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Original Research Article

Comparative study of lipid profile between clinical and subclinical hypothyroidism

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ABSTRACT

Background: Subclinical hypothyroidism (SH) is characterized by elevated levels of serum thyroid stimulating hormone in the presence of normal thyroxin levels. Subclinical hypothyroidism is often associated with elevated total cholesterol and other lipid profile parameters. This study was done to evaluate the lipid metabolism in subclinical hypothyroidism.
Methods: This case control study was done to compare the lipid profile parameters between subclinical and overt hypothyroidism cases attending the outpatient facility of our tertiary care hospital of our medical college in Puducherry. Newly diagnosed cases of hypothyroidism were selected by convenient sampling. A total of 37 SH cases and 31 overt hypothyroidism cases were included. Blood samples were drawn to measure lipid profile. A 2D echocardiogram was done to evaluate cardiac function. Ultrasonogram was done to evaluate fatty liver.
Results: The mean age of the participants in the subclinical hypothyroidism group was 34.2±12.2 years while in the clinical hypothyroidism group was 35.7±9.8 years. About 13.5% of the participants in subclinical hypothyroidism group and 12.9% of the participants in clinical hypothyroidism had fatty liver in ultrasound. A significant difference was observed in the mean values of total cholesterol, triglycerides and LDL levels between clinical and subclinical hypothyroidism.
Conclusions: This study highlights the need for screening of subclinical hypothyroidism in order to prevent the incidences of cardiovascular complications and other diseases like metabolic syndrome.

Keywords: Hypothyroidism, L- Thyroxin therapy, Metabolic syndrome, Subclinical hypothyroidism, Thyroid stimulating hormone

INTRODUCTION

India as a developing nation is currently facing the burden of not only infectious diseases, but also of non-communicable and other metabolic diseases. Diseases like cardiovascular diseases, diabetes mellitus and hypertension are more prevalent and results in an increased morbidity and mortality. However, certain endocrine disorders, especially disorders of thyroid metabolism are also on the rise. Hypothyroidism is a broad clinical spectrum of disorder ranging from overt hypothyroidism or myxedema to subclinical disorders with abnormal or mild subclinical disease.

In India, hypothyroidism has been recognized as a public health problem for the past several decades and has been termed as Iodine Deficiency Disorders (IDD). A universal salt iodization programme was adopted in 1983

and since then, there has been a considerable reduction in the prevalence.[1]

The clinical presentation of hypothyroidism is varied and dependent on many factors. Thyroid disorders are common among women and are often associated with increased morbidity and mortality among elders. Subclinical hypothyroidism is an important phenomenon in the spectrum of thyroid disorders. It is the most prevalent thyroid disorder, affecting 3-15% of the adult population.[2] Subclinical hypothyroidism is often a biochemical diagnosis, as patients seldom present with signs and symptoms of thyroid dysfunction. A diagnosis of subclinical hypothyroidism is made when there is an elevated serum Thyroid Stimulating Hormone (TSH) levels with a normal free T4 level. The risk factors for subclinical hypothyroidism include advancing age, female gender and excess intake of dietary iodine.

The impact of overt hypothyroidism on various systems is well established. However, subclinical hypothyroidism also has its own consequences. Some of the studies have established that subclinical hypothyroidism is a potential risk factor for cardiac function and lipid metabolism. The other consequences include neuropsychiatric symptoms and transition into overt hypothyroidism.[3] The changes in lipid metabolism and cardiovascular physiology are alarming, not only in the context of untreated cases, but also among patients with L-thyroxine substitution therapy.[4]

Subclinical hypothyroidism is often missed during clinical practice, due to the absence of overt symptoms. This is important in order to prevent complications and transformation into overt hypothyroidism. For this reason, the American Thyroid Association recommends routine screening for people of both the sexes at 35 years of age followed by periodic screening once in 5 years for early detection and management of subclinical hypothyroidism.[5]

However, in Indian context, there is scant data to substantiate the burden of subclinical hypothyroidism. Moreover, little research has been done to explore the risk factors and biochemical derangements of these patients. Considering the morbidity and mortality associated with dyslipidemia and cardiovascular diseases, there is an imminent need to evaluate subclinical hypothyroidism from the perspective of cardiovascular diseases and lipid metabolism.

The objective of the present study was to compare the lipid profile between clinical and subclinical hypothyroidism.

METHODS

This study was carried out as a case control study in the outpatient facility of the Department of General Medicine of MGMCRI tertiary care hospital in Puducherry. The study was conducted between 2014 and 2017.

All the patients who attended the outpatient facility and were newly hypothyroidism during the study period were included for the study. Participants who were under treatment for hypothyroidism and other metabolic, systemic and endocrine disorders were excluded.

A total of 68 hypothyroidism patients were included. Among them, 31 were diagnosed with overt clinical hypothyroidism and 37 were diagnosed as subclinical hypothyroidism. The participants in the study were selected by convenient sampling.

Data collection tools

A structured interview schedule was administered to each participant, which consisted of background information, history of medical illnesses like hypothyroidism, diabetes mellitus, hypertension and dyslipidemia. Height was measured in meters using a non elastic tape. Weight was measured in kilograms using a standardized weighing scale. Blood samples were drawn after overnight fasting. Thyroid function tests were carried out by chemiluminescence method using immunoassay analyzer. Serum total cholesterol and triglycerides were determined by enzymatic colorimetric assay.

High Density Lipoprotein (HDL) was determined enzymatically in the supernatant after dextran-magnesium induced precipitation of other lipoproteins. Low Density Lipoprotein (LDL) was determined using Friedewald formula. A 2D Echocardiogram was carried out by trained cardiologist to detect the presence of coronary artery disease. Ultrasonogram was carried out by trained sonologist to detect the presence of fatty liver.

Operational definition

Hypothyroidism was classified as clinical (overt) or subclinical based on Thyroid Stimulating Hormone (TSH) and Free T4 levels.[6] A diagnosis of clinical (overt) hypothyroidism was made when the TSH levels were >4.5 μIU/ml and Free T4 levels were <0.620 ng/dl. A diagnosis of subclinical hypothyroidism was made when the TSH levels were >4.5 μIU/ml and Free T4 levels were within the normal range. Standard normal ranges were applicable for all the lipid profile parameters.

Statistical analysis

Data was entered and analyzed using SPSS version 15 software. All the clinical and biochemical profile parameters were expressed as mean values. Chi square test was used to examine association between medical illnesses and hypothyroidism. Independent sample t test was done to evaluate the association between lipid profile and hypothyroidism.

RESULTS

This study was carried out among 68 participants who were diagnosed with hypothyroidism. Clinical hypothyroidism was present in 31 (45.6%) participants while subclinical hypothyroidism was present in 37 (54.4%) participants.

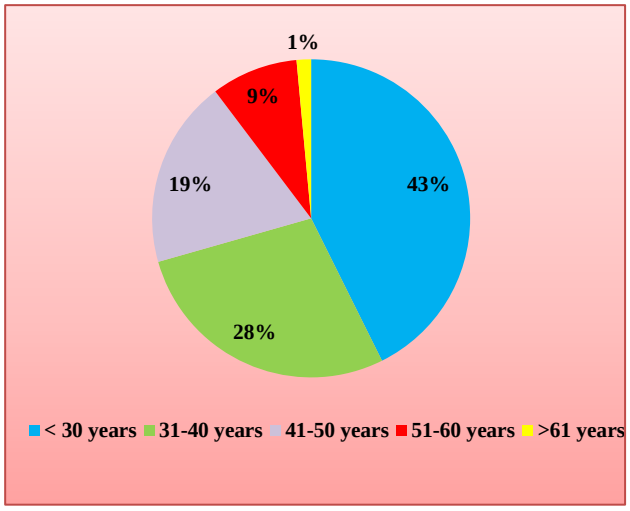

Figure 1: Age distribution of the study participants.

Majority of the participants belonged to <30 years of age (43%), followed by 31-40 years (28%). Very few participants (1%) were over 60 years of age. The age distribution of the study participants is given in Figure 1.

Table 1: Mean scores of the parameters.

Parameter	Subclinical hypothyroidism (n=37)		Clinical hypothyroidism (n=31)		p value
	Mean	SD	Mean	SD	
Age	34.2	12.2	35.7	9.8	0.585
Body mass index	25.3	4.5	27.3	4.9	0.086
TSH levels	15.6	7.6	65.3	34.8	0.0001*
Free T3	2.4	0.7	1.6	0.6	0.0001*
Free T4	1.4	1.3	0.8	0.5	0.025*
Total Cholesterol	195.4	31.9	230.8	43.9	0.0001*
Tri-glycerides	193.6	58.2	150.7	81.6	0.014*
HDL	47.5	7.9	42.3	9.8	0.021*
LDL	107.1	29.5	155.7	31.2	0.0001*
VLDL	38.7	11.4	25.7	9.7	0.0001*

The mean values of various clinical and biological parameters are given in Table 1. The mean age of the participants in the subclinical hypothyroidism group was 34.2±12.2 years while in the clinical hypothyroidism group was 35.7±9.8 years. There was no difference between both the groups (p 0.585). There was a significant difference in the lipid profile values between both the groups (p 0.0001).

Table 2: Clinical parameters of the study participants.

Parameter	Subclinical hypothyroidism (n=37)		Clinical hypothyroidism (n=31)	
	N	%	N	%
Body Mass Index				
Underweight (<18.5 kg/m^2)	2	5.4	1	3.2
Normal (18.5-23 kg/m^2)	9	24.3	5	16.1
Overweight (23-25 kg/m^2)	7	18.9	4	12.9
Obese (>25 kg/m^2)	19	51.4	21	67.7
Diabetes mellitus				
Present	1	2.7	0	0.0
Absent	36	97.3	31	100.0
Hypertension				
Present	3	8.1	1	3.2
Absent	34	91.9	30	96.8
Dyslipidemia				
Present	0	0.0	0	0.0
Absent	37	100.0	31	100.0
Echocardiogram				
Normal	37	100.0	31	100.0
CAD	0	0.0	0	0.0
Ultrasound				
Normal	31	83.8	0	0.0
Fatty liver	5	13.5	4	12.9
Not done	1	2.7	27	87.1

The frequency of clinical parameters of the study participants is given in Table 2. About 51.4% of the participants in subclinical hypothyroidism group and 67.7% of the participants in clinical hypothyroidism group were obese. Moreover, 8.1% of the participants in subclinical hypothyroidism group and 3.2% of the participants in clinical hypothyroidism were hypertensives. Also, 13.5% of the participants in subclinical hypothyroidism group and 12.9% of the participants in clinical hypothyroidism had fatty liver in ultrasound.

The association between various clinical parameters and hypothyroidism is given in Table 3. It was observed that fatty liver is a significant risk factor for subclinical hypothyroidism compared to clinical hypothyroidism. The observed difference was statistically significant (p 0.0001). The association between lipid profile and hypothyroidism is given in Table 4.

A significant difference was observed in the mean values of total cholesterol, triglycerides and LDL levels between clinical and subclinical hypothyroidism. The associated difference was statistically significant (p<0.05).

Table 3: Association between clinical parameters and hypothyroidism.

Parameter	N	Subclinical hypothyroidism N (%)	Clinical hypothyroidism N (%)	Chi sq.	p value
Age (in years)					
<35	39	22 (56.4)	17 (43.6)	0.1	0.701
>35	29	15 (51.7)	14 (48.3)		
Sex					
Males	5	3 (60.0)	2 (40.0)	0.07	0.794
Females	63	34 (54.0)	29 (46.0)		
Diabetes mellitus					
Present	1	1 (100.0)	0 (0)	0.8	0.356
Absent	67	36 (53.7)	31(46.3)		
Hypertension					
Present	4	3 (75.0)	1 (25.0)	0.7	0.394
Absent	64	34 (53.1)	30 (46.9)		
Ultra-sonogram					
Fatty liver	9	5 (55.6)	4 (44.4)	15.3	0.0001*
Normal	31	31 (100.0)	0 (0)		

*p value significant at 95% level

Table 4: Association between lipid profile and hypothyroidism.

Parameter	Mean difference	Std. Error	t value	p value
Total cholesterol	-35.4	9.2	3.8	0.0001*
Triglycerides	42.9	16.9	2.5	0.014*
LDL levels	-48.6	8.4	-5.8	0.0001*

*p value significant at 95% level

DISCUSSION

Subclinical hypothyroidism (SH) is one of the common forms of thyroid disorders is widely prevalent in upto 10% of the adult populations.[7] Though SH is a biochemical diagnosis, several precursor conditions such as chronic autoimmune thyroiditis, subacute thyroiditis or post-partum thyroiditis or drug induced thyroiditis could be implicated. However, the progression of SH to overt hypothyroidism is most often definite, ranging from 33-55% in 10 years.[8]

While most of the biochemical and physiological alterations are common with overt hypothyroidism, several studies have been reporting a link between derangement of lipid profile and subclinical hypothyroidism. Since lipid profile is an established, independent risk factor for cardiovascular diseases, its derangement in subclinical hypothyroidism may imply an increase in the risk for cardiovascular diseases in this patient group. Present study demonstrated a statistically significant correlation between SH and lipid profile parameters like total cholesterol, triglycerides and LDL levels ($p<0.05$). A meta-analysis done by Lu et al has reported that elevated total cholesterol levels were significantly present in SH group compared to euthyroid group.[9] Similarly, LDL levels were also significantly higher in the SH group. The observations were found to be statistically significant.[9] The Colorado USA study also demonstrated that SH patients had elevated total cholesterol and LDL-C levels. This study also demonstrated that the lipid levels increased in a graded manner, with declining thyroid function.[10]

The several studies which have established association between lipid profiles and subclinical hypothyroidism have demonstrated the atherogenic inclination of patients with SH. Studies hypothesize that the observed difference could be in relation to the poor cholesterol clearance among patients with SH.[11] However, the response of lipid profile to L-thyroxine therapy is another important aspect to be considered. A number of studies have demonstrated a decline in total cholesterol and LDL-C values after L-thyroxine substitution. The response to therapy was directly proportional to the severity of SH. Nevertheless, the response to L-thyroxine on HDL-C and triglyceride levels remains obscure.[4]

Present study demonstrated a statistically significant association between fatty liver and SH (χ^2 - 15.3, p= 0.0001). A study done by Posadas Romero-C also demonstrated the incidence of fatty liver to be 27.8% in the SH group. This study also established that presence of fatty liver in SH is a significant risk factor for metabolic syndrome (OR- 2.73; 95% CI- 1.26-5.92).[12] A study done by Lee et al demonstrated that Non-Alcoholic Fatty Liver Disease (NAFLD) was present in 11% of the participants with SH. This attribute was explained as a linkage

mechanism between SH and metabolic syndrome.[13] The underlying mechanism for this observation has been proposed that the thyroid hormones stimulate the expression of uncoupling proteins in the mitochondria of fat and skeletal muscle through modulate adrenergic receptors by enhancing responsiveness of catecholamines.[14] Thereby thyroid hormones influence the body weight, thermogenesis, lipolysis and fat metabolism, indirectly culminating in atherogenic risk.

Present study did not evaluate the parameters in comparison with euthyroid patients. Also, a further explorative analysis by matching for age, sex and other demographic factors would have provided the results eliminating possible confounders.

CONCLUSION

Thyroid disorders have a systemic manifestation causing derangements in the functioning of various organs. The thyroid hormones have an indirect influence on the lipid metabolism at the cellular level, more in subclinical hypothyroidism compared to euthyroid and overt hypothyroidism. This association between lipid profile and subclinical hypothyroidism results in an elevation in various lipid profile parameters like total cholesterol, LDL-cholesterol and triglycerides. Therefore, subclinical hypothyroidism is implicated in the causative mechanism of atherosclerosis and coronary artery diseases. Moreover, subclinical hypothyroidism impairs the cholesterol clearance, resulting in Non-Alcoholic Fatty Liver Disease, thereby resulting in features pathognomonic of metabolic syndrome. This study highlights the need for screening of subclinical hypothyroidism in order to prevent the incidences of cardiovascular complications and other diseases like metabolic syndrome.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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