Original Article

Association between circulating leptin and insulin resistance, the lipid profile, and metabolic risk factors in North Indian adult women

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Summary **Leptin plays an important role in the regulation of body weight and operates by inhibiting food intake and stimulating energy expenditure. The purpose of the present study was to ascertain the relationship between serum leptin levels and the lipid profile, insulin resistance, and metabolic risk factors in North Indian adult women. In a transactional case-control study of 390 women, subjects were 186 women with metabolic syndrome according to National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) guidelines and 204 healthy control women without metabolic syndrome, all of whom were between 20-40 years of age. Circulating leptin levels were determined by sandwich enzyme-linked immunosorbent assay, insulin resistance was determined by homeostasis model assessment for insulin resistance (HOMA-IR), and the lipid profile was determined using an enzymatic method. Results indicated that circulating leptin (13.38 ± 9.00 *vs.* 8.16 ± 6.31 ng/mL, $p < 0.001$), HOMA-IR (2.68 ± 2.05 *vs.* 1.72 ± 1.20, $p < 0.001$), the lipid profile, and other metabolic risk factors (waist circumference, waist-to-hip ratio, body mass index, and fasting plasma insulin) were significantly higher in women with metabolic syndrome than in women without the syndrome ($p < 0.001$). Further, in women with metabolic syndrome serum leptin was significantly ($p < 0.05$ or $p < 0.001$) and positively correlated with HOMA-IR ($p = 0.000$) and other metabolic risk factors but negatively correlated with fasting plasma glucose, triglycerides, and high-density lipoprotein cholesterol. Circulating leptin was found to be significantly associated with hyperlipidemia, insulin resistance, and other metabolic risk factors in North Indian adult women.**

Keywords: Leptin, insulin resistance, lipid profile, metabolic risk factors

1. Introduction

Metabolic syndrome describes the clustering of abdominal obesity, lipid abnormalities, hypertension, and hyperglycemia and is a strong, independent contributor to the onset of coronary heart disease and type 2 diabetes (*1*). Although the mechanisms underlying metabolic syndrome are not well understood, current evidence suggests that obesity plays a central role (*2*,*3*). As an endocrine organ, adipose tissue produces a number of adipokines, such as leptin, that are mainly associated with cylindrical obesity (*4*), whereas others such as interleukin-6, tumor necrosis factor-α, resistin, and adiponectin may be more closely linked to abdominal adiposity (*5*).

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However, there is evidence that leptin is associated with metabolic syndrome and/or with the factors related to it. "Adipokines" are hypothesized to be a possible link between obesity and other components of metabolic syndrome (*6*). Although the prevalence of metabolic syndrome is greater in obese people, not all obese persons suffer from metabolic syndrome, and nonobese individuals may also be affected.

Leptin is a 16 kDa metabolic hormone produced by the leptin gene, whose name is derived from the Greek word "leptos", which means "thin". It was discovered at the end of the year 1994 (*7*). It is produced and released mainly by adipocytes (*8*) and it circulates in serum in both free and bound form. Sinha *et al.* (*9*) noted the presence of leptin-binding proteins and reported that in lean subjects the majority of leptin circulated in the bound form, whereas in obese subjects the majority of leptin circulated in free form.

Leptin is produced at many sites but the amount of body fat is the main determinant of the circulating levels of this hormone. Leptin plays a central role in maintaining the energy balance in humans (*10*). It also regulates energy homeostasis and body weight by adipose tissue mass regulation (*8,11*). The leptin serum concentration has been found to be proportional to body mass but may be lowered rapidly by fasting or inflammatory reaction. It has a central role in energy storage regulation and fertility (*12*). It has several systemic effects such as body mass control, reproduction, angiogenesis, immunity, and cardiovascular function (*13,14*).

In humans, the circulating leptin level increases with obesity (*13*) and has been shown to be directly proportional to the amount of body fat mass, suggesting that a hallmark of obesity is not leptin deficiency but leptin resistance. Hyperleptinemia and/or leptin resistance may play an important role in insulin resistance by causing insulin resistance. Compared to males, females have higher leptin levels if leptin levels are expressed as a percentage of body adiposity (*15*). In recent years, the presence of leptin has been found to be associated with diabetes, glucose metabolism, and insulin metabolism (*16,17*). The association between plasma leptin and insulin in adults has also been examined (*18*).

The present study measured serum leptin levels in North Indian women with metabolic syndrome. These women were classified on the basis of National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) III criteria, and the relationship between metabolic syndrome and homeostasis model assessment for insulin resistance (HOMA-IR), the lipid profile, and other metabolic risk factors was investigated in these women and age-matched healthy controls. The relationship between leptin levels and insulin resistance was also investigated, as were clinical and metabolic parameters in healthy controls.

2. Materials and Methods

2.1. *Subject characteristics*

A case-control study was conducted with North Indian adult women ages 20-40 years. A total of 390 adult women were enrolled in this study and consisted of 186 women with metabolic syndrome (wMetS) according to NCEP-ATP III criteria and a control group of 204 age-matched healthy women without metabolic syndrome (woMetS) who were non-alcoholic, non-diabetic, and who had no cardiac, respiratory, inflammatory, endocrine, or metabolic disease. Pregnant and lactating women with any gynecological or obstetrical problems and women receiving medication such as hormone replacement therapy were excluded from this study.

A structured form was completed to collect information regarding subjects' medical, personal, family, dietary, and menstrual history. This study was approved by the Ethics Committee of this Institute and the Department of Biotechnology (DBT), New Delhi, India and "all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research". Written informed consent was obtained from all participants.

2.2. *Criteria for metabolic syndrome*

The NCEP-ATP III criteria for metabolic syndrome (*19*) are based on simple clinical and biochemical parameters. The current subjects were classified as having metabolic syndrome if they had three or more risk factors, which included any 3 of the following: 1) waist circumference (WC) > 88 cm (35 in); 2) triglycerides (TG) ≥ 150 mg/dL (1.69 mM); 3) high-density lipoprotein cholesterol (HDL-C) < 50 mg/dL (1.29 mM); 4) systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg; and 5) fasting plasma glucose (FPG) ≥ 110 mg/dL (6.1 mM). For adult Asian Indian women (*20*), the cut-off point for waist circumference was > 80 cm and that for body mass index (BMI) was > 23 kg/m^2 (modified with various components of NCEP-ATP III).

2.3. *Anthropometric measurements*

BMI, height, weight, WC, and hip circumference (HC) were evaluated in all subjects. The waist-to-hip ratio (WHR) was calculated from the WC and HC. The WHR is an indicator for measuring central/visceral obesity (WC was measured at the narrowest point superior to the hip and was divided by the circumference of the hips measured at their greatest gluteal protuberance). BMI was calculated as the ratio of body weight to body height squared and was expressed in kg/m^2. Using

an appropriate cuff size, a physician measured blood pressure on the right arm in a sitting position after 5 min of rest. The first and fourth Korotkoff sounds were recorded as systolic and diastolic BP. Blood pressure was measured again after 5 min of rest and the average was used in analysis.

2.4. *Biochemical measurements*

Blood samples for measuring serum biochemical parameters were obtained from all women in the morning after 12 h of fasting on the 10th day of menstruation. Serum and plasma were separated out from a total sample of 4.0 mL blood. Blood plasma glucose and the serum lipid profile were estimated using a glucose oxidase-peroxidase and enzymatic method, respectively (Randox Laboratories Ltd., Antrim, UK). Fasting plasma insulin (FPI) was estimated using an immuno-radiometric assay (Immunotech Radiova, Prague, Czech Republic). Insulin resistance, which indicates proneness to developing metabolic syndrome, was evaluated using the HOMA-IR method (*21*) was determined using the formula: [FPG (mM) × fasting insulin (μU/mL)]/22.5.

2.5. *Detection of serum leptin levels*

In a total of 541 women, leptin levels were determined by a sandwich enzyme-linked immunosorbent assay (ELISA) (Version 6.0, Cat No. CAN-L-4260, Diagnostics Biochem Canada Inc., London, UK). A monoclonal antibody specific for leptin was immobilized onto a microtiter plate and another specific for a different epitope of leptin was conjugated to biotin. Biotin-conjugated anti-leptin antibody, streptavidin-horseradish peroxidase conjugate, and corresponding substrate were used for yellow color development. A colored product formed in proportion to the amount of leptin present in the serum sample. The absorbance was measured on a microtiter plate reader at a wavelength of 450 nm. The intra-assay and inter-assay coefficients of variation were 4.3% and 5.8%, respectively.

2.6. *Statistical analysis*

Quantitative variables are expressed as mean ± standard deviation (S.D.). An unpaired *t*-test was performed to assess differences between the two groups in terms of biochemical parameters. Groups were also compared by one-way analysis of variance (ANOVA) followed by a Newman-Keuls post-hoc test. Pearson's correlation coefficient (*r*) was calculated to determine the association between the serum levels of circulating leptin level and insulin resistance, the lipid profile, and metabolic risk factors. As most of the parameters were not normally distributed, all parameters were log-transformed before analysis. A two-tailed ($\alpha = 2$) probability value of $p < 0.05$ was considered statistically significant. All statistical analysis was performed with STATISTICA (version 6.0) software.

3. Results

Out of a total of 390 North Indian adult women (age 20-40 yrs), 204 did not have metabolic syndrome (control group: woMetS) and 186 had metabolic syndrome (study group: wMetS).

3.1. *Clinical and biochemical characteristics in women wMetS and woMetS*

Differences between women wMetS and woMetS (Table 1) in terms of biochemical and anthropometric parameters, *i.e.*, weight (64.65 ± 12.02 *vs.* 52.33 ± 9.54), BMI (27.22 ± 5.07 *vs.* 22.06 ± 4.05), HC (99.32 ± 12.18 *vs.* 88.17 ± 7.45), WHR (0.87 ± 0.05 *vs.* 0.82 ± 0.06), FPI (10.31 ± 6.95 *vs.* 7.56 ± 4.86), and HOMA-IR (2.68 ± 2.05 *vs.* 1.72 ± 1.20), were highly significant ($p < 0.001$) but differences were not significant in terms of age (28.32 ± 5.94 *vs.* 27.18 ± 6.87), height (154.23 ± 6.28 *vs.* 154.15 ± 5.78) and pulse rate (78.90 ± 6.50 *vs.* 77.89 ± 6.48). Further comparison of women with and without metabolic syndrome revealed that serum leptin concentrations increased significantly with metabolic syndrome (13.38 ± 9.00 *vs.* 8.16 ± 6.31, $p < 0.001$) (Table 1).

3.2. *Metabolic risk factors in women wMetS and woMetS*

Comparison of metabolic risk factors revealed significant differences between women wMetS and woMetS (Table 2) in terms of WC (86.35 ± 13.98 *vs.* 72.14 ± 9.48, $p < 0.001$), SBP (132.40 ± 11.36 *vs.* 118.46 ± 9.01, $p < 0.001$), DBP (88.46 ± 7.81 *vs.* 80.46 ± 6.54, $p < 0.001$), high TG (142.59 ± 35.98 *vs.* 105.28 ± 23.27, $p < 0.001$), low

Table 1. Comparison of demographic and biochemical parameters for groups woMetS and wMetS

Variables	Women woMetS ($n = 204$)	Women wMetS ($n = 186$)
Age (yrs)	27.18 ± 6.87	28.32 ± 5.94
Height (cm)	154.15 ± 5.78	154.23 ± 6.28
Weight (kg)	52.33 ± 9.54	64.65 ± 12.02*
BMI (kg/m^2)	22.06 ± 4.05	27.22 ± 5.07*
HC (cm)	88.17 ± 7.45	99.32 ± 12.18*
WHR	0.82 ± 0.06	0.87 ± 0.05*
PR (count/min)	77.89 ± 6.48	78.90 ± 6.50
FPI (μU/mL)	7.56 ± 4.86	10.31 ± 6.95*
HOMA-IR	1.72 ± 1.20	2.68 ± 2.05*
Serum leptin (ng/mL)	8.16 ± 6.31	13.38 ± 9.00*

Data are shown as mean ± S.D. * $p < 0.01$. Abbreviations: BMI, body mass index; HC, hip circumference; WHR, waist-to-hip ratio; PR, pulse rate; FPI, fasting plasma insulin.

HDL-C (41.98 ± 4.66 *vs.* 43.92 ± 6.18, $p < 0.001$), and FPG (101.09 ± 17.25 *vs.* 90.54 ± 10.42, $p < 0.001$).

3.3. *Serum lipid parameters in women wMetS and woMetS*

Lipid profiles including serum total cholesterol (172.13 ± 34.64 *vs.* 145.14 ± 29.51), low-density lipoprotein-cholesterol (LDL-C; 101.88 ± 31.80 *vs.* 80.16 ± 28.48), very low density lipoprotein (28.52 ± 7.20 *vs.* 21.06 ± 4.65), the TC/HDL-C ratio (4.15 ± 0.97 *vs.* 3.36 ± 0.80), the HDL-C/LDL-C ratio (2.47 ± 0.87 *vs.* 1.87 ± 0.75), and a low LDL-C/HDL-C ratio (0.46 ± 0.19 *vs.* 0.64 ± 0.35) differed significantly ($p < 0.001$) between women wMetS and woMetS (Table 3).

3.4. *Metabolic risk factors in women woMetS and wMetS sub-grouped according to BMI*

When the women were divided into groups woMetS and wMetS according to BMI and sub-grouped into BMI < 23 kg/m^2 and > 23 kg/m^2, there was a significant difference ($p < 0.001$) between sub-groups woMetS and wMetS (Table 4) in terms of WC, WHR, and serum leptin levels, and there was no significant difference ($p > 0.05$) in terms of HOMA-IR and serum HDL-C. In contrast, serum TG was not significant in the group wMetS but was significant in the group woMetS (Table 4).

3.5. *Comparative summary of WC, BMI, and leptin levels on the basis of the number of metabolic syndrome determinants according to NCEP-ATP III guidelines*

The circulating level of leptin, WC, and BMI were compared among individuals with different numbers of metabolic syndrome determinants (according to the NCEP-ATP III guidelines) (Figure 1). Individuals with 0 (Control), 1, 2, 3, and 4-5 metabolic risk components numbered 22 (5.64%), 139 (35.64%), 43 (11.02%), 153 (39.23%) and 33 (8.46%), respectively. *p* values were significant and a linear trend in the serum level of leptin and WC was observed with an increasing number of metabolic syndrome determinants (Table 5).

3.6. *Correlation between circulating leptin levels and HOMA-IR, the lipid profile, and metabolic risk factors in women with metabolic syndrome (study group)*

Pearson's correlation coefficient (*r*) showed that the leptin level had a highly significant inverse relationship with FPG ($r = -0.09$, $p = 0.251$), TG ($r = -0.01$, $p = 0.913$), HDL-C ($r = -0.08$, $p = 0.259$), and the HDL-C/LDL-C ratio ($r = -0.05$, $p = 0.481$) but a positive correlation with WC ($r = 0.74$, $p < 0.001$), WHR ($r = 0.53$, $p < 0.001$), BMI ($r = 0.63$, $p < 0.001$), SBP ($r = 0.06$, $p = 0.428$), DBP ($r = 0.10$, $p = 0.159$), TC ($r = 0.09$, $p = 0.215$), LDL-C ($r = 0.11$, $p = 0.131$), the TC/HDL-C ratio ($r = 0.12$, $p = 0.120$), the LDL-C/HDL-C

Table 2. Comparison of metabolic risk factors for groups woMetS and wMetS

Variables	Women woMetS (*n* = 204)	Women wMetS (*n* = 186)
Age (yrs)	27.18 ± 6.87	28.32 ± 5.94
WC (cm)	72.14 ± 9.48	86.35 ± 13.98*
TG (mg/dL)	105.28 ± 23.27	142.59 ± 35.98*
HDL-C (mg/dL)	43.92 ± 6.18	41.98 ± 4.66*
SBP (mmHg)	118.46 ± 9.01	132.40 ± 11.36*
DBP (mmHg)	80.46 ± 6.54	88.46 ± 7.81*
FPG (mg/dL)	90.54 ± 10.42	101.09 ± 17.25*

Data are shown as mean ± S.D. * $p < 0.01$. Abbreviations: WC, waist circumference; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose.

Table 3. Comparison of serum lipid parameters for groups woMetS and wMetS

Variables	Women woMetS (*n* = 204)	Women wMetS (*n* = 186)
TC (mg/dL)	145.14 ± 29.51	172.13 ± 34.64*
LDL-C (mg/dL)	80.16 ± 28.48	101.88 ± 31.80*
VLDL (mg/dL)	21.06 ± 4.65	28.52 ± 7.20*
TC/HDL-C	3.36 ± 0.80	4.15 ± 0.97*
HDL-C/LDL-C	1.87 ± 0.75	2.47 ± 0.87*
LDL-C/HDL-C	0.64 ± 0.35	0.46 ± 0.19*

Data are shown as mean ± S.D. * $p < 0.01$. Abbreviations: TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; VLDL, very low density lipoprotein; HDL-C, high-density lipoprotein cholesterol.

Table 4. Comparison of metabolic risk factors in women woMetS and wMetS sub-grouped according to BMI

Metabolic risk factors	Women woMetS (*n* = 204)		Women wMetS (*n* = 186)	
	BMI < 23 kg/m^2 (*n* = 119)	BMI > 23 kg/m^2 (*n* = 85)	BMI < 23 kg/m^2 (*n* = 36)	BMI > 23 kg/m^2 (*n* = 150)
WC	67.89 ± 7.01	78.08 ± 9.33*	69.78 ± 6.12	90.33 ± 12.31*
WHR	0.79 ± 0.04	0.85 ± 0.06*	0.80 ± 0.04	0.88 ± 0.04*
Serum leptin	5.92 ± 2.83	10.06 ± 5.36*	6.74 ± 3.46	16.29 ± 8.99*
HOMA-IR	1.63 ± 1.12	1.86 ± 1.30	2.59 ± 1.54	2.70 ± 2.16
Serum TG	100.59 ± 21.57	111.85 ± 24.08*	146.61 ± 32.08	141.63 ± 36.89
Serum HDL-C	44.38 ± 6.19	43.28 ± 6.14	41.99 ± 4.37	41.97 ± 4.74

Data are shown as mean ± S.D. * $p < 0.01$. Abbreviations: WC, waist circumference; WHR, waist-to-hip ratio; HOMA-IR, homeostasis model assessment for insulin resistance; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.

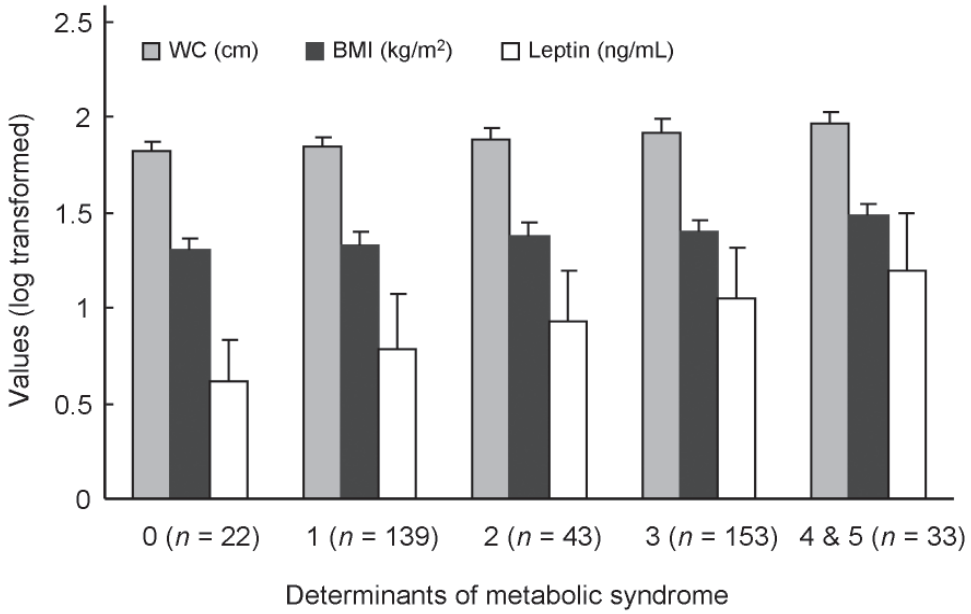

Figure 1. Comparison of serum leptin levels, WC, and BMI with the number of determinants of metabolic syndrome (NCEP-ATP III guidelines). Log-transformed data are expressed as mean ± S.D. In comparison to women with different numbers of determinants of metabolic syndrome, there was a significant increase in the serum leptin level with an increase in number of determinants of metabolic syndrome; this was attributed to an increase in waist circumference independent of BMI. However, women with 2 and 3 determinants had no significant change in BMI but a significant increase in the serum leptin level and WC.

Table 5. Comparison of WC, BMI, and leptin levels on the basis of number of metabolic syndrome determinants according to NCEP-ATP III guidelines

Parameters	Control (n = 22)	MRF 1 (n = 139)	MRF 2 (n = 43)	MRF 3 (n = 153)	MRF 4 and 5 (n = 33)
WC (cm)	66.5 ± 7.6	71.33 ± 7.42	77.63 ± 13.22[ab]	84.67 ± 13.6[abc]	94.15 ± 13.18[abcd]
BMI (kg/m^2)	20.39 ± 3.04	21.55 ± 3.27	24.04 ± 4.07[ab]	25.13 ± 3.47[ab]	30.57 ± 5.21[abcd]
Leptin (ng/mL)	4.53 ± 1.67	7.28 ± 3.73	10.26 ± 6.36[ab]	13.49 ± 8.09[abc]	19.07 ± 11.5[abcd]

Data are shown as mean ± S.D. [a] $p < 0.01$ compared to control. [b] $p < 0.01$ compared to MRF 1. [c] $p < 0.01$ compared to MRF 2. [d] $p < 0.01$ compared to MRF 3. Abbreviations: WC, waist circumference; BMI, body mass index; MRF, metabolic risk factors.

ratio (r = 0.12, p = 0.101), FPI (r = 0.17, p = 0.024), and HOMA-IR (r = 0.11, p = 0.032) (Figures 2 and 3).

4. Discussion

After the discovery of leptin secretion from adipose tissue, leptin's role has been further elucidated in the field of endocrinology. Even though leptin limits food ingestion and increases energy expenditure, it has been found at high levels in obese individuals. The present study noted a relationship between serum leptin levels and insulin resistance, the lipid profile, and metabolic risk factors in adult women, and these three indices indicate a greater risk of developing metabolic syndrome. Using a North Indian population of 390 adult women, this study found that leptin was strongly associated with metabolic syndrome in women wMetS. Women wMetS have higher leptin levels compared to subjects without metabolic syndrome. Furthermore, serum leptin level increased with the number of determinants of metabolic syndrome. Leptin levels were also found to be positively correlated with WHR, BMI, WC, SBP, DBP, TC, TG, FPG, FPI, and HOMA-IR but inversely correlated with HDL-C.

Leptin is an adipocyte secretory product that is not only involved in food intake and energy metabolism but also clearly has a role in glucose metabolism. Leptin may also act as a positive modulator of insulin. In skeletal muscle and beta cells, leptin may promote lipid oxidation and inhibit lipid synthesis, thus improving insulin sensitivity.

The present study found significant differences between women wMetS and woMetS in terms of WHR, BMI, fasting glucose, insulin, insulin resistance, and higher serum leptin levels ($p < 0.001$) (Table 1). However, there is only limited evidence regarding the association between leptin and metabolic syndrome as defined by conventional criteria because a high serum leptin level is associated with central obesity, which accompanies other components of metabolic syndrome like insulin resistance and dyslipidemia, after adjustment for body composition (*22,23*). The increased serum leptin level in obesity may be secondary to 'leptin resistance'. Resistance to the action

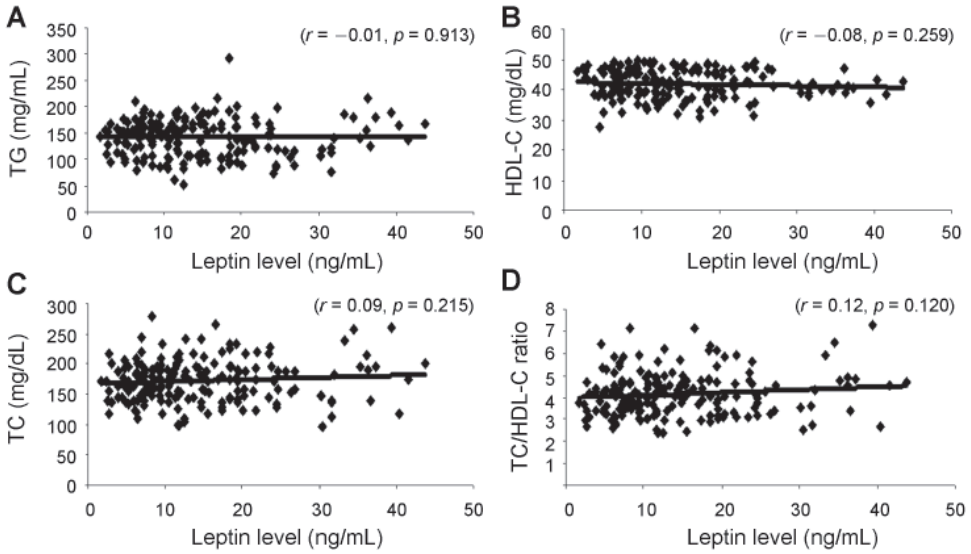

Figure 2. Relationship between serum leptin levels and TG (A), HDL-C (B), TC (C), and TC/HDL-C ratio (D) in North Indian women with metabolic syndrome.

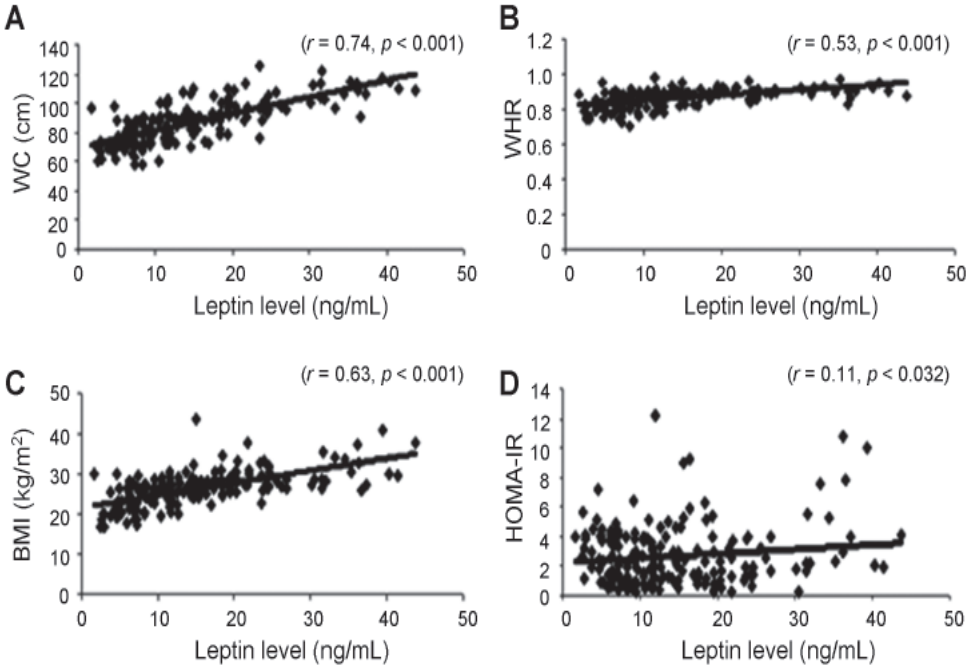

Figure 3. Relationship between serum leptin levels and various metabolic risk factors in North Indian women with metabolic syndrome. (A) WC; **(B)** WHR; **(C)** BMI; **(D)** HOMA-IR. Leptin was positively correlated with these metabolic risk factors.

of leptin could promote obesity *via* decreased energy expenditure and a failure to decrease food intake (*24*). Furthermore, leptin acts *in vivo* to lower glucose and insulin throughout the body, so resistance to this action could induce insulin resistance. One explanation for the insulin resistance seen in obesity might be that the high leptin levels interfere with insulin signaling. Another possibility is that there is diminished activation of AMPK in myocytes due to impaired leptin signalling. The resulting decrease in fatty acid oxidation will lead to an increase in intra-myocellular lipids and thus to insulin resistance.

That said, comparing the metabolic risk factors according to the NCEP-ATP III guidelines in women wMetS and woMetS revealed a significant difference in all risk factors for the development of metabolic syndrome. The current results also indicated that circulating leptin increases with an increase in the determinants of metabolic syndrome ($p < 0.001$). When women were stratified according to the presence of an increasing number of determinants of metabolic syndrome, a significant increase in the

serum leptin level was observed with an increasing number of determinants of metabolic syndrome. This was attributed to an increased waist circumference independent of BMI. There was no significant change in BMI for subjects with 2 and 3 determinants. However, the serum leptin level and WC increased significantly in these subjects (Figure 1 and Table 5). This shows that the presence and number of determinants of metabolic syndrome are closely associated with high levels of circulating leptin and a large WC but are independent of BMI in well-functioning adult women. The association between the presence of metabolic syndrome and leptin is partially attenuated by fat mass and visceral fat area.

The present study and other previous studies have shown that increased serum leptin levels are associated with metabolic abnormalities including abdominal obesity, glucose intolerance, IR, and high blood pressure. The present study found that serum leptin levels were negatively correlated with HDL-C and positively correlated with anthropometric variables, blood pressure, total cholesterol, triglycerides and insulin, and insulin resistance. Strong correlations between leptin and BMI and body fat distribution (waist and WHR) were observed. Similar associations were seen with leptin and body compositions in Asian Indian immigrants compared to Caucasians (*25*). Esteghamati *et al.* (*26*) found that high leptin levels are associated with insulin resistance and metabolic syndrome independent of BMI but that these associations are significantly mediated by the effects of central obesity. Similar to a study by Baratta *et al.* (*27*), the present study found a weak relationship between leptin and lipid parameters but a strong one between BMI and HOMA-IR. In humans, leptin has been found to be associated with factors for cholesterol metabolism (*28*). Leptin specifically represses the gene coding for stearoyl-CoA desaturase-1, an enzyme involved in the synthesis of triglycerides and very low density lipoprotein in the liver (*29*). The causal relationship between leptin and lipid levels has yet to be explained. Further studies are needed to define the factors that affect how leptin and insulin resistance interact, but some authors have posited a strong correlation between leptin and insulin sensitivity (*30*).

Previous studies and this study also suggest that control of metabolic risk factors warrants attention and caution to prevent metabolic syndrome in healthy individuals. Therefore, future studies need to consider how these risk factors influence the relationship between metabolic syndrome and leptin and between the syndrome and other adipokines as well.

As shown here, circulating leptin was significantly associated with obesity, the lipid profile, insulin resistance, and metabolic risk factors in adults of North India. Future studies are needed to identify other genetic or lifestyle risk factors that may contribute to this association and to determine the best strategies for lowering inflammation and the prevalence of metabolic syndrome in adults.

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