



STUDY OF VITAMIN B12 LEVELS IN THYROID DISORDER PATIENTS

General Medicine

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ABSTRACT

Background: Thyroid disorder is one of the most common encountered endocrinological disorder. Vitamin B-12 has the largest and most chemically complex structure of all the vitamins. Deficiency of vitamin B12 in thyroid disorder patients might exaggerate the clinical outcome.

Objective:

- To evaluate vitamin B12 levels in thyroid disorder patients.

Material and method: The study was done in 50 thyroid disorder patients of Sir Takhatsinhji Maharaj hospital, Bhavnagar. Patient clinical findings and history was noted. Patient blood routine investigations CBC, RFT, with serum vitamin B12 levels and Thyroid function test were done.

Result: We screened 50 thyroid disorder patients. Vitamin B12 deficiency was found among 30 patients having thyroid disorders.

Conclusion: Thyroid disorders adversely affect the vitamin B12 levels, so routine assessment of vitamin B12 levels will help doctor for better management and favorable outcome.

Summary: This study was carried out in Department of Medicine, Government Medical College, and Sir Takhatsinhji General Hospital, Bhavnagar.

The study was done on 50 patients with thyroid disorders with a measurement of vitamin B12 levels in admitted and outdoor patients at Sir Takhatsinhji General Hospital, Bhavnagar. Detailed history and examination were done. Routine blood investigations, serum vitamin B12 levels, serum TSH, T3 and T4 levels was done in all patients.

Following are the salient features of the present study

- Thyroid disorder and vitamin B12 deficiency are both, more common among 41 – 50 years people.
- Thyroid disorder is more common among the females.
- Subclinical hypothyroidism is among the more common thyroid disorder.
- Vitamin B12 deficiency is more common in the Hypothyroid patients.

Macrocytic hypochromic anemia is more prevalent among the people with thyroid disorder having vitamin B12 deficiency.

KEYWORDS

INTRODUCTION

Vitamin B-12 (B-12) has the largest and most chemically complex structure of all of the vitamins. Also called cobalamin, B-12 is the only active substance in the body containing an atom of cobalt. ¹ B-12 is synthesized by anaerobic microorganisms in the gut of animals, and as a result, is found naturally in foods of animal sources, including meat, fish, poultry, eggs, and dairy. It is also available in the crystalline form in supplements and fortified foods. ²

Forms of the vitamin include cyanocobalamin and hydroxocobalamin, which may convert to either of the two cofactor forms of B-12: methylcobalamin, the cofactor of methionine synthase, or adenosylcobalamin, the cofactor of L-methylmalonyl-CoA. These reactions are essential for the synthesis of nucleic acids, myelination of the central nervous system, and effective erythropoiesis in bone marrow. An adequate B-12 supply is required to maintain these reactions. ³

B-12 deficiency is associated with a wide range of hematological and neurological, as well as psychiatric and cardiovascular symptoms. ^{4,5} The classic manifestations of deficiency include glossitis, megaloblastic anemia, and myelin deterioration. ⁴ Neurological and psychiatric manifestations, which may include myelopathy, neuropathy, impaired memory, depression, and dementia, are particularly serious, as they can occur even with subclinical deficiency and may become irreversible if left untreated. In addition, the increased concentration of homocysteine associated with B-12 deficiency indicates a risk factor for atherosclerotic and thrombotic events. ⁶

B-12 has a complicated mechanism of absorption beginning with the vitamin being split from its proteinbound form by pepsin and gastric acid. The free vitamin then binds to R-proteins, or haptocorrins, secreted by the salivary glands for transport from the stomach to the intestinal lumen, where B-12 is released to bind with intrinsic factor. Intrinsic factor, which is secreted by gastric parietal cells, forms a complex with B-12 for transport into the small intestine where it is

absorbed at a specific site in the terminal ileum. B-12 then enters the enterocyte and is released to bind with plasma binding proteins transcobalamin I, II, or III for circulation in the blood, delivery to the tissues, or storage in the liver. This process of absorption is complex and is likely to be adversely affected by disorders of the gastrointestinal system. ^{3,7}

Inadequate dietary intake and malabsorption are the most common causes of B-12 deficiency. Inadequate dietary intake is less likely to occur in developed countries, where foods of animal sources compose a major portion of the diet. Strict vegetarians and the elderly, especially those who are malnourished, are more likely to be deficient due to inadequate intake. ⁸

Vitamin B-12 and thyroid dysfunction

The symptoms of B-12 deficiency in patients with thyroid disorders have not been evaluated in detail.

The goal of this review is to describe the prevalence of B-12 deficiency among patients with thyroid dysfunction.

AIM AND OBJECTIVES

AIMS

- Study of vitamin b12 levels in thyroid disorder patients.

OBJECTIVES

- Study of vitamin b12 levels in thyroid disorder patient.
- Study of clinical manifestation in patient with altered vitamin b12 levels and thyroid disorder.

MATERIAL & METHOD

Study will be carried out on patients diagnosed as thyroid disorder on the basis of Serum Thyroid function test in opd or admitted to Medicine wards of Sir T. General Hospital, Bhavnagar after taking permission from Institutional review board and scientific committee, government medical college, Bhavnagar.

Sample Size: 50 cases.

Study Design: Cross-sectional, observational, prospective study

Duration: January 2018 to January 2019.

Inclusion criteria:

- patient > 12 yrs of age
- patient with thyroid disorder on opd basis and admitted in sir t hospital bhavnagar
- patient giving consent

Exclusion criteria:

- patient not giving consent

Method of collection of data: Clinical History, Examination and data from case sheet.

All patients had their thyroid function assessed at admission or on opd basis. Patients with altered thyroid levels were further assessed thoroughly for their clinical signs and symptoms. Patient routine investigations for CBC , serum vitamin B12 , USG neck, were performed. Peripheral smear of blood was done.

Patient was categorized as per the criteria given in the Harrison 19th edition into thyroid disorders like subclinical thyroid, hypothyroid, and hyperthyroid. And into vitamin B12 deficiency and normal Vitamin B12 levels accordingly.

If needed biopsy and ATG were done.

STATISTICAL ANALYSES

For descriptive statistical analysis, mean, standard deviation, and frequencies were calculated.

Different characteristics were represented as numbers or percentage wherever required.

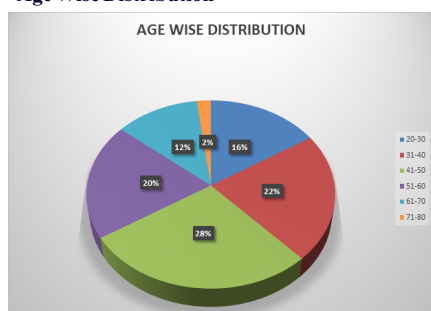
Statistical analysis was done by statistical software SPSS for Windows v16.0 (SPSS, Chicago, IL, USA). Comparisons between groups were performed using the Student t-test continuous variables and the chi-square test (χ^2). P-Value shows the significance level ($p < 0.05$).

LIMITATIONS OF THE PRESENT STUDY

The review included studies which assessed vitamin B12 status using only the serum Vitamin B12 assay, the accuracy of which has been debated. Other markers such as MMA, Holo-TC II , and tHcy were not utilized. The study reviewed did not report performing a complete dietary evaluation prior to beginning the study, so the factor of diet in vitamin B12 deficiency and thyroid disorder cannot be completely ruled out. Study subject consisted of 50 people which was a small group of patients, so a further evaluation of study in larger group might provide us with better orientations

OBSERVATION AND RESULT

Graph 1 – Age Wise Distribution

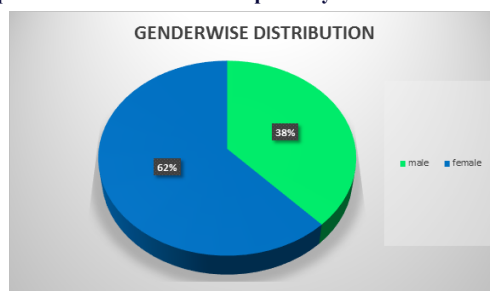


AGE	FREQUENCY	PERCENT
20-30	8	16
31-40	11	22
41-50	14	28
51-60	10	20
61-70	6	12
71-80	1	2
TOTAL	50	100

The study group consisted of participants more of in the age group of 41 years to 50 years followed by an age group of 31 years to 40 years.

Gender Distribution:

Graph 2 – Distribution Of Participants By Gender



Graph 2 – Graph Showing Gender Distribution

SEX	FREQUENCY	PERCENT
Male	19	38
Female	31	62
Total	50	100

The study group consist of females were about 62 % while males were 38 % of the study group.

Graph : 3 Distribution Of Patients According Thyroid Dysfunction

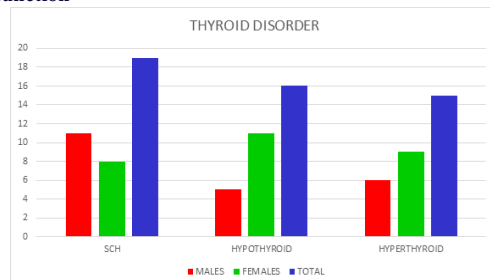
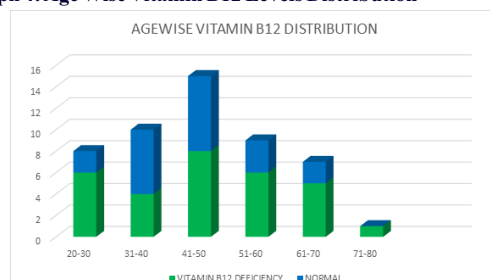


Diagram 3 : Thyroid Dysfunction Distribution

Thyroid Function	Males	Females	Number Of Patients	Percentage Of Patients
SCH	11	8	19	36
HYPOTHYROID	5	11	16	34
HYPERTHYROID	6	9	15	30
TOTAL	22	28	50	100

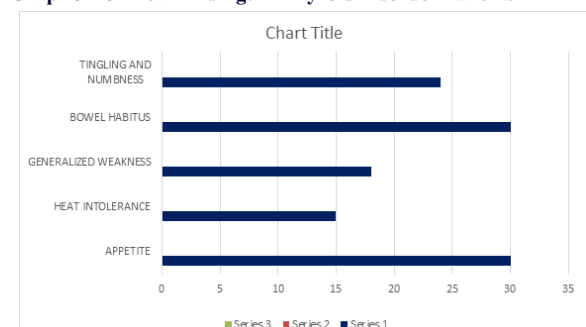
Thyroid distribution showed a maximum patient were subclinical hypothyroidism of the study group, followed by hypothyroid and hyperthyroid patients.

Graph 4: Age Wise Vitamin B12 Levels Distribution



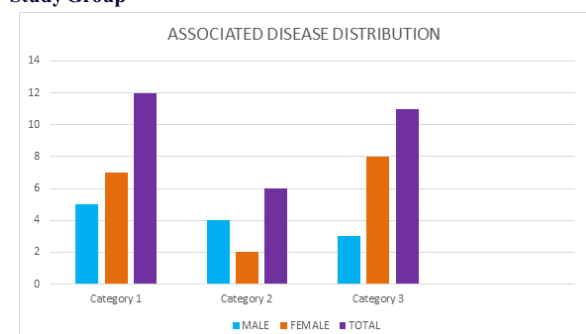
AGE	VITAMIN B12 DEFICIENCY	NORMAL VITAMIN B 12 LEVELS
20-30	6	2
31-40	4	6
41-50	8	7
51-60	6	3
61-70	5	2
71-80	1	0
TOTAL	30	20

Maximum VITAMIN B12 deficient age group found to be of 41 years to 50 years.

Graph 5 – Clinical Findings In Thyroid Disorder Patients

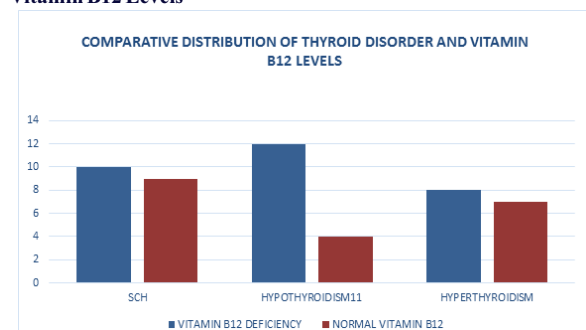
CLINICAL FEATURES	TOTAL	PERCENTAGE
APPETITE	30	60 %
HEAT INTOLERANCE	15	30 %
GENERALIZED WEAKNESS	18	36 %
BOWEL HABITUS	30	60 %
TINGLING AND NUMBNESS	24	48 %

Altered bowel habitus and altered appetite was the most common clinical finding observed in the study group. 13 patients out of 15 hyperthyroid patients had increased appetite while, 22 patients of subclinical hypothyroidism and hypothyroidism had decreased appetite.

Graph 6 - Gender Wise Distribution Of Associated Diseases In Study Group

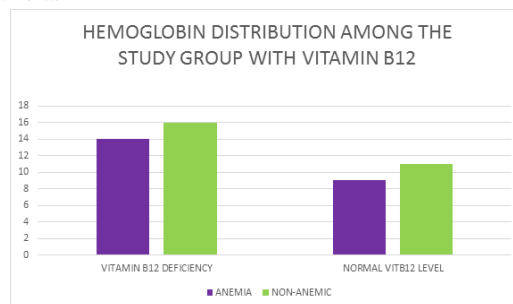
ASSOCIATED DISORDER	MALE	FEMALE	TOTAL
IHD	5	7	12
HYPERTENSION	4	2	6
DM	3	8	11

IHD, Hypertension and Diabetes mellites were studied among the study group.

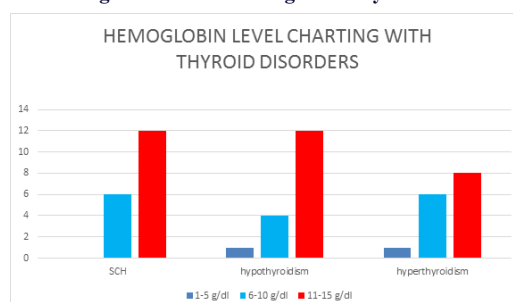
Graph 7 - Comparative Distribution Of Thyroid Disorder And Vitamin B12 Levels

	Vitamin B12 Deficiency	Percentage	Normal vitamin b12	Percentage
SCH	10	20 %	9	18 %
Hypothyroidism	12	24 %	4	8 %
Hyperthyroidism	8	16 %	7	14 %

Highest of 26 % of subjects showed vitamin B12 deficiency among hypothyroid group and 16 % of subjects showed vitamin B12 deficiency among hyperthyroid group.

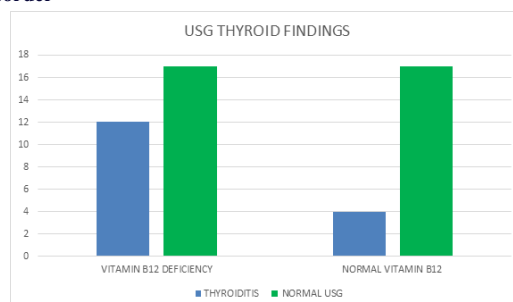
Graph 8 - Hemoglobin Distribution Among The Study Group With Vitamin B12

The number of patients with vitamin B12 deficiency and thyroid disorder were found to be 28 % as anemic.

Chart 9 Hemoglobin Level Charting With Thyroid Disorders

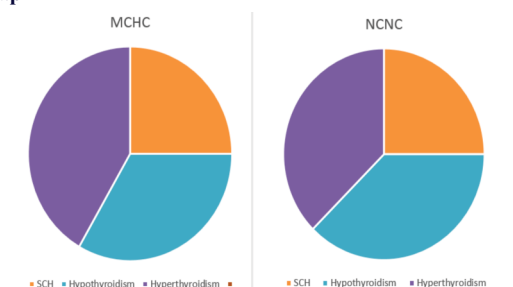
Hemoglobin Levles -	1-5 g/dl	6-10 g/dl	11-15 g/dl
SCH	0	6	12
Hypothyroidism	1	4	12
Hyperthyroidism	1	6	8

The chart implies the distribution of the hemoglobin ranges among the different thyroid disorder among the present study group .

Graph 10 Thyroid Ultrasonography Distribution With Thyroid Disorder

	Thyroiditis	Percentage	Normal	Percentage
Vitamin B12 Deficiency	12	24	17	34
Normal Vitamin B12 Levels	4	8	17	34
Total	16	32	34	68

24 % of the patients with vitamin B12 deficiency with underlying thyroid disorder were found to have thyroiditis in USG findings.

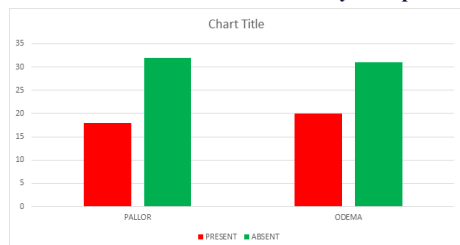
Graph 11

Types of anemia with vitamin B12 deficiency in thyroid disorder patients.

Types of anemia	MCHC	NCNC
SCH	3	2
Hypothyroidism	4	3
Hyperthyroidism	5	3

Comparative study of types of anemia in the study group, suggestive of macrocytic hypochromic anemia is more common in all the three types of thyroid disorder.

Graph 12: General Examination In The Study Group



	PRESENT	Percent	ABSENT	Percent
PALLOR	18	36	32	64
OEDEMA	20	40	31	62

Edema was present in 40 % of the patient and pallor among 36 % of patients.

DISCUSSION

Due to the non-specificity of symptoms and possibly severe consequences of untreated vitamin B-12 deficiency, screening is important for at-risk patients to ensure the prompt delivery of treatment. In this review, studies assessing the prevalence of vitamin B-12 deficiency in thyroid dysfunction are evaluated to determine whether regular vitamin B-12 screening is necessary.

This study was conducted on a group of 50 thyroid disorder patients to

	Present Study		Singapore			Rio de Janeiro, Brazil		P value
Thyroid Function	Males	Percent	Females	Percent	Total	Males	Females	
SCH	11	22	8	16	18	51	47	0.0239
Hypothyroid	5	10	11	22	17	30	39	0.0149
Hyperthyroid	6	12	9	18	15	39	19	0.0772
Total	19	38	31	62	50	200	186	0.0243

P value of subclinical hypothyroidism is 0.0239 and hypothyroidism is 0.0149 which is clinically significant.

Clinical findings among the study group were as follows:

	Present study		Karachi Pakistan	
	Present	Percent	Present	percent
PALLOR	18	36	9/102	8.82
OEDEMA	20	40	23/71	32.39

The p value of the clinical findings of the 2 study is 2.2834, which is clinically not-significant.

Among the age group division according to vitamin B12 deficiency, middle age group 41 years to 50 years followed by 31 years to 40 years are more deficient in vitamin B12 than other age groups. This finding is consistent with other study published at NCBI done on Taiwan people with an average age of sample was 36.5 years.

Average sample age	Taiwan	Present
Vitamin B12 deficiency	36.5	32.8
P value	Not available	0.04489

P value of the present study is clinically significant with the average sample age of patient to be 32.8, which is consistent with the study of NCBI Taiwan

Thyroid disorders and Vitamin B12 deficient patients often have common symptoms of change in appetite, tingling and numbness, altered bowel habitus and generalized weakness. Approximately 60 % of our patients has experienced changed in appetite and bowel habitus.

	Present		Karachi	
Clinical Features	Total	Percentage	Total	Percentage
Appetite	30/50	60 %	15/114	13.15

find out any correlation between serum vitamin B12 levels and thyroid disorders.

The most affected age group by thyroid disorders is between 31 years to 40 years, followed by age group of 21 years to 30 years.

AGE related comparative analysis

	Taipen study	Greenville USA	Karachi pakistan	Present
Patients sample size	190	116	116	50
P value	Not available	Not available	Not available	3.7298
Mean Age with SD	60.1 ± 11.6 years	44 ± 13.7 years	44 ± 13.7	45 ± 14.2

As the p value is 3.7298 which is more than 0.05, hence the age criteria is insignificant compared with the other studies. But the mean with SD was consistent with the karachi and USA study groups.

As far as the gender is concerned, thyroid disorder is more prevalent among the female group with around 62 % which was twice compared to the thyroid disorder among males with around 38 %.

SEX	Karachi, Pakistan	Erdogan et al	Present
Female	101	85	62
Male	15	15	38
Total	116	100	8100
P value	0.08266	2.5596	0.0163

The p value of the study at present is 0.0163 which is significant, compared to the study group of patients in karachi and erdogen et al study group based on gender. Genderwise females were more affected by thyroid disorders in all of the comparative studies including the present one.

In this study prevalence of SCH was more common among the study group of present which was consistent with the study of Rio de Janeiro.

Heat Intolerance	15/50	30 %	8/116	6.89
Generalized Weakness	18/50	36 %	61/113	53.98
Bowel Habitus	30/50	60 %	6/113	5.3
Tingling And Numbness	24/50	48 %	15/111	13.51

P Value of comparison of the two studies was 8.8288 which was non-significant. Which applies that the present study results in not consistent with the study carried out in Karachi.

Associated Disorders	Present Study	Percent	Palak , Vadodara	Percent	P Value
IHD	12	24 %	3	5.1	2.87152
Hypertension	6	12 %	12	20	
DM	11	22 %	1	1.7	

The p value of the study comparison between the palak et al and the current study is non-significant. The p value stands to be 2.87152.

Study of anemia in the study group

	Riyad Saudi		Present	
	MEAN ± SD	P Value	MEAN ± SD	P Value
Age	29.53 ± 9.22	0.515	45 ± 14.2	
Hemoglobin	13.43 ± 1.69	0.924	11.29 ± 1.88	
Vitamin B12	289 ± 187.93	0.002	224.16 ± 165.78	0.0049
MCHC	--	0.001	--	0.0324
NCNC	--	5.723	--	2.043

Macrocytic hypochromic anemia is a significant finding in the present study group as consistent with Riyad Saudi studies as the p value is 0.0324.

Study of USG was done among the study group of thyroid disorder patients

	Thyroiditis	Percentage	Normal	Percentage
Vitamin B12 Deficiency	12	24	17	34
Normal Vitamin B12 Levels	4	8	17	34
Total	16	32	34	68

P value is 2.8358 of the patients in the group having thyroid disorders which is insignificant.

Thyroid disorder comparison with the vitamin B12 deficiency

	Vitamin B12 Deficiency	Percentage	Normal Vitamin B12	Percentage
SCH	10	20 %	9	18 %
Hypothyroidism	12	24 %	4	8 %
Hyperthyroidism	8	16 %	7	14 %

The p value of vitamin b12 deficiency in thyroid disorder present study group is 0.01534, which is clinically significant.

Author	Prevalence Of Vitamin B12 In Study Group (percent)	Study Group	Mean Sd Age Of Patients	P Value	Country
Jabbar et al	40.5	116	44 ± 13.7	Not provided	Pakistan
Erdogan et al	25.6	100	44.9 ± 14.2	0.002	Turkey
Das Et al	10	60	36.5	0.002	East India
Ness Abramof	28	115	47 ± 15	Not provided	Israel
Jaya kumari et al	55.5	350	32.2	Not provided	South India
Wang et al	6.2	190	60.5 ± 11.7	Not provided	Taiwan
Present study	60	50	45 ± 14.2	0.01534	India

Study of Erdogan et al, Das et al, and the present study has a significant P value, suggestive that vitamin B12 deficiency is observed in thyroid disorder patients.

CONCLUSION

This study shows that most affected age group by thyroid disorders is between 31 years to 40 years, more prevalent among females. Prevalence of thyroid disorder was more common in females. Change of appetite was the most common presenting complaints with increased appetite was seen among hyperthyroid and decreased appetite was seen among subclinical hypothyroid and hypothyroid patients. The prevalence of vitamin B12 was more common among age group of 41 to 50 years and more among the female gender. IHD, hypertension and DM was among the associated disorders in the present study group. 60 % of cases had vitamin B12 deficiency among the thyroid disorder in present study group. Macrocytic hypochromic type of anemia is more prevalent among patients with thyroid disorders with vitamin B12 deficiency in present study group.

Thyroid disorders adversely affect the vitamin B12 levels, so routine assessment of vitamin B12 levels will help doctor for better management and favorable outcome of the patients.

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- prevalence of vitamin B 12 deficiency among patients with thyroid dysfunction, Roman Pawlak, Greenville, NC, USA
- vitamin B12 deficiency with anti-thyroid autoantibodies, Hung pin lin, Taiwan
- Association of vitiligo with anemia , vitamin B12 deficiency in Saudi arab patients, Riyadh, Saudi arabia.