Research Article

Pancytopenia- A clinicopathological analysis of 132 cases

Sharma Anjana[1], Ravindranath M[2], Maheep B[3]

[1]Dr Anjana Sharma, Assistant Professor, Department of Pathology, C. C. M. Medical College, Durg (C.G.), [2]Dr Ravindranath M, Head of Department, Department of Pathology, J. L. N. Hospital & Research Centre, Bhilai (C.G.), [3]Bhalla Maheep, Ex Joint Director, J. L. N. Hospital & Research Centre, Bhilai, C. G, India.

Address for Correspondence: Dr. Anjana Sharma, Block-13, Plot- 6, ML Nehru Nagar (East), Bhilai, Distt- Durg, Email id- anj_sh2000@yahoo.co.in

Abstract

Introduction: Pancytopenia is a challenging clinical entity for both clinicians and hematologists. The severity of pancytopenia and the underlying pathology determine the management and prognosis of these patients. Laboratory plays central role in determining the etiology of pancytopenia and thereby guiding the clinician in proper management of patient. The objective of the present study was to study the etiological factor, clinical features, peripheral blood picture, hematological parameters and bone marrow findings in different causes of pancytopenia in this region. **Materials and Methods:** In the prospective study carried out, a total of 132 patients of pancytopenia were evaluated for clinical features, hematological parameters, peripheral smear and bone marrow findings in Department of Pathology, Jawaharlal Nehru Hospital and Research Center, Bhilai, C .G. during a two years study period from March 2009 to April 2011. **Results:** Among the 132 cases studied, the age of patients studied ranged from 2.5 to 76 years with a mean age of 38.10 years. The maximum number of patients (53.7%) were noted in 2nd to 4th decade of age**.** Slight male preponderance was observed with male: female ratio 1.5:1. On analyzing for the specific causes of pancytopenia, majority of cases were found to be due to megaloblastic anemia (50.7%), followed by hypersplenism (10.6.%), malaria (9.8%), leukemia (9.0%) and aplastic anemia (7.5%) cases. Other rare causes includes Wilson disease, Kala azar, HIV, alcoholism etc. Clinical presentation of the patients with pancytopenia varied but pallor was the most common clinical finding (96.9%) followed by fever (59.8%). Dimorphic with macrocytic anemia was the predominant peripheral blood picture. Bone marrow aspiration was done in 101 cases and biopsy in 10 cases. The commonest finding was hypercellularity in marrow with megaloblastic erythropoiesis. **Conclusion:** The present study concludes that detailed clinical examination along with readily available diagnostic tools like hematological parameters, peripheral smear and bone marrow aspiration can help in prompt diagnosis and treatment in patients with pancytopenia.

Keywords: Bone marrow aspiration, Megaloblastic anemia, Pancytopenia.

Introduction

Pancytopenia is the simultaneous presence of anemia, leucopenia and thrombocytopenia [1,2]. It is an important hematological entity encountered in clinical practice. Anemia, bleeding and infection are the cardinal signs of pancytopenia [3]. The initial presenting symptoms are usually attributable to anemia or thrombocytopenia whereas leucopenia becomes the most serious threat to life during the subsequent course of the disorder [1]. The severity of pancytopenia and the underlying pathology determine the management and prognosis of these patients [4]. Pancytopenia covers a large number of pathological entities [5]. In most cases the etiology can be determined from consideration of the clinical features, blood examination, examination of the bone marrow aspirate and trephine biopsy. Occasionally extensive investigations and prolonged observation are necessary before a definitive diagnosis can be established [1].

Laboratory plays a central role in guiding the clinician for proper management of pancytopenia. There has been scarce literature in this region on Pancytopenia. Therefore the study "Pancytopenia- A. Clinico-

Manuscript received 10th July 2016
Reviewed: 24th July 2016
Author Corrected: 4th August 2016
Accepted for Publication 16th August 2016

pathological study of cases" has been undertaken so that data of various prevalent causes of pancytopenia can be established. The data can be of help in planning the diagnostic and therapeutic approach for these patients in this institution.

Objective

The objective was to study the etiological factors, clinical features, peripheral blood picture, hemato-logical parameters and bone marrow findings in different causes of pancytopenia.

Material and Methods

The present study was carried out in the Department of Pathology, Jawaharlal Nehru Hospital and research centre Bhilai, BSP, C.G. A total of 132 cases which includes all the cases of pancytopenia observed during two years study period (April 2009- March 2011) were recorded.

The sample technique was random sampling. Data was collected from the indoor patient population and both male and female were included in study. Patients were mostly from urban areas and nearby rural areas. Both children and adults were included in study.

Criteria for inclusion

- All ages and both the sexes
- Anemia (Hb <10gm/dl)
- Leucopenia (WBC<$4x10^9$/l)
- Thrombocytopenia (Platelets <1,50,000/$mm^{\wedge 3}$).

Criteria for exclusion

- Already on the treatment for diseases like aplastic anemia and leukemia.
- Patients on radiotherapy and chemotherapy.

Data was collected by interviewing patients about complaints, checking patient record and examining the patient and making observational chart.

Data was analyzed using Microsoft Excel spread sheet with simple statistical methods like Mean and Standard Deviation.

Observations

Demographic Profile- The total blood samples received in our laboratory for various haematological investigations including complete blood cell count during the study period was 108000.

The age of patients studied ranged from 2.5 to 76 years (Mean age was 38.10years; SD± 20.03).

The maximum number of patients (53.7%) were noted in 2nd to 4th decade of age. (**Table 1).** Slight male preponderance was observed (male: female ratio was 1.5:1).

Table-1: Showing age and sex distribution of total 132 patients with Pancytopenia.

Sr. No.	Age (Yrs)	Females	Males	Total no of cases (%)
1	0 -10	3	1	4(3)
2	11-20	12	19	31(23.4)
3	21-30	6	19	25(18.9)
4	31-40	10	5	15(11.3)
5	41-50	4	15	19(14.3)
6	51-60	9	10	19(14.3)
7	61-70	5	4	9(6.8)
8	71-80	3	7	10(7.5)
	Total	**52**	**80**	**132**

Causes of Pancytopenia- The analysis for the specific causes of pancytopenia is shown **(Table II).**

Table-II: Showing causes of pancytopenia in total 132 cases.

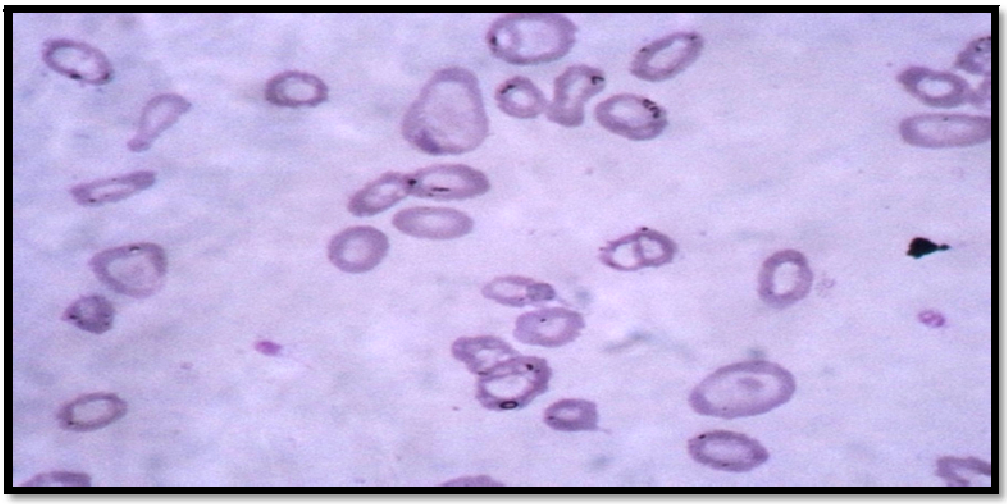
S. No.	Cause	Males	Females	Total No. of cases (%)
1.	Megaloblastic anemia	43	24	67 (50.7%)
2.	Hypersplenism	7	7	14 (10.6%)
3.	Malaria	9	4	13 (9.8%)
4.	Aplastic anemia	5	5	10(7.5%)
5.	Subleukaemic phase of acute leukemia (AL)	6	6	12 (9.0%)
6.	Kala –azar (KA)	1	0	1 (0.75%)
7.	Infection and sepsis (INF)	1	1	2(1.5%)
8.	Drug induced	0	1	1 (0.75%)
9.	Hepatitis (HBsag)	0	1	1 (.75%)
10.	HIV infection	1	-	1 (.75%)
11.	Alcoholism	1	-	1 (.75%)
12.	Chronic renal failure (CRF)	1	1	2 (1.5%)
13.	Myelodysplastic syndrome	2	1	3 (2.2%)
14	SLE	0	1	1(0.75%)
15	Trauma	2	0	2(0.75%)
16	Wilson Disease	1	0	1(0.75%)
	Total	**80**	**52**	**132**

Megaloblastic Anemia - Clinically all the 67 patients of megaloblastic anemia presented with symptoms of anemia with fatigue, lassitude and pallor. Peripheral smears in megaloblastic anemia patients showed, apart from pancytopenia, macrocytic and ovalocytic red cells in most of the cases (**photomicrograph 1),** anisocytosis, poikilocytosis, in all cases and circulating erythroblast in 7.4% of cases (**Table III).**

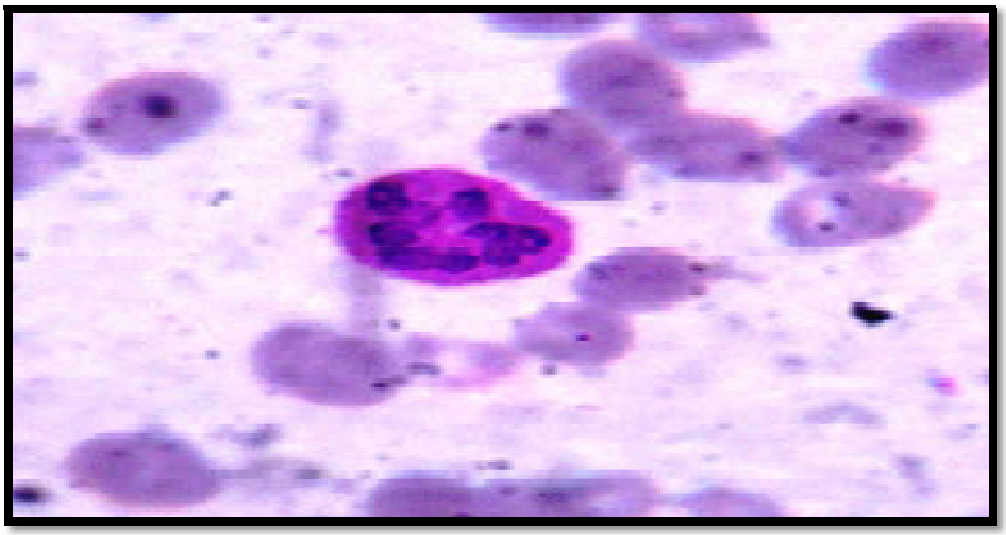
Macrocytic Features and dimorphic blood picture was seen in 58 (86.5%) and 9 (13.4.%) cases respectively. Hypersegmented neutrophils (**photomicrograph-2)** were frequent finding seen in 55 (82%) cases (**Table III**) Bone marrow examination was done in 58 cases. Bone marrow was found to be normocellular in 13 cases and hypercellular in 43 cases, two were diluted. Total 43 (74%) cases showed erythroid hyperplasia. Erythropoiesis was megaloblastic in 49 cases and predominantly megaloblastic. (**photomicrograph-3)** with micronormoblastic in 9 cases. Leucopoiesis showed presence of giant stab cells in most of the cases.

Table- III -Showing Peripheral smear Findings common causes of Pancytopenia.

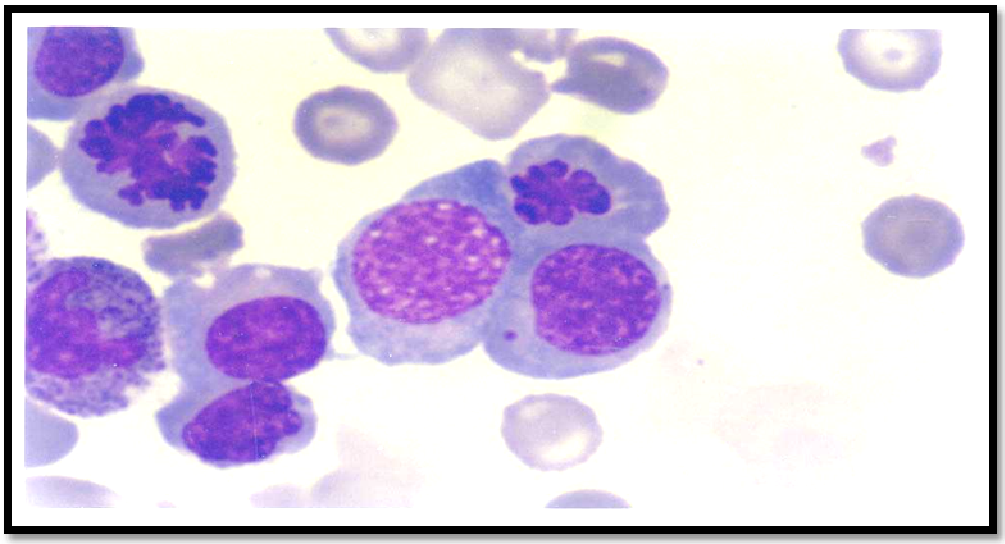
CAUSE		Anisopoikio-Cytosis	Circulating Erythroblast	Hypersegmented Neutrophil
Megaloblastic Anemia	67	67(100)	5(7.4)	55(82)
Malaria	13	3(23.0)	1(7.6)	-
Hyperspleenism	14	7(50)	1(7.1)	-
Aplastic Anemia	10	2(20)	-	-
Acute leukemia	12	2(16.3)	-	-
Myelodyaplastic syndrome	3	2(66.6)	-	-
Infection	2	-	-	1(50)



Photomicrograph -1 showing Macroovalocyte in Peripheral Blood



Photomicrograph -2 showing Hypersegmented Neutrophil



Photomicrograph -3: Showing a megaloblast in bone marrow smear

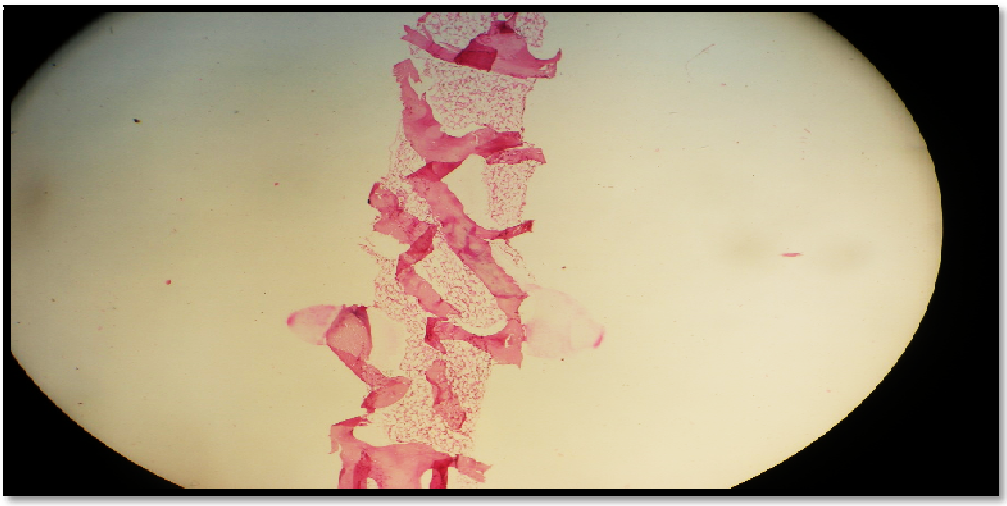
Malaria- Five hundred and sixty five patients were malaria positive during the study period out of which 13(10.6%) cases presented with pancytopenia i.e. 2.3% of total cases. There were 9 males and 4 females with male to female ratio as 1.6:1. Age ranged between 6-44 years (mean 17.2 years, SD ±9.85). Maximum 11 (84.5%) cases were seen in 2nd and3rd decade. The P. falciparum accounted for malaria in 11 and P. vivax accounted for 2 cases. Bone marrow Examination was done in 2 cases and it showed active hematopoiesis in both.

Hypersplenism- Fourteen cases of hypersplenism with peripheral pancytopenia were noted in the present study. The underlying cause revealed that all the cases were of secondary hyperspleenism. The commonest cause being portal hypertension with congestive splenomegaly in 12 (85%) cases, followed by tropical splenomegaly in 2 (14.2%) cases. Of the 12 cases of portal hypertension, 4 cases had cirrhosis with history of alcoholism, 2 had idiopathic cirrhosis, 5 cases had non cirrhotic portal hypertension/ IPF and 1 case had EHPVO**.** Bone marrow findings, which were available in 10 cases showed a hypercellular marrow in 6 and normocellular marrow in 4 cases. Erythoid hyperplasia was seen in 5 cases. Three cases showed micronomoblastic erythropoiesis.

Aplastic Anemia- Ten cases of aplastic anemia were diagnosed during the study period. No history of any causative agent or occupational exposure could be elicited in any of these cases. The average age showed a leaning towards middle age group (mean 41.2 years, ranging from 10-78 years). Male and female were equally affected. All 10 cases presented with features of anemia and pallor. Six patients had fever and four had bleeding manifestations in the form of fundal hemorrhages, menorrhagia etc. The hematological parameters are as in **Table IV**. Bone marrow examination was undertaken in all cases. The aspiration biopsy was hypo cellular in all the cases and diagnosis was confirmed on trephine biopsy. The trephine biopsy in 9 cases showed hypocellular marrow with suppression of haemopoiesis and increase in marrow fat cell (**Photomicrograph 4).** Increased number of mature lymphocytes was seen in the marrow of 2 cases.

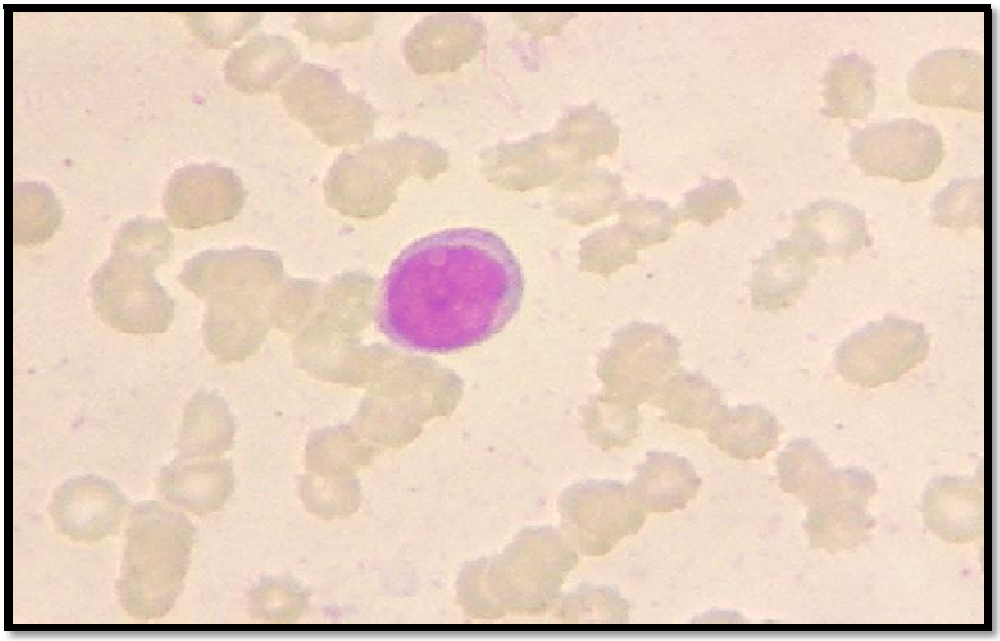
Table-IV: Showing haematological parameters in 10 cases of Aplastic anemia with pancytopenia

Sr.No.	Parameter	Range	Mean (±SD)
1	TLC (x 10^3/µL)	1.8-3.8	2.7(.92)
3	Haemoglobin (gm/dl)	3.8-10.0	6.5(1.6)
4	Haematocrit (%)	11.8-30.0	21.1(5.7)
5	MCV (fl)	79.8-96.5	93(3.2)
6	MCH (pg)	21.3-31.2	30(.9)
7	MCHC (gm/dl)	26.7-34.1	33(1.6)
8	Platelet count (x 10^3/µL)	3-100	35.0(25.9)
9	Reticulocyte count (%)	0.4-1	0.7(.3)



Photomicrograph 4- showing acellular trabecular space in bone marrow biopsy in Aplastic anemia

Sub leukemic phase of acute leukemia- Twelve patients (6 males and 6 females) presented in the subleukaemic phase of acute leukemia. The mean age was 44 years (range 6-75 years SD±19.6). Male and female were equally affected. The peripheral smear showed pancytopenia in all the 12 cases. Only 7 cases showed presence of occasional blast cell (**photomicrograph-5)**, 2 cases increased blast, 1 case showed promyelocytes. In 7 cases there was relative lymphocytosis. Bone marrow was hyper cellular in all cases and showed suppression of other haemopoietic cells by malignant cells All were diagnosed as AML, with immunophenotyping done in 7 cases helped in, further sub classification as AML-M3 in 2, AML-M2 in 3, AML-M5 in 1, and AML-M1 in 1case.



Photomicrograph-5: Showing blast in Subleukemic leukemia in pancytopenia in peripheral smear

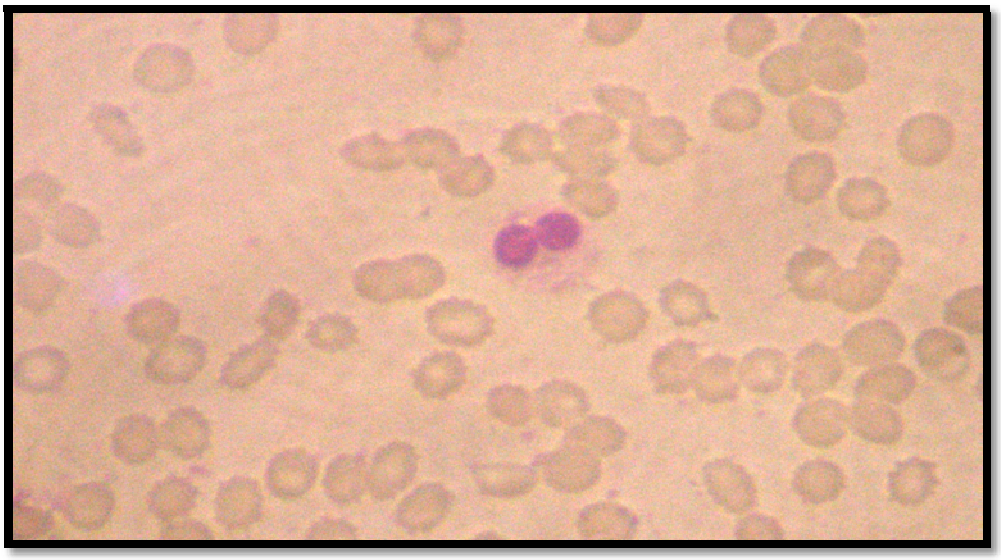
Clinical presentation in pancytopenia- Clinical presentation of the patients with pancytopenia varied. Pallor was noticed in almost all the cases (96.9%) except in 4 cases of which three were suffering from malaria and one had hypersplenism. Fever was the second most common presentation seen in 79 (59.8%) cases **(Table V)**.

Table-V: Showing comparison of clinical features in different common causes of Pancytopenia.

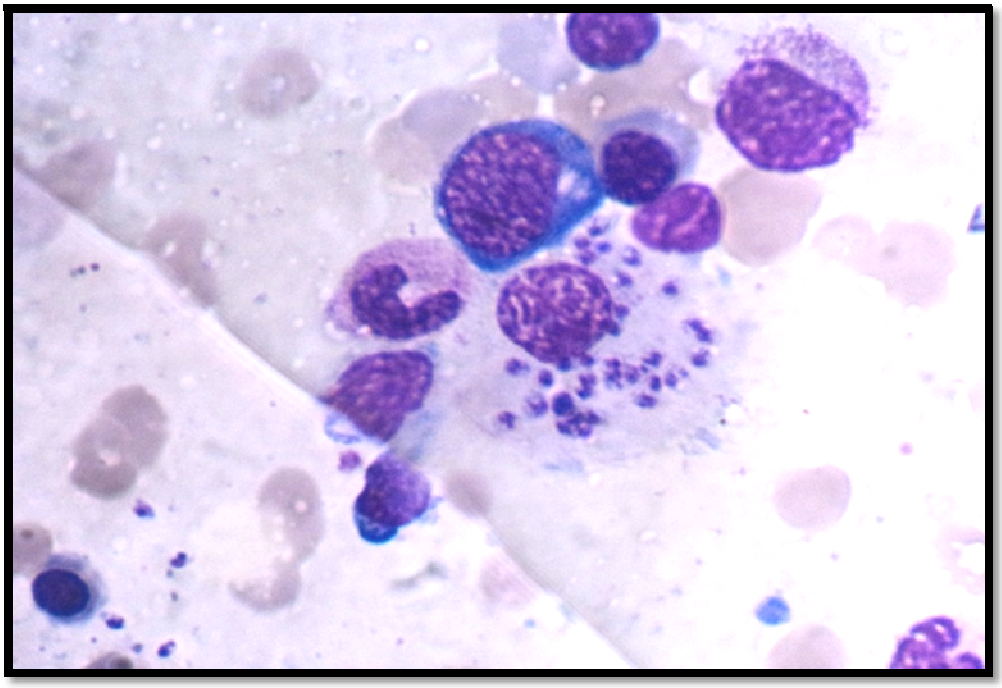
Cause	Clinical Presentation						
	Total Cases	Fever %	Pallor %	Bleeding %	Icterus %	Spleen %	Liver %
Megaloblastic Anemia	67	39(58.2)	67(100)	4(5.9)	15(22.3)	17(25.3)	17(25.3)
Malaria	13	13(100)	10(76.9)	1(7.6)	5(38)	3(23)	5(38)
Hyperspleenism	14	4(28.5)	13(92)	2(14)	4(28)	14(100)	4(28)
Aplastic anemia	10	6(60)	10(100)	4(40)	0	0	0
Acute leukemia	12	7(58.3)	12(100)	3(25)	1	2(16.6)	1(8.3)
Myelodyspalstic syndrome	3	2(66.6)	3(100)	0	0	0	0
Infection	2	1(50)	2(100)	0	0	2(100)	2(100)

Hematological parameters, peripheral smear findings and bone marrow findings in pancytopenia.

Hematological parameters and peripheral smear findings were as observed in (**Table VI, Table III).** Bone marrow examination was undertaken in 101 patients. The aspiration was found to be inadequate in 10 cases. In these, trephine biopsy helped in the diagnosis of 9 cases and one biopsy was inadequate. Of the total 101 cases, in which bone marrow was available for examination, the cellularity was normocellular in 24 cases (23.7%), hypercellular in 61 (60.3%) cases, hypocellular in 10 (9.9%) cases and diluted in 6 (5.9%) cases. (**Table VII)**. Leucopoiesis showed presence of giant band forms in cases of megaloblastic anemia. The bone marrow examination was found to be of diagnostic importance in cases of aplastic anemia, leukemia, MDS (**photomicrograph 6) and** Kala-azar. **(photomicrograph 7).**



Photomicrograph 6- Showing Pseudo Pelger huet anamoly in MDS in bone marrow



Photomicrograph 7- showing LD bodies in bone marrow smear in kala Azar

Other rare causes of pancytopenia- Other conditions, which were infrequently associated with peripheral pancytopenia, found in the present study included 1caseof HIV infection, 1case of chronic alcoholism, 2 case each of chronic renal failure, 3 cases of myelodysplastic syndrome, 2 cases trauma, 1 case of kala-azar, Wilson disease 1 case, 1 case of SLE, 1 case of drug induced pancytopenia and 1 case of-HBV hepatitis. **(Table II)**

Table-VI: Showing comparison of mean (standard deviation) of Hematological parameter in different common causes of Pancytopenia. (n=132).

Cause	TLC(X10^3/µl)	HB(gm/dl)	HCT(%)	MCV(fl)	MCH(pg)	MCHC (gm/dl)	PLTx103/µl)
Megaloblstic Anemia	3.2(.75)	5.0(1.8)	17.8(5.18)	102.3(10.1)	32.5(5.3)	34(2.8)	69.5(36.0)
Malaria	3.6(.50)	8(2)	24.1(5.6)	79.1(3.5)	27(3.1)	29(.5)	56.0(22.8)
Hyperspleenism	3.4(.95)	7.0(2.4)	23(6.9)	75.3(15.4)	24(8.3)	32(2.5)	64.3(37.7)
Aplastic Anemia	2.7(.92)	6.5(1.6)	21.1(5.7)	93(3.2)	30(.9)	33(1.6)	35.0(25.9)
Acute Leukemia	2.7(.96)	6.6(1.5)	20(4.9)	90(4.0)	30(2)	32(.9)	52.3(22.5)

Table-VII: **Showing pattern of erythropoiesis in bone marrow of 101Cases**.

	Maturation	No. of cases (%)
1	Normoblastic	32 (31.6)
2	Megaloblastic	57 (56.4)
3	Predominantly megaloblastic with micronormoblastic	12 (11.8)
	Total no. of cases	101 (100)

Discussion

The incidence of pancytopenia in our laboratory was found to be 0.12% or approximately one case per 820 blood samples, Very few studies have estimated the overall incidence of pancytopenia. Tilak and Jain from Chandigarh, India have reported the incidence of pancytopenia as 374 per million hospital attendance per year. [4]

Sex ratio- In the present study, slight male preponderance was observed with a male to female ratio as 1.5:1 **(Table I**). The findings in present study are comparable with that of Tilak and Jain and Khodke et al who observed a male to female ratio in pancytopenia as 1.1:1 and 1.3:1 respectively. [4,6]

Age- Wide variation in age of the patients from 2.5 to 76 years **(Table I)** was observed which correlates well with that reported by other workers Tilak and Jain, 5-70 years; Khodke et al, 3-69 years, Kumar et al, 12-73 years [4,6,7]. Maximum cases in the present study (54%) were seen in the age group between 2nd to 4thdecade (**Table I**). This was similar to the findings Khodke et al, where 44% cases were found to be between 12-40 years. [6]

Causes of Pancytopenia- Analysis of the specific causes for pancytopenia in the present study showed that megaloblastic anemia was the most frequent cause (50.7%) followed by hypersplenism (10.6%) and by malaria (9.8%), in this region (**Table II).** From Zimbabwe, Savage eta al observed megaloblastic anaemmia as the most common cause of pancytopenia. Similarly, from India, Tilak and Jain and Khodke et al observed megaloblastic anemia as the most common cause of pancytopenia with 68.8% and 44.0% cases respectively [4,6]. Moreover, Kumar et al and Varma and Dash also observed megaloblastic anemia in 23.26% and 22.2% cases respectively as the second most common cause of pancytopenia. [7,8].

The finding in the present study correlates well with that of other workers. There is a higher prevalence of nutritional anemia in Indian population which may explain megaloblastic anemia as the most common cause in these studies. However, studies from abroad did not support this finding. [9,10,11,12].

In the present study, malaria was observed as the third most common cause of pancytopenia, seen in 9.8% cases (**Table II).** From India, Tilak and jain from Chandigarh and Kumar et al from Delhi observed malaria as a cause of pancytopenia in only 3.9% and 3.0% cases respectively [4,7]. However, Hossain et al, from Bangladesh, observed malaria and kala Azar as a common cause of pancytopenia [11]. Regions in an around Durg District are endemic for malaria. Thus malaria accounted for a large number of cases presenting with pancytopenia in our study.

Hypersplenism as a cause of pancytopenia was noted in 10.67% cases in the present study which is in accordance with the findings of Kumar et al who observed it in 11.9% cases. [7].

Aplastic anemia constituted only 7.5% cases of pancytopenia in the present study. Varma and Dash Kumar et al, Keisu and Ost found aplastic anemia in 40.6%, 29.5% and 19% cases respectively. [7,8,12]. However, Imbert et al and Tilak and Jain also observed aplastic anemia as a cause of pancytopenia in 10% and 7.7% cases respectively, which correlates with present study. [4,10] Thus, the present study observed aplastic anemia as a less common cause of pancytopenia in this region as compared to other studies. The patients attending our hospital are from suburban areas and smaller towns and are less likely to be exposed to environmental pollutants and industrial toxins which are implicated as major cause of aplastic anemia and thus explains the present findings.

Present study found 9% cases in the subleukaemic phase of acute leukaemia as a cause of pancytopenia **(Table II).** The number of cases in this group reported by different workers show a great variation. Imbert et al found malignant myeloid disorders (AML, MDS, AML with myelofibrosis) in 42% cases and malignant lymphoid disorders in 18% cases. [10] Varma and Dash and Kumar et al observed subleukaemic leukaemia as a cause of pancytopenia in 12.8% and 12% cases respectively, which is near to present study. [7,8] However, Tilak and Jain and Khokde et al observed 1 case each of AML and erythroleukaemia in the subleukaemic phase accounting for 1.29% and 2.0% cases, respectively, in their study of pancytopenia. [4,6] The regional variation in incidence of hematological malignancies in different geographic areas could be responsible for these differences.

Over whelming infection and sepsis was seen in 2 (1.52%) cases in the present study **(Table II)** including cases of sepsis and viral infection. These findings are comparable to that of Tilak and Jain who observed only 3(3.89%) cases of toxic change. [4] Majority of the patients in our hospital are from suburban background and they tend to attend the hospital in late stages of infection. These patients (especially children) are already suffering from varying degree of nutritional deficiency, which make them more susceptible to these infections. Other rare causes of pancytopenia noted in the present study were 1 (.76%) case of HIV infection**.** Khodke et al also noted HIV infection in 1 (2.0%) case which supports the present findings. [6] However, Savage et al from Zimbabwe found HIV infection as the third most common cause of pancytopenia in their study probably because of high HIV prevalence rate in their region.

Another important finding was association of chronic alcoholism and pancytopenia in 1 (0.75%) cases in the present study **(Table II**). Keisu and Ost observed 6% cases of alcohol related disorders associated with pancytopenia [12]. Weston and Hall have also observed that chronic alcoholics with liver disease who are frequently folate deficient are at risk of life threatening pancytopenia.

Three cases of myelodyspastic syndrome (2.2%) were noted in the present study. From India, Khodke et al and Kumar et al also observed MDS as a cause of pancytopenia in 2% and 3.61% cases respectively [6,7]. However MDS comprised a prominent group in studies from abroad [9,12].

Two cases of chronic renal failure associated with pancytopenia was observed in the present study, the finding which has also been noted by the International Agranulocytosis and Aplastic Anemia Study group[13].

Clinical Features- Clinical features were observed collectively in all the cases of pancytopenia. Pallor was present in almost all the cases (96.9 %) a finding similar to the other studies. Fever was present in 59.84% cases (**Table V).** Khodke et al also observed 40% cases of pancytopenia with fever. [6]

Similarly, jaundice which was seen in 19.6% of our cases **(TableV)**. As the present study observed high number of malaria and hypersplenism, which showed jaundice in 38% cases and 28% cases each, these two conditions were responsible for high number of cases of pancytopenia with jaundice in the present study. Kumar et al who observed icterus in 6 (3.61%) cases of megaloblastic anemia [7].

Splenomegaly was seen in 31% cases in the present study (**Table V**), a finding similar to the observation by Khodke et al who noted it in 40% cases. [6] However, Tilak and jain observed splenomegaly in 50.66% cases of pancytopenia [4]. Hepatomegaly was present in 23.4% cases in the present study (**Table V)** which was lower than that reported by Tilak and jain and Khodke et al, who observed it in 41.5% cases and 47.5% cases respectively [4,6]. B N Gayathri and Kadam

Satyanarayan Rao observed splenomegaly (35.57%) and hepatomegaly (26.92%) in 104 cases of pancytopenia which is comparable to present study. Hussain also observed splenomegaly in 25% cases.

Peripheral Smear Findings- In the present study, peripheral smear examination showed anisopoikiocytosis in 65% cases of pancytopenia. It was prominent feature in megaloblastic anemia (100%), hypersplenism (50%) and malaria (23%.). Both Khodke et al and Tilak and Jain observed anisopoikiocytosis in 60% and 89.61% of cases respectively which matches with current study and it was prominent feature in smears from megaloblastic anemia in both studies [4,6]. Also, relative lymphocytosis in aplastic anemia was noted in 52.63% of the cases in our study compared to 50% in Tilak V et al study and 85.71% in Khunger JM et al. study [4,13].

Circulating erythroblast was seen in 5.3% cases, a finding similar to Khodke et al who observed it in 8% cases of pancytopenia [6]. However Tilak and jain who observed circulating erythroblasts in 12% cases of pancytopenia [4].

Hypersegmented polymorphs were seen in 43.1% cases, mostly in smears from patients in megaloblastic anemia, which correlates with Khodke et al who observed it in 40% cases of pancytopenia. Tilak and Jain, observed hypersegmented polymorphs in 58.43% cases. Hypersegmented neutrophils were noted in 82% of cases of megaloblastic anemia compared to 84.9% in Tilak V et alstudy [4]. Dimorphic blood picture was seen in 9.8% cases of pancytopenia which is lower than that observed by Khodke which was 20%. [6]

Haematological parameters- Haematological parameters revealed, as expected, a depression in all the cell counts. On comparing the haematological parameters of different causes of pancytopenia, anemia appeared to be more severe in cases of megaloblastic anemia, aplastic anemia, subleukaemic leukaemia, whereas, patients of malaria, hypersplenism and showed less severe anemia. Total leukocyte count was most severely depressed in cases of patients of aplastic anemia. Similarly, platelet count, although it showed wide variation, it was most severely depressed in patients of malaria and aplastic anemia (**Table VI).** Kumar et al in their study also found hypersplenism with less severe anemia than in aplastic anemia, megaloblastic anemia and leukaemia and lymphoma and thus supporting the present findings. [7]

Bone marrow examination-Bone marrow examination was conducted in 101 cases. Since inconclusive aspirates were seen in 10 cases and trephine biopsy helped in diagnosis of 9 out of them, 100 marrows were available for examination.

Normocellular marrow in 24% and hypercellular marrow smears were seen in of 61% cases, (Total- 85% cases) which is much higher than the observation by Imbert et al who observed normo- and hypercellular marrow in 66% cases. The higher number of cellular marrow smears in the present study is likely to be because of the much lower number aplastic anemia cases as compared to the number of cases of megaloblastic anemia. [10].

Out of 101 marrow available, the erythropoiesis was megaloblastic in 57 (56.4%) cases. Various authors Tilak and Jain, Savage, Khodke et al and Kumar et al have also found megaloblastic erythropoiesis in maximum number of cases. [4,6,7,15]. As the present study observed megaloblastic anemia as the most frequent cause of pancytopenia and hence maximum cases have shown megaloblastic erythropoiesis.

Conclusions

The following study concluded that Megaloblastic anemia is the most common cause of pancytopenia in this region and nearby areas followed by hypersplenism and malaria. Large numbers of cases of megaloblastic anemia observed in the present study indicate the wide prevalence of nutritional anemia in our population. Various uncommon causes of pancytopenia were identified in present study which includes HIV, Kala-Azar, Wilson disease, SLE, CRF etc. The hematological parameters, age and sex distribution of various causes in present study are comparable to other studies. The following recommendations can be made.

1. Simple diagnostic technique such as peripheral smear examination, hematological parameters along with detailed clinical examination can help in prompt diagnosis and cure.

2. If the bone marrow aspiration does not permit a morphological diagnosis, it should be followed up with repeated marrow investigations. A bone marrow biopsy should be taken early if the findings in the bone marrow aspiration do not explain pancytopenia especially if aplastic anaemia or myelodysplastic syndrome is suspected.

3. In case of megaloblastoid changes in marrow with unilineage or trilineage dysplasia, a trial of Vit B12 and folic acid therapy should be given, in case if patient not responding to treatment then, MDS should be suspected and bone marrow biopsy should be done at earliest.

4. Bone marrow aspiration is not beneficial for cases of malaria, Hypersplenism due to portal hypertension etc where clinical features combined with hematological parameters generally gives a clue to diagnosis.

5. Nutritional anemia should always be considered as an important cause of pancytopenia in patient showing hypersegmented neutrophil and macrocytes in peripheral blood and a therapeutic trail should always be given.

Funding: Nil, **Conflict of interest:** None initiated,
Permission from IRB: Yes

References

1. Firklin F, Chesteman C, Penington D, Rudj B, Pancytopenia; Aplastic anemia. In: de Gruchy's Clinical Haematology in Medical Practice, 5th edition. Oxford: Blackwell Scientific Publication, 1989: 119-136.

2. Adamson JW, Erslev AJ. Aplasticanemia. In: Hematology, 7th edition. William WJ, Beutler E, Lichtman HA, eds. New York: McGraw Hill. 419-436.

3. Kar M, Ghosh A. Pancytopenia. Journal of Indian Academy of Clinical Medicine 2001; 3(1): 29-34.

4.Tilak V, Jain R. Pancytopenia--a clinico-hematologic analysis of 77 cases. Indian J Pathol Microbiol. 1999 Oct;42(4):399-404.

5. Bello-González SA, Bergés-García A. [Peripheral pancytopenia]. Bol Med Hosp Infant Mex. 1990 Nov;47(11):737-45.

6. Khodke K, Marwah S, Buxi G, Yadav RB, Chaturvedi NK. Bone marrow examination in cases of pancytopenia. Journal Indian Academy of clinical Medicine 2001; 2:55-59.

7. Kumar R, Kalra SP, Kumar H, Anand AC, Madan H. Pancytopenia--a six year study. J Assoc Physicians India. 2001 Nov;49:1078-81.

8. Varma N, Dash S. A reappraisal of underlying pathology in adult patients presenting with pancytopenia. Trop Geogr Med. 1992 Oct;44(4):322-7.

9. Incidence of aplastic anemia: the relevance of diagnostic criteria. By the International Agranulocytosis and Aplastic Anemia Study. Blood. 1987 Dec; 70 (6):1718-21.

10. Imbert M, Scoazec JY, Mary Jy, Jeuzult H, Rochant H, Sultan C. Adult patients presenting with pancytopenia : A reappraisal of underlying pathology and diagnostic procedures in 213 cases. Haemotol Pathol 1989; 3(4): 159-167.

11. Hossain HA, Akond AK, Chowdhury MK. Pancytopenia-a study of 50 cases. Bangladesh journal of pathology 1992; 7(1):9-12.

12. Keisu M, Ost A. Diagnoses in patients with severe pancytopenia suspected of having aplastic anemia. Eur J Haematol. 1990 Jul;45(1):11-4.

13. Khunger JM, Arunselvi S, Sharma U, Ranga S, Talib VH: Pancytopenia – a clinicohematological study of 200 cases. Lin CK, Hsu HC,Chau WK, Jiang ML, Chiu CE. Reticulocyte count with maturation fraction in pancytopenic evaluation by a fully automated counter. Clin Lab Anal 1993; 7(6):371-375.

14. Lin CK, Hsu HC, Chau WK, Jiang ML, Chiu CF. Reticulocyte count with maturation fractions in pancytopenic evaluation by a fully automated counter. J Clin Lab Anal. 1993;7(6):371-5.

15. Savage DG, Allen RH, Gangaidzo IT, Levy LM, Gwanzura C, Moyo A, Mudenge B, Kiire C, Mukiibi J, Stabler SP, Lindenbaum J. Pancytopenia in Zimbabwe. Am J Med Sci. 1999 Jan;317(1):22-32.

…….....

How to cite this article?

Sharma Anjana, Ravindranath M, Maheep B. Pancytopenia- A clinicopathological analysis of 132 cases. *Int J Med Res Rev* 2016;4(8):1376-1386.doi:10.17511/ijmrr.2016.i08.16.

…….