



Effect Of Subclinical Hypothyroidism On Indices Of Metabolic Syndrome

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Abstract: Subclinical hypothyroidism is defined as an elevation in serum thyroid-stimulating hormone above the upper limit of the reference range (0.45-4.5 mIU/L) with normal serum free T4 and T3 hormone concentrations. Here we present a cross-sectional, observational study of 100 patients that was conducted in a tertiary care hospital, over a period of 18 months. The aim of this article is to study the clinical and biochemical changes, assess metabolic syndrome, BMD, body composition and hormonal profile in patients with subclinical hypothyroidism. The data collected were analyzed by using Pearson's chi square test and unpaired T test. Our study found 72% patients to be symptomatic, 29% patients to be obese, 31% patients to have goiter and 13% patients with deranged lipid profile. It was observed that waist circumference, body weight, BMI, insulin levels, C-peptide levels and polysomnography had a significant association with subclinical hypothyroidism as the p-value was observed to be less than 0.05. On assessment of data for presence of metabolic syndrome, it was observed that 8% of the patients of subclinical hypothyroidism had an associated metabolic syndrome. Our study observed that subclinical hypothyroidism has a significant correlation with various metabolic syndrome parameters.

Keywords: Subclinical hypothyroidism, metabolic syndrome, obesity, thyroid

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I. INTRODUCTION

Thyroid hormones are key regulators of many metabolic processes through their effect on protein and carbohydrate metabolism.¹ The clinical signs and symptoms of hypothyroidism are manifested when the disease is fully developed. Although even in the earliest (subclinical stage), one or more of these findings might occur. In one study of 69 female patients with subclinical hypothyroidism, a clinical index based on symptoms and physical signs, was shown to be more abnormal in patients with higher TSH levels, even though all patients had normal serum levels of free T₄.² These studies suggest that some patients with subclinical hypothyroidism indeed have clinical manifestations of mild thyroid failure. Signs and symptoms of thyroid hormone insufficiency includes weakness, lethargy, fatigue, dry skin, coarse hair, cold intolerance, constipation, weight gain, muscle cramps, edema of eyelids, face, legs (non-pitting) hoarseness, hearing loss, menorrhagia, slowing of return phase of reflexes (e.g., knee jerk).¹ Subclinical hypothyroidism (SCH) is defined as an elevation in serum thyroid-stimulating hormone (TSH) above the upper limit of the reference range (0.45-4.5 mIU/L) with normal serum free T₄ and T₃ concentration. The prevalence of subclinical hypothyroidism has been estimated to be from 1.4% to 8%, and being linked with a number of metabolic abnormalities. The causes of subclinical hypothyroidism are various and the important ones are Autoimmune (Hashimoto's) Thyroiditis, persistent TSH elevation in subacute thyroiditis, postpartum thyroiditis. Some drugs like amiodarone, lithium, etc. have also been implicated to cause this, apart from thyroid injury due to surgery, radiation. Infiltrative disease like sarcoidosis, hemochromatosis can also be responsible.³ Subclinical hypothyroidism is supposed to be a risk factor for cardiovascular diseases, hyperlipidemia, hypercoagulability and low grade inflammation including atherosclerotic disease⁴, altered total and low-density-lipoprotein cholesterol (LDL-C) and atrial fibrillation.⁵ Colorado Thyroid Disease Prevalence Study (25,862 subjects from statewide health fair) which revealed that 9% patients had SCH (TSH >5.1 mIU/L and normal T₄).⁶ For every 1 mIU/L elevation in TSH, in men there is an increase in total cholesterol of 6.2 mg/dl whereas in women there is increase in total cholesterol of 3.5 mg/dl.⁷ One of disorders with which it is supposed to be linked is metabolic syndrome. Metabolic syndrome is a cluster of disorders including central obesity, glucose intolerance, hypertension and dyslipidemia.⁸ The metabolic syndrome criteria according to the 2001 National Cholesterol Education Program /ATP III defines metabolic syndrome as the presence of any three of the following five traits:⁹

1. Abdominal obesity, defined as waist circumference in men >102 cm (40 in) and in women >88 cm (35 in).
2. Serum triglycerides ≥ 150 mg/dL (1.7 mmol/ L) or drug treatment for elevated triglycerides.
3. Serum HDL cholesterol < 40 mg/ dL (1 mmol/L) in men and <50 mg/ dL (1.3 mmol/ L) in women or drug treatment for low HDL-C.
4. Blood pressure $\geq 130/ 85$ mmHg or drug treatments for elevated blood pressure.
5. Fasting plasma glucose (FPG) ≥ 100 mg/dL (5.6 mmol/ L) or drug treatment for elevated blood glucose.

The pathophysiology of thyroid function on lipid and glucose metabolism and blood pressure for subjects with thyroid disorder is well known, associations between thyroid function and parameters of metabolic syndrome have been reported but are limited.¹⁰

2. MATERIALS & METHODS

Cross-sectional, observational study of 100 patients over 18 months, in the endocrinology department of a tertiary care hospital was conducted, after taking informed consent from the patients.

2.1 Inclusion criteria

1. Male and females, 18-70 yrs of age
2. Thyroid profile showing subclinical hypothyroidism i.e. elevation in serum thyroid-stimulating hormone (TSH) above the upper limit of the reference range (0.45-4.5 mIU/L) and normal serum free T₄ and T₃ concentration.

2.2 Exclusion criteria

1. History of therapy for Type 2 DM, hypothyroidism or hyperthyroidism, dyslipidemia, chronic respiratory, cardiovascular, neurological, renal or malignant diseases.
2. Patients on steroids, antidepressants

2.3 Investigations done

- Hb, TLC, DLC, Platelet, ESR, CRP
- Complete Biochemistry [sodium, potassium, chloride, bicarbonate, blood urea nitrogen (BUN), magnesium, creatinine, glucose]
- Total and Direct bilirubin
- Lipid profile
- Calcium, phosphate and ALP
- T₃, T₄, TSH.
- LH, FSH, Testosterone, Prolactin, estrogen, Cortisol, Insulin and C –peptide
- Body composition analysis
- BMD DXA
- USG Abdomen
- Polysomnography

2.4 Methodology

Thorough examination of the patient including general examination and systemic examination was done and documented after taking proper patient consent and institutional approval. Lab parameters including hematological count and biochemical parameters as per list given above were checked, documented and assessed.

3. STATISTICAL ANALYSIS

The data collected were analyzed by using Pearson's chi square test and unpaired T test. P value > 0.05 was considered significant. Wherever necessary, the results were depicted in the form of percentages with tables and graphs. Statistical software namely SPSS 15.0 were used for the analysis of the data and Microsoft Word and Excel to generate graphs and tables.

4. RESULTS AND DISCUSSION

4.1 Demographic data

Table I. Age distribution		
Age group	No.	Percentage
20-30 Yrs	32	32
31-40 Yrs	34	34
>40 Yrs	34	34
Total	100	100

Table II. Gender distribution		
Gender	No.	Percentage
Male	23	23
Female	77	77
Total	100	100

4.2 Clinical data

4.2.1 History

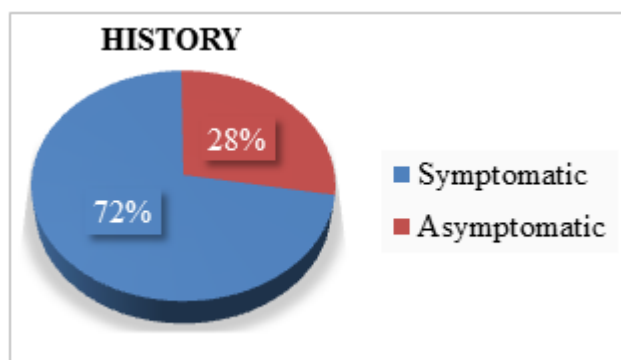


Fig 1. History

4.2.2 BMI

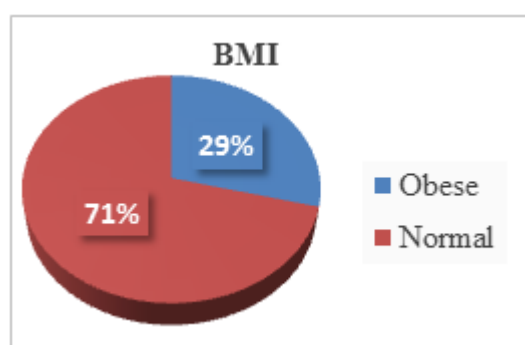


Fig 2. BMI

4.2.3 Polysomnography

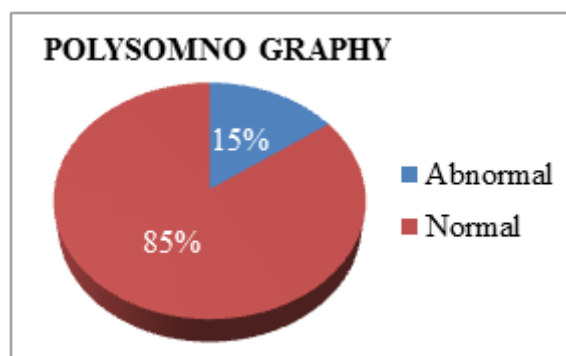


Fig 3. Polysomno Graphy

Table III. Analysis of relationship between subclinical hypothyroidism and altered hormone levels

Variable	History	No.	Mean	Standard Deviation	Standard Error mean	T Value	P Value
INSULIN	Symptomatic	72	20.74	7.02	0.83	2.118	0.037
	Asymptomatic	28	17.71	4.50	0.85		
C-PEPTIDE	Symptomatic	72	2.03	0.69	0.08	2.517	0.013
	Asymptomatic	28	1.67	0.46	0.09		
WT	Symptomatic	72	63.81	11.71	1.38	2.498	0.014
	Asymptomatic	28	57.43	10.79	2.04		
BMI	Symptomatic	72	23.81	4.08	0.48	1.297	0.198
	Asymptomatic	28	22.72	2.72	0.51		
WC	Symptomatic	72	27.89	5.48	0.65	2.002	0.048
	Asymptomatic	28	25.63	3.77	0.71		

Table IV. Association with Metabolic Syndrome

Variables	Percentage of patients		
	Male	Female	Total
Having metabolic syndrome	0	8	8
Abnormal waist circumference	0	11	11
Abnormal TG levels	4	6	10
Abnormal HDL-C levels	0	7	7
Abnormal BP	5	48	53
Abnormal fasting glucose	1	21	22

The present study is a cross sectional study of clinical, biochemical, metabolic and anthropometric parameters of 100 patients of established subclinical hypothyroidism (SCH). Correlation of SCH with metabolic syndrome was also observed in this study. Our study demonstrated affliction of young individuals, that too predominantly females as shown in table-I and II. Similar results were also seen in the study conducted by Chih-Cheng Lai *et al.*¹¹ where they found the prevalence of subclinical thyroid dysfunction was significantly higher amongst females as compared to the male subjects (9.9% vs 6.3%, respectively; $p < 0.05$). Another study by Nehal Hamdy *et al.* also revealed that the prevalence of subclinical hypothyroidism was more among the females.⁹ The types of clinical presentation, anthropometric analysis, biochemical and metabolic profile were observed. These were found to be having similar consistency of distribution as various other related studies. Only 28% of the patients were reported to be symptomatic, rest 72% patients did not have symptoms of thyroid disorder as depicted in Fig- 1. BMI was found to be high in twenty nine percent of our patients as shown in Fig-2. And on estimating body composition 27% of patients in our study were found as obese. Though the association is strong but it is not significant and is low in comparison to other studies. The blood sugar levels were found to be high in six percent of our patients and neither the Fasting Blood sugar nor Post prandial Blood sugar showed any significant association with the occurrence of symptoms as shown in table- IV. Similar result was found in the study by Nehal Hamdy *et al.*⁹ Some other recent studies also found a significant association between indices of metabolic syndrome and subclinical hypothyroidism.¹² Amongst the inflammatory markers that were studied, there were no significant associations drawn, and ESR was found to be raised in only three percent of the subjects. Lipid profile was found to be altered in thirteen percent of our patients, with abnormal triglyceride levels in 10% and reduced HDL-C in 7 percent of the patients but no significant relation was observed with presence of symptoms. Among the pituitary hormones,

prolactin was found to be elevated in sixteen percent of patients, Insulin was found to be elevated in 12% along with C- peptide in 10%. Out of all the hormones evaluated, only insulin and C-peptide levels were observed to have significant relation with presence of symptoms. On application of unpaired T test for the analysis of relationship between subclinical hypothyroidism and altered hormone levels, it was observed a significant relationship was present between subclinical hypothyroidism and increase in, insulin and C-Peptide i.e. p value was less than 0.05 as shown in table-III. A study by Nehal Hamdy *et al.*⁹ demonstrated insulin levels to be significantly higher in SCH patient group than in control group. Another recent study also found a significant association between altered hormone levels and subclinical hypothyroidism.¹³ In our study, estimation of bone mineral density by using DXA scan showed 17% patients had low bone mass and 7% patients were recorded to have osteopenia. On evaluation by polysomnography, 15% of the total patients were found to have abnormalities in their sleep pattern as shown in fig-3. In our study we observed that 8% of the patients of subclinical hypothyroidism had an associated metabolic syndrome. Other patients showed presence of variable components; most common were presence of increased BP in 53% patients, followed by increased blood sugar levels in 22% patients, increased waist circumference in 11%, increased TG in 10% and reduced HDL-C in 7% of the patients as shown in table-IV. Fahimeh Ramezani Tehrani *et al.*¹⁴ in their study found no evidence of an association between thyroid status and the prevalence of metabolic syndrome, but subclinical thyroid dysfunction was related with two components of Metabolic syndrome namely low HDL and high TG. Another study conducted recently by also found an association between lipid derangement and subclinical hypothyroidism.¹⁵

5. CONCLUSION

Subclinical hypothyroidism was found in sixty six percent

individuals with age less than forty years and a female preponderance was observed. Obesity is associated with some cases of SCH and alteration of metabolic profile as levels of AST, total proteins as well as other hormonal profile like prolactin, and insulin levels is observed in SCH patients. It was observed that SCH has significant correlation with metabolic syndrome parameters- WC, FBS, TG, HDL-C, and BP. Also C-peptide levels showed a positive correlation with SCH. We conclude that subclinical hypothyroidism has now emerged as one of the highly prevalent diseases, and is often undetected. It has also been observed to have a significant association with metabolic syndrome, so screening of thyroid

levels is important in all patients presenting with metabolic syndrome.

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6. AUTHORS CONTRIBUTION STATEMENT

All authors provided significant contribution in the form of data collection, analysis and gave necessary inputs for the designing of the manuscript.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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