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Impact of a mother's ABO blood group on fetal growth and pregnancy-induced hypertension

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Abstract
Background: Blood type, as defined by the ABO system, has been identified as a potential contributor to various medical conditions. However, its influence on pregnancy complications remains under-explored, particularly regarding fetal growth and hypertensive disorders of pregnancy. This research seeks to investigate whether an individual's ABO blood group plays a role in unfavorable pregnancy outcomes, with a specific focus on infants born smaller than expected and the development of preeclampsia.
Methods: Medical records, encompassing ABO blood group classifications, were obtained from the hospital's records and subjected to a backward-looking examination. The study concentrated on two particular pregnancy-related complications: hypertensive disorder of pregnancy and neonates with suboptimal weight. The duration of gestation at the time of delivery was also documented for each study participant.
Results: Analysis of 2552 maternal medical records from our institution revealed the following blood type distribution: O (27.7%, N=708), A (48.5%, N=1236), B (17.2%, N=440), and AB (6.6%, N=168). Notably, offspring of type B mothers exhibited significantly reduced birth weights compared to those of O, A, and AB mothers. Gestational length at delivery showed no statistically significant variation among blood groups. The study identified 200 cases of gestational hypertensive disorders. No correlation was found between ABO blood classification and the incidence of this pregnancy complication.
Conclusions: While a link was observed between maternal blood group and reduced neonatal weight, no such relationship was evident between blood type and hypertensive disorders of pregnancy. We theorize that genetic factors in maternal and fetal immune systems, which are closely tied to ABO blood group determination, may influence gestational processes, leading to variations in fetal growth and subsequent birth weight.

Keywords: ABO blood type, birth weight, pregnancy, preeclampsia

Introduction

Numerous investigations have demonstrated a robust link between ABO blood classifications and heightened vulnerability to specific health conditions. These include cardiac incidents, pathogenic infections, malignancies of the large intestine, cerebrovascular anomalies, and thrombotic events [1-4]. Furthermore, scientific literature has documented connections between ABO blood groups and pregnancy-related complications, such as gestational hypertensive disorders, inflammation of fetal membranes, venous clot formation, and excessive bleeding following childbirth [5]. However, conflicting results have emerged from these studies exploring the potential relationship between blood types and gestational outcomes, leading to ongoing debate in the field.

The ABO blood classification system, identified approximately 100 years ago, categorizes individuals based on specific antigens present on various cellular and tissue surfaces throughout the body [5, 6]. This categorization is determined by the presence or absence of two genetic elements, A and B. These genes encode distinct variants of an enzyme called glycosyltransferase, which is responsible for producing A and B antigens. The O variant of this gene results in a non-functional enzyme, leaving the antigen precursor unaltered. These antigens are found in diverse bodily structures, including erythrocytes, blood vessel linings, skin cells, thrombocytes, and nerve cells [7, 8]. Given their widespread distribution, ABO antigens have become a subject of interest beyond transfusion and organ transplantation, extending into the realm of reproductive health. In this field, gestational hypertensive disorders have received significant attention regarding potential associations with blood types.

Initial research suggests that a pregnant individual's blood classification may independently influence pregnancy outcomes. However, despite years of investigation, studies examining the relationship between ABO blood groups and hypertensive disorders of pregnancy have yielded inconsistent and sometimes contradictory results [9, 10].

Pregnancy-related complications such as preeclampsia, premature delivery, and infants born underweight pose a significant global health challenge. While these issues often stem from underlying maternal health conditions like unmanaged hypertension and diabetes, they can also be attributed to fetal and placental factors [11]. In particular, low birth weight (LBW) is a persistent and clinically significant complication in human pregnancies, leading to elevated rates of newborn mortality and morbidity. LBW is defined as any live birth where the infant weighs 2500 g or less, irrespective of gestational duration. These underweight newborns face a considerably higher risk of death, contributing to elevated perinatal mortality and morbidity rates [12].

Although numerous risk factors have been identified in connection with LBW, the precise mechanisms remain elusive in 40% of cases [13]. Given the observed link between ABO blood groups and unfavourable pregnancy outcomes, we theorized that blood group antigens might play a role in the development of LBW infants. Consequently, our research aimed to investigate the relationship between ABO blood types and several common pregnancy complications, including preeclampsia, low birth weight, and preterm delivery.

Methods

This retrospective analysis was performed at the Obstetrics and Gynecology Department of RNT medical college Udaipur, India. Following approval from the Ethics Committee, researchers accessed the hospital's digital records, which contained various demographic and clinical data fields for both mothers and their newborns. The study examined 2552 women who delivered at the hospital from November 2023 through January 2024. Only mothers with known ABO blood types were included in the analysis.

The study excluded women who had taken any medications (with the exception of vitamins, iron, and folic acid supplements), those with multiple pregnancies, and cases involving erythroblastosis fetalis. Preeclampsia was characterized as hypertension during pregnancy accompanied by proteinuria. Low birth weight was classified as any birth weight below 2500 g, including 2499 g, irrespective of gestational duration. Births were categorized as full-term if occurring at or after 37 weeks, and preterm if occurring at or before 36 weeks and 6 days of gestation.

Statistical evaluation was conducted using SPSS software, version 19. Continuous variables were expressed as means with standard deviations, while categorical variables were presented as percentages. The threshold for statistical significance was set at a P-value less than 0.05.

Results

The study encompassed 2552 expectant mothers. The average age of participants was 28.8 years, with a standard deviation of 5.4 years. Table 1 presents the mean ages of participants categorized by their ABO blood types. In our study cohort, type A emerged as the predominant blood group, accounting for 48.5% of participants. (Table 1).

Table 1: ABO blood types of study participants

Blood type	Mean age (Years)	N	%
O+	28.9 +-5.1	636	24.9
O-	29.1+-6.1	72	2.8
A+	28.9+-5.4	1122	44.0
A-	28.8+-5.5	114	4.5
B+	28.5+-5.3	322	12.6
B-	29.2+-6.1	118	4.6
AB+	28.2+-5.2	148	5.8
AB-	29.1+6.1	20	0.8
Total		2552	100

Among the 2552 pregnant women, 708 had type O blood, 1236 possessed type A, 440 were type B, and 168 were identified as type AB. Table 2 outlines the average birth weight and gestational age at delivery for each blood group. Notably, women with type B blood gave birth to infants with significantly lower weights compared to those with types O, A, and AB. However, the gestational age at birth was comparable across all groups, showing no statistically meaningful differences. (Table 2)

Table 2: Birth week, birth weight and presence of preeclampsia according to blood groups

	Blood groups				
	O (N=708)	A (N=1236)	B (N=440)	AB (N=168)	P
Birth weight (gram)	3294+-562	3137+-543	3005+-571	3127+-489	<0.001*
Birth week	38.5+-1.8	38.3+-1.9	38.1+-2.6	38.3+-1.7	NS
Preeclampsia					NS
Yes (N, %)	56(7.9)	171(8.9)	41(9.4)	14(8.8)	
No (N, %)	44(92.6)	1147(93.3)	399(90.6)	154(91.2)	

*B blood type versus O, A and AB blood type.

Preeclampsia (PE) was documented in 200 cases, representing 7.8% of the total sample. The incidence of PE varied slightly among blood groups: 7.9% in type O, 6.7% in type A, 9.4% in type B, and 8.8% in type AB. Statistical analysis revealed no significant disparity in PE rates across the four blood groups (P=0.876).

Regarding low birth weight (LBW) infants, the rates differed among blood groups: 7.0% in type O, 10.2% in type A, 17.3% in type B, and 10.2% in type AB. Strikingly, mothers with type B blood demonstrated a significantly higher likelihood of delivering LBW babies (p<0.005).

Table 3: Low birth weight babies (< 2500 gram) according to maternal ABO blood group

	Blood groups	N	%
Low birth weight	O	49/708	7.0
	A	126/1236	10.2
	B	76/440	17.3
	AB	17/168	10.2

Discussion

Evidence from multiple sources had previously indicated a potential link between ABO blood type and the likelihood of experiencing adverse pregnancy outcomes, including preeclampsia, chorioamnionitis, and venous thromboembolism [5, 6, 14]. While researchers have proposed various physiological mechanisms to explain these connections, many contradictory findings remain unresolved. This investigation aims to synthesize the current state of knowledge and address existing gaps in this field of study.

|This study's primary discovery is the correlation between blood type B and low birth weight (LBW) in pregnant women without other health issues. While no previous research has directly linked ABO blood types to birth weight, it's theorized that ABO antigens on cell surfaces play crucial roles in immunity and blood clotting [15].

Specific combinations of maternal and fetal immune system genes, which are closely tied to ABO blood groups, might influence pregnancy outcomes, including birth weight variations. Fetal growth is partially dependent on maternal blood flow to the placenta, which requires changes in uterine spiral arteries [16]. The tendency of non-O blood types to form arterial clots may put pregnant women at particular risk based on their inherited blood antigens.

Our study found PE rates of 7.9% in O group, 6.7% in A group, 9.4% in B group, and 8.8% in AB group pregnancies. Despite no significant ABO-PE association here, other research has convincingly shown ABO blood type's partial role in PE development [14, 17].

The most likely factor connecting PE to ABO type is increased clotting tendency, especially in non-O groups. AB blood type women have higher levels of clotting factors like factor VIII and von Willebrand factor, potentially triggering or worsening PE-related events.

Another mechanism linking ABO to PE appears to be the maternal immune response to placental protein 13 (PP13), which binds differently to red blood cells of various ABO groups, with strongest binding to AB [15, 18]. Reduced PP13 expression in the placenta during the first trimester may contribute to early PE development

Despite numerous investigations into the potential causal link between maternal ABO blood types and preeclampsia (PE), a definitive association remains unestablished. A recent study by Phaloprakarn and Tangjitgamol identified an elevated PE risk in women with A or AB blood types, but not B, when compared to type O individuals [9]. Corroborating this, Spinillo *et al*. and Hiltunen *et al*. observed a 2.1- to 3.1-fold increase in PE risk among Italian and Finnish pregnant women with AB blood type versus those with type O [19, 20]. However, contradicting these findings, Hentschke *et al*. found no correlation between blood groups and PE development [21]. Given the multitude of variables and conflicting results, a definitive conclusion regarding ABO blood types and PE remains elusive.

We acknowledge several limitations in our analysis

1. The retrospective nature of the study, drawing from a single academic center's cohort.
2. The omission of analyzing associations between ABO blood groups and other adverse pregnancy outcomes such as chorioamnionitis, venous thromboembolism, and gestational diabetes mellitus.
3. Potential data gaps inherent to retrospective studies may have diluted the associations among the variables examined.

Conclusion

To summarize, our findings suggest a possible link between ABO blood types and infant birth weight. However, this relationship requires further examination through future prospective randomized studies to confirm and elucidate the nature of this association.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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