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## Original Research Article

Prevalence of vitamin B<sub>12</sub> deficiency in patients with thyroid disorders: A study from Himalayan regionRavinder Kaur<sup>1,\*</sup>, Harjitpal Singh<sup>2</sup>, Rajinder Singh Yadav<sup>3</sup><sup>1</sup>Dept. of Biochemistry, Dr Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India<sup>2</sup>Dept. of ENT, Dr Radhakrishnan Government Medical College, Hamirpur, Himachal Pradesh, India<sup>3</sup>Dept. of Biochemistry, Dr. Rajendra Prasad Government Medical College, Kangra, Himachal Pradesh, India

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## ABSTRACT

**Background:** Endocrine disorders are on the rise world over. Diseases of thyroid gland are among the most prevalent endocrine disorders in the world, second only to diabetes mellitus. In India, autoimmune thyroid disorders have been estimated to be the most frequent endocrine disorders. Thyroid diseases are more prevalent in the sub Himalayan region even in post iodination phase.

**Aim:** To assess the prevalence of auto immune thyroid disease and vitamin B12 deficiency in patients with thyroid disorders in Himalayan region.

**Materials and Methods:** Study population comprised of patients above 18 years of age, who were advised thyroid function tests by the clinicians on an outpatient basis. Patients who were critically ill were excluded from the study. Thyroid function tests (T3, T4, TSH) along with anti thyroperoxidase antibody (ATA) was done by chemiluminescence and vitamin B12 levels were done by chemiluminiscent enzyme immunoassay after serum separation of 120 subjects. ATA level >50uIU/ml was taken as positive and Vitamin B12 deficiency was taken as a value less than 160 pg/ml.

**Results:** Mean age of study population was 42.48 (± 12.32) years. Forty hypothyroid and forty hyperthyroid and 40 controls were recruited. ATA positivity was reported in 52.5% (63/120) of the samples. In the present study more than 50% of cases with thyroid disorder and ATA positivity showed deficiency of vitamin B12 (hypothyroidism 63.3% hyperthyroidism, 51.8%).

**Conclusion:** All patients with thyroid dysfunction should be screened for vitamin B12 status and treated accordingly.

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## 1. Introduction

Endocrine disorders are on the rise world over. Thyroid diseases are more prevalent in the sub Himalayan region even in post iodination phase. In India, autoimmune thyroid disorders have been estimated to be the most frequent endocrine disorders. Autoimmune hypothyroidism has been reported to be more common than iodine deficiency in areas which are iodine sufficient. Hashimoto's thyroiditis is the

most common form of autoimmune thyroiditis.<sup>1</sup>

There is compelling evidence for the increased prevalence of vitamin B12 deficiency in the population of patients with thyroid disease. Hashimoto's thyroiditis (HT) affects women more than men. It may be associated with hypothyroidism, euthyroidism or occasionally hyperthyroidism. However, most cases present with hypothyroidism. The presence of antithyroid antibodies has been reported in patients with this disorder. Antibody against thyroid peroxidase has also been detected in thyroid tissue.

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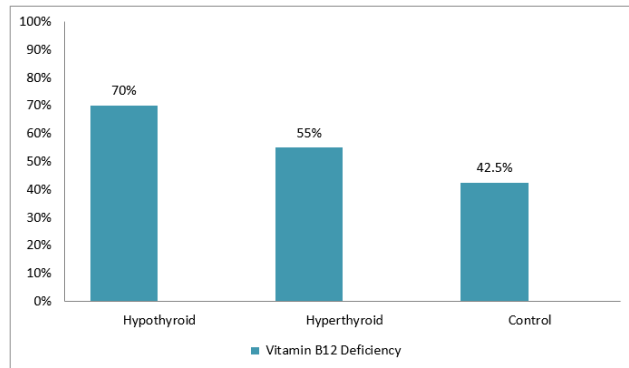
Present study was undertaken to estimate levels of vitamin B<sub>12</sub> in thyroid disorders and comparing it with euthyroid.

## 2. Materials and Methods

A hospital based case control study was conducted at a tertiary level hospital in Himachal Pradesh. A total of 120 subjects were enrolled (40 hypothyroid, 40 hyperthyroid and 40 controls (euthyroid) from patients attending hospital laboratory. Any patient, who was diagnosed afresh for thyroid disorder and not taking vitamin supplements, was included in the study. Informed consent was obtained from all the patients and any one, not giving consent was excluded from the study. Cases were diagnosed according to laboratory cut-off i.e. TSH more than 5.4  $\mu$ IU/ml as hypothyroid, TSH less than 0.5  $\mu$ IU/ml as hyperthyroidism. Thyroid profile along with ATA and vitamin B<sub>12</sub> was estimated by chemiluminiscent enzyme immunoassay.

Statistical analysis was done using standard methods (Epi info7) and expressed as percentages for discrete variables and mean  $\pm$ SD(Standard Deviation) for continuous variables. Chi square tests were used to test the significant difference in proportion. Statistical significance was assumed at  $p < 0.05$ .

## 3. Results



**Fig. 1:** Vitamin B<sub>12</sub> status among study groups

Vitamin B<sub>12</sub> deficiency was taken as a value less than 160 pg/ml. It was measured in all the cases and was found to be maximum in hypothyroidism cases, where it was 70%. In cases of hyperthyroidism the deficiency was 55%, whereas in controls it was only 42.5%

In 23 cases of hyperthyroidism, with T<sub>3</sub> value more than 202 ng/dl, vitamin B<sub>12</sub> deficiency was reported in 9 cases. In 23 cases of hyperthyroidism, with T<sub>4</sub> value more than 11.6  $\mu$ g/dl, vitamin B<sub>12</sub> deficiency was reported in 12 cases. In 40 cases of hyperthyroidism, with TSH value less than 0.53  $\mu$ IU/ml, vitamin B<sub>12</sub> deficiency was reported in 22 cases. In 27 cases of ATA positive hyperthyroidism, 14 cases were

**Table 1:** Vitamin B<sub>12</sub> deficiency among hyperthyroid

Hyperthyroid	Vitamin B <sub>12</sub> deficiency	Mean ( $\pm$ SD)
T <sub>3</sub> (>202 ng/dl)	9/23 (39.1%)	279.8(208.5)
T <sub>4</sub> (>11.6 $\mu$ g/dl)	12/23 (52.2%)	
TSH(<0.53 $\mu$ IU/ml)	22/40 (55.0%)	
ATA(Positive)	14/27 (51.8%)	

having vitamin B<sub>12</sub> deficiency. Mean level of vitamin B<sub>12</sub> among hyperthyroid was 279.8(208.5). (Table 1)

**Table 2:** Association of vitamin B<sub>12</sub> deficiency with hyperthyroidism

	Vitamin B <sub>12</sub> deficiency		Total	OR (95% CI), p value
	Present	Absent		
Hyperthyroid	22 (55%)	18 (45%)	40 (100%)	1.65 (0.68-4.00),
Controls	17 (57.5%)	23 (42.5%)	40 (100%)	0.37
Total	39	41	80	

As per our study, in hyperthyroid patients, there were 1.65 times more chances of vitamin B<sub>12</sub> deficiency than in controls. Association was positive and the reports were statistically not significant ( $p=0.37$ ). (Table 2)

**Table 3:** Vitamin B<sub>12</sub> deficiency among hypothyroid

Hypothyroid	Vitamin B <sub>12</sub> deficiency	Mean ( $\pm$ SD)
T <sub>3</sub> (<69 ng/dl)	9/13 (69.2%)	197.9(79.6)
T <sub>4</sub> (<4.4 $\mu$ g/dl)	16/20 (80%)	
TSH (>5.4 $\mu$ IU/ml)	28/40 (70%)	
ATA (Positive)	19/30 (63.3%)	

In 13 cases of hypothyroidism with T<sub>3</sub> value less than 69 ng/dl, Vitamin B<sub>12</sub> deficiency was reported in 9 cases. In 20 cases of hypothyroidism, with T<sub>4</sub> value less than 4.4  $\mu$ g/dl, Vitamin B<sub>12</sub> deficiency was reported in 16 cases. In 40 cases of hypothyroidism, with TSH value more than 5.4  $\mu$ IU/ml, Vitamin B<sub>12</sub> deficiency was reported in 28 cases. In 30 cases of ATA positive hypothyroidism, 19 cases were having vitamin B<sub>12</sub> deficiency. Mean level of vitamin B<sub>12</sub> among hypothyroid was 197.9( $\pm$ 79.6). (Table 3)

As per our study, in hypothyroid patients, there were 3.15 times more chances of vitamin B<sub>12</sub> deficiency than in controls. Association was positive and the reports were statistically significant ( $p=0.02$ ). (Table 4)

In the present study it has been found that hypothyroid patients had maximum deficiency of vitamin B<sub>12</sub> levels (70%). In the cases of hyperthyroidism, the deficiency was 55% whereas in the controls it was only 42.5%. In ATA positive cases of hypothyroidism, 63.3% cases were vitamin B<sub>12</sub> deficient, while in ATA positive case of

**Table 4:** Association of vitamin B<sub>12</sub> deficiency with hypothyroidism

	Vitamin B <sub>12</sub> deficiency		Total	OR (95% CI), p value
	Present	Absent		
Hypothyroid	28 (70%)	12 (30%)	40 (100)	3.15 (1.25-7.93), 0.02
Controls	17 (42.5%)	23 (57.5%)	40 (100)	
Total	45	35	80	

hyperthyroidism, 51.8% cases were vitamin B12 deficient.

#### 4. Discussion

Centanni et al<sup>2</sup> examined 62 patients with autoimmune thyroid disease. Patients with increased serum gastrin underwent endoscopic, pathologic and immunologic testing. Atrophic gastritis was confirmed in 22 cases (35%). Ness-Abramof et al<sup>3</sup> in their study found that patients with AITD have a high prevalence of Vitamin B12 deficiency and particularly of pernicious anemia

Jabbar et al<sup>4</sup> have shown that vitamin B12 deficiency to be common in hypothyroid patients (40.5%). They recommended that screening for B12 deficiency should be undertaken early in the diagnosis of hypothyroidism and periodically thereafter as hypothyroid and B12 deficient patients often have common symptoms of weakness, lethargy, memory impairment, numbness and tingling.

A study by Das et al<sup>5</sup> in the Eastern India has found that in cases of primary hypothyroid patients, vitamin B12 deficiency was 10%. It mostly occurs as a result of malabsorption due to pernicious anemia accompanying hypothyroidism. Similar results have been discussed by Wang et al.<sup>6</sup> Orzechowska-Pawilojc et al.<sup>7</sup> have also demonstrated reduced levels of vitamin B12 in hypothyroid patients.

On the other hand, Lippi et al<sup>8</sup> carried out a retrospective study and found that prevalence of vitamin B12 deficiency was not different in patients with hypo/hyperthyroidism. According to their study, the routine screening for B<sub>12</sub> deficiency in subjects with subclinical disturbances of thyroid function was not needed, however it could be useful in patients with overt thyroid dysfunction. Similarly, Erdogan et al<sup>9</sup> did not find an increase in vitamin B<sub>12</sub> deficiency in hypothyroid patients. However, it was recommended that, suspicion of hypothyroidism should be considered in anemia with uncertain etiology.

Orzechowska-Pawilojc et al<sup>10</sup> observed in their study of hyperthyroid patients that there was no deficiency of vitamin B12, but the mean value of vitamin B12 was significantly lower than in the control group. Fein HG et al<sup>11</sup> found that pernicious anemia had been strongly associated with hyperthyroidism.

But Demirbas et al<sup>11</sup> when studying hyperthyroid patients, did not find any differences in B12 levels between hyperthyroid and healthy subjects both before and after antithyroid therapy. Caplan et al<sup>12</sup> concluded that

abnormalities of thyroid function per se did not alter vitamin B12 levels in patients.

Jaya Kumari et al<sup>13</sup> in their study in southern part of India did not demonstrate any significant correlation between vitamin B12 levels and anti-TPO. However in their study they found that there was prevalence of low serum vitamin B12 levels in autoimmune thyroid disorders.

Stangl GI et al,<sup>14</sup> has observed in animals that vitamin B12 deficiency was associated with a slight reduction of type I 5'-deiodinase activity in liver and with a significant reduction of the T3 level. Similarly it was found that there is a high (approx 40%) prevalence of B12 deficiency in hypothyroid patients.<sup>15</sup> However in one study on primary hypothyroid cases in India, prevalence of vitamin B12 deficiency was 10% and it was postulated that the deficiency of vitamin B12 increases along with the age. Vitamin B12 deficiency mostly occurs as a result of malabsorption due to pernicious anemia accompanying hypothyroidism.<sup>16</sup>

There is compelling evidence for the increased prevalence of vitamin B12 deficiency in the population of patients with thyroid disease. Centanni et al<sup>17</sup> examined 62 patients with autoimmune thyroid disease. Patients with increased serum gastrin underwent endoscopic, pathologic and immunologic testing. Atrophic gastritis was confirmed in 22 cases (35%). Ness-Abramof et al<sup>18</sup> in their study found that patients with AITD have a high prevalence of Vitamin B12 deficiency and particularly of pernicious anemia.

Orzechowska-Pawilojc et al. found that both the hypothyroid<sup>19</sup> and hyperthyroid<sup>20</sup> state in women are associated with lower concentration of Vitamin B12 when compared to a healthy control group. Jabbar et al<sup>21</sup> concluded that there is high (approx. 40%) prevalence of B12 deficiency in hypothyroid patients and replacement of Vitamin B12 leads to improvement in symptoms.

#### 5. Conclusion

In our study more than 50% of cases with thyroid disorder and ATA positivity showed deficiency of vitamin B<sub>12</sub> (hypothyroidism 63.3% hyperthyroidism, 51.8%). All patients with thyroid dysfunction should be screened for vitamin B<sub>12</sub> status and treated accordingly.

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None.

## 7. Conflict of Interest

None.

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