Original Article

Triglyceride Glucose Index, its Modified Indices, and Triglyceride HDL-C Ratio as Predictor Markers of Insulin Resistance in Prediabetic Individuals

Rojeen Rasheed Suleiman, Sherwan Ferman Salih[2], Barhav Issa Abdullah[3], Ibrahim Hasan Ibrahim[1], Zindan Azeez Saeed[4]

Department of Medical Laboratory Technology, [1]College of Health and Medical Techniques / Sheckhan, Duhok Polytechnic University, [2]College of Medicine, [3]College of Health Science, University of Duhok, Duhok, Iraq, [4]Chemistry Department, Emergency Teaching Hospital, Duhok, Iraq

Abstract

Background: Prediabetes is a strong hazard for developing of both cardiovascular disorders and diabetes mellitus. Insulin resistant predisposes to prediabetes and type 2 diabetes mellitus that all are strongly correlated with development of cardiovascular disorders. Recently, the triglyceride glucose index, its modified indices and the ratio of triglyceride/ high density lipoprotein-cholesterol have been suggested as sensible surrogate markers of insulin resistant. **Objectives:** The current study aimed to evaluate the triglyceride glucose index, its modified indices and triglyceride/ high density lipoprotein-cholesterol ratio among individuals with prediabetes compared to healthy control. **Materials and Methods:** This study was carried out as a case control among 120 participants, 60 prediabetic individuals and 60 apparently healthy individuals as a control group. Prediabetic individuals were obtained from relatives of patients with diabetes mellitus visiting Endocrinology Unit at Azadi Teaching Hospital and 60 healthy individuals were chosen from medical staffs of Azadi Teaching Hospital. **Results:** There were statistically significant higher mean level of indices in individuals with prediabetes with exception of triglyceride/ high density lipoprotein-cholesterol ratio that was insignificantly higher. There was a significant positive correlation of abnormal homeostatic model assessment of insulin resistance with triglyceride/ high density lipoprotein-cholesterol ratio (r = 0.651), and triglyceride glucose index (r = 0.390) whereas insignificant positive correlation with its modified index. **Conclusion:** The mean level and prevalence of abnormal TyG index, TyG-BMI and TyG-WC were significantly higher in prediabetic individuals, whereas, TG/HDL-c was insignificantly higher compared to control individuals.

Keywords: Cardiovascular, prediabetes, triglyceride glucose index

Introduction

Prediabetes is hyperglycemic condition within normal glucose metabolism and diabetes mellitus and presented in two types; impaired glucose tolerance (IGT) and impaired fasting glucose (IFG). Prediabetes is predictor for the type 2 diabetes mellitus (T2DM) development and cardiovascular disease (CVD) development.[1]

Insulin resistance (IR) is characterized by decreased sensitivity and responsiveness of different tissues of the body to the metabolic effects of insulin, mostly muscle, adipose tissue, and liver. IR tends to several conditions such as prediabetes, T2DM, hypertension, dyslipidemia, and metabolic syndrome, that all are highly linked to the development of atherosclerosis and development of CVD.[2]

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Body mass index (BMI) and waist circumference (WC) were involved in the evaluation of the body fat and are commonly used for detecting prediabetic and T2DM development.[3] Recently, the triglyceride glucose (TyG) index, its modified indices (TyG-BMI and TyG-WC), and TG/ HDL-c ratio have been advocated as sensible and

Address for correspondence: Dr. Rojeen Rasheed Suleiman, Lecturer in Clinical Biochemistrym, Department of medical laboratory technology, College of Health and Medical Techniques/Shekhan, Duhok Polytechnic University, Duhok, Iraq.
E-mail: Rojeen.rasheed@dpu.edu.krd

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simple alternative indicators of IR.[4] The hyper insulinemic euglycemic clamp test and the homeostatic model assessment of insulin resistance are used to calculate the TyG index. TG/ HDL-c ratio depends up on triglyceride (TG) concentration and high-density lipoprotein-cholesterol (HDL-c) concentration, that are considered an index of CVD mortality, incidence of T2DM, atherogenic dyslipidemia, and metabolic syndrome.[5]

Different studies done in different areas in world have shown different results of using TyG index, TyG-BMI, TyG-WC, and TG/HDL-c ratio as predictors for IR in general and diseased population.[6,7] Therefore; the current study aimed to evaluate the IR, TyG index, TyG-BMI, TyG-WC, and TG/HDL-c ratio among individuals with prediabetes and compare between TyG index, TyG-BMI, TyG-WC, and TG/HDL-c ratio as predictors for IR among individuals with prediabetes.

Materials and Methods

A case control study was conducted among 120 participants, including 60 prediabetic participants and 60 healthy individuals as a control group. The study was conducted for 6 months interval from January 2022 to June 2022. Prediabetic individuals were identified from relatives of patients with T2DM visiting Endocrinology unit at Azadi Teaching Hospital and 60 healthy individuals were chosen from medical staffs of Azadi Teaching Hospital. The diagnosis of prediabetes depends on American Diabetes Association as IFG having FPG levels 100 mg/dl to 125 mg/dl or IGT as having glucose level 2 hours post OGTT of 140 mg/dl to 199 mg/dl with FPG less than that for the diagnosis of diabetes mellitus.[8]

All the participants were informed to be at Azadi Teaching Hospital – clinical biochemistry department in the morning and after overnight fasting for blood collection. Ten ml of blood was obtained from the participants for the analysis of serum lipid profile concentration, glucose, insulin, and blood HbA1c %. All biochemical parameters were measured by Cobas 6000 (Roche, Hitachi) depending on different principles. Serum glucose concentration and lipid profile depend up on enzymatic-colorimetric method, insulin was measured by electrochemiluminescence and blood HbA1c was measured by turbidimetric assay.[9]

We assessed anthropometric parameters such height, weight, and WC considering the standards of the World Health Organization. Calculation of BMI depends on the division of weight in kilogram by square of the height in meters (kg/m^2)[10]

HOMA-IR was computed from FPG and fasting insulin as follows: HAMA-IR = Glucose (mg/dl) × insulin (µu/l)/ 405 (HOMA-IR >3.0 was regarded as insulin resistance.[11] The following equation determines the TyG index: Ln [FBS (mg/dl) × TG (mg/dl)/2] (normal value was between 4 and 8).[12] TG/HDL-c ratio is calculated using Fasting TG/ fasting HDL-c (more than 3 indicate abnormal level).[13] TyG-BMI was estimated as TyG index × BMI (best cutoff value was 213.29), whereas, the TyG-WC was assessed as TyG index × WC (optimal cutoff point was 760.06).[14,15]

Statistics

SPSS was used for statistical analysis. The results were shown as a mean (SD) or as a percentage. Independent t-tests were utilized to compare the groups in study. In order to compare differences between two groups, the Pearson Chi-square test was used. A P value of 0.05 or less is considered statistically significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number 18082021-8-23 (including the number and the date in 18 August 2021.

Results

Basic features of studied individuals were expressed in [Table 1]. Mean age level in prediabetic individuals was (43.9 years) with male predominant (36, 60%). BMI and WC were significantly higher in prediabetes than control ($p < 0.0001$). Moreover; there were statistically significant higher mean level of indices in individuals with

Table 1: General characteristics of participants

Characters	Prediabetes (N=60) mean± SD, No%	Control (N= 60) mean± SD, No%	P value
Age (years)	43 ± 9	41 ± 6	0.201
Gender			
Male	36(60%)	31(51.7%)	0.362
Female	24(40%)	29(48.3%)	
BMI (kg/(m)2)	31.46 ± 5.37	24.82 ± 3.27	< 0.0001
W.C (cm)	104.75 ± 13.77	91 ± 11.99	< 0.0001
Glucose (mg/dl)	101.08 ± 7.59	81.05 ± 9.25	< 0.0001
Insulin (µIU/mL)	14.48 ± 8.38	12.26 ± 4.01	0.073
HbA1c (%)	6.01 ± 0.22	5.05 ± 0.34	< 0.0001
Triglyceride (mg/dl)	113.30 ± 65.05	91.14 ± 42.17	0.028
HDL-C (mg/dl)	50.07 ± 9.62	54.23 ± 18.35	0.058
TyG index	8.56 ± 0.56	6.8 ± 0.39	< 0.0001
TyG -BMI index	269.75 ± 50.57	200.69 ± 27.64	< 0.0001
TyG -WC index	898.06 ± 137.09	734.12 ± 96.79	< 0.0001
TG/HDL-c	2.39 ± 1.92	1.95 ± 1.03	0.117
HOMA-IR	3.81 ± 2.39	2.44 ± 0.81	< 0.0001

Table 2: Prevalence of biochemical indices and ratio in prediabetic individuals and healthy control

Biochemical indices	Prediabetes N=60 No%	Control N= 60 No%	P value
TyG index			
4.0-8.0	5 (43.3%)	37(61.7%)	< 0.001
≥ 8.0	55(91.7%)	23(38.3%)	
TG/HDL-c			
< 3.0	51(85%)	57(95%)	0.068
≥ 3.0	9(15%)	3(5%)	
HOMA-IR			
< 3.0	26(43.3%)	42(70%)	0.002
≥ 3.0	34(56.7%)	18(30%)	
TyG-BMI index			
< 213.29	9(15%)	45(75%)	< 0.0001
≥ 213.29	51(85%)	15(25%)	
TyG-WC index			
< 760.06	8(13.3%)	42(70%)	< 0.0001
≥ 760.06	52(86.7%)	18(30%)	

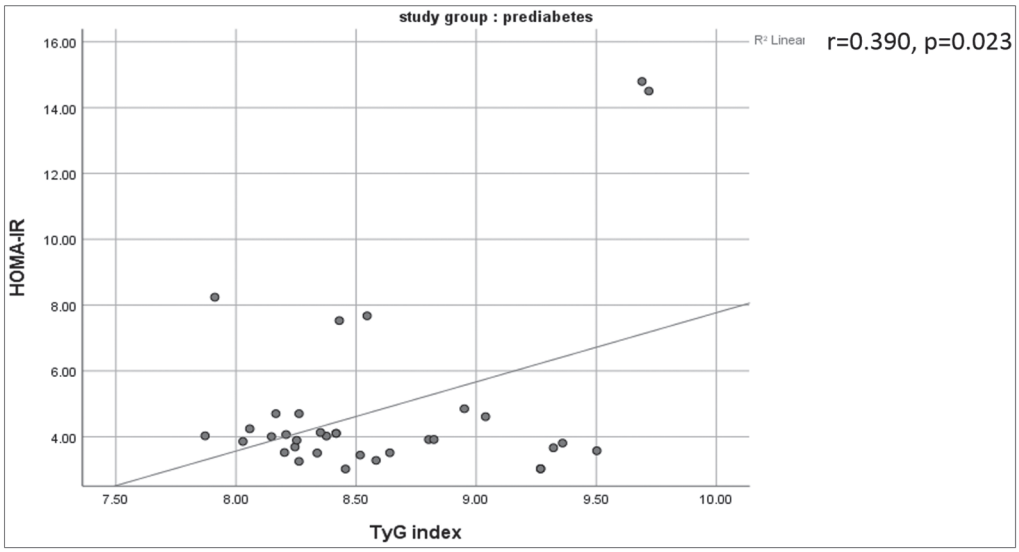

Figure 1: Correlation of HOMAR-IR with TyG index

prediabetes with exception of TG/HDL-c ratio that was insignificantly higher.

Prevalence of abnormal indices and ratio among individuals with prediabetes and healthy control were shown in [Table 2]. Majority of abnormal TyG index (55, 91.7%), TyG-WC (52, 86.7%), TyG-BMI (51, 85%) were found in prediabetic individuals, whereas, half of HOMA-IR (34, 56.7%) was abnormal comparing to control (p value < 0.05).

Correlation of indices and ratio with abnormal HOMA-IR (more than 3.0) among prediabetic individuals was shown in [Figures 1, 2, 3, and 4]. A significant positive correlation of abnormal HOMA-IR with TG/HDL-c (r = 0.651, p=< 0.001), and TyG index (r = 0.390, p=0.023) was found, whereas insignificant positive correlation with TyG-BMI (r = 0.245, p=0.163) and TyG-WC index (r = 0.139, p=0.432) was found.

Discussion

Prediabetes is a common cardiometabolic condition with increased risk of CVD.[16] Many studies demonstrated that the prevalence of prediabetes has been increasing all over the world, as they shown that one third to half of population have prediabetes as well as most of those were unaware of the condition.[17,18] Obesity is an inflammatory process and regarded as most modifiable environmental risk factor that associated with increase insulin demand and increase incidence of IR leading to prediabetes development.[19]

Our study showed a statistically significant higher mean WC and BMI in individuals with prediabetic than apparently healthy control. Moreover, the study indicated that central adiposity, high liver fat content, IR, high body triglycerides, and decreased serum adiponectin levels were linked with incidence prediabetes in obese people..[20] Our

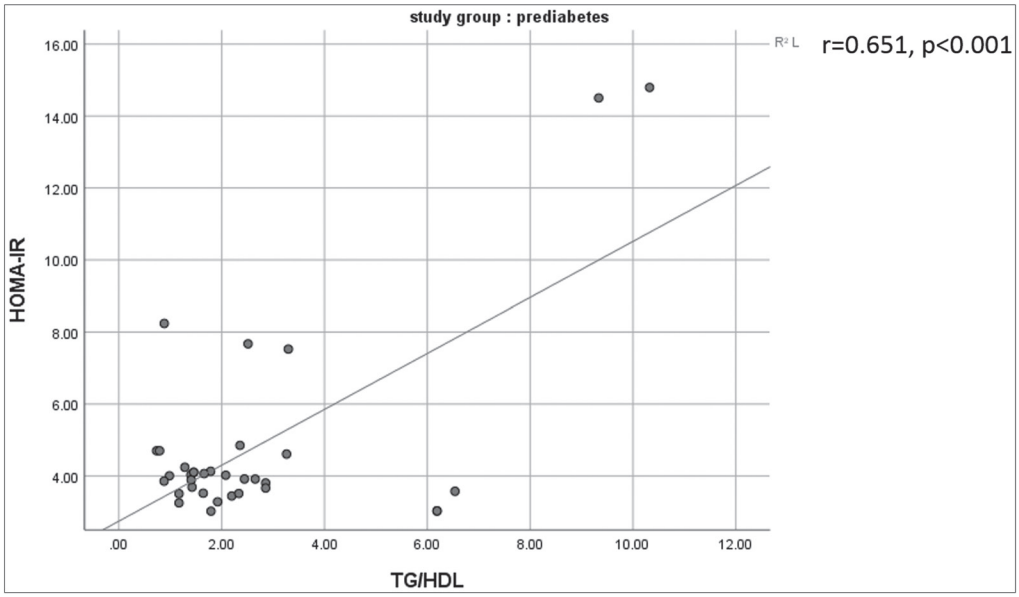

Figure 2: Correlation of HOMAR-IR with TG/HDL index

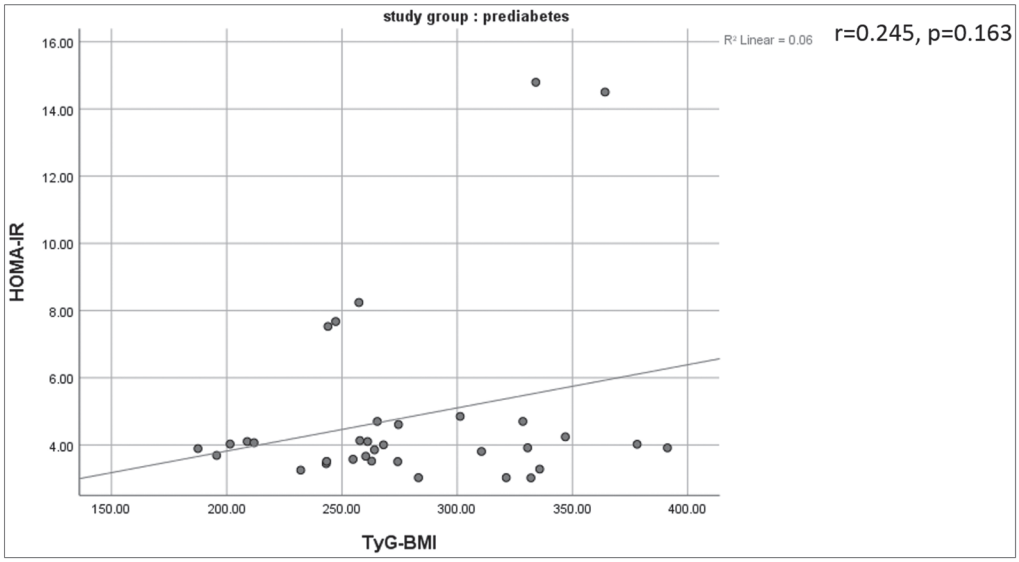

Figure 3: Correlation of HOMAR-IR with TyG-BMI index

finding was consistent with study done in US among Japanese American population by sun J *et al*. that shown increased visceral obesity was associated with increase incident of prediabetes and inconsistent with study done by Mainous *et al.* that had shown no association between obesity and prediabetes.[21,22]

The present study observed that the mean level of HOMA-IR and prevalence of IR were higher among prediabetic individuals compared to healthy control. However, more than half of prediabetic individuals had IR as the HOMA-IR was more than 3.0 as compared to the presence of less than one third of IR among healthy control individuals. In insulin resistance, several tissues and cells in the body such as muscle tissue, adipose tissue, hepatic tissue, and endothelial cells do not respond normally to insulin that mostly results from abnormal insulin signaling. Moreover, Insulin resistance can be caused by vascular endothelial dysfunction, which reduces insulin delivery to insulin-sensitive organs. Obesity-related inflammation increases endothelial dysfunction, extracellular matrix production, and alterations in capillary density and glucose absorption, all of which contribute to the development of insulin resistance.[23]

The most striking observation of our study was the presence of higher mean level and higher prevalent rate of abnormal indices and ratio among individuals with prediabetes. The mean level and prevalence of abnormal TyG index, TyG-BMI and TyG-WC were significantly higher in prediabetic individuals, whereas, the TG/HDL-c was insignificantly higher compared to control individuals.

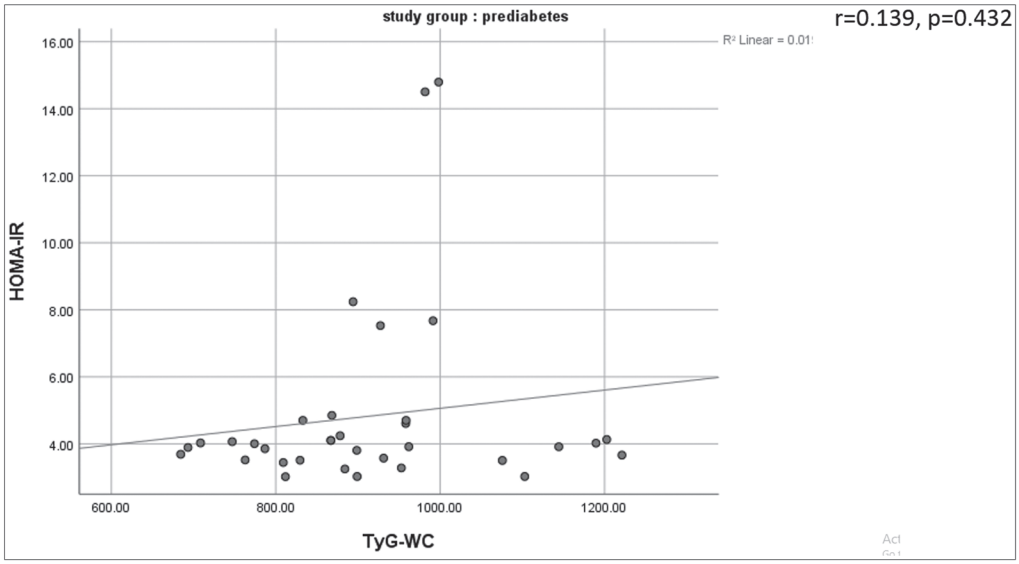

Figure 4: Correlation of HOMAR-IR with TyG index

Majority of prediabetic individuals had abnormal level of TyG index, TyG-BMI and TyG-WC, whereas, half of those individuals had abnormal level of TG/HDL-c. This is mostly related to obesity, abnormal high triglyceride level, and low HDL-c level. Increase triglyceride concentration resulting in decrease retention of free fatty acids (FFA) and increase FFA level in blood and increase flux of these FFA from adipose tissue to other tissue such as liver with increase synthesis of triglyceride and hepatic glucose output (vicious cycle).[6] Adipose tissue is regarded as an endocrine organ through secreting adipokines (leptin and adiponectin) that regulate the energy balance and insulin action. Abnormality in adipokines level such as hyperleptinemia and hypoadiponectinemia is associated with increase in central adiposity (visceral adipose tissue) that has a critical role in the development of IR.[24] Moreover, visceral adipose tissue responsible for secretion of various inflammatory cytokines that enhances the occurrence of insulin resistance and prediabetes.[25]

In relation to IR, the current study observed a significant positive correlation in the relation of IR with TyG index and TG/HDL-c ratio as well as insignificant positive correlation with TyG index-BMI and TyG index-WC. The relationship between TyG index and insulin resistance has been explained by a number of different probable processes. Increased FFA can result from higher triglyceride levels, with increased flux of FFA from adipose to non-adipose tissue, this may enhance insulin resistance.[26,27] Lee *et al.* found in their study that TyG index might serve as an indication for insulin resistance and assist in identifying those who are at a high risk of improving CVD even before they exhibit any symptoms.[28] Our study was inconsistent with study done by Janghorbani *et al.* as they found that TyG index did not improve impaired glucose metabolism prediction in an Iranian population.[29] Zhang *et al.* found that in Chinese normal-weight population, risk of incident of impaired glucose metabolism increased with increasing TyG index.[30] According to Gianini *et al*., the ratio of TG/ HDL-c was linked to insulin resistance and may be utilized in conjunction with other indicators to identify those who are more likely to develop complex insulin resistance morbidity.[31] According to Zhou M. *et al*., TG/ HDL-c would be a predictor of IR in the Chinese people with varying levels of glucose tolerance.[32]

According to research by Zheng *et al*., TyG-WC is a more accurate analyst used for identifying those at a high risk of developing prediabetes.[14] TyG-WC may achieve superiority since TG, FPG, and obesity are extensively proven of the involvement in IR and reasons of prediabetes. Affording to the Korean National Health and Nutrition Examination Survey, the TyG-BMI was a useful analysis to predict IR in healthy Koreans a cheapest as well as a less intrusive way.[33] In a cohort research, Jiang *et al*. discovered a higher TyG-BMI could substantially raise the causes of prediabetes in the general inhabitance, particularly in women, nonobese persons, and those below 50[34]

As evidence indicating visceral adipose tissue serves a further crucial role in the development of insulin resistance than fat in subcutaneous, WC may be much more beneficial than BMI. Visceral fat is thought to produce more FFA than subcutaneous fat, increasing the causes of IR.[35]

Conclusion

The current study concludes that more than half of individuals with prediabetes had insulin resistance compared with apparently healthy control. The mean level and prevalence of abnormal TyG index, TyG-BMI, and TyG-WC were significantly greater in prediabetic individuals, whereas, the TG/HDL-c was insignificantly

higher compared to control individuals. Moreover, a significant positive association of IR with TyG index and TG/HDL-c ratio as well as insignificant positive correlation with TyG index-BMI and TyG index-WC was found.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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