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Study of Serum Lipoprotein (a) in Hypothyroidism

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Hypothyroidism occurs when your body doesn't produce enough thyroid hormones. The thyroid is a small, butterfly-shaped gland that sits at the front of your neck. It releases hormones to help your body regulate and use energy. To this study compare Serum lipoprotein levels in hypothyroid patients and in control group. To find the correlation of Lp(a) with thyroid hormones status in hypothyroid patients. To find the hypothyroid patients. Levels of serum Lp (a), FT3, FT4, TSH, TC and TG were all estimated from the samples of the study group. The results of this study provide ample evidence that the levels of Serum Lp(a) are increased in hypothyroid patients.

Keywords: Hypothyroidism; carbohydrates; lipoproteins; triglycerides and dyslipidaemia.

1. INTRODUCTION

Hypothyroidism is one of the most common endocrine disorder in last few decades, it occurs in either subclinical or clinical form. According to the third National Health and Nutrition Examination Survey (NHANES III) the prevalence of hypothyroidism was 4.6% and it is more prevalent in women, which also increases with age, thus showing age and sex relation [1]. The thyroid hormones are involved in almost all major metabolic pathways, and hypothyroidism can lead to various metabolic abnormalities. Regulation of basal metabolic rate is maintained

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by thyroid hormones by their effect on carbohydrate, lipid and protein metabolism. Besides the direct effects of thyroid hormones on metabolism, it can also affect indirectly by influencing other regulatory hormones such as catecholamine and insulin [2]. It causes derangement of wide range of parameters in lipid profile, hemodynamic changes, endothelial dysfunction, coagulation disturbances, hormonal and metabolic change.

Hypothyroidism is commonly associated with dyslipidaemia, the metabolic abnormality which can occur either in overt or subclinical form. It accounts for the end effect of thyroid hormones in lipid metabolism resulting in various qualitative and or quantitative changes of cholesterol, triglycerides, phospholipids and lipoproteins which includes lipoprotein (a), apolipoprotein A1 and apolipoprotein B. In hypothyroidism, there is increased risk for cardiovascular disease due to dyslipidaemia and the coexisting metabolic abnormalities, in combination with the thyroid hormone- induced hemodynamic alterations [3–6].

In parallel with measures to control established cardiovascular risk factors, there is a need to identify novel risk markers that may have therapeutic or preventive utility. Lipoprotein (a) Lp(a) is one such novel marker that is receiving increasing attention as a potential causal factor and therapeutic target in CHD. Some studies regard Lp(a) as an independent risk factor for atherosclerosis of brain and coronary arteries. Clinical interest in Lp(a) has grown considerably in recent years, as various epidemiological studies have identified the association between plasma Lp(a) concentrations (≥ 300 mg/L) and the risk of suffering cardiovascular events, coronary events, peripheral artery disease and the early development of atherosclerosis in adolescents and children [7,8].

Lp(a) is an LDL- like particle to which specific apolipoprotein (a) is covalently bound to apolipoprotein B by disulphide linkage. Serum Lp(a) level is determined genetic variation of the Lp(a) genes, but it could also be affected by non-genetic factors. Several studies have shown the influence of diet, drugs and hormones on Lp (a) levels. In a number of previous studies, investigators have reported the effect of the thyroid status on the changes in the serum lipoprotein concentrations, whereas reports on serum Lp(a) levels are limited. The detail on how the serum Lp(a) levels are influenced by thyroid hormone are still not well explained. The present study was designed to determine the Lp(a) levels among the hypothyroid patient and healthy control and to compare the same, and to find any correlation between between Lp(a) and other lipid [9-11].

2. MATERIALS AND METHODS

This study was conducted in the Department of Biochemistry, Sree Balaji Medical College and Hospital, Chromepet, Chennai during the period of November 2016 – September 2018 among outpatients and healthy volunteers visiting the outpatient services of the Department of Medicine, Sree Balaji Medical College and Hospital, Chromepet, Chennai. Proper consents were taken from patients whose sample was included in the study. Patients' particulars, brief clinical history and clinical examination findings were recorded. The laboratory parameters that were measured includes serum Lipoprotein (a), serum FT 4, serum FT 3.

2.1 Inclusion Criteria

Known hypothyroid with (0- 5 years) duration including both sexes in the age group (20- 60 years) and healthy individuals of both sexes in the age group (20- 60 years).

2.2 Exclusion Criteria

Patients with Diabetes mellitus, Familial hypercholesterolemia, Malignant neoplasm, Liver diseases, Renal diseases, Cardiovascular diseases and patients on treatment with systemic steroids.

2.3 Sample Collection and Processing

The sample size of this study includes 100 subjects involving 50 hypothyroid patients and 50 healthy controls. The blood samples were collected from subjects after an overnight fasting by venepuncture under aseptic precautions. 5ml of blood was drawn from all the study subjects from the anterior cubital vein using vacutainer and collected in plain tube. The blood samples are allowed to clot adequately and then centrifuge for 10minutes at 3500 rpm. 1 ml of the separated serum was taken and preserved under - 20º C upto 4 weeks for Lp(a) estimation. From the remaining serum, analysis of parameters like serum FT3, FT4, TSH were carried out using ADVIA Centaur immunoassay analyser and serum lipid profile using fully automated BS 390 analyse on the same day.

The estimation of Glycerol phosphate dehydrogenase and Peroxidase (GPO- POD) was done by adopting the previous method [12].

2.4 DATA ANALYSIS

The statistical analysis was done with the help of Statistician using the Pearson' s correlation coefficient as the test of correlation and Independent Sample t- Test as the test of significance. The statistical software used for statistical interpretation was from Stata version 14. 1.

P ≤ 0.05 = Significant
P < 0.01 = Highly significant P > 0.05 = Not significant

3. RESULTS

A total of 100 subjects were selected as the study group for the present study. This includes 50 cases with hypothyroid and 50 healthy controls. Levels of serum Lp(a), FT3, FT4, TSH, TC and TG were estimated for all the samples of the study group. The values obtained in controls and cases are presented in the master chart I and II respectively. Serum FT3 (pmol/ L), S. FT4 (ng/ d L), S. TSH (m IU/ L), S. TC (mg/ dl), S, S. TG (mg/ dl), were found to be statistically significant in the control and hypothyroid patients with p < 0.001.

Serum Lp(a) levels among hypothyroid patients (23. 120± 12. 118) were significantly higher than control subjects (4 . 780 ± 3 . 691) with t- value = 10.2375 (p < 0.001). Serum TSH levels among hypothyroid patients (35. 715± 25. 156) were significantly higher than control subjects (2 . 633 ± 1. 001) with t- value = 9.2917 (p < 0.001). Serum FT3 level were significantly lower in hypothyroid patients (2.420±0.527) than the controls (3.479±0.858) with t- value = □7.4361 (p < 0.001).

Serum FT4 level were significantly lower in hypothyroid patients (0.841±0.187) compared to control subjects (1 .639 ± 0.647) with t-value = □8.3807 (p < 0.001).

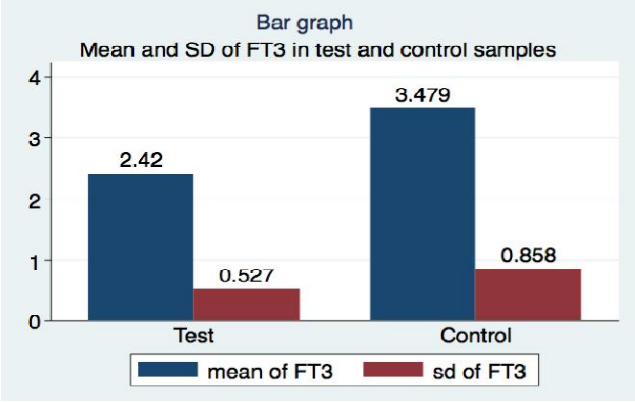

Fig. 1. Comparison of Serum FT3 levels in both test and control samples

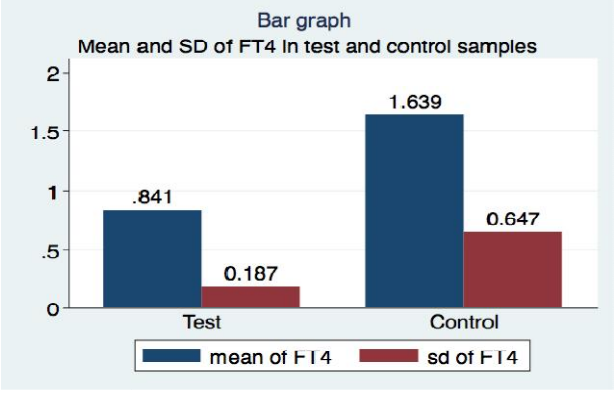

Fig. 2. Comparison of serum FT4 levels in both test and control samples.

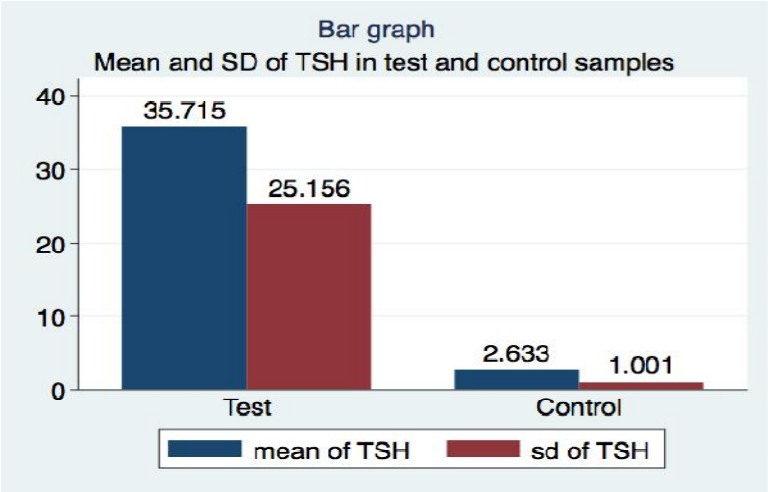

Fig. 3. Comparison of Serum TSH levels in both test and control samples

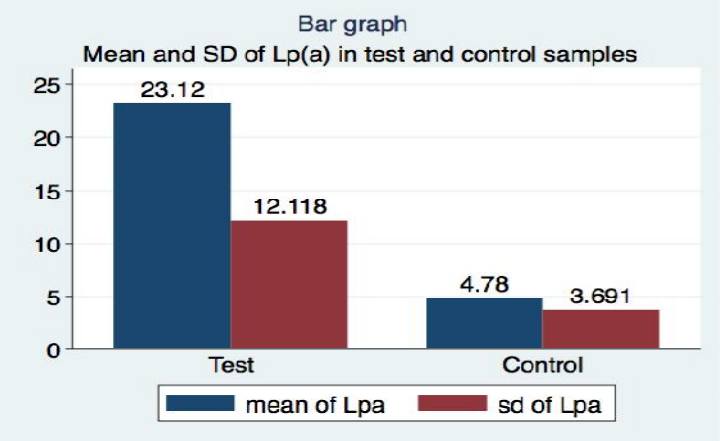

Fig. 4. Comparison of serum lipoprotein (a) levels in both test and control samples

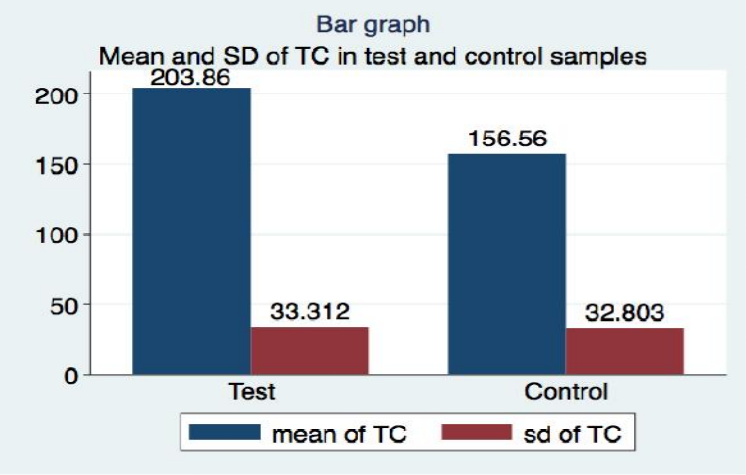

Fig. 5. Comparison of serum Total Cholesterol (TC) levels in both test and control samples

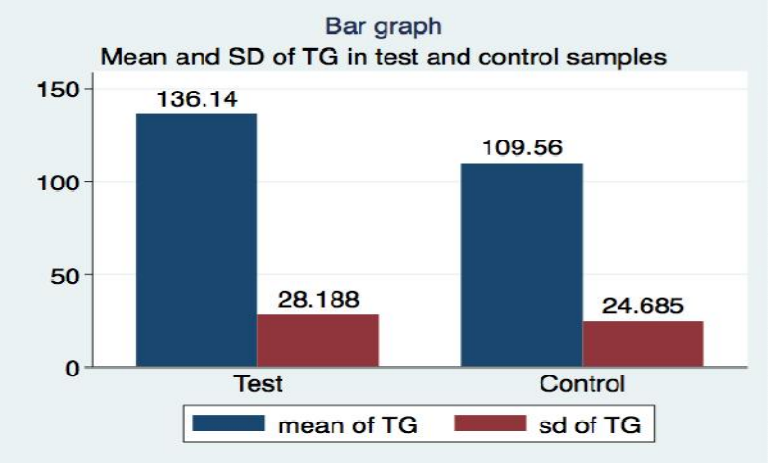

Fig. 6. Comparison of serum Triglyceride (TG) levels in both test and control samples

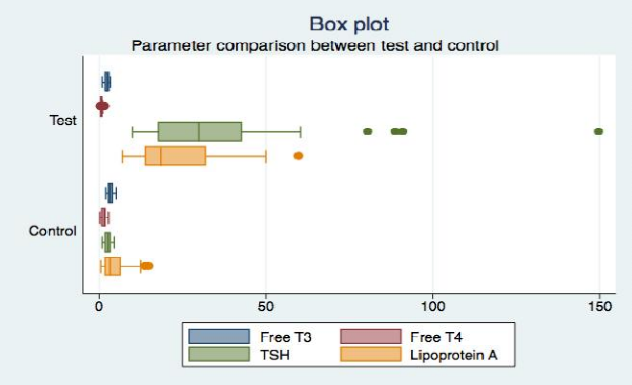

Fig. 7. Box plot showing median, quartiles and whiskers, comparing FT 3, FT 4, TSH and Lp(a) levels in test and control samples

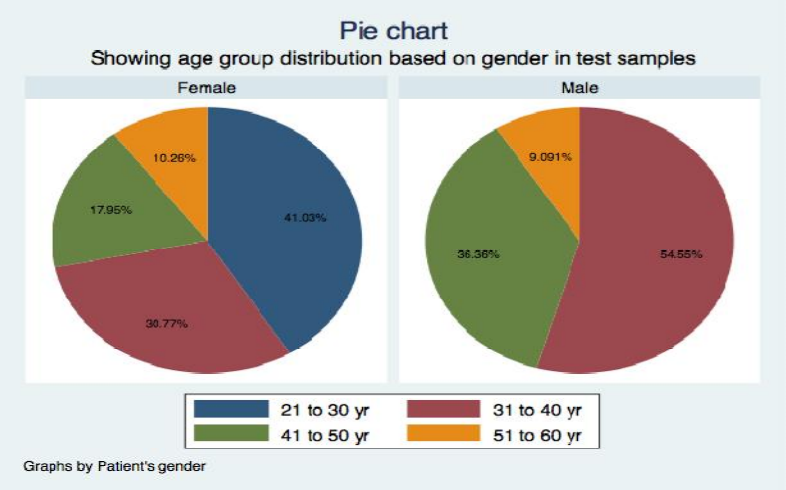

Fig. 8. A pie graph showing age distribution for each gender among test group

Table 1. Mean value of age in both test group and control group, and male female ratio

Parameters	Control (n=50)	Patients (n=50)
Age	40.54±11.72	36.18±9.74
M:F	1:9	1:3.545

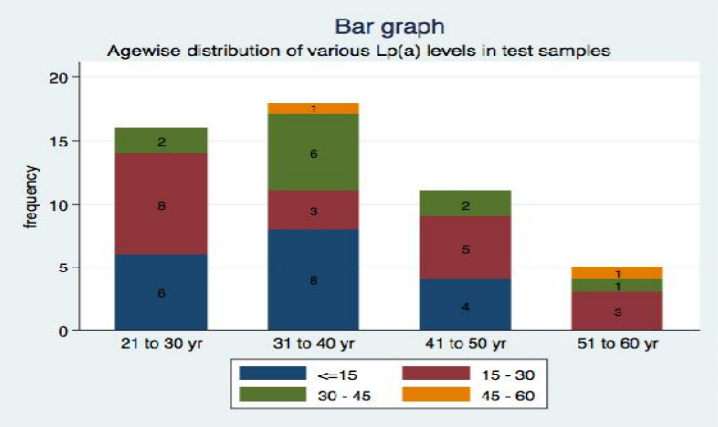

Fig. 9. Stacked bar graph showing Lp(a) level distribution in different age groups in test samples

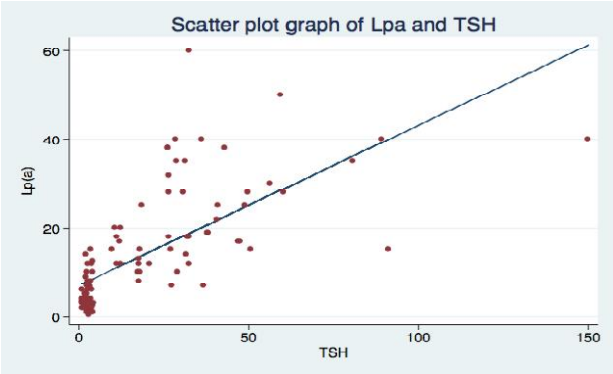

Fig. 10. Scatterplot with regression line of Lp (a) and TSH

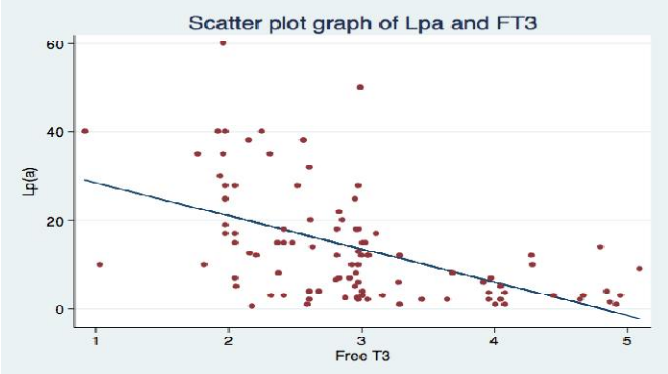

Fig. 11. Scatterplot graph with regression line of Lp (a) and FT 3

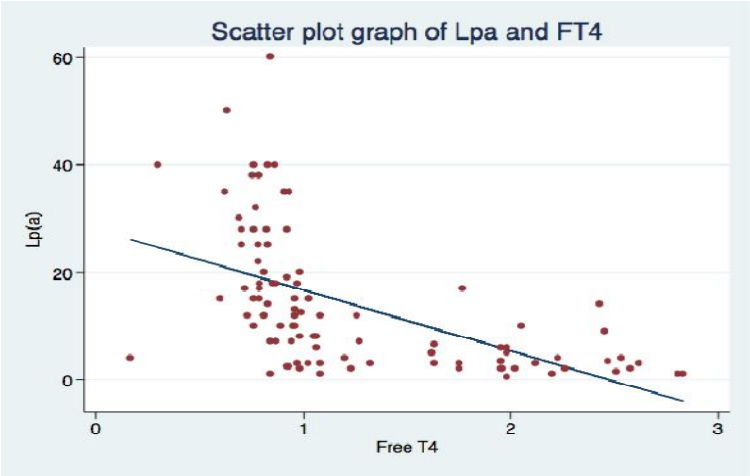

Fig. 12. Scatterplot with regression line of variable Lp(a) and FT 4

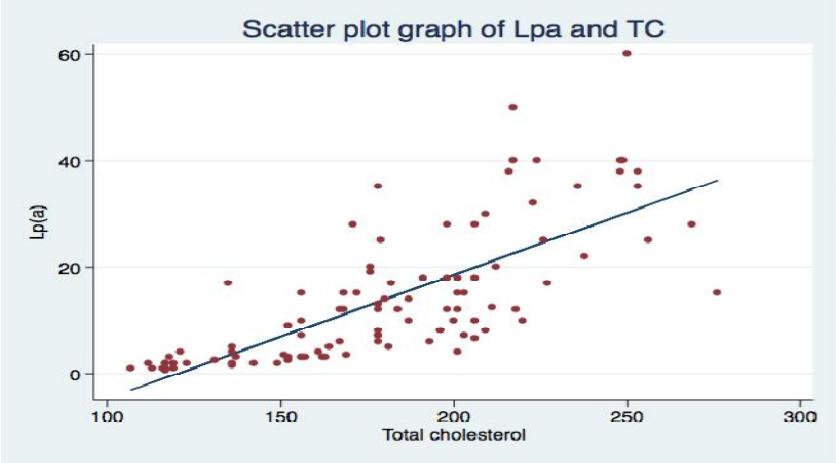

Fig. 13. Scatterplot with regression line of Lp (a) and TC

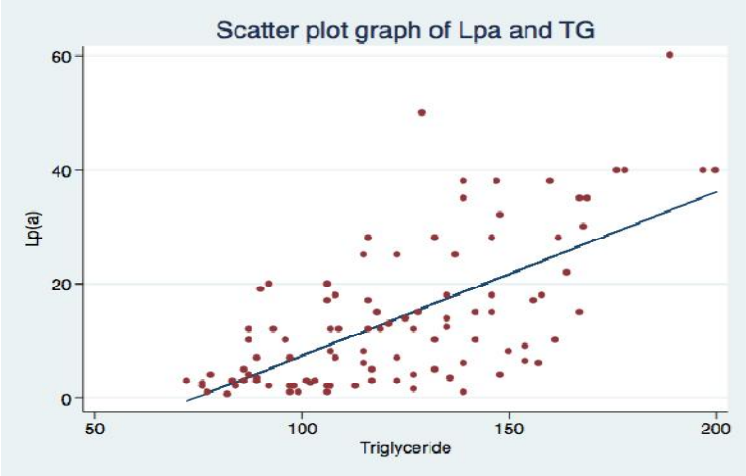

Fig. 14. Scatterplot with regression line of Lp (a) and triglyceride

4. DISCUSSION

This study was done on known cases of hypothyroidism, and healthy individuals taken as controls. Between the study group, biochemical parameters including serum Lp(a), serum TSH, serum fasting TC, and serum TG were found to be significantly higher in cases when compared to controls, while other parameters like serum free thyroxine (FT 4), free triiodothyronine (FT 3), were significantly lower in Hypothyroid patients when compared to control [13].

Pearson' s correlation between Lp(a) and serum thyroid stimulating hormone (TSH), serum fasting total cholesterol, serum triglycerides showed positive correlation. While a negative correlation is seen between Lp(a) and serum free thyroxine (FT 4), free iodothyronine (FT 3) [14]. This study showed that serum Lp(a) levels among hypothyroid patients were significantly (p= 0.0000) higher with a mean and standard deviation of (23. 12± 12.117) than control (4.78± 3.691). These findings were further supported by the highly significant positive correlation between Lp(a) and TSH in hypothyroid patients (r = 0.398, p= 0.0042) which is consistent with the finding of studies done by Maria L. Martinez et al. Hanna Engler and Walter F. Riesen et al. Sara Sandrio et al. It was also observed that serum Lp(a) levels were significantly increased in all age groups and in both genders of hypothyroid patients when compared to control, which suggested the influence of thyroid hormones on Lp(a) metabolism [15]. The potential association between Lp(a) and thyroid function status in the general population might be regarded as an important aspect for cardiovascular risk prediction and prevention. This hypothesis was supported by De Bruin et al. [16] who demonstrated an almost perfect correlation between free thyroxine index and Lp(a).

This study shows that the fasting serum TG levels among hypothyroid patients were significantly higher than the normal controls. The mean value of serum TG was 136.140 ± 28 .188 mg/ dl in hypothyroid group whereas for the control group it was 109.560±24.685 mg/dl. There was a positive correlation between serum TG and serum Lp(a) among hypothyroid cases with r value being - 0.646 (p= 0.00010). Further, the present study also showed that the thyroidism strongly related to the group of the people (races) and several previous studies emphasized the same point[19, 20]. This study also warranted for further analysis.

5. CONCLUSION

The results of this study provide ample evidence that the levels of Serum Lp(a) are increased in hypothyroid patients. The present study also observed that there is positive correlation of Lp(a) levels with Thyroid stimulating hormone (TSH) indicating that in uncontrolled hypothyroid condition the level of Lp(a) will tend to increase, which puts them at risk for developing cardiovascular events in future. As an outcome of this correlation study, a recommended screening can be advised to hypothyroid patients to estimate Lp(a) level along with lipid profile which may assist in early treatment and prevent them from developing cardiovascular diseases.

CONSENT AND ETHICAL APPROVAL

The ground work for the study was started after getting clearance from the research committee and the Institutional Human Ethical Committee (reference number for approval: 002/SBMC/IHEC/2016 /834 of Sree Balaji Medical College and Hospital, Chromepet, Chennai. The study was explained to the participants and informed consent obtained from them before taking the blood sample.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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