Research Article

Leptin-to-Adiponectin Ratio: A New Marker for Metabolic Syndrome in Northern Indian Population

Arjun Kumar Singhal*

Department of Microbiology, Indian Society for Atherosclerosis Research, New Delhi, India

Corresponding author:
Arjun Kumar Singhal,
Department of Microbiology,
Indian Society for Atherosclerosis Research,
New Delhi, India;
E-mail: singhal2075@yahoo.co.in

Received: 23-Aug-2023,
Manuscript No. AMHSR-23-111048;
Editor assigned: 25-Aug-2023,
PreQC No. AMHSR-23-111048 (PQ);
Reviewed: 08-Sep-2023,
QC No. AMHSR-23-111048;
Revised: 20-Jan-2025,
Manuscript No: AMHSR-23-111048 (R);
Published: 27-Jan-2025,
DOI: 10.54608.annalsmedical.2025.179

Abstract

Background: Urbanisation, sedentary lifestyles, and dietary changes have all contributed to an increase in the prevalence of metabolic syndrome in Indian populations during the past ten years. Numerous markers have been investigated to determine if a person is at risk for developing the metabolic syndrome, with the bulk of them having to do with adipose tissue. Recently, adiponectin and leptin, two biomarkers with a high correlation to cardiometabolic health or disease, are of particular interest. **Methods:** In the general population of India, 100 persons were included. Body mass index, waist circumference, systolic and diastolic blood pressure, fasting blood glucose, plasma lipids, adiponectin, leptin, insulin, and the homeostasis model were all measured for the purpose of assessing insulin resistance. We used binary logistic regression analysis to determine the connection between the researched factors and metabolic syndrome and Spearman's analyses to evaluate correlations. **Results:** In all, 200 participants-100 men and 100 women-were enrolled for the study. Men's and women's median ages were 53 and 48, respectively ($p<0.05$). Men had significantly greater WHR, SBP, and DBP ($p<0.05$, respectively). Women had significantly higher levels of triglycerides, LDL, insulin, adiponectin, leptin, and HOMA-IR ($p<0.05$, respectively). Leptin to adiponectin ratio was significantly and positively correlated with body mass index ($r=0.597$, $p<0.001$), waist circumference ($r=0.576$, $p<0.001$), triglycerides ($r=0.190$, $p=0.001$), insulin levels ($r=0.329$, $p<0.000$), and HOMA-IR ($r=0.301$, $p<0.000$). **Conclusion:** In this study, higher levels of LAR, together with higher levels of leptin and lower levels of adiponectin, were found to be significantly linked with metabolic syndrome. To properly determine whether LAR can be a predictor of metabolic syndrome or not, independent of confounding factors, research with adequate design must be conducted.

Keywords: Cardiometabolic health; Triglycerides; Insulin; Adiponectin; Leptin; Resistance

Introduction

Metabolic Syndrome (MetS) is a metabolic conditions, which increases the risk of atherosclerotic diseases, obesity, hypertension, dyslipidemia, and hyperglycemia [1-3]. The frequency of the metabolic syndrome and its components is increasing on a global scale. MetS is a significant global public health concern as a result [4,5]. Urbanisation, sedentary lifestyles, and dietary changes have all contributed to an increase in the prevalence of metabolic syndrome in Indian populations during the past ten years [6,7]. Numerous markers have been investigated to determine if a person is at risk for developing the metabolic syndrome, with the bulk of them having to do with adipose tissue [8-11]. Recently, Adiponectin and leptin, two biomarkers with a high correlation to cardiometabolic health or disease, are of particular interest. For instance, hypertrophic adipocytes secrete less adiponectin while producing more leptin in obese patients who are at risk for metabolic syndrome and insulin resistance [12-16]. Indeed, it has been discovered that the levels of leptin and adiponectin correlate, respectively, favourably and unfavourably, with obesity, diabetes mellitus, hypertension, and metabolic syndrome.

How to cite this article: Arjun KS. Leptin-to-Adiponectin Ratio: A New Marker for Metabolic Syndrome in Northern Indian Population. Ann Med Health Sci Res. 2025;15:1-6

Additionally, subclinical infammation and inflammatory markers are affected differently by leptin and adiponectin [17]. Since leptin upregulates pro-inflammatory cytokines including TNF and IL-6, it is regarded as an inflamatory cytokine [18,19]. Adiponectin, on the other hand, has anti-inflammatory characteristics by suppressing the production and release of pro-inflammatory mediators. The Leptin-to-Adiponectin Ratio (LAR) has the potential to be a unique predictor of cardio-metabolic outcomes, including metabolic syndrome, according to recent studies [8,20-21]. LAR has been linked to a number of conditions, including chronic renal disease, insulin resistance, metabolic syndrome, carotid intima-media thickness, "at-risk phenotype" in young, severely obese patients, and more. In comparison to adiponectin or leptin alone, some other studies revealed that this marker was a better tool for the diagnosis of metabolic syndrome and risk stratification of participants [22-24].

Therefore, current study aimed to investigates the association of LAR with metabolic syndrome in Northern Indian population.

Materials and Methods

Study subjects

This study was carried out in tertiary care center in northern India. The study's target subject was the general population of people of both sexes who were at least 20 years old. Women who were pregnant or nursing, those who had major chronic illnesses, ongoing or recent (within 7 days) acute illnesses, or those who were currently taking any medications were all excluded from the study.

Data collection

The following measurements were made for each subject: Height with a calibrated stadiometer, weight, waist circumference at the point where the lowest rib meets the iliac crest, hip circumference at the outermost points of the greater trochanters, and Waist-to-Hip Ratio (WHR), which is calculated as waist circumference divided by hip circumference. Weight (in kg) divided by height (in m^2) is how the Quetelet's method calculates Body Mass Index (BMI). We used the automated blood pressure measuring device to test the participant's blood pressure and bioelectric impedance measurement was used to calculate the percentage of Body Fat (%BF). After an 8-12 hour overnight fast, complete fresh blood samples were collected, and venous blood samples were taken from an vein. Blood glucose levels were then tested using the Accu-Chek® compact plus glucometer. Following this, serum was isolated and kept at 20°C for lipid assays and 80°C for additional biochemical investigation. Within one week of the sample's collection, serum lipids were analysed. Automated analyser were used to measure serum Triglycerides (TG), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL) and serum cholesterol (TC). While serum leptin and adiponectin levels were determined by Radio Immuno Assay (RIA) using Linco Research kits (commercially available), insulin levels were determined using an automated analyser (Roche Diagnostics). Each participant had their anthropometric and biochemical parameters taken once.

HOMA-IR, the homeostasis model assessment of insulin resistance:

HOMA-IR=Fasting insulin μ (UI/mL) × Fasting blood glucose (Mmol/L) ÷ 22.5.

Anthropomorphic obesity indicators definition

Obesity was defined by the World Health Organisation as having a BMI of 30 kg/m^2 or more, a waist circumference of >94 cm for men and >80 cm for women, and a waist-hip ratio of 0.90 for males and 0.85 for women [25,26]. The BF% cutoffs used to define obesity were BF% 25 for men and 35 for women, which are the numbers most frequently mentioned in international scientific literature [27].

Metabolic syndrome definition

The IDF/AHA/NHLBI consensus harmonised definition, which recommends three or more of any of the following criteria, was used to define the metabolic syndrome [26]. WC ≥ 80 cm (for women) ≥ 94 cm (for men), SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg, or blood pressure-lowering medication, fasting plasma glucose ≥ 101 mg/dL, or anti-diabetic medication, fasting triglycerides ≥ 154.5 mg/dL or triglyceride-lowering medications, and HDL ≥ 40 mg/dL (women), ≥ 52 mg/dL (men) [28].

Statistical analysis

The Statistical Package for Social Science (SPSS) version 20.0 for Windows (IBM Corp., 2011) was used to code, enter, and analyse the data. Version 20.0 of IBM SPSS for Windows. The variables' distribution pattern was examined. Variables having a normal distribution are stated as mean plus Standard Deviation (SD). The median (interquartile range) is reported for skewed variables. Variables with skewness were log converted. The absolute values of plasma leptin (ng/mL) and plasma adiponectin (g/mL) are split to create the L/A ratios. Men and women's clinical and biological factors were compared using the independent sample t test. The serum levels of leptin, adiponectin, and LARs were correlated using Spearman's correlations. Adiponectin, leptin, and LAR were utilised as dependent variables in a binary logistic regression analysis to find independent factors that could predict metabolic syndrome after adjusting for age, sex, and BMI. Two-tailed tests are used in statistics. Statistical significance was defined as a p value<0.05.

Results

The research population's clinical and metabolic features

In all, 200 participants-100 men and 100 women-were enrolled for the study. Men's and women's median ages were 53 and 48, respectively ($p<0.05$). Men had significantly greater WHR, SBP, and DBP ($p<0.05$, respectively). Women had significantly higher levels of triglycerides, LDL, insulin, adiponectin, leptin and HOMA-IR ($p<0.05$, respectively) (Table 1).

Table 1: Shows the study population's clinical and biochemical characteristics.

	Men (n=100)	Women (n=100)	p value
Age	53 ± 22.9	48 ± 19.1	<0.05*
*Weight (kg)	70.00 ± 22.00	68.00 ± 23.00	0.77
Height (m)	1.70 ± 0.10	1.50 ± 0.15	<0.05*
BMI (kg/m^2)	25.80 ± 5.45	27.00 ± 5.59	<0.05*
WC (cm)	88.90 ± 11.5	93.58 ± 13.8	0.08
WHR (cm)	0.89 ± 0.07	0.87 ± 0.08	<0.05*
BF (%)	21.89 ± 7.59	33.59 ± 9.88	<0.05*
SBP (mm Hg)	138 ± 35	126 ± 32	<0.05*
DBP (mm Hg)	84 ± 18	80 ± 19	0.05*
Blood glucose (mg/dL)	91.8 ± 21	86.5 ± 20.7	0.13
Total cholesterol (mg/dL)	167.3 ± 41.9	172 ± 43.5	0.05*
Triglycerides (mg/dL)	110.4 ± 40.5	112.8 ± 30.7	0.03
LDL (mg/dL)	58.2 ± 36.7	69.9 ± 44.5	0.04
HDL (mg/dL)	84.3 ± 38.5	86.3 ± 35.2	0.61
Insulin (µU/mL)	2.10 ± 1.91	2.65 ± 1.98	0.01
HOMA-IR	8.51 ± 0.31	10.49 ± 10.13	0.02
Adiponectin (µg/mL)	7.89 ± 4.45	9.89 ± 7.60	0.02
Leptin (ng/mL)	4.58 ± 6.34	17.45 ± 23.50	<0.05*

Note: WC: Waist Circumference; BF%: Body Fat percentage; BMI: Body Mass Index; WHR: Waist-Hip Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; LDL: Low Density Lipoprotein-cholesterol; HDL: High Density Lipoprotein-cholesterol; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance

Leptin-to-adiponectin ratio correlations with anthropometric measures of obesity, hypertension, blood lipids, and insulin resistance

Leptin to adiponectin ratio was significantly and positively correlated with body mass index ($r=0.597$, $p<0.001$), waist circumference ($r=0.576$, $p<0.001$), triglycerides ($r=0.190$, $p=0.001$), insulin levels ($r=0.329$, $p<0.000$), and HOMA-IR ($r=0.301$, $p<0.000$). The relationship between LAR and systolic or diastolic blood pressure, glycemia, or HDL cholesterol was not statistically significant (Table 2).

Table 2: Showing adiponectin, leptin, and LAR correlation with metabolic syndrome markers.

	Adiponectin		Leptin		LAR	
	R	P	R	P	r	p
BMI (kg/m^2)	−0.285*	0.001	0.657*	0.001	0.597*	0.001
WC (cm)	−0.285*	0	0.559*	0	0.576*	0
TG (mg/dL)	−0.139*	0.012	0.149*	0.006	0.189*	0.001
Insulin (µU/mL)	−0.122	0.056	0.328*	0	0.329*	0
HOMA-IR	−0.137*	0.029	0.286*	0	0.301*	0

Note: WC: Waist Circumference; BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; TG: Triglycerides; HDL: High Density Lipoprotein

Correlation between leptin-to-adiponectin ratio and metabolic syndrome

The metabolic syndrome was significantly linked with greater levels of leptin (OR=1.42, p=0.002), as well as lower levels of adiponectin (OR=0.45, p=0.002) and LAR (OR=1.49, p=0.000) in the binary logistic regression analysis (Table 3). In addition to being significantly linked with metabolic syndrome (OR=1.64, p value=0.000), lower levels of adiponectin (OR=0.34, p value=0.001), and higher levels of leptin (OR=1.44, p value=0.002), the LAR was also shown to be significantly associated with age and sex after adjusting for these factors.

Table 3: Binary logistic regression analysis was used to determine the unadjusted and adjusted (for age and sex) ORs (95% CI) for metabolic syndrome based on log-transformed leptin, adiponectin, and LAR levels.

Variables	Metabolic syndrome	P-value	Metabolic syndrome	P value
	Unadjusted OR (CI)	p	Adjusted OR (CI)	p
Leptin	1.422 (1.123–1.798)	0.002	1.442 (1.15–1.78)	0.002
Adiponectin	0.459 (0.298–0.719)	0.002	0.349 (0.219–0.489)	0.001
LAR	1.498 (1.124–1.787)	0	1.641 (1.278–1.862)	0

Discussion

It is now widely acknowledged that adipokines, primarily leptin and adiponectin, have a significant role in several physiological pathways, including the regulation of insulin in glucose metabolism [9,28]. These compounds have been shown to have the ability to predict the development of metabolic syndrome. Indeed, studies have shown that the metabolic syndrome is significantly related with reduced levels of adiponectin [8,12,13]. On the other hand, increased levels of leptin have been linked to metabolic syndrome. The leptin to adiponectin ratio may play a role in the prediction of cardiometabolic illnesses, including metabolic syndrome, despite the fact that these indicators are widely characterised in the literature [8,20-21]. The goal of this study was to evaluate the association between LAR and a variety of anthropometric measurements, blood lipid levels, blood pressure, and insulin resistance in a northern Indians.

Our research found a link between LAR and body mass index, waist size, lipids, and insulin resistance. These findings concur with those of Kotani, et al. who conducted a research in Japanese populations. The LAR was significantly and favourably correlated with metabolic syndrome factors like BMI and triglycerides, particularly in men [29]. However, in contrast to them, there was no significant relationship between glucose levels and LAR. Similar outcomes were obtained by Zyl, et al. in their study of urban South African women, LAR was significantly higher among those with high blood sugar levels [30]. It has been demonstrated in the literature that LAR is linked to both a reduced vascular response to acetylcholine and an increase in waist circumference [17]. Additionally, it has been discovered that the LAR is linked to a heightened vasoconstrictive response to angiotensin II [8].

LAR, leptin, and adiponectin were significantly linked with metabolic syndrome both with and without adjusting for age and sex. However, both the LAR and leptin levels were significantly greater in metabolic syndrome participants compared to non-metabolic syndrome subjects.

Adiponectin levels were noticeably lower in patients with metabolic syndrome, meanwhile. These findings resemble those of Kotani, et al. who discovered that even after adjusting for sex, LAR was significantly greater in those with metabolic syndrome [20,28]. In a study by Zhuo, et al. discovered that LAR and leptin may be more accurate markers for the diagnosis of metabolic syndrome than adiponectin [19]. The authors also discovered that LAR, rather than adiponectin or leptin alone, had a greater capacity for classifying people with and without metabolic syndrome. In comparison to adiponectin or leptin alone, several other research have found that LAR serves as a useful marker of obesity, diabetes mellitus, insulin resistance, and metabolic syndrome [23,31]. With a stronger connection with CRP and HOMA-IR than leptin or adiponectin alone, LAR has also been demonstrated to be connected to low grade inflammation and insulin resistance irrespective of obesity.

Our research had some limitations. First, the small sample size may have had an effect on the study's statistical significance. Second, because the patients from northern India were not necessarily representative of all Indians, this result might not hold true for patients from different racial or ethnic origins. Further investigation is necessary to discover whether the findings hold true for other Indian groups. Despite these drawbacks, our study-which identified the potential use of LAR as a diagnostic marker of metabolic syndrome in Indians.

Conclusion

In this study, higher levels of LAR, together with higher levels of leptin and lower levels of adiponectin, were found to be significantly linked with metabolic syndrome. To properly determine whether LAR can be a predictor of metabolic syndrome or not, independent of confounding factors, research with adequate design must be conducted.

Financial Support

Nil.

Conflicts of Interest

There are no conflicts of interest

References

1. Klein BE, Klein R, Lee KE. Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. Diabetes Care. 2002;25:1790-1794.
2. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA. 2002;288:2709-2716.
3. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. Diabetes Care. 2005;28:385-390.
4. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA. 2002;287:356-359.
5. Park HS, Kim SM, Lee JS, Lee J, Han JH. Prevalence and trends of metabolic syndrome in Korea: Korean National Health and Nutrition Survey 1998–2001. Diabetes Obes Metab. 2007;9:50-58.
6. Satoh N, Naruse M, Usui T, Tagami T, Suganami T. Leptin-to-adiponectin ratio as a potential atherogenic index in obese type 2 diabetic patients. Diabetes Care. 2004;27:2488-2490.
7. Kotani K, Sakane N, Saiga K, Kurozawa Y. Leptin: Adiponectin ratio as an atherosclerotic index in patients with type 2 diabetes: relationship of the index to carotid intima–media thickness. Diabetologia. 2005;48:2684-2686.
8. Srikanthan K, Feyh A, Visweshwar H, Shapiro JI, Sodhi K. Systematic review of metabolic syndrome biomarkers: A panel for early detection, management, and risk stratification in the West Virginian population. Int J Med Sci. 2016;13:25.
9. Grundy SM. Metabolic syndrome update. Trends Cardiovasc Med. 2016;26:364-373.
10. Dallmeier D, Larson MG, Vasan RS, Keaney Jr JF, Fontes JD, et al. Metabolic syndrome and inflammatory biomarkers: A community-based cross-sectional study at the Framingham Heart Study. Diabetol Metab Syndr. 2012;4:28.
11. Al-Hamodi Z, Al-Habori M, Al-Meeri A, Saif-Ali R. Association of adipokines, leptin/adiponectin ratio and C-reactive protein with obesity and type 2 diabetes mellitus. Diabetol Metab Syndr. 2014;6:1-8.
12. Kaur J. A Comprehensive Review on Metabolic Syndrome. Cardiol Res Pract. 2014;2014:943162.
13. Rasmussen-Torvik LJ, Wassel CL, Ding J, Carr J, Cushman M, et al. Associations of body mass index and insulin resistance with leptin, adiponectin, and the leptin-to-adiponectin ratio across ethnic groups: the Multi-Ethnic Study of Atherosclerosis (MESA). Ann Epidemiol. 2012;22:705-709.
14. Fantuzzi G. Adiponectin and inflammation: Consensus and controversy. J Allergy Clin Immunol. 2008;121:326-330.
15. Mangge H, Almer G, Truschnig-Wilders M, Schmidt A, Gasser R. Inflammation, adiponectin, obesity and cardiovascular risk. Curr Med Chem. 2010;17:4511-4520.
16. Robinson K, Prins J, Venkatesh B. Clinical review: Adiponectin biology and its role in inflammation and critical illness. Crit Care. 2011;15:1-9.
17. Lopez-Jaramillo P, Gomez-Arbelaez D, Lopez-Lopez J, Lopez-Lopez C, Martinez-Ortega J. The role of leptin/adiponectin ratio in metabolic syndrome and diabetes. Horm Mol Biol Clin Invest. 2014;18:37-45.
18. Paz-Filho G, Mastronardi C, Franco CB, Wang KB, Wong ML. Leptin: Molecular mechanisms, systemic pro-inflammatory effects, and clinical implications. Arq Bras Endocrinol Metabol. 2012;56:597-607.
19. Iikuni N, Kwan Lam QL, Lu L, Matarese G, Cava AL. Leptin and inflammation. Curr Immunol Rev. 2008;4:70-79.
20. Zhuo Q, Wang Z, Fu P, Piao J, Tian Y, et al. Comparison of adiponectin, leptin and leptin to adiponectin ratio as diagnostic marker for metabolic syndrome in older adults of Chinese major cities. Diabetes Res Clin Pract. 2009;84: 27-33.
21. Falahi E, Rad AH, Roosta S. What is the best biomarker for metabolic syndrome diagnosis?. Diabetes Metab Syndr. 2015;9:366-372.
22. Hughes JT, O'Dea K, Piera K, Barzi F, Cass A. Associations of serum adiponectin with markers of cardio-metabolic disease risk in Indigenous Australian adults with good health, diabetes and chronic kidney disease. Obes Res Clin Pract. 2016;10:659-672.
23. Gauthier A, Dubois S, Bertrais S, Gallois Y, Aube C, et al. The leptin to adiponectin ratio is a marker of the number of metabolic syndrome criteria in French adults. J Metabolic Syn. 2012;1:101.
24. World Health Organization. Obesity: Preventing and managing the global epidemic: Report of a WHO consultation. 2000.
25. Consultation WE. Waist circumference and waist-hip ratio. Report of a WHO Expert Consultation. Geneva: World Health Organization. 2008;2008:8-11.
26. Okorodudu DO, Jumean MF, Montori VM, Romero-Corral A, Somers VK. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: A systematic review and meta-analysis. Int J Obes (Lond). 2010;34:791-799.
27. Von Frankenberg AD, Do Nascimento FV, Gatelli LE, Nedel BL, Garcia SP, et al. Major components of metabolic syndrome and adiponectin levels: A cross-sectional study. Diabetol Metab Syndr. 2014;6:1-9.

28. Kotani K, Sakane N. Leptin: Adiponectin ratio and metabolic syndrome in the general Japanese population. Korean J Lab Med. 2011;31:162-166.
29. van Zyl S, van der Merwe LJ, van Rooyen FC, Joubert G, Walsh CM. The relationship between obesity, leptin, adiponectin and the components of metabolic syndrome in urban African women, Free State, South Africa. South Af J Clin Nut. 2017;30:8-13.
30. Oda N, Imamura S, Fujita T, Uchida Y, Inagaki K, et al. The ratio of leptin to adiponectin can be used as an index of insulin resistance. Metabolism. 2008;57:268-273.
31. Chou HH, Hsu LA, Wu S, Teng MS, Sun YC, et al. Leptin-to-adiponectin ratio is related to low grade inflammation and insulin resistance independent of obesity in non-diabetic Taiwanese: A cross-sectional cohort study. Acta Cardiol Sin. 2014;30:204.