Original Article

Primary care perspectives on leptin and adiponectin in north Indian families with metabolic syndrome

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Abstract

Background: Urbanization, sedentary lifestyles, and dietary changes have all contributed to an increase in the prevalence of metabolic syndrome (MetS) in Indian populations during the past 10 years. Numerous markers have been investigated to determine if a person is at risk for developing MetS, 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 (BMI), waist circumference, systolic and diastolic blood pressure, fasting blood glucose, plasma lipids, adiponectin, leptin, insulin, and the homeostasis model were measured to assess insulin resistance. We used binary logistic regression analysis to determine the connection between the researched factors and MetS and Spearman's analyses to evaluate correlations. **Results:** In all, 200 participants (100 men and 100 women) were enrolled in 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 BMI (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 MetS. To properly determine whether LAR can be a predictor of MetS, independent of confounding factors, research with adequate design must be conducted.

Keywords: Adipoleptin, leptin, metabolic syndrome

Introduction

An increase in the risk of atherosclerotic diseases, obesity, hypertension, dyslipidemia, and hyperglycemia is caused by the metabolic state known as metabolic syndrome (MetS).[1-3] Globally, the prevalence of MetS and its elements is rising. As a result, MetS is a substantial global public health issue.[4,5] The frequency of MetS has increased during the past 10 years in Indian populations due to urbanization, sedentary lifestyles, and dietary changes.[5-7] The majority of the markers examined to evaluate whether a person is at risk of developing MetS relate to adipose tissue.[8-11] Adiponectin and leptin, two biomarkers with a strong link to health or disease in the cardiometabolic system, have recently attracted a lot of attention. For instance, in obese patients who are at risk of MetS and insulin resistance,

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hypertrophic adipocytes produce less adiponectin while generating more leptin.[11-16] Leptin and adiponectin levels have been found to correlate positively and unfavorably, respectively, with obesity, diabetes mellitus, hypertension, and MetS.[13-15] Leptin and adiponectin also have varied effects on inflammatory and subclinical inflammation markers.[17] Leptin is classified as an inflammatory cytokine as it upregulates pro-inflammatory cytokines such as TNF- and IL-6.[18,19] Contrarily, adiponectin exhibits anti-inflammatory properties by inhibiting the synthesis and release of pro-inflammatory mediators.[14,15,17] Recent research[8,9] has shown that the leptin-to-adiponectin ratio (LAR) has the potential to be a distinct predictor of cardio-metabolic outcomes, including MetS.[8,20,21] Chronic renal illness, insulin resistance, MetS, carotid intima-media thickness, the "at-risk phenotype" in young, extremely obese people, and other diseases have all been related to LAR.[18-20] Other studies showed that this marker was a better method for the identification of MetS and risk categorization of participants than adiponectin or leptin alone.[21-24]

Therefore, the current study aimed to investigate the association of LAR with MetS in the northern Indian population.

Materials and Methods

Study subjects

This study was carried out in a 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 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 a vein. Blood glucose levels were then tested using a glucometer. Following this, serum was isolated and kept at 20°C for lipid assays and 80°C for additional biochemical investigation. Within 1 week of the sample's collection, serum lipids were analyzed. Automated analyzers 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 radioimmunoassay (RIA), insulin levels were determined using an automated analyzer. Each participant had their anthropometric and biochemical parameters taken once.

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

$$\text{HOMA} - \text{IR} = \text{Fasting insulin } \mu \text{ (UI/mL)} \times \text{Fasting blood glucose (Mmol/L)} \div 22.5$$

Anthropomorphic obesity indicators definition

Obesity was defined by the World Health Organization 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 WHR 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 harmonized definition, which recommends three or more of any of the following criteria, was used to define MetS:[26] WC ≥80 cm for women and WC ≥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 for women and HDL ≥52 mg/dL for men.

Statistical analysis

The statistical package for social science (SPSS) version 20.0 for Windows (IBM Corp., 2011) was used to code, enter, and analyze the data. Version 20.0 of IBM SPSS for Windows. The serum levels of leptin, adiponectin, and leptin-adipoleptin ratio (LARs) were correlated using Spearman's correlations. Two-tailed tests are used in statistics. Statistical significance was defined as a *P* value of <0.05.

Results

The research population's clinical and metabolic features

In all, 200 participants (100 men and 100 women) were enrolled in 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].

Relationships between the leptin-to-adiponectin ratio and anthropometric indicators of insulin resistance, hypertension, obesity, and blood lipids

BMI ($r = 0.597$, $P = 0.001$), 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) were substantially and positively linked with LAR. There was no statistically significant correlation between LAR and systolic or diastolic blood pressure, glycemia, or HDL cholesterol [Table 2].

Relationship between metabolic syndrome and the leptin-to-adiponectin ratio

In the binary logistic regression analysis [Table 3], higher levels of leptin (OR = 1.42, *P* = 0.002) and lower levels of adiponectin (OR = 0.45, *P* = 0.002) and LAR (OR = 1.49, *P* = 0.000) were significantly associated with MetS. After adjusting for these variables, the LAR was shown to be significantly associated with age and sex in addition to being significantly associated with MetS (OR = 1.64, *P* = 0.000), lower levels of adiponectin (OR = 0.34, *P* = 0.001), and higher levels of leptin (OR = 1.44, *P* = 0.002).

Discussion

Adipokines, especially leptin and adiponectin, are now widely accepted to have a substantial role in a number of physiological pathways, including the control of insulin in glucose metabolism.[9,28] There is evidence that these substances can foretell the onset of MetS. Research has found a strong correlation between MetS and low adiponectin levels.[8,12,13] Conversely, elevated leptin levels have been connected to MetS. Although these indicators are extensively described in the literature,[8,20,21] the LAR may be useful in the prediction of cardiometabolic diseases, including MetS. Examining the relationships between LAR and various anthropometric parameters, blood cholesterol levels, blood pressure, and insulin resistance in a population of northern Indians was the aim of this study.

According to our study, LAR is associated with BMI, waist size, cholesterol levels, and insulin resistance. These results are consistent with a study on Japanese populations conducted by Kotani *et al.*[29] Particularly in men, the LAR was strongly and favorably linked with elements of MetS such as BMI and triglycerides. There was no discernible connection between glucose levels and LAR, in contrast to them. In a study of urban South African women, van Zyl *et al.*[30] found similar results and found that LAR was considerably higher among those with high blood sugar levels. The relationship between LAR and both a decreased vascular response to acetylcholine and an increase in waist circumference has been shown in the literature.[17] In addition, it has been discovered that the LAR is linked to a heightened vasoconstrictive response to angiotensin II.[8]

Both with and without controlling for age and sex, there was a substantial correlation between LAR, leptin, and adiponectin and MetS. However, when compared to people without MetS, participants' LAR and leptin levels were both noticeably higher.

While this was happening, adiponectin levels were noticeably lower in patients with MetS. These results are similar to those of Kotani *et al.*,[29] who found that LAR was considerably higher in people with MetS even after controlling for sex.[20] Zhuo *et al.*[20] found that LAR and leptin may be more reliable diagnostic indicators for MetS than adiponectin.[19] The authors also found that LAR had a better ability to distinguish between individuals with and without MetS than adiponectin or leptin alone. Several other studies have discovered that LAR acts as a helpful marker of obesity, diabetes mellitus, insulin resistance, and MetS when compared to adiponectin or leptin alone.[23,31]

Table 1: Study population's clinical and biochemical characteristics

	Men (*n*=100)	Women (*n*=100)	*P*
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 (mmHg)	138±35	126±32	<0.05*
DBP (mmHg)	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*

*Statistical Significant. 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

Table 2: 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*	0.000	0.559*	0.000	0.576*	0.000
TG (mg/dL)	−0.139*	0.012	0.149*	0.006	0.189*	0.001
Insulin (µU/mL)	−0.122	0.056	0.328*	0.000	0.329*	0.000
HOMA-IR	−0.137*	0.029	0.286*	0.000	0.301*	0.000

*Statistical Significant. WC=waist circumference, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, TG=triglycerides, HDL=high-density lipoprotein

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*	Metabolic syndrome	*P*
	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)	0.000	1.641 (1.278–1.862)	0.000

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.[32] This study on leptin and adiponectin in north-Indian families with MetS is pertinent for family medicine physicians as it informs risk assessment, facilitates tailored treatment approaches, supports patient education, enables effective monitoring, and encourages a holistic approach to family health.

Our study has some limitations. First, the statistical significance of the study might have been impacted by the small sample size. Second, this finding might not apply to individuals with other racial or cultural backgrounds because the patients from northern India were not necessarily representative of all Indians. To determine whether the results apply to other Indian communities, more research is required. Despite these limitations, our study found that LAR may be used to diagnose MetS in Indians.

Conclusion

In this study, it was discovered that MetS was substantially correlated with greater levels of LAR, higher levels of leptin, and lower levels of adiponectin. Research with an appropriate design is required to accurately assess whether or not LAR may predict the development of MetS, irrespective of confounding factors.

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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;25:1790-4.
2. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, *et al.* The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 2002;288:2709-16.
3. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI, East HE, *et al.* The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. Diabetes Care 2005;28:385-90.
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;287:356-9.
5. Park HS, Kim SM, Lee JS, Lee J, Han JH, Yoon DK, *et al.* Prevalence and trends of metabolic syndrome in Korea: Korean National Health and Nutrition Survey 1998-2001. Diabetes Obes Metab 2007;9:50-8.
6. Satoh N, Naruse M, Usui T, Tagami T, Suganami T, Yamada K, *et al.* Leptin-to-adiponectin ratio as a potential atherogenic index in obese type 2 diabetic patients. Diabetes Care 2004;27:2488-90.
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;48:2684-6.
8. Srikanthan K, Feyh A, Visweshwar H, Shapiro JI, Sodhi K. Systematic review of metabolic syndrome biomarkers: A panel for early detection, manage- ment, and risk stratification in the West Virginian population. Int J Med Sci 2016;13:25-38.
9. Grundy SM. Metabolic syndrome update. Trends Cardiovasc Med 2016;26:364-73.
10. Dallmeier D, Larson MG, Vasan RS, Keaney JF, Fontes JD, Meigs JB, *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 adi- pokines, leptin/adiponectin ratio and C-reactive protein with obesity and type 2 diabetes mellitus. Diabetol Metab Syndr 2014;6:99.
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, Jenny N, *et al.* Associations of BMI 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;22:705–9.
14. Fantuzzi G. Adiponectin and inflammation: Consensus and controversy. J Allergy Clin Immunol 2008;121:326–30.
15. Mangge H, Almer G, Truschnig-Wilders M, Schmidt A, Gasser R, FuchsD. Inflammation, adiponectin, obesity and cardiovascular risk. Curr Med Chem 2010;17:4511–20.
16. Robinson K, Prins J, Venkatesh B. Clinical review: Adiponectin biology and its role in inflammation and critical illness. Crit Care 2011;15:221.
17. López-Jaramillo P, Gómez-Arbeláez D, López-López J, López-López C, Martínez-Ortega J, Gómez-Rodríguez A, *et al.* The role of leptin/adi- ponectin ratio in metabolic syndrome and diabetes. Horm Mol Biol Clin Investig 2014;18:37-45.
18. Paz-Filho G, Mastronardi C, Franco CB, Wang KB, Wong M-L, Licinio J. Leptin: Molecular mechanisms, systemic pro-inflammatory effects, and clinical implications. Arq Bras Endocrinol Amp Metabol 2012;56:597-607.
19. Iikuni N, Lam QLK, Lu L, Matarese G, La Cava A. Leptin and inflammation. Curr Immunol Rev 2008;4:70-9.
20. Zhuo Q, Wang Z, Fu P, Piao J, Tian Y, Xu J, *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, Khalkhali Rad AH, Roosta S. What is the best biomarker for meta- bolic syndrome diagnosis? Diabetes Metab Syndr 2015;9:366-72.
22. Hughes JT, O'Dea K, Piera K, Barzi F, Cass A, Hoy WE, *et al.* Associations of serum adiponectin with markers of cardio-metabolic disease risk in indig- enous Australian adults with good health, diabetes and chronic kidney disease. Obes Res Clin Pract 2016;10:659-72.
23. Satoh N, Naruse M, Usui T, Tagami T, Suganami T, Yamada K, *et al.* Leptin- to-adiponectin ratio as a potential atherogenic index in obese type 2 diabetic patients. Diabetes Care

2004;27:2488-90.

24. Gauthier A, Dubois S, Bertrais S, Gallois Y, Aube C, Gagnadoux F, *et al.* The leptin to adiponectin ratio is a marker of the number of metabolic syndrome criteria in French adults. J Metab Syndr 2011;31:1-6.
25. World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Geneva: World Health Organization; 2000.
26. WHO Expert Consultation. Waist Circumference and Waist-hip Ratio. Geneva: World Health Organization; 2011.
27. Okorodudu DO, Jumean MF, Montori VM, Romero-Corral A, Somers VK, Erwin PJ, *et al.* Diagnostic performance of body mass index to identify obesity as defined by body adiposity: A systematic review and metaanaly- sis. Int J Obes (Lond) 2010;34:791-9.
28. Von Frankenberg AD, do Nascimento FV, Gatelli LE, Nedel BL, Garcia SP, de Oliveira CS. Major components of metabolic syndrome and adiponectin levels: A cross-sectional study. Diabetol Metab Syndr 2014;6:2.
29. Kotani K, Sakane N. Leptin: Adiponectin ratio and metabolic syndrome in the general Japanese population. Korean J Lab Med 2011;31:162-6.
30. 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 Afr J Clin Nutr 2017;30:68-73.
31. Oda N, Imamura S, Fujita T, Uchida Y, Inagaki K, Kakizawa H, *et al.* The ratio of leptin to adiponectin can be used as an index of insulin resistance. Metabolism 2008;57:268-73.
32. Chou H-H, Hsu L-A, Wu S, Teng M-S, Sun Y-C, Ko Y-L. Leptin-to-adiponectin ratio is related to low grade inflammation and insulin resistance inde- pendent of obesity in non-diabetic Taiwanese: A cross-sectional cohort study. Acta Cardiol Sin 2014;30:204-14.