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STUDY TO KNOW THE VITAMIN B12 DEFICIENCY IN PATIENTS HAVING MEGALOBLASTIC ANEMIA

[1]Dr Aaisha Qadir, [2]Dr Sidra Khan, [3]Dr Muhammad Usman Hasan

[1]Pak Red Crescent Medical and Dental College, Lahore

[2]Sheikh Zayed Medical College, Rahim Yar Khan

[3]MO at DHQ Hospital, Okara

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Abstract:

Objective: *To evaluate the vitamin B 12 deficiency frequency in individuals with high mean corpuscular volume and anemia.*

Study design: *A cross-sectional study.*

Place and Duration: *In the Medicine Unit II of Services Hospital Lahore for one year duration from September 2017 to September 2018.*

Methods: *113 samples were included according to the exclusion and inclusion criteria. The deficiency of Vitamin B 12 in serum was determined according to standard methods. By Sysmex KX 21 hematology analyzer, Blood samples were analyzed and by Tukey-Cramer and ANOVA test continuous variables were analyzed and analysis of categorical variables was done by Chi-square test. The relationship among variables was determined by Pearson correlation. Statistically significant $p \leq 0.05$ was obtained.*

Results: *Of the 113 subjects, 37 (32.7%) were male, female were 76 (67.2%), 34.48 ± 6.71 years was the mean standard and anemic patients were 89.3% (n = 101). The mean hematocrit, red blood cells and hemoglobin were 3.0 million, dl, 33.1% / µL, 11.3 g respectively. Vitamin B12 deficiency was observed in 65 of 113 subjects (57.5%); In addition, 19.4% and 37.9% respectively are divided into sub-sections as limit and absolute deficiency. Mean corpuscular volumes of up to 139 fl and low levels of vitamin B12 up to <30 pg / ml were observed. In 11 (9.7%) patients¸ Pancytopenia was observed with severe deficiency of vitamin B 12 (<100 pg / ml). A strong negative association was noted between mean corpuscular volume and vitamin B 12 ($p = 0.0001$, $r = -0.79$). Poikilocytosis, anisocytosis, hypersegmented neutrophils and megaloblast were seen in peripheral blood film.*

Conclusion: Vitamin B 12 deficiency is an important factor contributing to mega-loblastic anemia.

Key words: *Megaloblastic anemia, Vitamin B 12 deficiency.*

Corresponding author:

Dr. Aaisha Qadir,

Pak Red Crescent Medical and Dental College, Lahore

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INTRODUCTION:

Vitamin B12 belongs to the cobalamin family. A basic micronutrient for DNA synthesis and cell proliferation, especially for the rapid proliferation of bone marrow hematopoietic cells[1-2]. The animal origin foods have high vitamin B 12 content[3]. The vitamin B 12 daily requirement is 3 µg and 5 µg is the daily absorption. Vitamin B 12 reserves in the hepatocytes of liver are 2000-5000 µg and are sufficient 3-5 years before the symptoms of deficiency occur[4]. vitamin B12 deficiency causes are terminal ileum surgery, dietary deficiency, chronic gastritis, lack of internal factor, pancreatitis, infection with Helicobacter pylori, invasion of transcobalamin II, fish cassette worms (Diphyllobothrium latum) and excessive bacterial growth syndrome[5]. Vitamins B 12 act as coenzymes and catalyze 2 main biochemical processes in the human body[6]. Coenzyme forms include S-adenosylcobalamin and methylcobalamin. Adenosylkobalamin is a coenzyme for the L-methylmalonyl-CoA-coenzyme A activity that converts methylmalonyl-CoA to succinyl-CoA and synthesis of methionine, a coenzyme for methionine synthetase, which catalyzes the conversion reaction of methylcobalamine[7]. Clinically, vitamin B 12 deficiency is manifested by various gastrointestinal, neurological and hematological findings. Deficiency of Vitamin B12 results in anemia with variable intensity, which can sometimes be very serious[8]. The average corpuscular volume (VMC) is surprisingly high; It can be between 110-140 fl. However, it is not possible to have a normal VCM and vitamin B 12 deficiency[9]. Peripheral blood radiography shows poikilocytosis, macro ovalocytes and anisocytosis. In the bone marrow, distinct erythroid hyperplasia is noted in response to a problem in erythropoiesis called ineffective erythropoiesis[10].

MATERIALS AND METHODS:

This cross-sectional study was held in the Medicine Unit II of Services Hospital Lahore for one-year duration from September 2017 to September 2018. A sample consisting of 113 subjects was selected by exclusion and inclusion criteria and an appropriate sampling technique. The sample size for the study was calculated using the sample rate formula. Hemoglobin <12 g / dl in both sexes over 12 years of age, <13 g / dl in females, male and mid-volume corpuscular ≥ 96 fl, megaloblast and hyper segmented neutrophils were included. Subjects older than 80 years, diabetic subjects, vegetarians, heart disease, hypertension, gastrointestinal disorders and pulmonary tuberculosis were excluded. Dimorphic blood, iron deficiency anemia and Folic acid deficiency were also not included. According to the guidelines of WHO Anemia was analyzed. By venous puncture 3 blood samples were taken from the antecubital vein. From the Sysmex KX 21 hematology analyzer, whole blood was autolyzed, and Vitamin B 12 serum levels were measured. Vitamin B 12 levels; Group I: normal> 240 pg / ml, Group II: border 169-239 pg / ml, Group III: <170 pg / ml deficiency and severe deficiency in Group IV: <100 pg / ml. The data were entered into the SPSS version 18.0 statistical package. Continuous variables were determined by Tukey-Cramer and ANOVA tests and recorded as mean ± SD, while categorical variables and chi-square test were taken as percentage and frequency. Using Pearson correlation, the relationship among variables was analyzed.

RESULTS:

113 total cases, male was 37 (32.7%) and female were 76 (67.2%). The M:F ratio was 1: 2.1 approximately. The 34.48 ± 6.71 years was the mean age. The average age of the study subjects was 34.5 ± 6.6 years ± SD. (Table I). In 89.3% Anemia was noted. The mean hematocrit, red blood cells and hemoglobin were 3.0 million, 36.1% and 11.3 g / dl, respectively (Table I). Demographic features are elaborated in the table I.

TABLE I: DEMOGRAPHIC CHARACTERISTICS OF STUDY POPULATION (n=113)

	Mean	Std. Dev	Range
Age (years)	34.48	6.71	24-29
Hemoglobin (g/dl)	11.32	2.15	4-16
Hematocrit (Hct)(%)	36.16	8.04	19-47
RBC (million/µL)	3.0	0.57	2.3-4.0
Mean corpuscular volume (fl)	100.64	19.27	70-134
Mean corpuscular hemoglobin (pg/dl)	31.92	4.50	24-39
Mean corpuscular hemoglobin con-centration(%)	29.38	4.62	23-38
RDW*(%)	12.5	2.5	11.5-15.5
Vitamin B12 (pg/dl)	171.18	82.64	27-298

Patients with severe B 12 deficiency (<100 pg / ml) showed a mean volume of 139 fl corpus (Table II).

TABLE II: RED BLOOD CELL INDICES IN DIFFERENT GROUPS (n=113)

	MCV	MCH	MCHC
Normal (>240pg/ml)	84.7±5.3	29.2±3.1	27.5±3.6
Borderline deficiency (170-240 pg/ml)	97.3±4.8	28.9±3.5	26.6±4.0
Vitamin B12 deficiency (<170 pg/ml)	119±5.8	36.4±2.9	32.3±2.8
Severe Vit. B12 deficiency (<100pg/m)	121.8±8.5	35.1±3.0	32.2±4.5

The value of Vitamin B12 was as below as <30 pg / ml. There were vast differences in vitamin B 12 between the groups (p = 0.00001) (Table III).

TABLE III: ANALYSIS OF VARIANCE OF VITAMIN B_{12} BETWEEN AND AMONG GROUPS

	Sum of Squares	df	Mean Square	F-value	p=value
Between Groups	556048.468	3	185349.489	148.042	0.0001
Within Groups	120192.292	96	1252.003		
Total	676240.760	99			

The details of the measured levels of vitamin B 12 are shown in the table IV.

TABLE IV: VITAMIN B12 LEVELS MEASURED IN STUDY POPULATION (n=113)

	n (%)	Mean	Std. Dev	p=value
Group I. Normal (> 240pg/ml)	48 (42.4%)	245.22	50.3	p<0.002 (for all groups)
Group II. Borderline deficiency (170-240 pg/ml)	22 (19.4%)	210.22	31.5	
Group III. Vit. B12 deficiency (<170 pg/ml)	15 (13.2%)	139.20	22.1	
Group IV. Severe Vit. B12 deficiency (<100pg/ml)	28 (24.7%)	65.07	15.3	

There was a significant negative correlation between vitamin B 12 and mean corpuscular volume (r = -0.79, p = 0.0001) (Table V).

TABLE V: PEARSON`S CORRELATION OF VITAMIN B_{12} (n=113)

	MCV	MCH	MCHC
Correlation coefficient (r-value)	-0.79	-0.43	-0.58
p=value	0.0001	0.001	0.001

Pancytopenia was observed in 11 (9.7%) of the peripheral blood sample with a decrease in lymphocyte count. Oval macrocytes, Megaloblasts, poikilocytosis, hypersensitive neutrophils and anisocytosis were seen in the peripheral blood shown in Figures 1 and 2.

FIGURE I: OVAL MACROCYTES (a) AND MEGA-LOBLASTIC CHANGES (b)

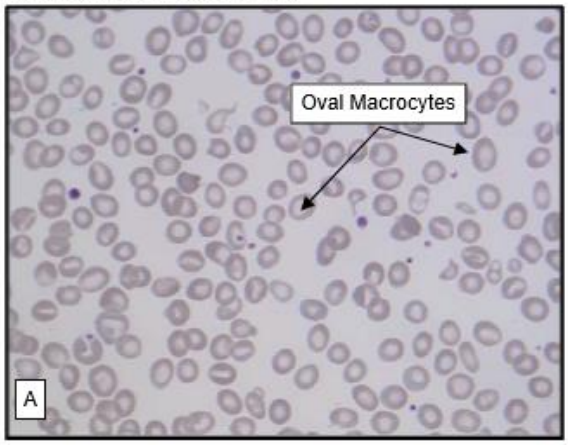

FIGURE II: NEUTROPHIL SHOWING HYPERSEG-MENTED NUCLEUS AS SEEN IN PERIPHERAL BLOOD FILM

DISCUSSION:

Vitamin B 12 is important for the nucleotide's synthesis of RNA and DNA from body cells. Vitamin B12 deficiency rapidly proliferates the bone marrow cells and the resulting ineffective erythropoiesis causes the large red blood cells formation in immature form known as megaloblasts. B 12 vitamin deficiency is very common among the Pakistan population[11]. In a recent study on 95 subjects; Vitamin B 12 deficiency was noted in the study population up to 72.6%. Iqbal SP et al. At Ağa Khan Karachi Hospital, do A retrospective study which shows the ratio of vitamin B 12 deficiency among non-vegetarians and vegetarians was 85% and 78.5%, respectively[12]. This study results were divided into 19.4% and 37.9%, respectively, and the deficiency of the B 12 vitamin in 57%. (Table IV). This study reveals that the vitamin B 12 deficiency incidence is relatively low compared to previous studies. In another study conducted in the hospital, vitamin B12 and 76% folate deficiencies were reported and the outcomes were not compatible with this analysis. Most likely, the variation is due to the addition of vitamin B12 and folate and a small sample size (n = 49)[13]. This study results indicate that deficiency of vitamin B 12 is much common. The population studied shows up to 57% was found to be deficient in vitamin B12. For this reason, vitamin B12 deficiency should be considered in clinical cases with a mean corpuscular volume greater than 96 fl[14]. Although the results regarding the frequency of vitamin B12 deficiency in megaloblastic anemia represent a large population of Sindh patients, a similar trend has been reported in other parts of Pakistan. Sarode et al. Showed that the prevalence of vitamin B12 deficiency in a study in a hospital was 76% in 102 cases of feeding megaloblastic anemia[15]. This study is comparable with the study conducted in a study conducted by Khudduri and Sharma reporting vitamin B 12 deficiency, a hospital in India and 65% B12 vitamin deficiency. Naeem et al. The lack of vitamin B 12 from Gilgit agency in northern Pakistan is reported to be 31.8%. The results of this study are relatively high.

CONCLUSION:

B 12 vitamin deficiency is an important factor contributing to megaloblastic anemia. Early diagnosis should be emphasized by doctors in selected patients. Additional studies are suggested to assess the etiology of deficiencies in the community.

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