SUBCLINICAL THYROID DISORDERS AND ITS ASSOCIATION WITH DYSLIPIDAEMIA AT A TERTIARY CARE INSTITUTE

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ABSTRACT

BACKGROUND

Subclinical thyroid disorders with altered Thyroid Stimulating Hormone (TSH) level, yet normal circulating levels of free thyroid hormones (FT_4) include subclinical hypothyroidism and subclinical hyperthyroidism. The prevalence of subclinical thyroid disorders is found to be increasing in our country and subclinical hypothyroidism is known to be linked with hypercholesterolemia. Hence, we intend to find the prevalence of subclinical thyroid diseases and its association with lipid profile.

MATERIALS AND METHODS

This study was done on 253 female medical students of PES institute of medical Sciences and research who were willing to participate in the study. Free T_4 (FT₄) and Thyroid Stimulating Hormone (TSH) levels were estimated by Enzyme Linked Immuno-Fluorescent Assay (ELFA). Lipid Profile of the subjects including total cholesterol, serum triglyceride, HDL, LDL, VLDL was estimated using VITROS instrument. Based on the levels of TSH and FT₄ the students were categorized as euthyroid, subclinical hypothyroid and subclinical hyperthyroid.

RESULTS

The prevalence of subclinical hypothyroidism and subclinical hyperthyroidism was found to be 8.3% and 1.58% respectively among the study population. A statistically significant decrease in FT_4 levels as the TSH levels increased was seen. As the TSH value increased, HDL levels significantly decreased, and the LDL levels were found to be increased significantly.

CONCLUSION

Prevalence of subclinical hypothyroidism is found to be high in our study. The students with subclinical hypothyroidism were found to have significantly increased levels of LDL and decreased levels of HDL, which is an important risk factor for atherosclerosis, hypertension and coronary heart disease. Hence early detection of subclinical thyroid disorders would help us prevent the individual from developing the overt disease and its complications.

KEYWORDS

Subclinical Hypothyroidism, Subclinical Hyperthyroidism, Atherosclerosis, Coronary Heart Disease. **HOW TO CITE THIS ARTICLE**: Sindhu R, Vastrad S, Vinay AV, et al. Subclinical thyroid disorders and its association with dyslipidaemia at a tertiary care institute. J. Evid. Based Med. Healthc. 2019; 6(2), 77-81. DOI: 10.18410/jebmh/2019/15

BACKGROUND

Subclinical Hypothyroid and subclinical Hyperthyroid individuals are asymptomatic. These thyroid disorders can be diagnosed only by measuring the levels of TSH and FT₄.

Financial or Other, Competing Interest: None. Submission 18-12-2018, Peer Review 21-12-2018, Acceptance 29-12-2018, Published 08-01-2019. Corresponding Author: Dr. Santosh Vastrad, Assistant Professor, Department of Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka. E-mail: drsantoshvastrad@gmail.com DOI: 10.18410/jebmh/2019/15 Individuals with elevated TSH and normal FT_4 levels are diagnosed as subclinical Hypothyroid and those with decreased TSH and FT_4 within the normal range as subclinical hyperthyroid.^{1,2} Advancing age, female gender and excess intake of dietary iodine are the risk factors for developing subclinical hypothyroidism.³ Several studies have established that subclinical hypothyroidism is the most prevalent thyroid disorder, affecting 3-15% of the adult population.⁴

Thyroid hormones play an important role in regulating lipid metabolism. It has been thought that subclinical hypothyroidism could be associated with altered lipid profile.⁵ Several studies have also reported that subclinical hypothyroidism leads to hyperlipidemia.⁶⁻⁹

Recent studies shows that subclinical hypothyroidism is linked with an increased risk of coronary heart disease (CHD) events and CHD mortality in those with higher TSH levels.¹⁰ As subclinical hypothyroidism has been associated hypercholesterolemia¹¹ and atherosclerosis,08 with screening of subclinical hypothyroid individuals for LDL, VLDL, Total cholesterol, Triglycerides and HDL and treatment has to be advocated to prevent cardiovascular disease.12 The changes in lipid metabolism and cardiovascular physiology are alarming, not only in the context of untreated cases, but also among patients with Lthyroxine substitution therapy.¹³

As the individuals with subclinical thyroid disorders do not present with symptoms, screening the general population, especially the female population for their TSH, FT₄ and lipid profile would greatly reduce the incidence of overt thyroid disorders and the complications associated with it. Hence, we intend to find the prevalence of subclinical thyroid diseases and its association with lipid profile.

Aims and Objectives

- 1. To determine the prevalence of subclinical hypothyroidism and subclinical hyperthyroidism among female medical students.
- 2. To determine the association of subclinical hypothyroidism with Dyslipidaemia.

MATERIALS AND METHODS

This study was done on 253 female medical students within the age group of 18-25 years of PES Institute of medical Sciences and Research, Kuppam who were willing to participate in the study. After obtaining institutional ethical clearance, written informed consent was obtained from the participants. All the individuals participating in the study were instructed to give 5 ml of venous blood after overnight fasting. TSH and FT₄ levels were estimated by Enzyme linked immuno-fluorescent assay (ELFA) using VIDAS FT₄ and TSH kit. The normal ranges of TSH and FT₄ were 0.25-5.5 µIU/ml and 9-24 pmol/L respectively. Asymptomatic individuals with TSH more than 5.5 µIU/ml and FT₄ within the normal range were diagnosed as subclinical hypothyroidism and asymptomatic individuals with TSH less than 0.25 µIU/ml and FT₄ within the normal range were diagnosed as subclinical Hyperthyroid.

Lipid Profile of the subjects including total cholesterol, serum triglyceride, HDL, LDL, VLDL were estimated using VITROS instrument.

Inclusion Criteria

Students willing to participate in the study within the age group 18-25 years.

Exclusion Criteria

Subjects with ischemic heart disease, cerebrovascular and neurological diseases, Diabetes mellitus, chronic renal impairment, known psychological illnesses, previous H/O thyroid disease or previous thyroxine therapy were excluded.

The data was entered into MS Excel 2007 version and the values of the FT₄, TSH, Total cholesterol, serum triglyceride, HDL, LDL, VLDL was expressed as Mean± SD and prevalence of subclinical Hypothyroid and subclinical Hyperthyroid individuals was expressed in percentage. Correlation of TSH with lipid profile was performed by Pearson's correlation and simple regression analysis.

RESULTS

This study was carried out among 253 female medical students. Table 1 shows the Mean \pm SD values of Age, TSH, FT₄ and lipid profile. The prevalence of subclinical hypothyroidism and subclinical hyperthyroidism were found to be 8.3% and 1.58% respectively as shown in table 2. Pearson's correlation (table 3) and simple regression analysis (Figure 1 - Figure 6) were done. A statistically significant decrease in FT₄ levels as the TSH levels increased was seen. As the TSH value increased, HDL levels significantly decreased, and the LDL levels were found to be increased significantly.

Parameters	Mean±SD	
Age (Years)	21.19±1.31	
TSH (µIU/ml)	2.75±2.3	
FT₄ (pmol/L)	15.2±2.5	
Total Cholesterol (mg/dl)	149.64±25.31	
Serum TGL (mg/dl)	79.6±31.19	
HDL (mg/dl)	45.98±8.67	
LDL (mg/dl)	87.33±21.71	
VLDL (mg/dl)	16.04±6.2	
Table 1 Anthronometric and Baseline Biochemical		

Table 1. Anthropometric and Baseline Biochemical Parameters of the Study Population

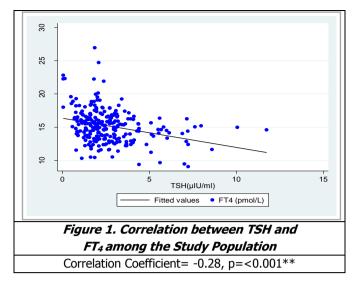
	Total Number	Prevalence among Study Population
Sub-clinical Hyperthyroidism	4	1.58%
Euthyroid	228	90.12%
Sub-Clinical Hypothyroidism	21	8.3%
Total Study Population	253	-

Table 2. Prevalence of Sub-Clinical Hyperthyroidism, Euthyroid and Sub-Clinical Hypothyroidism among the Study Population

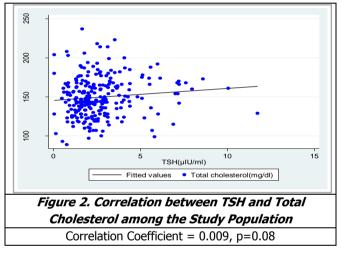
Parameters	r-Value	p-Value	
FT4 (pmol/L)	-0.31	< 0.001**	
Total Cholesterol (mg/dl)	0.10	0.08	
Serum TGL (mg/dl)	0.08	0.19	
HDL (mg/dl)	-0.14	0.02*	
LDL (mg/dl)	0.14	0.02*	
VLDL (mg/dl)	0.06	0.28	
Table 3. Pearson's Correlation between TSH and			
Various Parameters among the Study Population			

*, ** P value <0.05 is Statistically Significant.

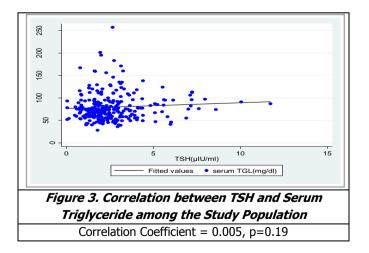
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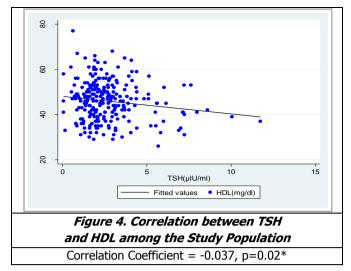
As the TSH value increases the FT_4 levels decreases and it is found to be statistically significant among the study population.



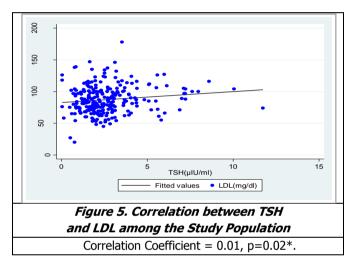
As the TSH value increases the Total Cholesterol levels increases among the study population, but not found to be statistically significant.



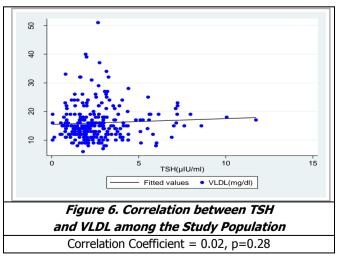
As the TSH value increases the serum Triglyceride levels increases among the study population, but not found to be statistically significant.



As the TSH value increases the HDL levels decreases and it is found to be statistically significant among the study population.



As the TSH value increases the LDL levels increases and it is found to be statistically significant among the study population.



As the TSH value increases the VLDL levels increases among the study population but not found to be statistically significant.

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DISCUSSION

The prevalence of subclinical hypothyroidism and subclinical hyperthyroidism were found to be 8.3% and 1.58% respectively in our study showing that subclinical hypothyroidism is more common than subclinical hyperthyroidism. It is also established that subclinical hypothyroidism is more common than overt hypothyroidism.^{14,15,16} 8.02% of the study population was found to have subclinical hypothyroidism in an epidemiological study in eight cities of India.¹⁷ Another reports 9.4% prevalence of subclinical study hypothyroidism and it was noted that women were affected more than men. It was also found that the prevalence of subclinical hypothyroidism increased with age.¹⁸ The progression of subclinical hypothyroidism to overt hypothyroidism is definite among 33- 55% of cases in 10 vears.19

Thyroid hormones play a very important role in the regulation, absorption, and metabolism of lipid synthesis. Several studies have reported the link between subclinical hypothyroidism and alteration in the lipid profile. Abnormal lipid profile is considered as an independent risk factor for cardiovascular diseases. Hence its association with subclinical hypothyroidism may imply an increase in the risk for cardiovascular diseases like coronary heart disease. It has been established that total cholesterol, LDL levels will be higher in subclinical Hypothyroid individuals.³ In our study, a linear increase in LDL levels and a linear decrease in HDL levels with increasing TSH was seen which is similar to other studies.^{20,21} Rise of serum LDL levels is mainly due to impaired clearance of LDL, probably reflecting decreased LDL receptor expression.²²

Subclinical hypothyroidism has been associated with increased systemic vascular resistance, arterial stiffness, altered endothelial function, increased atherosclerosis and altered coagulability which in turn may accelerate development of coronary heart disease.¹⁰ Therefore screening the young adult females for TSH, FT₄ and lipid profile would greatly reduce the burden of overt hypothyroidism and the complications associated with it like atherosclerosis, hypertension, coronary heart disease.

Further study can be undertaken to know the relationship between dietary habits like excessive intake of iodized salt and its relationship to development of subclinical Hypothyroidism.

CONCLUSION

Subclinical hypothyroidism is found to be more common than overt hypothyroidism or subclinical hyperthyroidism. The individuals with subclinical hypothyroidism were found to have significantly increased levels of LDL and significantly decreased levels of HDL. Subclinical hypothyroidism may be considered as potentially modifiable risk factor for cardiovascular diseases. Hence its early detection would prevent the individual from developing the overt disease and its complications.

REFERENCES

- [1] Fatourechi V. subclinical hypothyroidism: an update for primary care Physicians. Mayo Clin Proc 2009;84(1):65-71.
- [2] Hoogendoorn EH, den Heijer M, van Dijk AP, et al. subclinical hyperthyroidism: to treat or not to treat? Postgrad Med J 2004;80(945):394-398.
- [3] Tumbanatham A, Jayasingh K, Varun V. Comparative study of lipid profile between clinical and subclinical hypothyroidism. Int J Adv Med 2018;5(4):978-982.
- [4] Ayala AR, Danese MD, Ladenson PW. When to treat mild hypothyroidism. Endocrinol Metab Clin North Am 2000;29(2):399-415.
- [5] Alireza RH, Mahdis S, Tavakali MH. Correlation between subclinical hypothyroidism and dyslipidemia. Iran J Pathol 2017;12(2):106-111.
- [6] Kung AW, Janus ED. Thyroid dysfunction in ambulatory elderly Chinese subjects in an area of borderline iodine intake. Thyroid 1996;6(2):111-114.
- [7] Staub JJ, Althaus BU, Engler H, et al. Spectrum of subclinical and overt hypothyroidism: effect on thyrotropin, prolactin and thyroid reserve and metabolic impact on peripheral target tissues. Am J Med 1992;92(6):631-642.
- [8] Hak AE, Pols HA, Visser TJ, et al. subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam Study. Ann Intern Med 2000;132(4):270-278.
- [9] Althaus BU, Staub JJ, Ryff-De Leche A, et al. LDL/HDL- changes in subclinical hypothyroidism: possible risk factors for coronary heart disease. Clin Endocrinol (Oxf) 1988;28(2):157-163.
- [10] Rodondi N, den Elzen WP, Bauer DC, et al. subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA 2010;304(12):1365-1374.
- [11] Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev 2008;29(1):76-131.
- [12] Gharib H, Tuttle RM, Baskin HJ, et al. subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. J Clin Endocrinol Metab 2005;90(1):581-585.
- [13] Efstathiadou Z, Bitsis S, Milionis HJ, et al. Lipid profile in subclinical hypothyroidism: is L-thyroxine substitution beneficial? Eur J Endocrinol 2001;145(6):705-710.
- [14] Cooper DS. subclinical thyroid disease: a clinician's perspective. Ann Intern Med 1998;129(2):135-138.
- [15] Brabant G, Beck-Peccoz P, Jarzab B, et al. Is there a need to redefine the upper normal limit of TSH? Eur J Endocrinol 2006;154(5):633-637.
- [16] Gibbons V, Lillis S, Conaglen JV, et al. Do general practitioners use thyroid stimulating hormone assay for opportunistic screening? N Z Med J 2009;122(1301):25-30.

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- [17] Unnikrishnan AG, Kalra S, Sahay RK, et al. Prevalence of hypothyroidism in adults: an epidemiological study in eight cities of India. Indian J Endocrinol Metab 2013;17(4):647-652.
- [18] Usha Menon V, Sundaram KR, Unnikrishnan AG, et al. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc 2009;107(2):72-77.
- [19] Raza SA, Mahmood N. subclinical hypothyroidism: controversies to consensus. Indian J Endocrinol Metab 2013;17(Suppl 3):S636-S642.
- [20] Ozcan O, Cakir E, Yaman H, et al. The effects of thyroxine replacement on the levels of serum

asymmetric dimethylarginine (ADMA) and other biochemical cardiovascular risk markers in patients with subclinical hypothyroidism. Clin Endocrinol (Oxf) 2005;63(2):203-206.

- [21] Kim SK, Kim SH, Park KS, et al. Regression of the increased common carotid artery-intima media thickness in subclinical hypothyroidism after thyroid hormone replacement. Endocr J 2009;56(6):753-758.
- [22] Duntas LH. Thyroid disease and lipids. Thyroid 2002;12(4):287-293.