver function tests, renal function tests and serology for HIV and HBsAg. CXR and ultrasound was done in all patients. Additional investigations for malaria, dengue, enteric fever, ANA, sputum examination and blood culture were done when deemed necessary. Bone marrow examination was done on patients who did not respond to initial therapy guided by above investigations.

RESULTS

We enrolled 69 patients of pancytopenia out of which 33 were males and 36 were females. Bone marrow examination was done in 19 patients. Age distribution is as shown in Figure 1.

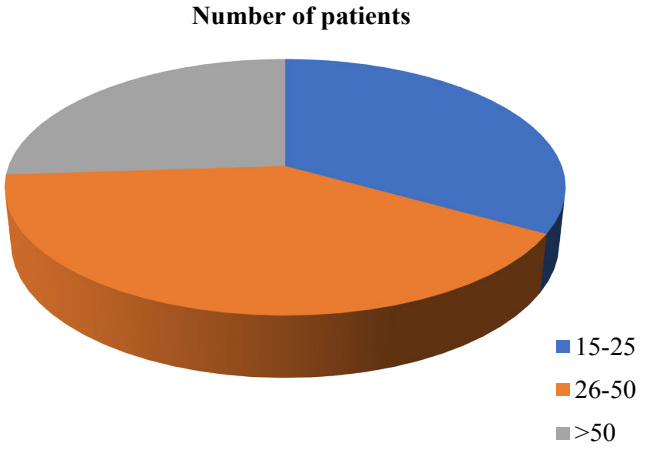

Figure 1 Pie chart depicting age distribution of pancytopenia-age in years with respect to number

Twenty-three patients were in the age group of 15-25, 28 patients were in between 26-50 and 18 were more than 50 years of age.

Generalised weakness was the major presenting complaint present in 64 patients, followed by fever seen in 29 cases. None of patients presented with any bleeding tendencies.

On physical examination pallor was present in 55 cases. Icterus was present in 20 cases. Clinically detectable hepatomegaly was in 5 patients whereas splenomegaly in 7 cases. Lymphadenopathy seen in only one case. Other symptoms like oedema, dyspnoea, skin lesions were seen in 13 cases. Investigation details are shown in Tables 1-5.

Table 1 Haemoglobin range and number of individuals

Haemoglobin in gram/dl	No. of patients
Less than 4.9	30
5-7.9	21
8-10.9	12
More than 11	6

Table 2 Leucocyte counts range and number of individuals

Total leucocyte count/cu mm	No. of patients
Less than 500	1
501-1000	2
1001-2000	13
2001-3999	53

Table 3 Platelets counts range and number of individuals

Platelet count/cu mm	No. of patients
Less than 20000	8
20001-40000	17
40001-60000	9
60001-80000	6
80001-100000	17
100001-120000	7
More than 120001	5

Bone marrow was performed in 19 cases. One case was myelodysplasia and others were suggestive of megaloblastic anaemia and dual deficiency marrow. Remaining cases showed improvement with aetiology specific treatment. Hence bone marrow was not performed in these cases.

Table 4 Aetiology of pancytopenia is as tabulated below

Aetiology	Number of cases
Dimorphic anemia	25 (36.23%)
Megaloblastic anemia	24 (34.78%)
Vivax malaria	3 (4.34%)
Falciparum malaria	4 (5.79%)
Tuberculosis	1 (1.44%)
HIV	1 (1.44%)
Pneumonia with sepsis	1(1.44%)
Dengue	2 (2.89%)
Enteric fever	2 (2.89%)
Myelodysplasia	1 (1.44%)
SLE	1(1.44%)
Chronic kidney disease	2 (2.89%)
Tuberculosis with HIV	2 (2.89%)

Table 5 Sex distribution of aetiology (aetiologies in males and females)

Aetiology	Male	Female
Dimorphic anemia	12	13
Megaloblastic anemia	12	12
Malaria	4	3
Tuberculosis	0	1
HIV	0	1
Pneumonia with sepsis	1	0
Dengue	0	2
Enteric fever	0	2
Myelodysplasia	1	0
SLE	0	1
CKD	1	1
Tuberculosis with HIV	2	0

DISCUSSION

Pancytopenia is not a disease but a manifestation of various illnesses. It has varied manifestations which may be due to anaemia, thrombocytopenia and sometimes life threatening leukopenia. It can be an incidental finding too. This study was undertaken to make an effort to find out possible aetiologies of pancytopenia. There are various studies on pancytopenia and the causes of pancytopenia are varied with respect to geography, methods of studies, drug exposure, infections, and habits of an individual.

In our study, nutritional anaemia was the most common cause of pancytopenia which includes dimorphic anaemia and megaloblastic anaemia in 36.23% and 34.78% cases respectively based on complete hemogram. These individuals were given aetiology specific treatment in the hospital and followed up. Those who did not respond to treatment, those who had significant clinical findings and in those individuals where nutritional deficiency was unlikely were subjected to bone marrow examination. Bone marrow studies reveal 13 subjects with pancytopenia had megaloblastic anaemia, 5 cases were having marrow suggestive of dual deficiency-iron and vitamin B_{12}/folate and one was diagnosed as myelodysplastic syndrome.

Table 6 Comparison of various studies on megaloblastic anaemia

Studies	Megaloblastic anaemia as aetiology
Mir, et al. GMC, Srinagar, J&K [5]	72.72%
Akshata, et al. Vydehi IMS RC [6]	20%
Thakkar, et al. C U Shah MC [4]	37%
Sankepally, Gandhi hospital [7]	53%
Khunger, et al. [3]	72%
Tilak, et al. [8]	68%
Gayathri, et al. [9]	74%
Deepak Kumar, et al. [10]	18.75%
Present study	34.78%

The high incidence of megaloblastic anaemia correlates with nutritional deficiencies common in subcontinent [11] (Table 6).

Megaloblastic anaemia should be considered in all patients of pancytopenia, thus peripheral smear should be considered and presence of macrocytes, hyper-segmented neutrophils favour the diagnosis. These cases generally show improvement with vitamin B_{12} and folic acid [7].

Dimorphic anaemia is more common than megaloblastic anaemia in pancytopenia cases. This finding is correlating with other studies [9].

In such cases, invasive procedures like bone marrow examination can be avoided and may be considered if there is no improvement with iron, vitamin B_{12}/ folate treatment.

Infections are known to cause pancytopenia. In our study, malaria as an aetiology for pancytopenia was noted in 7 cases which accounted 10.13%. Others studies showing malaria as aetiology of pancytopenia is tabulated below (Table 7).

Table 7 Comparison of various studies on malaria

Studies	Malaria as aetiology in %
Gayatri, et al. [9]	1.93%
Khunger, et al. [3]	1%
Tilak, et al. [8]	3.90%
Kumar, et al. [10]	3%
Akshata, et al. [6]	8%
Thakkar, et al. [4]	19%
Our study	10.13%

In many parts of India, TB has been postulated as an aetiological agent in pancytopenia. Table 8 gives us correlation between TB and pancytopenia.

Table 8 Comparison of various studies on tuberculosis

Studies	Tuberculosis as aetiology
Tariq, et al. [5]	3.03% (4 cases)
Thakkar, et al. [4]	5 % (5 cases)
Khunger, et al. [3]	1 case
Kumar, et al. [10]	1 case
Khodke, et al. [11]	1 case
Tilak, et al. [8]	1 case
Pasam, et al. [12]	1 case
Our study	1.44% (1 case)

HIV as an aetiological agent for disorder of haematopoietic system is well known (Table 9). It may be due to direct result of infection itself or indirectly through drugs, neoplasms, or secondary infections [13,14].

Table 9 Comparison of various studies on HIV

Studies	HIV as aetiology
Sankepally, et al. [7]	1 case (3%)
Akshatha, et al. [6]	1 case (2%)
Khodke, et al. [11]	1 case
Thakkar, et al. [4]	1 (5.56%)
Our study	1 (1.44%)

Sepsis is very well associated with pancytopenia. Table 10 compares few studies on sepsis and pancytopenia.

Table 10 Comparison of various studies on sepsis

Studies	Sepsis association in %
Akshatha, et al. [6]	2%
Sankepally, et al. [7]	3%
Our study	1.44%

Viral fever cause pancytopenia. There are different viruses which cause pancytopenia. In our study 2 cases are associated with pancytopenia (Table 11).

Table 11 Comparison of various studies on viral fever

Studies	Viral fever as aetiology
Akshatha, et al. [6]	4% (dengue)
Thakkar, et al. [4]	1%
Our study	2.89% (dengue)

Enteric fever another common infection in our country is associated with pancytopenia. Table 12 shows comparative data for enteric fever with various studies.

Table 12 Comparison of various studies on enteric fever

Studies	Enteric fever as aetiology
Kumar, et al. [10]	2 cases
Thakkar, et al. [4]	3 cases (3%)
Our study	2 cases (2.89%)

Myelodysplastic syndrome (MDS) occurs in 5 per 100000 population in general population, where as in more than 70 years it occurs in 22-45 per 100000 population (Table 13) [13].

Table 13 Comparison of various studies on myelodysplastic syndrome

Studies	MDS as aetiology
Sankepally, et al. [7]	1 case (3%)
Akshatha, et al. [6]	2 cases (4%)
Tariq, et al. [5]	4 cases (3.03%)
Deepak kumar, et al. [10]	8.30%
Lakhey, et al. [13]	7.40%
Khunger, et al. [3]	4 cases
Kumar, et al. [10]	6 cases
Khodke, et al. [11]	1 case
Our study	1 case (1.44%)

Systemic lupus erythematosus (SLE) is associated with pancytopenia in our study in 1 case (Table 14).

Table 14 Comparison of various studies on systemic lupus erythematosus

Studies	SLE as aetiology
Akshatha, et al.	3 cases (6%)
Sankepally, et al.	1 case (3%)
Our study	1 case (1.44%)

In our study pancytopenia was seen in 2 cases (2.89%) who had chronic kidney disease.

Our study noted 2 cases (2.89%) of pancytopenia in patients who were co infected with HIV and TB.

In chronically ill patients, folic acid deficiency precipitates marrow changes which is manifested as pancytopenia [13].

CONCLUSION

Pancytopenia is caused by various conditions. In our study, nutritional anaemia was most common cause. Nutritional anaemia includes dual deficiency (iron and vitamin B_{12}/folate) and megaloblastic anaemia. There are various predisposing factors for these anaemias like alcoholism, hypothyroidism, self-limiting illnesses, puberty, pregnancy etc. which are noted in our study. Hence it is necessary to treat such cases with iron and/or vitamin B_{12}/folate, to repeat hemogram after few weeks and if necessary further evaluation with invasive procedure like bone marrow may be considered. There are other treatable causes like dengue, malaria, enteric fever, and TB. In such cases pancytopenia resolves over a period

of time after aetiology specific treatment is given. However, bone marrow becomes necessary if there is no improvement or there are signs which are suggestive of severe diseases like leukaemia, MDS etc.

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