

Association between intrauterine fetal growth restriction and ABO blood groups at King Abdulaziz University Hospital, Saudi Arabia

Retrospective study

Nedaa M. Bahkali, MD, Maisam H. Alhammadi, MBBS, Wehad S. Jambi, MBBS, Hadeel A. Albaradei, MBBS, Nadin A. Alharbi, MBBS, Banan A. Alsaif, MBBS, Duaa M. Bahkali, MD, Nabeel S. H Bondagji, FRCS.

ABSTRACT

الأهداف: دراسة العلاقة المحتملة بين فصائل الدم ABO وتأخر النمو داخل الرحم بين النساء الحوامل اللاتي ولدن في مستشفى جامعة الملك عبد العزيز (KAUH) في جدة، المملكة العربية السعودية. يمكن أن ينجم تقييد نمو الجنين داخل الرحم (IUGR) عن عوامل مرتبطة بالمشيمة أو الأم أو الجنين. تم ربط فصائل الدم ABO بالعديد من المضاعفات المرتبطة بالحمل والتي يمكن التنبؤ بها ومنعها بسهولة.

المنهجية: هذه الدراسة الحشدية بأثر رجعي قامت بتحليل السجلات الطبية للنساء الحوامل اللاتي ولدن في KAUH، وقامن بزيارات متابعة بعد الولادة. تم استكمال البيانات المفقودة عن طريق إجراء مقابلات هاتفية مع المرضى.

النتائج: تم تضمين ما مجموعه 436 مريضا بمتوسط عمر 31.2 ± 5.5 سنة في الدراسة. كانت 50.7% من النساء لديهن فصيلة دم O، و28.4% لديهن فصيلة دم A، و16.5% لديهن فصيلة دم B، و4.4% لديهن فصيلة دم AB. كانت نتيجة الغالبية (94.7%) إيجابية لمستضد الريسوس. على الرغم من أنها ذات دلالة إحصائية، فإن النساء ذوات فصيلتي الدم AB وB أظهرن معدلات أعلى من تأخر النمو داخل الرحم (31.6%، و27.8%، على التوالي) مقارنة بأولئك الذين لديهم فصيلتي الدم A وO، الذين لديهم معدلات أقل من تأخر النمو داخل الرحم (26.6%، و24%، على التوالي).

الخلاصة: أظهرت نتائج دراستنا أن النساء ذوات فصيلتي الدم AB وB لديهن معدلات أعلى قليلاً من تأخر النمو داخل الرحم مقارنة بأولئك اللاتي لديهن A وO، اللاتي لديهن معدلات أقل من تأخر النمو داخل الرحم. قد توفر دراسة أكبر تقارن فصيلة الدم O بالمجموعات الأخرى مزيداً من الفهم للعلاقة بين فصائل الدم ABO وIUGR.

Objectives: To investigate the potential association between ABO blood groups and intrauterine fetal growth restriction (IUGR) among pregnant women who delivered at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia.

Methods: This is a retrospective cohort study analyzed the medical records of pregnant women who delivered at KAUH and had postnatal follow-up visits. Missing

data were completed by conducting phone interviews with patients.

Results: A total of 436 patients with a mean age of 31.2 ± 5.5 years were included in the study. 50.7% of the women had blood type O, 28.4% had blood type A, 16.5% had blood type B, and 4.4% had blood type AB. The majority (94.7%) tested positive for the Rhesus antigen. Although statistically significant, women with blood groups AB and B exhibited higher rates of IUGR (31.6%, and 27.8%, respectively) compared to those with blood groups A and O, who had lower rates of IUGR (26.6%, and 24%, respectively).

Conclusion: Our study results showed that women with blood groups AB and B had slightly higher rates of IUGR than those with A and O, who had lower rates of IUGR. A larger study comparing blood group O to other groups may provide more insight into the relationship between ABO blood groups and IUGR.

Keywords: ABO, blood group, IUGR, pregnancy

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From the Department of Obstetrics and Gynecology, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Nedaa M. Bahkali, Obstetrics and Gynecology Department, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.
E-mail: Nmbahkali@kau.edu.sa
ORCID ID: <https://orcid.org/0000-0002-6561-8616>

Intrauterine fetal growth restriction (IUGR) has been defined as a fetal weight, less than the 10th percentile of gestational age (normal range between the 10th and 90th percentile), with pathological consequences. Many factors lead to the occurrence of IUGR, including placental, maternal, and fetal factors. Placental factors, such as placental insufficiency, tend to be the most common cause of IUGR. Besides, maternal factors including smoking during pregnancy, diabetes mellitus, hypertension, and anemia are also important causes of IUGR. In addition, genetic diseases and congenital anomalies are also important risk factors for IUGR.¹ Furthermore, intrauterine fetal demise (IUID), which is a fetal death in utero after 20 weeks of gestation with a birth weight of more than 500 g, shares the same risk factors as IUGR.²

The ABO blood group is a system and is determined by cell surface antigens expressed in human blood. Particularly, 4 main blood groups exist, which are A, B, AB, and O, differentiated by the type of carbohydrate on cell surface. Blood type distribution varies across countries.³ In Saudi Arabia, the most common blood type among the population is type O+.⁴

Several studies have investigated the relationship between ABO blood types and pregnancy-related complications in pregnant women and newborns, with wide variations in the results. Multiple systematic reviews have shown positive statistically significant differences between the maternal ABO blood group and pregnancy complications.^{5,6} Some authors reported an association between ABO blood types and risks for preeclampsia.⁷⁻⁹ On the other hand, a study by Sajan et al¹⁰ found a link between ABO blood types and pregnancy-related complications regarding the risk of preterm delivery, low birth weight (LBW), and small for gestational age (SGA), but not with gestational diabetes (GDM) and preeclampsia. Another study found that pregnant females with AB blood type have a higher risk of developing GDM.¹¹ Furthermore, Seyfizadeh et al¹² have studied risk factors of pregnancy-related complications and found an association between these risk factors and ABO blood type. In contrast, Clark et al¹³ demonstrated that there was no association between maternal ABO and fetal growth restriction.

Although ABO blood groups are considered significant risk factors for several pregnancy

complications, few studies have investigated ABO blood groups among IUGR and IUFD cases. Our study aims to determine the relationship between ABO blood groups and the occurrence of IUGR among pregnant women who underwent delivery at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia.

Methods. This is a retrospective cohort study of pregnant women who gave birth in KAUH during a period of 5 years from 2017 to 2022. ABO blood groups and rhesus antigens were the exposure variables, while IUGR was the outcome variable. All women who gave birth and had follow-up visits after delivery at KAUH were eligible for inclusion. Incomplete records and multiple pregnancies were excluded from the data collection. The sample size was calculated using Epi info. The equation for cohort studies was built with 95% confidence level, 80% power, 40% risk among unexposed, and 60% risk among exposed. With 2:1 unexposed to exposed ration, the minimum required sample size using Kelsey was 221. Medical records of female patients who met the inclusion criteria were retrospectively inspected for age, past medical and obstetric history, mode of delivery, pregnancy complications, and birth outcomes. Data on comorbidities such as gestational diabetes mellitus, pregnancy-induced hypertension, preeclampsia, antepartum and postpartum hemorrhage, and number of previous pregnancy losses were collected. Birth outcomes included birth weight, APGAR scores, neonatal intensive care unit (NICU) admission, and congenital anomalies. Phone calls were made to gather data that could not be obtained from the patients' files. The outcome variables of interest were IUGR, and exposure variables included both the ABO blood group and rhesus antigens. This study was reviewed and approved by the Committee of Research Ethics at King Abdulaziz University (Reference No 75-22). The data were obtained after obtaining administrative permission of the gynecology and Obstetrics Department at KAUH. Data were kept securely, and personal identifiers were removed before proceeding to data analysis to protect patient confidentiality and privacy. The collected data were used for research purposes only.

Statistical analysis. The data analysis was carried out using the Statistical Package For The Social Sciences, Version 29.0 (IBM Corp, Armonk, NY, USA). Categorical variables were described using frequency tables and percentages. The Shapiro-Wilk normality test was used to test for normal distribution. Continuous variables were summarized using mean and standard deviation (SD) or median and interquartile range (IQR) as appropriate. Chi-square independence

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and Fisher-Freeman-Halton exact tests were used to test associations between categorical variables. The significance level was set at 0.05.

Results. A total of 436 Saudi women were included in the analysis, with a mean age of 31.2±5.5 years. The majority (83.3%) were of Saudi nationality. The median gestational age was 39 weeks and (interquartile [IQR] 38-40) and the median gestational days was 3 (IQR 0-5). The patients' gravida had a median of 3 (IQR 2-4), and para had a median of 2 (IQR 1-3). Of the total, 17.7% had a history of one pregnancy loss, 7.3% had 2 pregnancy losses, and 3.9% had more than 2 pregnancy losses. The most common comorbidity was hypothyroidism (9.9%), followed by bronchial asthma (3.7%). The comorbidities are further detailed in (Table 1).

History of GDM was present among 9% of the total, and 6.7% had a history of abortion. Current pregnancy was complicated by GDM among 13.9% and hypertension among 3.4%. See the obstetric-related history of the patients in (Table 2).

More than half (56.7%) had normal vaginal delivery, 3.9% had assisted vaginal delivery, and 39.4% had caesarean delivery (18.8% elective and 20.6% emergent). Labor was induced for 14% of the women. Only 1.6% of the newborns were admitted to neonatal intensive care unit (NICU). Of the total, 25.7% had IUGR while 0.7% had intrauterine fetal death. See the maternal and neonatal outcomes showed in (Table 3).

Table 1 - Nationality and comorbidities among the patients (study group).

Comorbidities	n	%
<i>Nationality</i>		
Saudi	363	83.3
Non-Saudi	73	16.7
<i>Chronic hypertension</i>		
Yes	12	2.7
No	434	97.3
<i>Bronchial asthma</i>		
Yes	16	3.7
No	419	96.3
<i>Autoimmune diseases</i>		
Yes	2	0.5
No	433	99.5
<i>Hypert thyroidism</i>		
Yes	3	0.7
No	432	99.3
<i>Hypothyroidism</i>		
Yes	43	9.9
No	392	90.1

ABO blood grouping showed that half (50.7%) of the women had blood type O, 28.4% had blood type A, 16.5% had blood type B, and 4.4% had blood type AB. Rhesus antigen was positive among 94.7%. ABO

Table 2 - Past and current pregnancy-related complications

Comorbidities	n	%
<i>Past history</i>		
Gestational diabetes mellitus	37	9.0
Pregnancy induced hypertension	13	3.1
Preeclampsia	14	3.4
Hemorrhage during pregnancy	6	1.5
Ectopic pregnancy	6	1.4
Abortion	29	6.7
Preterm labor	16	3.9
History of congenital anomaly	5	1.2
<i>Current pregnancy</i>		
Gestational diabetes mellitus	59	13.9
Pregnancy induced hypertension	15	3.4
Eclampsia	3	0.7
Antepartum hemorrhage	6	1.4

Table 3 - Showing maternal, neonatal, and delivery-related findings.

Maternal and neonatal outcome	n	%
<i>Mode of delivery</i>		
Vaginal delivery	247	56.7
Assisted vaginal delivery	17	3.9
Total cesarean section	172	39.4
Elective cesarean section	82	18.8
Emergency cesarean section	90	20.6
<i>Analgesia/anesthesia type</i>		
Inhaler	114	26.1
Regional	301	69.0
General	21	4.8
<i>Baby gender</i>		
Male	209	47.9
Female	227	52.1
<i>Resuscitation</i>		
C-PAP	1	0.2
PPV & suction	10	2.3
C-PAP & PPV	2	0.5
PPV & intubation	1	0.2
C-PAP + PPV + intubation	1	0.2
<i>Neonatal outcome</i>		
Live birth	433	99.3
Intrauterine fetal death	3	0.7
<i>Neonatal complication</i>		
No complications	425	97.5
Neonatal intensive care unit admission	7	1.6
Neonatal death	3	0.7
<i>IUGR</i>		
Yes	112	25.7
No	324	74.3

C-PAP: continuous positive airway pressure, PPV: positive pressure ventilation, IUGR: ntrauterine fetal growth restriction

Table 4 - The distribution of intrauterine growth restriction (IUGR) rate across ABO blood groups and rhesus antibodies

	IUGR	Normal	P-value
<i>Blood group</i>			
A	33 (26.6)	91 (73.4)	0.826
B	20 (27.8)	52 (72.2)	
AB	6 (31.6)	13 (68.4)	
O	53 (24)	168 (76)	
<i>Rhesus</i>			
Positive	106 (25.7)	307 (74.3)	0.964
Negative	6 (26.1)	17 (73.9)	
Values are presented as numbers and percentages (%). The significance level <i>p</i> -value at 0.05.			

blood groups and rhesus antigens were investigated for statistical association with IUGR. Among ABO blood groups, while the IUGR rates were similar across the groups, women with blood groups O, had lower IUGR rate than groups. However, the results were not statistically significant ($p=0.826$). Analyses also showed a slightly higher IUGR rate among Rhesus positive women compared to Rhesus negative women (26.1% vs. 25.1%). Again, the results were not statistically significant. The related results are demonstrated in (Table 4).

Discussion. The significant role of ABO blood groups in the pathogenesis of several diseases has been extensively addressed in various studies. Among these diseases, the impact of ABO blood groups on the complications of pregnancies and their associated outcomes for both the mother and newborns numerous studies has garnered particular attention. These complications include gestational hypertensive disorders, preterm delivery, low birth weight (LBW), and small for gestational age (SGA).⁸⁻¹⁰ Several studies have reported associations between specific blood groups and particular pregnancy outcomes. For instance, a highly regarded study has stated that pregnant women with AB blood group may have a potentially higher risk for complications of placenta previa.¹⁴ Furthermore, a published meta-analysis has concluded that blood group O is a protective factor against pre-eclampsia, while blood group AB is a potential risk factor for pre-eclampsia.¹⁵

The primary objective of this study was to explore the possible association between different blood groups and IUGR. Focusing on gestational outcomes is particularly relevant due to the limited amount of research in this area. Our findings showed that the majority of the study population belongs to blood group O, which

aligns with the results of a previous study carried out in Saudi Arabia.⁴ Furthermore, the present study identifies GDM as the most common complication during the current pregnancy, indicating a high prevalence of GDM. Indeed, this high prevalence is consistent with another published study in Saudi Arabia, which showed a prevalence of GDM to be 19.6%.¹⁶ Additionally, it is well-established that pregnant women with GDM are at higher risk of developing several pregnancy complications, including preterm delivery, induction of labor, intrauterine fetal, and infant death.¹⁷

Although the study results do not reveal any significant association between the different ABO blood groups with IUGR or IUFD, this link is plausible since our analysis revealed some interesting findings. First, we found that women belonging to blood group O exhibited a lower IUGR rate than other groups. Second, women who are Rhesus positive had a slightly higher IUGR rate. These associations were proposed in a previously published article, stating that since the difference in blood groups and IUGR are significantly associated with cardiovascular disease, the link is probable.¹³ Moreover, a highly regarded study concluded that although the maternal blood group is considered a confounding factor in predicting the risk of pre-eclampsia, it is important to take it into account for the risk assessment of IUGR particularly in the first trimester.¹⁸

The best explanation for our findings is that the majority of our population were Rhesus positive, in addition to the low sample size across the different blood groups. The strengths of our study include the scarcity of studies regarding the association between blood groups and IUGR, particularly in Saudi Arabia.

Study limitations. There are limitations that needs to be addressed. First, the statistical comparison was limited across groups due to variations in sample sizes. Second, the study population showed a very low prevalence of intrauterine fetal death (0.7%), which limited the analysis of this variable. Additionally, one of the important limitations of this study is that the cohort was selected from a single center, which may not reflect the true pattern across Saudi Arabia and may affect the generalizability of our findings.

In conclusion, several studies have established the impact of ABO blood groups on pregnancy complications and their associated outcomes. Our findings showed a lower rate of IUGR among pregnant women belonging to the O blood group, and a higher rate of IUGR among Rhesus-positive women. However, these associations were not statistically significant, indicating that neither blood groups nor Rhesus status

were associated with IUGR. These findings have raised new hypotheses regarding the association between ABO blood groups and IUGR.

We recommend further prospective studies with a larger, multi-center population to determine the true impact of ABO blood groups on IUGR and IUFD, and help obstetricians identify the higher-risk patients to apply the required preventive measures for such patients.

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