

Original Article

The association of hypertriglyceridemic waist phenotype with type 2 diabetes mellitus among individuals with first relative history of diabetes

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Abstract

BACKGROUND: Anthropometric measures with biochemical indicators have been used as screening tools for metabolic abnormalities in adolescents and adults. A few studies have assessed the relation of EWET (Enlarge waist Elevated triglyceride) phenotype with diabetes, especially among individuals with first relative history of diabetes. This study aimed to evaluate the association of EWET phenotype with diabetes among individuals with family history of diabetes.

METHODS: Anthropometric and biochemical measurements were evaluated in a population – based cross – sectional study of 332 male and 991 female Isfahani adults aged 35-55 year. The EWET phenotype was defined as serum triglyceride concentrations ≥ 150 mg/dl and concurrent waist circumference (WC) ≥ 88 cm in females and ≥ 102 cm in males.

RESULTS: The prevalence of EWET phenotype was respectively 9.6% and 23.6% among male and female. Individuals with the phenotype had significantly higher BMI and WHR (waist to hip ratio) as compared to other groups. After control for age and physical activity, male with EWET phenotype were significantly more likely to have high serum triglyceride levels ($p < 0.001$), cholesterol ($p < 0.001$). Even after additional control for BMI, the significant associations remained except for low HDL Cholesterol. Female with EWET phenotype had significantly adverse metabolic risks as compared to other groups, either before or after control for BMI ($p < 0.001$). Individuals with the phenotype were more likely to have diabetes (both gender) and (IGT) Impaired Glucose Tolerance (female only).

CONCLUSIONS: Our results showed that EWET phenotype has significantly associated with diabetes. This phenotype could be used for early identification of diabetes and IGT.

KEYWORDS: Enlarge waist Elevated triglyceride, IGT, Obesity and Anthropometric.

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Diabetes is one of the most common metabolic abnormalities causing mortality in developed and developing countries.¹ This metabolic abnormality leads to heart, kidney and eye complications.² World Health Organization (WHO) has estimated that more than 2 million diabetic individuals were living in Iran in 2000. This figure has been estimated to be increased to more than 6.4 million in 2030.³⁻⁵ Studies have shown the prevalence of diabetes in Iran is 5-16.3%.⁶ Preva-

lence of diabetes in Tehran population with family history of diabetes was 32.3% and 40.7% among men and women, respectively.⁷ As diabetes is a threat for health, early diagnosis using simple screening Methods is of great importance.^{8,9}

Several screening methods have been used for identification of at risk patients for DM. Recent studies introduced anthropometric indicators as a useful screening method for early identification of metabolic abnormalities^{10,11} of

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commonly used ones is BMI, a measure of general obesity. Recent reports demonstrated that measures of central adiposity predict metabolic abnormalities risk more strongly than BMI.^{12,13} Among these measures, WC has been introduced as a useful and easy-to-measure indicator for assessing risk diabetes risk.¹⁴ Some investigators have combined these anthropometric measures with high triglyceride levels to make a new method for diabetes screening named EWET. Others reported this marker as a simple and cheaper method for screening of patients with diabetes and coronary heart disease. Originally, Canadian researchers showed that this phenotype is a strong screening tool for predicting metabolic triad (hyperinsulinemia, high levels of small dense low density lipoprotein particles, and ApoB).¹⁵ The EWET phenotype is highly prevalent in Iran, such that 32% of Iranian women,¹⁶ 19% of men and 6.5% of adolescents are affected.¹⁷

The relation of this phenotype and CHD risk factors have been shown. Although abdominal obesity and hypertriglyceridemia have separately been known as risk factors for type 2 diabetes, limited data are available relating EWET phenotype to diabetes, especially among individuals with first relative history of diabetes. One may assume that EWET are two factors of the metabolic syndrome, a well-known risk factor for diabetes, but it must be kept in mind that EWET is a simple and inexpensive marker than the metabolic syndrome for predicting diabetes. Furthermore, even for the relation of metabolic syndrome and diabetes, the existing evidence come from western societies, while the picture of cardiovascular risk factors is a little bit different in middle-Eastern from that in western countries. To stop increasing prevalence of diabetes in the world, early identification of high-risk groups is necessary. Therefore, this research aimed to estimate the relation of EWET phenotype with diabetes and other metabolic abnormalities among individuals with first relative history of diabetes in Isfahan, Iran.

Methods

Subjects: This research was performed within the framework of the (DPP) Diabetes Prevention Project, in Isfahan, Iran. Our aim in DPP was to prevent diabetes by some lifestyle measure or even medication interventions among at risk individuals (IFG/IGT patients). In the DPP, participants divided into three treatment groups. The first group was the lifestyle intervention that received intensive training in diet and physical activity. Our aim was, losing 7 percent of their body weight and maintaining that loss. The second group took metformin. The third group was control group. Baseline examinations in this cohort were conducted from 2003. Males and females 30 to 55 year of age who were first relative history of type 2 diabetes were invited to study via community announcement. This population-based cross-sectional study was performed among 1450 people with first relative history of diabetes (F.H.D). After excluding peoples using medications that would influence serum lipids, current analysis was done among 1323 individuals with F.H.D (332 males and 991 females). The criterion for participants was having ≥ 1 first-degree relative with a diagnosis of diabetes after 30 years old.

This study was approved by the Research Council of Endocrine and Metabolism Research Center (EMRC) of Isfahan University of Medical Science and each participant filled in consent.

Anthropometric Assessment: Weight was measured by Seca scale while subjects were lightly clothed and without shoes and recorded to the nearest .1Kg. Height was measured by Seca stadiometer while subjects were in a standing position without shoes and their shoulders were in a normal position. Body mass index was calculated as weight (in kg) divided by height square (in m²). WC was measured at minimal waist after a normal exhale and hip circumference was measured at the widest point over the buttocks with an unscratched tape measure and without any

Table 1. General characteristics of male participants by different phenotype of serum triacylglycerol concentration and waist circumference*

	Phenotypes of TG and WC				P †
	NWNT	EWNT	NWET	EWET	
n = 332	n = 124	n = 21	n = 143	n = 44	
Age (y)	42.7 ± 6.6	43.3 ± 5.3	42.9 ± 6.2	44.4 ± 5.8	0.5
BMI (kg/m ²)	26.1 ± 3	32 ± 2.9	26.9 ± 2.5	31.4 ± 2.6‡	< 0.001
Waist (cm)	90 ± 7.2	107.2 ± 4	92.4 ± 6.7	105.4 ± 4.4‡	< 0.001
WHR	0.88 ± 0.05	0.03 ± 0.94	0.90 ± 0.06	0.94 ± 0.03‡	< 0.001

BMI; Body mass index; WC: waist circumference; NWNT: Normal Waist Circumference < 102 cm and Normal Triglyceride < 150 mg/dL; EWNT: Enlarged Waist ≥ 102 cm and Normal Triglyceride < 150 mg/dL; NWET: Normal Waist < 102 cm and Elevated Triglyceride ≥ 150; EWET: Enlarged Waist ≥ 102 cm and Elevated Triglyceride ≥ 150.

* Mean ± SD unless indicated

† By using ANOVA

‡ P < 0.001 as compared to NWNT and NWET

pressure to body surface; measurements were recorded to the nearest 1 cm. Data on physical activity were gathered by using participants' responses to one query: How much time do you exercise in a week? We categorized the replies of this query as never, < 3 h/wk, and ≥ 3 h/wk.

Definition of Terms: Participants were categorized in 4 phenotype groups on the basis of the mentioned cutoff points:

NWNT (normal waist normal triglyceride): Normal WC < 102 for man and for women < 88 and normal serum triglyceride concentrations (< 150 mg/dl).

EWNT (Enlarged waist normal triglyceride): Enlarged WC for men ≥ 102 and for

women ≥ 88 and normal serum triglyceride concentration (< 150 mg/dl).

NWET (normal waist elevated triglyceride): Normal WC for men < 102 and for women < 88 and elevated triglyceride ≥ 150 mg/dl.

EWET (Enlarged waist elevated triglyceride): Enlarged WC for men ≥ 102 and for women ≥ 88 and hyper serum triglyceride concentration (≥ 150mg/dl).

Biochemical Assessment: Blood samples were taken after >10h overnight fasting while the participants were in a sitting and relax position and were centrifuged within 5 min. Blood lipid analyses were done at the EMRC laboratory on the same day. Oral Glucose tolerance test was done by 75gr glucose. The samples was ana

Table 2. characteristics female with phenotypes of serum triacylglycerol concentration and waist circumference

	Phenotypes of TG and WC				P †
	NWNT	EWNT	NWET	EWET	
n = 891	n = 259	n = 206	n = 176	n = 250	
Age (y)	41.7 ± 5.9‡	43.1 ± 6.6	42.8 ± 6.6	43.8 ± 6.1	< 0.001
BMI (kg/m ²)	26.5 ± 2.9	33.1 ± 3.7	27.1 ± 2.2	33 ± 4.1§	< 0.001
Waist (cm)	5.1 ± 80.4	95.4 ± 5.9	82 ± 3.9	96.1 ± 6.9§	< 0.001
WHR	0.88 ± 0.05	0.03 ± 0.94	0.06 ± 0.9	0.94 ± 0.03‡	< 0.001

BMI; Body mass index; WC: waist circumference; WHR: waist-to-hip ratio; NWNT: Normal Waist Circumference < 88 cm and Normal Triglyceride < 150 mg/dL; EWNT: Enlarged Waist ≥ 88 cm and Normal Triglyceride < 150 mg/dL; NWET: Normal Waist < 88cm and Elevated Triglyceride ≥ 150; EWET: Enlarged Waist ≥ 88 cm and Elevated Triglyceride ≥ 150.

* Mean ± SD unless indicated otherwise (ANOVA test and chi-square test)

† ANOVA

‡ P < 0.05 in comparison other Groups

§ P < 0.001 in comparison NWNT and NWET

lyzed by using autoanalyzer BT 3000 (Rome, Italy) by Enzymatic Glucose Method using commercial kits (Chem Enzyme, Tehran, Iran). Serum cholesterol and triglyceride levels were measured by enzymatic reagents (Chem Enzyme, Tehran, Iran) adapted to the Selecta auto analyzer. High-density lipoprotein cholesterol levels were measured using kits (Pars Azmoon, Tehran, Iran). Plasma LDL cholesterol levels were estimated with Fried Wald formula (18). Inter-assay coefficients of variations (CVs) were 1.25 for TG, 1.2 for cholesterol and 1.2% for glucose. The corresponding intra-assay CVs were 1.97, 1.6 and 2.2%, respectively. Glycated hemoglobin levels (HbA1C) were assessed with DS5 and DS5 analyzer uses low pressure cation exchange chromatography in conjunction with gradient elution to separate human hemoglobin subtypes and variants from haemolysed whole blood.^{19,20}

Statistical analysis:

Statistical package for social sciences (SPSS) was used for statistical analyses. Data have separately been analyzed for males and females. General characteristics of individuals across different phenotypes of EWET were compared by one-way analysis of variance (ANOVA) with Tukey post-hoc correction. Multivariate-adjusted means for metabolic variables across various phenotypes of EWET was obtained by the use of analysis of covariance (ANCOVA) in four models. In first model, we adjusted age (y) and physical activity (never, < 3 hour/week, and \geq 3 hour/week). In the second one, we controlled our analysis for BMI. Chi-square test was used for comparing prevalence of different phenotypes of EWET across different categories of OGTT test.

Results

Mean age of men and women was 43.5 ± 5.5 and 43.0 ± 5.6 y, respectively. Mean BMI, WC, WHR and TG among men were 27.6 ± 3.3 kg/m², 94.4 ± 8.6 cm, 0.9 ± 0.06 and 192.7 ± 110 respectively and among women 29.6 ± 4.5 kg/m², 87.9 ± 9.1 cm, 0.8 ± 0.05 and 158 ± 83 respectively. Of the 1450 adult 332 (9.6%) of men

and 234 (23.6%) of women had EWET phenotype. General characteristics of male subjects separately in different phenotypes of WC and serum triglyceride levels have been presented in Table 1. There wasn't any significant difference in the age of participants across different phenotypes. Those with EWET phenotype had higher BMI, WC and WHR as compared to other phenotypes ($p < 0.01$ for all).

Women's general characteristics have been shown in Table 2. Those with the EWET phenotype were older and higher BMI, WC and WHR as compared to other phenotypes.

Men with the EWET phenotype had higher levels of serum triglyceride, cholesterol, and lower levels of HDL-cholesterol as compared to other groups (Table 3). The differences remained significant after controlling for age and physical activity. Such adjustments revealed significant differences in 2h-PG and HBA1C between the EWET phenotype and other groups. Even after further adjustment for BMI, all the mentioned differences were significant except for serum HDL-cholesterol that was marginally non significant ($p = 0.057$). Crude means of all metabolic variables were of higher levels among women with the EWET phenotype as compared to other phenotypes (Table 4). Controlling for age and physical activity and additional control for BMI had little impacts on these differences and they were still significant.

The prevalence of impaired glucose tolerance (IGT) and diabetes across different phenotypes of WC and serum triglyceride levels have been provided in Table 5. Both men and women with the EWET phenotype had higher prevalence of type 2 diabetes compared to other phenotypes. The prevalence of IGT was not significantly different in four phenotypes of WC and serum TG concentration.

Discussion

Findings of the current study suggest a positive association between hypertriglyceridemic waist phenotype and diabetes prevalence. We observed that males and females with the EWET phenotype had higher metabolic abnormalities

Table 3. Multivariate – adjusted means for metabolic risk factors across four phenotypes of serum triglycerol concentration and waist circumference in men

	Phenotype of TG and WC				P*	
	NWNT (n = 124)	EWNT (n =21)	NWET (n =143)	EWET (n = 43)		
Fasting blood sugar (mg/dl)	Model I †	99.6 ± 3.9	102.9 ± 8.8	110 ± 3.5	110 ± 6.3	0.085
	Model II ‡	101.1 ± 4	98.7 ± 9.5	110.6 ± 3.5	106.3 ± 7	0.086
2h-post prandial (mg/dl)	Model I	106.9 ± 5.7	121.3 ± 12.7	116.1 ± 5.1	140.2±9.3	< 0.01
	Model II	109.8 ± 6	113.5 ± 13.7	117.3 ± 5.2	133.1 ± 10.3	< 0.01
Hemoglobin A _{1c}	Model I	4.9 ± 0.13	5.5 ± 0.29	5.3 ± 0.12	5.4±0.23	< 0.01
	Model II	4.98 ± 0.14	5.4 ± 0.31	5.3 ± 0.12	5.2±0.26	< 0.01
Triglyceride (mg/dl)	Model I	111.3 ± 8.2	111.2 ± 18.9	239.5 ± 7.4	296.2 ±13.4	< 0.001
	Model II	109.6 ± 8.7	116.1 ± 20.4	238.8 ± 7.5	300.6 ±15	< 0.001
High density lipoprotein (mg/dl)	Total	46 ± 12.3	43.9 ± 8.6	42.3 ± 11	39.4 ± 9.4	< 0.01
	Model I	45.8 ± 1.1	43.9 ± 2.5	42.5 ± 1	39.5± 1.8	< 0.01
	Model II	45.5 ± 1.1	44.9 ± 2.7	42.3 ± 1	40.5±2	0.057
Cholesterol (mg/dl)	Model I	184.3 ± 3.7	187.7 ± 8.5	206.5 ± 3.3	213.2 ± 6.1	< 0.001
	Model II	186.1 ± 3.9	182.5 ± 9.2	207.3 ± 3.4	208.6 ± 6.8	< 0.001
Low density lipoprotein (mg/dl)	Model I	117.6 ± 3.2	121.4 ± 7.2	119.5 ± 3	118.9 ± 5.8	0.407
	Model II	119.8 ± 3.3	115.2 ± 7.8	120.4 ± 3	112.7 ± 6.5	0.157

NWNT: Normal Waist Circumference < 102 cm and Normal Triglyceride < 150mg/dL; EWNT: Enlarged Waist ≥ 102 cm and Normal Triglyceride < 150 mg/dL; NWET: Normal Waist < 102 cm and Elevated Triglyceride ≥ 150; EWET: Enlarged Waist ≥ 102 cm and Elevated Triglyceride ≥ 150.

* By using ANOVA for crude values and ANCOVA (Bonferroni correction) for adjusted values

† Adjusted for age and physical activity

‡ Further adjusted for BMI

** Mean ± standard deviation for crude values and Mean ± standard error for adjusted values

as compared to those without this phenotype. This study is among the first study relating hypertriglyceridemic waist phenotype to IGT and diabetes in a sample of individuals with first relative history of diabetes.

Hypertriglyceridemic waist phenotype has been suggested as a screening tool for metabolic risk factors.²¹ Considering the increasing trend in the prevalence of heart diseases and diabetes all over the world, developing simple and cheap screening tools for early identification of these chronic diseases is of great importance.¹⁷ EWET phenotype has the ability to recognize

more subjects characterized by the metabolic triad than the presence of the metabolic syndrome.²¹ Some investigators have used this simple screening tool for the identification of metabolic triad and cardiovascular risk.¹⁵ Among Tehrani people, this phenotype have been reported as a valid predictor of cardiovascular disease, not only among adult,^{16,17} but also among adolescents,²² such that those adolescents with the EWET phenotype had higher prevalence of other metabolic risks as well. This phenotype has also been demonstrated as a simple method for early identification of those

Table 4. Multivariate – adjusted means for metabolic risk factors across four phenotypes of serum triglyceride concentration and waist circumference in Women

	Phenotype of TG and WC				P*
	NWNT (n = 259)	EWNT (n =206)	NWET (n =176)	EWET (n = 250)	
Fasting blood sugar (mg/dl)	Model I † 95.6 ± 1.3	103 ± 1.8	97.9 ± 1.9	104.8 ± 1.6	< 0.001
	Model II ‡ 95.6 ± 1.5	103 ± 2	98.1 ± 2	104.7 ± 1.8	< 0.001
2h-post prandial (mg/dl)	Model I 118.1 ± 2.5	134.4 ± 3.2	122 ± 3.5	137.6 ± 2.9	< 0.001
	Model II 118 ± 2.9	134.4 ± 3.6	122 ± 3.7	137.4 ± 3.2	< 0.001
Hemoglobin A _{1c}	Model I 4.8 ± 0.05	5 ± 0.07	4.9 ± 0.8	5.3 ± 0.06	< 0.001
	4.8 ± 0.06	5.1 ± 0.08	4.9 ± 0.08	5.3 ± 0.07	< 0.001
Triglyceride (mg/dl)	Model I 103.5 ± 3.3	108.6 ± 4.3	220.7 ± 4.6	229 ± 3.8	< 0.001
	Model II 105.5 ± 3.7	106.4 ± 4.7	221.8 ± 4.9	226.6 ± 4.2	< 0.001
High density lipoprotein (mg/dl)	Model I 50.3 ± 0.6	49.3 ± 0.86	46.1 ± 0.95	45.2 ± 0.7	< 0.001
	Model II 50.7 ± 0.7	48.8 ± 0.9	46.6 ± 1	44.6 ± 0.8	< 0.001
Cholesterol (mg/dl)	Model I 188.4 ± 2.1	195.1 ± 2.7	200.8 ± 2.3	211.5 ± 2.4	< 0.001
	Model II 188.9 ± 2.4	194.8 ± 36.4	201.3 ± 3.1	210.7 ± 2.7	< 0.001
Low density lipoprotein (mg/dl)	Model I 118.2 ± 1.8	125.1 ± 2.4	112 ± 2.7	123.8 ± 2.2	< 0.001
	Model II 118.3 ± 2.1	124.9 ± 2.7	112.3 ± 2.9	123.6 ± 2.5	< 0.001

BMI: Body mass index; WC: waist circumference; NWNT: Normal Waist Circumference < 88cm and Normal Triglyceride < 150mg/dL; EWNT: Enlarged Waist ≥ 88cm Normal Triglyceride < 150mg/dL; NWET: Normal Waist < 88 cm and Elevated Triglyceride ≥ 150; EWET: Enlarged Waist ≥ 88cm Elevated Triglyceride ≥ 150.

* By using ANOVA for crude values and ANCOVA (Bonferroni correction) for adjusted values

† Adjusted for age and physical activity

‡ Further adjusted for BMI

Table 5. Prevalence of diabetes and impaired Glucose tolerance in male and female participants across different phenotypes of triacylglycerol concentration and waist circumference

	Phenotypes of TG and WC				P*
	NWNT	EWNT	NWET	EWET	
Men (%)					
Normal	38.5	4.5	47.4	9.6	0.06
IGT †	33.3	8.9	40	17.8	0.7
IFG §	42.5	11	34.2	12.3	0.1
Diabetic †	18.2	3	48.5	30.3	< 0.01
Women (%)					
Normal	41.2	18.2	19.1	21.5	< 0.001
IGT †	30.3	26.4	15.2	28.1	0.1
IFG §	34.1	22.2	16.5	27.3	0.9
Diabetic †	15.4	23.1	16.7	44.9	< 0.001

NWNT: Normal Waist Normal Triglycerid; EWNT: Enlarged Waist (men ≥ 102 cm; Women ≥ 88 cm) and Normal Triglycerid. NWET: Normal Waist Elevated Triglycerid; EWET: Enlarged Waist Elevated Triglyceride

* By using chi-square test

† Diabetes was defined as FBS ≥ 126 mg/dl in two repeated measurements and 2-h PG ≥ 200 mg/dl in two separate measurements.

‡ 140 ≤ 2-h post prandial blood Glucose ≤ 200 IGT

§ 100 ≤ Fasting plasma glucose (FPG) ≤ 125

at higher risk of diabetes.⁹ Lemieux et al have reported that two simple measures, waist and TG, might be a cheap clinical method identifying males with elevated insulin, APOB and LDL concentration, and hence, increased CHD and diabetes risk.¹⁵ However, this is the first among individuals with first relative history of diabetes relating this phenotype to IGT and diabetes, among individuals with FHD. We found that those with this phenotype were more likely to have diabetes. Therefore, such a simple index can be used by health professionals in health care system to early identify those at higher risk of diabetes. Although waist circumference has been used as a screening measure for this purpose, it has been shown that the addition of a biomarker like serum triglyceride to this measure would increase its accuracy, sensitivity and specificity in this regard.²²

In the current study, participants with the EWET phenotype had higher prevalence of metabolic risks. Prevalence of diabetes and IGT were higher among these people. Although such findings have previously been reported by other investigators, the population studied in previous publications was not individuals with FHD. The prevalence of EWET phenotype was respectively 9.6% and 23.6% among men and women in this study. Lemieux et al²³ have reported the phenotype among 19% of 907 participants in the Quebec Health Survey. Among 3430 French men, the phenotype has been reported to be 12.1%.²⁴ Sumner et al²⁵ found 21% of postmenopausal black women, 28.3% of white women and 42.3% of Mexican women with this phenotype. In Tehran Lipid and Glucose Study, the phenotype has been reported among 19% of adult men¹⁷ and 31.9% of women.¹⁶ This figure in Isfahani women was 24%.²⁶ As it comes from these figures, the prevalence is considerably different in different populations. Ethnicity might explain these differences to some extent. It seems that the pattern of obesity among Middle Eastern population is something different from those in other places of the world. In other words the so-called Middle Eastern pattern of obesity is highly

prevalent in these countries. This pattern of obesity is characterized by larger fat accumulation in the abdomen, particularly among women, such that women in these countries have higher prevalence of both general and central obesity. Different prevalence of this phenotype could also be explained by the use of different cut-off points for WC and serum triglyceride in the studies. The age range of the studied population must also be taken into account.

In this study, prevalence of diabetes among those with the EWET phenotype was 30.3% for men and 44.9% for women, respectively. Just 18.2% and 15.4% of those with NWNT phenotype were diabetic men and women, respectively. Prevalence of IGT among those with the EWET phenotype was 17.8% for men and 15.2% for women, respectively.

St-pierre et al,⁹ assessing 1190 individuals, introduced EWET phenotype as a predictor of cardiovascular risks among type 2 diabetic and IGT patients. They found that nearly 53% of males and 80% of females with the phenotype were diabetics or IGT. In a study in US population, 25.4% of those with the phenotype were diabetics and just 8% of diabetics were free of this phenotype.²⁷ However all these studies have been performed among individuals without family history diabetes. All mentioned studies are in line with our findings in the current study suggesting the higher prevalence of diabetes among those with the phenotype.

The mechanism by which EWET affects the risk of diabetes is unknown. It seems that enlarged waist circumference is associated with increased intra-abdominal fats which in turn could result in higher production of lipid products in the liver and therefore increasing levels of LDL and VLDL. On the other hand, high intra-abdominal fat would cause free fatty acid levels to increase in circulation which in turn could result in developing insulin resistance and hyperinsulinemia.²² The gene expression of Fat/CD36 as a carrier of long chain fatty acids is regulated by insulin. Previous researches have shown that destruction of this protein is closely related to insulin resistance.²⁸ Others have shown that the activity of lipo-

protein lipase (LPL) as a key enzyme for controlling serum TG levels is decreased among individuals with insulin resistance.²⁹ Increase levels of free fatty acids in beta cells could result in decreased insulin secretions and therefore increased risks of diabetes.³⁰

Some points needed to be considered in the interpretation of our findings. The important limitation of this study is its cross-sectional nature which does not allow inferring causal relations. Other point that must be kept in mind is the definition of EWET phenotype which might be different from other studies. While the WHO Expert Committee³¹ on Physical Status recommends measurement midway between the lower rib and the iliac crest, the NHANES III guidelines³² prescribe use of a point just above the right ileum and the recommendation of the North American Association for the Study of Obesity (NAASO) and the National Heart, Lung and Blood Institute

(NHLBI) (33) is to use the right iliac crest. The shortage of standard measurement for WC is problem, and makes comparison with other researches difficult. It is believed that the use of narrowest waist measurement offers greater ease of acceptance and interpretation by the public and may facilitate self-measurement in addition to clinical use. We measured WC at the point of noticeable waist because no standard location has been reported for waist circumference measuring. We did not measure serum insulin levels and insulin sensitivity of tissues in the current study. Therefore further studies in this field are warranted.

In conclusion, there was a significant positive association between hypertriglyceridemic waist phenotype and prevalence of diabetes. Therefore, using this phenotype for early identification of individuals at high-risk of diabetes has important public health implications for prevention.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

MA, MS, NM and MA participated in the collection of data, conception and design. AE and MZ contributed to conception and design, statistical analysis and data interpretation and manuscript drafting. All authors approved final manuscript for submission.

References

1. Qiao Q, Hu G, Tuomilehto J, Nakagami T, Balkau B, Borch-Johnsen K, Age- and sex-specific prevalence of diabetes and impaired glucose regulation in 11 Asian cohorts. *Diabetes Care*. 2003; 26: 1770-80.
2. Zandbergen AA, Sijbrands EJ, Lamberts SW, Bootsma AH. Normotensive women with type 2 diabetes and microalbuminuria are at high risk for macrovascular disease. *Diabetes Care*. 2006; 29(8): 1851-5.
3. World Health organization. Diabetes estimates and projections. [[http:// www.who.int/ncd/dia/databases4.htm#EMRo](http://www.who.int/ncd/dia/databases4.htm#EMRo)]. Accessed April 23, 2007.
4. Amini M, Afshin-Nia F, Bashardoost N, Aminorroaya A, Shahparian M, Kazemi M. Prevalence and risk factors of diabetes mellitus in the Isfahan city population (aged 40 or over) in 1993. *Diabetes Res Clin Pract*. 1997; 38: 185-90.
5. Saadat N, Salehi P, Emami H, Azizi F. The relationship between Glucose intolerance and blood pressure, body mass index, and waist to hip ratio in Tehran urban population: *Tehran lipid disorders 2002*; 1: 1-8.
6. Larijani B, Zahadi F. epidemiology of diabetes mellitus in Iran. *Iranian journal of diabetes and lipid disorders 2002*; 1: 1-8.
7. Najafipour F, Azizi F, Zareizadeh M. epidemiological study of familial diabetes type 2 in Tehran. *Iranian Journal of diabetes and lipid disorders 2003*; 35-42.
8. Asghar S, Hussain A, Ali SM, Khan AK, Magnusson A Prevalence of depression and diabetes: a population-based study from rural Bangladesh. *Diabet Med*. 2007; 24: 872-7.
9. St-Pierre J, Lemieux I, Perron P, Brisson D, Santure M, Vohl MC, Relation of the "hypertriglyceridemic waist" phenotype to earlier manifestations of coronary artery disease in patients with glucose intolerance and type 2 diabetes mellitus. *Am J Cardiol* 2007; 99: 369-73.

10. Mirmiran P, Azizi F, Hatami H, Gnghorbani M, Epidemiology and obesity in prevalent disease control in Iran. 2nd ed. Tehran: Eshtiagh, 2000; 56-62.
11. Misra A, Wasir JS, Vikram NK. Waist circumference criteria for the diagnosis of abdominal obesity are not applicable uniformly to all populations and ethnic groups. *Nutrition*. 2005; 21: 969-76.
12. Kahn H. Correction: The "lipid accumulation product" performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. *BMC Cardiovasc Disord* 2006; 6(1): 5.
13. Esmailzadeh A, Mirmiran P, Azizi F. Waist-to-hip ratio is a better screening measure for cardiovascular risk factors than other anthropometric indicators in Tehranian adult men. *Int J Obes Relat Metab Disord* 2004; 28: 1325-32.
14. Ho SC, Chen YM, Woo JL, Leung SS, Lam TH, Janus ED. Association between simple anthropometric indices and cardiovascular risk factors. *Int J Obes Relat Metab Disord* 2001; 25: 1689-97.
15. Lemieux I, Pascot A, Couillard C, Lamarche B, Tchernof A, Almeras N, Hypertriglyceridemic waist: A marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? *Circulation* 2000; 102: 179-84.,
16. Solati M, Ghanbarian A, Rahmani M, Sarbazi N, Allahverdian S, Azizi F. Cardiovascular risk factors in females by serum level of triglycerides and waist circumference (Tehran lipid and Glucose study). *Iranian Journal of Diabetes and lipid Disorders*. 2003; 2: 121-127. [In Persian].
17. Solati M, Ghanbarian A, Rahmani M, Sarbazi N, Allahverdian S, Azizi F. Cardiovascular risk factors in males with hypertriglyceridemic waist (Tehran Lipid and Glucose Study). *Int J Obes Relat Metab Disord* 2004; 28: 706-9.
18. Puavilai W, Laorugpongse D, Deerochanawong C, Muthapongthavorn N, Sriert P. The accuracy in using modified Friedewald equation to calculate LDL from non-fast triglyceride: a pilot study. *J Med Assoc Thai* 2009; 92(2): 182-7.
19. Frank EL, Moulton L, Little RR, Wiedmeyer HM, Rohlfing C, Roberts WL. Effects of hemoglobin C and S traits on seven glycohemoglobin methods. *Clin Chem* 2000; 46: 864-7.
20. Roberts WL, De BK, Brown D, Hanbury CM, Hoyer JD, John WG, et al. Effects of hemoglobin C and S traits on eight glycohemoglobin methods. *Clin Chem* 2002; 48: 383-5.
21. Gazi IF, Filippatos TD, Tsimihodimos V, Saougos VG, Liberopoulos EN, Mikhailidis DP, et al. The hypertriglyceridemic waist phenotype is a predictor of elevated levels of small, dense LDL. *Cholesterol* 2006; 41: 647-54.
22. Esmailzadeh A, Mirmiran P, Azizi F. Clustering of metabolic abnormalities in adolescents with the hypertriglyceridemic waist phenotype. *American Journal of Clinical Nutrition* 2006; 83: 36-46.
23. Lemieux I, Alméras N, Mauriège P, Blanchet C, Dewailly E, Bergeron J, et al. Prevalence of 'hypertriglyceridemic waist' in men who participated in the Quebec Health Survey: association with atherogenic and diabetogenic metabolic risk factors. *Can J Cardiol* 2002; 18: 725-32.
24. Czernichow S, Bruckert E, Bertrais S, Galan P, Hercberg S, Oppert JM. Hypertriglyceridemic waist and 7.5-year prospective risk of cardiovascular disease in asymptomatic middle-aged men. *Int J Obes (Lond)* 2007; 31: 791-6.
25. Sumner AE, Cowie CC. Ethnic differences in the ability of triglyceride levels to identify insulin resistance. *Atherosclerosis*. 2007 Jan 23; [Epub ahead of print].
26. Tavassoli N. Hypertriglyceridemic waist in an Iranian women sample: Isfahan Healthy Heart Program (IHHP). *Atherosclerosis* 2006; 7: 53-54.
27. Kahn HS, Valdez R. Metabolic risks identified by the combination of enlarged waist and elevated triacylglycerol concentration. *Am J Clin Nutr* 2003; 78: 928-34.
28. Bonen A, Tandon NN, Glatz JF, Luiken JJ, Heigenhauser GJ. The fatty acid transporter FAT/CD36 is upregulated in subcutaneous and visceral adipose tissues in human obesity and type 2 diabetes *Int J Obes (Lond)*. 2006; 30: 877-83.
29. Sumner AE, Vega GL, Genovese DJ, Finley KB, Bergman RN, Boston RC. Normal triglyceride levels despite insulin resistance in African Americans: role of lipoprotein lipase. *Metabolism* 2005; 54: 902-9.
30. Little P, Byrne CD. Abdominal obesity and the "hypertriglyceridemic waist" phenotype. *BMJ* 2001; 322: 716-20.
31. WHO Expert Committee on Physical Status. The use and interpretation of anthropometry. Report of a WHO Expert Committee. Geneva: WHO; 1995.
32. Chumlea NC, Kuczmarski RJ. Using a bony landmark to measure waist circumference. *J Am Diet Assoc* 1995; 95: 12.
33. National Heart, Lung and Blood Institute. The practical guide: identification, evaluation and treatment of overweight and obesity in adults (online), June 1998; www.nh/bi.nih.gov/guidelines/obesity/practgde.htm.