Association of ABO ,Rh Blood Groups with the Susceptibility of Gestational Diabetes in the Yazd-Iran Population

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Abstract

Objective: Today, the association of blood groups as genetic traits has been confirmed in many diseases. However, its association with gestational diabetes mellitus (GDM) has not been investigated. Therefore, in this study, we investigated the relationship between blood groups and GDM.

Materials and Methods: In this analytical cross-sectional study, pregnant women referred to Baqaeipur Clinic and Yazd Diabetes Research Center in 2015-2018Based on the information related to the results of the one-hour OGTT test and the two-hour glucose levels recorded in the file were divided into two groups (GDM, non GDM). Then other information about the participants in the study, including demographic information, medical history, ABO and Rh blood groups, abortion, delivery, and number of pregnancies were extracted from the file and analyzed using SPSS version 23 software.

Results: Out of 1708 pregnant women, 244 (14.3%) had GDM, and 1464 (85.7%) did not. There was a statistically significant difference between these two groups in terms of age ($P< 0.001$), weight ($P< 0.001$), number of pregnancies ($P< 0.001$), delivery ($P< 0.001$), previous diseases ($P< 0.001$), and Rh ($P= 0.01$). While in terms of the ABO blood group system ($P= 0.3$) and abortion rate ($P= 0.067$), no statistically significant difference was observed.

Conclusion: Finally, we concluded that the frequency of the B+ blood group is higher in the GDM group, however, there is no statistically significant relationship between ABO blood groups and GDM.

Keywords: Blood groups, Gestational diabetes mellitus, Metabolic disease

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Introduction

Gestational diabetes mellitus (GDM) is the most common metabolic disorder during pregnancy, which occurs mainly due to the exacerbation of physiological changes in glucose metabolism. (1,2). Known risk factors for GDM include a family history of diabetes, obesity, maternal age, glycosuria, also adverse outcomes in previous pregnancies such as stillbirth, macrosomia, and other risk factors that are not yet known. The prevalence of GDM in the world is increasing significantly and its prevalence has been reported from 1 to 14% depending on the screening test. (3,4) According to a study, the prevalence of GDM in Iran is reported to be 3.41% (5) while in Yazd province in a study in 2012 was reported to be 12% (6).

Possible maternal side effects include Preterm delivery, hydramnios and hypertension, type 2 diabetes, and neonatal complications including fetal death, congenital anomalies, polycythemia, hyperbilirubinemia, cardiomyopathy, dystrophic syndrome and unexplained neonatal death, abnormalities Metabolic, effect on fetal growth, such as macrosomia, is intrauterine growth retardation (7,8). Meanwhile, type 2 diabetes is one of the most common possible complications, just as type 2 diabetes is more common in communities with a higher prevalence of GDM. About 40% of maternal with GDM develop overt diabetes within 30 years. The probability of recurrence of GDM in the next pregnancy is 30 to 69%. The lifetime risk of type 1 diabetes in these infants is estimated at 6% (9-11).

GDM, like type 2 diabetes, is a multifactorial disease influenced by various environmental and genetic factors, many of which are still unknown (9-11). Blood type exists as a genetic trait that has been suggested in many studies to be related to type 2 diabetes and other diseases (12-15) and considering the many complications caused by this disorder and its high prevalence, identifying risk factors for its control and effectiveness is essential. According to the explanations given about blood groups, one of the possible risk factors that are less discussed in this field is ABO and Rh blood groups.

Material and methods

The present study was an analytical -cross sectional study that investigated the relationship between mother's blood group in terms of ABO and RH with GDM. In this study, pregnant women referred to Bagaipur Clinic and Yazd Diabetes Research Center during 2015-2018were examined. The sampling method in this study is census. The information required from the records of pregnant women includes age, weight, previous medical history, ABO and Rh blood groups, one and two hour blood sugar, fasting blood sugar before and during pregnancy, and history of abortion and delivery. Exclusion criteria included eclampsia and pre-eclampsia pregnancy, type 1 diabetes, twins and multiples, taking medications that affect the patient's blood sugar, smoking during pregnancy or 6 months before pregnancy, some chronic diseases including cardiac, vascular, hepatic, renal. The results of one-hour and two-hour OGTT and blood sugar test of pregnant women were also analyzed to diagnose GDM. People with fasting blood sugar$\geq$ 92, blood sugar at one time$\geq$ 180, or blood sugar at two hours$\geq$ 153 were registered in the GDM group and the rest in the non-GDM group. Data were entered into Excel and SPSS V23 so descriptive data analysis was performed using appropriate tests to evaluate frequency, mean and standard deviation. Other data were analyzed using independent T-test and Chi square.

Ethical considerations

The study was based on the checklists completed by the researcher, no additional costs were incurred for the patients in this study. Also, the patient's file information

remained confidential and was used only for research purposes. This study was approved by the ethics committee of Yazd University of Medical Sciences (code: IR.SSU.MEDICINE. REC.1396.228).

Results

In this study, out of 1708 pregnant women, 244 (14.3%) had GDM, and 1464 (85.7%) were non-GDM. The mean (±SD) age of the studied population was 29.15 years (±6.2). The most abundant blood type ABO in the studied population is related to blood type o+. Other demographic information about the study population is shown in Table 1.

In this study, the mean age in the non-GDM group was 31.1 (±6.3), and in the GDM group 28.7 (±6.15) which was statistically significant (*P*< 0.001). The mean weight of the GDM group was 75.5 (±11.8) and non-GDM 68.3 (±12.9) which was statistically significant (*P*< 0.001). Also, the number of pregnancies in the GDM group was 2.7 (±1.5) and 2.36 (±1.38) in the non-GDM group, which was statistically significant (*P*< 0.001). The results also showed that the number of deliveries in the GDM was 1.25 (±0.99) and in the non-GDM group 0.93 (±0.89), which was statistically significant (*P*< 0.001). The results showed that

the number of abortions in the GDM group was 0.55 (±0.9) and non-GDM group 0.43 (±0.8), witch not statistically significant compared to the non-GDM group (*P*= 0.067). (Table 2)

Also, in this study, previous disease records such as thyroid, blood pressure, infertility, and Type 2 diabetes were evaluated using the Chi square. The results showed that there is a significant statistical relationship between the GDM and non-GDM groups in terms of the history of the mentioned diseases (*P*< 0.001). In addition, in terms of blood groups ABO and RH, were also examined using the chi-score test. The results of this study showed that in the GDM group, blood group B+ was the most common, and blood group AB- was the least frequent. Although there was no significant relationship between ABO blood groups and GDM (*P*= 0.33). While there was a statistically significant relationship between the Rh blood group and GDM using the Chi-square test (*P*= 0.01) so that Rh + blood group showed a higher frequency (Table 3).

Discussion

GDM is a type of metabolic disorder during pregnancy. Due to the increasing prevalence of this disorder (16,17) and also despite

Table 1. Description of the information of the pregnant women participating in the study

Group		Mean (±SD)/ Frequency (%)
Age		29.15 (± 6.2)
Weight		69.3 (±13)
GDM	No	1464 (85.7)
	Yes	244 (14.3)
ABO blood group	A	511 (29.9)
	B	519 (30.4)
	AB	87 (5.1)
	O	591 (34.6)
Rh blood group	Rh+	168 (9.8)
	Rh-	1540 (90.2)

The values are reported as mean (±SD) or content (percentage)

Table 2. Comparison of age, weight, number of pregnancies, deliveries, and abortions between two groups of pregnant women with GDM and non-GDM

Group	GDM	Non-GDM	*P*
Age	28.7 (±6.15)	31.3 (±6.3)	<0.001
Weight	75.5 (±11.8)	68.3 (±12.9)	<0.001
Pregnancy number	2.7 (±1.5)	2.36 (±1.38)	<0.001
deliveries	1.25 (±0.99)	0.93 (±0.89)	<0.001
Abortion	0.55 (±0.9)	0.43 (±0.8)	0.067

The results were obtained using the independent T-test. Values are reported as mean (±SD)

Table 3. Comparison of a frequency distribution of variables between two groups of pregnant women with GDM and non-GDM

Group		GDM	Non-GDM	*P*
Previous Diseases	Hypothyroidism	42 (17.2%)	202 (82.8%)	0.001
	High blood pressure	3 (8.3%)	33 (91.7)	
	Infertility	0 (0%)	17 (100%)	
	Type 2 diabetes	48 (48.9%)	50 (50.1%)	
Blood group	A	66 (12.9%)	445 (87.1%)	0.3
	B	83 (16%)	436 (84%)	
	AB	16 (18.4%)	71 (81.16%)	
	O	79 (13.4%)	512 (86.6%)	
Blood group	Rh+	205 (13.3%)	1334 (86.7%)	0.01
	Rh-	39 (16%)	130 (84%)	

The results were obtained using the independent Chi square test. Values are reported as contetnt (±percent)

numerous studies that indicate the important role of blood groups in susceptibility to other diseases such as infection, cancer, cardiovascular disease, and disorders of the nervous system (18-21). Only limited studies have been conducted on the association of GDM with the blood group, showing conflicting results (22). Accordingly, in this study, we examined the relationship between ABO and RH blood groups with GDM in pregnant women referred to Baghaeipour Clinic and Yazd Diabetes research Center.

One of the valuable results of this study is the prevalence of GDM, which is equal to 14.3%. As in a meta-analysis study conducted for the 9th edition of the Diabetes Atlas of the International Diabetes Federation (IDF) by Wang et al., in 2021, the global standard prevalence of GDM was 14.0%, in addition, the prevalence of this disease was separately for each world region, the highest prevalence, was examined. Which is 27.6% related to the Middle East and North African countries. In this study, one of the possible reasons for this large difference in prevalence is the difference in screening strategies and diagnostic criteria used to identify GDM cases in different regions and countries (23).

The results of this study showed a higher prevalence of GDM in women with B+ 83 (34.01%) blood group, although it was not statistically significant, as in the study of Phalopark et al. In 2012, the blood group was not significantly associated with GDM (24). But in the study of Anderson et al., this frequency was more significant in blood type

O in GDM (25). Also in the study of Tedeschi et al., the results showed that diabetes is more common in people with blood type B (26). However, McConnell's study found that blood type A was significantly associated with diabetes compared to blood type B (26). Although that the distribution of ABO groups varies significantly among races, ethnicities, and socioeconomic groups. One of the reasons for the conflicting results of the relationship between the ABO blood group and the risk of GDM in different studies can be considered. The association between ABO blood groups and the risk of diabetes may be due to a combination of several factors, including genetic diversity, inflammatory markers, intestinal microbiota composition, and other unknown factors (27-29). Their biological mechanisms may not be well known. One possible mechanism is the presence of polymorphisms at the site of the ABO-encoding gene, which strongly suggests an association with inflammatory cytokines such as E-selectin, P-selectin, TNF-a, soluble-cell adhesion molecule-1 and interleukin Increase insulin resistance (30,31).

Another result of this study is a significant association between Rh blood type and GDM. Given that Rh-negative phenotypes are very different in different parts of the world, for example, about 15% of Caucasians are Rh-negative, while only 0.5% of the Japanese population is Rh-negative. Accordingly, this type of blood group classification has been considered in fewer studies, and even in limited studies, the relationship between this

phenotype and other groups of diabetes has been investigated. One of these studies is the study of Meo et al. And Rh blood group was evaluated and this relationship was not statistically significant (12). Also, in the study of Fagrazi et al., it was stated that people with blood groups A+, A-, B+, and AB+ are at risk of more likely type 2 diabetes (32). While in the present study, blood groups B + and O + were higher in the group with GDM, the association was not significant.

In this study, by examining the records of diseases such as thyroid, hypertension, infertility, and type 2 diabetes, it was shown that they have a significant relationship with GDM. In this regard, it has been shown in several studies that gestational diabetes and type 2 diabetes share some characteristics, including risk factors, pathophysiological mechanisms, and genetic susceptibility (33,34). In societies with a higher prevalence of GDM, type 2 diabetes is also They are more common, and in fact, the course of GDM follows that of type 2 diabetes, but the risk and time of onset of this disease are variable (35,36).as in the study by Wang et al. in 2021 to investigate the relationship between thyroid dysfunction during pregnancy and the risk of developing GDM and preeclampsia, the results show a significant relationship between some thyroid disorders and GDM On the other hand, regarding the relationship of infertility, according to the studies conducted so far, no study has investigated it, and only one study in 2021 has introduced GDM as one of the complications of infertility treatment by the ivf/icsi method (37). Also, in a meta-analysis study by Wang et al. in 2022, it has been shown that the history of abortion was associated with an increased risk of GDM in pregnant women, so that it may be a risk factor for predicting GDM (38). In the present study, the history of abortion is more in the group of mothers with GDM. Although this relationship was not statistically significant. In addition, in this study, the variables of the number of pregnancies and deliveries in the group of mothers with GDM were significantly higher,

although the clear mechanism of this relationship has not been determined yet, and more studies are needed in this field.

In a 2022 study by Birukov et al., it has been shown that a history of high blood pressure before or during early pregnancy was associated with an increased risk of gestational diabetes (GDM). The World Health Organization has also confirmed this connection. In addition, this relationship seems to be stronger in overweight pregnant women (39). As in the present study, the results show that weight is significantly higher in GDM women, as in the results of several studies consistent with this finding (40,41). But the results of this study show that the age of the mother is significantly lower in the group of mothers with GDM. One possible reason for this inconsistency with most studies is that maternal age should be combined with other maternal characteristics and obstetric history when calculating individual adjusted risk for adverse pregnancy outcomes (42). Also, considering that in this research, the census method was used to check the samples. In the studied statistical population, the history of diabetes, BMI, gestational age, etc. have not been compared between the two groups, which can explain this contradiction.

Conclusions

Generally investigating the mechanisms involved in this disease, in turn, can be helpful in the field of prevention and treatment. In addition, the suggestion of other future studies could be to examine the relationship between other blood grouping categories and GDM. It can also be interesting to examine the relationship between blood types and other problems after pregnancy.

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Conflict of Interest

The authors express that there are no competing interests

References

1. ADA American Diabetes Association. Gestational diabetes mellitus. Diabetes care. 2004;27(suppl 1):S88-90.

2. McGovern A, Butler L, Jones S, van Vlymen J, Sadek K, Munro N, et al. Diabetes screening after gestational diabetes in England: a quantitative retrospective cohort study. British Journal of General Practice. 2014;64(618):e17-23.

3. American Diabetes Association. 11. Microvascular complications and foot care: standards of medical care in diabetes—2019. Diabetes Care. 2019;42(Supplement_1):S124-38.

4. Siegel KR, Bullard KM, Imperatore G, Ali MK, Albright A, Mercado CI, et al. Prevalence of major behavioral risk factors for type 2 diabetes. Diabetes Care. 2018;41(5):1032-9.

5. Jafari-Shobeiri M, Ghojazadeh M, Azami-Aghdash S, Naghavi-Behzad M, Reza PI, Pourali-Akbar Y, et al. Prevalence and risk factors of gestational diabetes in Iran: a systematic review and meta-analysis. Iranian journal of public health. 2015;44(8):1036-44.

6. Sayehmiri F, Bakhtiyari S, Darvishi P, Sayehmiri K. Prevalence of gestational diabetes mellitus in Iran: a systematic review and meta-analysis study. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2013 Feb 19;15(40):16-23.(in Persian)

7. Doupis J. Gestational diabetes from A to Z. World Journal of Diabetes. 2017;8(12):489-511.

8. Johns EC, Denison FC, Norman JE, Reynolds RM. Gestational diabetes mellitus: mechanisms, treatment, and complications. Trends in Endocrinology & Metabolism. 2018;29(11):743-54.

9. Yan J, Yang H. Gestational diabetes mellitus, programing and epigenetics. The Journal of Maternal-Fetal & Neonatal Medicine. 2014;27(12):1266-9.

10. Kawai VK, Levinson RT, Adefurin A, Kurnik D, Collier SP, Conway D, et al. A genetic risk score that includes common type 2 diabetes risk variants is associated with gestational diabetes. Clinical endocrinology. 2017;87(2):149-55.

11. Rosik J, Szostak B, Machaj F, Pawlik A. The role of genetics and epigenetics in the pathogenesis of gestational diabetes mellitus. Annals of human genetics. 2020;84(2):114-24.

12. Meo SA, Rouq FA, Suraya F, Zaidi SZ. Association of ABO and Rh blood groups with type 2 diabetes mellitus. European Review for Medical & Pharmacological Sciences. 2016;20(2):237-42.

13. Cooling L. Blood groups in infection and host susceptibility. Clinical microbiology reviews. 2015;28(3):801-70.

14. Wu O, Bayoumi N, Vickers MA, Clark PA. ABO (H) blood groups and vascular disease: a systematic review and meta-analysis. Journal of thrombosis and haemostasis. 2008;6(1):62-9.

15. Mandato VD, Torricelli F, Mastrofilippo V, Ciarlini G, Pirillo D, Farnetti E, et al. Prognostic impact of ABO blood group on type I endometrial cancer patients-results from our own and other studies. Journal of Cancer. 2017;8(14):2828-35.

16. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes research and clinical practice. 2018;138:271-81.

17. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes research and clinical practice. 2017;128:40-50.

18. Capuzzo E, Bonfanti C, Frattini F, Montorsi P, Turdo R, Previdi MG, et al. The relationship between ABO blood group and cardiovascular disease: results from the Cardiorisk program. Annals of translational medicine. 2016;4(10):189.

19. Teshome Y, Mekonen W, Birhanu Y, Sisay T. The association between ABO blood group distribution and peptic ulcer disease: a cross-sectional study from Ethiopia. Journal of blood medicine. 2019:193-7.

20. Chen Z, Yang SH, Xu H, Li JJ. ABO blood group system and the coronary artery disease: an updated systematic review and meta-analysis. Scientific reports. 2016;6(1):23250.

21. Yu H, Xu N, Li ZK, Xia H, Ren HT, Li N, et al. Association of ABO blood groups and risk of gastric cancer. Scandinavian Journal of Surgery. 2020;109(4):309-13.

22. Franchini M, Mengoli C, Lippi G. Relationship between ABO blood group and pregnancy complications: a systematic literature analysis. Blood Transfusion. 2016;14(5):441-8.

23. Wang H, Li N, Chivese T, Werfalli M, Sun H, Yuen L, et al. IDF diabetes atlas: estimation of global and regional gestational diabetes mellitus prevalence for 2021 by International Association of Diabetes in Pregnancy Study Group's Criteria. Diabetes research and clinical practice. 2022;183:109050.

24. Phaloprakarn C, Tangjitgamol S. Maternal ABO blood group and adverse pregnancy outcomes. Journal of Perinatology. 2013;33(2):107-11.

25. Andersen J, Lauritzen E. Blood groups and diabetes mellitus. Diabetes. 1960;9(1):20-4.

26. Tedeschi G, Cavazzuti F. Casuistic contribution on the study of the relations between diabetes mellitus & the ABO & Rh blood groups. Il Progresso medico. 1959;15(3):76-82.

27. Alanazi MA, Alkhidhr MA, Alhadhari AM, Al-Hathloul AW, Alsharif EJ, Albahli SF, et al. Association of diabetes mellitus with ABO blood groups & Rh with. The Egyptian Journal of Hospital Medicine. 2018;73(4):6535-40.

28. Öner C, Doğ an B, Telatar B, Çelik Yağ an CF, Oğ uz A. Frequency of ABO/Rhesus blood groups in patients with diabetes mellitus. Journal of the College of Physicians and Surgeons--Pakistan. 2016;26(1):74-5.

29. Al-Ganimi AKA. Evaluation of the Relationship between ABO Blood Groups, Rh Factor and Diabetes Mellitus Type 2. International Journal of Medical Research & Health Sciences. 2018;7(11):110-4.

30. Qi L, Cornelis MC, Kraft P, Jensen M, van Dam RM, Sun Q, et al. Genetic variants in ABO blood group region, plasma soluble E-selectin levels and risk of type 2 diabetes. Human molecular genetics. 2010;19(9):1856-62.

31. Hu FB, Meigs JB, Li TY, Rifai N, Manson JE. Inflammatory markers and risk of developing type 2 diabetes in women. Diabetes. 2004;53(3):693-700.

32. Fagherazzi G, Gusto G, Clavel-Chapelon F, Balkau B, Bonnet F. ABO and Rhesus blood groups and risk of type 2 diabetes: evidence from the large E3N cohort study. Diabetologia. 2015;58:519-22.

33. Sapanont K, Sunsaneevithayakul P, Boriboonhirunsarn D. Relationship between ABO blood group and gestational diabetes mellitus. The Journal of Maternal-Fetal & Neonatal Medicine. 2021;34(8):1255-9.

34. Mohammadzade F, Maryam F, Alireza S, Mohammadali V. Relationship Between ABO Blood Group and the Incidence of Gestational Diabetes in Pregnant Women in Gorgan, North of Iran.West Indian Medical Journal.2016:1-11.

35. Song C, Lyu Y, Li C, Liu P, Li J, Ma RC, et al. Long-term risk of diabetes in women at varying durations after gestational diabetes: a systematic review and meta-analysis with more than 2 million women. Obesity reviews. 2018;19(3):421-9.

36. Okba A, Hosny SS, Elsherbeny A, Kamal MM. Study of Possible Relation between Fasting Plasma Glucagon, Gestational Diabetes and Development of Type 2 DM. Current Diabetes Reviews. 2020;16(2):148-55.

37. Hu L, Xie R, Wang M, Sun Y. Patients with IVF complicated by moderate-to-critical OHSS experience increased thrombosis, GDM and neonatal NICU admission but slightly shorter gestation compared with matched IVF counterparts: A retrospective Chinese cohort study. Reproductive Biology and Endocrinology. 2021;19:1-8.

38. Wang H, Guo X, Song Q, Su W, Meng M, Sun C, et al. Association between the history of abortion and gestational diabetes mellitus: A meta-analysis. Endocrine. 2023;80(1):29-39.

39. Birukov A, Glintborg D, Schulze MB, Jensen TK, Kuxhaus O, Andersen LB, et al. Elevated blood pressure in pregnant women with gestational diabetes according to the WHO criteria: importance of overweight. Journal of Hypertension. 2022;40(8):1614-23.

40. Dalrymple KV, El-Heis S, Godfrey KM. Maternal weight and gestational diabetes impacts on child health. Current opinion in clinical nutrition and metabolic care. 2022;25(3):203.

41. Basu A, Feng D, Planinic P, Ebersole JL, Lyons TJ, Alexander JM. Dietary blueberry and soluble fiber supplementation reduces risk of gestational diabetes in women with obesity in a randomized controlled trial. The Journal of Nutrition. 2021;151(5):1128-38.

42. Khalil A, Syngelaki A, Maiz N, Zinevich Y, Nicolaides KH. Maternal age and adverse pregnancy outcome: a cohort study. Ultrasound in Obstetrics & Gynecology. 2013;42(6):634-43.