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Evaluation of serum vitamin b_{12} level in primary hypothyroidism

Pritam Prakash[1], Rekha Kumari[2*], Sanjay kumar[3], Santosh kumar[4]
[1] Assistant Professor, Department of Biochemistry, IGIMS, Patna, Bihar, India
[2] Additional Professor, Department of Biochemistry, IGIMS, Patna, Bihar, India
[3] Associate Professor, Department of microbiology, NMC Patna, Bihar, India
[4] Senior Resident, Department of Biochemistry, IGIMS, Patna, Bihar, India

Abstract
Objective: To assess the prevalence of vitamin B_{12} deficiency in patients of primary hypothyroidism
Material and Method: 110 patients of primary hypothyroidism and 110 healthy control were evaluated for B_{12} deficiency. TPO were also evaluated in B_{12} deficient hypothyroid person.
Result: Prevalence of vitamin B_{12} deficiency was 45.2% in my study. There was a statistically significant decrease in vitamin B_{12} level as compared to control group. (196.65±74.33 µg/ml vs 344.918±73.946µg/ml). 12.7% of hypothyroid patient have vitamin B_{12} level less than 100µg/ml. 45.25 of vitamin B_{12} deficient hypothyroid patients have TPO positive. But there is no correlation between level of vitamin B_{12} and TPO.
Conclusion: Because of high prevalence of vitamin B_{12} deficiency and confusing sign and symptoms screening of vitamin B_{12} should be done at the time of diagnosis of primary hypothyroidism. And it should be repeated thereafter at periodic interval.

Keywords: vitamin B12, Primary hypothyroidism, autoimmune thyroid disease (AITD), TPO

Introduction
Primary hypothyroidism and anaemia both are very prevalent in our country. Hypothyroidism is common endocrine disorder characterised by decreased production of thyroid hormone and primary hypothyroidism is defined as a manifestation of hypothyroidism with increase in TSH and low level of T_3 and T_4. [1]. The prevalence of hypothyroidism is 13.1% in 46 – 54 year while the people of 18 – 35 year is less affected. The prevalence in these age group is only 7.5% [2]. In India overall prevalence of hypothyroidism is 11%. It is very high as compared with UK and USA which is 2% and 4.6% respectively [3]. Vitamin B_{12} is also known as cobalamine. Its chief function is normal brain and nerve development, formation of red blood cell and helps in the synthesis and regulation of DNA [4]. Vitamine B_{12} deficiency may occur in hypothyroid patients is due to autoantibody present against partial cell or due to gut oedema, sluggish movement or decreased intestinal absorption [5]. Patients of hypothyroidism usually present with symptoms of numbness, paraesthesia, poor memory, poor focus, and neuropathy even if adequate replacement doses of thyroxin is given. In general population the deficiency of vitamin B_{12} is 4%.Most frequently pernicious anaemia occurs with primary autoimmune hypothyroidism which is associated with around 12% of cases of hypothyroid. Both of condition have grave medical implication. And evaluation of vitamin B_{12} deficiency in patient has not been done. So we have evaluated level of vitamin B_{12} level in patients of primary hypothyroidism

Material and Method
Cross sectional study design was adopted to evaluate vitamin B_{12} level in primary hypothyroidism. The study was conducted in department of biochemistry in IGIMS, Patna. 220 subjects were taken, out of which 110 cases were of primary hypothyroidism considered as cases and 110 euthyroid subjects were taken as control. The severity of hypothyroidism was moderate to severe.

Inclusion Criteria
TSH level > 5.5 µIU/ml
Patient willingness to study

Exclusion Criteria
Patient with history of haemolytic anaemia, Peptic ulcer, chronic infections, bone marrow suppression
Patient with history of illial resection.
Blood transfusion in last three month.

Sample Collection
Detailed history was taken and venous blood sample was collected after informed consent by patients. Serum was used for analysis of vitamin B_{12} and TPO level by fully automated chemiluminescence method on ACCESS 2. Diagnosis of thyroid disease (AITD) was confirmed by the presence of thyroid autoantibody in serum. Normal level of TPO is 0 – 9 IU/ml. The biochemical vitamin B_{12} deficiencywas defined at a concentration below200 ng/ml.

Statistical technique
Microsoft excel was used for data storage and analysis The data were expressed as mean ± SD. P value was calculated.

Result
Age of hypothyroid patients were in the range of 31- 89 years with mean age 62±16.74 years. Mean age of control group was 61±15.45years.There was no difference in mean age.Vitamin B_{12} is significantly reduced in hypothyroid patients as compared to control group. In my study the level

of vitamin B_{12} in hypothyroid patient was 196.65±74.33 µg/ml. While it is 344.918±73.946µg/ml in healthy control (Table1) (Graph -1). It is statistically significant (p<0.001). 14 out of 110 patients (12.7%) has vitamin B_{12} level less than 100 µg/ml while 28 out of 110 hypothyroid patients have their vitamin B_{12} value in between 100-200 µg/ml. (Table2)

Table 1: showing level of vitamin B_{12} level in case and control

	Case	Control	p Value
Vitamin B_{12} (ng/ml)	196.65±74.338	344.918±73.946	<0.001

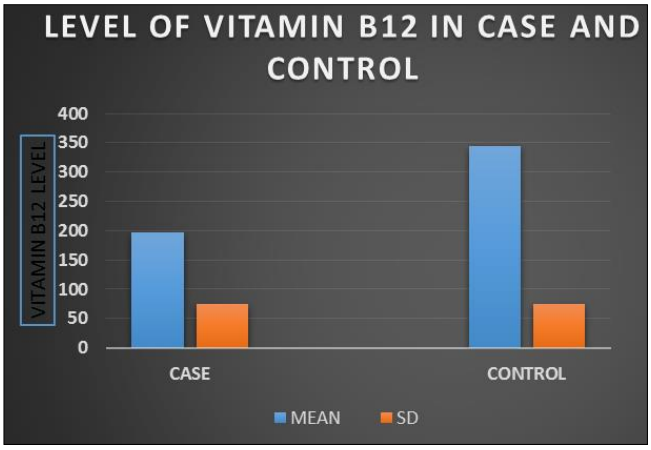

Fig 1: showing level of vitamin B_{12} in hypothyroid patients and control group

Table 2: Distribution level of vitamin B_{12} in hypothyroid patients

Level of Vitamin B_{12} (ng/ml)	Number of Hypothyroid Patients	Percentage
>200	68	61.8
100-200	24	25.45
<100	14	12.7

45.2% of patients who were hypothyroid and and low vitamin B_{12} were TPO positive. But no correlation is found between low TPO levels and low vitamin B_{12} levels in our study. (graph 2) (R^2 =0)

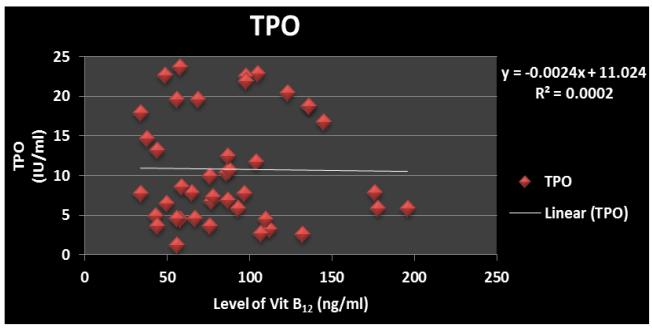

Fig 2: showing no correlation between level of TPO and vitamin B_{12} level

Discussion

Primary hypothyroidism is very common disorder which is prevalent in middle aged female. Prevalence of vitamin B_{12} deficiency in these patients are reported 15-25% in elderly [7]. In my study the prevalence of vitamin B_{12} deficiency in hypothyroid patients was 45.2%.The prevalence of vitamin B_{12} deficiency in hypothyroidism was as 10%, 18.6%,and 40,5% in India, Turkey, and Pakistan.[8, 9, 5].

The level of vitamin B_{12} in hypothyroid patients was significantly reduced in my study. The pernicious anemia may be associated with primary hypothyroidism due to autoimmune pernicious anemia, malnutrition, malabsorption, PPI or metformin. Metformin has effect on receptor of illial mucosa, so it cause malabsorption.. Overall, 35–40% of patients with autoimmune thyroid diseases have atrophic gastritis [5], while 33% of patients with primary hypothyroidism have been shown to have antibodies to gastric parietal cells, and 12% have pernicious anaemia. Intrinsic factor antibodies have also been observed in patients with autoimmune hypothyroidism [10].The prevalence of vitamin B_{12} deficiency in autoimmune thyroid disease was reported 6.3, 28 and55.5% in three different study.in my study 45.2% of vitamin B_{12} deficient patients were TPO positive [11, 12, 13].The symptom of vitamin B_{12} deficiency is very variable.It may be either hematological or neurological abnormality, or they may coexist. For some time they may be asymptomatic, Sosome researchers like Ness Abamof *et al* [13]. and Collins Pawlak [14]. Recommend vitamin B_{12} screening at time of diagnosis of autoimmune hypothyroidism after 3-5 years.

Limitation

One of limitation of this study is its sample size. I have assessed vitamin B_{12} statusby serum vitamin B_{12} level. But other markers such as MMA, TCII have better accuracy. So to investigate better relationship between vitamin B_{12} and primary hypothyroidism a large sized study

Conclusion

In our study we concluded that the level of vitamin B_{12} is significantly decreased in patient of hypothyroidism compared to control. Both have common with vitamin B_{12} will prevent long term sequel of vitamin B_{12} deficiency. Vitamin B_{12} screening should be done in every case of hypothyroidism early in diagnosis. Then patient should be followed up. Because initiation of treatment of vitamin B_{12} early in the diagnosis results in marked improvement of symptoms as reported by some researchers. But larger study should be undertaken to evaluate whether initial therapy therapy with vitamin B_{12} will prevent long term sequel of vitamin B_{12} deficiency.

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