RESEARCH ARTICLE

Association of ABO blood group with gestational diabetes mellitus in Pakistan: A case control study

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Abstract

Objective: To investigate the association between blood group and development of gestational diabetes mellitus among pregnant women.

Method: The retrospective, case-control study was conducted from August 2021 to May 2022 at The Aga Khan Hospital for Women, Garden Karachi, and comprised data from January to December 2020 related to women who had given live birth. All the women had been screened for gestational diabetes mellitus. Data included blood type and rhesus factor phenotype. The risk of gestational diabetes mellitus was assessed. Data was analysed using SPSS 19.

Results: Of the 1,899 pregnant women, 303(16%) had gestational diabetes mellitus and 1,596(84%) were free of it. Blood type had no significant association (p=0.406) with gestational diabetes mellitus, while rhesus positivity tended to be significantly higher in the gestational diabetes mellitus group (p=0.051). Parity was the only parameter for which significant difference was found among the blood groups (p<0.05).

Conclusion: There was a higher incidence of gestational diabetes mellitus in women with rhesus positivity.

Keywords: Blood group, Gestational diabetes mellitus, GDM, Type 2 diabetes mellitus, Risk factors, ABO system.

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Introduction

Pregnancy is a state marked by insulin resistance (IR) principally facilitated by hormones, including the human placental lactogen (hPL), growth hormone, corticotrophin-releasing hormones, prolactin and progesterone. Gestational diabetes mellitus (GDM) occurs during pregnancy in women whose pancreatic function fails to overcome IR, and it often leads to maternal complications and even foetal outcomes.[1] Similar to type 2 diabetes mellitus (T2DM), GDM is a multifactorial condition influenced by a combination of environmental and genetic factors, many of which remain unidentified. It is estimated that 2-5% of pregnancies globally are affected by GDM, and its prevalence has risen significantly over the past decade. Although the exact cause of the disease is not fully understood, GDM is thought to result from complex interactions among genetic, epigenetic and environmental factors.[2]

Blood group antigens are considered to be among the hereditary determinants, and play a pivotal role in understanding genetics and disease susceptibility.[3] Along with their expression on red blood cells (RBCs), ABO antigens are also expressed on the surface of many human cells and tissues, including epithelium, sensory neurons, platelets and vascular endothelium. ABO blood types have some association with various infectious[4] and non-infectious diseases.[5]

Moreover, the possible association between ABO blood group and T2DM has also been studied, and a higher frequency of blood group B in T2DM patients was found compared to the control population.[6] Although pathophysiological mechanism for the association between ABO blood group phenotypes with T2DM and associated factors are not well-researched, there is a possible assumption that the ABO blood groups are linked to specific molecules related to T2DM. Increased level of plasma lipid and inflammatory markers, such as intercellular adhesion molecule-1 (ICAM-1), E-selectin, P-selectin and tumour necrosis factor-2 (TNF-2), have an association with the ABO system of blood groups. The variant at ABO gene loci has an association with the rise in these inflammatory markers. These molecules affect insulin and its receptor, and contribute to the development of diabetes.[7]

A recent study in Iran reported an increased incidence of GDM in AB group patients,[8] whereas low incidence of GDM was found in AB blood group patients in Saudi Arabia.[9] A study in France showed that rhesus (Rh) positivity in group AB women have a greater risk of GDM.[10]

The current study was planned to investigate the association between blood group and GDM development among Pakistani pregnant women.

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Subjects and Methods

The retrospective, case-control study was conducted from August 2021 to May 2022 at the Aga Khan Hospital for Women, Garden Karachi, which is one of secondary care hospitals associated with the Aga Khan University Hospital (AKUH), Karachi, and comprised data from January to December 2020 related to women who had given live birth. After approval from the AKUH ethics review committee, the sample size was calculated using OpenEpi calculator 3.01 in line with a previous study[8] with level of significance 0.05, power 80%, and controls-to-cases ratio 3. The sample size was inflated by >60% to improve the validity of the findings. Data was retrieved from the institutional electronic health records. Data of women who had a live birth with chromosomal or congenital abnormality was excluded.

Data was collected using a predesigned proforma covering maternal age, parity, body weight at first visit, body mass index (BMI) at first visit, singleton pregnancy, past or present history of hypertension (HTN), family history of diabetes, ABO blood group, and Rh blood type.

Standard blood group serology analysis had been employed to determine the ABO system of the patients, and hospital protocols were followed for GDM screening. Fasting blood glucose (FBG) levels were tested and GDM in the first trimester was identified at the cut-off value of 92mg/dL. A 75g oral glucose tolerance test (OGTT) after an overnight fast was performed in the second trimester to reach a definite diagnosis of GDM. If the patients were on oral anti-hypertensive medications before the pregnancy or had blood pressure (BP) >140/90mmHg on more than two occasions before 20 weeks of gestation, they were labelled as chronic hypertensive. Patients with one or more first-degree relatives with diabetes were considered to have family history of diabetes.

Data was analysed using SPSS 19. Normality of continuous data was checked using Kolmogorov-Smirnov test, and it was visualised by histogram and Q-Q plot. Normal data was reported as means±standard deviation. Independent sample t test was used for further analysis of normal data, and analysis of variance (ANOVA) was performed. Mann-Whitney U test was applied to analyse data that was not normally distributed, and this data was reported as median with interquartile range (IQR). Quantitative data was reported as frequencies and percentages, and it was analysed using chi-square test or Fisher exact test. P<0.05 was considered statistically significant. Besides, variables with p<0.20 in univariate analysis were considered for adjustment in the multivariable model using logistic regression. Multiple logistic regression was performed to estimate the association between ABO system of blood group and GDM after controlling the effect of age, BMI, parity, singleton baby, HTN and family history of diabetes.

Results

Of the 1,899 pregnant women, 303(15.95%) had GDM, while 1,596(84.04%) were free of it. Mean age, body weight, BMI, party, family history of diabetes, fasting blood sugar (FBS) level, HTN and Rh blood type were significantly between GDM and non-GDM groups (Table 1).

Among the GDM patients, 57(18.8%) had blood group A, 115(37.9%) had group B, 109(35.9%) had group O and

Table-1: Comparison of demographic and clinical characteristics between GDM and non-GDM groups.

Variables	GDM (n=303)	Non-GDM (n=1596)	*p*-value
Mean Age (years)	29.37±5.26	26.62±4.96	0.0005†
Age Groups (years) (%)			0.0005‡
<30	184(60.7)	1266(79.3)	
31-34	63(20.8)	219(13.7)	
>34	56(18.5)	111(7)	
Mean Body height (cm)	156.95±6.85	156.84±6.68	0.780†
Mean Body weight (kg)	70.70±12.91	63.20±12.77	0.0005†
Mean BMI (kg/m^2)	28.74±5.23	25.72±5.57	0.0005†
Fasting blood glucose level (mg/dl)	(n=228)	(n=980)	
Median [75-95 percentile]	89[82-96]	79[75-83]	0.0005¥
Parity (%)			0.022‡
0-1	193(63.7)	1122(70.3)	
2-6	110(36.3)	474(29.7)	
Pregnancy (%)			0.397‡
Single	298(98.3)	1578(98.9)	
Twin	5(1.7)	18(1.1)	
Hypertension (%)	27(8.9)	97(6.1)	0.067‡
Family history of diabetes (%)	107(35.3)	465(29.1)	0.032‡
Rh blood type (%)			
Positive	295(97.4)	1512(94.7)	0.051‡
Negative	8(2.6)	84(5.3)	

GDM: Gestational diabetes mellitus; BMI: Body mass index; †Independent sample t test; ‡Chi-square or fisher exact test; ¥Mann Whitney U test.

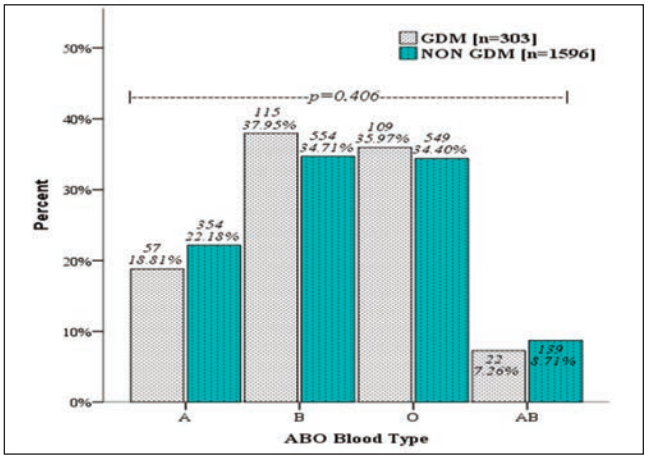

Figure: Association of blood type and gestational diabetic mellitus (n=1899).

Table-2: Comparison of demographic and clinical characteristics across blood groups.

Variables	Blood Type				*p*-value
	A (n=411)	B (n=669)	O (n=658)	AB (n=161)	
Age Groups (years) (%)					0.086‡
<30	309(75.2)	520(77.7)	502(76.3)	119(73.9)	
31-40	75(18.2)	93(13.9)	86(13.1)	28(17.4)	
>34	27(6.6)	56(13.9)	70(10.6)	14(8.7)	
Mean BMI (kg/m^2)	26.45±6.57	26.01±5.31	26.30±5.43	26.17±5.02	0.544†
Parity (%)					0.047‡
0-1	287(69.8)	462(69.1)	440(66.9)	126(78.3)	
2-6	124(30.2)	207(30.9)	218(33.1)	35(21.7)	
Pregnancy (%)					0.606‡
Single	407(99)	663(99.1)	648(98.5)	158(98.1)	
Twin	4(1)	6(0.9)	10(1.5)	3(1.9)	
Hypertension (%)	32(7.8)	34(5.1)	48(7.3)	10(6.2)	0.260‡
Familial history of diabetes (%)	117(28.5)	207(30.9)	213(32.4)	35(21.7)	0.053‡

BMI: Body mass index;†One-way analysis of variance (ANOVA); ‡Chi-square test.

Table-3: Logistic regression models showing the association between ABO blood type and GDM.

Models	Odds Ratio	95%CI	*p*-value
Model 1: Crude			
A	1.02	0.59-1.73	0.949
B	1.31	0.80-2.14	0.280
O	1.25	0.76-2.05	0.369
AB	Ref		
Model 2: Adjusted by age and BMI			
A	0.99	0.57-1.70	0.966
B	1.37	0.82-2.26	0.227
O	1.25	0.75-2.07	0.394
AB	Ref		
Model 3: Adjusted by age, BMI, Parity, Singleton baby, HTN			
A	1.03	0.59-1.78	0.919
B	1.44	0.86-2.38	0.163
O	1.31	0.78-2.19	0.296
AB	Ref		
Model 4: Adjusted by Age, BMI, Parity, Singleton baby, HTN and FHD			
A	1.01	0.58-1.75	0.968
B	1.40	0.84-2.33	0.192
O	1.27	0.76-2.13	0.354
AB	Ref		

CIL Confidence interval; BMI: Body mass index; HTN: Hypertension, FHD: Family History of Diabetes

22(7.3%) had blood group AB. The corresponding numbers in the non-GDM group were 354(22.2%), 554(34.7%), 549(34.4%) and 139(8.7%) (*p*=0.406) (Figure). Parity was the only parameter for which significant difference was found among the blood groups (Table 2).

Multivariate analysis showed no significant association of GDM with maternal age, parity, BMI, singleton pregnancy, HTN and family history of diabetes (Table 3).

Discussion

Earlier research has found a connection between genetically determined ABO blood groups and an elevated risk of various infectious and non-infectious diseases. In addition, ABO blood groups have been associated with increased susceptibility to conditions, such as cancer, cardiovascular diseases, infections, metabolic disorders and malaria.[11] Although, an association between T2DM and ABO system of blood groups has been evident, further research is required to determine an association between ABO blood group and GDM.

In the current study, the prevalence of GDM was 15.95%, which is comparable to 16.3% reported earlier.[12] In contrast, a European study reported a prevalence of 5.4%.[13] The observed variation may stem for several factors, such as differences in screening practices, study settings, risk factors associated with GDM, variations in dietary management plans, discrepancies in medication use, inconsistencies in antenatal care (ANC) follow-up, and differences in clinical, dietary and environmental factors. The higher incidence of GDM found in the current study emphasises the need to address this common condition for better maternal and prenatal health.

Other factors, such as maternal age, raised BMI and family history, can predict GDM development. Increasing maternal age is a known risk factor for GDM.[14,15] GDM was diagnosed in pregnant women aged ≤30 in the current study. Based on this finding, healthcare providers can incorporate maternal age as a screening factor to identify women at GDM risk. Women in preconception clinics can be advised about the risk factors for GDM and its implications based on maternal age, allowing them to make informed choice with respect to childbearing.

Moreover, fetomaternal complications are increased in GDM patients.[16] Hyperinsulinaemia, large for gestational age, hypoglycaemia, hyperbilirubinaemia and respiratory distress syndrome are common neonatal complications. Development of diabetes and obesity in later life is also reported in children born to women with GDM.[17] This further emphasises the importance of improved screening for GDM risk factors, thus ensuring preventive strategies to avoid fetomaternal complications.

In the current study, majority of the patients had blood group B, followed by O, A, and AB groups. This is in line with another study.[11]

In the current study, pregnant women with blood group B had higher GDM frequency compared to the other blood groups. An earlier study in Iran found raised blood glucose values in fasting pregnant women (13-26 weeks of gestation) in the AB blood group.[18] Another study showed

that the AB blood group had a lower GDM risk.[19]

A significant association was found in the current study between Rh positivity and GDM. Glucose metabolism can have an association with the Rh blood system, and can influence the clinical manifestation. The contribution of specific genes on the control of blood glucose metabolism and sensitivity to T2DM needs further research.

The current study has limitations as it comprised patients from a single centre. Large multicentre studies are required to validate the current findings.

Conclusion

Pregnant women having blood group with Rh positivity had an increased GDM frequency, while low frequency of GDM was observed in those with the AB blood group. Pregnant women with high-risk blood groups can be screened at the time of booking, and counselled for healthy lifestyle measures.

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Author Contribution:

ES: Concept, design, drafting, revision, final approval and agreement to be accountable for all aspects of the work.
SN: Data acquisition, analysis and interpretation.
SI: Drafting, revision and final approval.
AR: Data analysis and interpretation.