RESEARCH ARTICLE

The relationship of maternal age, BMI, serum Tenascin-C, and HOMA-IR values with gestational diabetes mellitus

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Abstract

Objective: To explore the relationship, if any, of gestational diabetes mellitus with maternal age, body mass index, serum tenascin-C and homeostatic model assessment for insulin resistance, and to see if these could act as predictive markers for gestational diabetes mellitus.

Method: The case-control study was conducted from February to August 2022 at the outpatient department of gynaecology and obstetrics at the Civil Hospital, Karachi, and comprised pregnant females aged 18-40 years having gestational age 20-34 weeks. After noting down baseline characteristics and anthropometric measurements, the participants were subjected to oral glucose tolerance test on the basis of which they were divided into three groups; pregnant healthy controls in group 1, those with gestational diabetes mellitus on diet control in group 2, and those with gestational diabetes mellitus taking medicines for the condition in group 3. Fasting serum samples were used for further analysis using enzyme-linked immunosorbent assay kits. Data was analysed using SPSS 21.

Results: Of the 90 subjects, 30(33.3%) were in group 1 with mean age 26.0±4.9 years, 30(33.3%) were in group 2 with mean age 30.7±5.6 years, and 30(33.3%) were in group 3 with mean age 29.1±5.5 years. Age, gestational age, body mass index and homeostatic model assessment for insulin resistance values were significantly higher in groups 2 and 3 compared to group 1 ($p<0.05$), while serum Tenascin-C values were not significantly different ($p>0.05$).

Conclusion: HOMA-IR values and BMI were more reliable in diagnosing GDM before its onset, and should be included in the screening test for GDM in early pregnancy.

Key Words: Diabetes, Gestational, Tenascin, Gynecology, Fasting, Enzyme, Immunosorbent, Diet

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Introduction

Diabetes mellitus (DM), a critical health problem, is regarded as the 9th leading cause of mortality worldwide. Persistent hyperglycaemia is a symptom of DM, which is a metabolic disorder that affects the body's ability to produce adequate insulin or to respond to the circulating insulin[1]. The International Diabetes Federation (IDF) has anticipated that by the year 2045, nearly 783.2 million people aged 20-79 years will develop DM.[2]

Gestations DM (GDM), which has a considerable impact on the rates of morbidity and mortality, is one of the most common pregnancy complications among Pakistani women. According to a study done in 2017, there are more than 374 million hyperglycaemic patients worldwide, of which 21.3 million have been diagnosed with GDM[3,4]. Another finding showed that[4] women with GDM had a higher risk of later-life cardiovascular disease (CVD) and type 2 DM (T2DM). A systemic review across 10 nations found that the prevalence of GDM was 5.1%, 24.2%, 10%, 5.1%, 15.3%, 8.6%, 14.7% and 12.2% in Yemen, Egypt, Oman, Morocco, Pakistan, Iran, Qatar and Bahrain, respectively[4]. A cross-sectional study in various primary, secondary and tertiary care hospitals in Karachi and Hyderabad showed high GDM frequency to be 11.8%[5]. Another study done in 2018 showed that the prevalence of GDM has increased from 6.3% to 19% over 5 years.[6] A cross-sectional study at a tertiary care hospital in Lahore reported GDM prevalence to be 9.47%.[7]

GDM is caused by insulin resistance (IR) and cell dysfunction, albeit the precise mechanism of cell dysfunction differs. GDM can be caused by increased maternal age, obesity and polycystic ovarian (PCO) diseases, and certain cytokines can also give rise to increased IR. [8] Among these cytokines, the one large extracellular matrix glycoprotein known as tenascin-C (TN-C), is expressed in developing tissues. It participates in a variety of pathological and developmental processes,

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aids in the regulation of cell behaviour, promotes tissue remodelling, and is noticeably unregulated at the site of tissue injury and inflammation [9].

A study in 2016 showed a correlation between elevated serum TN-C levels and the severity of proliferative diabetic retinopathy (DR). This indicates that prolonged DM is related to elevated blood TN-C levels, while it is still unclear whether DM itself causes elevated serum TN-C levels[10].

The current study was planned to explore the relationship, if any, of GDM with maternal age, body mass index (BMI), serum TN-C and homeostatic model assessment for insulin resistance (HOMA-IR), and to see if these could act as predictive GDM markers.

Subjects and Methods

The case-control study was conducted from February to August 2022 at the outpatient department (OPD) of gynaecology and obstetrics at the Civil Hospital, Karachi (CHK). After approval from the institutional ethics review board, the sample size was calculated using PASS software[11] with 95% confidence interval (CI) and 5% margin of error. The sample was raised using non-probability convenience sampling technique. Those included were pregnant females aged 18-40 years having gestational age 20-34 weeks. Those with a previous history of GDM, DM, PCOs, and other chronic illnesses were excluded.

After obtaining informed consent from the participants, data was collected using a questionnaire that covered demographic characteristics and obstetrical history. Anthropometric measurements were also noted for each participant. An oral glucose tolerance test (OGTT) was performed after 12-13 hours of fasting, following the guidelines of the International Association of Diabetes and Pregnancy Study Group (IADPSG)[12]. Fasting serum samples were collected for analysis of serum TN-C and insulin using enzyme-linked immunosorbent assay (ELISA). The patient was considered normal with a fasting blood glucose (FBG) level <92mg/dl, after 1 hour <180mg/dl, and after 2 hours <153mg/dl. Patients who had 2 or more abnormal values were identified as having GDM.[12] The subjects were divided into three groups; pregnant healthy controls in group 1, those with GDM on diet control alone in group 2, and those with GDM taking medicines for the condition in group [3]. Body mass index (BMI) was calculated and the subjects were categorised as per standard values.[13] HOMA-IR was calculated using the formula:[14] {fasting insulin (µIU/ml) ×fasting plasma glucose (mg/dl)}/405.

Data was analysed using SPSS 21. Chi-square test and one-way analysis of variance (ANOVA) were used to evaluate the data. P<0.05 was considered significant.

Results

Of the 90 subjects, 30(33.3%) were in group 1 with mean age 26.0±4.9 years, 30(33.3%) were in group 2 with mean age 30.7±5.6 years, and 30(33.3%) were in group 3 with mean age 29.1±5.5 years. There was a significantly (p=0.004) higher number of females aged >30 years (Figure 1). Age, gestational age and BMI were significantly higher in groups 2 and 3 compared to group 1 (Table 1).

Table-1: Demographic data of the participants (n=90).

Variables N=90	Group 1 (Healthy pregnant female)	Group 2 (GDM on Diet)	Group 3 (GDM on Medicine)	*P*-value
Mean Age (years ± SD)				
<30yrs				
>30yrs	26.07 ± 4.96	30.70 ± 5.64	29.13± 5.52	0.004
Occupation				
Housewives	30	27	29	0.160
Working women	0	3	1	
Gravidity				
Primigravida	3	2	3	
Multigravida	27	28	27	0.870
Gestational Age in weeks (Mean ± SD)	27.0 ± 4.3	25.4 ± 4.0	30.1 ± 5.3	0.001
BMI (Mean ± SD)				
<18.5 Underweight				
≥18.5-22.9 Normal	26.8 ± 5.5	29.9 ± 5.9	29.5 ± 6.5	0.033
≥23-24.9 Overweight				
≥25 Obese				

GDM: Gestational diabetes mellitus, BMI: Body mass index, SD: Standard deviation.

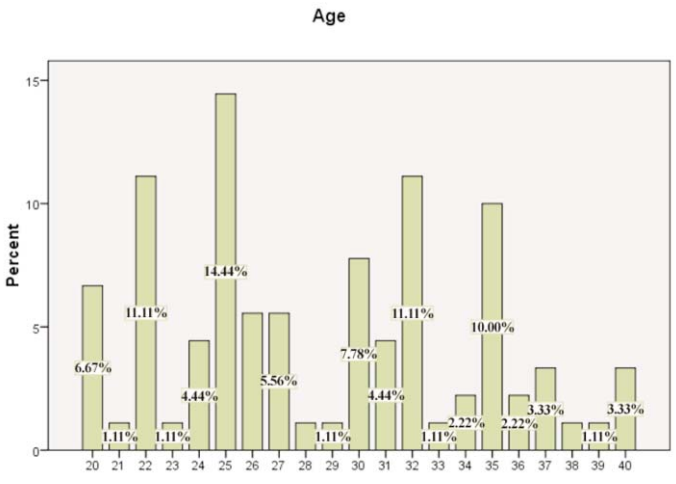

Figure: Age distribution of the study sample.

Table-2: Serum levels of TN-C, Fasting insulin, fasting blood glucose (FBG), and HOMA-IR values of the participants.

Biochemical Parameters N=90	Group 1 (Healthy pregnant female)	Group 2 (GDM on Diet)	Group 3 (GDM on Medicine)	*P*-value
Serum TN-C (ng/L) (Mean ± SD)	2383 ± 649.8	2376 ± 768.7	2305 ± 872.3	0.91
Serum Fasting insulin (µIU/ml) (Mean ± SD)	6.81 ± 1.0	15.05 ± 5.7	11.8 ± 3.0	0.0005
Fasting blood Glucose (mg/dl) (Mean ± SD)	93.7 ± 9.6	114.9 ± 31.9	110.1 ± 20.9	0.001
HOMA-IR >1.9 early IR >2.9 significant IR (Mean ± SD)	1.57 ± 0.2	4.16 ± 1.6	3.25 ± 1.2	0.0005

SD: Standard deviation, HOMA-IR: Homeostatic model assessment for insulin resistance, TN-C: Tenascin-C.

Serum fasting insulin, FBG and HOMA-IR values were higher in GDM groups compared to controls, while serum TN-C levels were not significantly different (Table 3).

Discussion

GDM is a major complication of pregnancy and it is associated with severe maternal and foetal complications. The prevalence of GDM is increasing, and needs early diagnosis for timely intervention. Various studies have shown an increased prevalence of GDM associated with increased maternal age and raised BMI[15,16]. The current study showed the majority of GDM patients were aged 29-30 years, and it had no relationship with the GDM. However, raised BMI was associated with GDM.

Many studies have tried to find a biomarker that can have involvement with the occurrence of GDM, like leptin, angiopoietins family, and many more, but none of them proved their association with GDM.[17]

In the present study, the serum levels of TN-C were not associated with GDM. In previous studies, serum TN-C levels were found to be raised in complicated pregnancies, like GDM with preeclampsia and other cardiovascular diseases and infections.[18,19] The current study excluded all GDM patients with history of hypertension and other metabolic disorders. Probably this explains why the current study did not find any association between the two factors.

The current study emphasised the importance of HOMA-IR value as it was strongly correlated with GDM, especially those who were controlling their glucose levels with diet restrictions. A few recent studies have reported similar findings.[19,20]

Conclusion

HOMA-IR values and BMI were more reliable in diagnosing GDM before its onset, and should be included in the screening test for GDM in early pregnancy.

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