

Assessment of Lipid Profile in Sub-Clinical Hypothyroidism Subjects in Rural and Urban Population of Northern India**Sunil Kumar¹, Singh Satyendra Prasad², Yadav Gajraj Singh^{*3}, Gupta R. C.⁴**¹Assistant Professor, Department of Biochemistry, Late Shri Lakhiram Agrawal Memorial Government Medical College, Raigarh (C.G)²Assistant Professor, Department of Community Medicine, Late Shri Lakhiram Agrawal Memorial Government Medical College, Raigarh (C.G)³Assistant Professor, Department of Biochemistry, Raipur Institute of medical science (RIMS), Raipur, (C.G)⁴Ex-professor and Head, Department of Biochemistry, National Institute of medical science and Research (NIIMS University), Jaipur, Rajasthan

Received: 20-05-2023 / Revised: 11-06-2023 / Accepted: 05-07-2023

Corresponding author: Dr. Gajraj Singh Yadav

Conflict of interest: Nil

Abstract:**Introduction:** Sub-clinical hypothyroidism (SCH) can be defined as normal Free Thyroxine (FT₄) and Free Triiodothyronine (FT₃) concentrations and high serum TSH concentration associated with few or no signs and symptoms of hypothyroidism. The level of lipid profile and lipoprotein is higher in sub-clinical hypothyroidism which was associated with cardiovascular disease in addition also increase the incidence of coronary risk factor, so newly diagnosed SCH subjects must monitor their lipid profile to prevent cardiovascular manifestation.**Material and Methods:** This paper is a cross-sectional study of 800 subjects (including rural and urban areas) of Amber Tehsil in Jaipur District. The blood samples (lipid profile and lipoprotein) were analyzed at the National Institute of Medical Sciences and Research, Jaipur.**Result:** Using a T-test it was found that total Cholesterol (TC) and Low-Density Lipoprotein Cholesterol (LDL-C) of rural and urban populations were significantly higher in the SCH group as compared to the Euthyroidism (EuT) group (p<0.05).**Conclusion:** Serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were significantly higher in SCH subjects as compared to subjects with normal thyroid function in urban as well as rural populations. The difference in triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and very low-density lipoprotein cholesterol (VLDL-C) in SCH subjects and subjects with normal thyroid function was not significant.**Keywords:** Sub-clinical hypothyroidism (SCH), Mortality, lipid profile, and lipoprotein, Euthyroidism.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

The diagnosis of sub-clinical hypothyroidism is confirmed by serum TSH is high and FT₃, and FT₄ within the normal range [1]. On the basis of TSH level SCH is categorized into two groups first moderately raised TSH (4.0-10.0 mIU/L) and second significantly elevated TSH (above 10.0 mIU/L)[2]. Moderate SCH level is found in the majority (90%) of the subjects. Sub-clinical hypothyroidism has been reported to have a prevalence of about 4-10% in the general population and 7-26% in the geriatric population[3]. The prevalence of sub-clinical hypothyroidism is about 4 to 8.5% in females aged more than 60 yrs[4]. The cardiovascular system is one of the main body systems affected by changes in the thyroid hormone level, which both directly and indirectly affect its function. It is well known

that thyroid hormones regulate many biological and metabolic activities including lipoprotein metabolism directly or indirectly which affects many cardiovascular risk factors and fallout in neuro-hormonal activation, including sympathetic nervous system activation[5]. Screening for sub-clinical thyroid disease, although not recommended routinely, is strongly advocated in the high-risk group as it has a risk of progression to overt thyroid disease from sub-clinical hypothyroidism. Sub-clinical hypothyroidism has a particular effect on the heart and may be associated with cardiac dysfunction and atrial fibrillation[6]. Sub-clinical hypothyroidism affects the heart by disturbing both the systolic and diastolic functions of the heart[7]. The most frequent cause of hypothyroidism is autoimmune thyroid disease (AITD) manifested by

elevated thyroid antibodies, namely thyroid peroxidase antibodies. Thus, an increase in thyroid antibodies may potentially influence the coronary risk. About the association between sub-clinical thyroid dysfunction and CAD new data have emerged during the last decade. The influence of sub-clinical thyroid dysfunction on CAD progression is significant, but the findings are still controversial to make a definitive decision [8]. To resolve this controversy, subjects found to have sub-clinical hypothyroidism in the present study will also be screened for major coronary risk factors like dyslipidemia, hypertension, obesity, smoking, diabetes, hyperhomocysteinemia, etc.

Material and Methods: This cross-sectional study was conducted on 400 subjects from rural areas (area under Gram Panchayat) and 400 subjects from urban areas (area under Municipal Corporation or Municipal Committee) of Amber Tehsil in Jaipur District. The blood samples were analyzed at the National Institute of Medical Sciences and Research, Jaipur.

Inclusion Criteria: Adult subjects from urban and rural populations, Subjects were included from every fiftieth house in the study area; Subjects were enrolled after taking written consent from them on the prescribed format.

Exclusion Criteria: Pregnant women, Persons who refused to fill out consent forms, and Those who were not willing to participate in the study.

Subject Selection: Simple randomization method was used for the selection of subjects. Every fiftieth house was selected for this study in a defined area. If the total number of houses in any village were less than 50, then randomly any one house was selected. The subjects were selected for the study after proper examination and personal clinical

history with the help of a proforma at the time of examination.

Blood Sample Collection: 5ml venous blood samples after 12 hours of fasting were collected in plain vials from the antecubital vein under aseptic conditions. The blood was centrifuged at 4000 rpm for 5 minutes and the serum was removed and stored at - 20°C. The serum was subjected to estimation of the following parameters on a fully automatic analyzer (Human fully automatic analyzer) using standard kits and enzymatic methods.

Estimation of lipid profile and lipoprotein: Estimation Total Cholesterol[9], Estimation of High-Density Lipoprotein Cholesterol[9], PEG-CHOD-PAP, END point Assay with liquid clearing factor (LCF), Determination of Triglycerides [10], Determination of LDL-C and VLDL-C is done by Friedewald's equation[11].

Results

This study were conducted in 400 urban and 400 rural population in the Amber Tehsil of Jaipur District (Rajasthan) and the main objective of this study was to estimate the lipid profile and lipoprotein in SCH subject in both populations. Serum lipids and lipoproteins in the Euthyroid group and Sub-clinical hypothyroidism group in urban areas were compared (Table-1).

Using T-test the Total Cholesterol (TC) and Low-Density Lipoprotein Cholesterol (LDL-C) were found to be significantly higher in SCH group as compared to EuT group ($p < 0.05$) but the difference in High-Density Lipoprotein Cholesterol (HDL-C), Triglycerides (TG) and Very Low-Density Lipoprotein Cholesterol (VLDL-C) was not statistically significant ($p > 0.05$).

Table 1: Comparison of serum lipids and lipoproteins in Euthyroid (EuT) and Subclinical hypothyroidism (SCH) groups in an urban area

Lipid	Thyroid Status	N	Mean	SD	Mean difference	P value
TC	EuT	342	165.96	24.98	20.04	<0.0001 (HS)
	SCH	39	186	16.82		
HDL-C	EuT	342	48.63	4.69	0.53	0.506 (NS)
	SCH	39	48.10	5.07		
TG	EuT	342	156.02	24.79	7.72	0.056 (NS)
	SCH	39	163.74	19.20		
LDL-C	EuT	342	86.13	24.90	19.02	<0.0001 (HS)
	SCH	39	105.15	18.44		
VLDL-C	EuT	342	31.20	4.95	1.54	0.0604 (NS)
	SCH	39	32.74	3.79		

Serum lipids and lipoproteins in the Euthyroid group and the Subclinical hypothyroidism group in rural areas were compared (Table-2). Using a T-test it was found that in urban subjects, Total Cholesterol (TC) and Low-Density Lipoprotein Cholesterol (LDL-C) were significantly higher in the SCH group as compared to the EuT group ($p < 0.05$) while the difference in High-Density Lipoprotein Cholesterol (HDL-C), Triglycerides (TG) and Very Low-Density Lipoprotein Cholesterol (VLDL-C) was not statistically significant ($p > 0.05$).

Table 2: Comparison of serum lipids and lipoproteins in Euthyroid (EuT) and Subclinical hypothyroidism (SCH) groups in a rural area

Lipid	Thyroid Status	N	Mean	SD	Mean difference	P value
TC	EuT	345	171.20	27.29	17.91	<0.0001 (HS)
	SCH	43	189.12	29.90		
HDL-C	EuT	345	51.21	7.00	0.66	0.66 (NS)
	SCH	43	50.55	5.37		
TG	EuT	345	129.69	30.11	3.16	0.50 (NS)
	SCH	43	126.53	25.28		
LDL-C	EuT	345	94.04	28.15	19.21	<0.0001 (HS)
	SCH	43	113.25	32.80		
VLDL-C	EuT	345	25.94	6.03	0.64	0.50 (NS)
	SCH	43	25.30	5.05		

A comparison was made between serum lipids and lipoproteins of all the urban subjects (N=400) and all the rural subjects (N=400). Using a T-test it was found that. Total cholesterol, HDL-C, and LDL-C were found to be significantly higher in rural subjects as compared to urban subjects. TG and VLDL-C were found to be significantly higher in urban subjects as compared to rural subjects (Table-3).

Table 3: Comparison of serum lipids and lipoproteins in all rural and all urban subjects (all the values are Mean \pm SD)

Lipid	Urban Popu ⁿ (N=400)	Rural Popu ⁿ (N=400)	p-value
Triglycerides (TG)	156.78 \pm 24.39	129.35 \pm 29.65	<0.0001(HS)
Total Cholesterol (TC)	167.92 \pm 25.03	173.13 \pm 28.1	<0.01(S)
LDL-C	87.98 \pm 24.99	96.11 \pm 29.3	<0.0001(HS)
VLDL-C	31.36 \pm 4.88	25.87 \pm 5.93	<0.0001(HS)
HDL-C	48.59 \pm 4.73	51.15 \pm 6.85	<0.0001(HS)

Discussion

Alteration in thyroid hormones affects the metabolism of lipids [12]. Moreover, Thyroid disorders can affect cardiovascular health. SCH may also increase the risk of several abnormalities like elevated serum levels of LDL cholesterol and triglycerides and may increase the chances of coronary artery disease and associated mortality [13]. However, the evidence about the relationship between sub-clinical hypothyroidism and coronary artery disease is not unequivocal. Therefore, a primary objective of this study was to investigate and compare coronary risk factors in subjects having SCH and normal subjects. For assessment of the risk of coronary artery disease, serum lipids, and lipoproteins were investigated. Since sub-clinical hypothyroidism may affect cardiovascular health.

Moreover, the effect of sub-clinical hypothyroidism on coronary risk factors was also investigated that subclinical hypothyroidism is associated with higher CVD risk [14]. When serum lipids and lipoproteins in normal (Euthyroid) subjects and subjects with sub-clinical hypothyroidism in urban areas were compared, Total Cholesterol (TC) and Low-Density Lipoprotein Cholesterol (LDL-C) were found to be significantly higher in SCH group as compared to normal group ($p < 0.05$) but the difference in High-Density Lipoprotein Cholesterol

(HDL-C), Triglycerides (TG) and Very Low-Density Lipoprotein Cholesterol (VLDL-C) was not statistically significant ($p > 0.05$). Similar results were found in the rural population. Thus, subjects with sub-clinical hypothyroidism were found to have an adverse lipid profile as compared to euthyroid subjects. This is in conformity with an earlier study in which Total Cholesterol and LDL-Cholesterol levels in serum were found to be significantly higher in subjects with sub-clinical hypothyroidism than in euthyroid subjects [15]. Moreover, Rahman et al concluded their related findings between in rural and urban population in India [16].

Conclusion

Serum total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were significantly higher in SCH subjects as compared to subjects with normal thyroid function in urban as well as rural populations.

The difference in triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and very low-density lipoprotein cholesterol (VLDL-C) in SCH subjects and subjects with normal thyroid function was not significant.

Ethical approval: Yes, the study was approved by institutional ethical committee of NIMS University, Jaipur, Rajasthan (India).

References

1. Cooper DS. Sub-clinical hypothyroidism. *N Engl J Med.* 2001; 345(4): 260-65.
2. Hollowell JG, Staehling NW, Flander WD, Hannon WH, Guter 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 Metab.* 2002; 87(2):489-99.
3. Ayala C, Cozar MV, Rodriguez JR, Silva H, Pereira JL, García-Luna PP. Sub-clinical thyroid disease in institutionalized healthy geriatric population. *Med Clin (Barc).* 2001; 117(14):534-35.
4. Nakajima Y, Yamada M. Sub-clinical thyroid disease. *Nihon Rinsho.* 2012;70 (11):1865-71.
5. Rizos CV, Elisaf M. S, Liberopoulos E. N. Effects of Thyroid Dysfunction on Lipid Profile. *Open Cardiovasc Med J.* 2011; 5: 76-84.
6. Rodondi N, Newman AB, Vittinghoff E, de Rekeneire N, Satterfield S, Harris TB, et al. Sub-clinical hypothyroidism and the risk of heart failure, other cardiovascular event and death. *Arch Intern Med.* 2005; 165(21):2460-66.
7. Rizos CV, Elisaf MS, Lieberopoulos EN. Effect of thyroid dysfunction on the lipid profile. *The Open Cardiovascular Medicine Journal* 2011; 5:76-84.
8. Ladenson PW, Singer PA, Ain KB, Bagchi N, Bigos ST, Levy EG, et al. American thyroid association guideline for detection of thyroid dysfunction. *Arch Intern Med.* 2000; 160(11): 1573-75.
9. Buccolo G, David M. Quantitative determination of serum triglyceride by the Use of Enzyme. 1973 19(5) 476-82.
10. Friedewald W, Levy R, Fredrickson D. Estimation of concentration of low density lipoprotein Cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972; 18:499-515.
11. Friedewald W, Levy R, Fredrickson D. Estimation of concentration of low density lipoprotein Cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972; 18:499-515.
12. Duntas LH, Brenta G. The effect of thyroid disorders on lipid levels and metabolism. *Med Clin North Am.* 2012; 96:269-81.
13. Althaus BU, Staub JJ, Ryff-deleche A, Oberhänsli A, Stähelin HB. LDL/HDL changes in sub-clinical hypothyroidism: Possible risk factors for coronary heart disease. *ClinEndocrinol (Oxf).* 1988;28(2):157-63.
14. Rodondi N, den Elzen WPJ, Bauer DC, et al; Thyroid Studies Collaboration. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. *JAMA.* 2010; 304(12): 1365-1374.
15. Efstathidou Z, Bitsis S, Milionis HJ, et.al. Lipid profile in sub-clinical hypothyroidism: is L-thyroxine substitution beneficial? *Eur J Endocrinol.* 2001.145(6)705-10.
16. Rahman Adil, Niranjan Singh, Sushil Kumar Shukla, Hypothyroidism and Lipid Profile: A Comparative Study between Rural & Urban Hypothyroid Individuals, *International Journal Dental and Medical Sciences Research*, Jan-Feb 2021;3(1): 189-194.