

Original Article

Evaluation of lipid accumulation product in relation to thyroid hormone levels in hypothyroid patients: a cardiovascular risk perspective

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Abstract

Hypothyroidism, a prevalent endocrine disorder leads to complications such as hypertension, bradycardia, dyslipidemia and increased cardiovascular risks. Lipid Accumulation Product (LAP) index, which combines waist circumference (WC) and triglycerides (TG), has been under researched in context to hypothyroidism. This study aims to evaluate LAP levels across euthyroid, subclinical and overt hypothyroid individuals and analyze their correlation with Thyroid stimulating hormone (TSH) levels to determine LAP's effectiveness in predicting cardiovascular risk related to hypothyroidism. A cross-sectional descriptive study was conducted at Tertiary Care Centre, India. It involved 150 participants in three groups, 50 individuals in each (Euthyroid, subclinical and overt hypothyroid). Age, weight, thyroid parameters, TG, WC and LAP were assessed. The TG, WC and LAP values showed significant increase across all the three study groups ($p < 0.001$). Highest LAP values found in overt hypothyroid patients while lowest found in euthyroid controls. Pearson's correlation analysis showed a significant positive correlation between LAP and TSH levels. Our study showed an association between LAP and TSH levels indicating hypothyroidism is associated with elevated lipid accumulation, reflecting early metabolic disturbances and increased cardiometabolic risk. LAP may serve as a practical screening tool for cardiovascular risks in hypothyroid patients.

Keywords: hypothyroidism, lipid accumulation product, thyroid hormones, cardiovascular diseases, Healthcare (SDG 3)

Abbreviations: T3 – triiodothyronine; T4 – thyroxine; TSH – thyroid-stimulating hormone; LDL – low-density lipoproteins; TG – triglycerides; CVD – cardiovascular diseases; WC – waist circumference; BMI – body Mass Index; LAP – Lipid accumulation product; FPG – fasting plasma glucose; ROC – Receiver operating Characteristic; AUC – area under the curve; CI – confidence intervals

Introduction

Thyroid hormones are crucial for regulating metabolic balance and cardiovascular function, primarily triiodothyronine (T3) and Thyroxine (T4). These hormones produced by the thyroid gland, impacts on several conditions including lipid metabolism, vascular resistance and myocardial contractility [1, 2]. Hypothyroidism, marked by decreased levels of thyroid

hormones may leads to conditions including hypertension, bradycardia and dyslipidemia, an elevated risk of heart failure and atherosclerosis [1–3]. Subclinical thyroid disorders, marked by abnormal thyroid-stimulating hormone (TSH) levels along with normal FT4 levels poses a significant challenge to cardiometabolic health by impacting on lipid metabolism and vascular function [4]. Elevated TSH values signifies hypothyroidism, while free T4 & free T3 can differentiate between overt



and subclinical disorder, exhibiting low and normal levels respectively [3].

In the cases of hypothyroidism, hyperlipidemia is evident with elevated low-density lipoproteins (LDL) and triglycerides (TG) levels which facilitates the development of atherosclerotic plaque, worsening cardiovascular diseases (CVD) [5]. A significant cardiovascular risk is underscored by the rising incidence of the thyroid disorders, notably in South Asia, which gets worsened by metabolic syndrome and high rates of type 2 diabetes mellitus [6].

Thyroid hormones are crucial for cardiovascular homeostasis, as thyroid hormone receptors found in vascular smooth muscle cells, endothelial cells and cardiac myocytes. Even minor changes in serum thyroid hormone levels adversely affect the cardiovascular system, contributing to the increased risk of CVD [1]. These fluctuations can alter the gene expression linked to the heart function, which complicates in treating the thyroid disorder patients [1, 2].

There are two principle mechanisms that connects hypothyroidism to CVD, first theory suggests that lipid profile disturbances arise from the altered adipokine effects of LDL receptor affinity, coupled with inadequate thyroid hormone signaling leading to reduced levels of ester transfer protein levels and subsequent LDL accumulation. Second theory suggests that reduced nitric oxide production causes endothelial dysfunction, increasing systematic vascular resistance, impairing myocyte function and potentially resulting in cardiac malfunction or mortality [3, 6].

In adults, waist circumference (WC) and serum TG are the crucial metrics for assessing the lipid accumulation risks. Conventional obesity assessing methods such as body Mass Index (BMI) and WC both poses limitations in assessing the Lipid accumulation product (LAP), because BMI assess overall fat but fails to distinguish the specific body composition and WC assess abdominal fat but fails to differentiate between subcutaneous and visceral fat [7, 8].

To address these limitations, a researcher named Kahn in 2005 introduced an index called LAP index which combines both WC and fasting TG levels, these parameters are stable and cost effective to acquire. As both WC and TG values tend to increase with age, they reflect cumulative changes over time and are linked to metabolic insulin resistance, chronic triglyceridemic and risks related to cardiovascular health [9–11]. This makes the LAP, a suitable tool for clinicians to assesses patients for identifying individuals at the cardiac related risks [8].

Research shows that LAP is associated with various health issues including polycystic ovarian syndrome, diabetes mellitus, cardiovascular diseases, mild cognitive impairment and chronic obstructive pulmonary disease [4, 7, 8, 12]. Although previous studies have focused mainly on LAP in relation to above conditions, there is a lack of studies examining hypothyroid conditions. Notably there is a gap in research concerning the Indian population and the influence of LAP scores in hypothyroid patients. This study aims to investigate LAP levels among euthyroid, subclinical hypothyroid and overt hypothyroid groups, assessing their correlation with TSH levels. ultimately, the objective is to establish the potential of LAP scores in predicting cardiovascular risk in the context of hypothyroidism.

Material and methods

Study design and population

The total of 150 participants were included in this cross-sectional descriptive study, among them 50 were euthyroid controls, 50 were subclinical hypothyroid and 50 were overt hypothyroid individuals. The healthy individuals without any current or previous history of thyroid disorder were classified as control group who have attended the master health check-up services at Tertiary Care Centre, India.

The Institutional Ethics Committee of Sri Ramachandra Institute of Higher Education and Research granted the ethical permission (Reference No: CSP/21/AUG/97/421) and prior to enrolment, written informed consent was obtained from all study participants.

Inclusion and exclusion criteria

This study included patients aged 18 years and above; who were diagnosed with hypothyroidism who routinely visiting the department of Endocrinology.

The study excluded individuals who have the history of diabetes mellitus, pre-existing cardiovascular diseases or any metabolic syndrome and in order to avoid confounding bias, patients under hypolipidemic medications were also excluded.

Study parameters

The information on demographic characteristics and clinical history was collected using a questionnaire.

Anthropometric measures such as weight, height and waist circumference were collected by trained technicians using standardized protocols. A standard analog weighing machine was used to measure the body weight and a digital stadiometer with an adjustable headpiece and fixed vertical backboard was used to measure the standing height. Waist circumference was measured using a flexible measuring tape. Fasting plasma glucose and serum triglyceride levels were evaluated using standard laboratory methods. Lipid accumulation product (LAP) was calculated using the following formulae (6,9).

$$\text{For men: LAP} = [\text{Waist circumference (cm)} - 65] \times [\text{Triglyceride concentration (mmol/L)}]$$

$$\text{For women: LAP} = [\text{Waist circumference (cm)} - 58] \times [\text{Triglyceride concentration (mmol/L)}]$$

Statistical analysis

Data collection was done using Microsoft Excel and the statistical analysis were done using SPSS software version 24.0. The mean and standard deviation (SD) was used to express numerical variables and independent T-test were used to compare quantitative variables. The relationship between variables was analyzed using Pearson correlation analysis. A statistically significant p-value is defined as <0.05.

Results

Baseline characteristics of study population

In this study total of 150 participants included and they were classified into three groups: Euthyroid controls, Subclinical hypothyroidism and overt hypothyroidism groups. 50 participants in each group. Of these

22 (44%) males and 28 (56%) females in euthyroid control group; 6 (12%) males and 44 (88%) females in subclinical hypothyroidism group; while 7 (14%) males and 43 (86%) females in overt hypothyroidism group.

Table 1 summarizes the baseline characteristics of study population including age, weight, thyroid profile parameters, fasting plasma glucose (FPG), serum triglycerides and BMI. Age, weight, serum TSH, FT4, TG and FPG levels showed significant difference across all three groups ($p < 0.005$). There was no significant difference observed in BMI between groups ($p = 0.102$).

Waist circumference and lipid accumulation product across study groups

Table 2 summarizes the LAP and WC values across the groups. The LAP values also showed significant increase across all the three study groups ($p < 0.001$). Highest LAP values found in overt hypothyroid patients while lowest found in euthyroid controls.

All the three study groups showed substantial increase in WC values. Higher WC values were found in subclinical and overt hypothyroidism groups than euthyroid control group. Among all the groups, highest WC values were found in overt hypothyroid patients ($p < 0.001$).

Correlation between LAP and other parameters

According to Pearson correlation analysis, LAP and WC had a strong positive correlation among the study population ($r = 0.935$, $p < 0.001$) suggesting that higher central adiposity was linked with increased LAP values. Additionally, WC showed a positive correlation with BMI ($r = 0.448$, $p = 0.001$).

Serum TSH levels were positively correlated with both LAP ($r = 0.390$, $p < 0.001$) and WC ($r = 0.365$, $p < 0.001$) values. The positive association was observed between

Table 1: Baseline characteristics and biochemical parameters of the study population across euthyroid, subclinical and overt hypothyroid groups.

Parameters	Euthyroid controls (n=50)	Subclinical hypothyroidism (n=50)	Overt hypothyroidism (n=50)	P-value
Age (years)	41±9.11	39.16±13.13	32.60±9.99	<0.001**
Weight (kg)	63.18±14.02	63.15±13.61	70.16±12.77	0.013*
TSH (mIU/L)	1.94±0.78	5.67±1.83	17.35±7.56	<0.001**
FT4 (ng/dL)	1.36±0.39	1.21±0.30	0.65±0.28	<0.001**

Table 1: Continued.

Parameters	Euthyroid controls (n=50)	Subclinical hypothyroidism (n=50)	Overt hypothyroidism (n=50)	P-value
TG (mg/dL)	127.1±5.47	137.6±19.49	142.1±16.48	<0.001**
FPG (mg/dL)	94.5±15.78	142.4±39.63	139.1±18.08	<0.001**
BMI (kg/m ²)	26.2±3.85	24.7±5.27	26.7±4.59	0.102

Note: TSH – Thyroid stimulating Hormone; FT4 – free Thyroxine; TG – Triglycerides; FPG – fasting plasma glucose; BMI – Body Mass Index; kg – kilograms; mIU/l – milli-international units per Liter; ng/dL – nanograms per deciliter; mg/dL – milligrams per deciliter; kg/m² – kilograms per square meter. * – denotes statistically significant.

LAP and TSH, indicating a trend toward increased lipid accumulation with raising TSH levels. Age and LAP values do not significantly correlate ($r=-0.206$, $p=0.028$). LAP and BMI have weak and inconsistent association ($r=0.132$, $p=0.163$).

ROC analysis of LAP, WC and TG

Receiver operating Characteristic (ROC) curve analysis was conducted to evaluate the predictive performance of LAP, WC and TG for cardiovascular risk. The area under the curve (AUC) for LAP was 0.765 (95% CI:0.683–0.846), WC was 0.769 (95% CI: 0.688–0.805) and TG was 0.777 (95% CI: 0.704–0.849), demonstrating a similar predictive performance among the parameters (Figure. 1).

Discussion

The purpose of this study was to analyse the metabolic characteristics of euthyroid and hypothyroid participants and to determine cardiovascular risk using the LAP values and TSH levels. We found that in comparison to euthyroid controls, hypothyroid individuals had noticeably higher LAP levels. Pearson’s correlation analysis showed a significant positive correlation between LAP and TSH levels.

The present study findings underscore a significant link between thyroid dysfunction, particularly elevated TSH levels and increased lipid accumulation, as reflected by higher LAP values. LAP, which incorporates both anthropometric and biochemical factors related to lipid dysregulation and is derived from WC and TG levels, becoming more widely acknowledged as an indicator of central adiposity and metabolic risk.

Our results show a strong correlation between LAP and TSH levels are in agreement with previous research. Elevated TSH levels are consistently associated with higher lipid accumulation in South Asian populations, such in India, Nepal and Pakistan. Studies conducted in Indian hospitals show a significant positive association between TSH and LAP, indicating a direct link between the severity of thyroid disease and central adiposity [10].

In 2021, Rajaragupathy *et al.* found that hypothyroid patients had significantly higher LAP values than euthyroid controls in a hospital-based study from southern India. They also found a strong positive correlation between TSH and LAP, indicating a direct substantial increase in lipid accumulation with worsening thyroid dysfunction and these emphasizing LAP as a cardiovascular risk indicator [10]. In 2025, similarly an investigation carried out in Nepal by Pandey *et al.* found that hypothyroid people have noticeably higher LAP levels. Multivariate regression findings showed

Table 2: Comparison of waist circumference and lipid accumulation product values among euthyroid, subclinical and overt hypothyroid groups.

Parameters	Euthyroid controls (n=50)	Subclinical hypothyroidism (n=50)	Overt hypothyroidism (n=50)	P-value
WC (cm)	83.35±3.10	88.22±15.76	96.86±13.21	<0.001*
LAP	34.09±5.85	42.24±17.52	51.26±16.99	<0.001*

Note: WC – waist circumference; LAP – Lipid Accumulation Product; cm – centimeter. * – denotes statistically significant.

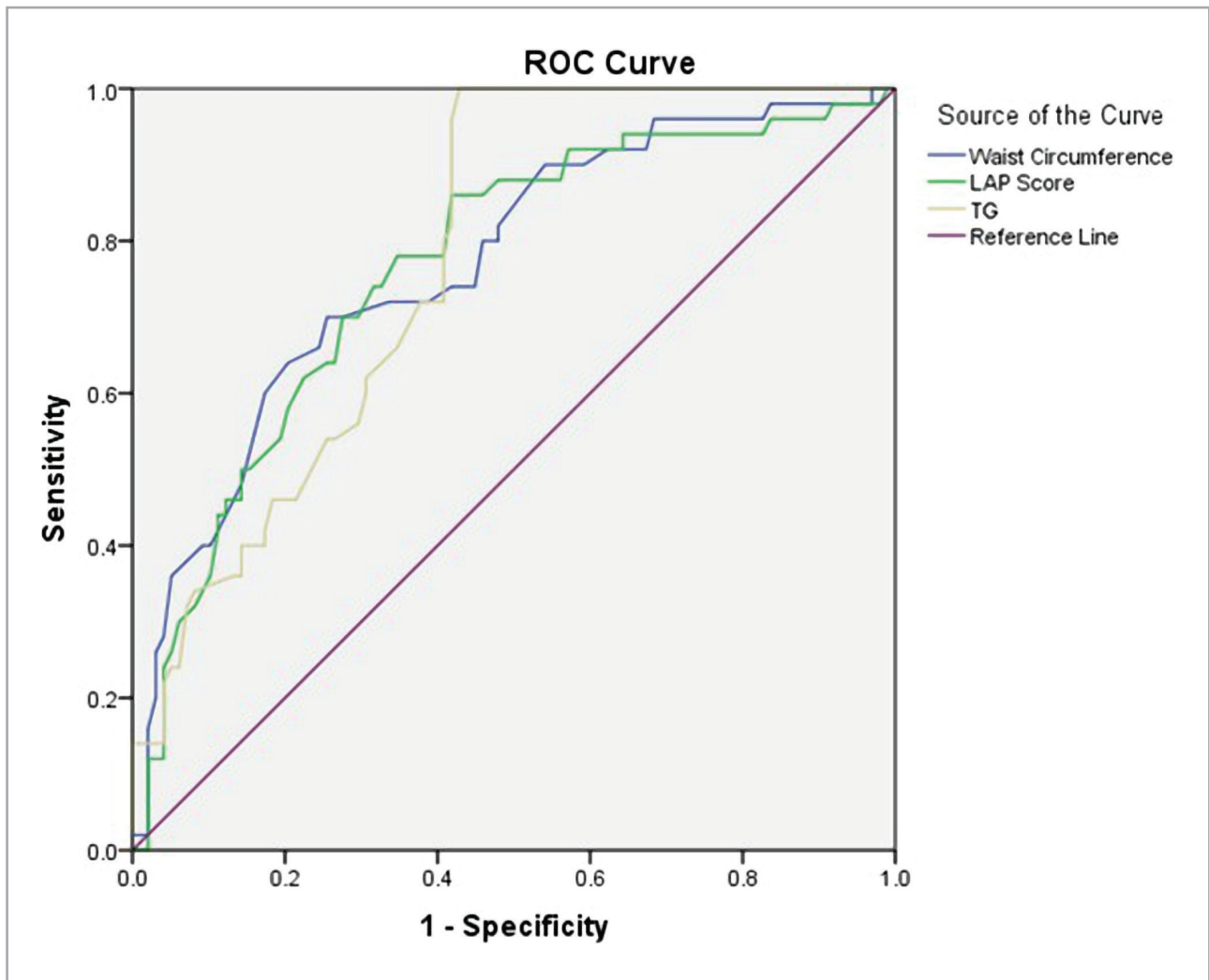


Figure 1: Receiver operating characteristic (ROC) curve analysis showing the area under the curve (AUC) of waist circumference, lipid accumulation product (LAP), and triglycerides (TG) in predicting metabolic risk.

that TSH independently predicted higher LAP values after adjusting for confounders [6].

The involvement of thyroid dysfunction in lipid dysregulation and cardiometabolic risk is further supported by population-based studies, as demonstrated by Anwar *et al.*, 2024 who conducted a prospective cohort study in Pakistan population and found a high correlation between hypothyroidism and dyslipidaemia and hypertension [2]. All of these results support the usefulness of LAP as an easy-to-use, affordable marker of metabolic risk in those with high TSH levels. The observed trend of lipid abnormalities in those with raise in TSH levels serves as pathophysiological evidence for increased LAP in hypothyroid conditions. Considering all studies together, greater TSH levels are associated with increased lipid accumulation and metabolic risk in South Asian population.

In hypothyroid individuals, rising levels of LAP suggest that thyroid disorders elevate metabolic risk

beyond traditional lipid indicators. LAP measures the integrated burden of visceral fat accumulation and excess circulating lipids, both vital to insulin resistance and cardiometabolic health, unlike separate measurements of triglycerides or waist circumference [8].

The persistent correlation between TSH and LAP in South Asians suggests that LAP can be a basic, affordable and quickly reproducible marker for early identification of metabolic risk in resource limited settings. Incorporating LAP assessment into routine screening for those with thyroid dysfunction may enable early identification and subsequent lifestyle or treatment modifications to address the cardiometabolic risks.

This cross-sectional study design restricts the ability to determine the relationship between TSH levels and lipid accumulation. These results from single-center study might not be applicable to all population. Significant confounding factors were not evaluated, which includes diet pattern, exercise and insulin

resistance. Long-term cardiometabolic outcomes were not investigated and thyroid function was assessed at a single time point.

Conclusion

Our study showed a positive correlation trend between LAP and TSH levels and also demonstrates that hypothyroidism is associated with elevated lipid accumulation, reflecting early metabolic disturbances and increased cardiometabolic risk. Considering its simplicity, LAP may serve as a practical screening tool in resources limited settings. Larger prospective and multicentre studies were warranted to set optimal LAP cut-off values and to evaluate its predictive value for future cardiovascular outcomes. This research aligns with the United Nations Sustainable Development Goal 3 (Good Health and Well-Being) and contributes to healthcare-related research.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Institutional Ethics Committee of Sri Ramachandra Institute of Higher Education and Research, Chennai. (Reference No: CSP/21/AUG/97/421), Dated: 14.09.2021.

Consent to participate

Written informed consent was obtained from all the participants.

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