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Original Article

TyG index a promising biomarker for glycemic control in type 2 Diabetes Mellitus

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1. Introduction

Diabetes Mellitus (DM) is increasing at an alarming rate throughout the world . The assessment of glycemic control is of prime importance because of its key role in the management of type 2 DM. Diabetics with poor glycemic control have adverse effects on the life expectancy and quality of life [1,2].

Glycated hemoglobin (HbA1c) has been considered as a good indicator of overall glycemic control and possible risk for long-term complications. It is a validated, however, laboratory determinations of plasma HbA1c are yet not widely available and standardized in all services [3] in addition to its high cost.

Recently, the TyG index, a product from the fasting levels of triglycerides and glucose, presented promising results as a surrogate marker for the assessment of insulin resistance (IR) [4] with a good correlation with gold standard hyperglycemic clamp according to a study in Brazilian [5] and Mexician [6]. In addition, it has been used as a tool to recognize metabolically obese normal weight individuals [7] and as a predictor of coronary artery calcification and subclinical atherosclerosis [8], and non alcoholic fatty liver disease [9] on the other hand, hypertriglycerdemia is a well known risk factor for coronary heart disease [10] and one of the component of metabolic syndrome [11]. so, measuring serum TG level as part of TYG index or alone can be a useful and cost effective marker and represent the glycemic and cardiovascular status of an individual simultaneously.

Given the need for markers with accessibility and with good discriminating ability for the assessment of glycemic control, we evaluate the potential of using TyG index and TyG derived indices (TyG-WC, TYG-BMI) to assess glycemic control and its correlation with HbA1C in a sample of Iraqi subjects with type 2 DM.

2. Subjects and methods

2.1. Subjects

This study is a cross sectional study conducted in Baghdad medical city during the period from January 2018–September 2018.

Initially, 350 T2DM subjects were assessed for eligibility. Among these, 57 subjects were excluded because of the presence of missing data or certain diseases as renal, liver, thyroid or any endocrine abnormalities or if they were pregnant, on insulin therapy or any other medications that affect the tested parameters. . Final analyses were performed in 293 subjects (154 men and 129 women).

Based on the criteria of the American Diabetes Association (ADA) diabetes was defined as levels of fasting glucose $\geq$ 126 mg/dL or HbA1c $\geq$ 6.5% and/or the current use of antihyperglycemic drugs [12].

The subjects provided their written informed consent for use of their health screening data in the research. This study was reviewed and approved by the scientific and ethical committee in AL-Kindly college of Medicine-University of Baghdad and was carried out in accordance with the Helsinki Declaration of 1975.

2.2. Anthropometric measurements

Anthropometric measurements were performed while the participants wore light clothes, and the height and body weight were measured to the nearest 0.1 cm and 0.1 kg respectively. The BMI was calculated as the weight in (kg) divided by the height in (m) squared. The waist circumference (WC) was measured to the nearest 0.1 cm midpoint between the iliac crest and the costal margin at the end of expiration.

2.3. Biochemical measurement

Venous blood samples were collected from all the subjects in

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serum separator tubes after 12h fasting. Serum was separated to clot and was centrifuged at 5000 rpm for 10min. The supernatant clean serum was then pipetted and stored in dry thin walled vials at −20 °C until further analysis. Hemolysed samples wereexcluded. The sera were analyzed for fasting serum glucose(FSG), total cholesterol(TC), triglyceride(TG) and high density lipoprotein(HDL-C) using an auto analyzer (Roche Modular P-800, Germany). The serum level of LDL cholesterol was determined using the Friedewald formula: LDL-c (mg/dL)TC (mg/dL)HDL-c (mg/dL)TG (mg/dL)/5 [13].

HbA1c was estimated by high performance liquid chromatography(supplied by Variant company, USA) insulin was measured by Enzyme linked immune assay (DRG kit, Germany).

The effect of glycemic control on different parameters was evaluated by categorizing all the patients into two categories on the basis of HbA_1c levels; < 7% good glycemic control, ≥ 7% poor glycemic control. The selection of these cutoff values of HbA_1c was based on earlier studies [14].

TyG indices were calculated according to the followings formula [4,15,16]:

$$\text{TyG index} = \ln(\text{fasting TG [mg/dL]} \times \text{fasting glucose [mg/dL]}/2)$$

$$\text{TyG-WC} = \text{TyG index*WC}$$

$$\text{TYG-BMI} = \text{TyG index*BMI}$$

Insulin resistance was assessed by HOMA-IR: fasting Glucose (mg/dl) x fasting Insulin(μU/mL)/405.

2.4. Statistical analysis

Statistical software SPSS version 21.0 software (Chicago, IL, USA) was used for statistical analysis. A value of $p < 0.05$ was considered statistically significant.

Baseline characteristics were calculated for the total number of subjects. All data were presented as mean ± SD Independent samples *t*-test (2-tailed) was used to compare means of different parameters. Pearson's correlation test was performed to assess correlations between different parameters. Receiver operating curve (ROC) were used to compare the strength of TYG indices in discriminating the glycemic control state and the insulin resistance state depending on the area under the curve (AUC) and 95% confidence interval (CI) were calculated.

3. Result

The baseline characteristics of the studied subjects are described in https://www.nature.com/articles/nutd201446 Table 1. A total of 293 subjects aged 22–78 years (51.86 ± 9.8) participated in this study. 154 (52.6%) were male 0.54% had good glycemic control (HbA1C < 7). 29.3% were normal weight, 25.6% overweight and 45.1% were obese.

Table 2 shows the characteristics of the patients according to their glycemic control; HOMA −IR, TYG index,TYG-WC and TYG-BMI were significantly increased in diabetics with poor glycemic control.

Table 3 illustrates that TyG Index, TyG-BMI, TyG-WC correlate significantly with HbA1c and HOMA-IR in addition TyG index showed significant correlation with HDL-C,LDL-C,VLDL-C.

The ROC analysis in Table 4 shows that the TyG index have a better performance in comparison with the TyG −WC and TYG-BMI in identifying glycemic control. (AUC for TYG index:0.839,TYG-WC: 0.710 and TYG-BMI:0.651)respectively.

4. Discussion

In the present study we evaluated whether TyG index and TyG derived indices (TYG−WC and TYG-BMI) correlate with long term glycemic control in term of HbA1c in type 2 diabetic patients and their possible use as surrogate markers of glycemic control. The novel insight of this study is that TyG indices showed positive significant correlations with HbA1c and IR. We also found that TYG index; TYG−WC and TYG-BMI were significantly increased in the diabetics with poor glycemic control In addition, the ROC curve analysis showed that TyG index had the largest AUC (0.839), followed by TYG-WC (0.710) and TYG-BMI(0.651) respectively Beside, TYG-INDEX showed significant correlations with all the tested cardiometabolic risk factors (HDL-C, non HDL-C,TC, IR). Thus TYG index demonstrated its superior performance in identifying glycemic control.

The predicating ability of TYG index has been studied in different metabolic state. Guerrero-Romero et al. proposed that TYG index could be a marker of IR with an excellent correlation with the gold standard euglycemic-hyperinsulinemic clamp test [6]. In addition, another study suggested that TYG index can predict the risk of future DM [17]. All the studied TYG derived indices showed a significant correlation with HbA1c, IR and a good AUC, but, the TYG index showed the best performance.

Several possible mechanisms have been suggested to explain the correlation between TyG index and glycemic control. Increased triglyceride levels can lead to increased free fatty acids and, thus, increased flux of free fatty acids from adipose to nonadipose tissue, which may affect the glycemic control [18]. Many studies have confirmed that higher levels of triglycerides in the liver and muscle may affect glucose metabolism in each target organ [19,20]. In this study, TyG index had the largest AUC for IR followed by TyG −WC then TyG-BMI, so TyG index was the most efficient surrogate marker for identification of IR. In contrast, a previous study in nondiabetic Taiwanese people demonstrated that TyG BMI had the largest AUC followed by TyG-WC and then TyG index [21]. This difference may be due to difference in the studied population (diabetic subjects vs nondiabetic subjects).

The rationale to use the TyG index in the clinical setting is that its routinely measured easy, cost effective, and reflect

Table 1
Baseline characteristics of the studied population.

	Mean	SD
Age (years)	51.86	9.8
Gender male No.(%)	154 (52.6%)	
Duration of diabetes (years)	6.96	0.47
Weight(kg)	92.52	8.9
Height (m)	1.74	0.
Body mass index(kg/m$^{2)}$	30.15	1.03
Waist circumference(cm)		11.2
male	103.5	9.4
female	101.8	
Fastng serum glucose (mg/dL)	193.5	4.49
HbA1c (%)	8.12	1.4
Total cholesterol (mg/dL)	201.62	3.37
Triglycerides (mg/dL)	161.58	5.2
HDL-C (mg/dL)	42.3	4.1
LDL-C (mg/dL)	125.46	30.3
VLDL-C (mg/dL)	24.54	0.98
TYG index	9.46	0.68
TYG-BMI	273.85	40.3
TYG-WC	924.67	90.4
Insulin (mU/mL)	12.81	3.5
HOMA-IR	5.3	1.6

Result expressed as mean ± standard deviation (SD).

Table 2
Comparison between patients with good and poor glycemic control.

	Good glycemic control	Poor glycemic control	P value
Number (%)	135(46%)	158 (54%)	
Male No (%)	74 (48%)	80(52%)	
Age (years)	50.94 ± 9.44	52.69 ± 10.27	0.135
Duration of DM (years)	7.37 ± 0.9	6.362 ± 0.6	0.156
Weight(kg)	84.70 ± 20	82.80 ± 13.35	0.620
Height (m)	1.65 ± 0.12	1.63 ± 0.09	
Body mass index(kg/m$^{2)}$	30.64 ± 3.4	31.31 ± 6.09	0.568
Waist circumference (cm)			
Male	96.8 ± 9.9	108 .75 ± 9.9	0.000
female	102.36 ± 5.7	101.4 ± 9.2	0.785
Fasting serum glucose (mg/dL)	150.40 ± 30.7	230.22 ± 40.8	0.000
HbA1c (%)	6.426 ± .84	9.581 ± 1.30	0.000
Triglycerides (mg/dL)	155.37 ± 43.60	167.23 ± 44.15	0.261
Total colesterol (mg/dL)	192.04 ± 29.236	209.62 ± 55.462	0.009
LDL-C (mg/dL)	117.02 ± 39.9	132.60 ± 44.9	0.003
HDL-C (mg/dL)	42.21 ± 3.42	42.35 ± 4.7	0.763
VLDL-C (mg/dL)	25.16 ± 1.23	24.05 ± 3.6	0.580
TYG index	9.19 ± .67	9.69 ± .61	0.000
TYG-WC	865.27 ± 183.7	976.08 ± 114.7	0.002
TYG-BMI	276 ± 48	291.93 ± 57	0.043
Insulin (mU/mL)	9.9 ± 2.1	15.4 ± 2.3	0.01
HOMA-IR	2.6 ± 0.2	7.9 ± 1.1	0.000

Result are expressed as mean ± SD.
P less than 0.05 is statistically significant.

Table 3
Correlation between the studied parameters.

		HbA1C	HOMA-1	TC	Non HDL-C	LDL-C	HDL-C	VLDL-C
TYG index	r	0.444**	0.629**	0.427**	0.305**	0.216**	−0.431**	0.580**
	p	0.000	0.000	0.000	0.006	0.000	0.000	0.000
TYG-WC	r	0.318**	0.283*	0.128	0.138	0.053	−0.056	0.293**
	p	0.005	0.012	0.260	0.225	0.646	0.625	0.009
TYG-BMI	r	0.281*	0.239*	0.227*	0.257	0.138	−0.106	0.422**
	p	0.013	0.036	0.044	0.022*	0.224	0.354	0.000

r = pearson correlation coefficient.
P less than 0.05 is statistically significant.

Table 4
The areas under the curves and 95% confidence interval for the potential markers.

Test variable	Area under the curve	Asymptotic 95% Confidence Interval		*P*-value
		Upper Bound	Lower Bound	
For glycemic control				
TyG index	0.833	0.745	0.922	0.000
TyG-WC	0.702	0.522	0.774	0.002
TyG-BMI	0.648	0.583	0.821	0.027
For Insulin resistance				
TyG index	0.833	0.861	0.978	0.000
TyG-WC	0.648	0.705	0.897	0.000
TyG-BMI	0.702	0.776	0.939	0.000

P less than 0.05 is statistically significant.

many cardiometabolic risk factors in addition, the epidemic increase in type 2 diabetes predict that diabetes will have a worldwide increase, including people in undeveloped countries [22]. Because the HbA1 is expensive, and not available in most laboratories of the hospitals of undeveloped countries. Thus, an alternative test that is inexpensive and routinely available is required to provide the opportunity for follow up of long term glycemic among the individuals of low income and undeveloped countries.

Limitation: first the study is cross sectional, second we included only patient type 2 diabetic mellitus, we may extend the study in the future to include healthy individuals.

5. Conclusions

The TyG index represents a useful and accessible tool for assessment of long term glycemic in T2DM patients with good correlation with both HbA1c and IR., This index has the advantage of being applicable into clinical practice since both glucose and triglyceride determination are inexpensive and routinely measured.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.11.030.

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