



## WHR: COMMON ANTHROPOMETRIC INDICATORS FOR IDENTIFYING INSULIN SENSITIVITY AND RESISTANCE IN FEMALE

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**Abstract:** Diabetes mellitus has reached epidemic level worldwide. South Asians are known for increased predisposition of diabetes which has become an important health problem. Obesity is a well-established risk factor for diabetes mellitus and Insulin resistance. Early detection of reduced insulin sensitivity (IS) and insulin resistance (IR) is need of the time. The aim of the present study was to assess most suitable anthropometric indicator for identifying IR or IS and determine the cutoff points of the most effective indicators. A total of 742 subjects were included in this cross-sectional study. Hormone and glucose levels were estimated using standard protocols. Body mass index (BMI), waist circumference (WC), waist-to-hip ratio, waist-to-height ratio (WHtR) and the HOMA-IS and HOMA-IR were determined. The correlations between the anthropometric indices and IS and IR were determined. ROC analysis was used to determine the areas under the curve (AUC) and cutoff points. Among the obese non diabetic females, WHR ( $r = -0.386$ ;  $P = <0.001$ ) showed substantially significant correlation with HOMA-IS (homeostasis model assessment of insulin sensitivity). The ROC curve demonstrated statistical significance for BMI, WC and WHR, and the best cutoff points were 28.06 kg/m<sup>2</sup>, 94.75 cm and 0.91, respectively. It also showed substantial significance for WHR (AUC =  $0.65 \pm 0.06$ ;  $P = 0.021$ ), and the best cutoff points was 0.85 in all studied anthropometric indices. Among the obese non diabetic female, WHR showed substantially greater correlation with IR/IS.

**Key Words:** Insulin resistance, Body mass index, Waist circumference, Waist to hip ratio, Diabetes, Obesity

### INTRODUCTION

Over recent decades, it has come to be considered that there is a worldwide pandemic of diabetes mellitus (DM). Data from the World Health Organization (WHO) indicate that the prevalence of DM is 2.8% among the worldwide population over 20 years of age (1). Pre-diabetes, characterized by abnormal fasting plasma glucose, glucose intolerance, or both, is often asymptomatic and the time that elapses between the early stages of these conditions and the diagnosing of DM ranges from four to seven years (2). Over this period, the complications relating to inadequate glucose metabolism progress and tissue damage becomes established before DM is diagnosed (3). Within this context, early detection of alterations in glucose metabolism is desirable, such that prophylactic interventions can be implemented (4) (5).

A prospective study demonstrated that reduced insulin sensitivity (IS), evaluated through the homeostasis model assessment of insulin sensitivity (HOMA-IS) index (6), was present the appearance of abnormal fasting plasma glucose, glucose intolerance, or both, in previously normal individuals from the point of view of glucose metabolism. Moreover, during the transition from normal to abnormal metabolism, IS

presented an additional decrease (7). Another index, called the homeostasis model assessment of insulin resistance (HOMA-IR), provides an indirect assessment of glucose metabolism, through evaluating endogenous insulin and plasma glucose homeostasis, as well as fasting plasma glucose (FPG) (8) (9).

Obesity is a condition that involves a risk of such metabolic alterations (10) (11). Therefore, anthropometric indicators among obese individuals are associated with a greater possibility of developing DM and metabolic syndrome. The indicators include body mass index (BMI) (12), waist circumference (WC) (13), waist-to-hip ratio (WHR) (14), waist-to-height ratio (WHtR) (15) and the conicity index (CI) (16). However, such associations have been described both in normal healthy populations and in nutritionally heterogeneous populations.

The objective of the present study was to evaluate the correlation of anthropometric indicators for identifying abnormalities of glucose metabolism in a group of non-diabetic females who were overweight or presented abdominal and generalized obesity (evaluated through BMI and WC) and among

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individuals who were at risk of developing DM, but with normal fasting plasma glucose.

## MATERIALS AND METHODS

### Subjects and data collection

This study is a population-based cross-sectional study, all individuals were of north Indian origin and the population was homogeneous with regard to ethnic background. A total of 742 subjects were enrolled initially from the out patients department of K. G. Medical University UP, Lucknow, India and volunteers from general population of Lucknow (North India). Out of these, only 342 obese/overweight (BMI =  $33.62 \pm 3.60$ ) non diabetic female subjects were selected for the present study. In all subjects' body height, body weight, waist circumferences and hip circumferences were measured for calculation of BMI and WHR. Informed consent was obtained from each participant and the study was carried out in accordance with the local ethics committee.

All study participants were subjected to a thorough screening program that included assessment of a detailed personal and family history, physical examination, determination of anthropometric indices and measurement of various biochemical parameters.

### Measurements

We evaluated weight, height, WC, hip circumference, blood pressure (BP), among the individuals included in study. BMI, WHR, and WHtR were calculated. All the data were evaluated by physicians with training on measurements of weight and height using standard techniques (17). WC was evaluated with the patient standing, at the end of exhalation, at the midpoint between the lower costal border and top of the iliac crest. Hip circumference was measured at the level of the greater trochanter in order to calculate WHR; the mean of 2 measurements was calculated for both WC and hip circumference.

Hypertension was measured in accordance with the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (18). Hypertension was diagnosed when the systolic or diastolic BP was  $\geq 140/\geq 90$  mm Hg on a repeated single-day measurements or when the individual was a known hypertensive. Diabetes was diagnosed when a subject provided history of previously diagnosed diabetes or the fasting blood glucose was  $\geq 126$  mg/dL. Diagnoses of dyslipidemia were evaluated in accordance with the laboratory criteria established in the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, or were defined as

situations of hypolipidemic drug use, regardless of serum lipoprotein cholesterol levels and triglyceride levels (19). Subjects with established diabetes mellitus, coronary artery disease and pregnant women were excluded.

### Estimation of body fat composition

The Body fat analyzer (Bioelectrical impedance was obtained using a device, Tanita-TBF-310, Tanita, Tokyo, Japan; calibrated to suit Indian population) was used for assessing the percentage body fat and fat mass (FM).

### Biochemical Parameters

Venous blood was collected after an overnight fast, and plasma and serum samples were either used immediately for analysis or were stored frozen at  $-80^{\circ}\text{C}$ . Insulin level was determined by enzyme-linked radio immunosorbent assay (RIA) (Linco Research, Inc. USA). The mean intra- and inter assay coefficients of variation for insulin were 5.7 and 9 % (20). The mean intra-assay coefficient of variation (CV) of leptin was 3.4 to 8.3% (21). Insulin resistance (IR) was calculated as follows:  $\text{IR} = \text{Fasting Insulin (FI)} (\mu\text{U/l}) \times \text{FPG (mmol/l)}/22.5$ ; (22). Insulin sensitivity (IS) was calculated as follows:  $\text{IS} = 1/[\text{FI (mU/l)} \times \text{FPG (mmol/l)}/22.5]$  (6). Insulin sensitivity were considered to be preserved when  $\text{HOMA-IS} \leq 0.37$  and insulin resistance was considered to be present when  $\text{HOMA-IR} > 2.7$ , in accordance with a study on prevalence carried out among a Brazilian population (23).

The fasting glucose concentration was measured by Glucose oxidase-Peroxidase (GOD-POD) method (24), the inter assay coefficient of variation was less than 5.0% (25), hypertension were measured twice on the right arm, after a 15-min rest, using a mercury sphygmomanometer (26). All protocols were approved by the Institutional Review Board or Ethical Committee at King George's Medical University Lucknow, Uttar Pradesh, India.

### Statistical analysis

Statistical analyses were performed using the SPSS, version 15.0. The level of statistical significance was set at  $P < 0.05$ . In order to evaluate the correlations of anthropometric data with HOMA-IS and HOMA-IR among the continuous variables, Pearson's coefficient was used on continuous variables with normal distribution and Spearman's coefficient was used on continuous variables that did not follow normal distribution. Fisher's exact test was used for categorical variables.

ROC (receiver operating characteristic) curves were constructed and the areas under the curve (AUC) were calculated, with a 95% confidence interval (CI)

(27). The Z test was used for comparisons of AUCs. Sensitivity (Sn) and specificity (Sp) values relating to detection of lower IS or higher IR were calculated for each cutoff point present in the sample. The cutoff value that presented the highest sum of Sn and Sp was chosen since it optimized the ratio between these two parameters (28).

### RESULTS

The mean age of the 742 subjects with normal FPG was 43.09 ± 12.28 years, and 400 of them were males. The general characteristics of the sample studied are shown in Table 1. Reduced insulin sensitivity was found in 32.35% of the subjects, and the mean HOMA-IS for all subjects was 0.62±0.47, a value that was well above the level that is considered appropriate (≤ 0.37).

**Table 1:** Characterization of the individuals with normal fasting plasma glucose evaluated according to clinical, anthropometric and laboratory data (742)

Variables	Mean ± SD	Median (min-max)
Age (years)	43.09±12.28	44.00 (19.00-78.00)
Weight (kg)	74.10±14.25	74.00 (40.00-115.00)
Height (m)	159.97±9.65	160.00 (136-181)
BMI (kg/m <sup>2</sup> )	29.01±5.77	29.43 (14.69-54.89)
SBP (mmHg)	124.32±13.21	120.00 (90.00-180.00)
DBP (mmHg)	83.03±7.75	80.00 (70.00-110.00)
WC (cm)	98.19±11.41	98.00 (57.00-138.00)
HC (cm)	102.67±10.43	102.00 (65.00-171.08)
WHR	0.95±0.09	0.96 (0.57-1.57)
WHtR	0.61±0.08	0.61 (0.35-0.87)
FPG (mg/dl)	97.86± 8.53	99.20 (60.03- 109.60)
FI (mIU/ml)	10.98±7.99	9.30 (1-70)
HOMA-IS	0.62±0.47	0.45 (0.05-4.75)
HOMA-IR	2.67±1.94	2.19 (0.26-014.52)
% body fat	32.22±7.51	32.40 (16.90-53.60)
FM (kg)	25.18±9.19	24.10 (8.30-56.60)

BMI=Body Mass Index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; WC=Waist circumference; HC=Hip circumference; WHR=Waist to hip ratio; WHtR=Waist-to-height ratio; FPG=Fasting plasma glucose; FI=Fasting Insulin; HOMA-IS=Homeostasis model assessment of insulin sensitivity index; HOMA-IR=Homeostasis model assessment of insulin resistance index; FM=Fat mass.

In parallel, we evaluated 342 non-diabetic obese/over-weight females, of mean age 44.30 ± 10.53 years. The prevalence of insulin resistance in the sample studied was 26.32%, with mean HOMA-IR of 4.44±3.04, which were also above-normal values (≤ 2.7). The general characteristics of the female population studied are shown in Table 2. Regarding nutritional status, according to BMI data, 51.8% were overweight and 48.2% were obese. The correlation with HOMA-IS in the group of subjects with normal FPG was demonstrated using BMI (r = -0.296; P = <0.001) and WHR (r = -0.386; P = <0.001) (Table 3). A ROC curve was constructed for the anthropometric indicators

evaluated and HOMA-IS was calculated in order to assess IS (Figure 1). Data on AUC, standard error (SE), 95% CI, cutoff points and the respective Sn and Sp demonstrated statistical significance in relation to BMI (AUC = 0.65±0.03; P = <0.001), WHR (AUC = 0.63±0.04; P = <0.001) and WC (AUC = 0.65±0.03; P = <0.001), and the best cutoff points found were 28.06 kg/m<sup>2</sup>, 0.91 and 94.75 cm, respectively (Table 4).

**Table 2:** General characteristics of the group of obese non-diabetic females (n=342)

Variables	Mean ± SD	Median (min-max)
Age (years)	44.30±10.53	45.00 (20.00-75.00)
Weight (kg)	75.96±13.45	77.50 (37.40-105.00)
Height (m)	153.90±8.32	153.50 (136-180)
BMI (kg/m <sup>2</sup> )	33.62±3.60	32.60 (30.04-47.57)
SBP (mmHg)	130.23±13.82	130.00 (90.00-180.00)
DBP (mmHg)	87.28±7.54	88.00 (70.00-110.00)
WC (cm)	101.25±12.15	102.00 (57.00-130.00)
HC (cm)	108.35±12.38	110.00 (65.00-155.00)
WHR	0.93±0.08	0.93 (0.67-1.20)
WHtR	0.66±0.08	0.67 (0.35-0.87)
FPG (mg/dl)	98.02±8.58	99.30 (60.03-110.00)
FI (mIU/ml)	15.94±9.92	14.00 (1.00-45.00)
HOMA-IS	0.51±0.52	0.37 (0.09-4.75)
HOMA-IR	4.44±3.04	3.69 (0.26-13.34)
% body fat	38.01±6.30	37.85 (20.50-53.60)
FM (kg)	32.42±8.92	30.90 (8.70-56.60)

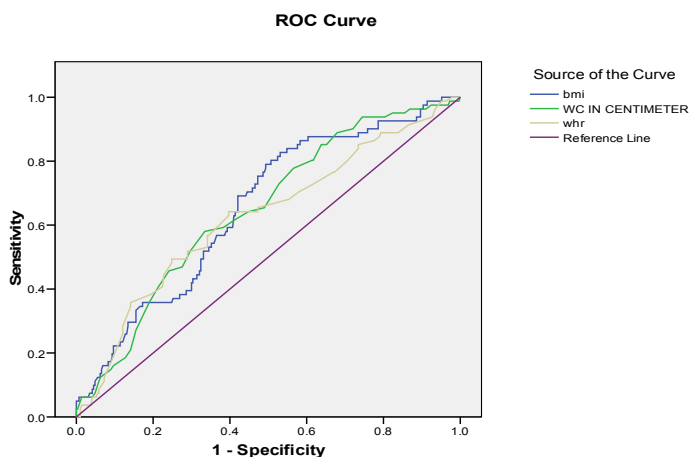
**Table 3:** Bivariate correlation analyses between HOMA-IS, and the variables (n=342)

Variables	HOMA-IS	
	r	P value
BMI (kg/m <sup>2</sup> )	-0.296	<0.001
WC (cm)	-0.326	<0.001
WHR	-0.386	<0.001
WHtR	-0.288	<0.001
% body fat	-0.284	<0.001
FM (kg)	-0.314	<0.001

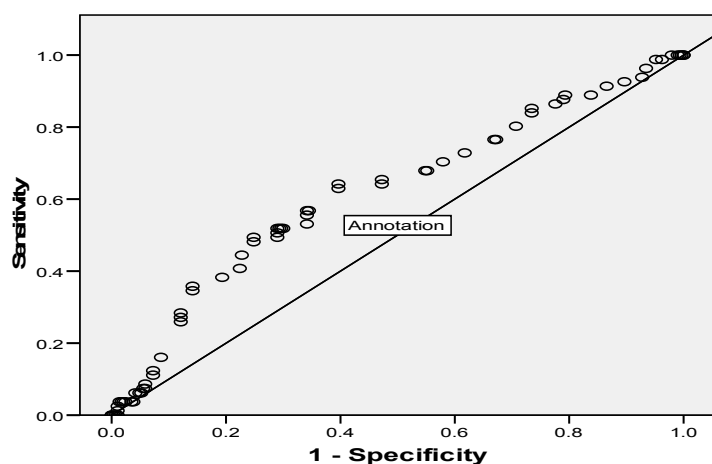
**Table 4:** Efficacy of the anthropometric indicators evaluated and fasting plasma glucose in assessing insulin sensitivity

Variables	Area ± SE (95% CI)	COP	Sn	Sp	Sn + Sp	P value
BMI (kg/m <sup>2</sup> )	0.65±0.03 (0.59-0.72)	28.06	80.2	50.7	130.9	<0.001
WHtR	0.65±0.03 (0.58-0.72)	0.59	80.2	61.4	141.6	<0.001
WHR	0.63±0.04 (0.55-0.70)	0.91	80.2	70.7	150.9	<0.001
WC (cm)	0.65±0.03 (0.58-0.71)	94.75	80.2	61.4	141.6	<0.001
FPG (mg/dl)	0.64±0.04 (0.57-0.72)	96.90	80.2	61.7	141.9	<0.001
% body fat	0.64±0.03 (0.58-0.71)	28.85	81.5	60.3	141.8	<0.001
FM (kg)	0.67±0.03 (0.61-0.73)	21.50	81.5	52.8	134.3	<0.001

SE = standard error; CI = confidence interval; COP = cut off point; Sn = Sensitivity (95% CI); Sp = Specificity (95% CI).



**Figure 1:** ROC (receiver operating characteristic) curve for the anthropometric indicators evaluated for assessing insulin sensitivity.



**Figure 2:** ROC (receiver operating characteristic) curve for waist-to-hip ratio for assessing insulin resistance through the HOMA-IR (homeostasis model assessment of insulin resistance) index.

In the group of obese females, the most statistically significant correlation with the HOMA-IS index was demonstrated by the waist-to-hip ratio (WHR). The remaining anthropometric indicators of obesity and body composition that were evaluated demonstrate correlations with the HOMA-IS index but it is less significant in comparison to WHR. A ROC curve was constructed for WHR, in order to assess IS, through HOMA-IR (Figure 2). In assessing the cutoff point with the greatest accuracy, WHR reached the greatest sum between Sn and Sp values for the cutoff point 0.85 (AUC = 0.65 ± 0.06; P = 0.021) (Table 5).

**Table 5:** Efficacy of waist-to-hip ratio for evaluating insulin sensitivity in the group of obese females

Variables	Area ± SE (95% CI)	COP	Sn	Sp	Sn + Sp	P value
WHR	0.65±0.06 (0.53-0.77)	0.85	86.7	82.0	168.7	0.021

SE = standard error; CI = confidence interval.

## DISCUSSION

In the present study, BMI and WHR demonstrated relevant negative correlations with HOMA-IS in individuals with normal FPG but presenting conditions that indicated that they were at risk of developing diabetes mellitus. The most promising anthropometric indicators for assessing IS/IR were BMI, WHR and WC. BMI and WC are widely used in clinical practice. However, WHR still has not been incorporated into routine anthropometric assessment.

Previous studies already reported associations between WHR and conditions such as left ventricular hypertrophy (29), hypertension (30), diabetes (31), and IR (32). Another important finding from the present study was the correlation between IS, evaluated through the HOMA-IS index, among overweight non diabetic females. Several previous studies have associated abdominal obesity with metabolic alterations and high cardiovascular risk, regardless of generalized obesity indicators (33) (34) (35).

Imaging techniques such as nuclear magnetic resonance and computed tomography make it possible to observe different adipose tissue deposits at waist level. Among these are visceral and subcutaneous adiposity: the first of these is highly correlated with IS reduction and increased IR (36) (37). In turn, WHR has demonstrated a strong correlation with adiposity and was therefore it is a reliable marker of central adiposity and higher risk of adverse health (38). Yu *et al.*, (2013), (39) observed that WHR showed the highest AUC for the prediction of cardiovascular disease except for age and WC in women, suggesting that WHR may be a helpful as significant marker for early detection atherosclerosis. The Dallas Heart Study also discovered that WHR was independently associated with cardiovascular disease and WHR predict as a more precise indicator than either BMI or WC. The previous literature explained fully the reason for the association of visceral fat with metabolic abnormalities. Although obesity as defined by BMI is certainly connected with an increased risk of metabolic abnormalities, but at the same time studies also emphasized on the metabolic differences between different types of obese subjects. For example, Samocha-Bonet *et al.*, (40) reported a subset of obese subjects who are obese but metabolically healthy. The fat depots is responsible for this significant difference reported between the “metabolically healthy obese” and “metabolically unhealthy obese” subjects. “Metabolically healthy obese” subjects share same BMI levels with to “metabolically unhealthy obese” subjects, but they have less fat accumulate in the abdomen region, and more subcutaneously. So, abdominal obesity could negatively affect metabolic status and surly the vascular health.

Dasgupta et al., (32) also reported that WHR was the only significant predictors for an increased insulin resistance. They also suggested that abdominal obesity is a better predictor for insulin resistance than the overall body fat distribution. Previous studies have suggested that female subjects matched for BMI have greater WHR and insulin resistance (41). It is because WHR is more directly related to the visceral adipose tissue that, so it also associated with an increased production of different functional molecules, it is involved, at least in part, in both insulin resistance and low-grade inflammation.

IS reduction and increased IR are subclinical conditions that have been considered to be precursor alterations of pre-diabetic status (7), that justifies active surveillance to diagnose such conditions. However, the laboratory analyses available and involved in the detection of IR are expensive. Therefore, every effort should be made towards determining cost-effective and easily interpreted criteria to identify such conditions. To this end, further studies should be encouraged in different populations, with the aim of validating the use of anthropometric indicators that were shown to be effective in the present study.

Like others this study has some limitations. First, since the study sample contains only female subjects, a main limitation of this study, the differences in environments between female subjects studied in our study and male which may represent the more general population in addition to potential sex-related effects so the study population was not representative of the whole population. Second, lack of participants' history, such as smoking, past medical history and medication so this information were not available for analysis. Third, because of the cross-sectional nature of the study, a cause-and-effect relationship cannot be rule out from the study. More prospective or longitudinal studies are required to determine the future risk of development of metabolic risk factors related to adiposity. Finally, the method used for the measurement of body composition analyses, BIA was not as accurate as dual X-ray absorptiometry; so the assessment of specific components of body composition could have had some limitations.

### CONCLUSION

In conclusion, we found that WHR showed a significantly higher correlation with IS, among overweight female, and the best cutoff point was 0.85, compared with other metabolic parameters. This result suggests the superiority of WHR as a marker for early detection of metabolic disorders in comparison to other parameters that assess adiposity status. These indicators involve simple, fast and easily interpreted

anthropometric assessments, which may form an alternative to the present indices in clinical practice. In addition, abdominal obesity may have significant deleterious effects, particularly the development of metabolic disorder with the potential for future risk.

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