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Hematologic Analysis of Pancytopenia and Correlation with Bone Marrow Findings: Study in a Tertiary Care Centre

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Abstract
Background: *Pancytopenia is one of the most common haematological disorders, which is characterized by decrease in all the formed elements of blood. Pancytopenia occurs either due to certain primary conditions affecting the bone marrow or involvement of bone marrow secondarily by various systemic pathological process.*
Objectives: *The main objectives of the study are to evaluate the incidence and pattern of pancytopenia by analyzing the haematological data available during one year in the central laboratory of a tertiary care hospital in Navi Mumbai and to correlate the haematological findings with bone marrow findings.*
Methods: *The present prospective study, consists of an analysis of haematological data over a period of one year and analysing the incidence and pattern of pancytopenia and to correlate the haematological findings with bone marrow findings.*
Results: *In this study, 100 cases of Pancytopenia are diagnosed with an incidence of 0.47%. Bone marrow findings are available in only 15% cases of pancytopenia, and maximum incidence of pancytopenia, 5 cases (33.3%) is associated with chronic liver disease, followed by association with megaloblastic anaemia, 2 (13.3%) cases. In rest of the cases, definitive diagnosis of pancytopenia is not available, though the patients are being treated for various clinical conditions.*
Conclusion: *The highest incidence of pancytopenia is found in age group of 40-70 years. Bone marrow findings confirmed the diagnosis in 15% cases, showing Dysmegakaryopoiesis maximum incidence of cases associated with erythroid hyperplasia with megaloblastoid changes and chronic liver disease accounted in 21 cases of pancytopenia.*
Keywords: *Pancytopenia, Megaloblastoid change, Dysmegakaryopoiesis*

Introduction

Pancytopenia, literally meaning decrease in all cells of blood, is one of the relatively most common haematological disorders in clinical practice, which is characterized by decrease in all the formed elements of blood. Pancytopenia is not a specific clinical entity but conglomeration of decreased haematological values of formed elements of blood, occurs as primary clinical entity or may occur secondarily to other

haematological or non-haematological disorders, and is an amalgamation of a haematological triad of concurrently occurring anaemia, leukopenia and thrombocytopenia, often defined as a concurrent decrease in all the formed elements of the blood and a patient is considered to have pancytopenia if a haematological triad with following criteria is fulfilled: Haemoglobin is less than 13.5 gm/dl in male and 11.5 gm/dl in female, WBC count is less than 4×109/L and platelet lower than 150×109/L[1-3].

Pancytopenia, being not a specific entity, is characterized by fatigue, weakness and dyspnoea due to anaemia and increase vulnerability to infections as a result of leucopenia and bleeding and bruising tendencies attributable to low platelet count[4-6].

In the present study an attempt is being made to find out the incidence and causes of pancytopenia in a tertiary care hospital in Navi Mumbai and correlate the haematological findings with bone marrow findings in cases where bone marrow findings are available.

Aims and Objectives

The main aims and objectives of the present study are to find out the overall incidence of pancytopenia and to determine the causes of pancytopenia by analyzing the hematological dataavailable in the Central Laboratory of a tertiary care hospital in Navi Mumbai region and co-relate the findings with available bone marrow findings in cases wherever such findings are available.

Materials and Methods

The present prospective is conducted for a period of one year from 1st July 2015 to 30th June 2016. The study essentially consisted of analysis of hematological data and bone marrow examination data available in the Central Laboratory of a tertiary care hospital located in a peripheral most part of Navi Mumbai, an area which consists of unique demographic composition of diverse population of multiple ethnic and socioeconomic background. During the period of study, the haematological data and bone marrow findings, the latter wherever available, with inclusion criteria essential for categorizing a patient to be having pancytopenia such as a Haemoglobin level below 13.5g/dl for males and 11.5g/dl for females and leukocyte count less than 4,000 cells/cu.mm and a platelet count lower than 150,000/cu.mm are included in the study. The patients receiving therapeutic blood or blood components and also patients who are known to be under chemotherapy for prolonged debilitating illnesses including malignant neoplastic conditions or radiotherapy for obvious reasons are excluded from the study.

Results

In the present study a total of 21,250 blood samples received in the central laboratory were analyzed, out of which 100 cases with evidence of pancytopenia are noted with an overall incidence of pancytopenia of 0.47%. Maximum incidence of pancytopenia is noted in males, 59 (0.27%) cases, while the incidence is found to be much lower in females, 41 (0.19%) cases, with a male to female ratio of 1.4: 1. Though the present study showed pancytopenia could affect any age group, the incidence of pancytopenia is found to be highest, 33 (0.15%) cases, in the age group of 40-60 years [Chart 1], while the incidence of pancytopenia is found to be lowest, 3 (0.014%) cases, in the age group of 0-10 years.

Bone marrow findings are available in only 15 (15%) cases of a total 100 cases of pancytopenia [Chart 2]. Bone marrow findings in a maximum of 5 (33.3%) cases showed features of erythroid hyperplasia with megaloblastoid change. Two (13.3%) cases each with features of Dyserythr-opoiesis with megakaryocytic hyperplasia and dyserythropoiesis, dysmyelopoiesis with megakaryocytic hypoplasia respectively are also noted. Two (13.3%) cases of dyserythropoiesis with megakaryocytic hypoplasia are also found, along with one (6.6%) case each with a diagnosis of Dyserythropoiesis with increased eosinophilic precursors and mixed (normoblastic and micro-

normoblastic) erythropoiesis with megakaryocytic dysplasia respectively. In other remaining 85% of cases, no definitive diagnosis is not available inasmuch as bone marrow findings are being unavailable all the remaining cases.

In the present study, the main attributable, direct or indirect, causes of pancytopenia included chronic liver diseases in highest number of cases of pancytopenia, 21 (21%) cases, followed by infections 21 (21%) cases, including chronic infections such as tuberculosis, which are form bulk of second most common causes of pancytopenia. Anaemia, 18 (18%) cases, which included three cases of megaloblastoid anaemia and two cases of aplastic anaemia are another most common causes of pancytopenia.; nine (9%) cases of chronic renal disease and eight (8%) cases of splenomegaly respectively are found to be associated with pancytopenia. One (1%) case of pancytopenia is found to be occurring in a known case of acute lymphoblastic leukaemia which was previously diagnosed in another outside health care centre. In a large group of 22 (22%) cases, which included three senile patients, of pancytopenia no definite aetiological or pathogenetic factors could be determined.

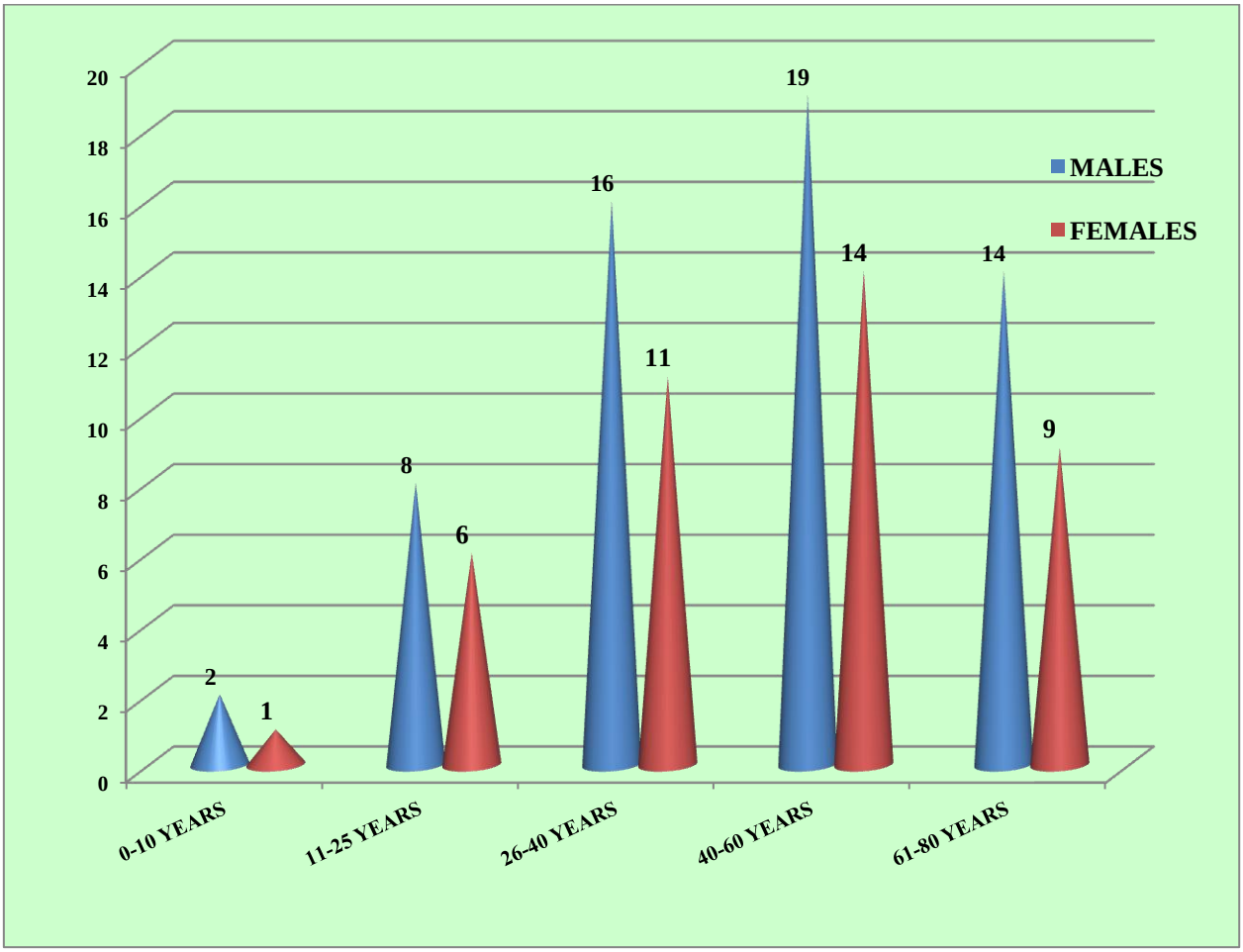

Chart 1: Chart showing age and sex incidence of pancytopenia

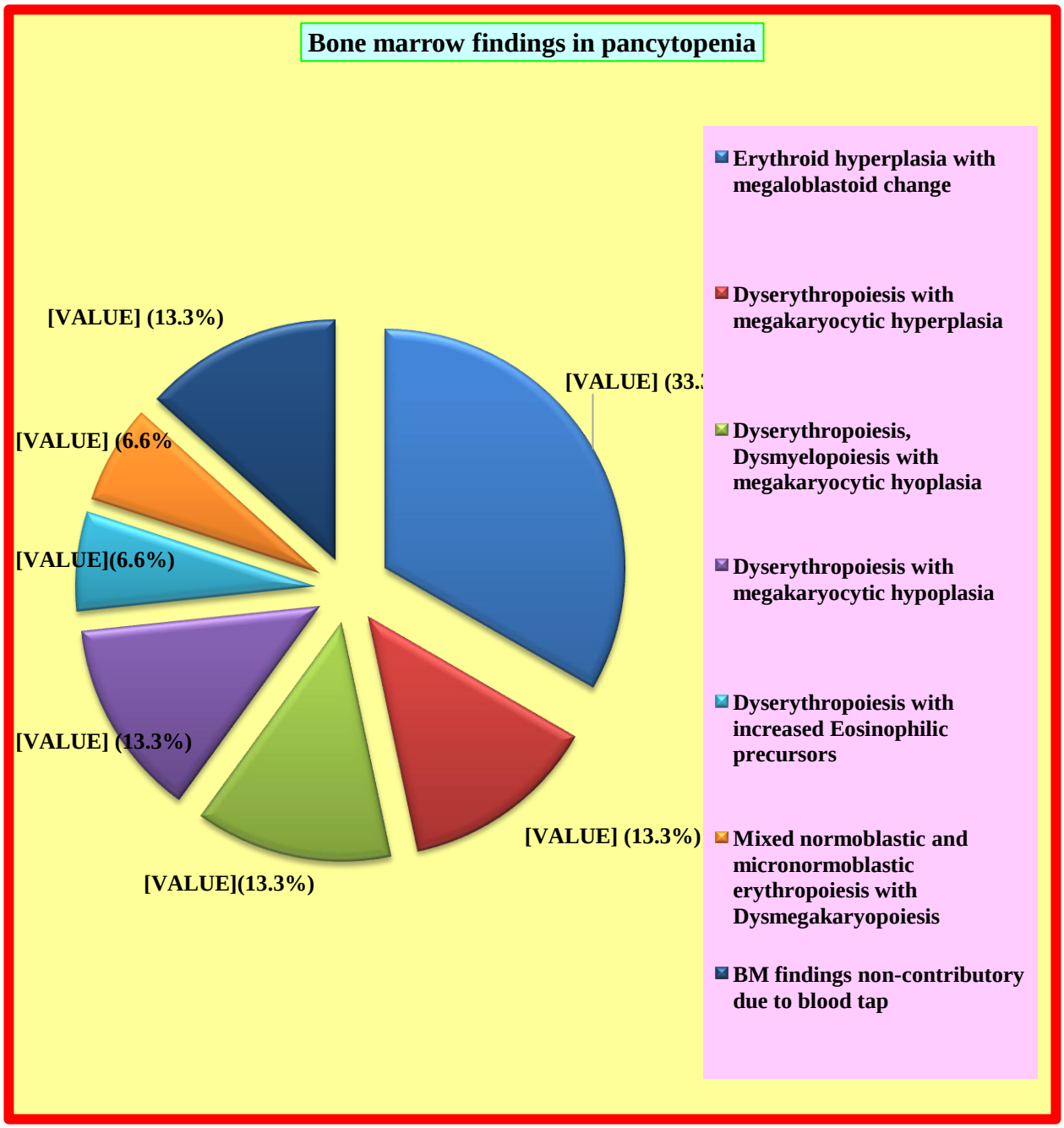

Chart 2: Chart showing bone marrow findings in pancytopenia

Table 1. Causes Of Pancytopenia

S.No	Causes Of Pancytopenia	Number Of Cases	Percentage
1	Chronic liver disease	21	21%
2	Anemia	18	18%
3	Infections including pulmonary tuberculosis and pleura effusion	21	21%
4	Chronic Kidney disease	9	9%
5	Splenomegaly	8	8%
6	Acute Lymphoblastic Leukemia	1	1%
7	Miscellaneous including senile individuals	22	22%
	Total	100	100%

.

Table 2. Table Showing Comparative Study of Number of Cases, Age-Wise and Gender-Wise Incidence and Most Common Causes of Pancytopenia

Study	Year	No. Of cases	Male to Female ratio	Highest incidence seen in age group	Most common cause (%)	Second common cause (%)
Tilak et al [6]	1999	205	1.13:1	5-20 years (32.4%)	Megaloblastic anaemia (68%)	Aplastic anaemia (7.7%)
Khodke et al [5]	2000	50	1.3:1	12-30 years	Megaloblastic anaemia (44%)	Aplastic anaemia (14%)
Khudair Abbas et al [14]	2004	105	1.3:1	21-30 years	Acute leukaemia (30.47%)	Aplastic anaemia (17.14%)
Pathak R.et al [10]	2009	102	1: 1.2	15-30 years (29.4%)	Hypoplastic anaemias (32.3%)	Erythroid hyperplasia (20%)
Gayathri and Rao [12]	2011	104	1.2:1	2-18 years (29.04%)	Megaloblastic anemia (74%)	Aplastic anemia (18%)
Deepak Kumar et al [13]	2011	100	1.8:1	30-49 Years (41%)	Megaloblastic anaemia (68%)	Aplastic Anaemia(7.7%)
Deepa T. et al [15]	2010-14	100	1.7: 1	10-80 years	Megaloblastic anaemia (78%)	Aplastic anaemia (12%)
Sweta et al [11]	2014	100	1.5:1	21-35 years (43%)	Megaloblastic anaemia (66%)	Aplastic anaemia (18%)
Current study	2016	100	1.4:1	40-60 years (35%)	Chronic liver disease (21%)	Infections including chronic infections such as tuberculosis (21%)

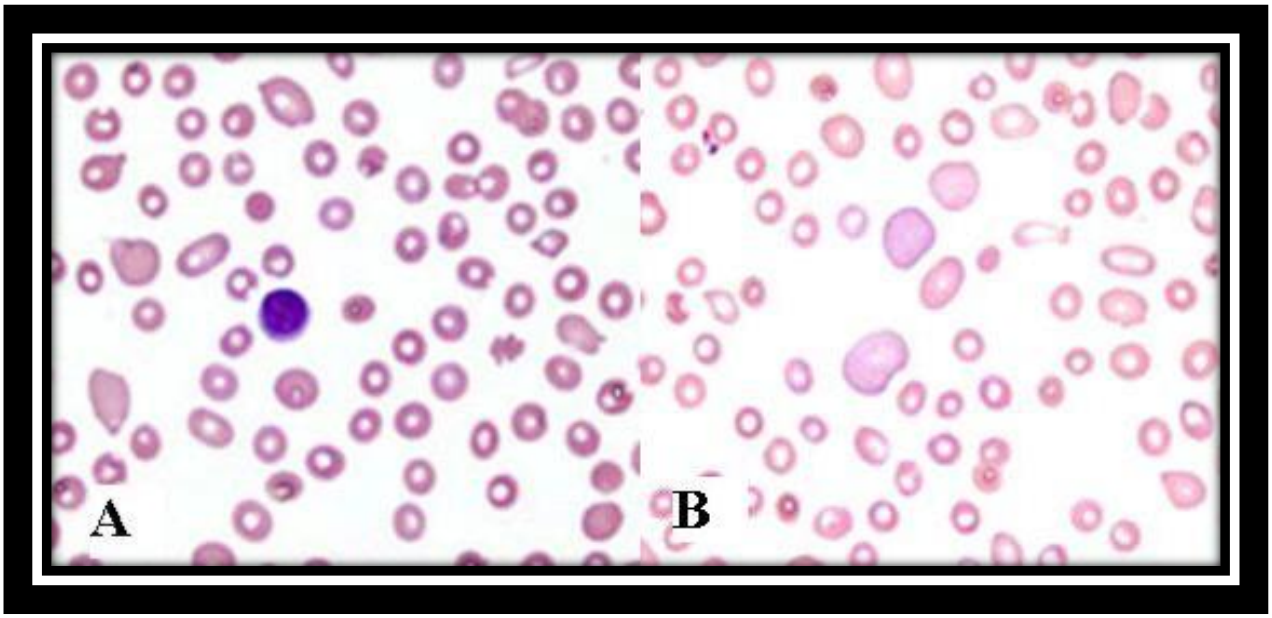

Figure 1. Photomicrograph Showing Blood Picture with A. Marked Anisopoikiloctosis; B. Marked Polychromasia

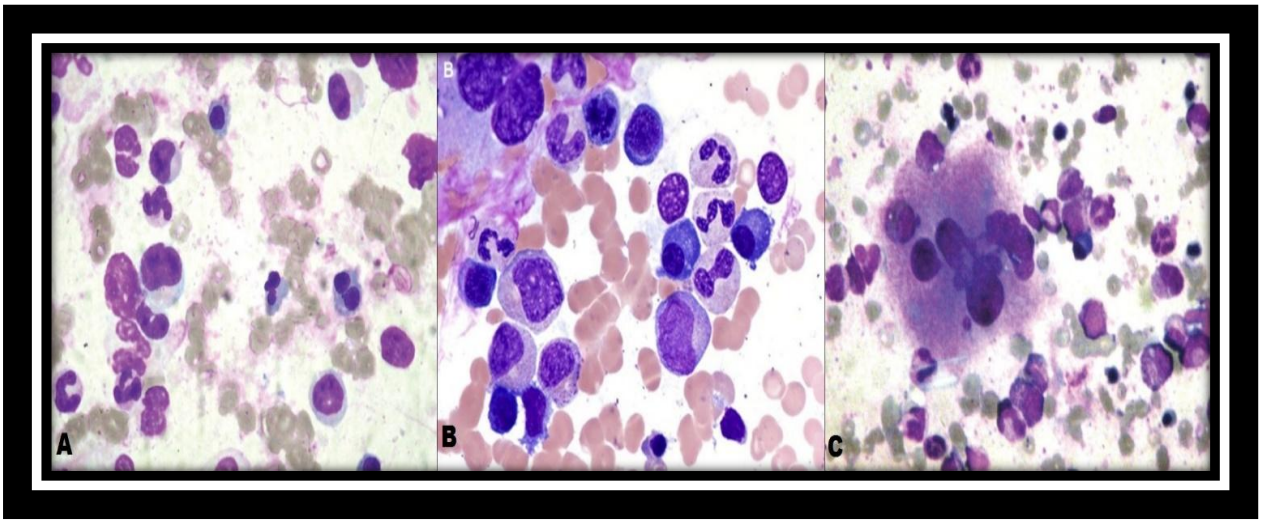

Figure 2. Photomicrograph of Bone Marrow Smeaars Showing A. Dyserythropoiesis; B. Dysmyelopoiesis; C. Dysmegakaryopoiesis

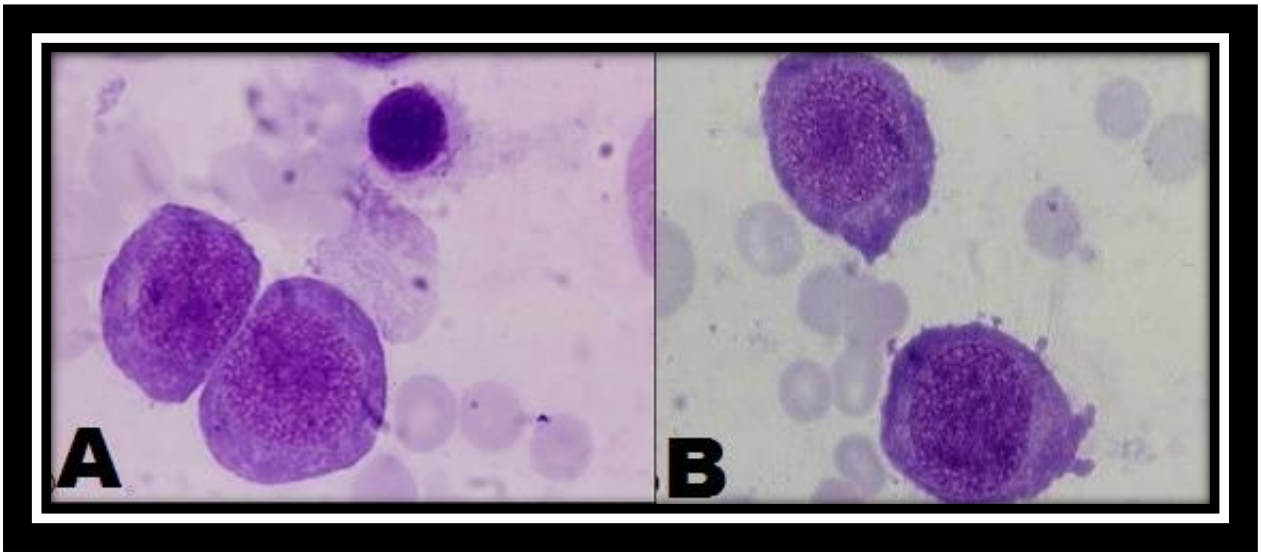

Figure 3. Photomicragraphs of Bone Marrow Smears Showing A. Erythroblasts with Megaloblastoid Changes in Varying Stages of Development; B. Two Megaloblasts

Discussion

Pancytopenia, not being a specific disease, is clinico-haematological entity consisting of a triad of haematological findings resulting from decrease in all the formed elements of blood, which could occur as a result of host of varied disease processes [7-9]. In the present study, an attempt is being made to find the overall incidence of Pancytopenia by analysis of haematogical data of blood samples received in the central laboratory of a tertiary care Hospital and thereby establish causes of Pancytopenia and correlate the haematological findings with bone marrow findings in cases wherever bone marrow studies are available. In the present study, a total of haematological data from 21,250 blood samples is analyzed and 100 cases of pancytopenia are diagnosed with an incidence of 0.47%. The highest incidence by age, 33 (0.15%) cases, is seen in the age group of 40-60 years, which is slightly higher than incidence (29.4%) for the age group of 15-30 years in the studied conducted by Pathak et al[10] (Table 2) and15-35 years with an incidence of 43% in studies conducted by Sweta et al [11]. The highest incidence (29.04%) by age according to a study by Gayatri and Rao et a[12] is noted in the age group of 2-18 years. The highest age incidence of pancytopenia in the current study

is nearly similar to the findings of Deepak Kumar et al [13] which is 30-49 years. Highest incidence of pancytopenia in the present study is found in males, 59 (0.27%) cases than in females, 41 (0.19%) cases, with male to female ratio being 1.4:1 which is almost similar(Table 2)to the ratio found in the studies of Khodke et al [5] Sweta at al [11] and Khudair et al [14]. In the present study, the most common cause of pancytopenia is found to be chronic liver disease (21%) and the second commonest causeis the category of infections (21%) including chronic infections such as pulmonary tuberculosis and pleural effusion. The commonest causes of pancyotopenia in the present study are highly distinct from the commonest causes of pancytopenia furnished in all other comparative studies by various authors [Table 2]. In the present study bone marrow findings are available in only 15% of pancytopenia cases and highest number (33.3%) are diagnostic of erythroid hyperplasia with megaloblastoid change.

In a study by Khodke et al megaloblastic anaemia (44%) and aplastic anaemia (14%) accounted as most common and second most common cause of pancytopenia respectively. Similarly, Tilak et al[6]in their study conducted in 1999 found that the most common cause of pancytopenia was megaloblastic anaemia (68%) with aplastic anaemia being second most common cause (7.7%). Megaloblastic anaemia was found to be main cause of pancytopenia in the studies of Gayatri et al[12], Deepak kumar et al [13] in 74% and 68% of cases of pancytopenia respectively. Studies conducted by Deepa T. et al[15] and Sweta at al[11] found megaloblastic anaemia as main causative factor in pancytopenia in 78% and 66% respectively. Khudair et al[14] in their studyin Iraq found acute leukaemias (30.47%) to be the main cause of pancytopenia. Pathak et al[10] in his study conducted in Nepal found hypoplastic anaemias (32.3%) as the predominant cause of pancyt-openia. Other authors such as Kumar et al [16] reported aplastic anaemia (29.5%) to be the main cause of pancytopenia. Bhaskar Thakkar et al [17] found megaloblastic anaemia (37%) to be the primary predominant aetiological factor for pancytopenia while malaria (19%) interestingly was found as second commonest cause. Savage et al [18] from Zimbabwe found megaloblastic anaemia (35.8%) to be the predominant clinical entity responsible for pancytopenia while Pine at al[19] in their study conducted in the United States of America found entirely different causative factor for pancytopenia in the form of infectious diseases in a whopping 64% of pancytopenia patients which compares favourably with the most common cause of pancytopenia found in the present study.

Conclusion

Pancytopenia which presents as a constellation of clinical features arising out of concurrent decrease in the formed elements of blood is commonly encountered in clinical practice in the backdrop of many of the clinical disorders. The present prospective study brings out certain interesting facts regarding the incidence and causes of pancytopenia.

In the current study the highest incidence of pancytopenia, 35%, is noted in the age group of 40-60 years, which is relatively a higher age group to be affected by pancytopenia as per the comparative statistics of similar studies by other authors. Another interesting observation is that the most common and the second most cause of pancytopenia are chronic liver disease and infections including chronic infections such as tuberculosis and pleural effusion, respectively, each being responsible for 21% pancytopenia cases. The most common and second most common cause of pancytopenia are distinctly different from common causes of pancytopenia found in different comparative studies conducted by various authors. In the present study, bone marrow studies are available in only 15% of cases of pancytopenia, out of which the highest number of cases, 33.3%, are diagnosed as erythroid hyperplasia with megalablastoid change.

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