Original Article

The Role of Waist-to-Height Ratio in Screening for Hyperinsulinemia in Normoglycemic Individuals

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Abstract

Objective: This study evaluates the correlation between insulin resistance and WHtR in normoglycemic individuals with and without a family history of T2DM.

Methodology: A cross-sectional study was conducted with 80 normoglycemic adults (20-50 years) recruited from a diabetes screening camp at District Headquarters Hospital, Gujranwala. Participants were categorized into Group A (40 individuals with a first-degree relative diagnosed with T2DM) and Group B (40 individuals without a familial history). Normal glucose tolerance was confirmed via an oral glucose tolerance test (OGTT) as per inclusion criteria, whereas diagnosed diabetes, cardiovascular diseases, hypertension, chronic renal diseases, malignancies, pregnancy, and acute illnesses were excluded. Anthropometric assessments, including height, waist circumference, and WHtR, were recorded alongside fasting plasma glucose, fasting insulin, and insulin resistance using homeostatic model assessment of insulin resistance (HOMA-IR).

Results: WHtR demonstrated a significant positive correlation with insulin resistance ($p=0.001$). Strong associations were observed between waist circumference, WHtR, fasting insulin, and HOMA-IR ($p<0.0001$). However, mean differences between groups were not statistically significant.

Conclusion: WHtR holds potential as a practical screening tool for hyperinsulinemia, particularly in individuals with a genetic predisposition to T2DM. Further large-scale and longitudinal studies are recommended.

Keywords: Blood glucose, Insulin resistance, Mass screening, Type 2 diabetes mellitus, Waist-height ratio.

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Introduction

Hyperinsulinemia is characterized by excessive insulin levels in circulation, often triggered by insulin resistance, wherein tissues exhibit reduced responsiveness to insulin. This condition is linked to metabolic disorders such as type 2 diabetes and obesity, impairing glucose metabolism and increasing cardiovascular risk. Contrary to conventional understanding, recent research suggests that hyperinsulinemia may precede insulin resistance in T2DM progression.[1]

Obesity contributes significantly to insulin resistance through inflammatory pathways and adipokine release, impairing insulin function in various tissues.[2] Traditional metrics like body mass index (BMI) provide a general measure of obesity but fail to reflect central fat distribution.[3] WHtR, however, is a more reliable marker of abdominal obesity, demonstrating a strong correlation with metabolic risks and proving superior to BMI in various studies.[4] Body mass index (BMI) commonly identifies obesity but lacks central obesity information, which is crucial for cardiovascular risks. Waist circumference faces challenges due to age, gender, and ethnicity variations in setting universal cutoffs. Waist-to-height ratio (WHtR) emerges as a reliable surrogate for abdominal obesity, offering consistent cutoffs across demographics, correlating well with body fat, and predicting hypertension. BMI's criticism includes failure to adjust for muscle mass, bone density, and fat distribution. An observational study on Asian heart failure patients revealed an "obesity paradox," suggesting lower morbidity and mortality risks in obese individuals by BMI, contrasting elevated WHtR linking to heart disease and diabetes risks. Patients with high WHtR and low BMI had the poorest outcomes, highlighting dual BMI and WHtR assessments for health risks.[5]

WHtR proves robust in identifying central obesity and predicting cardiometabolic risks, advocated by NICE as an early health marker.[6] Biomarker dependence overlooks early metabolic disorder detection, demanding insulin sensitivity assessment methods for T2DM prevention. WHtR anticipates insulin resistance or hyperinsulinemia before blood glucose changes.[7] One of the studies investigated anthropometric cutoff points for screening diabetes and metabolic syndrome (MetS) in Arab and South Asian ethnic groups in Kuwait, comparing ethnic-specific waist circumference (WC) cut points with International Diabetes Federation (IDF) and American Heart Association/National Heart, Lung, and Blood Institute criteria. It analyzed data from a national survey of Kuwaiti adults aged 18–60 years and found similar ROC values for WC, waist-to-height ratio (WHtR), and BMI in distinguishing diabetes and ≥3 cardiovascular disease (CVD) risk factors. While findings were specific to Kuwait, they underscore the need for similar studies in Pakistan to establish tailored anthropometric guidelines for screening metabolic health risks.[8] In Pakistan, a study on children aged 5-12 years identified cutoff values for waist-to-height ratio (WHtR) to detect overweight and obesity. For overweight, the WHtR cutoff values were 0.46 for boys and 0.47 for girls, while for obesity, the values were 0.47 for boys and 0.48 for girls.[9] Similarly, another study conducted at King Edward Medical University in collaboration with Mayo Hospital Lahore found that raised Body Mass Index (BMI) is associated with insulin resistance, particularly among females, whereas Waist-to-Hip Ratio (WHR) is not significantly associated with insulin resistance.[10]

Given the need for early detection of metabolic risks, this study investigates the association between WHtR and insulin resistance in normoglycemic individuals with and without a family history of T2DM.

Methodology

This comparative study was conducted at the University of Health Sciences, Lahore, from December 22, 2020, to July 2, 2021. Participants were recruited from the outpatient section of the District Headquarters Hospital, Gujranwala, during a diabetes screening camp. The sample size estimates were derived from article 11 using the standard sample size formula WHO sample size calculator. Although the calculated sample size in each group was 15, it was increased to 40 participants per group to ensure research validity.

Participants in Group A were eligible if they had a family history of diabetes and normal glucose tolerance confirmed by OGTT, whereas those in Group B had no diabetic background. Nonetheless, individuals with acute illnesses at the time of the study and known cases of any type of diabetes, cardiovascular diseases, cerebrovascular diseases, peripheral arterial diseases, hypertension, chronic renal illnesses, malignancies, bone diseases, and pregnancy were excluded.

Variables included anthropometric measurements (height, waist circumference), fasting and post-prandial blood glucose levels, fasting insulin levels, and insulin resistance (HOMA-IR). Participants were stratified into two groups based on family history of diabetes.

Anthropometric Measurements

Height was measured in centimeters (cm) using a stadiometer. Waist circumference (WC) was measured following WHO recommendations using a flexible, non-stretchable measuring tape positioned at the midpoint between the lower margin of the last palpable rib and the iliac crest. Participants maintained an upright posture with a relaxed abdomen to ensure measurement accuracy and consistency.

Waist-to-height ratio (WHtR) was calculated by dividing waist circumference (cm) by height (cm).12For adults with central obesity, a cutoff value of 0.5 is generally accepted.[13]

Blood Sample Collection

Participants arrived in a fasting state. Blood samples (3-5 ml) were collected from the vein to measure fasting blood glucose and insulin levels. Blood samples (3 ml) were collected again after administering 75g of oral glucose to measure 2-hour post-prandial glucose levels.

Laboratory Procedures

Blood samples were transported to the laboratory of the Department of Physiology and Cell Biology at the University of Health Sciences, Lahore, on the same day of sample collection. The serum was separated by centrifugation, aliquoted into Eppendorf tubes, and stored at -40°C. The concentration of blood glucose was assessed using the glucose oxidase enzymatic technique. Fasting insulin concentrations were quantified using an enzyme-linked immunosorbent assay (ELISA) kit, ensuring precise and reliable assessment. The sandwich ELISA technique was employed, where insulin in test sera was conjugated with both enzyme and solid-phase antibodies.

Calculation of Insulin Resistance (HOMA-IR)

Insulin resistance was calculated using the HOMA-IR equation: [(Fasting insulin * Fasting glucose) / 22.5].14

Ethical Considerations

Current research was handled in alignment with the Helsinki Declaration of Human Rights. It was duly approved by the Ethical Review Committee of the University of Health Sciences, Lahore (letter NO: UHS/REG-20/ERC-2991 dated December 11, 2020).

Statistical Analysis:

SPSS version 25 was used for statistical analysis. Normality was tested using Shapiro-Wilk's test. Independent sample t-tests compared normally distributed data, while the Mann-Whitney U test was used for non-normally distributed data. Correlation analysis was conducted between WHtR and HOMA-IR, with statistical significance set at $p<0.05$[7].

Results

This investigation involved comprehensive anthropometric measurements and biochemical analyses, detailed in Table 1, providing a foundational understanding of the study cohort. Among participants, 44.4% (36) were aged 20-30 years, 37% (30) were aged 30-40 years, and 17% (14) were aged 40-50 years. Group A comprised 62.5% (25) males and 37.5% (15) females, while Group B included 57.5% (23) males and 42.5% (17) females.

Regarding family history, 47% (19) had a maternal history of T2DM, 40% (16) had T2DM in their paternal side, while 12.5% (5) had T2DM in both parents. A pivotal observation revealed a significant positive correlation between waist-to-height ratio (WHtR) and critical metabolic indicators, including fasting insulin, homeostatic model assessment of insulin resistance (HOMA-IR), age, waist circumference, and fasting plasma insulin levels.

In Table 1, the anthropometric and biochemical parameters of participants were analyzed and compared between the two mentioned groups. The average age was similar in both groups, with Group A at 32 ± 8.4 years and Group B at 33 ± 9.7 years (p=0.56). Waist circumference, height, and waist-to-height ratio did not show significant variations, with p-values of 0.14, 0.2, and 0.07(Fig: 1), respectively. Fasting plasma glucose and 2-hour post-prandial glucose levels were comparable between the groups (p=0.45 and p=0.43). Likewise, fasting insulin levels and HOMA-IR scores exhibited no notable differences, with p-values of 0.52 and 0.61. Overall, these findings suggest that there are no significant disparities in the measured parameters between individuals with normal glucose tolerance, irrespective of their familial history of diabetes.

The correlation analysis reveals significant interrelationships between various anthropometric and biochemical parameters (Table 2). Age is strongly correlated with waist circumference and WHtR, suggesting age-related changes in body fat distribution. Gender showed a significant positive correlation with fasting plasma glucose ($r = .289$, $p < 0.01$), HOMA-IR ($r = .304$, $p < 0.01$), fasting insulin ($r = .324$, $p < 0.01$), and a significant negative correlation with family history of diabetes (FH) ($r = -.530$, $p < 0.01$). Insulin resistance (HOMA-IR) was strongly correlated with fasting insulin ($r = .984$, $p < 0.01$) and waist-to-height ratio (WHtR) ($r = .364$, $p < 0.01$), highlighting the potential utility of WHtR as a predictor of insulin resistance. Waist circumference and WHtR are closely linked to each other and are also significantly associated with fasting plasma insulin and HOMA-IR, indicating that central obesity plays a crucial role in insulin resistance. Height shows an inverse relationship with WHtR, fasting plasma insulin, and HOMA-IR, highlighting potential protective factors of greater stature against metabolic disturbances. Fasting plasma glucose is strongly correlated with 2-hour post-prandial glucose, fasting plasma insulin, and HOMA-IR, emphasizing its role as a key marker of glucose metabolism and insulin resistance. Overall, these findings underscore the complex interplay between body composition and metabolic parameters in assessing metabolic health.

Waist circumference also showed a strong positive correlation with WHtR ($r = .938$, $p < 0.01$) and fasting insulin ($r = .366$, $p < 0.01$). Interestingly, family history was negatively correlated with fasting plasma glucose ($r = -.374$, $p < 0.01$), HOMA-IR ($r = -.281$, $p < 0.05$), and fasting insulin ($r = -.240$, $p < 0.05$), suggesting that subjects without a family history of diabetes might exhibit higher levels of these metabolic indicators. In the current study, the IQR of WC was higher in group B,

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Table 1. Anthropometric and Biochemical parameters of Participants

Parameters	Group A		Group B		p-value
	Mean ± SD	Median(IQR)	Mean ±SD	Median(IQR)	
Age(years)	32±8.4	32(20-50)	33±9.7	30(20-50)	0.56
WC(cm)	95±14	89 (69-130)	91±21	89 (50-152)	0.14
Height(cm)	162±12	166(132-183)	167±10	170(145-185)	0.2
WHtR	0.6±0.12	0.56(0.4-0.9)	0.5±0.12	0.54(0.3-0.9)	0.07
FPG(mg/dl)	78±8.2	78(63-99)	76±7.4	75(63-99)	0.45
2HRPP(mg/dl)	104±12	100(87-145)	107±13	105(89-140)	0.43
Fasting Insulin(Mu/L)	15±12	10(1.31-54)	17±14	11(2.61-75)	0.52
HOMA-IR	2.8±2.3	2.06	3.2±3.2	2.14	0.61

Group A: Normal glucose tolerant with diabetic family history, Group B: Normal glucose tolerant without diabetic family history, SD: Standard deviation, IQR: Interquartile range, WC: Waist circumference, WHtR: Waist-to-height ratio, FPG: Fasting plasma glucose, 2HRPP: 2-hour post-prandial glucose, HOMA-IR: Homeostasis model of assessment of insulin resistance, sFRP-4: Secreted frizzled related protein-4. The independent sample t test and Mann Whitney U test was used was used to evaluate the p value accordingly.

Table 2. Spearman's correlation of anthropometric and biochemical parameters

		WC	Height	WHtR	FPG	2hrpp	HOMA-IR	FPI
Age	r	.46**	.02	.41**	.16	.014	.296**	.306**
	p	.001	.89	.001	.201	.902	.008	0.001
WC	r		-.04	.94**	.06	.121	.355**	.366**
	p		.73	.001	.6	.28	.001	0.001
Height	r			-.34	-.19	-.04	-.16	-.15
	p			.002**	.09	.67	.15	.186
WHtR	r				.07	.08	.364**	.372**
	p				.5	.46	.001	0.001
FPG	r					.64**	.229*	.09
	p					.001	.04	.41
2hrpp	r						0.12	.01
	p						0.28	.889
HOMA-IR	r							.98**
	p							.001

** Significant at p=0.01 level.

* Significant at p=0.05 level.

WC: Waist circumference, WHtR: Waist-to-height ratio, FPG: Fasting plasma glucose, 2hrpp: 2-hour post-prandial glucose, HOMA-R: Homeostasis model of assessment of insulin resistance, FPI: Fasting plasma insulin

representing a higher abdominal fat percentage that could have some implications on the results of Waist to height ratio.

Discussion

This study identified a statistically significant positive correlation between waist-to-height ratio (WHtR) and key metabolic indicators, including fasting insulin, HO-

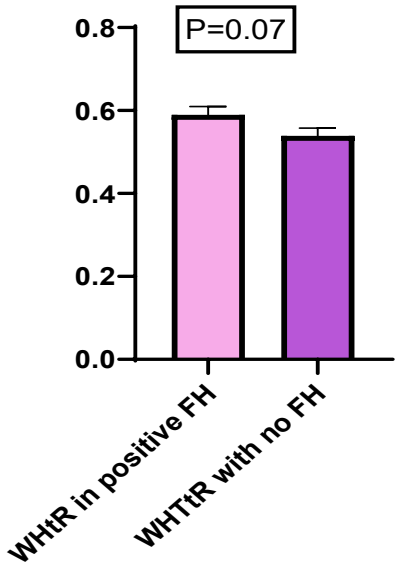

Figure 1: Comparison of WHtR in people with and without diabetic background

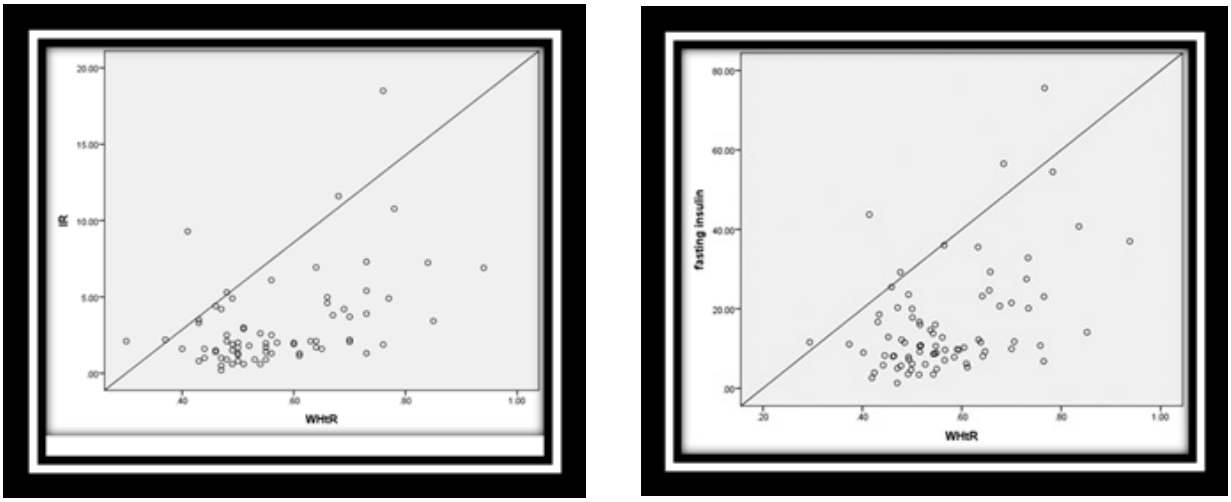

Figure 2: Scatter Plots showing Positive Co- Relation of WHtR with HOMA-IR and Fasting Plasma Insulin

MA-IR, age, waist circumference, and fasting plasma insulin levels (Table 1). However, despite finding higher mean values of waist circumference and WHtR among individuals with a positive family history (FH) of type 2 diabetes mellitus (T2DM), our analysis did not show significant differences in HOMA-IR and fasting plasma insulin levels between those with and without a family history, as indicated by the Mann-Whitney U test.

The non-significant differences between the FH and non-FH groups in terms of HOMA-IR and fasting plasma insulin might be attributed to the relatively small sample size or variability within the groups. Other studies have demonstrated varying results, which may be influenced by different methodologies or sample characteristics. The lack of significant findings in our study underscores the complexity of metabolic indicators and suggests that family history alone may not be a sufficient predictor without considering additional factors. Furthermore, other studies have produced mixed results regarding the relationship between FH and these metabolic indicators, reflecting the complex nature of insulin resistance and its predictors.[18,19]

A key contribution of our study is the demonstration of WHtR as a valuable screening tool for identifying hyperinsulinemia, even in individuals with normal glucose tolerance and a family history of T2DM. This reinforces WHtR's role as a more specific and sensitive marker compared to traditional indicators like BMI. The correlation between WHtR and insulin resistance aligns with findings from various studies but adds new insight by focusing on individuals with normal glucose tolerance, which is relatively underexplored.

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This finding supports its role as a more sensitive and specific marker compared to BMI. While existing literature highlights its effectiveness in various contexts, our study adds new insights by focusing on individuals with normal glucose tolerance, an area less frequently explored.[25,26]

Several studies support WHtR as an effective tool for screening insulin resistance. Research from India[14] and Indonesia[15] indicates its positive correlation with insulin resistance and hyperinsulinemia. Studies correlate WHtR positively with hyperinsulinemia in non-diabetics[16] and diabetics,[17] superior in PCOS detection compared to BMI in India.[14] In a long-term study, individuals with T2DM had a higher incidence of cardiovascular disease associated with elevated WHtR.[18] West African research also supports WHtR and waist circumference (WC) as strong indicators for type 2 diabetes risk.[19]

Another study highlighted significantly higher body weight, BMI, waist circumference, and type 2 diabetes mellitus risk among individuals with a diabetic background compared to those without. Factors such as ethnicity, fiber intake, and awareness significantly influence susceptibility to diabetes. The study also underscored the inferior nutritional status among individuals with a diabetic background.[20] In a cross-sectional study involving 9605 respondents from Northern China, WHtR emerged as a superior indicator associated with carotid artery stenosis (CAS), suggesting its efficacy in early identification and intervention for carotid artery atherosclerosis in high-risk individuals.[21] However, the Karachi study highlighted the limitations in correlating WHtR specifically with hyperinsulinemia among metabolic syndrome individuals.[22]

However, recent studies highlight its relevance in different populations. A 2020 study in Brazil confirmed its association with metabolic syndrome and its potential as a screening tool in diverse ethnic groups.[23] Similarly, research from 2021 in China demonstrated that it was a better predictor of insulin resistance compared to BMI in a large cohort of adults.[24]

In summary, while our study reinforces the utility of WHtR in identifying hyperinsulinemia, especially among individuals with normal glucose tolerance, it also highlights the need for further research to clarify these relationships fully. The findings suggest that while WHtR is a promising tool, its effectiveness and application may vary depending on individual and contextual factors.

The relatively small sample size may limit the generalizability of findings. Results may not be fully representative of broader populations as it is a single center study. Variables such as dietary habits, physical activity, and broader genetic predispositions were not considered. Future research should focus on multi-center, longitudinal studies with larger cohorts to further explore WHtR's role in metabolic risk assessment.

Conclusion

In conclusion, the strong correlations between WHtR, fasting insulin, and HOMA-IR highlight the significant impact of central obesity on insulin metabolism. These findings emphasize the importance of WHtR as a practical and reliable measure for assessing the risk of hyperinsulinemia and related metabolic conditions. Monitoring and managing WHtR could be crucial for early detection and intervention in individuals predisposed to metabolic syndrome and type 2 diabetes.

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Authors' Contribution Statement

SA contributed to the conception, design, acquisition, and data analysis. SK contributed to the supervision, data analysis, and proofreading. AS contributed as a co-supervisor of the study. HU contributed to laboratory work. All authors are accountable for their work and ensure the accuracy and integrity of the study.

Confilct of Interest

Authors declared no conflict on interest

Grant Suppport and Financial Disclosure

None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.