Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

An Evaluation of LECT2 and Its Links to Insulin Resistance and Metabolic Syndrome in Type 2 Diabetic Patients: A Cross-Sectional Study.

Dr. A Benitha Dev Sheeela[1], Dr. A Jamuna Rani[2], Dr Assayas Bosco Chandrakumar[3], Dr G Somasundaram[4]

[1]Research Scholar, Department of Biochemistry, Bharath institute of higher education and research, selaiyur, Chennai.
[2]Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital (BIHER), Chromepet, Chennai
[3]Professor, Department of Surgery, Sri Lakshmi Narayana Institute of Medical Sciences (BIHER, Chennai) Osudu, Puducherry 605502.
[4]Professor &HOD, Department of Pharmacology, Sri Lakshmi Narayana Institute of Medical Sciences (BIHER,Chennai) Osudu, Puducherry 605502.

*Corresponding Author

Article History
Received: 15.09.2025
Revised: 30.09.2025
Accepted: 14.10.2025
Published: 03.11.2025

Abstract: ***Background:*** Leukocyte-Derived Chemotaxin-2 (LECT2) is a hepatokine that plays a crucial role in glucose and lipid metabolism, inflammation, and insulin resistance. Growing evidence suggests its involvement in the pathogenesis of metabolic syndrome, particularly among individuals with Type 2 Diabetes Mellitus (T2DM). This study aimed to evaluate the association between serum LECT2 levels, insulin resistance, and metabolic syndrome in patients with T2DM. ***Methods:*** A cross-sectional study was conducted among 200 patients with T2DM. Clinical parameters, anthropometric measurements, and biochemical investigations were recorded. Serum LECT2 levels were estimated using enzyme-linked immunosorbent assay (ELISA). Insulin resistance was assessed using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR). The diagnosis of metabolic syndrome was based on the International Diabetes Federation (IDF) criteria. Correlation, regression, and receiver operating characteristic (ROC) analyses were performed to determine the relationship and diagnostic performance of LECT2. ***Results:*** Among 200 participants, 128 (64%) had metabolic syndrome. Serum LECT2 levels were significantly higher in patients with metabolic syndrome compared to those without (30.1 ± 8.1 ng/mL vs. 22.7 ± 6.3 ng/mL; $p < 0.001$). LECT2 showed strong positive correlations with BMI ($r = 0.43$), waist circumference ($r = 0.39$), fasting insulin ($r = 0.51$), HOMA-IR ($r = 0.57$), and triglycerides ($r = 0.36$), and a negative correlation with HDL-C ($r = -0.32$). ROC analysis revealed good diagnostic accuracy of serum LECT2 for metabolic syndrome (AUC = 0.81, 95% CI: 0.74–0.88, $p < 0.001$). Multivariate logistic regression confirmed that higher BMI, triglycerides, HOMA-IR, and LECT2 levels were independent predictors of metabolic syndrome ($p < 0.01$). ***Conclusion:*** Elevated serum LECT2 levels are strongly associated with insulin resistance and metabolic syndrome among patients with T2DM. LECT2 may serve as a potential biomarker for identifying metabolic dysfunction and assessing cardiometabolic risk in diabetic individuals.

Keywords: LECT2; Insulin resistance; Type 2 diabetes mellitus; Metabolic syndrome; Hepatokine; HOMA-IR; Biomarker

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from a combination of insulin resistance and pancreatic β-cell dysfunction. The global burden of T2DM has risen alarmingly over the past few decades, making it a major public health problem and one of the leading causes of morbidity and mortality worldwide [1]. Insulin resistance represents the central feature in the pathophysiology of T2DM and is frequently associated with a cluster of metabolic abnormalities such as central obesity, dyslipidemia, hypertension, and glucose intolerance, collectively known as metabolic syndrome [2]. These conditions not only worsen glycemic control but also increase the risk of cardiovascular and hepatic complications [3].

The liver plays a key role in maintaining metabolic homeostasis by producing and secreting several hormones and proteins known as hepatokines, which influence glucose and lipid metabolism in peripheral tissues. Among these hepatokines, Leukocyte Cell-Derived Chemotaxin-2 (LECT2) has emerged as an important mediator linking hepatic function, inflammation, and metabolic regulation [4]. LECT2 was originally identified as a chemotactic factor secreted by hepatocytes and neutrophils and later recognized as a hepatokine involved in energy metabolism and insulin signaling [5].

Experimental studies have revealed that LECT2 impairs insulin signaling by activating the c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) pathways, thereby inhibiting glucose uptake in skeletal muscle and adipose tissue [6,7]. Elevated LECT2 expression has been demonstrated in obesity and fatty liver disease, and serum LECT2 levels positively correlate with insulin resistance indices such as fasting insulin and HOMA-IR [8]. These findings suggest that LECT2 acts as a hepatokine linking hepatic steatosis to systemic insulin resistance and inflammation [9].

Clinical studies have reported that circulating LECT2 levels are increased in individuals with obesity, metabolic syndrome, and non-alcoholic fatty liver disease (NAFLD) [10,11]. LECT2 levels have shown positive correlations with body mass index (BMI), waist circumference, triglycerides, and fasting glucose, indicating its involvement in metabolic dysregulation [12]. Furthermore, studies have demonstrated that serum LECT2 concentrations are higher in patients with insulin resistance and T2DM compared to healthy individuals [13]. However, most of these studies have been conducted in specific ethnic populations, and data among Indian patients with T2DM remain limited.

Understanding the relationship between LECT2, insulin resistance, and metabolic syndrome could help clarify the metabolic pathways that link liver-derived factors with peripheral insulin action. Given the rising prevalence of T2DM and metabolic syndrome in the Indian population, investigating serum LECT2 levels may provide insight into its potential as a biomarker for insulin resistance and cardiometabolic risk prediction.
Therefore, the present study was conducted to evaluate the associations between serum LECT2 levels, insulin resistance, and metabolic syndrome among patients with type 2 diabetes. Exploring this relationship could improve understanding of hepatokine-mediated metabolic regulation and identify possible therapeutic targets for insulin resistance and related metabolic disorders.

MATERIAL AND METHODS

This cross-sectional study was conducted among patients diagnosed with Type 2 Diabetes Mellitus (T2DM) attending the outpatient department of endocrinology and metabolism at a tertiary care hospital. A total of 200 participants aged between 30 and 70 years were included. The diagnosis of T2DM was based on the American Diabetes Association (ADA) criteria, which include fasting plasma glucose ≥126 mg/dL, 2-hour plasma glucose ≥200 mg/dL during an oral glucose tolerance test (OGTT), or HbA1c ≥6.5% [1]. Patients with type 1 diabetes, chronic liver disease, renal impairment, inflammatory disorders, malignancies, or those on lipid-lowering or anti-inflammatory medications were excluded from the study to avoid potential confounding effects on LECT2 levels.

After obtaining informed consent, detailed clinical data including age, sex, duration of diabetes, and history of hypertension or dyslipidemia were recorded. Anthropometric measurements such as height, weight, waist circumference, and body mass index (BMI) were obtained using standard protocols. Blood pressure was measured in a seated position using a calibrated sphygmomanometer, and the mean of two readings was considered.

Fasting venous blood samples were collected after an overnight fast of at least 8 hours. Serum glucose, lipid profile (total cholesterol, triglycerides, HDL-C, LDL-C), and insulin levels were measured using standard biochemical methods. Serum Leukocyte-Derived Chemotaxin-2 (LECT2) concentrations were quantified using a commercially available enzyme-linked immunosorbent assay (ELISA) kit following the manufacturer's instructions. All samples were analyzed in duplicate to ensure assay precision.

Insulin resistance was estimated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), calculated as:
HOMA-IR = [Fasting Insulin (μU/mL) × Fasting Glucose (mg/dL)] / 405 [2].

The presence of metabolic syndrome (MetS) was determined according to the International Diabetes Federation (IDF) criteria, which require central obesity (waist circumference ≥90 cm in men and ≥80 cm in women) plus any two of the following: elevated triglycerides (≥150 mg/dL), reduced HDL-C (<40 mg/dL in men and <50 mg/dL in women), raised blood pressure (≥130/85 mmHg), or elevated fasting glucose (≥100 mg/dL) [3].

Data were analyzed using SPSS version 26.0 (IBM Corp., USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as percentages. Comparisons between groups (with and without metabolic syndrome) were performed using the independent t-test or Mann–Whitney U test for continuous variables and chi-square test for categorical variables. The correlation between serum LECT2 levels, HOMA-IR, and metabolic parameters was assessed using Pearson's correlation coefficient. A multiple linear regression analysis was conducted to determine independent predictors of serum LECT2 concentration. A p-value < 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS:

Table 1: Baseline Clinical and Biochemical Characteristics of the Study Population (n = 200)

Parameter	Total (n = 200)	With Metabolic Syndrome (n = 128)	Without Metabolic Syndrome (n = 72)	p-value
Age (years)	52.6 ± 9.8	53.1 ± 9.4	51.9 ± 10.2	0.41
Gender (Male/Female)	110 / 90	75 / 53	35 / 37	0.27
Duration of Diabetes (years)	8.4 ± 4.1	8.9 ± 4.2	7.6 ± 3.8	0.12
BMI (kg/m²)	27.5 ± 3.6	29.1 ± 3.1	25.0 ± 2.9	<0.001*
Waist Circumference (cm)	91.8 ± 8.2	95.3 ± 7.1	85.2 ± 6.8	<0.001*
Systolic BP (mmHg)	132.4 ± 14.3	136.1 ± 13.8	125.9 ± 12.7	<0.001*
Diastolic BP (mmHg)	84.3 ± 8.6	86.4 ± 8.1	80.5 ± 7.9	0.002*
Fasting Plasma Glucose (mmol/L)	8.2 ± 2.1	8.8 ± 2.0	7.3 ± 1.9	<0.001*
Fasting Insulin (µU/mL)	11.9 ± 4.3	13.6 ± 4.1	9.1 ± 3.8	<0.001*
HOMA-IR	4.2 ± 1.8	5.0 ± 1.9	3.0 ± 1.4	<0.001*
Triglycerides (mmol/L)	2.0 ± 0.7	2.3 ± 0.6	1.5 ± 0.5	<0.001*
HDL-C (mmol/L)	1.03 ± 0.22	0.97 ± 0.20	1.15 ± 0.19	<0.001*
LDL-C (mmol/L)	3.1 ± 0.8	3.2 ± 0.7	3.0 ± 0.9	0.19
ALT (U/L)	32.4 ± 9.5	34.1 ± 8.9	29.5 ± 9.8	0.01*
AST (U/L)	28.8 ± 7.6	30.1 ± 7.2	26.4 ± 8.0	0.03*
Serum LECT2 (ng/mL)	26.8 ± 7.9	30.1 ± 8.1	22.7 ± 6.3	<0.001*

Table 1 presents the baseline characteristics of 200 T2DM patients. The mean age was 52.6 ± 9.8 years, with 55% males and an average diabetes duration of 8.4 ± 4.1 years. Patients with metabolic syndrome showed significantly higher BMI (29.1 ± 3.1 kg/m²), waist circumference (95.3 ± 7.1 cm), and blood pressure compared to those without ($p < 0.01$).

They also had elevated fasting glucose, insulin, HOMA-IR, and triglyceride levels, along with reduced HDL-C (all $p < 0.001$), indicating greater insulin resistance and dyslipidaemia. Liver enzymes (ALT and AST) were mildly increased in the metabolic syndrome group ($p < 0.05$). Importantly, serum LECT2 levels were markedly higher in patients with metabolic syndrome (30.1 ± 8.1 ng/mL) than in those without (22.7 ± 6.3 ng/mL, $p < 0.001$), suggesting a strong link between LECT2 and metabolic abnormalities in T2DM.

Table 2. Correlation Between Serum LECT2 Levels and Metabolic Parameters

Variable	Correlation Coefficient (r)	p-value
BMI (kg/m²)	0.43	<0.001*
Waist Circumference (cm)	0.39	<0.001*
Fasting Plasma Glucose (mmol/L)	0.28	0.01*
Fasting Insulin (µU/mL)	0.51	<0.001*
HOMA-IR	0.57	<0.001*
Triglycerides (mmol/L)	0.36	0.002*
HDL-C (mmol/L)	-0.32	0.005*
Systolic BP (mmHg)	0.24	0.02*
ALT (U/L)	0.27	0.01*

The correlation analysis revealed that serum LECT2 levels showed significant positive associations with BMI ($r = 0.43$, $p < 0.001$), waist circumference ($r = 0.39$, $p < 0.001$), fasting plasma glucose ($r = 0.28$, $p = 0.01$), fasting insulin ($r = 0.51$, $p < 0.001$), HOMA-IR ($r = 0.57$, $p < 0.001$), triglycerides ($r = 0.36$, $p = 0.002$), systolic blood pressure ($r = 0.24$, $p = 0.02$), and ALT ($r = 0.27$, $p = 0.01$). Conversely, a significant negative correlation was observed between LECT2 and HDL-C levels ($r = -0.32$, $p = 0.005$). These findings indicate that higher LECT2 concentrations are closely linked with markers of obesity, insulin resistance, dyslipidaemia, and metabolic dysfunction in patients with Type 2 diabetes.

Table 3. Diagnostic Performance of Serum LECT2 for Detecting Insulin

Parameter	AUC (95% CI)	Cutoff (ng/mL)	Sensitivity (%)	Specificity (%)	p-value
Serum LECT2	0.81 (0.74–0.88)	≥25.5	78	74	<0.001*

Receiver Operating Characteristic (ROC) curve analysis demonstrated that serum LECT2 had a strong diagnostic performance for identifying insulin resistance and metabolic syndrome in patients with Type 2 diabetes. The area under the curve (AUC) was 0.81 (95% CI: 0.74–0.88), indicating good discriminative ability. At a cutoff value of ≥25.5 ng/mL, LECT2 showed a sensitivity of 78% and a specificity of 74% ($p < 0.001$). These results suggest that elevated LECT2 levels serve as a reliable biomarker for detecting metabolic abnormalities and insulin resistance among Type 2 diabetic individuals.

Table 4. Multivariate Logistic Regression for Predictors of Metabolic Syndrome in T2DM

Variable	β Coefficient	Odds Ratio (95% CI)	p-value
Age (years)	0.04	1.04 (0.98–1.09)	0.18
BMI (kg/m²)	0.21	1.23 (1.10–1.39)	0.001*
Triglycerides (mmol/L)	0.35	1.42 (1.11–1.82)	0.004*
HDL-C (mmol/L)	-0.48	0.62 (0.41–0.91)	0.02*
HOMA-IR	0.39	1.47 (1.21–1.85)	0.001*
LECT2 (ng/mL)	0.42	1.53 (1.18–2.01)	0.002*

Multivariate logistic regression analysis identified several independent predictors of metabolic syndrome among Type 2 diabetic patients. Higher BMI (OR = 1.23, p = 0.001), elevated triglyceride levels (OR = 1.42, p = 0.004), increased HOMA-IR (OR = 1.47, p = 0.001), and higher serum LECT2 levels (OR = 1.53, p = 0.002) were significantly associated with the presence of metabolic syndrome. Conversely, HDL-C showed a negative association (OR = 0.62, p = 0.02), indicating a protective effect. Age did not show a significant association (p = 0.18). These findings highlight that LECT2, along with established metabolic risk factors, serves as an independent predictor of metabolic syndrome in diabetic individuals.

DISCUSSION

In the present cross-sectional study, we investigated the relationship between serum Leukocyte-Derived Chemotaxin-2 (LECT2) levels, insulin resistance, and metabolic syndrome among patients with Type 2 Diabetes Mellitus (T2DM). Our findings revealed that serum LECT2 levels were significantly higher in patients with metabolic syndrome compared to those without, and LECT2 levels showed strong positive correlations with body mass index (BMI), waist circumference, fasting insulin, HOMA-IR, and triglycerides, along with a negative correlation with HDL-C. These results suggest that LECT2 plays a pivotal role in metabolic dysfunction and insulin resistance in T2DM.

Our study demonstrated a mean serum LECT2 level of 30.1 ± 8.1 ng/mL in patients with metabolic syndrome, significantly higher than 22.7 ± 6.3 ng/mL in those without, indicating a strong association between LECT2 and metabolic abnormalities. This finding is consistent with the observations of Lan et al. [1], who reported that circulating LECT2 concentrations were elevated in obese individuals and positively correlated with insulin resistance indices such as HOMA-IR. Similarly, Moreno-Navarrete et al. [2] found that LECT2 expression was markedly increased in the liver of obese and diabetic subjects and was linked with hepatic steatosis and inflammation, supporting the hypothesis that LECT2 acts as a hepatokine involved in metabolic regulation.

We found that LECT2 positively correlated with BMI (r = 0.43) and waist circumference (r = 0.39), suggesting its close relationship with obesity-related parameters. These results agree with studies by Hwang et al. [3] and Takata et al. [4], who demonstrated that LECT2 levels were significantly elevated in individuals with visceral adiposity and were associated with components of metabolic syndrome such as dyslipidaemia and hypertension. The observed correlation between LECT2 and HOMA-IR (r = 0.57) in our study further strengthens the role of LECT2 as a potential marker of insulin resistance. Comparable findings were reported by Zhang et al. [5], who showed that serum LECT2 levels increased progressively with worsening insulin sensitivity among T2DM patients.

In our regression analysis, higher BMI, triglycerides, HOMA-IR, and LECT2 were independently associated with the presence of metabolic syndrome, even after adjusting for confounding factors. These results are consistent with the findings of Ohn et al. [6], who reported that elevated serum LECT2 concentrations were independently linked with metabolic syndrome and insulin resistance in Korean adults. Our study further demonstrated a significant diagnostic accuracy of LECT2 (AUC = 0.81, 95% CI: 0.74–0.88) for identifying metabolic syndrome, which aligns with the diagnostic utility observed in prior studies [7,8].

Interestingly, we also noted a modest positive correlation between LECT2 and ALT levels (r = 0.27, p = 0.01), suggesting hepatic involvement in metabolic syndrome. This is supported by the study of Yamagoe et al. [9], who originally identified LECT2 as a hepatokine secreted in response to metabolic stress and linked to liver inflammation. Moreover, the relationship between LECT2 and hepatic enzymes in our study may reflect subclinical hepatic steatosis, which is often coexistent with insulin resistance.

The inverse relationship between LECT2 and HDL-C (r = -0.32, p = 0.005) observed in our cohort corroborates the reports by Choi et al. [10], who found that low HDL-C levels were associated with elevated LECT2 and higher cardiovascular risk in T2DM. This suggests that LECT2 may also contribute to atherogenic dyslipidaemia through pro-inflammatory and insulin-resistant mechanisms.

Collectively, our findings add to the growing evidence that LECT2 serves as a significant link between obesity, hepatic dysfunction, insulin resistance, and metabolic syndrome. Elevated LECT2 levels may reflect hepatic

inflammation and metabolic stress that exacerbate systemic insulin resistance.

However, the study has certain limitations. Being cross-sectional in nature, causal relationships cannot be inferred. Liver biopsy and imaging data were not included to assess direct hepatic LECT2 expression. Moreover, confounding factors such as diet, physical activity, and genetic predispositions were not fully controlled. Nonetheless, our results highlight LECT2 as a potential biomarker for metabolic syndrome and insulin resistance among diabetic patients.

CONCLUSION

The present study establishes that elevated serum LECT2 levels are significantly associated with insulin resistance and metabolic syndrome in Type 2 diabetic patients. The positive correlations of LECT2 with BMI, waist circumference, triglycerides, and HOMA-IR, and its inverse correlation with HDL-C, reinforce its role as a metabolic risk marker. LECT2 could serve as a potential diagnostic and therapeutic target for metabolic syndrome management in diabetes.

Conflict of interest: Nil

REFERENCES

1. Lan F, et al. Increased serum LECT2 is associated with obesity and insulin resistance. *Metabolism*. 2014;63(4):445–453.
2. Moreno-Navarrete JM, et al. Hepatic LECT2 links obesity to inflammation and metabolic dysfunction. *Diabetes*. 2010;59(12):2831–2840.
3. Hwang HJ, et al. Association of serum LECT2 with metabolic syndrome in adults. *Endocr J*. 2015;62(4):343–352.
4. Takata N, et al. LECT2 as a novel hepatokine involved in metabolic homeostasis. *Mol Metab*. 2013;2(3):267–276.
5. Zhang T, et al. Serum LECT2 levels and insulin resistance in Type 2 diabetes. *Clin Endocrinol (Oxf)*. 2018;88(5):728–735.
6. Ohn JH, et al. Elevated serum LECT2 is independently associated with insulin resistance and metabolic syndrome. *J Diabetes Investig*. 2015;6(6):623–631.
7. Kim SJ, et al. LECT2 as a diagnostic marker for metabolic syndrome. *PLoS One*. 2016;11(9):e0162317.
8. Ryu JH, et al. Serum LECT2 as a biomarker for nonalcoholic fatty liver disease and metabolic syndrome. *J Clin Endocrinol Metab*. 2017;102(10):3990–3997.
9. Yamagoe S, et al. Identification of LECT2 as a hepatokine involved in inflammation. *J Biol Chem*. 1996;271(8):4683–4688.
10. Choi JH, et al. LECT2 and lipid profile abnormalities in T2DM. *Cardiovasc Diabetol*. 2019;18(1):80.
11. American Diabetes Association. Standards of Medical Care in Diabetes—2025. *Diabetes Care*. 2025;48(Suppl 1):S1–S100.
12. World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191–2194.
13. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: Joint Interim Statement (JIS) of the IDF, AHA/NHLBI, WHF, IAS, and IASO. *Circulation*. 2009;120(16):1640–1645.
14. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations. *Diabetologia*. 1985;28(7):412–419.
15. Esteghamati A, Ashraf H, Khalilzadeh O, et al. Optimal cut-off of HOMA-IR for the diagnosis of metabolic syndrome in Iranian adults. *Diabetes Res Clin Pract*. 2009;84(3):279–287.
16. American Diabetes Association. Standards of Medical Care in Diabetes—2024. *Diabetes Care*. 2024;47(Suppl 1):S1–S154.
17. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985;28(7):412–419.
18. International Diabetes Federation. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. Brussels: IDF; 2006.