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Study of Vitamin B12 Levels in Patients of Sickle Cell Disease in a Tertiary Care Hospital, Jharkhand

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Abstract
Introduction: *Cobalamine is required mainly for two important conversion reactions in the body1.for methymalonylcoA isomerization, 2.for methylation of homocysteine. Deficiency of these two reactions in the body has widespread implications. While the deficiency of folic acid in sickle cell anemia has been comprehensively studied, vitamin b12 has been widely overlooked leading to undefined morbidity patterns*
Material and methods: *seventy patients with sickle cell disease were selected for the study.50 were males and 20 females. Complete blood counts, hemograms, vitamin b12 and folic acid levels were obtained and compared with 100 controls. Patients were devided into two groups*
1. Group A-patients with low vitamin B12 levels<160
2. Group B-patients with low-normal vitaminB12 levels>160
Results: *vitamin b12 levels in control group was between 146-860mg/dl(319+_160)Vitamin b12 in study group A was (70.4+-30.6), Vitamin B12 in study group B was(215+_68.6)mean value 153.4. The results were statistically significant difference placed at p<=0.03*
Conclusions: *A High index of suspicion has to be maintained for Vitamin B12 deficiency in sickle cell anemia patients. Supplementation and monitoring is essential to prevent disease.*
Key Words: *Cobalamine, sickle cell anemia*

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I. Introduction

Sickle cell disease refers to hemoglobinopathy arising from a single DNA mutation within beta globin gene. Approximately, 30,000 children are born each year with sickle cell anemia or it's variant. The most common of these diseases are sickle cell anemia (HbSS), hemoglobin sickle cell disease (HbSC) and hemoglobin SB thalassemia (minor and major)

Today, the sickle hemoglobin has interacted with diverse genes and environmental factors producing a multisystemic disease with several phenotypes.

Since hBSS was first described in 1910, efforts have mounted to develop clinical care to lessen the severity of clinical problems., mainly pain episodes and recurrent hospital admissions..Under nutrition was not reviewed as clinically important before 1980's.Now it has been realized that nutrition may be optimized to lessen complications.India reports a 33% prevalence rate of vitamin B12 and 6% prevalence rate of folic acid deficiency.

VitB12 or cobalamin is a water soluble vitamin. It is required for mainly two conversion reactions in the body
1.methylmalonyl coA conversion
2.methylation of homocysteine., It is a cofactor in DNA synthesis and fatty acids as well as amino acid metabolism, nervous system function and red cell formation.

Subjects with sickle cell disease may be at a higher risk of cobalamine deficiency because of increased demand, inadequate supply and coexisting folate deficiency and malabsorption. The anemia of the chronic hemolytic process may mask the classical findings of megalobastic anemia in such patients. Such patients may suffer undiagnosed aches and pains and neuropsychiatric manifestations if vitamin B12 deficiency is not suspected.

The prevalence of subclinical vitamin B12 deficiency in sickle cell disease is not known.

II. Materials And Method

Ethical clearance was obtained from the institute. Sickle cell disease patients were subjected to blood tests and other investigations.

Seventy patients (50 males and 20 females) with sickle cell disease were selected for the study. They all belonged to age group 14-50 years. Mean age was 25 years. Patients less than 14 years of age were excluded from the study. Patients who were already supplemented with vitamin b12, either oral or parenteral and with severe illness and malnutrition were also excluded from the study. Subjects were recruited on basis of medical history.

All patients were on supplementation folic acid 5mg per day. CBC, Ironstudies, vitamin b12, reticulocyte count, hemoglobin electrophoresis, creatinine, bilirubin, serumiron, ferritin, TIBC, folic acid levels were obtained in patients with sickle cell disease. Vit b12 was also obtained in healthy blood donors (70 males and 30 females) aged 14-50 years as normal control group

Patients were devided into two groups according to vit b12 levels

1.Group A-patients with low vitB12 levels<160pg/ml

2.Group B-patients with normal vitB12 levels>160pg/ml

The statistical significance level was set at $p<0.05$, using student T tests, chi square test, Fischer exact test.

III. Results

Mean age of sickle cell disease patients was 25 years.50 males and 20 females were examined in the study group.70 males and 30females were there in control group.

30 cases belonged to age group 14-22 years.20 patients belonged to age group of 23-32 years.10 patients belonged to age group 33-43 years.05patients belonged to age group 45 years and above.

Table 1: Age Distribution

Age in years	Study group		Control group	
	No of cases	Percentage of cases	No of cases	percentage of cases
14-22	30	42.8%	30	30%
23-32	20	28.57%	37	37%
33-43	10	14.28%	22	22%
45 and above	10	14.28%	11	11%

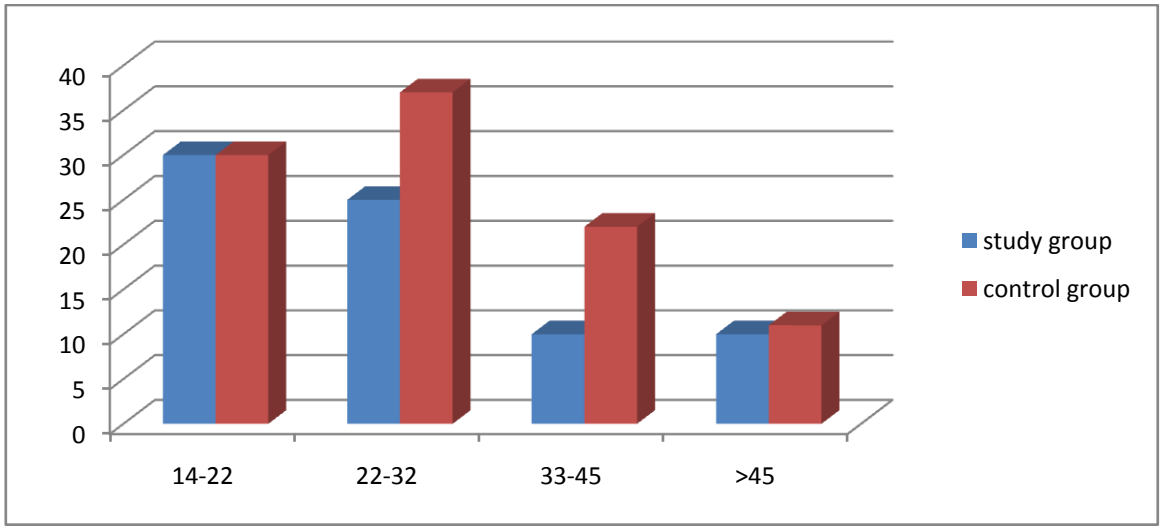


Figure 1: Age Distribution

SEX DISTRIBUTION OF STUDY AND CONTROL GROUP

Study group consisted of 50 males and 20 females, while the control group consisted of 70 males and 30 females

Table 2: SEX DISTRIBUTION OF STUDY AND CONTROL GROUP

SEX	Study group	Control group
Male	50	70
Female	20	30

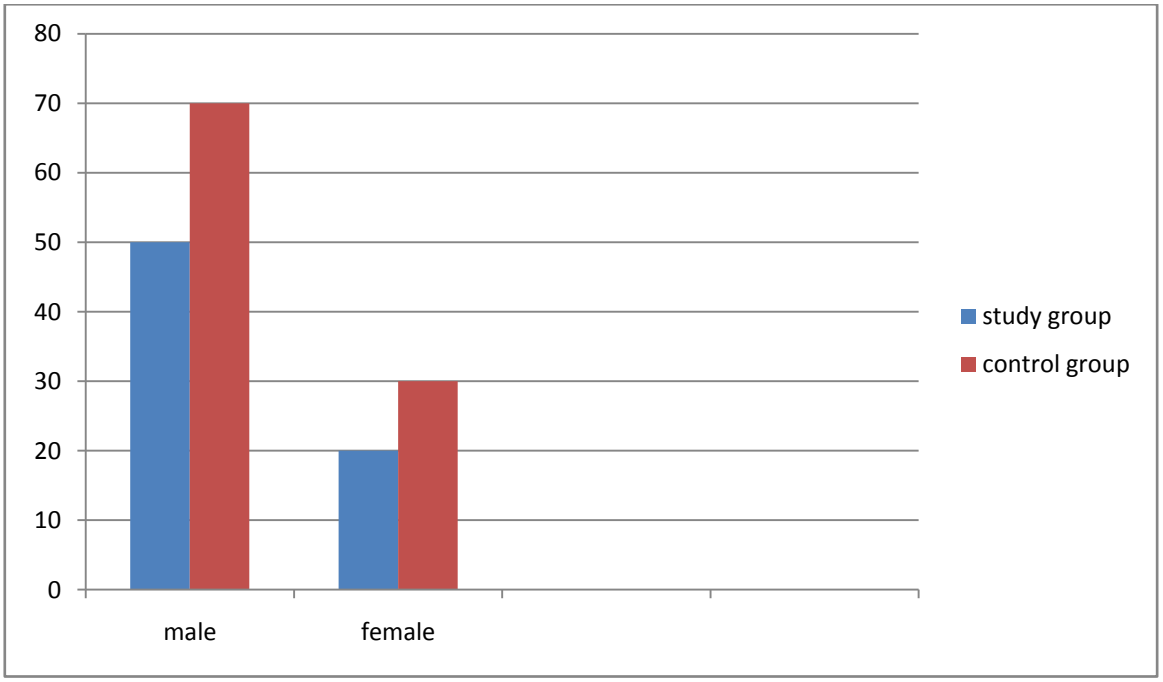


Figure 2: SEX DISTRIBUTION OF STUDY AND CONTROL GROUP

Symptoms and signs of patients on admission

2% of the patients presented with oral conditions including glossitis and altered taste sensation.Clinically, patients with very low vitamin b12 presented with features of loss of taste with soreness of tongue in 3% (groupA) and 2% (groupB). p value was 0.2%.They complained of tingling sensation of hands and feet and difficulty in walking(66%)14% had anxiety ,irritability and other neuropsychiatric disturbances.11% had paresthesias and tingling and 33% patients had reduced sense of position and vibration.

Hemoglobin levels ranged between (7.5+_1.2)mg/dl in study group, and MCV was between (72.4+_10.0)

Iron deficiency was seen in few patients (5), with a prevalence of iron overload in few patients.

Table 3: Symptoms on Day of Admission

Sore tongue	3
Smooth tongue	3
anxiety	14
paresthesia	11
Reduced sense of position	33
Reduced sense of vibration	33

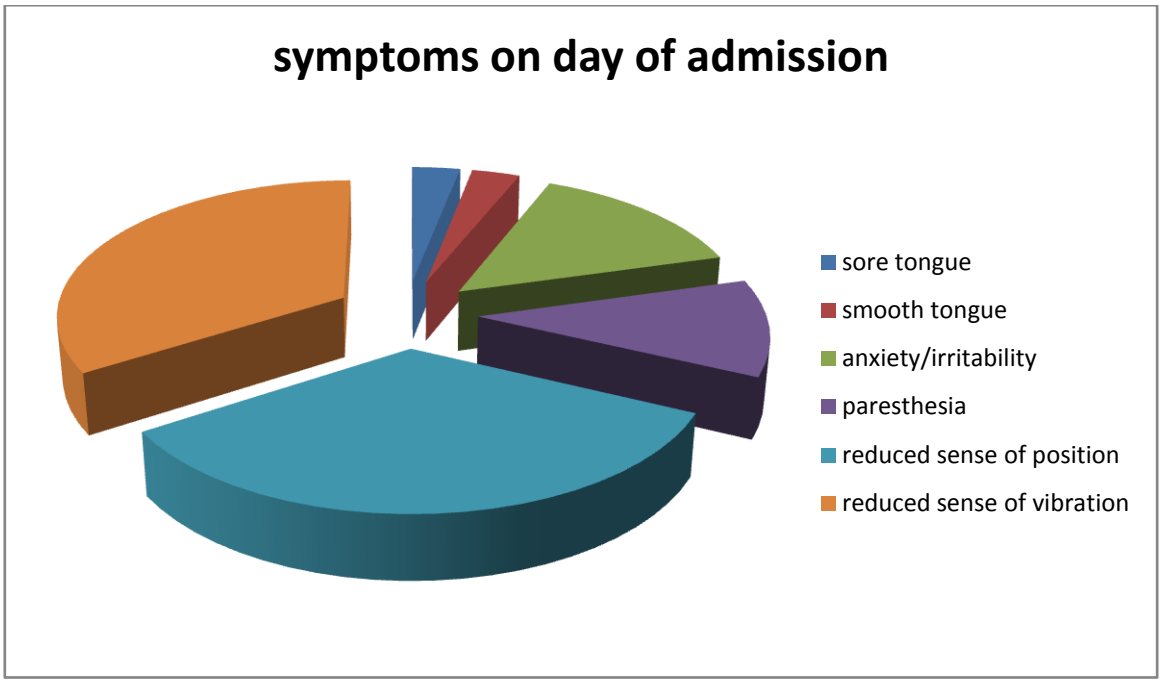
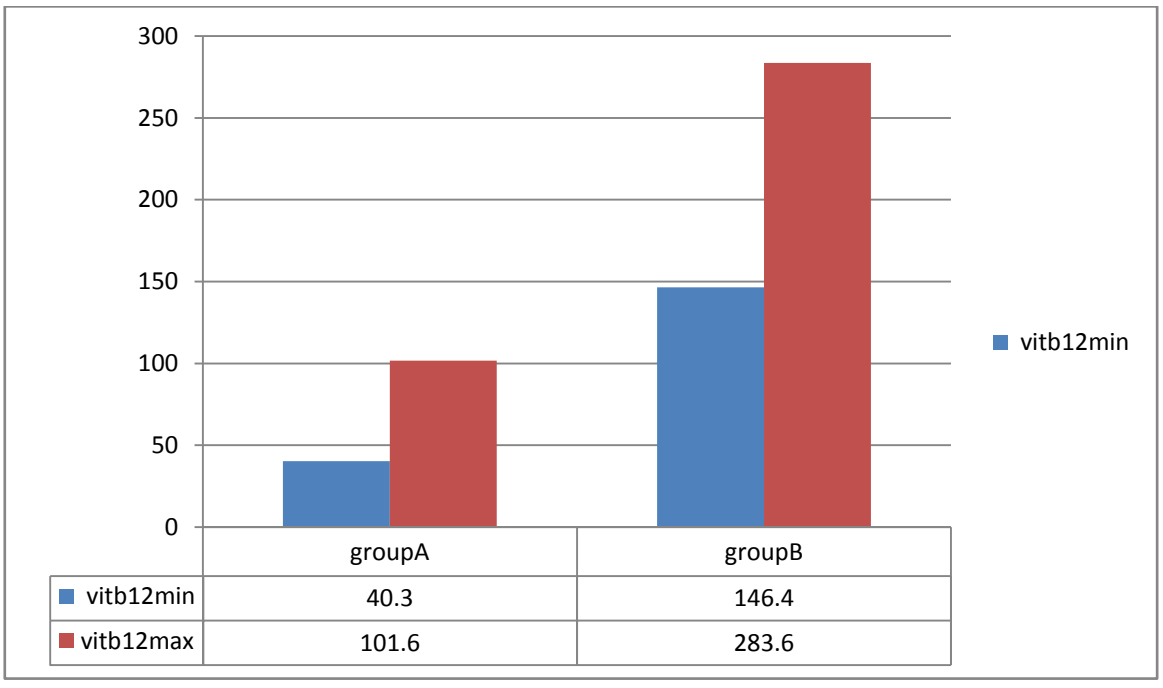


Table 3: Symptoms on Day of Admission

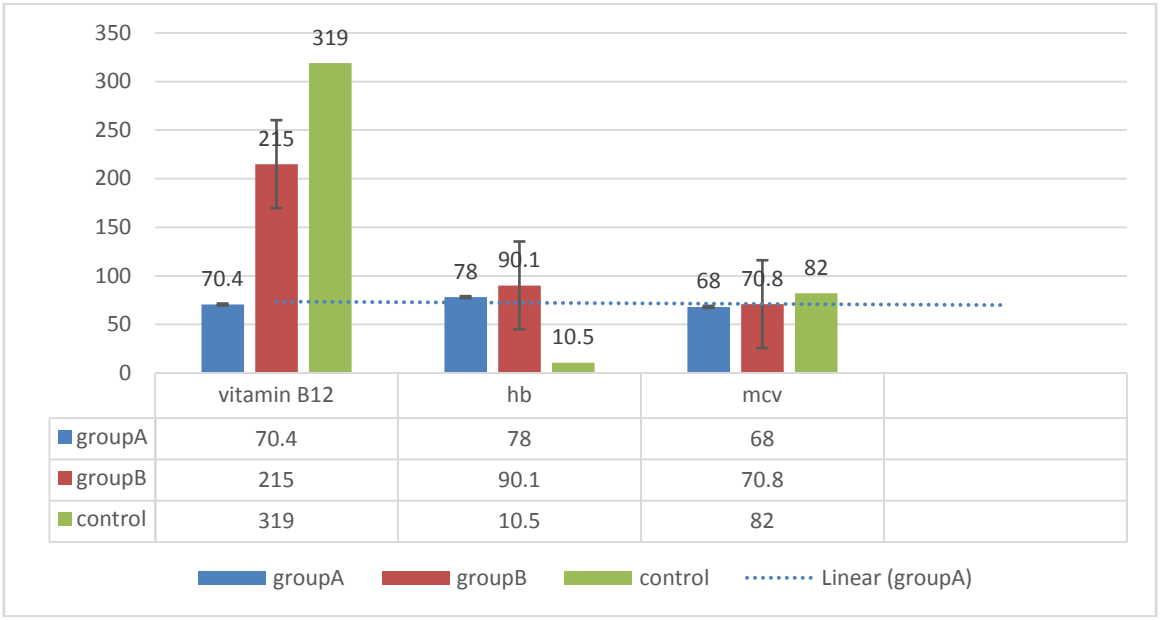
IV. Results

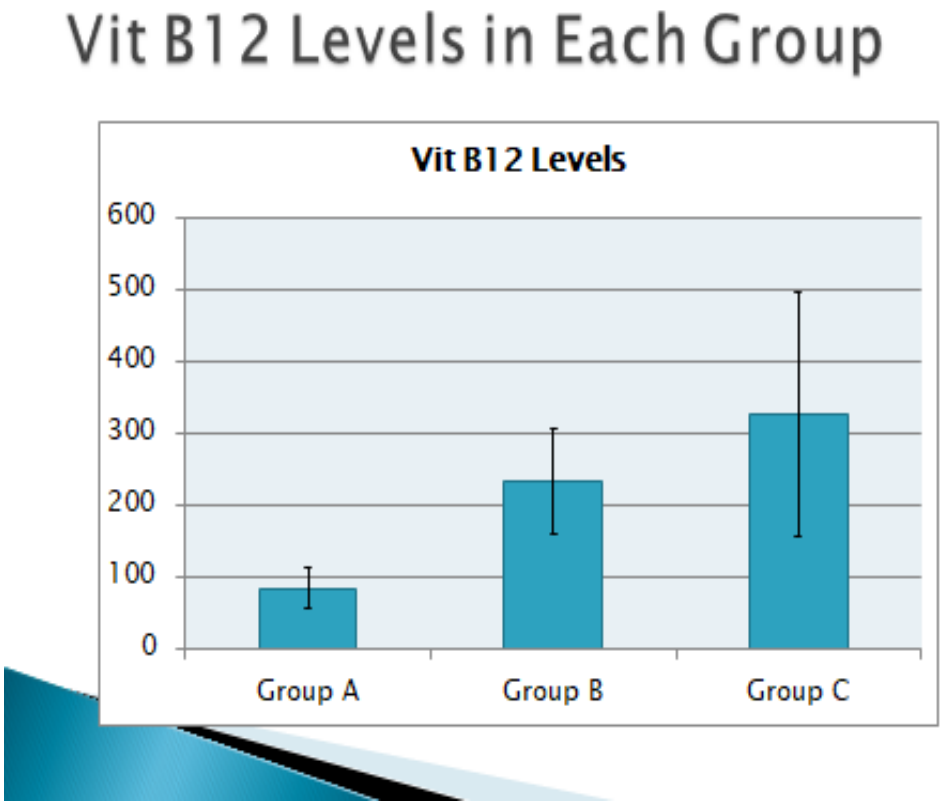
	Group A	Group B	controls	P value
Serum vitb12	70.4±30.1	215±68.6	319±160	0.001
Hb%	78±11.9	90. ±11.1	10.2±2.5	0.197
MCV	68±20	70.8±22.3	82.0±4.1	0.241

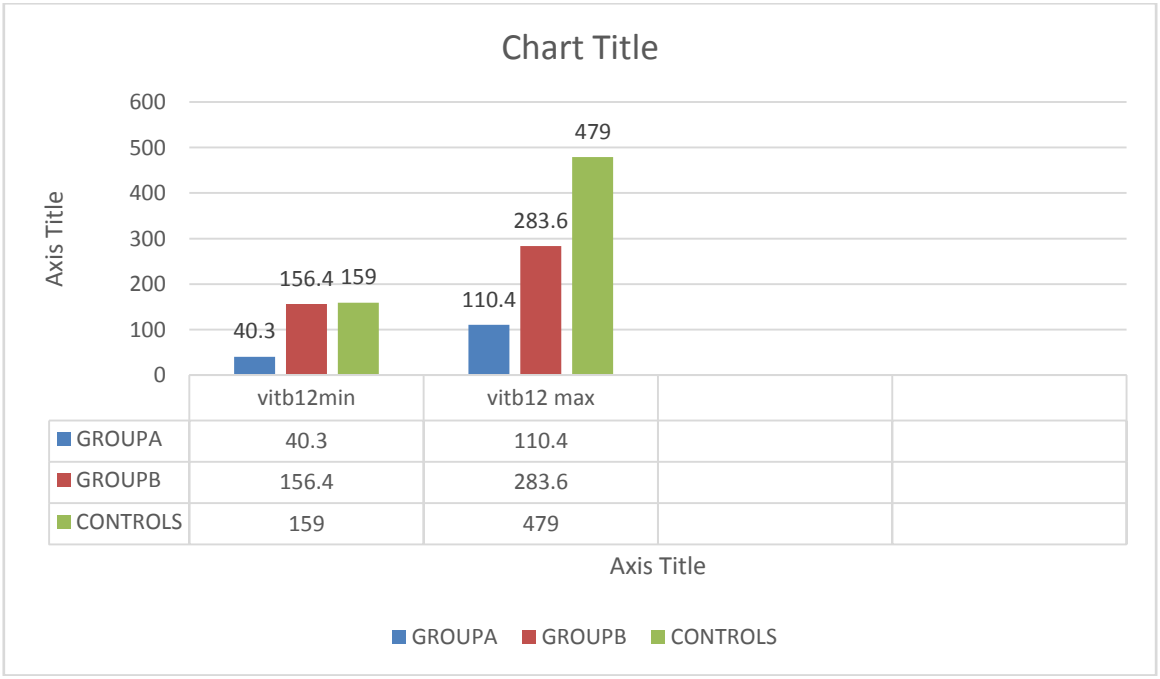
The meancobalamine level in sickle cell study group up was much less than normal contols. Vit b12 levels in study group A was 70.4±30.6 and in study group B ranged from 215±68.6 and the mean value was 153.4.hemoglobin levels were 78±11.9 and MCV was 68±20
Vit b12 levels amongst the control group ranged between ranged between 146-860 (mean 319.2±160



VITAMIN B12 LEVELS IN GROUP A AND GROUP B(MAXIMUM AND MINIMUM)



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GROUPA
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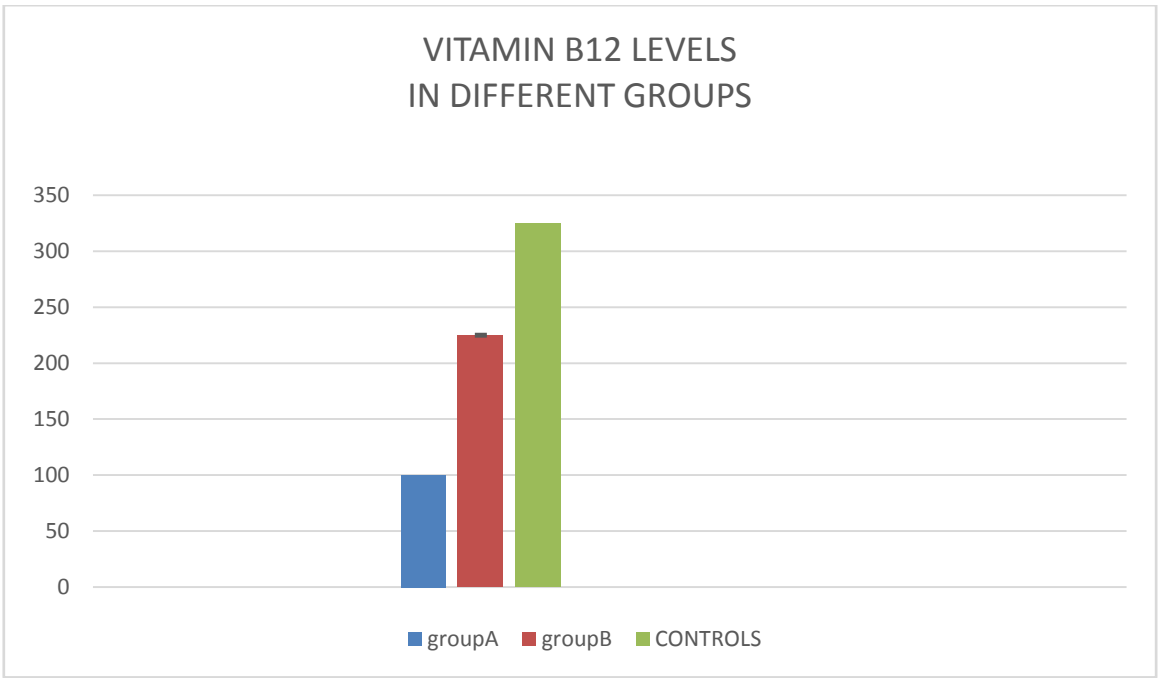
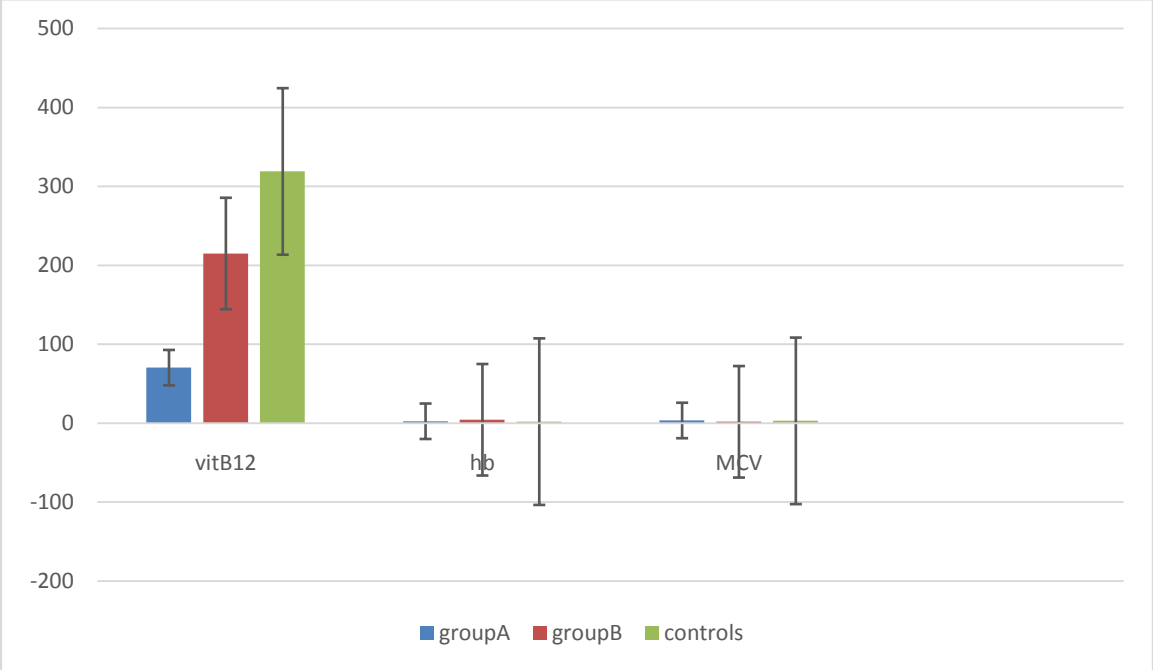

VITAMIN B12 LEVELS
IN DIFFERENT GROUPS
350
300
250
200
150
100
50
0
groupA
groupB
CONTROLS



V. Discussion

Vitamin b12 deficiency is common in individuals with increased demand, in adequate supply, break-down, and decreased absorption. There is routine supplementation of folic acid in sickle cell anemia, which also leads to functional vitamin b12 deficiency. Increased requirement of vitamin b12 is seen in sickle cell disease patients because of ongoing hemolysis and erythrocyte a functional b12 depletion.

Repeated sickling in gastric blood vessels, leading to micro vascular infarcts causes decreased functioning of gastric parietal cells causing reduced production of intrinsic factor

Same mechanism may lead to reduced production of transcobalamin Reduced absorption from the terminal ileum for the same reason causing possible reduced levels of transcobalamine proteins (B12 binders) may all contribute to deficiency states.

It is difficult to suspect vitamin B12 deficiency in sickle cell anemia patients as they usually present with microcytosis. Anemia is usually explained by the sickle cell disease process itself or by other associated phenomenon such as folate deficiency. Chronic pains and vague neurological symptoms are common in both sickle cell disease states as well as vitamin b12 deficiency.

We were unable to provide some ancillary tests in this study such as homocysteine, urinary methylmalonic acid, methylmalonic acid and decreased leucocyte alkaline phosphate levels, which would have given more accurate results.

VI. Conclusion

In conclusion, we derive that we have to keep a High index of suspicion, especially in patients with vague neurological or psychiatric symptoms and look for vitamin b12 deficiency also in addition to folic acid deficiency and provide for routine supplementation in such cases. We should also not hesitate in providing for additional tests when neccessary such as leukocyte alkaline phosphate (LAP), methylmalonic acid and total homocysteine levels in suspected cases. Folic acid supplementation should be regularly monitored as well.

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