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Original Research Article

Study of Clinical and Laboratory Profile of Patients of Subclinical Hypothyroidism

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Abstract

Background: Subclinical hypothyroidism is more common than overt hypothyroidism and it is associated with Coronary artery disease and many biochemical abnormalities. The aim of this study is to evaluate the clinical and laboratory profile of patients of subclinical hypothyroidism.

Methods: Total number of 75 patients with established subclinical hypothyroidism who were admitted in the Department of General Medicine in Tertiary Care Hospital during the period of August 2018 to September 2020 were enrolled for the study.

Results: The age group taken for study was 18 to 70 years. The mean age of patients suffering from subclinical hypothyroidism was 45.46. Out of 75 patients, 69(92%) patients were women while 6(8%) patients were men. In our study of 75 patients, 61.33% patients were asymptomatic, 10.67% patients reported having fatigue, 6.67% patients had musculoskeletal symptoms (proximal weakness, fatigue, slowed movements and reflexes, stiffness, myalgia, and less commonly, cramps and muscle enlargement), neck swelling(1.33%), cold intolerance(4%), constipation(4%), voice change(2.67%), depression(1.33%), infertility(2.67%), menorrhagia(1.33%) and weight gain(4%). Enlarged thyroid and dyslipidemia were also recorded. The mean of TSH (mIU/L) was 7.05±1.22 and the mean of FT4 (ng/dl) was 1.61±0.45. Finally, the mean of TPOAb (IU/mL) was 1.32±0.46. TPOAb was positive in 49(65.33%) patients.

Conclusion: It is very important to timely detect the subclinical hypothyroidism and to treat them adequately to prevent them from converting into frank hypothyroidism and other complications.

Keywords: Subclinical Hypothyroidism, Fatigue, Coronary Artery Disease, Tertiary, Dyslipidemia

Introduction

Thyroid disorders are amongst the most common endocrine diseases in India[1]. Subclinical hypothyroidism (SCH) is defined as a condition where biochemically thyroid stimulating hormone (TSH) is elevated above the reference value but thyroid hormones including thyroxine (T4) and triiodothyronine (T3) are normal[2-4]. Subclinical hypothyroidism (SCH) is a metabolic disorder with prevalence about 4-10% in general population[5]. Thyroid disorders are more common in women than in men. The higher prevalence of thyroid disorders in females may be associated with estrogen and progesterone [6]. Subclinical hypothyroidism is more common than overt hypothyroidism and it is associated with Coronary artery disease and many biochemical abnormalities [7]. Research shows that hypothyroidism can contribute to morbidity from Osteoporosis, Hyperlipidemia, Hypercholesterolemia, Cardiovascular and Neuropsychiatry disease in the population [8]. Subclinical hypothyroidism may be transient condition because these levels can return to normal or develop into overt hypothyroidism. According to established guidelines, SCH should not be diagnosed unless its manifestations are confirmed in two tests that are at least 3 months apart [9]. Owing to its ability to control and modulate metabolism, thyroid is often called as master gland of metabolism in common parlance[10]. Thyroid hormones are recognized as catabolic hormones and they regulate various processes of metabolism including the synthesis, mobilization, and breakdown of lipids. Hypothyroidism is reported to be associated with an increased risk for cardiovascular disease. Thyroid is also considered to have an effect on reproductive hormones and is often associated with diseases like polycystic ovarian syndrome. It also has an impact on psychological and psychiatric well-being of the individual. Subclinical hypothyroidism in children has also been shown to be associated with intellectual, cognitive and physical growth impairment[11,12].

Normal thyroid-stimulating hormone (TSH) levels generally fall between 0.4 and 4.0 milliunits per liter (mU/L).TSH levels higher than 4.5 mU/L usually indicate an underactive thyroid (hypothyroidism), and low TSH levels below 0.4 mU/L indicate an overactive thyroid (hyperthyroidism)[13]. The consequences of subclinical hypothyroidism are variable at several levels and may depend on the duration and the degree of elevation of the serum TSH. Although various studies have suggested it to be a cardiovascular risk factor, yet a number of important questions about subclinical hypothyroidism remain, including whether it increases cardiovascular (CV) risk or mortality, whether it negatively influences metabolic parameters and whether it should be treated with L-thyroxine. The effect of T4 replacement on lipids is uncertain. However, in several randomized trials of patients with subclinical hypothyroidism treated with T4 versus placebo, serum total and LDL cholesterol and apoprotein B-100 concentrations decreased significantly whereas serum HDL cholesterol, triglyceride, and lipoprotein(a) concentrations did not change[14].

Methodology

Source of data: The study consists of 75 patients who were admitted in the department of general medicine in tertiary care hospital during the period of August 2018 to September 2020.

Patients satisfying inclusion and exclusion criteria were enrolled for this study and after providing written informed consent, a thorough medical history, physical examination, ECG, laboratory investigations were performed on the

patient. Biochemical tests done were thyroid profile, total cholesterol, triglyceride, random blood sugar was done by immuno chemiluminescensce method using standard kits and protocols mentioned in them. The simple statistics was employed to calculate the percentage and ratio of clinical symptoms and signs. The p-value of <0.05 was considered to be significant for all statistical analysis.

Inclusion criteria:

- All the patients between 18-70 years of age with high concentration of TSH (thyroid-stimulating hormone or thyrotropin) in blood sample with values between 4 to 10 with normal FT4 levels.

Exclusion criteria:

- Pregnant women are excluded from this study.
- Patients less than 18 years of age.
- Patients more than 70 years of age.
- Patients taking L-thyroxine supplements.
- Patients with TSH values more than 10.

Reference range for lipid profile

- Total cholesterol: 50-200 mg/dL
- Triglyceride: 50-150 mg/dL
- HDL-C: 40-60 mg/dL
- LDL-C: <100 mg/dL

Results

In the present study, total 75 patients fulfilling the inclusion criteria and diagnosed with subclinical hypothyroidism were enrolled in the study. The patients were aged 18-70 years old (Mean age 45.46±11.65 years). The proportion of patients were highest in the age group 41-50 years (40%) followed by age group of 51-60 years (22%) and 18-30 years (16%). Out of 75 cases female predominates 69(92%) in comparison to male 6(8%) cases. Male to female ratio was 6/69 (0.086). TSH values ranged from 4.44-9.91mIU/ml with a mean of 7.05±1.22 mIU/ml. FT4 values ranged from 1.17-2.06 ng/dl with a mean of 1.61±0.45 ng/dl. Anti TPO antibodies were present in 49(65.33%) patients. All the patients were treated with replacement therapy as per the standard guidelines for subclinical hypothyroidism.

Table 1: Age Profile of Study Population

Age (in years)	No. of Patients (n=75)
18-30	12 (16.0%)
31-40	10 (13.3%)
41-50	30 (40.0%)
51-60	17 (22.6%)
>60	06 (08.0%)
Total	75 (100%)
Mean Age (Years)	45.46±11.65

Table 2: Gender wise Distribution

Gender	No. of Patients
Male	06 (8%)
Female	69 (92%)
Total	75 (100%)

Table 3: Age Group and Gender wise Distribution

Age in years	Female	Male	Total
<40	19	3	22
>40	50	3	53
Total	69	6	75

Table 4: Tc and Age Group wise Distribution

Group	<40 Years	>40 Years	Total
TC <200 mg/dl	7	16	23
TC >200 mg/dl	15	37	52
Total	22	53	75

Table 5: Symptoms and Gender wise Distribution

Group	Female	Male	Total
Asymptomatic	41	5	46
Symptomatic	28	1	29
Total	69	6	75

Table 6: Mean of Tsh, Ft4 and Tpoab

Group	No. Of patients	Min	Max	Mean
S. TSH	75	4.44	9.91	7.05±1.22
S.FT4	75	1.17	2.06	1.61±0.45
TPOAb	75	10.19	26.77	26.32±0.46

Table 7: Tsh and Age Group wise Distribution

Group	<40 Years	>40 Years	Total
TSH <7 mIU/ml	11	27	38
TSH >7 mIU/ml	11	26	37
Total	22	53	75

Table 8: Tpoab and Symptoms wise Distribution

Group	Asymptomatic	Symptomatic	Total
TPOAb +VE	29	20	49
TPOAb -VE	17	9	26
Total	46	29	75

The p-value is 0.599721. This result is not significant at $p<0.05$.

Table 9: Tpoab and Tc wise Distribution

Group	TC<200	TC>200	Total
TPOAb +VE	11	38	49
TPOAb -VE	12	14	26
Total	23	52	75

The p-value is 0.034108. This result is significant at $p<0.05$.

The clinical manifestations of subclinical hypothyroidism were varied.

In this study of 75 patients, 61.33% patients were asymptomatic while 10.67% patients reported having fatigue, 6.67% patients had musculoskeletal symptoms (proximal weakness, fatigue, slowed movements and reflexes, stiffness, myalgia, and less commonly, cramps and muscle enlargement), 1.33% reported neck swelling, 4% suffered from cold intolerance, 4% complained of constipation, 2.67% reported having voice change, 1.33% reported having depression, 2.67% suffered from infertility, 1.33% had menorrhagia and lastly, 4% reported having weight gain.

Table 10: Clinical Symptoms wise Distribution

Clinical Symptoms	No. of Patients (n=75)
Asymptomatic	46 (61.33%)
Tiredness	8 (10.67%)
Musculoskeletal	5 (6.67%)
Neck Swelling	1 (1.33%)
Cold Intolerance	3 (4%)
Constipation	3 (4%)
Voice Change	2 (2.67%)
Depression	1 (1.33%)
Infertility	2 (2.67%)
Menorrhagia	1 (1.33%)
Weight Gain	3 (4%)

In this study, 10(13.33%) patients with history of Hypertension suffered from subclinical hypothyroidism followed by 07(9.33%) patients with DM and 07 (9.33%) patients with IHD.

Table 11: Comorbidity wise Distribution

Group	Female	Male	Total
Hypertension	8	2	10
Dm	7	0	7
IHD	6	1	7

All patients were evaluated for dyslipidemia. The triglyceride levels and serum cholesterol levels were deranged in 51(68%) and 52(69.33%) patients respectively of all cases. The average cholesterol levels were 213.86 mg/dl (range161-259mg/dl). The mean triglyceride levels were 166.2mg/dl (range 122-210mg/dl).

Table 12: Serum Lipid wise Distribution

S. LIPIDS	No. of Patients (n=75)
TC (mg/dl)	213.86±27.74
TG (mg/dl)	166.2±21.99
LDL (mg/dl)	125.94±45.02
HDL (mg/dl)	47.01±13.23

Table 13: Tc and Tsh wise Distribution

Group	TSH <7 mIU/ml	TSH >7 mIU/ml	Total
TC <200 mg/dl	14	9	23
TC>200 mg/dl	24	28	52
Total	38	37	75

The p-value is 0.239835. The result is not significant at $p<0.05$.

Table 14: Vital Parameters and General Examination wise Distribution

Vital Parameters + General Examination	No. of Patients (n=75)
Pulse	
• Normal	75 (100%)
• Bradycardia	0
BP	
• Normal	65 (86.67%)
• Hypertension	10 (13.33%)

Goiter • Yes • No	 37 (49.33%) 38 (50.67%)
Dry Skin • Yes • No	 28 (37.33%) 42 (62.67%)
Puffy Eyes • Yes • No	 14 (18.67%) 61 (81.33%)
Delayed reaction of ankle jerk • Yes • No	 10 (13.33%) 65 (86.67%)

Table 15: Tpoab and Goiter wise Distribution

Group	Goiter +nt	Goiter -nt	Total
TPOAb+VE	23	26	49
TPOAb-VE	14	12	26
Total	37	38	75

The p-value is 0.569068. This result is not significant at $p<0.05$.

Table 16: Gender and Goiter wise Distribution

Group	Goiter +nt	Goiter -nt	Total
Male	4	2	6
Female	33	36	69
Total	37	38	75

The p-value is 0.375949. This result is not significant at $p<0.05$.

Discussion

The study clearly shows that the disease is prevalent across all age groups but more in greater than 40 year age group. Our study also indicates that females are more likely to have subclinical hypothyroidism as compared to males. This is similar to the study done by Bandhopadhay et al[15] where females constituted 78% of total study population. In study done by Mishra S et al[16] females are more likely to have subclinical hypothyroidism as compared to males.

Out of 69 females, 50 females were in >40 year age group. This shows that females suffer from subclinical hypothyroidism more than males as age advances. This was supported by Whickham Study[17], the Colorado[18] study and Nhanesiii[19] study where women with increasing age were affected more.

In our study, the disease is more in >40 year age group females which makes it inconsistant with study done by Mishra S et al[16] in which the disease is prevalent more in adolescent females and females of reproductive age group. Only 19 females were in <40 year age group. These young females having subclinical hypothyroidism have increased chances of infertility. It is very important to recognize them and treat them with Levothyroxine for their proper growth and development and for future pregnancies.

In this study, 46(61.33%) patients were asymptomatic while 29(38.67%) patients were having symptoms. Most common symptoms were fatigue followed by musculoskeletal symptoms.

Other symptoms were neck swelling, cold intolerance, constipation, voice change,

depression, infertility, menorrhagia and lastly weight gain which makes it inconsistant with study done by Mishra S et al[16] where none of the patients were asymtomatic. In this study, most common symptom is tiredness which is consistant with Mishra S et al[16] study.

Study by Pipliwal et al[20] mean TSH value was 7.44±1.30 microIU/ml which is consistant with our study in which mean TSH 7.05±1.22.

The comparision between this study and Saha K et al[21] is as below.

Table 17: Comparative Study of Serum Lipids

S. LIPIDS	No. of Patients (n=75)	Saha K et al (n=60)
TC (mg/dl)	213.86±27.74	162.07±42.32
TG (mg/dl)	166.2±21.99	148.90±65.27
LDL (mg/dl)	125.94±45.02	98.81±33.26
HDL (mg/dl)	47.01±13.23	34.27±13.21

Owing to these severe health related implications, treatment of hypothyroidism is essential. Levothyroxine is the treatment of choice for hypothyroidism. It has a 7-day half-life, allowing daily dosing[16]. It is also used as a treatment modality in subclinical hypothyroidism. The patients who developed symptoms and were TPOAb positive with TSH levels between 4-10mIU/L were started on low dose L-Thyroxine supplements and were called again after three months which showed their serum TSH levels to have returned to normal and they reported being asymptomatic. Therefore, our study shows that administering low dose L-Thyroxine supplements to patients suffering from subclinical hypothyroidism renders them asymptomatic but requires a stringent eye on thyroid function tests in the follow-up period.

Conclusion

Large number of patients are of subclinical hypothyroidism presenting in the outpatient department are having non-specific clinical presentation. Therefore, to diagnose these patients there should be high index of suspicion. Subclinical hypothyroidism patients commonly presented with generalized weakness, lethargy, tiredness and generalized body ache. They also complained of weight gain, constipation and menstrual disturbances. These symptoms caused poor quality life style and poor outcome. Treatment of these patients can help in improving their quality of life and work efficiency. It is well known that increase in atherogenic lipid profile is a risk factor for cardiovascular diseases, cerebrovascular disease thereby increased mortality. Hence subclinical hypothyroidism should be considered in all elderly people with nonspecific complaints and considered for treatment with low dose of thyroxine and lipid lowering drugs especially when serum TSH level is >10 mIU/L, thereby to reduce the risk of progression to overt hypothyroidism, decrease atherosclerotic events, improve their quality of life. However, there is an absolute need for larger prospective studies designed to answer the question as to whether subclinical hypothyroidism is associated with increased risk for coronary heart disease and whether therapy for subclinical hypothyroidism might reduce cardiovascular morbidity and mortality.

In this study, the patients who were having TPOAb positive and having symptoms like infertility, menorrhagia were improved after giving L-thyroxine supplements. There are no universally accepted recommendations for the management of subclinical hypothyroidism, but levothyroxine is recommended if the patient is a woman who wishes to conceive or is pregnant, or when TSH levels are above 10 mIU/L[22]. Otherwise, when TSH

levels are below 10 mIU/L, a trial of treatment may be considered when patients have suggestive symptoms of hypothyroidism, positive TPOAb or any evidence of heart disease. It is important to confirm that any elevation of TSH is sustained over a 3-month period before treatment is given. Treatment is administered by starting with a low dose of levothyroxine (25–50 µg/d) with the goal of normalizing TSH [22]. If levothyroxine is not given, thyroid function should be evaluated annually.

The limitation of the study is that this is a single centered study at tertiary care center, where majority of the patients are referred from other centers. Thus, this may not represent the holistic prevalence of subclinical hypothyroidism in the society. However, the findings of this study and earlier studies will promote researchers to do larger and multicentre studies.

Abbreviations

TSH – Thyroid Stimulating Hormone.
SCH – Subclinical Hypothyroidism.
FT3 – Free Triiodothyronine.
FT4 – Free Thyroxine.
TPO – Thyroid Peroxidase.
TC – Total Cholesterol.
TG – Triglycride.
LDL – Low Density Lipoprotein.
HDL – High Density Lipoprotein.

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