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Fetomaternal Complications of Rh-Negative Blood Group

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ABSTRACT

Objective: To determine the frequency of fetomaternal outcomes in Rh-negative pregnant patients. **Research Design:** A descriptive study. **Duration and Place of Study:** The study was conducted in the Department of Obstetrics and Gynecology at Lady Reading Hospital, Peshawar, from August 15, 2023, to February 15, 2024. **Methodology:** This study included 133 women aged 18–40 years with singleton pregnancies, a gestational age of >28 weeks, and Rh-negative blood type. Women with congenital anomalies or who refused consent were excluded. Data on demographic details, such as age, gestational age, and parity, were collected, along with fetomaternal outcomes like cesarean section, oligohydramnios, neonatal anemia, stillbirth, and neonatal jaundice. **Results:** The mean age of participants was 27.77 years, with a mean gestational age of 36.52 weeks and a mean parity of 1.44. The most common fetomaternal complication was cesarean section (56.4%), followed by neonatal anemia (12%), neonatal jaundice (11.3%), oligohydramnios (6.8%), and stillbirth (4.5%). Stratification revealed significant associations between gestational age and complications: neonatal anemia and stillbirth were more prevalent in later gestations (>36 weeks), while oligohydramnios was more common in earlier gestations (28–36 weeks). **Conclusion:** Rh-negative pregnancies are associated with various fetomaternal complications, including cesarean section, neonatal anemia, jaundice, and stillbirth. Gestational age plays a significant role in determining the prevalence of these complications.

INTRODUCTION

The Rh-negative blood group presents significant challenges, particularly during gestation, due to the potential for Rh alloimmunization between a Rh-negative gravida and a Rh-positive conceptus.[1] This immunological response occurs when the maternal immune system identifies Rh-positive erythrocytes of the fetus as non-self and mounts an adaptive immune reaction.[2] Alloimmunization—or the synthesis of anti-D immunoglobulins by the maternal immune system against the Rh (D) antigen—can be triggered during antenatal periods, parturition, spontaneous or induced abortion, or invasive obstetrical interventions.[3] If untreated, these immunoglobulins may traverse the placenta in subsequent gestations, targeting fetal erythrocytes and resulting in hemolytic disease of the fetus and newborn (HDFN).[4] HDFN can lead to fetal anemia, hyperbilirubinemia, or severe sequelae such as hydrops fetalis, characterized by pathologic fluid accumulation within fetal compartments.[4] Beyond direct fetal morbidity, Rh alloimmunization can significantly complicate gestational outcomes. The production of anti-D antibodies heightens the probability of adverse perinatal events, including spontaneous abortion, intrauterine fetal demise, and preterm delivery, secondary to the systemic maternal immune activation and its disruptive impact on fetal growth and maturation.[5] Hydrops fetalis, often a critical manifestation of severe HDFN, necessitates preterm termination of pregnancy to mitigate progression and neonatal morbidity.[6] Additionally, profound fetal anemia may require intrauterine transfusion, a procedure associated with iatrogenic risks such as infectious morbidity, preterm prelabor rupture of membranes, or iatrogenic uterine activity precipitating premature delivery.[7] Advancements in clinical protocols have substantially improved prognostic outcomes in Rh incompatibility through prophylaxis and therapeutic strategies. Administration of Rh(D) immunoglobulin (Rho(D) immune globulin) to Rh-negative patients during antenatal care and postpartum, following the delivery of an Rh-positive neonate, effectively prevents alloimmunization.[8] Early detection through maternal antibody titration and fetal evaluation using ultrasonography and Doppler velocimetry plays a pivotal role in risk stratification and management.[9] In cases of pronounced HDFN, neonatal intensive care interventions, including exchange transfusion, have further reduced neonatal morbidity and mortality.[10]

In a cross-sectional study conducted by Yadav M. and colleagues in the Department of Obstetrics and Gynecology at Nobel Medical College Teaching Hospital, an analysis

was performed involving singleton Rhesus-negative mothers. The findings revealed that the prevalence of cesarean sections was 53.6%, oligohydramnios occurred in 6.5% of cases, neonatal anemia was observed in 7.3%, stillbirths accounted for 6.3%, and neonatal jaundice was reported in 3.2% of Rh-negative pregnancies.[11]

In Pakistan, access to anti-RhD immunoglobulin IgG remains limited due to its high cost, making it unaffordable for many. While some studies have explored this issue in various regions of the country, no research has been conducted in the study area to assess the epidemiological distribution of Rh blood groups or the neonatal outcomes associated with Rh incompatibility.[12-14] Consequently, this study aims to evaluate the frequency of fetomaternal outcomes among Rh-negative pregnant women. The findings will contribute to the development of community-based guidelines for identifying Rh D antigen status, offering protection to pregnant women—particularly those who do not attend antenatal care or deliver at healthcare facilities.

METHODOLOGY

This descriptive case series was conducted in the Department of Obstetrics and Gynecology at Lady Reading Hospital (LRH), Peshawar, over a six-month period from August 15, 2023, to February 15, 2024. A total of 133 participants were included in the study. The sample size was calculated using WHO sample size software, based on a 95% confidence interval, a 3% margin of error, and an expected frequency of neonatal jaundice of 3.2% in Rh-negative pregnant patients.[11] Eligible participants included women aged 18 to 40 years with singleton pregnancies, a gestational age of >28 weeks, and Rh-negative blood group status. Women who refused to provide consent or whose pregnancies involved congenital anomalies detected on ultrasound were excluded. After obtaining ethical approval and informed consent, eligible participants were enrolled from the Gynecology labor room at LRH. Baseline demographic data, including age, gestational age, and parity, were collected. Fetomaternal outcomes were assessed based on predefined operational definitions. Cesarean section was defined as delivery of the baby via abdominal incision. Oligohydramnios was defined as an amniotic fluid index ≤5.0 cm on ultrasound. Neonatal anemia was diagnosed when hemoglobin was <14 g/dL within the first week of life. Stillbirth was considered as fetal loss at ≥28 weeks based on LMP or dating scan, confirmed by ultrasound showing absent cardiac activity. Neonatal jaundice was identified by yellowish skin discoloration after digital blanching, with serum bilirubin >13 mg/dL within the first week after birth. All outcomes and demographic data were recorded by the principal investigator using a structured proforma. Data analysis was performed using SPSS version 27. Categorical variables, including cesarean section, oligohydramnios, neonatal anemia, stillbirth, and neonatal jaundice, were expressed as frequencies and percentages. Quantitative variables such as age, gestational age, and parity were summarized as means and standard deviations.

RESULTS

Demographically, the patients had a mean age of 27.774 ± 3.32 years, mean gestational age of 36.519 ± 1.74 weeks, and mean parity of 1.444 ± 1.47 (as shown in Table-I).

Table I

Mean±SD of patients according to age, gestational age and parity (n=133)

Demographics	Mean±SD
1 Age (years)	27.774±3.32
2 Gestational age (weeks)	36.519±1.74
3 Parity	1.444±1.47

Regarding fetomaternal complications, the most frequent was Cesarean Section at 56.4% (75 patients), followed by Neonatal Anemia at 12% (16 patients), Neonatal Jaundice at 11.3% (15 patients), Oligohydramnios at 6.8% (9 patients), and Still Birth at 4.5% (6 patients) (as detailed in Table-II).

Table II

Frequency and %age of patients according to fetomaternal complications.

Fetomaternal Complications	Frequency	%age
Cesarean Section	75	56.4%
Oligohydramnios	9	6.8%
Neonatal Anemia	16	12%
Still Birth	6	4.5%
Neonatal Jaundice	15	11.3%

Stratification analyses revealed several notable observations: Cesarean Section rates were similar across age groups (54.5% in 18-30 years vs. 62.5% in >30 years, p=0.424), but significant differences emerged in gestational age comparisons. Specifically, Oligohydramnios was significantly more prevalent in 28-36 weeks (12.7%) compared to >36 weeks (0%, p=0.004), Neonatal Anemia was markedly higher in >36 weeks (25.8%) compared to 28-36 weeks (0%, p=0.000), and Still Birth was more common in 28-36 weeks (8.5%) versus >36 weeks (0%, p=0.019) (as presented in Table-III).

Table III

Stratification of Fetomaternal Complications with respect to age, gestational age and parity

	Age		
Fetomaternal Complications	**18-30 years**	**>30 years**	**P value**
Cesarean Section	54.5%	62.5%	0.424
Oligohydramnios	8.9%	0%	0.080
Neonatal Anemia	9.9%	18.8%	0.180
Still Birth	4%	6.2%	0.587
Neonatal Jaundice	11.9%	9.4%	0.696
Gestational Age Fetomaternal Complications	**28-36 weeks**	**>36 weeks**	**P value**
Cesarean Section	62%	50%	0.165
Oligohydramnios	12.7%	0%	0.004
Neonatal Anemia	0%	25.8%	0.000
Still Birth	8.5%	0%	0.019
Neonatal Jaundice	7%	16.1%	0.098
Parity Fetomaternal Complications	**0-2**	**>2**	**P value**
Cesarean Section	55.2%	59.5%	0.658
Oligohydramnios	9.4%	0%	0.054
Neonatal Anemia	9.4%	18.9%	0.129
Still Birth	4.2%	5.4%	0.758
Neonatal Jaundice	10.4%	13.5%	0.613

DISCUSSION

This research adds to the growing body of evidence on the management and outcomes of Rh-negative pregnancies. By incorporating demographic trends, clinical outcomes, and stratified results, it bridges existing gaps in the literature. Sharma et al. [15] conducted a study on 100 Rh-negative pregnant women and found that 3% were sensitized, with complications including preeclampsia (9%), oligohydramnios (12%), and neonatal jaundice (20%). In comparison, our study reported a lower neonatal jaundice rate (11.3%). Interestingly, oligohydramnios in our cohort (6.8%) was less prevalent than in Sharma et al.'s population, possibly reflecting differences in gestational management practices. Additionally, our study stratified these complications by gestational age, finding a significantly. Nagamuthu et al. [16] highlighted that 4.29% of pregnant women were Rh-negative, with hemolytic disease of the newborn (HDN) and erythroblastosis fetalis as key complications. Our study recorded neonatal anemia in 12% of cases, with significantly higher rates in pregnancies >36 weeks (25.8%, p=0.000), providing an additional stratified perspective. Maruta et al. [17] found an alloimmunization prevalence of 17.1% among Rh-negative women, with complications such as jaundice (47.1% in current pregnancies, 71.8% in previous pregnancies), hydrops fetalis (5.9% in current pregnancies), and stillbirth (5.9%). In contrast, our study documented lower neonatal jaundice (11.3%) and stillbirth rates (4.5%), but gestational-age stratification revealed that stillbirth was significantly more common in pregnancies <36 weeks (8.5%, p=0.019). Aliyo et al. [18] observed a 6.4% prevalence of Rh-negative pregnancies, with neonatal jaundice affecting 14.3% of neonates born to Rh-negative mothers. This was slightly higher than the jaundice rate in our cohort (11.3%). While Aliyo et al. focused on neonatal outcomes, our study expanded on maternal complications, noting a high cesarean section rate (56.4%) and stratified analysis showing no significant difference in cesarean rates between age groups (54.5% in 18–30 years vs. 62.5% in >30 years, p=0.424).

Our study contributes novel insights, particularly through stratification by gestational age, uncovering trends like the increased prevalence of neonatal anemia in later gestations (>36 weeks: 25.8%, p=0.000) and stillbirth in earlier gestations (28–36 weeks: 8.5%, p=0.019). This level of granularity enriches the existing literature and underscores the importance of targeted management strategies tailored to specific gestational periods. In summary, this study highlights the importance of integrating stratified analyses into routine evaluations of Rh-negative pregnancies to identify and address specific risk factors at varying gestational stages.

CONCLUSION

Our study has concluded that Rh-negative blood group is associated with significant fetomaternal complications, demonstrating the complex immunological challenges in pregnancy. The research reveals a substantial risk of adverse outcomes, particularly related to immune-mediated hemolytic processes affecting both maternal and fetal health

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Authors' Contributions

The authors have made the following significant contributions to this manuscript:

- **Dr. Sobia Khalil** led the conceptualization of the study, drafted the manuscript with meticulous attention to detail, and was primarily responsible for the acquisition and organization of hospital data.
- **Dr. Aiysha Humayun** contributed to the development of the study design, assisted in refining the research methodology, and played a key role in interpreting the findings.
- **Dr. Wajeeha Syed** played an integral role in the study by contributing to its conceptual framework, conducting in-depth data analysis and interpretation, and providing substantial input to the manuscript's development.
- **Dr. Nabeela Naz** provided valuable insights into the manuscript, particularly in relation to the clinical aspects of the study, and contributed significantly to the manuscript's final review.

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