

Original Research Article

Study of subclinical hypothyroidism in elderly and its correlation with lipid profile

Namita Mohanty, Satyajit Parhi*

Department of General Medicine, Maharaja Krishna Chandra Gajapati Medical College, Berhampur, Odisha, India

Received: 17 December 2019

Accepted: 23 December 2019

***Correspondence:**

Dr. Satyajit Parhi,

E-mail: drsatyajitparhi@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Although hypothyroidism accompanying dyslipidemia previously recognized as important risk factor for cardiovascular disease, but now subclinical hypothyroidism emerged as important risk factor for atherosclerosis and myocardial infarction especially in elderly people. Subclinical Hypothyroidism (SCH) is a state characterized by normal serum T3 and T4 level with elevated TSH level having minimal signs and symptoms. There are limited studies on SCH and dyslipidemia in elderly people in India, so this study was undertaken to correlate thyroid function abnormality with lipid profile in elderly population.

Methods: This observational study was conducted in 74 elderly people more than 60 years age group having symptoms of SCH i.e. fatigue, weakness mild thyroid swelling, weight gain etc. who did not previously have a diagnosis of hypothyroidism, diabetes mellitus, previous thyroidectomy, renal failure, hepatic failure, systemic hypertension etc. They had normal T3, T4 level and raised TSH value. Cases with TSH value >5 mIU/L but normal T3, T4 level were evaluated further for lipid profile.

Results: Elderly females suffered more from SCH in the age group of 60-70 years. Participants with SCH had significantly higher cholesterol (p value=0.0216), higher LDL (p value=0.0241) and higher triglyceride (p value =0.0004) with increasing TSH showing positive correlation. There is no significant correlation between decreasing HDL and TSH value.

Conclusions: All elderly people should be routinely screened for thyroid function abnormality. Those have SCH should also be evaluated for dyslipidemia so that they can be treated with lipid lowering drugs and low dose thyroxine judiciously to prevent atherosclerosis.

Keywords: Correlation, Dyslipidemia, Elderly, Subclinical hypothyroidism

INTRODUCTION

Thyroid disorders are the most common endocrine disorders second only to diabetes mellitus which may occur at any stage of life, it may be overt or subclinical. Subclinical Hypothyroidism (SCH) is defined as serum TSH concentration above the statistically defined upper limit of reference range when serum free T4 concentration is within its reference range in presence of a few or no definite clinical signs and symptoms suggestive of hypothyroidism.^{1,2} Overall prevalence is 4-

20% in general population. In elderly prevalence is 20%. Females are at greater risk for SCH 21% than male 16%, after 74 years of age.³ Persistent altered thyroid hormone level leads to various metabolic abnormalities like hyperlipidemia due to modification of other regulating hormones like insulin, catecholamines. Overt hypothyroidism leading to elevated lipid profile is well known, which is a risk factor for atherosclerosis and cardiovascular diseases. SCH patients also have lipid abnormalities though less pronounced but still important risk factor for severe cardiac diseases (2-3-fold risk for

myocardial infarction and left ventricular diastolic dysfunction).⁴ There are few Indian studies regarding SCH in elderly and hyperlipidemia. Moreover, there are no studies regarding TSH cut off for association with lipid. With this background this study was undertaken to study thyroid profile and lipid profile of elderly SCH patients and to study the correlation between thyroid function abnormalities and lipid profile in these patients.

METHODS

The present cross-sectional observational study was undertaken in the department of General Medicine M.K.C.G. Medical College, Berhampur, Odisha from September 2017 to August 2019. Study subjects: Seventy-four SCH patients of age more than 60 years.

Inclusion criteria

- SCH patients >60 years of age having minimal symptoms like fatigue, tiredness, myalgia etc.
- Both males and females

Exclusion criteria

Patients with following clinical signs and symptoms were excluded from the study

- Patients with overt hypothyroidism
- Thyroidectomy
- External radiation to neck
- Previous radioactive iodine therapy
- Primary, secondary dyslipidemia
- Diabetes mellitus
- Hypertension
- Renal and hepatic failure
- Drugs like statins and other drugs altering thyroid function and lipid level etc.

Laboratory analysis

After taking consent from the patients, and permission from Institutional Ethical Committee, detailed history, physical examination, routine laboratory investigations were done. Fasting thyroid profile (T3, T4, TSH) and fasting lipid profile were done in all patients. IMMULITE kit (chemiluminescent immune assay) was used for thyroid hormone estimation. Total cholesterol and serum triglycerides were estimated by oxidase/peroxidase method. LDL and HDL cholesterol were estimated by cholest test kit.

The reference value of each parameters are as follows:

Reference range for thyroid profile

- Serum TSH: 0.27-5 mIU/L
- Serum T3: 1.3-3.1nmol/L
- Serum T4: 66-181nmol/L

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

Statistical analysis

Generated data were analyzed statistically by nonparametric Mann-Whitney u' test, Chi-square test. Correlations between two continuous variables were calculated by Pearson Correlation. All the statistical analysis was performed by using Graph Pad Instat version 3 for window. The value of <0.05 was considered to be significant for all statistical analysis.

RESULTS

In this study, out of 74 cases female predominates 63(85.14%) in comparison to male 11(14.86%) cases. Patients were in the age group of 60-87 years, mean age in male 67.55±4.93 years, and in female 70.00±6.24 years showing no significant difference in age group between male and female (p=0.2329). Out of 11 male cases 8(72.73%) are in the age group 60-70 years (group1) and 3(27.27%) cases are in the age group of >70 yrs (group 2). Similarly, out of 63 females 38(60.32%) are in group 1 and 25(39.68%) in group 2. This shows no significant difference in sex distribution in two age groups of patients (p=0.6551).

All the patients have clinical signs and symptoms like mild weight gain (62.16%), generalized weakness (66.21%), fatigue (21.62%), dry skin (10.81%), cold intolerance (9.45%), constipation (8.10%) and mild thyroid swelling (4.05%). Thyroid profiles of all the patients were analyzed. The mean T3 value in males and females was found to be 1.8±0.55 nmol/liter and 1.78±0.39 nmol/liter respectively (p=0.6872). The mean T4 value in males and females was found to be 92.09±30.8 nmol/liter and 103.08±29.49 nmol/liter respectively (p=0.0932). Similarly the mean TSH value in males and females was found to be 9.90±3.98 mIU/liter and 11.51±4.49 mIU/liter respectively (p=0.3015).

Thyroid profile of this patients showed serum T3 varies from minimum 1.00 nmol/L to maximum 2.99 nmol/L. Mean T3 was 1.75±0.40 nmol/L in age group 60-70 years and 1.84±0.44 nmol/L in age group >70 years, showing no statistically significant difference between two age groups. Mean T4 was 94.36±24.5 nmol/L in group 1 and 113.09±33.98 in group 2 showing statistically significant difference (p=0.0168). Mean TSH in age group 60-70 years is 9.38±3.31 mIU/L. Mean TSH in age group >70 years is 14.37±4.32 mIU/L. comparison of TSH in two age groups found to be statistically significant (p <0.0001). The comparison of thyroid profile in two age groups was shown in Table 1.

Table 1: Comparison of thyroid profile in two age groups of patients with SCH (n-74).

Thyroid profile	Min	Max	Mean ±SD	Group-1 (60-70 Years)	Group-2 (>70 years)	p Value
T3 (nmol/liter)	1.000	2.99	1.78±0.42	1.75±0.40	1.84±0.44	0.3907
T4 (nmol/liter)	66.00	181.00	101.44±29.68	94.36±24.5	113.09±33.98	0.0168
TSH (mIU/liter)	5.20	20.35	11.27±4.43	9.38±3.31	14.37±4.32	<0.0001

Depending upon TSH value, patients were divided into two categories 1 (TSH value being 5-10 mIU/lit) and Category 2 (TSH value being >10 mIU/lit). In Category 1 and 2 there were 42(56.76%) and 32 (43.24%) patients respectively. The lipid profiles were compared between the two categories of TSH. Cholesterol, LDL and triglycerides values were found to be significantly high in

CAT-2 as compared to CAT-1 (p<0.05). However, HDL value was comparable in both the categories (p=0.3594). The detail comparison of lipid profile in two categories of TSH along with its minimum and maximum values was depicted in Table 2. The mean value of Cholesterol, LDL, HDL and triglycerides were comparable between male and female patients (p>0.05).

Table 2: Comparison of Lipid profile in two categories of TSH in patients with SCH (n-74).

Lipid profile	Min	Max	TSH (CAT-1) 5-10 mIU/L Mean±SD	TSH (CAT-2) >10 mIU/L Mean±SD	Statistics p value
Cholesterol (mg/dl)	67.00	584.00	205.60±91.50	235.44±79.01	0.0094
LDL (mg/dl)	52.00	204.00	124.40±37.92	152.13±39.81	0.0052
HDL (mg/dl)	11.00	106.00	41.07±16.98	38.06±13.40	0.3594
Triglycerides (mg/dl)	43.00	454.00	186.71±65.46	256.81±95.48	0.0002

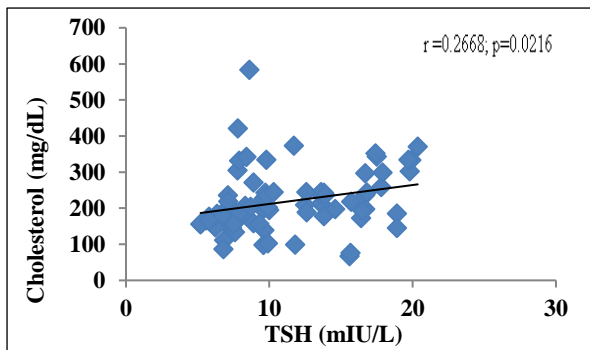


Figure 1: Correlation of cholesterol with TSH in the study subjects (n=74).

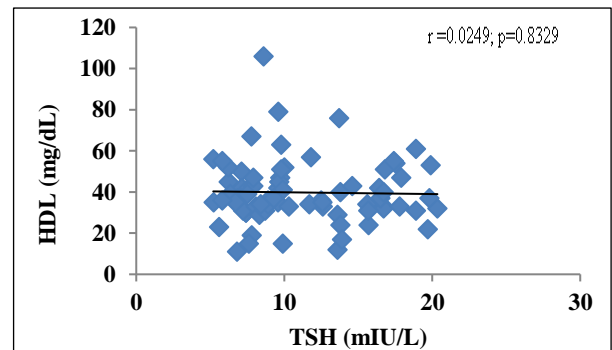


Figure 3: Correlation of HDL with TSH in the study subjects (n=74).

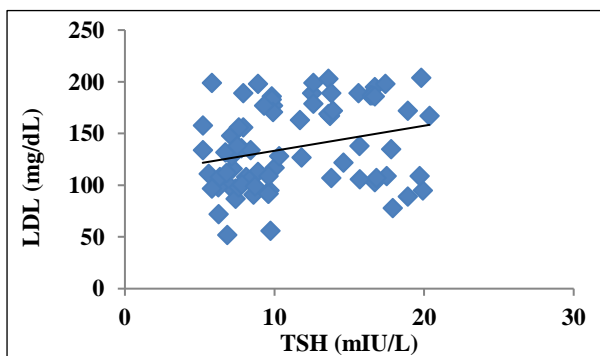


Figure-2: Correlation of ldl with tsh in the study subjects (n=74).

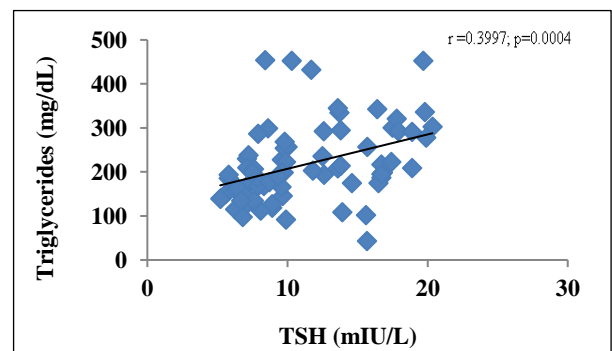


Figure 4: Correlation of triglycerides with TSH in the study subjects (n=74).

Further, we have correlated each lipid profile with TSH in study subjects. Total cholesterol ($r=0.2668$; $p=0.0216$), LDL ($r=0.2621$; $p=0.0241$) and triglycerides ($r=0.03997$; $p=0.0004$) have positive correlation with TSH. However, HDL was found to be decreasing with increasing TSH, though it did not reach to a statistically significant ($r = -0.0249$; $p=0.8329$). Graphs depicting the correlation of lipid profiles with TSH was shown in Figure 1,2,3 and 4.

DISCUSSION

This is a cross sectional observational study in 74 cases of SCH over a period of two years with subtle clinical features having normal T3, T4 levels and TSH level >5 mIU/L. Study showed females outnumbered male (85.14% Vs 14.86%) significantly. This is similar to the study done by Bandhopadhyay et al, where females constituted 78% of total study population.⁵ Age of study subjects lie between 60-87 years with mean age of males 67.55 ± 4.93 years and in female 70.00 ± 6.24 years which coincides with studies of Franklyn et al, and Jandu et al.^{6,7} Out of 11 male cases 8(72.73%) cases are in the age group 60-70 years and 3(27.27%) cases in the age group >70 years. Out of 63 female cases, 38(60.32%) cases were in the age group 60-70 years and 25(39.68%) cases are in the age group >70 years. It shows female suffer from SCH more than male as age advances. This was supported by WHICKHAM STUDY, the COLORADO study and NHANESIII study where women with increasing age were affected more.^{3,8,9} All the patients have minimal symptoms like generalized weakness, easy fatigability, weight gain, dry skin and mild thyroid swelling results similar to study by Kong et al.¹⁰

Regarding thyroid profile, mean serum T3 level being 1.78 ± 0.42 nmol/L shows no significant difference between sex and between two age groups. Studies by Pipliwal et al, showed the mean T3 value of 2.30 ± 0.60 ng/dL.¹¹ In this study, mean T4 was 101.44 ± 29.68 in males and females almost similar but when compared in different age group, in group 1 it was 94.36 ± 24.5 and group 2 it was 113.09 ± 33.98 , which indicates as age advances serum T4 increases minimally but within normal range.^{12,13}

Identifying the upper limit of normal TSH range is critical in defining SCH. In this study upper limit of normal is 5 mIU/L supported by study done by Singh et al. In NHANESIII study, TSH value of 4.5 mIU/L was taken as upper reference range.⁹ TSH value in this study varies from 5.20 mIU/L to 20.35 mIU/L with mean 11.27 ± 4.43 mIU/L, being similar in both the genders. Study by Pipliwal et al, mean TSH value was 7.44 ± 1.30 microIU/ml.¹¹ Author had categorized the patients on the basis of TSH value into two categories i.e cat 1 with a TSH value of 5-10 mIU/L and cat 2 with a TSH value of >10 mIU/L. Health aging and body composition based study and cardiovascular health study have taken 10mIU/lit as cut off value of severity.¹⁴ In this study

mean TSH in 60-70 years was 9.38 ± 3.31 mIU/L and in >70 years 14.37 ± 4.32 mIU/L. But the difference is statistically significant. Studies have shown serum T4 and TSH level minimally elevated with increase in age as adaptive response of the body.^{12,13}

Mean total cholesterol in cat 1 was 205.60 ± 91.50 mg/dl and mean total cholesterol in cat 2 was 235.44 ± 79.01 mg/dl which is similar to the study done by Houston et al, that is 222 mg/dl.¹ There is no statistically significant difference between male, female and different age groups. But while comparing between two categories of TSH value there is significant difference. This finding is consistent with that of Dubey et al.¹⁵ Mean LDL cholesterol value in cat 1 was found to be 122.40 ± 37.92 mg/dl and in cat 2, it was 152.13 ± 39.81 mg/dl. This showed similar in both sex and age group but significant difference between two TSH categories. Hence TC and LDL-C rose significantly with incremental increase in TSH level. Al Sayed et al, demonstrated LDL-C increased in SCH but did not study the correlation between TSH and LDL-C.¹⁶ Mean HDL cholesterol in cat 1 was 41.07 ± 16.98 mg/dl and mean HDL-C in cat 2 was found to be 38.06 ± 13.40 mg/dl. This is found to be similar in both sex and two age groups. With increasing in TSH, HDL-C decreases but not significantly which is concordant to NHANESIII study and study by Houston et al.^{1,9}

Mean serum triglyceride level in cat 1 was 186.71 ± 65.46 mg/dl and mean serum triglyceride in cat 2 was 256.81 ± 95.48 mg/dl. This shows no significant difference in different age groups. Study done by Jaisingh et al., showed mean triglyceride level of 115.4 mg/dl.¹⁷ When comparing between two categories of patients there is significant difference which indicates mean triglyceride level increases with increase in TSH value. This study was consistent with that of Pipliwal et al, who found that mild incremental change in TSH leads to higher level of triglycerides.¹¹ Howell et al, in NHANESIII STUDY Showed triglyceride was high in patients with SCH.⁹

Pathophysiology of dyslipidemia in SCH is not exactly known. However proposed mechanisms for dyslipidemia in SCH are as follows:¹⁸

- Primary accumulation of LDL-C due to reduction in number of cell surface receptors for LDL results in decreased in decreased catabolism of LDL.
- Reduced lipoprotein lipase activity is responsible for development of triglyceridemia in SCH although rate of TG synthesis is normal.
- Diminished secretion of cholesterol into bile has been demonstrated in hypothyroid rats.
- Reduced cholesteryl ester transfer (the net transfer of cholesterol from HDL to LDL and VLDL) in SCH may minimize the increase in serum LDL-Cholesterol concentrations.

Authors have certain limitations in this study as first, authors have estimated serum T3, T4, TSH not FT3, FT4,

Anti TPO Ab, Anti Tg Ab due to lack of facility and non-affordability of the patients. Second, as it is a cross sectional study difficult to say whether thyroid abnormality occurred first or lipid abnormality. Third, inclusion of small sample size and fourth, non-exclusion of smokers which might affect lipid abnormality.

CONCLUSION

Elderly people can present with subtle clinical signs and symptoms like tiredness, physical weakness and fatigue, mild weight gain attributable to SCH. More number of cases found in between 60-70 years with female predominance. There is positive correlation between total cholesterol, LDL cholesterol, serum triglyceride level and TSH value. It is well known that increase in atherogenic lipid profile is a risk factor for cardiovascular diseases, cerebrovascular disease thereby increased mortality. Hence SCH 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. Lipid profile parameters obtained in our study were comparable to similarly designed few Indian studies and few western studies. However, there is an absolute need for larger prospective studies designed to answer the question as to whether SCH is associated with increased risk for coronary heart disease and whether therapy for SCH might reduce cardiovascular morbidity and mortality.

ACKNOWLEDGEMENTS

Authors would like to thank to Dr. Prasanta Purohit for statistical analysis.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of M.K.C.G. Medical College, Berhampur, Odisha, India

REFERENCES

- Hueston WJ, Pearson WS. Subclinical hypothyroidism and the risk of hypercholesterolemia. *Annal Family Med.* 2004;2(4):351-5.
- Karmisholt J, Andersen S, Laurberg P. Variation in thyroid function in subclinical hypothyroidism: importance of clinical follow-up and therapy. *Europ J Endocrinol.* 2011;164(3):317-23.
- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Archiv Inter Med.* 2000;160(4):526-34.
- Hak L, Pols H, Visser T, Drexhage H, Witteman J, Hofman A. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. *Annal Inter Med.* 2000;1.
- Bandyopadhyay SK, Basu AK, Pal SK, Roy P, Chakrabarti S, Pathak HS, et al. A study on dyslipidaemia in subclinical hypothyroidism. *J Ind Med Associat.* 2006;104(11):622-4.
- Lee J, Chung WY. Subclinical Hypothyroidism; Natural History, Long-Term Clinical Effects and Treatment. In *Curr Topics Hypothyroid Focus Development* 2013;13.
- Franklyn JA. The thyroid-too much and too little across the ages. The consequences of subclinical thyroid dysfunction. *Clin Endocrinol.* 2013;78(1):1-8.
- Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. *Clin Endocrinol.* 1977;7(6):481-93.
- Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, et al. Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metabol.* 2002;87(2):489-99.
- Kong WM, Sheikh M, Lumb P, Naoumova RP, Freedman DB, Finer N. A randomized controlled trial of thyroxine treatment in mild subclinical hypothyroidism. In *Program and abstracts: the Endocrine Society's 82nd annual meeting, Toronto 2000.* *Am J Med.* 2002;112(5):348-54.
- Pipliwal PS, Mathur R, Mathur A, Kumar A. A study to compare the clinical profile and Laboratory Abnormalities in the subclinical hypothyroidism with healthy control. *IOSR J.* 2017;16(1):97-100.
- Hennessey JV, Espallat R. Diagnosis and management of subclinical hypothyroidism in elderly adults: A review of the literatures. *J Am Geriatric Soci.* 2015; 63(8):1663-73.
- Waring AC, Arnold AM, Newman AB, Bůžková P, Hirsch C, Cappola AR. Longitudinal changes in thyroid function in the oldest old and survival: the cardiovascular health study all-stars study. *J Clin Endocrinol Metabol.* 2012;97(11):3944-50.
- Waring AC, Rodondi N, Harrison S, Kanaya AM, Simonsick EM, Miljkovic I, et al. Thyroid function and prevalent and incident metabolic syndrome in older adults: The Health, Ageing and Body Composition Study. *Clin Endocrinol.* 2012;76(6):911-8.
- Dubey T, Upadhyay V, Deopujari K. Correlation of Subclinical Hypothyroidism with Dyslipidemia in Perimenopausal Women. *IJCMR.* 2016;3(7):1928-31.
- Al Sayed A, Al Ali N, Bo Abbas Y, Alfadhli E. Subclinical hypothyroidism is associated with early insulin resistance in Kuwaiti women. *Endocr J.* 2006;53(5):653-7.
- Jayasingh IA, Puthuran P. Subclinical hypothyroidism and the risk of hypercholesterolemia. *J Family Med Primary Care.* 2016;5(4):809.

18. Guntaka M, Hanmayyagari B, Rosaline M, Nagesh V. Lipid profile in subclinical hypothyroidism: A biochemical study from tertiary care hospital. *Chrismed J Health Res.* 2014;1(4):266.

Cite this article as: Mohanty N, Parhi S. Study of subclinical hypothyroidism in elderly and its correlation with lipid profile. *Int J Res Med Sci* 2020;8:444-9.