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A STUDY OF RELATIONSHIP BETWEEN (TRIGLYCERIDE-GLUCOSE) INDEX DURING THE FIRST TRIMESTER OF PREGNANCY AND THE RISK OF DEVELOPING GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is an increasingly global health problem and presence of suitable biomarkers for early diagnosis of GDM is considered crucial to improve final outcome. **Objective:** The aim of this study was to determine the predictive value of triglyceride glucose index (TyG index) in the first trimester for GDM. **Patients and Methods:** An analytical prospective cohort study was conducted for the period one year (May 2022-May 2023) at Tishreen University Hospital in Latakia-Syria. The study included all pregnant women in the first trimester who checked in the outpatient department of obstetrics and gynecology with assessment of fasting plasma glucose (FPG), lipid profile, and TYG index. **Results:** The prevalence of GDM among the study population was 17.3%. Women with GDM had significantly higher averages for age(p:0.001), body mass index BMI(p:0.001), parity(p:0.0001), abortions(p:0.02), family history of T2DM(p:0.002) and history of polycystic ovary syndrome PCOs(p:0.001). FPG and lipid profile parameters including total cholesterol (TC) and triglyceride (TG) were significantly higher in GDM group ($p<0.05$) compared to non-GDM. TyG index was significantly higher in women who developed GDM (4.73±0.1 versus 4.18±0.1,p:0.0001). When the peak TyG index reached 4.7, progressive of GDM could be predicted with an area under the ROC curve of 0.69(95% CI:0.96-1) with sensitivity 92.9% and specificity 100%. In addition to, all women who developed GDM were in the range of TyG index (4.49-4.87) whereas non-GDM women were distributed as follows; 3.90-4.20(41.9%), 4.21-4.48(45.2%), and 4.49-4.87(12.9%), p:0.0001. **Conclusion:** The current study demonstrated that TyG index in the first trimester of pregnancy provides non-invasive tool for identifying at risk pregnant women for GDM.

KEYWORDS: Gestational, diabetes mellitus DM, predictive, Syria, yYG index.

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as an abnormal glucose tolerance that first recognized in the second or third trimester of pregnancy.[1,2,3] Worldwide, the prevalence of GDM ranges from 1 to 30 percent and this varying in occurrence because of differences in the characteristics of population such as maternal age and body mass index, as well as race-ethnicity differences.[4,5,6,7] GDM is associated with increased risk of maternal and neonatal complications including: preeclampsia, operative delivery, maternal and/or birth trauma, future development of DM in mothers, metabolic complications in neonates such as hypoglycemia, hypocalcemia and hyperbilirubinemia, macrosomia, and obesity in adolescent offspring.[8,9,10] Diagnosis of GDM is made based on many diagnostic criteria in which International Association of Diabetes and Pregnancy Study Groups(IADPSG) is considered the most frequently used. According to the results of 75 gram oral glucose tolerance test (OGTT), GDM is diagnosed in presence one or more of the following; fasting plasma glucose FPG ≥92 mg/dL, one-hour glucose≥180 mg/dL, or two-hour glucose ≥153 mg/Dl.[11,12,13] There are many indices to access insulin resistance such as Hyperinsulinemic-Euglycemic Clamp Test(HIEC) and Homeostasis Model Assessment of Insulin Resistance(HOMA-IR) and each one has its own advantages and disadvantages.[14,15] Triglyceride glucose index (TYG index) represents a combination of FPG and triglyceride(TG) which used for detection of insulin resistance that plays an important role in GDM.[16] It has been reported that TYG index has valuable predictive value in early detection of type 2 diabetes mellitus (T2DM), non-alcoholic fatty liver disease, renal injury

resulting from microangiopathy and cardiovascular disease, and metabolic syndrome.[17,18,19,20] Early detection for GDM is considered crucial to reduce the risk for adverse pregnancy outcomes, and the best method for early screening and diagnosis continues to be controversial. Therefore, the aims of our study were: 1- to investigate the prognostic value of TYG index levels in early prediction of GDM. 2- to determine best cut-off point for prediction of GDM.

PATIENTS AND METHODS

This is an analytical prospective cohort study of a group of women attending department of obstetrics and gynecology at Tishreen University Hospital in Latakia-Syria during one-year period (2022-2023). The inclusion criteria were: all pregnant women in the first trimester of pregnancy who underwent screening for GDM. The exclusion criteria werepresence of one of the following: type 1 or type 2 diabetes mellitus (DM), pregestational thyroid dysfunction or dyslipidemia, treatment with glucocorticoids over the past six months, previous history of eclampsia or GDM, or women who diagnosed with GDM in the first trimester. Complete history, review of systems, and physical examination were performed. Weight and height were measured, and body mass index (BMI) was calculated as weight(kg) divided by height(m) squared(kg/m2). In the first trimester, FPG and levels of lipid were measured for all women, which included: Triglyceride TG (normal levels<150 mg/dL), Low-density lipoprotein LDL (normal<100 mg/dL), and High density lipoprotein HDL (low levels defined as <40 for men and <50 for women), with calculation of TYG index according the following formula: TyG index= Ln[TG(mg/dl) x FPG(mg/dl) /2]. 75 g OGT test was performed in all women in their 24th -28th week, with measurement of glucose before test, at 1st hour and at 2nd hour.

Ethical consideration: After discussing the study with the patients, all of them gave a complete and clear informed consent to participate in the study. This study was performed in accordance with the Declaration of Helsinki and approval for the study was obtained from the institutional ethics committee.

Statistical analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. To examine the relationships and comparisons between the two group, chi-square test was used. Independent t student test was used to compare 2 independent groups. Receiver operating curve (ROC) analysis was performed to determine a cut-off point of TYG-index in predicting of presence GDM with the best sensitivity and specificity. All the tests were considered significant at a 5% type I error rate($p<0.05$), β:20%, and power of the study:80%.

RESULTS

A total of 75 pregnant women who admitted to the department of obstetrics and gynecology from May 2022 to May 2023 were included in the study. Ages range from 18 years to 40 years (mean 28.58 ± 6.4 years) and BMI ranges from 18.6 to 33.3 kg/m2(mean 24.02±3.9 kg/m2). 53(70.7%) of the women were smokers with presence a history of PCOS in 17 cases(22.7%). In addition to, family history was detected in 24 cases(32%).

Table 1: Demographic characteristics of the study population.

Variable	Result
Age(years)	28.58±6.4
2BMI(kg/m)	24.02±3.9
Smoking	
Present	53(70.7%)
Absent	22(29.3%)
Family history of GDM	
Present	24(32%)
Absent	51(68%)
History of PCOS	
Present	17(22.7%)
Absent	58(77.3%)

GDM was developed in 13(17.3%) women, in which demographic characteristics and laboratory investigations were compared with the non-GDM group. The baseline characteristics of the participants were comparable between groups Table (2). There were significant differences between the groups in terms of age, BMI, family history of T2DM, parity, number of abortion and history of PCOs ($p<0.05$). In GDM group, a mean values of age and BMI were 33.84±5.6 years and 27.35±2.2 kg/m2 respectively with presence of family history of T2DM in 69.2%. Mean values for age and BMI were 27.48±6.1 years and 23.32±3.9 kg/m2 respectively with presence of family history of T2DM in 24.2% in non-GDM group. Presence of PCOs history was significantly higher in GDM group (46.2% versus 17.7%,p:0.001). In addition to, there were significant differences between the two group regarding of parity and mean number of abortions which were significantly higher in GDM group; (3.53±2.1 versus 1.6±1.37,p:0.0001) and (2.38±1.7 versus

1.8±1.12,p:0.02) respectively. Pregnant women with GDM presented no difference regarding presence of smoking(76.9% versus 69.4%,p:0.6).

Table 2: Demographic characteristics of the study population by comparison of the two groups.

Variable	GDM group (13 cases)	Non-GDM group (62 cases)	p-value
Age (years)	33.84±5.6	27.48±6.1	0.001
BMI(kg/m2)	27.35±2.2	23.32±3.9	0.001
Smoking Present Absent	 10(76.9%) 3(23.1%)	 43(69.4%) 19(30.6%)	0.6
Family history of GDM Present Absent	 9(69.2%) 4(30.8%)	 15(24.2%) 47(75.8%)	0.002
History of PCOS Present Absent	 6(46.2%) 7(53.8%)	 11(17.7%) 51(82.3%)	0.001
Parity	3.53±2.1(1-6)	1.6±1.37(0-5)	0.0001
Number of abortion	2.38±1.7(0-6)	1.8±1.12(0-5)	0.02

As shown in table (3), There were significant differences between two groups regarding the following laboratory investigations (GDM group versus non-GDM group); FpG(87.15±9.8 versus 77.98±8.2,p:0.001), TG(191.61±37.6 versus74.66±26.5,p:0.0001), TC(205.53±47.06 versus159.1±28.9,p:0.0001), TyG-index(4.73±0.1 versus4.18±0.1,p:0.0001) and TG/HDL(4.02±2.2 versus1.51±0.7,p:0.0001). There were no significant differences between two groups (GDM group versus non-GDM group) regarding of LDL(128.42±38.4 versus 110.46±55.6,p:0.4), HDL(54.87±18.06 versus53.54±16.2,p:0.9) and TC/HDL(4.06±2.3 versus3.17±1.1,p:0.05).

Table 3: Laboratory investigations of the study population by comparison of the two groups.

Variable	GDM group (13 cases)	Non-GDM group (62 cases)	p-value
FPG	87.15±9.8	77.98±8.2	0.001
TG	191.61±37.6	74.66±26.5	0.0001
TC	205.53±47.06	159.1±28.9	0.0001
LDL	128.42±38.4	110.46±55.6	0.4
HDL	54.87±18.06	53.54±16.2	0.9
TyG-index	4.73±0.1	4.18±0.1	0.0001
TG/HDL	4.02±2.2	1.51±0.7	0.0001
TC/HDL	4.06±2.3	3.17±1.1	0.05

Analysis of the ROC curve illustrated an 0.9 area under the curve (AUC) for TyG-index levels as a predictor of development of GDM (95% CI:0.96-1). The AUC of this biomarker indicated a high diagnostic value for GDM with the optimal threshold value being 4.7 with a sensitivity of 92.9% and specificity of 100%(figure 1).

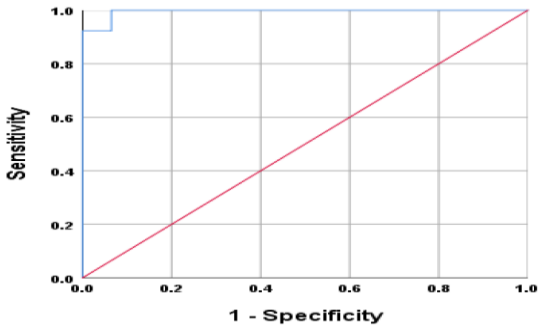

Fig. 1: Receiver operating curve of TYG-index: AUC 0.99[0.96-1]

The percentages of women in GDM groups versus non-GDM group according to FPG were as follows; 64-73(7.7% vs. 29%), 74-80(7.7% vs.50%), and 81-99(84.6% vs. 21%), p:0.0001. For TG groups, all women in GDM group were in the in the range 97-235 versus 19.4%in non-GDM group, p:0.0001. In addition to, the

percentages of women in GDM groups versus non-GDM group according to TyG index were as follows; 3.90-4.20 (0% vs. 41.9%),4.21-4.48 (0% vs.45.2%), and 4.49-4.87 (100% vs. 12.9%),p:0.0001

Table 4: Distribution of the study population according to GDM and tertiles of laboratory parameters.

Variable	GDM group (13 cases)	Non-GDM group (62 cases)	p-value
FPG 64-73 74-80 81-99	 1(7.7%) 1(7.7%) 11(84.6%)	 18(29%) 31(50%) 13(21%)	0.0001
TG 33-67 68-96 97-235	 0(0%) 0(0%) 13(100%)	 25(40.3%) 25(40.3%) 12(19.4%)	0.0001
index-TYG 3.90-4.20 4.21-4.48 4.49-4.87	 0(0%) 0(0%) 13(100%)	 26(41.9%) 28(45.2%) 8(12.9%)	0.0001

DISCUSSION

This analytical cohort study of 75 pregnant women assessed for the incidence of GDM, as well as the predictability of TYG index as a biomarker for early identification of GDM. This study showed the main findings: First, the prevalence of GDM was 17.3% in which demographic characteristics and laboratory parameters were compared according to presence of GDM. Second, women in GDM group were significantly older with elevated levels of BMI which might be explained by glucose tolerance that declines progressively with advancing age especially after the age of 35. In addition to, adiposity-induced alterations in β cell function, adipose tissue biology and insulin resistance that might be associated with chronic inflammation that results from an excessive amount of body fat with releasing of cytokines, adipokines and chemokines which altered insulin sensitivity. Third, family history of T2DM and presence of PCOs were significantly higher in GDM group. These findings might be explained by insulin resistance induced by normal pregnancy, which increased 25-70% in presence of PCOs due to excess weight gain during early stages of pregnancy. Furthermore, association between family history of diabetes and development of GDM reflects multifactorial pathogenesis of diabetes. Fourth, rates of abortions and births were significantly higher in GDM group compared to non-GDM women. Additionally, FPG, lipid profile parameters including TC and TG, TyG index and TG/HDL were significantly higher in GDM group. There are many supposed etiologies that can explain the association between levels of TYG index and development of GDM; abnormalities in β cell function and insulin resistance represent the main mechanisms of GDM, TyG index corporates both FPG and TG which are considered an important markers for insulin resistance which play key role in prediction initiation and development of GDM. The cutoff of TyG index 4.7 was the optimal value for accurate prediction of GDM development with AUC of 0.99 and this value corresponded to sensitivity:93 % and specificity:100%. Regarding GDM group, 85% of women were in the high tertile FPG and all were in the high tertile of TG and TyG index. These findings are comparable with results of previous studies.

Pazhohan et al(2017) demonstrated in a study conducted in Iran during two years period which included 954 pregnant women that prevalence of GDM was 18.4%. TyG index was significantly higher in GDM group(9.31±6.13 versus 8.34±5.04,p:0.001).[21]

Liu et al(2020) showed in a study conducted in China during one year period which included 352 pregnant women that GDM was occurred in 352 women(18.75%). Levels of TyG index was significantly higher in GDM group(8.3 versus 8,p:0.001).[22]

Garacia et al(2020) demonstrated in a study conducted in Mexico during 2 years period which included 184 pregnant women that prevalence of GDM was 17.7%. Levels of TyG index was significantly higher in GDM group(9.01±0.3 versus 8.73±0.3,p:0.001), but without an association between TyG index and the risk for development of GDM(RR:1.03,P:0.9).[23]

Kim et al(2021) showed in a study included 380.208 pregnant women that prevalence of GDM was 4.5% and The cutoff of TYG index 8.18 was the optimal value for accurate prediction of GDM development with sensitivity 47 % and specificity 68.2%.[24]

Song et al(2021) demonstrated in an analytic study conducted in China which included 382.213 pregnant women that elevated levels of TyG index was associated with the risk for development of GDM(OR:2.5,p:0.001).[25]

CONCLUSION

TyG index is considered an available, easy, and cheap method for early screening for GDM especially in presence of risk factors, which can be obtained through routine laboratory investigations.

Competing of Interests

All the authors do not have any possible conflicts of interest.

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