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Original Research Article

Correlation of triglyceride by HDL ratio as a marker of insulin resistance with BMI, waist to hip ratio, waist to height ratio and waist circumference, in South Indian population

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Abstract

Context: Type 2 diabetes mellitus (DM) and its pre runner, insulin resistance (IR) has become a pandemic problem, including the developing countries. Hence cost effective methods like anthropometric measures are needed to assess insulin resistance.

Aims: 1) To study the pattern of dyslipidemia in diabetics and non diabetic subjects. 2) To correlate the association of anthropometric markers (Body mass index (BMI), Waist/Hip ratio (WHR), Waist/height ratio (WHtR), Waist circumference (WC) with Triglyceride (TG) / High density lipoprotein (HDL) ratio as a surrogate marker of IR.

Settings and Design: 50 diabetics and 50 non diabetic subjects were enrolled prospectively and anthropometric and laboratory data were collected and analyzed in a tertiary care hospital.

Methods and Material: Statistical analysis used: Mean, Standard deviation, Frequency and Percentage. Pearson's correlation, Independent sample t test, Mann WhitneyU test.

Results: Elevated TC, LDL, TG/HDL, WHR and low HDL were significantly associated with diabetics. WC showed maximum correlation with TG/HDL among anthropometric markers in the whole study group and both study groups separately. The correlation of TG/HDL with WHtR (r=0.110) was higher in controls when compared with cases (r= 0.23) indicating that WHtR has high levels of correlation with IR in obese non diabetic population.

Conclusions: In this study, the above anthropometric measurements showed positive correlation with TG/HDL ratio. WC showed maximum correlation, though statistically not significant. We suggest using anthropometric measurements (WC, BMI, WHR, WHtR) as inexpensive and easy methods in clinical and epidemiological fields.

Keywords: Type 2 diabetes; fasting lipid profile; Body mass index; Waist hip ratio; Waist to height ratio, Waist circumference.

1. Introduction

Type 2 diabetes mellitus (DM) is a global public health crisis. It threatens the economies of all nations, particularly developing countries. Fueled by rapid urbanization, nutrition transition, and increasingly sedentary lifestyles, the epidemic has grown in parallel with the worldwide rise in obesity. [1]

According to the current estimates from the International Obesity Task Force, at least 1.1 billion people across the globe are overweight and 312 million of them are obese. It is now a well established fact that obesity, which is most commonly defined according to body mass index (BMI), substantially increases the risk of type-2 diabetes, hypertension, cardiovascular disease, and all-cause mortality. [2]

One of the important risk factors for cardiovascular diseases is insulin resistance (IR) syndrome. The evaluation of the insulin resistance has received tremendous attention in the last few years. The laboratory methods used for the determination of insulin resistance are expensive. [3] BMI and waist-to-hip ratio (WHR) are widely used as obesity indices for diabetes and cardiovascular risks. [4] Furthermore, the metabolic

alterations that finally result in metabolic syndrome are caused by insulin resistance which leads to metabolic syndrome (MetS) and prevalence of MetS is directly proportional to the obesity. [3]

While the determination of total cholesterol (TC), Serum triglyceride (TG), High density lipoprotein (HDL), low density lipoprotein (LDL), and blood glucose form part of the basic biochemical laboratory tests, there are however concerns about the reliability of some anthropometric measurements. BMI has routinely been used in clinical and public health practice to identify individuals at risk of future cardiovascular disease and diabetes. However, this measurement reflects both fat and lean mass and does not identify fat distribution. Other parameters usually used to assess obesity and abdominal obesity in particular, such as waist circumference (WC) and hip circumference (HC), may differ depending on the precise site at which they are measured. In the last few years, several large studies throughout different populations have shown that waist circumference-to-height ratio (WHtR) correlates more strongly with cardio-metabolic risk factors. Hence it is a simple and effective anthropometric index to identify obesity-associated metabolic risks. [5]

It is accepted now that the location of excess adiposity is a strong determinant of cardio metabolic risk. In comparison with overall obesity, the central deposition of excess weight specifically has been proven to be a stronger predictor of risk of morbidity and mortality, as defined by BMI alone. [2]

WC is often advocated as a simple and accurate anthropometric marker of central obesity. It is also associated cardio metabolic risk, and its use has been adopted into clinical screening guidelines. But the measure is not without limitations. First, WC cutoff points cannot be used universally across gender or race. The optimal WC cutoffs for assessing cardio metabolic risk may even differ between Asians from different countries. The application of WC to assess cardio metabolic risk also assumes, albeit erroneously, that risk stratification is not influenced by patient height. For example, it has recently been shown that the risk of metabolic syndrome within a given WC strata is significantly higher among shorter individuals. [2] Lower adult height was related to diabetes and stroke. [4]

An alternative anthropometric index of central obesity is WHtR circumvents the limitations of WC. First, due to the inclusion of height into the index, any potential confounding of cardio metabolic risk by height is avoided. Second, studies have found similar WHtR cutoffs for increased cardio metabolic risk among Caucasian and Asian populations as well as men and women. In fact, a WHtR cutoff value of 0.5 has been proposed as an indicator of cardio metabolic risk for Japanese, Korean, and British men and women. Finally, WHtR has also been shown to denote cardio metabolic risk among individuals who are not obese according to other anthropometric indices. [2]

The triglyceride-to-HDL cholesterol (TG/HDL-C) ratio has been reported to be closely related to IR in adults. However, although the association is widely described in white individuals, contrasting results have been reported in black adults and adolescents. Therefore, it is possible that given the racial/ethnic variations in both TG and HDL-C levels, the association of the TG/HDL-C with IR may be ethnicity dependent. [6]

As the present study is done in a poor resource setting, TG/HDL ratio has been used as a surrogate marker of IR for correlating with anthropometric markers.

1.1 Objective:

1) To study the pattern of dyslipidemia in diabetics and non diabetic subjects.
2) To correlate the association of obesity markers (BMI, WHR, WHtR, WC) with insulin resistance by using Triglyceride by HDL as a surrogate marker.

2. Methods

This is a prospective case control study conducted in a tertiary care hospital in Mangalore, after the approval from institutional ethical committee.

2.1 Study Group

50 known cases of Type 2 DM of either sex were included by random sampling method after an informed and written consent, duly signed by each participant.

2.2 Control Group

50 non diabetic subjects of either sex were included by random sampling method after an informed and written consent, duly signed by each participant.

2.3 Inclusion Criteria

50 cases of diagnosed type-2 DM and confirmed by biochemical investigations as per WHO criteria.

2.4 Exclusion Criteria

Causes of secondary dyslipidemia were excluded. Causes for obesity other than metabolic syndrome were excluded. Non consenting subjects were excluded.

A detailed history as per a preformed case performa was taken noting patient's past history about the patient's DM, its complications and its management from both outpatient and Inpatient department followed by a detailed systemic examination.

Estimation of total cholesterol was done by CHOD-POD method. Estimation of HDL was done by precipitation end point method. Estimation of Triglyceride was done by GPO-POD method. Estimation of LDL was calculated as follows:

LDL in mg/dl = TG - (HDL + VLDL)

Estimation of VLDL was calculated as follows:

VLDL = TG/5

2.5 Anthropometric Measurements

Height, weight, and waist and hip circumferences were taken as per the WHO STEPS protocol. The WHO STEPS protocol recommends that the subject stands with arms at the sides, feet positioned close together, and weight evenly distributed across the feet and should wear little clothing. The subject should be relaxed, and the measurements should be taken at the end of a normal expiration. WC is to be measured at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest. The HC measurement should be taken around the widest portion of the buttocks. BMI is the ratio between weight in kilograms and the square of height in meters. WHR was calculated as waist (cm)/hip (cm). [7]

Following are the accepted guidelines for the anthropometric measurements in Indians:

BMI in Indians: underweight (<18.5 kg/m^2), normal (18.5 - 22.9 kg/m^2), overweight (23-24.9 kg/m^2), obese (>25 kg/m^2). **WC:** 90 cm for men, 80 cm for women.

WHR: <0.88 in men and <0.80 in women. [8]

WHtR based on the following boundary values: 'no increased risk' (WHtR <0.5), 'increased risk' (WHtR ≥0.5 and <0.6) and 'very high risk' (WHtR ≥0.6). [9]

As per ATP III guidelines for lipid profile, TC 240 mg/dL and above, LDL 160- 189 mg/dL, TG 200- 499 mg/dL, HDL 60 mg/dL and above is considered high. HDL below 40 mg/dL is considered poor. [10]

If lipid values are expressed as mg/dl;

TG/HDL-C ratio less than 2 is ideal

TG/HDL-C ratio above 4 is too high

TG/HDL-C ratio above 6 is much too high

2.6 Statistical Analysis:

- Mean, Standard deviation, Frequency and Percentage.
- Pearson's correlation, Independent sample t test, Mann WhitneyU test

4. Results

It is a prospective case control study in which 100 subjects were included. Out of which 50 (38 males and 12 females) were diabetic and 50 (27males and 23females) were non-diabetic apparently healthy control subjects were confirmed by biochemical investigations as per WHO criteria. (Table 1). The age group of cases and controls were between 20-80 years with a mean age of 54 years for cases and 48 years for control (Table 1).

Table 1: Comparison of gender and age parameters in case and control groups:

Parameters	Groups	
Gender	Case (n=50)	Male = 38 Female = 12
	Control (n=50)	Male = 27 Female = 23
Age in years (Mean)	Case	54
	Control	48

Table 2 shows routine biochemical parameters such as fasting (FBS), post prandial blood sugars (PPBS), FLP done in all subjects. The values were significantly higher in cases than in controls for FBS, PPBS, TG, VLDL, TG/HDL. The mean value of FBS in case group was found to be 170.04 mg/dL and in control group it was 99.06 mg/dL. The mean value of PPBS in case group was found to be 249.38 mg/dL and in control group it was found to be 110.44 mg/dL. The mean value of total cholesterol in case group was found to be 174.08 mg/dL and in control group it was 208.54 mg/dL. The mean value of triglyceride in case group was found to be 159.74 mg/dL and in control group it was 139.26 mg/dL. The mean value of HDL in case group was found to be 35.92 mg/dL and in control group it was 47.22 mg/dL. The mean value of LDL in case group was found to be 110.124 mg/dL and in control group it was 135.66 mg/dL. The mean value of VLDL in case group was found to be 32.0 mg/dL and in control group it was 27.89 mg/dL. The mean value of TG/HDL in case group was found to be 5.77 and in control group it was 3.328 (Table 2).

3.1 Independent sample t test:

Table 2: Comparison of FBS, PPBS, TC, HDL, LDL parameters in case and control groups:

Parameters		Mean	Std Deviation	T	p Value
Fasting Blood Glucose (FBS) (mg/dL)	Case	170.04	59.104	8.421	<0.001*
	Control	99.06	7.67		
Post Prandial Blood Glucose (PPBS) (mg/dL)	Case	249.38	109.143	8.88	<0.001*
	Control	110.44	18.121		
Cholesterol	Case	174.08	47.584	-3.811	<0.001*
	Control	208.54	42.7131		
HDL	Case	35.92	12.466	1.249	<0.001*
	Control	47.22	13.961		
LDL	Case	110.124	41.76	-3.338	<0.001*
	Control	135.66	34.339		

*Indicates significant

BMI, WHR, WHtR, WC was measured in these subjects. Table 3 shows that the mean value of BMI in case group was found to be 25.85 kg/m^2 and in control group it was 24.88 kg/m^2. The mean value of WHR in case group was found to be 0.9697 and in control group it was 0.9102. The mean value of WHtR in case group was found to be 0.57 and in control group it was 0.5628. The mean value of WC in case group was found to be 94.28 cms and in control group it was 91.92 cms. (Table 3)

Table 3: Comparison of BMI, WHR, WHtR, WC parameters in case and control groups:

Parameters		Mean	Std Deviation	p Value
Body mass index (BMI) (kg/m^2)	Case	25.85	3.691	0.19
	Control	24.88	3.636	
Waist to hip circumference	Case	0.969	0.064	<0.001*
	Control	0.910	0.0519	
Waist to height ratio	Case	0.57	0.0735	0.573
	Control	0.56	0.0578	
Waist circumference	Case	94.28	12.44	0.281
	Control	91.92	9.073	

*Indicates significant

The independent sample t test was used to compare FBS, PPBS, Cholesterol, HDL, LDL, BMI, WHR, WHtR, WC between case and control groups. The obtained p values are less than 0.05 for FBS, PPBS, Cholesterol, HDL, LDL, WHR and hence there was a difference in mean of these outcome measures between case and control at 5% level of significance. For other parameters (BMI, WHtR, WC) the p value is more than 0.05 and hence there was no difference in the mean of these outcome measures between case and control (Table 2, 3).

The Mann WhitneyU test was used to compare TG, VLDL, TG/HDL he p values for TG and VLDL are >0.05 and hence there was no difference in these measures between case and control at 5% level of significance. (Table 4)

Mann WhitneyU test:

Table 4: Comparison of Triglyceride, VLDL, Tg/HDL parameters in case and control groups:

Parameters		Median	IQR	p Value
Triglyceride	Case	138	105 to 181	0.115
	Control	117	82.5 to 172.5	
VLDL	Case	27.8	21 to 36	0.12
	Control	23.5	16.6 to 34.25	
Tg/HDL	Case	3.869	2.632 to 6.35	0.003
	Control	2.6365	1.556 to 4.37	

Pearson correlation was used to find the linear relationship between TG/HDL with BMI, WHR, WHtR, WC. The p values are >0.05 and hence the findings are not significant at 5% level of significance. The degree of relationship was higher for TG/HDL vs. WC (r= 0.106) followed by BMI (r= 0.103), WHR (r=0.092), WHtR (r=0.057) when checked irrespective of the disease. The degree of relationship was higher for TG/HDL vs. WC (r= 0.048) followed by BMI (r=0.037), WHtR (r=0.023) in case group. However WHR (r = -0.099) showed inverse relationship. The degree of relationship was higher for TG/HDL vs. WC (r= 0.194) followed by BMI (r= 0.169), WHR (r=0.125), WHtR (r=0.110) in control group. The correlation of TG/HDL with WHtR (r=0.110) was higher in controls when compared with cases indicating high levels of IR in obese non diabetic population. (Table5)

Table 5: Pearson's correlation between TG/HDL and BMI, WHR, WHtR, WC:

Pearson Correlation	Irrespective of the disease		Case		Control	
	r Value	p Value	r Value	p Value	r Value	p Value
TG/HDL vs. BMI	0.103	0.310	0.037	0.799	0.169	0.241
TG/HDL vs. WHR	0.092	0.361	-0.099	0.492	0.125	0.386
TG/HDL vs. WHtR	0.057	0.576	0.023	0.873	0.110	0.447
TG/HDL vs. WC	0.106	0.294	0.048	0.738	0.194	0.178

5. Discussion

In our cross sectional study of 100 subjects, 50 diabetics (38 males and 12 females) and 50 non diabetics (27 males and 23 females) of 20-80 years age groups were included. The mean age of years for 54 years for case and 48 years for control group was observed. Routine biochemical parameters such as FBS, PPBS, FLP were done in all subjects.

Elevated TC, LDL, TG/HDL, WHR and low HDL were significantly associated with diabetics.

All anthropometric measurements showed a small positive correlation with TG/HDL ratio among the whole study group and also both groups separately. The correlation of TG/HDL with WHtR (r=0.110) was higher in controls when compared with cases (r= 0.23) indicating that WHtR has high levels of correlation with IR in obese non diabetic population.

WC showed highest correlation with TG/HDL in whole group and both groups separately. WHtR showed least correlation among the anthropometric measurements in the whole study group and in controls. WHR showed inverse correlation in diabetics. Hence in our study WC is the most correlating anthropometric measurement with TG/HDL though not statistically significant.

In a study done by MA Sayeed, et al (2003) involving 4923 (M/F=2321/2602) volunteers, the mean (SD) values of BMI, WHR and WHtR for subjects with diabetes and hypertension were significantly higher in either sex. The level significance was highest for WHtR. The prevalence of diabetes and hypertension increased significantly with higher quintiles of BMI, WHR and WHtR (chi sq values were largest in WHtR for both events). Partial correlation coefficients, controlling for age and sex, showed that BMI, WHR and WHtR significantly correlated with systolic and diastolic BP, FBG, TC and TG. In the entire correlation matrix, the 'r' values were the highest for WHtR. Taking diabetes and hypertension as dependent variables, logistic regression also showed the highest odds ratio in higher WHtR than BMI and WHR. [4]

In a study done by Zdenka Hertelyová, et al (2016), the average WHtR value for the whole group was 0.45 ± 0.06, with 0.46 ± 0.06 for men, and 0.44 ± 0.06 for women. WHtR values in respondents with all other parameters in normal range were from 0.41 to 0.52 for men and from 0.38 to 0.50 for women. Values are similar to those observed in other studies across diverse world populations. A positive correlation was observed between WHtR and atherogenic indices (AP1, AIP) uric acid levels and lipid profile parameters at $p < 0.001$, with the exception of glucose and HDL. WHtR and HDL were negatively correlated at $p < 0.001$. [5]

In a study done by Ali Chehrei, et al(2007)WC and W/Ht showed greater correlation with TC, TG, LDL-C, TC/HDL-C level than did BMI. Among lipid profile, TG showed the closest correlation with W/Ht ($r=0.309$, $p<0.001$) and WC ($r=0.308$, $p<0.001$). HDL-C level did not show any statistical relationship with W/Ht, but it was weakly correlated with WC ($r=-0.088$, $p<0.05$). [11]

In a study done by Wen-Cheng Li, et al (2013) showed the basic characteristics and the prevalence of cardio metabolic risk factors of the 21,038 men and 15,604 women in the study sample were comparable in terms of mean age (37.2 ± 9.4 and 37.3 ± 10.4 years, respectively, $P = 0.437$), prevalence of diabetes (1.3 vs. 1.2%, $P = 0.477$), and high total cholesterol (5.2 vs. 5.0%, $P = 0.467$). However, there were significant differences between the men and women in all other assessed variables (all $P < 0.001$). Specifically, men had a higher BMI (24.8 ± 3.5 vs. 22.5 ± 4.0 kg/m^2), WC (84.8 ± 9.1 vs. 73.3 ± 9.4 cm), and WHtR (0.49 ± 0.05 vs. 0.46 ± 0.06) in comparison with women. In both men and women, BMI, WC, and WHtR were all significantly correlated with each cardio metabolic risk factor ($P < 0.05$). In comparison with BMI and WC, the WHtR was a stronger correlate of FBG, TC, and TG in both men and women. [2]

In a study done by M B Snijder, et al (2004), after adjustment for age, body mass index and waist, a larger hip circumference was associated with a lower prevalence of undiagnosed diabetes, {odds ratio per one s.d. increase in hip circumference 0.55 (95% CI 0.41–0.73) in men and 0.42 (0.27–0.65) in women} and undiagnosed dyslipidemia {Odds ratio 0.58 (0.50–0.67) in men and 0.37 (0.30–0.45) in women}. Associations with undiagnosed hypertension were weaker {Odds ratio 0.80 (0.69–0.93) in men and 0.88 (0.70–1.11) in women}. As expected, larger waist circumference was associated with higher prevalence of these conditions. Similar associations were found using continuous metabolic variables as outcomes in linear regression analyses. Height partly explained the negative associations with hip circumference. When these analyses were performed stratified for age, associations became weaker or disappeared in the oldest age groups (age ≥75 y in particular), except for HDL-cholesterol. [12]

In a study done by Naveen Bhartia Porwal, et al (2015), the correlation analysis revealed that the Body mass index, Waist circumference, Waist-hip ratio and Waist-Height ratio were positively correlated with HOMA-IR an index of insulin resistance. [3]

In Sneha S, et al study (2016), found that the median HOMA – IR was >2.5 suggesting increased prevalence of insulin resistance among the study population. Common and simple anthropometric measurements like BMI, waist circumference and waist hip

ratio (visceral obesity) were found to have significant positive correlation with HOMA-IR. A significant positive correlation was also established between TG/HDL and HOMA-IR suggesting higher TG levels depict insulin resistance. A significant negative correlation was found between HOMA-IR and HDL emphasizing that insulin sensitivity decreases with HDL. TG and TG/HDL ratio can be used to identify insulin resistant individuals is shown in this study. These parameters were shown to have the same degree of specificity and sensitivity as plasma insulin. [13]

Inflammation and insulin resistance have shown to be forerunners of diabetes and cardiovascular diseases. Multiple linear regression analysis showed following parameters to have statistical significant relation with log HOMA -IR: • BMI (p = 0.04, 95%CI 0.001 – 0.058), WC (p = 0.030, 95%CI 0.002- 0.035), TG (p = 0.001, 95% CI 0.001 – 0.004) these could be surrogate clinical markers of insulin resistance. [13]

5.1 Limitations of the study

Present study is a hospital based study and may not be a true representation of the population at large.

6. Conclusions

In this study, anthropometric measurements showed positive correlation with TG/HDL ratio with WC showing maximum correlation, though statistically not significant. We suggest using anthropometric measurements (WC, BMI, WHR, WHtR) as inexpensive and easy methods in clinical and epidemiological fields.

Ethical issues: Nil
Conflict of interest: Nil

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