

Association of Vitamin B12 Levels among Patients with Hypo and Hyperthyroidism: Evidence from a Tertiary Care Teaching Hospital in South India

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ABSTRACT

Thyroid dysfunction, are on the increase in worldwide and also it's linked to deficiency of micronutrient. This study was evaluated the prevalence of vitamin B12 levels deficiency in thyroid dysfunction, cases in a teaching hospital in south India. A simple descriptive cross-sectional study was conducted in single-centric with thyroid dysfunction patients. Serum TSH was measured to confirm the thyroid dysfunction and confirmed thyroid cases were analyzed serum vitamin B12 by ELISA. Statistical analyses by descriptive analysis included Chi-square tests. A total of 396 cases were screened and found 107 (27%) male and 289 (73%) female patients. Higher numbers of patients were middle-aged about 48.2%. Among 396 cases, the hypothyroid was 81.6% and hyperthyroidism cases 18.4%. Female patients was found significant thyroid dysfunction cases than male. Vitamin B12 levels were 58.8% of < 200 pg/ml and 41.2% is more than 200 pg/ml in overall thyroid dysfunction (hypo and hyperthyroid) cases. In conclusion, the thyroid dysfunction cases vitamin B12 deficiency prevalence rate was higher, therefore routine vitamin B12 screening is recommended to thyroid dysfunction patients.

Keywords: Vitamin B12, Thyroid dysfunction, TSH, Hypothyroidism, Hyperthyroidism

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INTRODUCTION

The endocrine disorder is related to thyroid imbalance. Endocrine diseases have a substantial factor and influence in community health owing to associated long-term morbidity, lead to decline in quality of life, and mortality¹. Among endocrine disorder, thyroid dysfunction are the most common prevalence both in India and worldwide². The thyroid diseases include goiter, thyroiditis, thyroid nodules, hypothyroidism, hyperthyroidism, and thyroid malignancy. Among various thyroid dysfunction problem, hypothyroidism is the most frequent one in India and comprises 11%, compared to Western population with 2%–4.6% in adults³. There are higher hypothyroidism were observed in the coastal states (11.7% vs. 9.5%), compared than Inland states, may be deficiency of iodine⁴.

The occurrence rate for hypothyroidism was more in women than in men. Geographical factors, age, sex, ethnicity, and iodine consumption are the defining factors for the occurrence of thyroid complications⁵. Thyroid dysfunction affects peoples around 42 million in India, with 3–5% hypothyroidism prevalence was connected to autoimmune etiology². Many factors including vitamin B12 related with number of diseases and important to look and rule it out initially for starting treatment⁶.

Vitamin B12 deficiency causes neurologic and hematological complications that is often connected with autoimmune thyroid disease^{7,8}. Vitamin B12 deficiency is frequently start to be coexisting in hypothyroidism patients. The relation between autoimmune thyroid

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disorders and vitamin B12 deficiency is prospective due to the associated with other autoimmune problems and resulted in impaired vitamin B12 absorption⁹. There are many number of vitamin B12 deficiency cases in hypothyroid patients were increased with age¹⁰. Patients with a vitamin B12 deficiency and hypothyroidism typically have symptoms of weakness, poor memory retention, fatigue, itching, and loss of sensation, that are characteristic of both individual diseases. Therefore, our study aimed to assess the analysis of B12 among thyroid dysfunction patients to evaluate the deficiency status.

METHODS AND MATERIALS

Study design and sample size

Our study was a single-centric cross-sectional study, conducted in the Department of Biochemistry and Central Research Laboratory of Swamy Vivekanandha Medical College Hospital and Research Institute (SVMCHRI), a tertiary care teaching hospital in South India.

Sample size:

A total of 323 patients could be included in this study using this formula.

$$n = Z^2 \times (1 - p) \div d^2$$

p = Prevalence of vitamin B12 deficiency = 70% (Based on previous study)¹¹

d = allowance error = 5

Z= 1.96 (95% Confidence interval)

The study sample incorporated with low and high TSH abnormal cases of both hypothyroidism and hyperthyroid cases. The hypothyroid cases to attain the calculated sample size to reach until 323. During this period of hyperthyroid cases were included (73 cases) and collected for the evaluation.

Study participants:

Inclusion criteria: All patients aged ≥ 18 years with thyroid dysfunctions and patients who were not taking vitamin supplements for at least two week, was included in the study.

Exclusion criteria: The exclusion criteria as follows: (1) pregnant or lactating females; (2) below the

age 18 of any gender (3) above the age of 75 of any gender.

Ethical consideration

This research was executed after approved by the institutional ethical committee (IEC-SVMCHRI) and written informed consent was collected from the patients. Data confidentiality and no personally identifiable information were collected.

METHODOLOGY

The serum sample was collected from the thyroid dysfunction cases that was considered based on the low or high serum TSH concentrations (Hypo and hyperthyroid). TSH was measured in the central laboratory, Department of Biochemistry, through Autoanalyser (Vitros chemistry 5.1 and Vitros Eci, Japan). Cases were diagnosed with laboratory cut-off value. TSH more than 5.0 $\mu\text{IU/ml}$ was considered as hypothyroid, and less than 0.5 $\mu\text{IU/ml}$ as hyperthyroidism. Other general information's (sex, age) were collected from the patients. Serum vitamin B12 concentration was determined by ELISA (Enzyme-linked Immunosorbent assay) method by Vitamin B12 Quanti Microelisa (J. Mitra & Co. Pvt. Ltd., India), according to the kit manual.

DATA ANALYSIS

Statistical analysis will be performed using SPSS 25 version. All variables, including patients' demographic data, vitamin B12 level, TSH were subjected to descriptive analysis and percentage distribution and correlation was analysed by Chi-Square test. The continuous variables are presented as mean and standard deviation (mean \pm SD). A p value of <0.05 was considered statistically significant.

RESULTS

Vitamin B12 was analyzed in the thyroid dysfunction patients and considered deficiency was a value less than 200 pg/ml. The collected patients were about 323, hypothyroid and 73 hyperthyroidism. A total of 107 (27%) male and 289 (73%) female patients were participated in this study about the female population was more. Higher numbers of patients were middle-aged about 48.2%, while adolescents represented 35.1% of patients and about 16.7% of patients were more than 60 years older. The overall age distribution between male and female patients was depicted in the table.1.

Table1. Distribution of thyroid dysfunction patients based on age. Comparison of male and female thyroid dysfunction patients with was significant ($p < 0.05$) through Chi-square analysis.

Age Duration	Count	Sex		Total	Significance Pearson Chi-Square
		Male	Female		
18-40	No	29	110	139	p=0.036* (p<0.05)
	%	7.3	27.8	35.1	
40-60	No	53	138	191	
	%	13.4	34.8	48.2	
> 60	No	25	41	66	
	%	6.3	10.4	16.7	
Total	No	107	289	396	
	%	27.0	73.0	100.0	

RESEARCH PAPER

The mean for the age 46.18±14.34, vitamin B12, 46.68±14.35, vitamin B12, 210.46±148.51, TSH 221.32±185.89, TSH 32.89±40.94 in hypothyroid and age 0.098±0.128 in hyperthyroid respectively (Table 2).

Table 2. The mean and standard deviations (SD) of thyroid dysfunction patients for the variables.

Variables	Hypothyroid (n=323) Mean and SD	Hyperthyroid (n=73) Mean and SD
Age (Years)	46.18±14.343	46.68±14.35
B12 (pg/ml)	221.32±185.89	210.46±148.51
TSH (mIU/ml)	32.92±40.94	0.098±0.128

Among 396 cases hypothyroid was found to be 81.6% and hyperthyroidism cases 18.4%. The hypo and hyperthyroid dysfunction cases between male and female patients was found to be significant (p=0.024) (Table 3).

Table 3. Comparison of gender with hypo and hyper thyroid patients. Thyroid dysfunction by TSH in gender distribution was significant (p<0.05) through Chi-square analysis

Thyroid status	Count	Sex		Total	Significance Pearson Chi-Square
		Male	Female		
Hypothyroid (>5 mIU/ml)	No	95	228	323	p=0.024* (p<0.05)
	%	24.0	57.6	81.6	
(<0.5 mIU/ml) Hyperthyroid	No	12	61	73	
	%	3.0	15.4	18.4	
Total	No	107	289	396	
	%	27.0	73.0	100.0	

The vitamin B12 levels were analysed and found to be 58.8% of < 200 pg/ml in overall thyroid dysfunction (hypo and hyperthyroid) and 41.2% is more than 200 pg/ml. there was no significant changes was observed between both hypo and hyperthyroid cases (Table 4).

Table 4. Comparison of vitamin B12 deficiency in hypo and hyperthyroid patients. Vitamin B12 deficiency distribution was no significant between hypo and hyperthyroidism group through Chi-square analysis.

Thyroid status	Count	B12		Total	Significance Pearson Chi-Square
		< 200	> 200		
Hypothyroid (>5 mIU/ml)	No	194	129	323	p=0.298 No significance
	%	49	32.6	81.6	
(<0.5 mIU/ml) Hyperthyroid	No	39	34	73	
	%	9.8	8.6	18.4	
Total	No	233	163	396	
	%	58.8	41.2	100	

DISCUSSION

Water soluble vitamin B12 is mainly achieved from animal based foods, because humans are unable to synthesize and it's necessary for neurological function, red blood cell (RBC) formation and DNA synthesis¹². Deficiency of B12 is frequently associated with various problems including neurological disorder, mucosal alterations, megaloblastic anemia and thyroid dysfunction. There are number of studies continues to be a debate about the association of thyroid dysfunction with B12 deficiency. In our study, 40-60 age group was about 48.2% and the overall thyroid dysfunction cases for the male and female population was about 27 and 73% respectively (Table 1). Females correspond to the majority in thyroid dysfunction patients, which is compared than male population with the known high prevalence of hypothyroidism cases among the females¹³. Also another study, females were higher 54% than in males about 46% for the incidence rate¹⁴. They suggested that untreated *Helicobacter pylori* infection may also leads to vitamin B12 deficiency. A study found that deficiency of vitamin B12 in gastric neuroendocrine tumors¹⁵ and peripheral neuropathy in association with vitamin B12 levels¹⁶. The prevalence of vitamin B12 deficiency was increased with numerous studies

particularly in thyroid disorder case. Thyroid hormones has major role in cellular metabolism, gastrointestinal function and erythropoiesis. Therefore, thyroid dysfunction affects absorption and utilization of the vitamin B12. A meta-analysis study from 64 studies (n=28000) reported that vitamin B12 deficiency in hypothyroidism than healthy individual⁸.

A study conducted from a medical college in central India among the 100 hypothyroid cases, 69% were females and 31% were males. In this study, 68% were vitamin B12 deficient, among which 73.5% were females¹⁷. Previous studies have shown that vitamin B12 deficiency (40.5%) to be common in hypothyroid cases and recommended that screening of vitamin B12 should be undertaken in early stage of the diagnosis of hypothyroidism as well as required periodically¹⁸. Another studies reported that B12 deficiency was about 46% of hypothyroid patients¹⁹. Although some other studies reinforced that routine screening of hypothyroid patients for vitamin B12 deficiency estimation^{18,19}. Hyperthyroid patients also exhibited vitamin B12 deficiency, explained that imbalance of thyroid hormone in long time may influence cobalamin metabolism. A study reported a vitamin B12 deficiency was observed between in subclinical

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hypothyroidism and hyperthyroidism²⁰. Other second-line tests such as Methylmalonic Acid (MMA), homo cysteine, and holotranscobalamin before treatment²¹. But also, screening required for the cases of polyglandular autoimmune syndromes with autoimmune gastritis (PA) and celiac disease, because of their association may cause cobalamin deficiency²². A retrospective study evidenced that vitamin B12 deficiency was not different/or associated in patients with hypo/hyperthyroidism²³. In our study was also not significant of vitamin B12 (Table 4) deficiency between hypo and hyperthyroidism. A recent study conducted vitamin B12 deficiency in thyroid dysfunction cases was linked to autoimmune etiology and recommended that assessment of B12 and supplementation may require for prevention of complications in thyroid disorder management²⁴.

LIMITATIONS

Our study does not address confounding factors like lifestyle and dietary habit. Our study collected thyroid dysfunctions patients without taking vitamin supplements for more than two week was included and not studied about any subtype of thyroid disorder. Also, is a single-center, and other limitations including small sample size and autoimmune markers were not evaluated. Further multicentric longitudinal studies may include for better understand on vitamin B12 metabolism.

CONCLUSION

Deficiency of vitamin B12 in thyroid dysfunction, linked to autoimmune etiology. The association between thyroid dysfunction and vitamin B12 levels were of great importance. Hypo and hyperthyroidism patients are showed decreased vitamin B12 levels. Therefore, routine B12 assessment, along with surrogate markers including anemia and supplementation should be integrated into thyroid dysfunction for the disease management to prevent complications. Larger studies required to be undertaken for evaluate this further initiation of early therapy will prevent the long-term sequelae of vitamin B12 deficiency.

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Compliance with Ethical Standards:

Ethical Committee Approval: The study was approved by the institutional ethical committee of SVMCHRI (SVMCHRI/IEC/AUG/2023/005).

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Consent to participation declaration: Every human participant was provided their consent after being informed about the study procedures. The voluntary participation was included in this study.

Declarations:

Clinical trial number: Not applicable.

Competing interests: None.

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