

Detection of Subclinical Hypothyroidism In Jammu Region and Its Association With Hypercholesterolemia

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ABSTRACT

Previous studies showed patients with mild hypothyroidism, mainly elderly women, are at a higher risk of cardiovascular diseases because of lipid abnormalities. The present study conducted to find prevalence of subclinical hypothyroidism in apparently healthy patients and to determine whether hypercholesterolemia is more common in patients with subclinical hypothyroidism than in euthyroid. This observational study was conducted in Government Medical College, Jammu (Department of Biochemistry) over a period of four months. Biochemical investigations for thyroid function and lipid profile were conducted on 150 patients of either sex, aged 18 to 85 years. Based on serum TSH values, patients were divided into SCH (n=53) and EU group (n=97).

Quantitative variables were calculated and statistical significant result was considered for p-value less than 0.05. TSH values found to be elevated in patients with subclinical hypothyroidism. Similarly, serum TC and triglycerides found significantly elevated in SCH group than in EU group. On perspective of age, average total cholesterol values were elevated in all age-groups of SCH group. This study conclude that in SCH group, there is an increase in levels of atherogenic lipids, especially total cholesterol (TC). Female patients and patients above the age of 60 years are more at the risk of hypercholesterolemia, which suggests that all adults above 35 years with subclinical hypothyroidism should be asked to get their lipid profile investigated.

Key words: Subclinical hypothyroidism (SCH), euthyroidism (EU), hypercholesterolemia, thyroid-stimulating hormone (TSH), total cholesterol (TC).

INTRODUCTION

Subclinical hypothyroidism, a common thyroid dysfunction, has drawn an intensive interest due to its exaggerating prevalence which enhanced from 11.3% in 2003 to 19.3% in 2012 in India [1] and found to be more prevalent in females than in males [2]. Lipid abnormalities are commonly reported in patients with hypothyroidism and may contribute to disproportionate increase risk in cardiovascular conditions [4]. In an intervention study, subclinical hypothyroidism determined to be two to three times more prevalent in hypercholesterolemia patients with fasting serum samples [2]. Similarly, few studies of subclinical hypothyroid patients have shown elevations in their cholesterol levels. Canaris *et al.*, studied the prevalence of thyroid disease in statewide healthfair in Colorado among 25,862 participants and concluded that lipid profile were elevated in individuals with dysfunctional thyroid function, mainly in subclinical hypothyroidism than in euthyroidism [5].

In the study of Ball *et al.*, (1991), hypothyroidism found common in apparently healthy people with increased plasma cholesterol levels [6]. Hypothyroidism observed in both males and females resulted in changed LDL-C/HDL-C and TC/HDL-C ratios, found prominent in subclinical hypothyroid patients than in euthyroid one [7]. The reason for such abruptness is still unknown but few suggested that composition and transport of lipoproteins are disturbed in thyroid dysfunction [9]. In Rotterdam, study conducted on Elderly Women, conclude subclinical hypothyroidism proves to be major risk factor for atherosclerosis [8]. In middle aged women, subclinical hypothyroidism is related with hypertriglyceridemia and elevated TC/HDL-C levels, a resultant of hormonal imbalance or menopausal conditions, may enhance the risk of premature coronary artery disease (CAD) and atherosclerosis. In survey based study in Whickham, by W.M.G. Tunbridge *et al.*, hypothyroidism was found to be more prone in females than in males while higher ratio was of younger than the older one [21].

The main aim of this study was to determine whether hypercholesterolemia is more common in subclinical hypothyroidism patients when compared to euthyroid individuals of Jammu region. The study also compared lipid profile between subclinical hypothyroidism group and euthyroid group with respect to age, sex in relation with TSH value.

MATERIALS & METHOD

Present observational study conducted in Government Medical College, Jammu (Department of Biochemistry) over a period of four months. A total of apparently healthy 150 patients, aged 18-85 years were randomly selected. The study based on physical examination followed

by biochemical investigations for thyroid function and lipid profile, along with clinical data and medical history was also included. Based on TSH values, patients were divided into SCH group (n = 53) and EU group (n = 97). SCH considered for mild elevated TSH values between 5 - 10 mU/L and normal FT₄, while EU group referred with normal TSH values between 0.3-4.9 mU/L. Patients were considered to have hypercholesterolemia if serum values for cholesterol is >200 mg%, LDL >130 mg%, and triglycerides >150 mg%; and HDL <35 mg%.

Exclusion criteria:

Patients with a history of diabetes mellitus, CAD, hyperthyroidism on treatment, pregnancy, or on drug therapy like oral contraceptives, hormonal medication, amiodarone, lithium, and cholesterol lowering agents were omitted from present study.

Method:

1. **Thyroid Function Test:** The blood sample, under all aseptic conditions, was taken between 9 am and 11 am from non-fasting subjects because fasting causes a rapid fall in serum T₃ concentration [13]. At room temperature, samples were clotted for 30 minutes and centrifuged at 3000 rpm for about 20 minutes. Separated serum transferred to another tube for thyroid function estimation. Sampling, reagent delivery, mixing, processing and results were automatically performed by ARCHITECT I SYSTEM.
2. **Lipid Profile Test:** After 14 hours fasting, blood sample, from same subjects were taken under aseptic conditions. Serum was obtained by same procedure as TFT. Sampling, reagent delivery, mixing, processing and results were automatically performed by SIEMENS DIMENSION 16961 X PLU.

Statistical analysis:

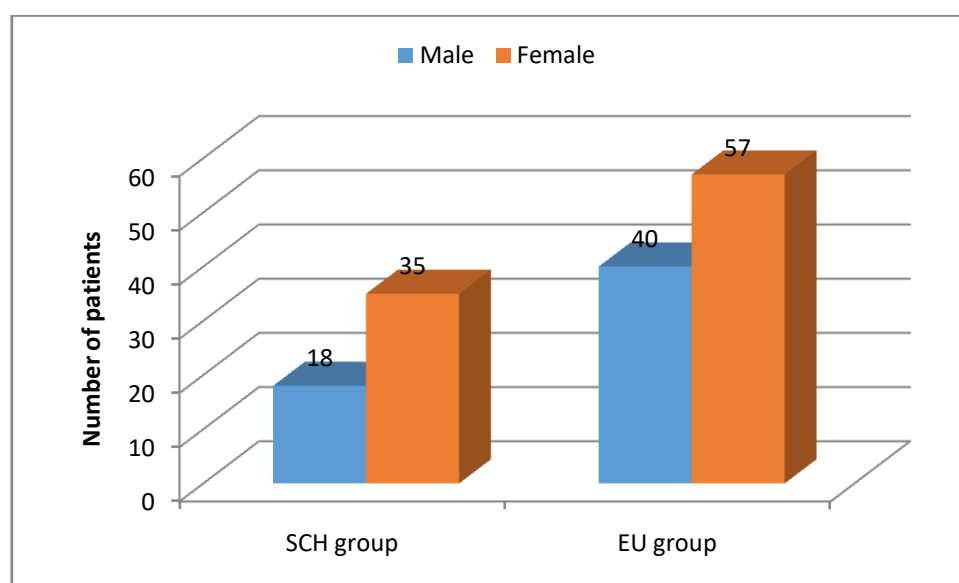
For windows, data was analysed using computer software IBM SPSS version 22.0 by ANOVA. 't'-test and Fischer's exact test was used for statistical difference and frequency comparison, respectively. Statistically significance is considered for p-value of <0.05.

RESULTS

The study for 150 patients of both gender and age (between 18-85 years) was conducted at Government Medical Hospital & College, Jammu. Out of 150 samples, 92 were females and 58 were males. In 1st part, among 150 samples, patients with high TSH were mentioned as subclinical hypothyroidism (SCH) group containing 53 patients while the remaining 97 were euthyroid (EU) group, having low TSH values. In 2nd part, these groups were further categorized different groups; namely on basis of sex, age& their co-relation with total lipid content.

Gender distribution of patients

Of 150 patients studied, SCH group (n=53) comprised of 18 males and 35 females while EU (euthyroid) group (n=97) comprised 40 males and 57 females. Both groups had predominantly female patients and prevalence of SCH in female was twice more than that in males. In study of *Canaris GJ*, males were less with female-male ratio in hypothyroidism condition, which is similar to the result of this study[17]. Similarly findings were obtained, concluding subclinical hypothyroidism is common among elderly women [14].

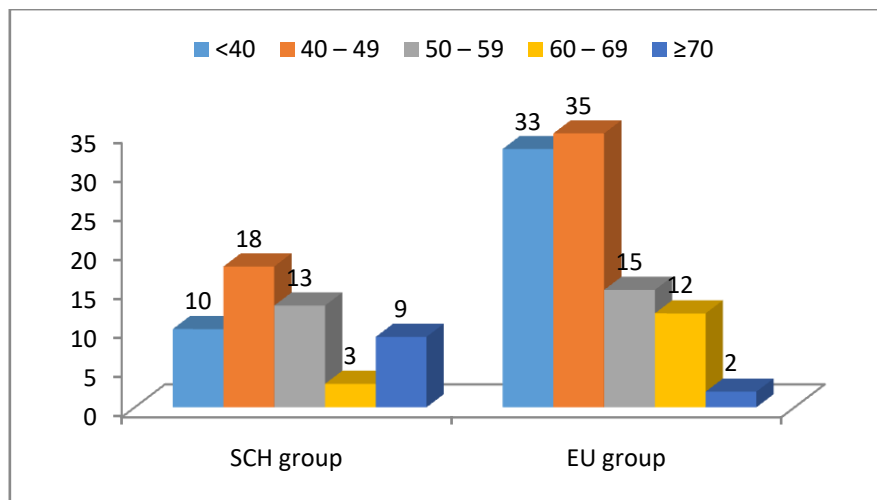


Graph 1. Gender distribution of patients

Age-wise distribution of patients

Both groups (SCH and EU) were divided, according, namely <40, 40-49, 50-59, 60-69, and >70. In SCH group, predominance were found in age group of 40-49 years is 18 (33.96%) while least observed in sub-group is 60-69 (5.66%). Or else, in EU group, predominance observed in 40-49 years is 35 (36.08%), followed by <40 group containing 33

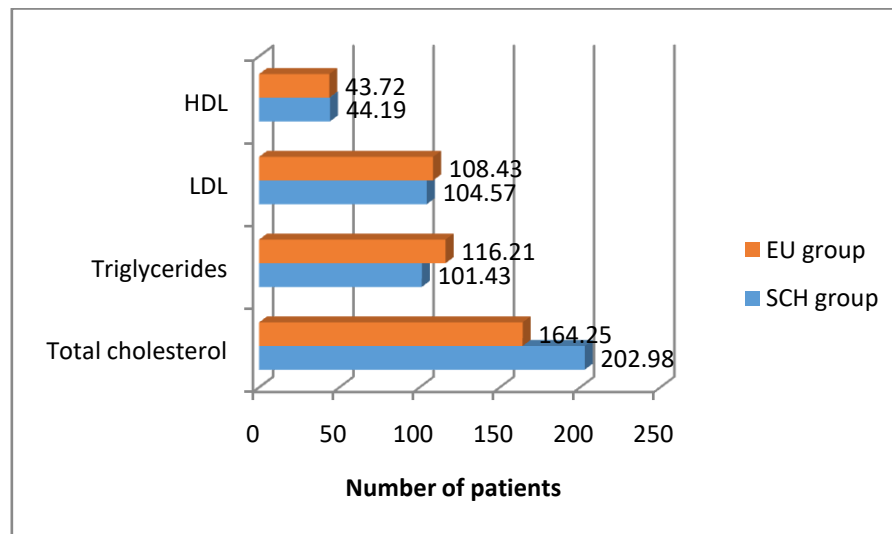
(34.02%). In study of Alexander J, *et al.*, prevalence of subclinical hypothyroidism is prominently found in middle-aged women as well in males which partially correlates with present study [17].



Graph 2. Age distribution of patients

Assessment of lipid values in SCH and EU group.

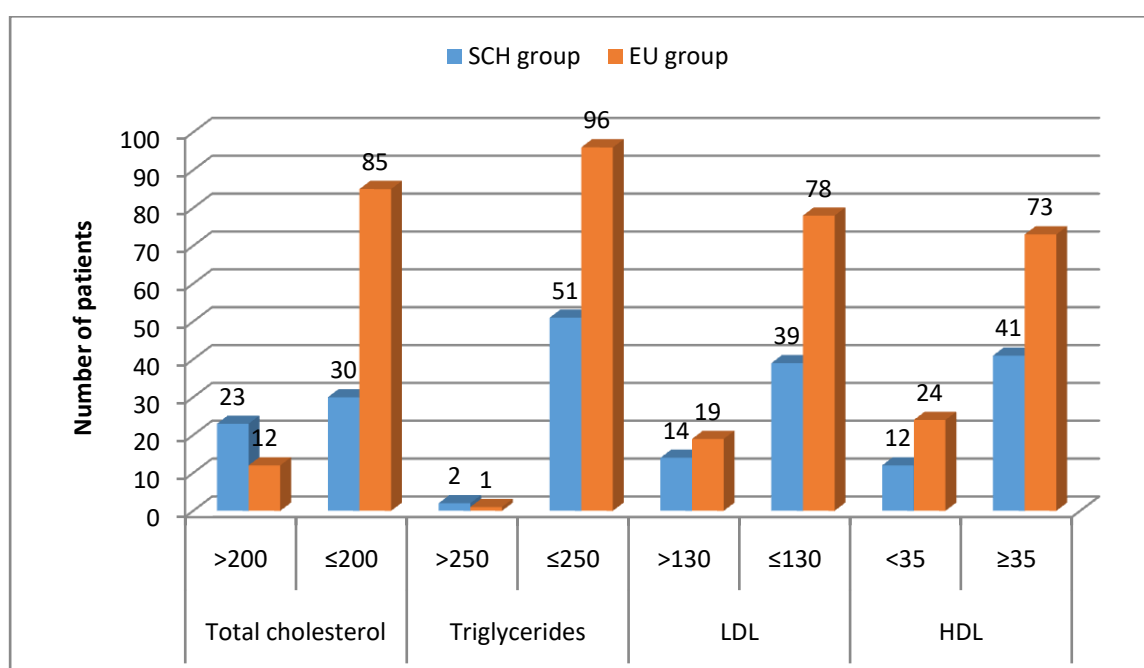
On analyzing mean lipid values in both groups, serum TC was found elevated in the SCH group. Using unpaired t-test, a significant value was observed between serum Total Cholesterol ($p=0.0001$) and Triglycerides ($p=0.003$). Although, no such values observed in another lipid parameters in relation with SCH condition. In contrast with the results, it was concluded that the main impact of the higher TSH levels correlates with cholesterol levels in the patients while no such effect was observed in EU group. Previous study suggested that SCH patients showed reduced activity of lipoprotein lipase, which could be a resultant of increased lipid values in such patients [16]. In study of Xiao-Li-Liu, *et al.* concluded that subclinical hypothyroidism correlated with altered lipid profile which relates with present study [15].



Graph 3. Assessment of lipid values in SCH and EU groups

Comparing non-standard lipid values between SCH and EU groups.

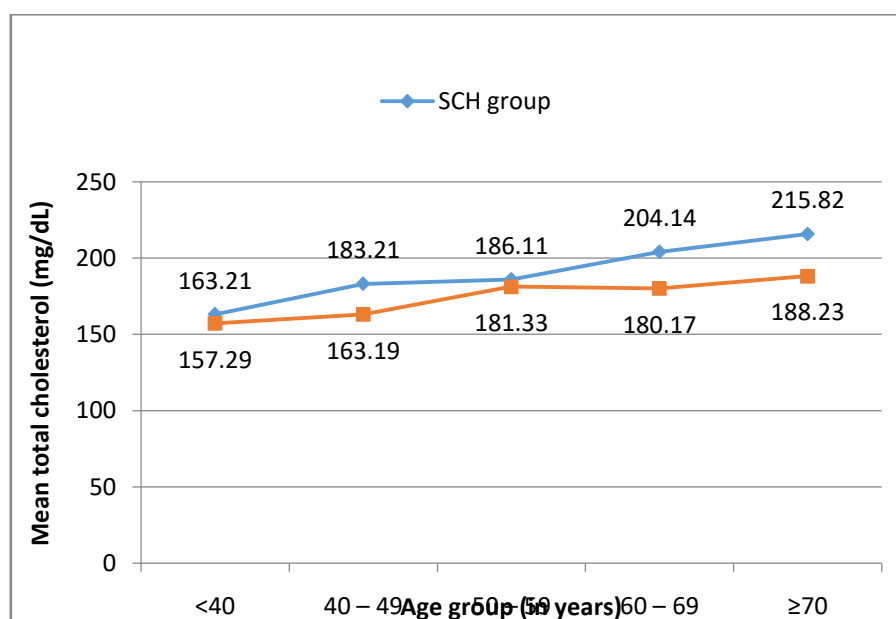
On evaluating lipid values, SCH patients showed elevation in serum TC levels indicating serum TC value >200 were in SCH group. In relation to their values, the statistical inference of such patients proved to be higher as having ($p < 0.0001$) high significant values but no positive significant results observed in remaining lipid parameters ($p > 0.05$). In study of Hueston WJ. & Pearson WH., hypercholesterolemia founds to be associated with SCH condition, which is almost similar in our study [11]. Similarly, other studies suggested the elevation in plasma cholesterol levels in subclinical hypothyroidism patients of either sex [17].



Graph 4. Comparing abnormal lipid values between SCH and EU groups

Comparison of mean total cholesterol values by age group between SCH and EU groups

Depending on age groups, mean TC values were compared between SCH and EU groups, values were found to be elevated for all five groups of SCH groups. On comparing statistically, a significant value ($p < 0.001$) observed in serum TC levels in the age group of 40–49 years while no other lipid parameters showed any significant elevation in either age group ($p > 0.05$). In the study of Sawin CT., Castelli WP. *et al.*, observed that cholesterol value were elevating with age with also suggested in my study. [5]

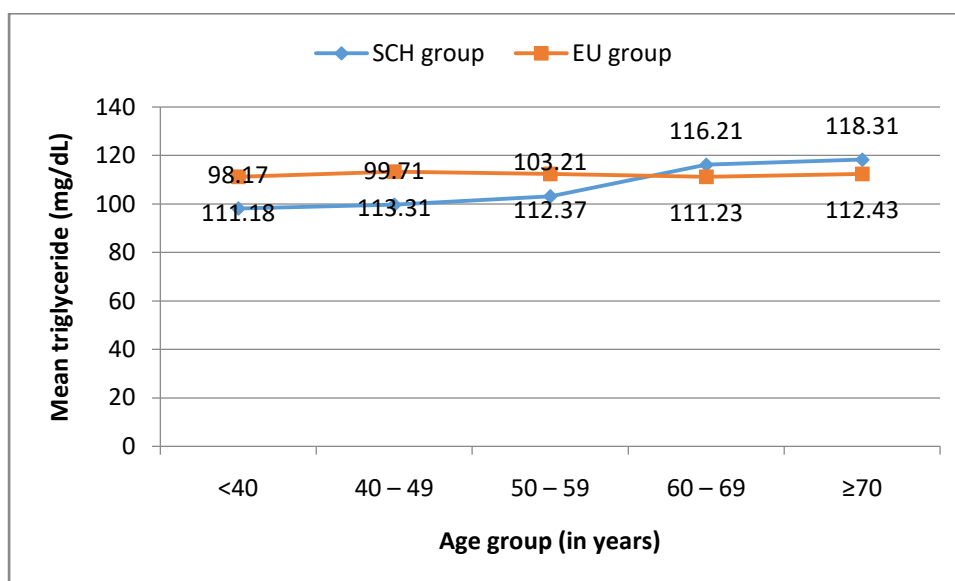


Graph 5. Comparing mean total cholesterol values in SCH & EU groups according to age

Evaluating mean triglyceride values by age groups between SCH and EU groups

Mean triglyceride value found to be diversified for all age groups resulting elevation in EU group as compared with SCH group. It was observed serum triglyceride values were elevated in >60 age group while showed decline with increasing age (<60 years). In contrast, SCH group showed inverse results providing higher value for >60 age group. On comparing statistically, a significant value ($p < 0.01$) observed in mean triglyceride levels in 40–49 years group while no other parameters showed significant elevation in either age group ($p > 0.05$). This indicates subclinical hypothyroidism patients, aged >60 years, may have risk of elevated

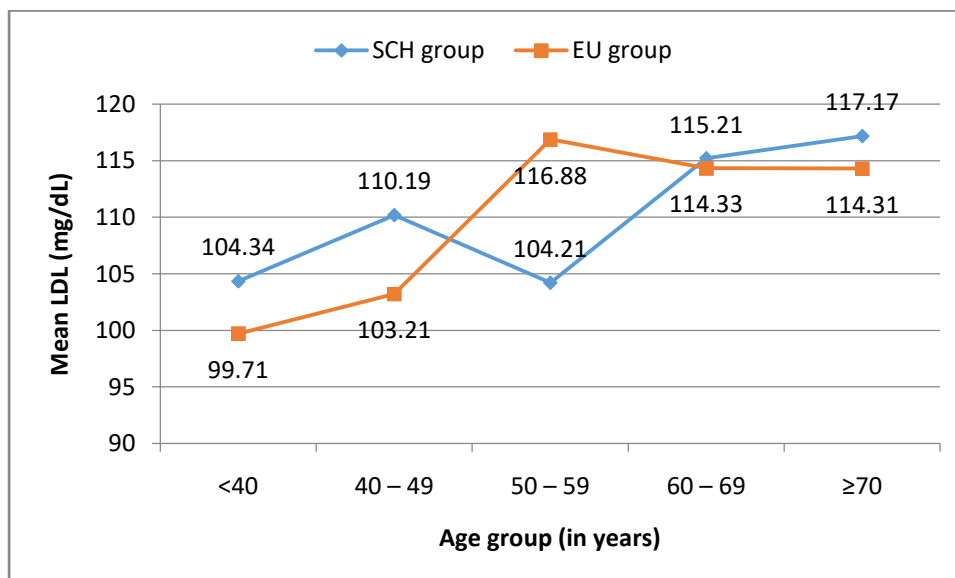
serum triglyceride levels, which was also demonstrated by J. Kvetny, P.E. Heldgaard, *et al.*, [19].



Graph 6. Evaluation of mean triglyceride values in SCH and EU groups according to age.

Comparison of LDL values by age groups between SCH and EU groups

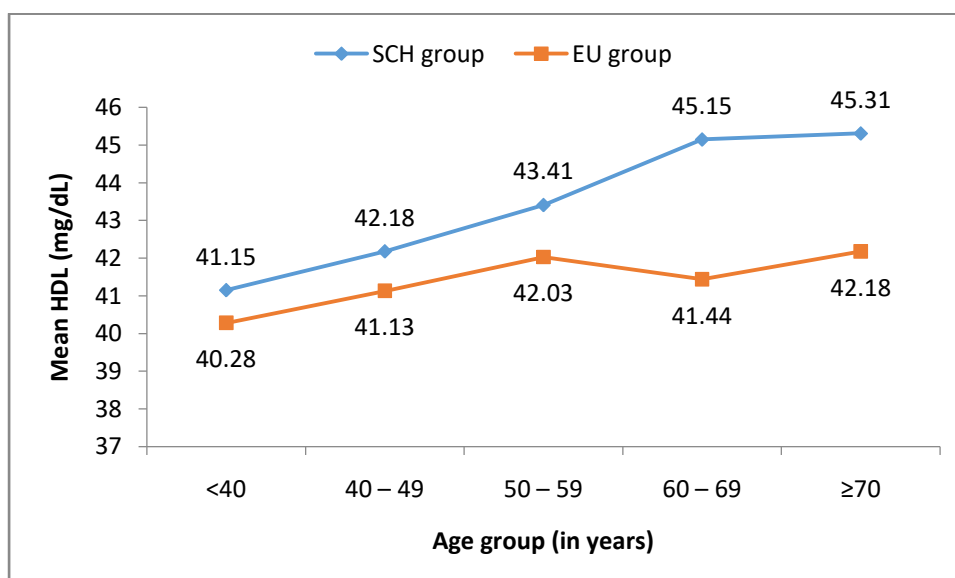
Depending upon age groups, mean LDL values of either groups, were compared. In this study, elevations were observed in all groups of SCH except one (50-59) while inverse results were obtained from EU group. In this age-group, the LDL values were observed to be lower in SCH group as compared to EU group. The statistical interference value of both groups came to be non-significant ($p > 0.05$) and conclusion is inconsiderable. While in the study of ChulSik Kim, *et al.*, concludes LDL levels are not significantly affected by thyroid dysfunction [18].



Graph 7. Comparing mean LDL values of SCH and EU groups by age

Comparison of mean HDL values by age groups between SCH and EU groups

With other lipid parameters, mean HDL values were compared in SCH and EU groups. The same impact of results was found as were observed in LDL values. No direct relation was observed in the mean HDL values with the high TSH levels in both the groups. In SCH group, mean HDL values observed to elevate in minute traces as compared with EU group. Due to non-significant values ($p>0.05$) in both groups, hence, considered to be negligible.



Graph 8. Comparing mean HDL values of SCH and EU groups by age

Assessment of total lipid profile by gender in SCH and EU groups

Comparing total lipid profiles between both groups, mean serum cholesterol found to be elevated in both gender of SCH group. While no other lipid parameters were elevated in either group. Statistically significant values observed in serum TC values ($p=0.02$) and triglycerides values ($p=0.01$) of male patients of either groups. Similar significant results were obtained in serum TC values ($p=0.001$) and triglycerides values ($p=0.03$) of female patients. Hence, statistically significant values were obtained in serum TC and triglyceride levels of both sexes, suggesting that serum TC and triglyceride elevated in SCH male patients which also correlates with previous studies. [19, 20].

Table 1. Assessment of total lipid profiles between SCH and EU groups in terms of gender

Gender	Lipids (mg/dl)	SCH group (n=53)		EU group (n=97)		Statistical inference
		No. of cases	Mean $\pm$ SD	No. of cases	Mean $\pm$ SD	
Male	TC	18	205.99 $\pm$ 74.02	40	167.44 $\pm$ 46.83	$p=0.02$ (significant)
	TG		98.58 $\pm$ 17.25		111.18 $\pm$ 18.31	$p=0.01$ (highly significant)
	LDL		104.17 $\pm$ 19.34		108.87 $\pm$ 20.78	$p=0.41$ (not significant)
	HDL		46.30 $\pm$ 9.21		44.22 $\pm$ 6.88	$p=0.34$ (not significant)
Female	TC	35	200.98 $\pm$ 72.01	57	160.05 $\pm$ 45.76	$p=0.001$ (highly significant)
	TG		104.71 $\pm$ 17.77		113.31 $\pm$ 18.87	$p=0.03$ (significant)
	LDL		105.10 $\pm$ 18.78		108.01 $\pm$ 17.12	$p=0.44$ (not significant)
	HDL		42.08 $\pm$		42.22 $\pm$	$p=0.93$ (not

			8.87		6.84	significant)
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CONCLUSION

Our study suggested that serum TC and triglycerides levels increased under subclinical hypothyroidism, indicating a high risk for CAD, CHD and atherosclerosis in both male and female patients. Elderly females were found to be more effected than male. Therefore, cardiovascular status of SCH patients should be monitored carefully. A positive association is reported between low TSH values with serum lipid parameters in our study group.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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