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Original Article

A study of anemia in hypothyroidism with reference to vitamin B12 deficiency

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ABSTRACT

Background: Hypothyroidism is the most common of thyroid disorders in India. Anemia and hypothyroidism often occur simultaneously. Only few studies have assessed the role of vitamin B12 deficiency in this anemia**.** So, we planned this study to assess prevalence of anemia in hypothyroidism and to see if there is any association between vitamin B12 deficiency and anemia in these patients.
Methods: It was an observational study. All hypothyroid patients attending the medicine OPD or admitted to medicine wards were enrolled for the study. Total 60 patients were included. Data was analyzed to assess the burden of anemia and B12 deficiency in hypothyroid and to find out any correlation between TSH level, anemia and vitamin B12 deficiency.).
Results: About one third of hypothyroid had decreased vitamin B 12 levels. TSH level showed significant positive correlation with hemoglobin value. 28% of the hypothyroid patients had vitamin b12 deficiency, but TSH levels itself did not correlate with vitamin B12 level. However, it was seen that those who had combined thyroid and B12 deficiency had significantly higher chances of developing generalized swelling and breathlessness.
Conclusions: Although there is no correlation between TSH level and B12 deficiency, it may be helpful to determine B12 level in hypothyroid patients who present with anemia, generalized swelling and/or breathlessness as B12 supplementation may give better symptomatic relief in them as compared to treating with thyroxine alone. More elaborative studies with larger sample size are required to explore this rather unattended relation of anemia in hypothyroidism with B12 deficiency.

Keywords: Anaemia, Hypothyroidism, Vitamin B12

INTRODUCTION

Hypothyroidism is a condition caused due to decreased synthesis, metabolism or decreased action of thyroid hormone. The highest prevalence of hypothyroidism (13·1%) is noted in people of 46-54 years of age; 18-35 years age group being less affected (7·5%).[1] The prevalence of hypothyroidism is 11% in India, compared to U.K & U.S.A, where it is 2% and 4·6% respectively.

Anemia is a frequently underestimated clinical condition accompanying thyroid diseases.[2] A study done by Omar et al reported 40.9% and 57.1% incidence of anemia accompanying hyperthyroidism and hypothyroidism respectively.[3] The prevalence of anemia in overt and subclinical hypothyroidism was 43% and 39% respectively in a study by Erdogan et al.[4]

Although macrocytosis might occur with thyroid disorder, the metabolic relationship between levels of thyroid stimulating hormone (TSH) and serum vitamin B12 is not known. One study comparing the vitamin B12

deficiency in primary hypothyroidism reported that 39.6% of hypothyroid patients had low vitamin B12 levels.[5] The association between AITD (Autoimmune thyroid disease) and vitamin B-12 deficiency is likely related to the presence of the autoimmune disorders like atrophic gastritis and/or pernicious anemia, both of which lead to impaired absorption of B-12.[6] The association between hypothyroidism and B-12 deficiency in the absence of AITD has not been evaluated in detail and may vary according to dietary habits across population groups.[5]

We conducted this study to assess prevalence of anemia in thyroid patients to assess the burden of anemia and B12 deficiency in hypothyroid and to find out any correlation between TSH level, anemia and vitamin B12 deficiency.

METHODS

It was an observational study, carried out in the Department of Medicine. The study was started after obtaining clearance from institutional ethical committee in March 2016.

Study duration and population

The study lasted for one and half year from April 2016 to September 2017. The study population came from patients attending a tertiary care hospital in the west of India.

Inclusion criteria

All hypothyroid patients attending the medicine OPD or admitted to medicine wards were enrolled for the study. The patients already diagnosed as hypothyroid, those >18 years in age and those who gave consent for participation in the study were included.

Exclusion criteria

Patients with known comorbid conditions like diabetes Mellitus on metformin, cirrhosis of liver, already on vitamin B12 supplementation and chronic alcoholics were excluded from the study. A detailed history was taken from all participants. All participants were subjected to complete blood count, thyroid function test, S. Vitamin B12 level. sickling, urine routine microscopy, renal function test, liver function test, s. ferritin and reticulocyte count. Anemia was defined as hemoglobin levels lower than 12 g/dl in women and 13 g/dl in men. Normal S. TSH was taken as 0.39-5.0 μIU/ml. Vitamin B12 deficiency was defined as serum vitamin B12 levels lower than 210 pg/ml as per AI 360 Immunoassay method (TOSOH).

Statistical analysis

Data so collected was analysed in SPSS to assess the burden of anemia in the hypothyroid patients and also to assess the relation between hypothyroidism and vitamin B12 deficiency. The proportion was presented as percentage while pearson's correlation coefficient was used to look for correlation between two quantities.

RESULTS

Total 60 patients of hypothyroidism were included. Out of these, maximum patients (30%) were in the age group of 51-60 years with female preponderance in overall population i.e. 48 (80%) and only 20% were males. 46 (76.7%) of patients had raised serum TSH while 23.3% had normal TSH level. 39 (65%) of these had anemia. Only 17 (28.3%) out of 60 hypothyroid patients had decreased vitamin B12 levels, rest 43 (71.7%) had vitamin B12 levels within normal limits.

Majority of the patients i.e. 20 each (33.3%) presented with fatigue and lethargy, followed by breathlessness seen in 13 (21.7%), generalized swelling seen in 10 (16.7%), weight gain seen in 8 (13.3%), paraesthesia's present in 7 (11.7%) and constipation seen in 6 (10%). Only 4 (6.7%) had complaint of decreased appetite, 2 (3.3%) had muscle cramps and excessive sweating and 1 (1.7%) had depression. None of the patients had complaint of cold intolerance. Most common sign was pallor seen in 16 (26.7%), followed by edema (15%), abnormal findings in respiratory examination (8.3%) and abnormal cardiovascular system findings (3.3%). None of the patient had icterus, cyanosis, clubbing, lymphadenopathy and abnormal per abdominal findings or abnormal central nervous system findings.

Mean of s-TSH of the study population was 22.78±31.379 IU/ml. Mean of Total T3 and Total T4 as present in 11 patients was 8.84±25.264 ng/ml and 7.326±3.807 μg/dl respectively. Mean of Free T3 and Free T4 as present in 34 patients was 2.41±1.222 pg/ml and 1.23±1.109 ng/dl respectively. Mean of Vitamin B12 levels in all patients was within normal range 447.92±456.585 pg/ml. Mean hemoglobin level of the study population was 11.168±2.411 gm%. Mean of Red cell distribution width (RDW) was 15.225±2.288% and mean of reticulocyte count was 1.750±1.055%. Rest of the lab parameters including RFT, LFT and other RBC indices were in the normal range (Table 1).

There was no significant correlation of total count with Vitamin B12 level (r 0.233, p 0.073) neither it showed correlation to TSH (r -0.123, p 0.347). There was no significant correlation even between PCV with Vitamin B12 or TSH (r -0.165, p 0.208) and (r -0.172, p 0.188); MCV with Vitamin B12 or TSH (r -0.053, p 0.690) ,(r 0.004, p 0.979); retic count with Vitamin B12 or TSH (r -0.299, p 0.345), (r -0.032, p 0.922) and Hemoglobin with vitamin B12 (r -0.158, p 0.228) however there was significant correlation between Hemoglobin and TSH levels (r -0.320, p 0.013) (Table 2).

Table 1: Lab parameters of the study population.

Lab parameters	Mean	Std. deviation
Hb (gm%)	11.168	2.411
Platelet count lacs/ mm^3	2.618	0.77
Hematocrit (%)	34.358	7.801
MCV (fL)	79.58	10.909
MCH (pg)	25.719	4.248
MCHC (%)	32.15	1.92
Total RBC (mil/µL)	4.381	0.998
RDW (%)	15.225	2.288
Retic count (%)	1.75	1.055
Vitamin B12 (pg/ml)	447.92	456.585
S. TSH (IU/ml)	22.78	31.379
Free T3 (pg/ml)	2.41	1.222
Total T3 (ng/ml)	8.84	25.264
Free T4 (ng/dl)	1.23	1.109
TOTAL T4 (g/dl)	7.326	3.807
RBS (mg%)	104.69	21.418
Urea (mg%)	31.38	19.938
Creatinine (mg%)	0.99	0.554
Bilirubin (mg%)	0.77	0.502
SGPT (IU/L)	27.57	12.936
SGOT (IU/L)	36	22.72
Urine RM	1.95	0.218

Some symptoms of hypothyroid patients were found to be significantly more common in those who also had vitamin b12 deficiency. There was >1.5 times chance of finding weight gain in patients with vitamin B12 deficiency (odds ratio 1.629; 95% CI 0.343-7.72), 1.13 times chances of finding fatigue (odds ratio 1.130; 95% CI 0.347-3.683), >5 times chances of developing generalized swelling (odds ratio 5.318; 95% CI 1.271-22.250) and >2 times chances of developing breathlessness (odds ratio 2.933; 95% CI 0.896-9.608) in patients with decreased b12 levels (Table 3).

Table 2: Correlation of TLC, PCV, MCV, Reticulocyte count and Hemoglobin with TSH and B12 levels.

Variable	Statistical variable	Vitamin B12	TSH
TLC	Pearson Correlation	0.233	-0.123
	P-value	0.073	0.347
PCV	Pearson Correlation	-0.165	-0.172
	P-value	0.208	0.188
MCV	Pearson Correlation	-0.053	0.004
	P-value	0.69	0.979
Reticulocyte count	Pearson Correlation	-0.299	-0.032
	P-value	0.345	0.922
Haemoglobin	Pearson Correlation	-0.158	-0.32
	P-value	0.228	0.013

Table 3: Odds of finding symptoms in hypothyroid patients with decreased vs normal vitamin B12 level.

Variable	Statistical variable	R value
Pallor	Pearson Correlation	0.021
	P-value	0.884
Breathlessness	Pearson Correlation	2.857
	P-value	0.048
Weight gain	Pearson Correlation	0.144
	P-value	0.704
Fatigue	Pearson Correlation	0.469
	P-value	0.494
Generalised swelling	Pearson Correlation	6.750
	P-value	0.009

Table 4: Correlation of combined deficiency of Vit. B12 and TSH with symptoms and signs.

Exposure	Decrease Vit. B12 (n= 17)	Normal Vit. B12 (n=43)	p-value	Confidence interval	Odds ratio
Weight gain	3(17.6)	5(11.6)	0.537	0.343-7.727	1.629
Fatigue	6(35.3)	14(32.6)	0.839	0.347-3.683	1.13
Lethargy	4(23.5)	16(37.2)	0.311	0.144-1.867	0.519
Generalized swelling	6(35.3)	4(9.3)	0.015	1.271-22.250	5.318
Muscle cramps	0(0)	2(4.7)	0.366	NA	NA
Breathlessness	8(47.1)	10(23.3)	0.07	0.896-9.608	2.933

On correlation analysis, we found no significant correlation between s-TSH and Vitamin B12 level (r 0.180, p 0.168). The association of generalized swelling and breathlessness with vitamin b12 level was confirmed by correlation analysis as the two also showed significant positive correlation with vitamin b12 level (r = 6.750; p = 0.009) and (r = 2.857; p = 0.048) respectively (Table 4).

DISCUSSION

In this observational study we included 60 hypothyroid patients during the study period. Approximately 28% of the patients had low serum vitamin B 12 levels. Previous studies have reported pernicious anemia to occur in about 10% of patients with hypothyroidism caused by chronic autoimmune thyroiditis.[7] It has been suggested that patients with autoimmune hypothyroidism may have concomitant vitamin B12 deficiency caused by autoantibodies to gastric parietal cells. Therefore, it may be meaningful to measure vitamin B12 level in patients with hypothyroidism who are anaemic.

Kawa et al, reported that in hypothyroidism RBC and Hb were decreased, while haematocrit was increased.[8] They also showed that MCH and MCHC were lower in patients with thyroid dysfunction and MCV was increased in two groups of hypothyroidism and hyperthyroidism. We found a strong significant correlation between hemoglobin value and TSH. However, the dose of thyroxine and years of known diagnosis had no correlation with any blood indices in our study. This may be because of small sample size and overall mild anemia seen in our study population which might not have reflected in changes in RBC indices.

Hypothyroidism and vitamin B12 deficiency have common set of symptoms of weakness, lethargy, memory impairment, numbness and tingling. Muscle involvement in adults with hypothyroidism is also common. Approximately, 33% of our patients reported symptoms of lethargy and fatigue and 22% of had complaints of breathlessness. Shortness of breath on exertion and decreased exercise capacity have been suggested to be due to impaired respiratory function. Weakness of respiratory muscles and decreased pulmonary responses to hypoxia and hypercapnia can result in hypoventilation.[9] It has been seen that several patients, despite being on adequate thyroxin replacement, have persistence of symptoms and are subsequently found to be vitamin B12 deficient.

In a study of 116 hypothyroid patients 40% had low vitamin B12 levels and generalized weakness, impaired memory, depression, numbness and decreased reflexes were more frequently noted in B12 deficient patients.[10] In our study also we found significantly higher chances of development of generalized edema and breathlessness in patients who also had B12 deficiency along with hypothyroidism.

Metabolism of homocysteine and methyl-malonyl acid (MMA) require vitamin B 12, thus both MMA and homocysteine levels increase in vitamin B12 deficiency.[11] When homocysteine levels are elevated other causes like coexisting folic acid deficiency, renal impairment and inadequate thyroid replacement need to be evaluated. We did not study homocysteine levels in our study, but this is an area of increasing interest. Studies have shown a relationship between hypothyroidism and hyperhomocysteinemia, which has also shown to improve with treatment of thyroid status.[12] We also analyzed the correlation between serum TSH level and vitamin B12, which failed to reach statistical significance.

CONCLUSION

Anemia is common among patients with hypothyroidism as is vitamin b12 deficiency. Although there is no correlation between TSH level and B12 deficiency, it may be helpful to routinely determine B 12 level in hypothyroid patients who present with generalized swelling and/or breathlessness as B12 supplementation may give better symptomatic relief in them as compared to treating with thyroxin alone. More elaborative studies with larger sample size are required to explore this rather unattended relation of hypothyroidism and B12 deficiency.

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