Correlation of Subclinical Hypothyroidism with Dyslipidemia in Perimenopausal Women

T.N. Dubey[1], Vibhor Upadhyay[2], K. Deopujari[3]

ABSTRACT

Introduction: Although overt hypothyroidism with its accompanying dyslipidemia is widely recognized as a risk factor for atherosclerosis and cardiovascular disease but now subclinical hypothyroidism emerged as an independent risk factor for aortic atherosclerosis and myocardial infarction in women. Subclinical hypothyroidism is characterized by dyslipidemia most commonly in elderly females but perimenopausal females are also at higher risk. There are limited studies on subclinical hypothyroidism in India on perimenopausal women which is done in our study. Objective: The objective of the study was to find the correlation of dylipidemia with subclinical hypothyroidism in perimenopausal women in central India.

Material and Methods: The study was conducted at department of medicine in Gandhi Medical College and Hamidia Hospital, Bhopal for one year from January 2015 to December 2015. It was an observational cross-sectional study. Females of 35-45 years of age group with raised TSH and normal T3 and T4 values were included in the study. 66 females patients of SCH were included in this study and subdivided in two groups according to their TSH values as group1 (5.5-10) and group2 (>10) and their fasting lipid profile and thyroid samples were measured.

Results: Significant results were observed in different parameters among both the groups of SCH. Total cholesterol, Triglycerides, LDL-cholesterol, TC/HDL ratio and LDL/HDL ratio was highly significant (<0.01) in both groups but HDL-cholesterol and TSH levels were not significant (>0.05) in the two groups of SCH. Group having TSH (>10μIU/ml) have the higher risk of developing atherosclerosis as compared to females with TSH (5.5-10μIU/ml). Total cholesterol, Triglycerides, LDL, TC/HDL ratio and LDL/HDL ratio were positively correlated with TSH values in both the groups of perimenopausal females whereas the HDL cholesterol had no correlation with TSH values among SCH perimenopausal females.

Conclusion: This study showed that perimenopausal women with subclinical hypothyroidism were characterized by dyslipidemia in the form of increased TC, TG and LDL. SCH groups having TSH (>10μIU/ml) have the higher risk of developing atherosclerosis as compared to perimenopausal females with TSH (5.5-10μIU/ml). TC/HDL ratio and LDL/HDL ratio were also higher in both SCH group suggesting the future development of cardiovascular disease in these females.

Keywords: Dyslipidemia, Perimenopausal, Subclinical hypothyroidism, Thyroid stimulating hormone

INTRODUCTION

By definition, subclinical hypothyroidism refers to biochemical evidence of thyroid hormone deficiency in patients who have few or no apparent clinical features of hypothyroidism.[1] This is a relatively common condition with a prevalence ranging from 4 to 15% in the general population.[2,3] Although overt hypothyroidism with its accompanying hypercholesterolemia, is widely recognized as a risk factor for atherosclerosis and cardiovascular disease.[4] In recent population based surveys subclinical hypothyroidism emerged as an independent risk factor for aortic atherosclerosis and myocardial infarction.[5] Subclinical hypothyroidism frequently occurs in females comparative to males.[6] Many of the perimenopausal symptoms e.g. weight gain, mood swings, insomnia, tiredness, anxiety etc. are quite similar to hypothyroidism, so evaluation of thyroid profile in these patient might show the presence of subclinical hypothyroidism which may progress to overt hypothyroidism and can be masked by perimenopausal symptoms.[7]

Thyroid hormone have a great impact on lipid metabolism as its needed for the catabolism and synthesis of lipids and its deficiency may create alteration in lipid metabolism mostly degradation rather than synthesis. Studies in the past have revealed that cardiovascular risk might be possible in subclinical hypothyroidism but the effect of TSH range is not clearly stated.[8,9] So the lipid metabolic changes affected by the severity of disease in terms of elevation in the TSH range are topic of debate. There are limited studies on subclinical hypothyroidism in India. The relationship of lipid profile abnormalities to subclinical hypothyroidism is not certain. In central Indian population there are no studies that have answered these questions. So, the purpose of this study is to assessment of various lipid parameters in perimenopausal women with Subclinical hypothyroidism with elevation in the range of TSH.

MATERIAL AND METHODS

The study was conducted in Gandhi Medical College and Hamidia Hospital, Bhopal. Newly diagnosed 66 perimenopausal SCH women were enrolled for the study from the medical and endocrine OPD of HH, which were divided in two groups on the basis of TSH range: SCH-I (5.5-10μIU/ml) and SCH-II (>10μIU/ml). The age group criteria for study population were 35-45 years of female. Those patients were excluded from the study who were having thyroid disorder, diabetes, hypertension, menopause or any cardiovascular risk and patients on thyroxine, hypolipidemic drugs or drugs causing dyslipidemia were also excluded. Ethical clearance from the institutional ethical board and informed consent from patients were obtained before the start of the study.

Thyroid profile and lipid profile were estimated in all the

[1]Professor and Head of Department, [2]Post Graduate Student, [3]Associate Professor, Department of Medicine, GMC, Bhopal, India

Corresponding author: Room No.-12, E-block, PG Hostel, Gandhi Medical College, Bhopal-462001 (M.P.), India

participants of study group by taking fasting samples. Thyroid stimulating hormone (TSH), T3 and T4 were measured by using enzyme linked immunosorbant assay (ELISA) technique. The patients with TSH range (>5.5µIU/ml), T3 and T4 within reference range were said to having SCH.

Total cholesterol (<200 mg/dl), Triglycerides (<150 mg/dl) and High density lipoprotein cholesterol (40-60 mg/dl) were measured by using CHOD/POD method, GPO-PAP method, and CHODPOD/ Phosphotungustate method respectively. LDL cholesterol (<130 mg/dl) was estimated by Friedewald formula. Total cholesterol/HDL-C and LDL-C/HDL-C ratio were also calculated by dividing TC and LDL-C with HDL-C respectively.[10]

STATISTICAL ANALYSIS

A SPSS (statistical package of social sciences) version 20.0 of IBM for windows was used for statistical analysis. All the variables were expressed in Mean ± SD. The variables of divided groups of subclinical hypothyroidism were analyzed by using one way ANOVA. Pearson correlation coefficient was performed between TSH and other parameters (TG, TC, TC/HDL-C ratio and LDL/HDL ratio). A p value <0.05 was considered statistically significant.

RESULTS

We found that that among 66 patients of subclinical hypothyroid females 28 were in group 1 (TSH 5.5-10) and 38 were in group 2 (TSH>10). The mean age of the patients in group 1 SCH was 39.72±2.72 yrs and group 2 SCH was 43.42±3.12 yrs. The mean age in SCH-2 was higher showing that as age increases thyroid failure also increases. Mean value of TSH in group 1 SCH females was 8.91±0.86 and in group 2 SCH was 14.31±1.24 µIU/ml which was statistically significant (p value<.001). When we compared fasting lipid profiles in these perimenopausal females of SCH, among it total cholesterol mean values were 199.4±16.11 mg/dl and 220.43±23.20 mg/dl in their respective groups which shows a significant relationship (p value<.005). When we correlated the total cholesterol values with TSH values, it shows a positive correlation as paerson correlation coefficient (r) was 0.31.

Similarly the triglycerides levels were compared among both the groups in which SCH group 1 TG were 122±27.63 mg/dl and in SCH group 2, TG were 139±25.56 mg/dl which was statistically significant as p value was less than .05. The value of TG were also correlated with the TSH values and a significant positive correlation was seen among them as pearson correlation coefficient (r) was 0.28. Coming to another variable of lipid profile, LDL, the mean values in group 1 SCH were 132±15.46 mg/dl and in SCH group 2 were 147.24±21.24 mg/dl which was statistically significant (p value=0.003). LDL values were also positively correlated with the TSH concentration as pearson correlation coefficient(r) was 0.31. There was no variations were found among the groups of SCH in HDL-cholesterol and the difference was not significant.

Now coming to ratios which are better marker of cardiovascular morbidity, the risk ratio (TC/HDL) ratio in group 1 SCH was 4.61±0.39 and in group 2 SCH, it was 5.21±0.49 and it has significant association (pvalue=0.001). It was found to have the positive correlation with the TSH concentration as pearson

correlation coefficient was found to be 0.40. LDL/HDL ratio was also evaluated in our study which is a better marker of cardiovascular morbidity, in group 1 SCH it was 3.23±0.47 and in group 2 SCH, the values were 3.51±0.49 and it was also found to be statisytically significant (p value=0.004). It was also having a positive significant correlation with the TSH values (r=0.34).

Thus all variables of lipid profiles were significantly different in both groups of subclinical hypothyroidism except HDL-Cholesterol. The mean value of total cholesterol was below the reference range in SCH-I and significant higher in group II of SCH. Triglycerides and Total cholesterol levels were also found to be positively correlated with TSH concentration and as TSH concentarion increases, their level were also found to be increasing but their lvels were below the refrence range in both groups. LDL-C level was significantly higher in each group above the reference range. TC/HDL and LDL/HDL ratios were significantly different in each group of SCH and consistently increasing along with the range of TSH. (Table-1 and 2)

DISCUSSION

Hypothyroidism is characterised by a decrease in both synthesis and catabolism of lipoprotients. In most patients with myxedema, the relative greater decreas in catabolism and the resulting preponderance of synthesis results in high cholesterol concentrations. The nature and degree of dyslipidemia in overt hypothyroidism has been demonstrated in many studies and there is no doubt about the beneficial effects of thyroid substitution on serum lipids and on the risk for CAD.[11,12] Although the relationship between SCH and an atherogenic lipoprotein profile is still under debate[6,13,14], a meta analysis of 13 intervention studies showed that levothyroxine (l-T4) therapy led to a significant reduction in both serum total and low-density lipoprotein (LDL) cholesterol levels.[15]

Parameters	Subclinical Hypothyroidism [#]		P Value
	SCH- 1*	SCH-2*	
Age (Yrs)	39.72±2.72	43.42±3.12	0.394
TSH (µ *lU/Ml*)	8.91±0.86	14.31±1.24	0.001
FT3 (ng/dl)	1.54±1.15	1.13±0.34	0.450
FT4 (ng/dl)	1.17±0.19	0.9±0.11	0.549
TC (mg/dl)	199.4±16.11	220±23.20	0.001
TG (mg/dl)	122±27.63	139±25.86	0.028
LDL (mg/dl)	132±15.46	147.24±21.27	0.003
HDL (mg/dl)	42.01±2.32	39.21±2.11	0.564
TC/HDL ration	4.61±0.39	5.21±0.49	0.001
LDL/HDL ratio	3.23±0.47	3.51±0.49	0.004

by ANOVA; *All the variables in Mean±SD; A p value < 0.05 was considered statistically significant

Table-1: Baseline characteristics among the various groups of SCH women

Parameters	r value
TSH - TG	0.29*
TSH-TC	0.31 *
TSH-TC/HDL ratio	0.40 **
TSH- LDL/HDL ratio	0.34 **

$By pearson correlation coefficien; *p value Significant at 0.05 level; **p value Significant at 0.01 level.

Table-2: Correlation between TSH and other variables [$]

Subclinical hypothyroidism has a great influence on derangement of lipid profile in perimenopausal women. The colarado thyroid disease prevalence study which is one of the largest study conducted on thyroid dysfunction also showed that there is derangement of lipid profile with increasing TSH values.[2] Similarly the Rotterdam study also concluded that SCH is independently associated with atherosclerosis and cardiovascular morbidity in post menopausal women which can be attributed to dyslipidemia.[16] In our study we also found that there is statistically significant increase in the Total cholesterol, triglycerides and LDL levels in SCH females. Celik C et al observed to support this study that SCH women are characterised by dyslipidemia.[15] Luboshitzky R et al also supported the findings of our study and they have also concluded that dyslipidemia and hypertension was associated with SCH in middle aged women.[17] Similar findings were also noted in the EPIC-Norfolk prospective study which found significantly increased concentrations of serum total cholesterol (TC), LDL cholesterol (LDLc) and triglyceride in SCH women only.[18]

In Indian setup, Senthilkumaran S et al also found that SCH is more common in female compared to overt hypothyroidism.[19] We have also found that Total cholesterol, triglycerides and LDL cholesterol have positive correlation with severity of disease as the elevation of TSH range. Karthik N et al observed a significant dyslipidemic changes in SCH women compared to control group.[20] Similarly when we compared the LDL/TC and HDL/TC ratios which are better indicator of cardiovascular morbidity, we found that these were positively correlated with TSH concentration. Gaurav et al also conducted a similar study in Punjab on perimenopausal middle aged women and supported or finding in these perimenopausal females.[21]

There is some controversy regarding the presence or the severity of SCH induced dyslipidemia as some studies have found no correlation between TSH concentration and dyslipidemia. Legrys et al did not find any evidence that SCH was associated with increased risk of myocardial infarction in postmenopausal women.[22] Data from NHANES III revealed increased levels of TC in SCH patients vs controls, however when adjusted for age,race,sex and use of lipid lowering drugs, no difference was observed between SCH and controls regarding lipid profile.[3]

We have found that SCH is associated with an atheogenic lipid and lipoprotein profile, characterised by an increase in concentration of total cholesterol, LDL and triglycerides but not with deranged HDL levels. However there are studies which have also found deranged levels of HDL in SCH patients.[23] It was observed in this study that SCH women with TSH >10μIU/ml have the higher dyslipidemic changes in comparison to those having TSH<10μIU/ml. Marwaha et al supported this study by observing that atherogenic lipid abnormalities was found in adult subjects of SCH with TSH>10mIU/L not in subjects with TSH<10mIU/L.[24]

CONCLUSION

In this study we found that the women in perimenopausal age group with subclinical hypothyroidism are more prone for atherosclerosis due to the fact that they have deranged lipid profiles. Among dyslipidemia, increased level of Total cholesterol, triglycerides and LDL-cholesterol might suggest a future development of cardiovascular diseases. There was also positive correlation of thyroid stimulating hormone with total cholesterol and triglyrides and as the value of TSH increases their concentration also increases. Similarly the LDL/TC and HDL/TC ratio which are better predictor of cardiovascular morbidity also found to be significantly associated with SCH and positive correlation with TSH values were also seen in our study and points towards the higher risk for atherogenicity. This study specify that SCH women with TSH>10μIU/ml have higher risk of developing cardiovascular risk in comparison to women having TSH<10μIU/ml.

REFERENCES

1. Cappola AR, Ladenson et al PW. Hypothyroidism and atherosclerosis. J ClinEndocrinol Metab. 2003;88:2438–2444.
2. Canaris GJ, Manowitz NR et al EC. The Colorado Thyroid Disease Prevalence Study. Arch Intern Med. 2000;160: 526-534.
3. Hollowell JG, Staehling NW et al. Serum TSH, T(4), and thyroid antibodies in the UnitedStates population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). J ClinEndocrinol Metab. 2002;87:489-499.
4. Bastenie PA, Vanhaelst L et al. Coronary artery disease in hypothyroidism: observation in preclinical myxoedema. Lancet. 1967;2:1221.
5. Neves C, Alves M et al. Thyroid diseases, dyslipidemia and cardiovascular pathology. Rev Port Cardiol. 2008;27: 1211-1236.
6. Papi G, Uberti ED, Betterle C, Carani C, Pearce EN, Braverman LE, Roti E: Subclinical hypothyroidism. Curr Opin Endocrinol Diabetes Obes. 2007;14:197–208.
7. Joshi SA, Bhalerao A, Somalwar S, Jain S, Vaidya M, Sherawat N. Journal of South Asian federation of Obstetrics and Gynaecology. 2011;3:14-16.
8. Fowler PBS, Swale J et al. Hypercholesterolaemia in borderline hypothyroidism: stage of premyxoedema. Lancet. 1970;2:488–491.
9. Hansson GK; Inflammation, atherosclerosis, and coronary artery disease. N. Engl. J. Med. 2005;352:1685–1695.
10. Burtis CA, Ashwood ER, Bruns DE. Teitz fundamentals of clinical chemistry. Saunders An imprint of Elsevier Inc., Pennsylvania, 2010, pp. 422-424.
11. Gillett M, Subclinical Hypothyroidism: Subclinical Thyroid Disease: Scientific Review and Guidelines for Diagnosis and Management, The Clin Biochem Rev. 2004; 25:191-194.
12. Shekhar R, Chowdary NVS, Das MC, Vidya D, Prabodh, prevalence of subclinical hypothyroidism in costal region of Andhra Pradesh, S. Biomed Res. 2011;22:471-474.
13. Gan SD, Patel KR, Enzyme immunoassay and enzyme-linked immunosorbent assay.J Invest Dermatol. 2013;133: e12.
14. Celik C, Abali R, Tasdemir N, Guzel S, Yuksel A, Aksu E et al. Is subclinical hypothyroidism contributing dyslipidemia and insulin resistance in women with polycystic ovary syndrome, Gynecol Endocrinol. 2012;28:615-8.
15. Tanis BC, Westendorp GJ, Smelt HM. Effect of thyroid substitution on hypercholesterolaemia in patients with subclinical hypothyroidism: A reanalysis of intervention studies. Clin Endocrinol (Oxf). 1996;44:643–9.
16. Hak AE, Pols HAP et al, JCM. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam

study. Ann InternMed. 2000;132:270–278.

17. Luboshitzky R, Aviv A, Herer P, Lavie L, Risk factors for cardiovascular disease in women with subclinical hypothyroidism, Thyroid. 2002;12:421-5.

18. Boekholdt SM, Titan SM, Wiersinga WM, et al: Initial thyroid status and cardiovascular risk factors: the EPIC-Norfolk prospective population study. Clin Endocrinol (Oxf). 2010;72:404–410.

19. Senthilkumaran S, Sathyaprakash V, Sundhararajan A. Study on Prevalence and Distribution of Subclinical Hypothyroidism in Rural Women, Sch J App Med Sci. 2015;3:287-290.

20. Karthick N, Dillara K, Poornima KN, Subhasini AS. Dyslipidaemic Changes in Women with Subclinical Hypothyroidism, J Clin Diagn Res. 2013;7:2122-2125.

21. Gaurav gupta, rajan gupta et al, lipidemic changes in perimenopausal middle aged women with subclinical hypothyroidism, RJPBCS. 2015:6:1909-12.

22. LeGrys VA, Funk MJ, Lorenz CE, et al. Subclinical hypothyroidism and risk for incident myocardial infarction among postmenopausal women, J Clin Endocrinol Metab. 2013;98:2308-2317.

23. Erem. C. Blood coagulation, fibrinolytic activity and lipid profile in subclinical thyroid disease: subclinical hyperthyroidism increase plasma factor X activity. Clin. Endocrinol. 2006;64:323-329.

24. Marwaha RK, Tandon N, Garg MK, Kanwar R, Sastry A, Narang A et al. Dyslipidemia in subclinical hypothyroidism in an Indian population, Clin Biochem. 2011;44:1214-1217.

International Journal of Contemporary Medical Research
ISSN (Online): 2393-915X; (Print): 2454-7379 | ICV: 50.43 | Volume 3 | Issue 7 | July 2016

1931