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PROPORTION OF MEGALOBLASTIC ANEMIA IN 40 PATIENTS WITH PANCYTOPENIA AT CMC HOSPITAL LARKANA

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ABSTRACT

INTRODUCTION: *Pancytopenia is common in Pakistan and refers to the combination of anemia, leucopenia and thrombocytopenia in the peripheral blood. Pancytopenia is said to exist in an adult when the hemoglobin level is less than 13.5gm/dl in males and 1l.5gm/dl in females, white cell count less than 4xl0^{9}IL and platelet count less than 150x10^9/L.*
The causes of pancytopenia are aplastic anemia, sub-leukemic leukemia, myelodysplasia, multiple myeloma, nutritional deficiencies leading to megaloblastic anemia, hypersplenism, paroxysmal nocturnal hemoglobinuria, AIDS, infections such as miliary tuberculosis, leishmaniasis, brucellosis etc.
OBJECTIVES: *i) To see the various causes and prevalence of megaloblastic anemia in relation to age and sex.*
ii) To give recommendations about its prevention and management.
STUDY DESIGN: *Randomized, Observational study.*
SETTING: *OPD & Medical Ward-II, Chandka Medical College Hospital Larkana.*
DURATION WITH DATES: *01 years study from February 2007 to February 2008.*
SUBJECT AND METHODS: *Patients of either sex, who attended medical ward-II of Chandka Medical College Hospital Larkana, either as inpatient or out patient department, from February 2007 to February 2008 and fulfilled the inclusion criteria, were included in this study.*
Pancytopenia was considered as hemoglobin value less than 13.5gm/dl in males or 11.5gm/dl in females, a white cell count less than 4x10^9/L and Platelets count less than 150x10^9/L.
The finding of mean corpuscular volume (MCV) > 110 fl with anemia was considered as megaloblastic anemia. Patients of less than 12 years and pregnant females were excluded from the study.
RESULT: *Out of 40 patients, 29 (72.5%) were males and 11 (27.5%) were females (P < 0.05).*
The mean ages of males were 29.10 + 16.46 years whereas of females 36.14 + 15.6 years (P<0.22).
Megaloblastic anemia was the common pathology encountered after aplastic anemia and hypersplenism. Megaloblastic anemia was the cause of pancytopenia in 06 (15%) patients.
CONCLUSION: *We concluded that megaloblastic anemia is common cause of pancytopenia in our patients.*

KEYWORDS: Pancytopenia; Megaloblastic anemia; Hypersplenism.

INTRODUCTION

Pancytopenia is common in Pakistan and refers to the combination of anemia, leucopenia and thrombocytopenia in the peripheral blood [1]. Pancytopenia is said to exist in an adult when the hemoglobin level is less than 13.5gm/dl in males and 1l.5gm/dl in females, white cell count less than 4xl0^9*IL* and platelet count less than 150x10^9/L [2].
The causes of pancytopenia are aplastic anemia, sub-leukemic leukemia, myelodysplasia, [3] multiple myeloma, nutritional deficiencies leading to megaloblastic anemia, hypersplenism, paroxysmal nocturnal hemoglobinuria, AIDS, infections such as miliary tuberculosis, leishmaniasis, brucellosis etc.
The megaloblastic anemia are disorders caused by impaired DNA synthesis, cells primarily affected are those having relatively rapid turnover especially hematopoietic precursors and gastrointestinal epithelial cells. Cell division is sluggish, but cytoplasmic development

progresses normally, so megaloblastic cells tend to be large, with an increased ratio of RNA to DNA [3].

Megaloblastic erythroid progenitors tend to be destroyed in the marrow. Thus, marrow cellularity is often increased but production of red blood cells is decreased, an abnormality termed as ineffective erythropoiesis.

Most megablastic anemias are due to deficiency of cobalamin (Vitamin B12) and/ or folic acid[3]. The finding of significant macrocytosis [mean corpuscular volume > 100 fl] suggests the presence of a megaloblastic anemia. Other causes of macrocytosis include hemolysis, liver disease, alcoholism, hypothyroidism and aplastic anemia. If macrocytosis is marked (MCV > 110 fl) the patient is much more likely to have a megaloblastic anemia [3]. Neutrophil hypersegmentation or abnormalities of erythrocyte morphology with low serum vitamin B 12 and folate confirms megaloblastic anemia. Clinical features of megaloblastic anemia usually include malaise, paraesthesias, breathlessness, sore throat, grey hair, smooth tongue, angular chellosis, vitiligo, skin pigmentation, impotence, poor memory, depression etc.

OBJECTIVES

i) To see the various causes and prevalence of megaloblastic anemia in relation to age and sex.

ii) To give recommendations about its prevention and management.

MATERIAL AND METHODS

Patients of either sex, those attended medical ward-II of Chandka Medical College Hospital Larkana, either as in patient or out-patient department, from February 2007 to February 2008 and fulfilled the inclusion criteria, were included after informed consent, in this randomized, Observational study.

All the data was noted on a especially designed proforma. All investigations were sent to a single laboratory. Pancytopenia was considered as hemoglobin value less than 13.5gm/dl in males or 11.5gm/dl in females, a white cell count less than $4x10^9$/ L and Platelets count less than $150x10^9$/L. The finding of mean corpuscular volume (MCV) > 110 fl with anemia was considered as megaloblastic anemia.

Patients were graded into mild, morerate and severe pancytopenia as per severity Criteria: [4].

1. Mild: Hemoglobin value less than 8gm/ dl, polymorphonuclear cell count more than 2. $0.5x10^9$/L and platelets more than $20x10^9$/ L.

2. **Moderate:** Hemoglobin value less than 7gmJdl, Polymorphoneuclear cell counts less

TABLE NO: I

AGE AND SEX DISTRIBUTION

n = 40

SEX	NO. OF CASES	AGE IN YEARS MEAN + SD
MALES	29(72.5%)	29.10 + 16.46
FEMALES	11(27.5%)	36.14+15.6
TOTAL	40	37.67+17.79
P-VALUE	P<0.05, CHI SQUARE=3.75	P>0.22 (non significant)
	significant	F=1.50

TABLE NO: II

PREVALANCE OF PANCYTOPENIA

n=40

CAUSE	MALE	FEMALE	BOTH	PERC-ENTAGE	95% CONFIDENCE INTERVAL
APLASTIC ANEMIA	10	3	13	32.5	19.41-48.03
HYPERSPLENISM	4	5	9	22.5	11.56-37.29
MEGALOBLASTIC ANEMIA	6	0	6	15	6.31-28.61
NON- HODGKIN'SL YMPHOMA	3	1	4	10	3.25-22.38
MYELODYSPLASTIC SYNDROME	2	0	2	5	0.84-15.55
DRUG INDUCED	2	0	2	5	0.84-15.55
MULTIPLE MYELOMA	1	0	1	2.5	0.12-11.71
MALARIA	0	1	1	2.5	0.12-11.71
MILIARY TUBERCULOSIS	0	1	1	2.5	0.12-11.71
HEMOPHAGOCYTIC SYNDROME	1	0	1	2.5	0.12-11.71

P<O.OOl, chi-square 42.78

TABLE NO: III

SEVERITY OF PANCYTOPENIA

n = 40

SEVERITY	AA	HS	MG	NHL	OTHERS	TOTAL
	n=13	N=9	N=6	n=4	n=8	
MILD	3(23.07%)	3(33.33%)	1(16.7%)	2(50%)	1(12.5%)	10(25%)
MODERATE	4(30.76%)	1(11.11%)	1(16.7%)	0%	2(25%)	8(20%)
SEVERE	6(46.15%)	5(55.56%)	4(66.69%)	2(50%)	6(46.15%)	22(55%)
P-VALUE	P>O.44	P>0.13	P>0.10	P>0.22	P>0.08	P<O.OO1
	Chi-square= 1.62	Chi-square= 4	Chi-square= 4.5	chi-square= 3	chi-square= 4.88	chi-square= 12.90
STATISTICALY			Non- significant			Significant

AA=Aplastic anemia
HS=Hypersplenism
MG=Megaloblastic anemia
NHL= Non-Hodgkin's lymphoma

than $0.5x10^9$/L and Platelets less than $20x10^9$/L.

3. Severe: White cell counts less than $0.2x10^9$/L and Platelets less than $l0xl0^9$1.

Patients of less than 12 years and pregnant females were excluded from this study.

All patients were thoroughly evaluated and emphasis was given on history of diet, bowel habits, paresthesias, memory and exposure to chemical agents, radiation either by occupational, accidental or by treatment. History of recent viral infection, fever, weight loss, bleeding from gums or else and blood transfusion were also noted.

Relevant points on physical examination were pallor, mouth ulcers, sensory disturbance, splenomegaly, hepatomegaly, lymphadenopathy and bone tenderness.

DATA ANALYSIS

The results were statistically analyzed in relation to specific disease, age and gender.

RESULTS

The patients included 29 (72.5%) were males and 11 (27.5%) were females. Female to male ratio was 1:2.6. The distribution of gender was found statistically significant, (P < 0 .05)

(Chi square =3.75) (Table no: I).

The age of patients ranged from 12 - 70 years. The mean age of females was 29.10+ 16.46 years (mean + SD) whereas of females 36.14 +15.6 years.

Megaloblastic anemia as cause of pancytopania was found in 06(15%) cases. (Table no:II).

04 (66.66%) patients out of 06 patients with megaloblastic anemia had evidence of vitamin B12 deficiency and remaining 02 (33.33%) patients, had folic acid deficiency. The average deficiency level of vitamin B12 was 140 pg /ml, (normal range was 200 to 950 pg / ml) and folic acid was below 120 ng / ml (normal range was 175 to 700 ng / ml). The exact cause of deficiency of these vitamins was not detected but response to treatment with vitamin B 12 and folic acid was documented. All these 06 patients were males with mean age 30.16 years.

Out of them 04 (66.66%) patients had severe pancytopenia and remaining 02 (33.33%) had moderate severity. These results are statistically non significant (P > 010, chi-square = 4.5) (Table no: III).

The clinical presentations of these cases were as follows: Palpitation and weight loss in all cases (100%), fever 28(70%), bleeding manifestations such as epistaxis, hematemesis, melena 28 (70%) and diarrhea 11 (27%) cases and History of repeated episodes of mouth ulcers in (17%) cases, 05 (12.5%) paients had history of sore throat. The results were statistically significant (P < 0.001, chi-square =14.4) (Table no: IV).

TABLE NO: IV

SYMPTOMS OF PANCYTOPENIA

n=40

SYMPTOMS	SEX		BOTH	PERCENTAGE
	MALE	FEMALE		
PALPITATION	29	11	40	100
WEIGHT LOSS	29	11	40	100
FEVER	20	8	28	70
BLEEDING MANIFESTATIONS	20	8	28	70
DIARRHEA	8	3	11	27
MOUTH ULCERS	6	1	7	17
SORE THROAT	3	2	5	12.5
DRUG HISTORY	2	0	2	5

P<0.001, chi-square 147.41

TABLE NO: V

SIGNS OF PANCYTOPENIA

N=40

SIGNS	SEX		BOTH	PERCENTAGE
	MALE	FEMALE		
ANEMIA	29	11	40	100
TEMPARETURE	20	8	28	70
SPLENOMAGALY	13	2	15	37.5
HEPATOMAGALY	12	2	14	35
PURPURIC RASHES	6	2	8	20
MOUTH ULCERS	6	1	7	17.5
LYMPADENOPATHY	5	1	6	15
JAUNDICE	3	1	4	10
GINGECAL HYPERTROPHY	2	1	3	7.5

P<0.001, chi-square 137.09

All patients were anemic (100%), 28 (70%) were febrile, 15 (37.5%) and 14 (35%) patients had splenomegaly and hepatomegaly respectively. The other phyical findings were noted as purpuric rashes 08 (17.5%), mouth ulcers 07 (17.5%), lymphadenopathy 06 (15%), jaundice

04 (10%). Gingival hypertrophy was detected in 03 (7.5%) patients. The results are statistically significant (P < 0.001, chi-square =137.09) (Table no: V).

DISCUSSION

The over all global studies showed that Megaloblastic anemia is more common in white people (and usually in older population [3]), but in UK and India, people have similar incidence [4]. In this study, the prevalence of Megaloblastic anemia was 15%. All the patients were male and their age ranges from 12-50 years. The mean age was 28.5 years. The studies conducted by Atif Beg in 1999, Megaloblastic anemia was the most common cause of pancytopanias, the incidence was 32% [5], Waseem Iqba11998 29% [6], male to female ratio were 1.28:1, comparable results were seen in Qaiser Hasnain in 1987 1.62:1 [7]. David et al 1997 in.

Zimbabwe [4] showed Megaloblastic anemia were the common cause with incidence of 48%. The age difference of our study is comparable to Waseem Iqbal 1998, that is 23.2 years but it is higher in Atif Beg that is 34.45 years. Most of our pancytopenic patients with Megaloblastic anemia had higher incidence of diarrhea, glossitis, mouth

ulcers, 66.66% of our patients presented with high grade fever, bleeding manifestations and severe pancytopenia.

The cause of Megaloblastic anemia was vitamin B12 deficiency in 33.33%, folic acid deficiency 33.33% and in 16.66% both vitamins were deficient, 16.66% were because of malabsorption due to Celiac disease. We were unable to detect the exact cause of these vitamin deficiencies. The cause in our population may be due to lack of knowledge about proper diet, malnutrition, and malabsorption or over cooking during food preparation. Our results were comparable other studies in Pakistan by M. Manan et al 1990 [5], Waseem Iqbal 1998 [6] revealed similar findings. But the studies of Chinese patients in HongKong [8] showed most common cause of Megaloblastic anemia were vitamin B 12 deficiency due to classical PA, even in alcoholics (Chinese), these patients were associated with other diseases like Hyperthyroidism, Hypothyroidism, Diabetes mellitus type-I, Thalassaemie trait Vitiligo etc none of our patient were associated with these diseases.

CONCLUSION & RECOMMENDATIONS

In light of the high frequency of defective cobalamin absorption in older people, some experts have recommended the use of 0.1mg oral crystalline cobalamin prophylaxis daily in people over age 6.5 years [3]. But we observed that the number of the male sufferers were more as compared to female and majority of our patients were, in contrast, younger or middle aged.

At times acute magaloblastic disease resembles as immune cytopenia with a rapidly developing thrambo cytopenia and/or leucopenia in the absence of anemia and blood smear may be completely normal, but the marrow is floridly magaloblastic, therefore bone marrow aspiration and trephine biopsy may be the hallmark for the diagnosis. It is easy and safe procedure and can be done even in severe thrombocytopenia without any complications.

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