International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-09-67*

Assessment of cardiometabolic index (CMI) and Lipid Accumulation Product (LAP) Index in metabolic syndrome patients.

Dr. Narayana Swamy Y N[1]*, Dr. Mallikarjun[2], Dr. Madhuvan HS[3].

[1]Associate Professor, Department of General Medicine, Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India.

[2]Associate Professor, Department of General Medicine, Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India.

[3]Professor & Unit Head, Department of General Medicine, Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India.

Correspondence:
Dr. Narayana Swamy Y N.
Associate Professor, Department of General Medicine, Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India.

Received: 07-08-2026
Revised: 18-08-2026
Accepted: 10-09-2026
Published: 12-09-2026

Abstract

Background: Metabolic syndrome (MetS), also known as syndrome X, a complex multifactorial disease. MetS usually occurs from unhealthy dietary habits and sedentary lifestyles. MetS, considered as a valuable health tool for assessing individuals at high risk of type 2 diabetes (T2DM), cardiovascular diseases, chronic kidney disease, some cancers, and early death. The preset study was undertaken to assess the cardiometabolic index (CMI), Lipid Accumulation Product (LAP) index in patients with metabolic syndrome and non-metabolic syndrome. ***MATERIALS AND METHODS:*** A total of 240 subjects were involved in this study. They were categorized into 120 patients with metabolic syndrome and 120 non- metabolic syndrome. This prospective cross-sectional study was conducted at in Department of General Medicine, Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India. The study has been approved by the Institutional Ethics Committee and informed consent was obtained from all the study participants. Body weight and height were measured. The BMI was calculated. Waist circumference (WC)was measured. Blood pressure (DBP) was measured. Under aseptic conditions, five ml fasting venous blood samples were collected from all the study subjects, transferred 2 ml into fluoride tube and 3 ml in plain tube. The samples were centrifuged at 3000rpm for five minutes to obtain plasma/serum. The obtained plasma/serum sample was used for estimation of glucose, total cholesterol, triglycerides, HDLC were estimated by using Biochemistry fully auto analyzer. LDLC and VLDLC were calculated by Frieldwald's formula. CMI index and LAP index were calculated. A detailed physical, clinical examination was done for all the study participants. Demographic details and anthropometric parameters of all the participants were be recorded. ***RESULTS:*** In the present study, mean age of 48.5±15.8 years, WC 124.2±13.1 cm, WHR 0.89±0.08 and BMI 29.8±2.1 kg/m2 were significantly increased in patients with metabolic syndrome compared to non-metabolic syndrome subjects. In this study, mean SBP 136.4±12.5 mmHg, DBP 78.5±8.7 mmHg, serum glucose 110.9±15.9 mg/dl, cholesterol 190.5±28.9 mg/dl, triglycerides 177.1±49.5 mg/dl, LDLC 125.5±15.2 mg/dl, VLDLC 35.4±10.1 mg/dl, CMI 1.75±1.0 and LAP index 117.5±51.2 were significantly increased whereas HDLC 30.2±8.5 mg/dl was significantly decreased in patients with metabolic syndrome compared to non- metabolic syndrome subjects. ***CONCLUSION:*** The present study may conclude that CMI and LAP index were significantly increased in patients with metabolic syndrome.

Keywords: Metabolic syndrome, Cardiometabolic syndrome, Lipid accumulation product index, Insulin resistance.

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INTRODUCTION

Metabolic syndrome (MetS), also known as syndrome X, a complex multifactorial disease associated with central obesity, insulin resistance (IR), abnormal glucose regulation, elevated blood pressure, low high-density lipoprotein (HDL) cholesterol and increased triglycerides. [1]

MetS, indicates a cluster of interrelated cardiometabolic risk factors, and bridging the transition from metabolic homeostasis to overt cardiovascular diseases (CVDs), causing the increased CVD risk. [2,3]

MetS usually occurs from unhealthy dietary habits and sedentary lifestyles and is also considered as a valuable health tool for assessing individuals at high risk of type 2 diabetes (T2DM), cardiovascular diseases, chronic kidney disease, some cancers, and early death. [4]

Globally, the prevalence of MetS is increasing, especially in low- and middle-income countries where urbanisation, unhealthy dietary habits and sedentary lifestyles have accelerated its burden. A very recent meta-analysis data collected between 1990 and 2018 and reported a global prevalence ranging from 12.5% to 31.4%, [5] In India, recent epidemiological study reported that approximately 30% of adults meet the MetS criteria. [6]

Wakabayashi et al., in 2015 proposed cardiometabolic index (CMI) as an innovative tool for evaluation of metabolic diseases. CMI integrates the waist-to-height ratio (WHR) and the triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C). [7] The CMI provides a comprehensive assessment of abdominal fat distribution and abnormalities in lipid metabolism. In contrast to conventional metrics such as BMI and waist circumference (WC), the CMI exhibits superior clinical utility in predicting metabolism-related chronic conditions. [8]

Recent studies have reported strong correlation of CMI with insulin resistance (IR) and suggested that CMI is superior to traditional indices like BMI in predicting metabolic syndrome. [9,10] The CMI reflects both dyslipidemia and central obesity, key components of insulin resistance (IR) and metabolic dysfunction. [11] In addition, CMI exhibits associations with non-alcoholic fatty liver disease (NAFLD), chronic kidney disease (CKD), CVD, and stroke [12–14].

In 2005, Kahn et al., introduced a new index "Lipid Accumulation Product (LAP) Index", a better indicator of MetS, as it reflects the central lipid accumulation. The LAP is based on waist circumference (WC) and fasting triglyceride levels. As the LAP index includes two of the five components of metabolic syndrome, it can serve as a reliable indicator of MetS. [15] A few studies have reported that LAP index may be an indicator of NAFLD, MetS, and also related to the risk of cardiovascular events. [16-18] However, a limited studies were conducted in relation with CMI, LAP index in patients with metabolic syndrome. Therefore, the preset study was undertaken to assess the cardiometabolic index (CMI), Lipid Accumulation Product (LAP) index in patients with metabolic syndrome and non-metabolic syndrome.

MATERIALS AND METHODS

Study subjects

A total of 240 subjects were involved in this study. They were categorized into 120 patients with metabolic syndrome and 120 non- metabolic syndrome. This prospective cross-sectional study was conducted at in Department of General Medicine, Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India. The study has been approved by the Institutional Ethics Committee (AIMSRC/IEC/97/2024-25) and informed consent was obtained from all the study participants.

Sample Size Calculation

The sample size was calculated by using the formula n= (Z21-α/2.P.Q/d2). Simple random sampling method was followed for recruiting the study subjects.

Inclusion Criteria

Subjects willing to participate in the study, individuals of both sexes aged > 18 years, subjects with metabolic syndrome, non-metabolic syndrome, non-alcoholic patients, diabetic patients without comorbidities were included in the study.

Exclusion Criteria

Subjects not willing to participate in the study, patients with secondary obesity brought on by genetic diseases, congenital heart disease, endocrine abnormalities, patients with hypothyroidism, celiac disease, history of myocardial infarction, dermatomyositis etc. were excluded.

Anthropometry

Body weight and height were measured using a scale with stadiometer. The BMI was calculated as weight (kg)/height (m)2. Waist circumference (WC)was measured at the midpoint between the last rib and the iliac crest and hip circumference (HC) was measured at the largest parts around the buttocks using a flexible tape measure.
Systolic (SBP) and diastolic blood pressure (DBP) was measured by using sphygmomanometer using appropriated sized cuffs.

Sample collection, laboratory and clinical measurements

Under aseptic conditions, five ml fasting venous blood samples were collected from all the study subjects, transferred 2 ml into fluoride tube and 3 ml in plain tube. The samples were centrifuged at 3000rpm for five minutes to obtain plasma/serum.

The obtained plasma/serum sample was used for estimation of glucose (GOD-POD) total cholesterol (cholesterol oxidase/peroxidase), triglycerides (glycerol phosphate oxidase/peroxidase), HDLC (HDLC- Direct) were estimated by using Biochemistry fully auto analyzer. LDLC and VLDLC were calculated by Frieldwald's formula.

Indexes

The CMI and LAP index wee calculated by using the following formulas. [7,15]

CMI index:

CMI (males/females): Triglyceride (mg/dl) /HDLC (mg/dl) x WHtR

LAP index:

Men: (Waist circumference (cm) - 65) x TG (mg/dl)

Women: (Waist circumference (cm) - 58) x TG (mg/dl)

A detailed physical, clinical examination was done for all the study participants. Demographic details and anthropometric parameters of all the participants were recorded.

Diagnosis of metabolic syndrome:

The diagnosis of metabolic syndrome was made based on the IDF criteria [19]

adult patients with obesity were identified as having metabolic syndrome if they had three or more of the following altered factors:

a) Abdominal obesity (WC ≥ 102 cm for males; ≥88 cm for females);
b) Elevated triglycerides: ≥150 mg/dL (1.7 mmol/L) or specific treatment for this
c) Lipid abnormality;
d) Reduced HDL-C: <40 mg/dL (1.0 mmol/L) in males; <50 mg/dL (1.3 mmol/L) in females, or specific treatment for this lipid abnormality;
e) Increased BP: SBP ≥ 130 mmHg or DBP ≥ 85 mmHg and/or the treatment of previously diagnosed hypertension;
f) An increased fasting plasma glucose (FPG) concentration ≥100 mg/dL (5.6 mmol/L)

or previously diagnosed type 2 diabetes mellitus.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and categorical variables as numbers and percentage. Mann-Whitney U test was applied. The p value ($p < 0.05$) was considered as statistically significant. Data analysis was done by using SPSS 22.0.

RESULTS

In the present study, mean age of 48.5±15.8 years, WC 124.2±13.1 cm, WHR 0.89±0.08 and BMI 29.8±2.1 kg/m^2 were significantly increased in patients with metabolic syndrome compared to non-metabolic syndrome subjects as shown in table 1.

Table 1. Comparison of demographic and Anthropometric parameters among of study subjects.

Parameters	MetS cases, (n=120) Mean±SD	Non-MetS, (n=120) Mean±SD	P-value
Demographic			
Age (Years)	48.5±15.8	44.2±12.5	<0.001
Male (n,%)	75 (62.5%)	70 (58.3%)	-
Female (n,%)	45 (37.5%)	50 (41.7%)	-
Anthropometric parameters			
WC (cm)	124.2±13.1	113.2±9.5	<0.001
HC (cm)	131.5±12.5	129.9±15.3	0.075
WHR	0.89±0.08	0.51±0.05	<0.001
BMI (kg/m^2)	29.8±2.1	22.3±3.2	<0.001

* p value<0.05 is considered as statistically significant.

In this study, mean SBP 136.4±12.5 mmHg, DBP 78.5±8.7 mmHg, serum glucose 110.9±15.9 mg/dl, cholesterol 190.5±28.9 mg/dl, triglycerides 177.1±49.5 mg/dl, LDLC 125.5±15.2 mg/dl, VLDLC 35.4±10.1 mg/dl, CMI 1.75±1.0 and LAP index 117.5±51.2 were significantly increased whereas HDLC 30.2±8.5 mg/dl was significantly decreased in patients with metabolic syndrome compared to non- metabolic syndrome subjects as shown in table 2.

Table 2. Comparison of Clinical and laboratory parameters among of study subjects.

Parameters	MetS cases, (n=120) Mean±SD	Non-MetS, (n=120) Mean±SD	P-value
SBP (mmHg)	136.4±12.5	110.2±10.1	<0.001
DBP (mmHg)	78.5±8.7	75.3±7.6	<0.001
Serum glucose (mg/dl)	110.9±15.9	80.5±12.4	<0.001
Total Cholesterol (mg/dl)	190.5±28.9	160.5±38.8	<0.001
Triglycerides (mg/dl)	177.1±49.5	105.3±20.8	<0.001
HDLC (mg/dl)	30.2±8.5	45.2±10.7	<0.001
LDLC (mg/dl)	125.5±15.2	93.8±23.1	<0.001
VLDL (mg/dl)	35.4±10.1	21.0±5.2	<0.001
CMI	1.75±1.0	0.91±0.5	<0.001
LAP index	117.5±51.2	70.1±25.9	<0.001

* p value<0.05 is considered as statistically significant.

DISCUSSION

Metabolic syndrome, is a complex disease that combines a variety of metabolic alterations. Due to its significant increase in the prevalence and in fact, that MetS is a high-risk complication. Therefore, its early identification could allow for proper nutritional or pharmacological treatments, which are crucial in preventing the occurrence of cardiovascular diseases and mortality associated with the progression of those conditions. [20]

For these reasons, the preset study was designed to assess the cardiometabolic index (CMI), Lipid Accumulation Product (LAP) index in patients with metabolic syndrome. In the current study, mean age, WC, WHR and BMI were significantly increased in patients with metabolic syndrome compared to non-metabolic syndrome. In this, mean SBP, DBP, serum glucose, cholesterol, triglycerides, LDLC, VLDLC, CMI and LAP index were significantly increased whereas HDLC was significantly decreased in patients with metabolic syndrome compared to non- metabolic syndrome subjects.

CMI and MetS share a common pathophysiology rooted in visceral adiposity, Insulin Resistance (IR) and chronic low-grade inflammation. In the case of obese subjects, an excess of free fatty acids (FFA) can impair the functions of insulin, and results in the development of IR. Additionally, subjects with abdominal obesity may experience a reduction in binding affinity and also the quantity of insulin receptors on target tissues, resulting in a diminished capacity to respond to glucose. Moreover, an increased triglyceride levels plays a role in the development of IR similar to that of abdominal obesity. Additionally, decreased levels of HDL-C may adversely affect the functioning of β-cells, and lead to decreased insulin output and sensitivity, there exists a "vicious cycle" between IR and high CMI. [21]

In support of our study findings, a study conducted by Tamini S et al., reported that a significant increase in CMI and LAP index. They suggested that LAP index and CMI performed better than BAI in ROC analysis in detecting MetS both in general population with obesity and in male/female subgroups. [22] Azarboo A et al., conducted as meta-analysis with ten studies with 51,037 participants. Individuals with Metabolic dysfunction-associated steatotic liver disease (MASLD) had significantly higher CMI compared to those without MASLD. CMI correlates strongly with MASLD, suggesting its potential as a non-invasive tool for early detection and risk stratification. [23] In a cohort study conducted by Li J et al., reported that elevated CMI index is significantly and positively associated with increased risks of all-cause and diabetes-related mortality among U.S. adults with cardiometabolic syndrome (CMS). [24]

Similarly, another cross-sectional study conducted by Wu L et al., reported that CMI was correlated with HOMA-IR in patients with T2DM. Through the multiple logistic regression analysis, CMI was significantly correlated with IR. In addition, a non-linear correlation between CMI and IR risk was identified. The AUC of CMI was the largest compared with traditional indexes of adiposity and blood lipids. According to the subgroup analysis, the two had a more significantly positive correlation in females, the elderly and subjects with HbA1c < 7%. [25] In a cross-sectional study by An-Bang Liu et al., reported that multivariate regression indicated a positive correlation between CMI and glucose metabolic biomarkers, including FBG, HbA1c, FSI, and HOMA-IR. There were also significant correlations between CMI and increased risk of IR, preDM, and DM. Inverse nonlinear L-shaped associations were found between CMI and IR, preDM, and DM, with saturation inflection points at 1.1, 1.45, and 1.6, respectively. Below these thresholds, increments in CMI significantly correlated with heightened risks of IR, preDM, and DM. They concluded that, CMI exhibited inverse L-shaped nonlinear relationships with IR, preDM, and DM, suggesting that reducing CMI to a certain level might significantly prevent these conditions. [26]

In this study, LAP index was also significantly increased in MetS patients than non-MetS patients. The LAP index is a simple parameter calculated from waist circumference and triglycerides and is associated with dysfunctional and lipolytic

adipose tissue, a key factor in the development of the MetS. Waist circumference, a parameter of the LAP, represents abdominal subcutaneous adipose tissue and visceral adipose tissue. [27] Current research suggests that MetS develops after an accumulation of abdominal fat, and dyslipidemia precedes the occurrence of MetS. Therefore, LAP may have an ability to predict MetS in the early stages. [28] The WHR requires only a single anthropometric measurement of waist and height, however, the use of LAP as a predictor of MetS is more advantageous. Waist circumference (WC) is unable to distinguish between visceral and subcutaneous adipose tissue. Visceral adiposity is strongly associated with cardiometabolic risks than subcutaneous adipose tissue. Visceral adipose tissue adipocytes have a higher rate of lipolysis and also produce more adipocytokines, like interleukin-6 (IL-6) and plasminogen activator inhibitor-1. Therefore, it is very important to include a routinely applicable indicator for evaluation of visceral adiposity. Triglyceride has been reported as a significant correlate of visceral adipose tissue in healthy subjects. [29] Furthermore, the use of triglyceride levels in combination with waist circumference, termed hypertriglyceridemic waist, has been shown to be able to identify individuals with the greatest amount of visceral fat and to be associated with increased risk of MetS. [30]

In support of our findings, a cross-sectional study conducted by Bohlouli Sardroudi S et al., assessed the association between lipid accumulation product (LAP) index and anthropometric indices, metabolic factors and hepatic function markers in obese subjects with NAFLD. They reported a significant difference in body weight, WC, fasting blood sugar (FBS) and lipid profile among LAP index quartiles. Moreover, the LAP index showed a positive correlation with body weight, liver function, with lipid profile in all of the subjects with NAFLD. [31] In a cross-sectional study by Mariana Amaral Raposo et al., aimed to assess the accuracy of the LAP index to identify metabolic syndrome in people living with HIV. A positive and significant correlation was found between the metabolic syndrome and LAP ($r=0.401$; $P<0.01$), metabolic syndrome and body mass index ($r=0.361$; $P<0.01$) and metabolic syndrome and waist circumference ($r=0.427$; $P<0.01$) in our sample. The analysis of the receiver-operating characteristic (ROC) curve revealed that the best cut-off value for LAP index to define metabolic syndrome was 59.4 (sensitivity 80%, specificity 79% and area under the curve (AUC) of 0.875. They concluded that ROC curves analysis demonstrated a good diagnostic accuracy of the LAP index in order to predict metabolic syndrome. [32] Yet, Jui-Kun Chiang et al., conducted a study with aim of investigate the use LAP index to predict MetS in Taiwanese adults. They reported that LAP showed the highest prediction accuracy among adiposity measures with an area under the ROC curve (AUC) of 0.901. This was significantly higher than the adiposity measure of waist-to-height ratio (AUC = 0.813). They concluded that LAP index was a simple and accurate predictor of MetS in Taiwanese people aged 50 years and over. LAP had significantly higher predictability than other adiposity measures tested. [33]

Hewage N et al., conducted a cross-sectional study to explore the effectiveness of the cardiometabolic index (CMI), lipid accumulation product (LAP) index and waist-to-thigh ratio (WTR) in identifying insulin resistance (IR) in females who are clinically not having diabetes mellitus (DM) by recruiting 282 females subjects. The participants were divided into two groups based on BMI as normal weight controls (n=142) and overweight/obese cases (n=140). They reported that significant associations were identified between all adiposity indexes, IR, and lipid profile parameters. They concluded that, CMI had highest accuracy for detecting IR. [34].

CONCLUSION

The present study may conclude that significant increase in mean age, WC, WHR and BMI, SBP, DBP, serum glucose, cholesterol, triglycerides, LDLC, VLDLC, CMI and LAP index whereas HDLC showed significant decrease in patients with metabolic syndrome compared to non- metabolic syndrome subjects. Further studies with large sample size are recommended.

Acknowledgements: We would like to thank the authorities of Akash Institute of Medical Sciences and Research Centre (AIMSRC), Bengaluru, Karnataka, India.
Conflict of interest: Nil
Funding: Nil.

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