

## **HYPERTRIGLYCERIDAEMIC WAIST PHENOTYPE: ASSOCIATION WITH PREDIABETES AND DIABETES AMONG ADULTS OF CENTRAL KERALA**

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### **ABSTRACT**

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#### **BACKGROUND**

Hypertriglyceridaemic waist (HTGW) phenotype has been suggested as a useful screening tool for metabolic abnormalities.

#### **AIMS AND OBJECTIVES**

This study evaluated the association of the hypertriglyceridaemic waist (HTGW) phenotype with prediabetes and diabetes (DM) among adults in central Kerala.

#### **SUBJECTS AND METHODS**

A cross sectional study carried out on adult subjects attending the general medicine outpatient department of a tertiary care centre located in central Kerala. Blood pressure, anthropometric and metabolic parameters were measured. HTGW was defined as elevated triglycerides and elevated waist circumference.

#### **RESULTS**

Participants with HTGW had odds ratio (95% confidence interval [CI]) of 6.21 (1.83-21.06) in total population, 14.78 (1.70-128.35) in men and 3.14 (0.59-16.67) in women for prediabetes compared to those without HTGW phenotype. Subjects with HTGW phenotype had an odds ratio (95% CI) of 11.60 (6.09-22.11) in total population, 10.23 (4.17-25.07) in men and 13.09 (5.15-33.27) in women for diabetes compared to those without HTGW phenotype. Multivariate analysis showed that age and gender were not independent predictors of Prediabetes and diabetes.

#### **CONCLUSION**

HTGW phenotype was strongly associated with DM and this phenotype could be used as a screening tool to identify adults with diabetes.

#### **KEYWORDS**

Hypertriglyceridaemic Waist Phenotype, Prediabetes, Diabetes, Central Kerala.

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**INTRODUCTION:** Type 2 diabetes is a leading cause of disability and mortality both in developed countries and developing countries.<sup>[1,2]</sup> Worldwide, the prevalence of diabetes (DM) is increasing very rapidly and International Diabetes Federation has estimated an increase from 366 million to 552 million diabetic people between 2011 and 2030.<sup>[3]</sup> Over 19% of world's diabetic subjects live in India.<sup>[4]</sup> where mostly younger individuals in their economically productive years are affected.<sup>[5]</sup> Lifestyle modifications would greatly help in preventing the onset of diabetes. Early identification of at-risk individuals using simple screening methods becomes important.

The hypertriglyceridaemic waist (HTGW) phenotype represented by the simultaneous presence of increased waist circumference and elevated serum triglycerides was reported to predict cardiovascular disease and DM better than the metabolic syndrome.<sup>[6,7,8,9]</sup> It was also suggested as a marker of excess visceral fat.<sup>[10]</sup> which is an independent risk factor for type 2 DM.<sup>[7]</sup> The HTGW phenotype is a cheap and simple tool, as it involves only waist circumference and fasting triglycerides measurements. Studies on HTGW phenotype in Kerala is limited. The present study is aimed to identify the association of HTGW phenotype with prediabetes and DM among adults attending the outpatient department of a tertiary care centre of central Kerala.

**SUBJECTS AND METHODS:** The study was cross sectional in design conducted in a tertiary care centre in central Kerala. 356 subjects aged 30- 70 years attending the general medicine outpatient department were included in the study. Informed consent of the participants were obtained. Blood pressure was recorded. Waist circumference was measured at the level of iliac crest after normal expiration.

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Fasting blood samples were collected and analysed for fasting plasma glucose and lipid profile using a fully automated analyser. Pregnant females and those with debilitating diseases were excluded from the study. The study was approved by institutional ethics committee.

**Definition of Terms:** In the present study, HTGW phenotype was defined as the simultaneous presence of waist circumference (WC)  $\geq 85.5$  cm and plasma triglyceride (TG) concentration  $\geq 151.5$  mg/dL for both genders. These values correspond to the optimal cut-offs of these parameters for detection of diabetes in the study population. Subjects without this phenotype was defined as having non-HTGW phenotype (Non-HTGW). Prediabetes was defined as fasting plasma glucose between 100-125 mg/dL. Diabetes was defined as fasting plasma glucose  $\geq 126$  mg/dL<sup>[11]</sup> or prior diagnosis.

**Analysis:** Data was analysed using SPSS version 17.0. ROC curve was plotted to determine the cut off values of waist circumference and triglyceride for the detection of diabetes. For waist circumference ROC curve was plotted separately for males and females, and for triglyceride the curve was plotted for total population. Continuous variables of the subjects at baseline were expressed as mean and standard deviation. Odd's ratio (OR) & and their respective 95% confidence interval (95% CI) was used to evaluate the association between HTGW, prediabetes and diabetes. Multivariate analysis was used to identify independent predictors of prediabetes and diabetes. For all analyses, p value  $< 0.01$  was considered as significant.

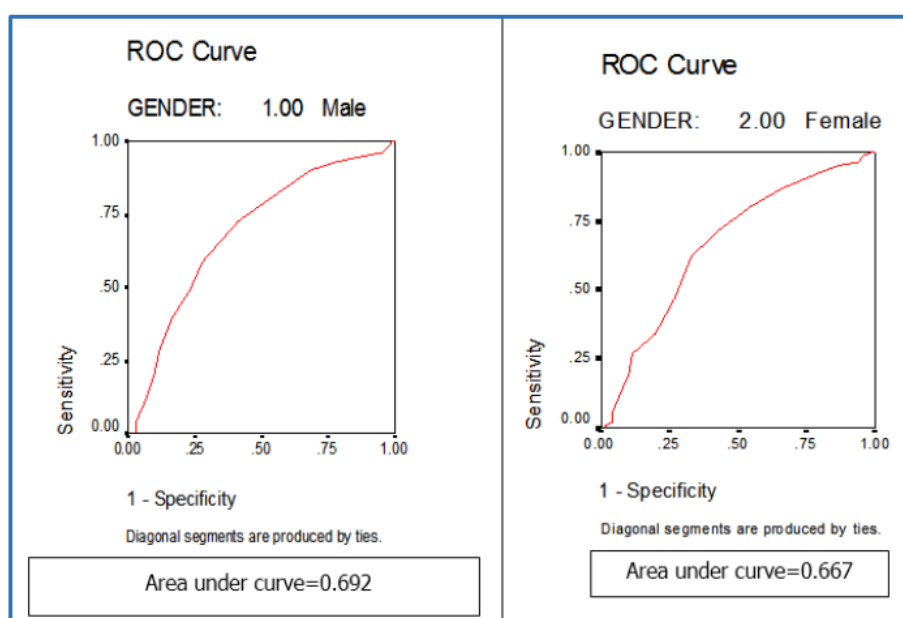
**RESULTS:** Cut-off values of Waist Circumference and Triglyceride: In the ROC curve analysis, optimal cut-off values were defined as the point at which the value of "Sensitivity + Specificity" was maximum. The optimum cut-off point for WC was 85.5 cm for both men and women. This

cut-off had a sensitivity and specificity of 59% and 72% respectively for men and 62% and 67% for women [Fig. 1]. The optimum cut-off point for serum triglyceride was 151.5 mg/dL. This value had a sensitivity of 70% and specificity of 80%. [Fig. 2]. These cut-off values were used to define HTGW phenotype in the present study.

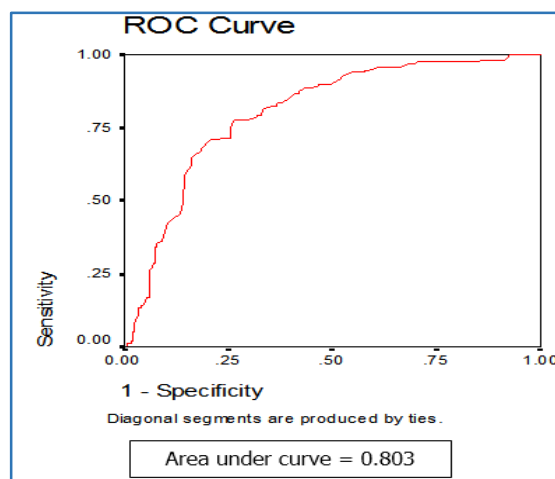
**Characteristics of the Subjects:** The baseline characteristics of the participants based on according to the HTGW phenotype are shown in Table 1. The age of the subjects was not statistically different between the two phenotype groups. Subjects with HTGW phenotype had higher levels of waist circumference, fasting blood sugar and serum triglycerides.

**Prevalence of HTGW:** Prevalence of HTGW in the study population was 23% with 95% CI: 18.6-27.4. Female participants showed higher prevalence of HTGW compared to males. [24.6% vs. 21.5%]. But the difference was not statistically different (p value=0.489). Prevalence of prediabetes and diabetes were 16.6% and 43.5% respectively.

**Association between Prediabetes and Diabetes and the HTGW:** The odds ratios between prediabetes and diabetes and the HTGW are shown in Table 2 and Table 3. Compared with the participants in the non-HTGW group, those in the HTGW group had an odds ratio (95% confidence interval [CI]) of 6.21 (1.83-21.08) in total population, 14.78 (1.70-128.35) in men and 3.14 (0.59-16.67) in women for prediabetes (Table 2). As shown in Table 3, participants in the HTGW group had an odds ratio (95% CI) of 11.60 (6.09-22.11) in total population, 10.23 (4.17-25.07) in men and 13.09 (5.15-33.27) in women for diabetes compared to those in the non-HTGW group. Result of Multivariate analysis is shown in Table 4 which shows that age and gender were not independent predictors of Prediabetes and diabetes.



**Fig. 1: ROC Curve for Waist Circumference**



**Fig. 2: ROC Curve for Serum Triglyceride**

| Characteristics | Non-HTGW<br>n=274 | HTGW<br>n=82 | P value |
|-----------------|-------------------|--------------|---------|
| Age             | 51.6±10.9         | 53.4±9.5     | 0.173   |
| FBS             | 115.4±44.3        | 166.7±48.4   | 0.000   |
| WC              | 84.2±3.4          | 88.5±2.0     | 0.000   |
| TG              | 122.6±45.1        | 181.8±36.7   | 0.000   |

**Table 1: Characteristics of Study Participants by HTGW Phenotype**

| Phenotype        | OR [95% CI]        | P value |
|------------------|--------------------|---------|
| Total Population |                    |         |
| Non-HTGW         | 1.00               |         |
| HTGW             | 6.21(1.83-21.06)   | 0.001   |
| Men              |                    |         |
| Non-HTGW         | 1.00               |         |
| HTGW             | 14.78(1.70-128.35) | 0.002   |
| Women            |                    |         |
| Non-HTGW         | 1.00               |         |
| HTGW             | 3.14(0.59 -16.67)  | 0.161   |

**Table 2: Odds Ratio (OR) between Prediabetes and the HTGW among Men and Women (Univariate Analysis)**

HTGW (Hypertriglyceridaemic waist phenotype) was defined as enlarged waist  $\geq 85.5$  cm and elevated triglyceride  $\geq 151.5$  mg/dL for men/women. Non-HTGW (Non-HTGW phenotype) includes subjects without this phenotype.

| Phenotype        | OR [95% CI]       | P value |
|------------------|-------------------|---------|
| Total Population |                   |         |
| Non-HTGW         | 1.00              |         |
| HTGW             | 11.60(6.09-22.11) | 0.000   |
| Men              |                   |         |
| Non-HTGW         | 1.00              |         |
| HTGW             | 10.23(4.17-25.07) | 0.000   |
| Women            |                   |         |
| Non-HTGW         | 1.00              |         |
| HTGW             | 13.09(5.15-33.27) | 0.000   |

**Table 3. Odds Ratio between Diabetes and the HTGW among Men and Women (Univariate Analysis)**

| Prediabetes   |                  |         |
|---------------|------------------|---------|
| Variable      | OR [95% CI]      | P value |
| Age (51-70)   | 1.38(0.73-2.59)  | 0.322   |
| Gender (Male) | 1.41(0.75-2.65)  | 0.283   |
| Diabetes      |                  |         |
| Variable      | OR [95% CI]      | P value |
| Age (51-70)   | 1.01(0.63 -1.62) | 0.963   |
| Gender (Male) | 1.16(0.73-1.85)  | 0.534   |

**Table 4: Independent Predictors of Prediabetes and Diabetes (Multivariate Analysis)**

**DISCUSSION:** The major finding of our study is strong association of HTGW phenotype with type 2 diabetes. In Chinese rural adults (OR: 2.10; 95% CI: 1.62–2.73),<sup>[12]</sup> Canadian Aboriginals (OR: 4.96; 95% CI: 2.49–9.88).<sup>[7,13]</sup> and in a group of Hispanics (OR: 7.28 ; 95% CI=(3.63-14.63)).<sup>[7]</sup> also HTGW phenotype showed significant association with type 2 diabetes. Okosun and Boltri observed a gender difference in the association between the HTGW phenotype and type 2 DM. In their study, Black women with the HTGW phenotype were at higher risk of developing DM (OR: 5.62; 95% CI: 1.04–9.42) compared to males (OR: 3.94; 95% CI: 2.85–3.90).<sup>[12,14]</sup> In our study, also women with the HTGW phenotype had higher odds for type 2 diabetes than males.

In Chinese rural adults, HTGW phenotype showed no association with prediabetes.<sup>[12]</sup> whereas in Hispanics HTGW phenotype was significantly associated with prediabetes (OR=5.55; 95% CI=3.38–9.13).<sup>[7]</sup> Only women with the HTGW phenotype were at higher risk for developing prediabetes in Chinese urban adults (OR: 1.51; 95% CI=1.04–2.19).<sup>[6]</sup> In our study, HTGW phenotype was significantly associated with prediabetes in total population and males. In women, no statistically significant association existed between HTGW phenotype and prediabetes. The mechanism of association of HTGW with diabetes is mostly unknown. It is believed that excess visceral fat causes increased release of free fatty acids into circulation, which can inhibit glucose uptake and oxidation by muscle and other organs. Increased insulin secretion can compensate temporarily for these alterations, but the continuous

presence of these triggering conditions may promote the development of type 2 DM.<sup>[6,7]</sup>

Prevalence of HTGW phenotype in this study was 23%. In studies from United Kingdom and Malaysia, prevalence of the phenotype was 30%.<sup>[7]</sup> and 19.7% respectively.<sup>[15]</sup> Among men and women in this study, the prevalence of HTGW phenotype was respectively 21.5% and 24.6%. The phenotype has been reported in 12.1% French men.<sup>[16]</sup> and 19% of participants in the Quebec Health Survey.<sup>[17]</sup> HTGW phenotype was present in 40.6% Canadian women.<sup>[7]</sup> and 31.9% of women.<sup>[18]</sup> in Tehran lipid and glucose study. Different prevalence could be due to use of different cut-off points for WC and serum triglyceride since reference values for WC and serum triglyceride varies with ethnicity and lifestyle factors.<sup>[10]</sup> This study was designed using the optimal cut-off for WC and serum triglyceride for detection of DM which could also be a limitation of our study.

Our study has several limitations including cross-sectional design, small sample size and lack of information regarding lifestyle, BMI, and family history of DM. Being hospital based, prevalence of HTGW, prediabetes and diabetes in the study could be higher than general population. In addition, the definition of HTGW phenotype might be different from other studies. Therefore, a more detailed population based study in this field is needed.

**CONCLUSION:** In summary, we found that the hypertriglyceridaemic waist phenotype is a useful tool to detect individuals at high risk for diabetes.

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