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ORIGINAL RESEARCH

Evaluation of iron profile level in subclinical hypothyroid: A pilot study

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) is preliminary state of thyroid disorder, in which the circulating levels of Thyroid Stimulating Hormone (TSH) are slightly above the normal range (4.6-10 mIU/lit), whereas thyroxine (T4) and triiodothyronine (T3) are still within the normal limits. Iron deficiency is reported in patients of hypothyroidism. Thus, routine screening, and early detection of iron profile can be helpful to prevent the further progression of Subclinical to Overt hypothyroidism. The present study aims to detect the prevalence of iron deficiency in cases of Subclinical hypothyroidism.**Methods:** 50 patients of subclinical hypothyroidism (58% female and 42% male) and equal number of age and sex matched controls were included in the study. Thyroid Profile (TSH, fT3, fT4) and Iron Profile (Total Iron, TiBC, Ferritin) were analysed on auto analyser which is based on the chemiluminescence immunoassay. The collected data was analysed statistically.**Result:** Significantly low levels of serum iron was found in cases of subclinical hypothyroidism (p-value=0.0036). Serum iron levels (r= -0.448; p-value =0.0011) and Serum ferritin (r= -0.485; p-value =0.0003) showed a highly significant negative correlation with serum TSH levels.**Conclusion:** Based on the results of our study we conclude that there is a higher prevalence of Iron deficiency in SCH patients, hence we hypothesize that by routine laboratory testing, early detection of Iron profile and appropriate therapeutic measures can be helpful in preventing the onset of overt hypothyroidism.

Key words: Serum Iron deficiency, ferritin, subclinical hypothyroidism, thyroid stimulating hormone

INTRODUCTION

"Hypothyroidism is a common endocrine disorder with reduced production of thyroid hormones." It is a most common disorders with different frequency between countries.

Subclinical hypothyroidism (SCH) is a condition of increased serum Thyroid Stimulating Hormone (TSH) levels, where the circulating form thyroxine (T_4) and tri-iodothyronine (T_3) concentrations fall within normal reference range. The consequences of SCH are different at numerous levels and may depend on the degree and the duration of increase in the serum TSH[1].

It is as well as noted that subclinical hypothyroidism has been long associated with atherosclerosis, hypercholesterolemia, infertility, cardiovascular neuropsychiatric symptoms, mortality, poor obstetric outcome, unprovoked deep vein thrombosis, and common bile duct stones[2-6].Around 3.9% adult are suffering from hypothyroidism and even more 9.4% are suffering from subclinical hypothyroidism. According to numerous studies, Subclinical hypothyroidism occurs in 10% of women and 6% of men population with >65 years of age[7, 8].As oestrogen has an anti-thyroid action, the prevalence of sub clinical hypothyroidism is more in females[9].

Subclinical hypothyroidism, despite its name suggesting the absence of symptoms, is typically diagnosed in patients when Thyroid Function Tests are conducted on a routine basis or due to the presence of mild hypothyroidism symptoms. Therefore, the diagnosis is primarily based on biochemical results[10].

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Anaemia is a major global health problem prevalent in underdeveloped, developing and developed countries which is a major cause of morbidity as well as socioeconomic development of the nation[11].
Hematopoietic system is one of the primary systems which is affected by hypothyroidism and anaemia is the most common manifestation. The most frequent type of anaemia is normochromic normocytic anaemia which is frequently caused due to the bone marrow repression which causes defective erythropoietin production which in turn is due to thyroid hormone deficiency, along with that micro and macrocytic anaemia also occurs[12].Thus, subclinical hypothyroidism and iron deficiency anemia are interdependent units which are clinically neglected until the "vicious cycle" augments both the disease processes.

MATERIAL AND METHODS

The present case-control study was conducted in the Department of Biochemistry and Pathology at a tertiary care centre in Northern India. The study was performed after obtaining the ethical clearance from the Institutional Ethical Committee (Ref No: SU/SMS&R/76-A/2022/112). Fifty (50) patients who were screened for subclinical hypothyroid from the samples received in Biochemistry laboratory were selected as per the selection criteria. Age and sex matched equal number of healthy individuals were taken as control in the present study. The selected cases and control subjects were contacted and screened for relevant clinical history, drug intake and examination was carried out. Detail information about the study and its risk and significance was explained to the subjects (case and control) and full written informed consent was taken.

INCLUSION CRITERIA: Sub-clinical hypothyroid patients in the age group30-60 years (either sex), non-diabetic, non-pregnant, TSH - >4 mIU/L and < 10 mIU/L were taken into consideration[13].
Age and sex matched healthy controls were selected from the staff of SMS&R, other patients whose thyroid profile were normal under investigation as well as attendants of the patients.

EXCLUSION CRITERIA: Individuals of age < 30yrs &>60yrs, pregnant women, patients suffering from diabetes milletus, hypertension, CKD, malignancy, rheumatologic disease, Congestive heart failure, coronary artery disease, usage of drugs like cephalosporins, NSAIDS, Penicillin and its derivatives, thyroid supplements etc.

LABORATORY METHODS:CBC, Hb levels were analysed on Sysmex XN1000. Thyroid Profile (TSH, fT3, fT4) and Iron Profile (Total Iron, TiBC, Ferritin) was analysed on auto analyser Fusion 5.6 which is based on the chemiluminescence immunoassay.

STATISTICAL ANALYSIS: In this study, data analysis was conducted using an appropriate computer software package. The qualitative variables were expressed in number (percentage), quantitative variables were expressed in mean ± SD. For comparison of quantitative variables between two groups, the unpaired Student t-test was utilized. To evaluate qualitative data, the $\chi 2$ test was performed. The prevalence of Iron deficiency was determined by calculating the Odds Ratio and 95% confidence interval. Pearson correlation coefficient was used to determine the relationship between serum TSH and iron profile levels among patients with subclinical hypothyroidism. A p-value of ≤ 0.05 was considered statistically significant, while a p-value of < 0.0001 was considered highly significant.

RESULTS

The study analysed 50 cases of subclinical hypothyroidism, with 58% being female and 42% male as shown in **Fig 1.** Additionally, 50 healthy controls were included in the study, and there were no significant demographic differences between the cases and control groups. Details given in **Table 2**.

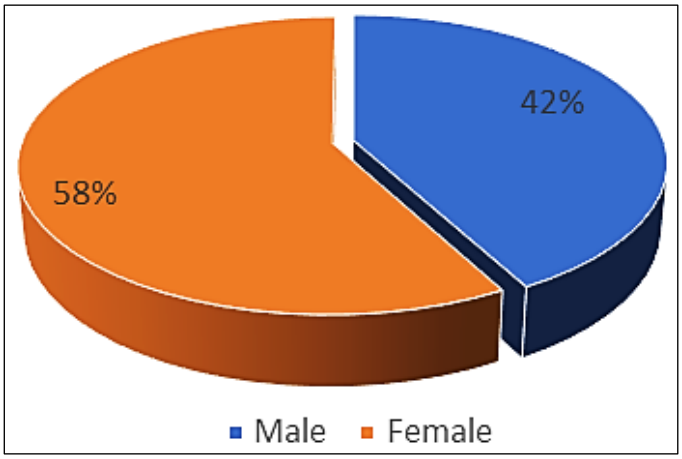

Fig 1: Sex Distribution among the cases

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ASSESSMENT OF SERUM IRON DEFICIENCY

Total Serum Iron deficiency was found out in 46 subjects (35 cases and 11 control), making the prevalence of Iron deficiency among Subclinical Hypothyroid to be statistically significant (Odd's ratio=8.27, 95%CI= 3.35 to 20.38; p-value=<0.001).

On analysis of the serum levels of TSH, Iron, ferritin and TiBC among cases and controls through unpaired student t-test, as shown in **Table 1,** it was found that there was significant increase (p= 0.0001)in serum TSH levels in cases and the serum Iron levels in cases were significantly decreased (p=0.0036) in comparison to controls but when the serum ferritin and serum TiBC levels were compared there was no significant difference among the two groups.

Pearson's correlation coefficient analysis was performed as given in **Table 2** for Serum Iron levels (R= -0.448;p-value of 0.0011) and ferritin levels (R= -0.485;p-value of 0.00035) in SCH patients showed an inverse relationship with TSH levels, whereas Total iron binding capacity levels in SCH patients showed apositive correlation(R= 0.2865;p-value of 0.0436) thereby proving all have statistical significant correlation with Serum TSH levels.

Table 1: The clinical characteristics and biochemical parameters of the study participants

Parameter	SCH	Control	P Value
AGE (years) (mean ± SD)	35.46±12.00	36.46±12.09	0.675
SEX **Male** **Female**	 42% 58%	 64% 36%	0.066
TSH (mean ± SD)	6.8002±1.61	1.7534±0.99	*0.0001
SERUM IRON (µg/dL) (mean ± SD)	72.14±39.17	95.5172±39.10	*0.0036
FERRITIN (ng/mL) (mean ± SD)	32.02±27.98	172.5±111.27	8.6578
TiBC (µg/dL) (mean ± SD)	389±77.27	392±63.8	0.2117

Table 2: Correlation of iron profile levels with TSH levels using Pearson's Correlation Coefficient

Parameter	Pearson's Correlation Coefficient	P-Value
Serum Iron vs TSH	-0.448	*0.0011
Ferritin vs TSH	-0.485	*0.0003
TiBCvsTSH	0.2865	*0.0436

*Represents the p-value is statistically significant.

DISCUSSION

Although various clinical studies have attempted to establish a correlation between serum Iron levels and hypothyroidism, no definitive results have been obtained thus far. To address this issue, this cross-sectional study enrolled 50 SCH cases and an equal number of healthy controls to eliminate the prevalence of iron deficiency due to nutritional causes. The cases (patients with SCH) had significantly higher mean serum TSH levels compared to the healthy controls, indicating that a lower proportion of patients with SCH were undergoing replacement therapy. This study's finding revealed that 70% of patients with SCH had serum iron level below the deficient range (< 60 µg/dL), which was significantly lower than the levels observed in the control group (p-value=0.0036). These findings corroborate the results of Arvind K. Mishra *et al.*, who also reported a high prevalence of iron deficiency in individuals with subclinical hypothyroidism [14].Additionally, a significant negative correlation was found between serum iron levels and TSH levels, consistent with the results of a study conducted by NawrasNooriBashboosh[15]. Another study by Wang F *et al.*,Haemoglobin (Hb) and serum ferritin (SF) showed a negative correlation with TSH but a positive correlation with FT3 and FT4[16].In contrast study conducted by Yavuz O *et al.*,found no correlation between thyroid hormone levels and iron levels[17].As most of the study commemorate the correlation of iron deficiency in thyroid disorder this study can project this effect on global population.

According to the present study's findings, iron deficiency is prevalent in patients with SCH. Therefore, it can be recommended to screen for iron deficiency at the time of SCH diagnosis and to periodically evaluate it.

LIMITATION

Despite the various efforts and interpretation there are certain limitations in the present study which are autoimmune aetiology has not been excluded as the

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underlying cause of SCH, hence the evaluation of Anti-Thyroperoxidase (TPO) antibodies should be recommended. A larger sample size should be taken into consideration for a more accurate representation of population. Also, this study does not examine the relationship between haemoglobin levels and transferrin saturation.

CONCLUSION

The manifestation of the subclinical hypothyroidism is not significant in initial stages so it is preferably done as in routine investigation for early detection. The initial two steps in thyroid hormone biosynthesis involves most of the enzymes that contains iron as a major component like thyroid peroxidase (TPO)[18].

The plasma concentrations of T3 and T4 will be decreased and *in vitro* hepatic rT3 deiodination will be increased which suggests decrease in the thyroid hormone metabolism due to deactivating effect of iron deficiency[19].Thefindings of the present study helps to justify the above pathophysiology of subclinical hypothyroidism beingone of the major risk factor for the development of severe iron deficiency anaemia at an early stage.Assessment of iron profile in patients with subclinical hypothyroidism can improve the treatment protocol and also support in monitoring the disease progression.

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CONFLICT OF INTEREST

There is no conflict of interest among the authors in the present study.

CONDUCTION OF STUDY

The study was conducted in School of Medical Sciences and Research, Sharda University, Greater Noida, UP during the period of March 2022 to December 2022.

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