



Outcomes of pregnancy in Rhesus Negative Mothers in DHQ Dera Ismail Khan

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ABSTRACT

Background: Rh negative pregnancy is a major concern in obstetrics, and it has increased risks of complications in mothers and babies. When the mother and father are Rh negative, pregnancy risks in the mother include maternal sensitization, which may cause problems in pregnancy as well as in the baby. The risks are higher in environments with low antenatal care and late booking. **Objective:** To determine the outcomes of pregnancy in rhesus negative mothers at District Headquarter Hospital Dera Ismail Khan. **Study Design:** Cross sectional descriptive study. **Duration and Place of Study:** This study was conducted from August 2023 to February 2024 in the Department of Obstetrics and Gynecology, District Headquarter Hospital, Dera Ismail Khan. **Methodology:** A total of 252 rhesus negative pregnant women aged 18 to 40 years with singleton pregnancy and gestational age more than 30 weeks were included. Pregnancy outcomes including caesarean section, fetal distress, neonatal anemia and stillbirth were noted. Data were analyzed using Statistical Package for Social Sciences version 26. Chi square test was applied after stratification and p-value ≤ 0.05 was taken as significant. **Results:** The mean age of participants was 28.83 ± 4.78 years and mean gestational age was 36.77 ± 2.22 weeks. Caesarean section was performed in 59.90% cases, fetal distress was observed in 25.00%, neonatal anemia was found in 9.90% and stillbirth occurred in 5.20% cases. **Conclusion:** Pregnancy in rhesus negative mothers is associated with high rates of caesarean section and notable adverse fetal outcomes such as fetal distress, neonatal anemia, and stillbirth.

INTRODUCTION

Rh-negative pregnant women can be described as those who have red blood cells that lack the RhD antigen, thereby having a Rh-negative blood type.¹ This problem has particular clinical significance in pregnant women in that a Rh-positive fetus, usually inherited from a Rh-positive father, allows for the possible passage of fetal erythrocytes into the maternal circulation, either during pregnancy or delivery.² This exposure can serve as an indication of maternal immune sensitization to Rh, with her producing anti-D antibodies.³ This occurs with higher chances in cases of miscarriage, abdominal trauma, invasive procedures, and antepartum or intrapartum bleeding.³ After the development of anti-D antibodies, these antibodies can cross the placenta during subsequent pregnancy and cause hemolysis of the Rh positive red blood cells of the infant.⁴

In pregnancy outcomes, Rh-negative mothers can show a higher rate of intervention procedures, especially within settings of sensitization or fetal monitoring suggestive of problems.⁵ Cesarean delivery can occur more often because of a decision to deliver earlier if fetal status worsens or reveals a non-reassuring fetal heart rate pattern associated with anemia and hypoxia.⁶ Fetal

distress is noted when the fetus has undergone severe hemolysis due to anemia, which reduces oxygen-carrying capacity, possibly leading to reduced variability of fetal heart rate, late decelerations, and bradycardia, necessitating emergency delivery.⁷ Pregnancies with sensitization usually involve intensive monitoring with ultrasound and Doppler studies of the middle cerebral artery for signs of anemia, and if severe, intrauterine transfusion or planned early delivery becomes necessary.⁸ The postnatal consequences resulting from Rh-incompatibility include anemia of the newborn, jaundice, hydrops fetalis disease in its severe forms, and stillbirth, particularly among mothers who have not received adequate management.⁹ Neonatal anemia is caused by the destruction of fetal and newborn erythrocytes by anti-D antibodies from the mothers.¹⁰ Clinical features among affected newborns include pallor, weak cry, failure to thrive due to lack of feeding, rapid rate of respiratory rate, and low hemoglobin levels measured by laboratory tests.¹¹ These can be relieved through phototherapy, exchange transfusion, or packed cell transfusion depending on their intensities.¹² Stillbirth can result if the process is severe enough to cause congestive heart failure and associated hemhydros due to unrelieved fetal distress,¹³ particularly if

antenatal care is inadequate and no antenatal anti-D prophylaxis is undertaken; thus, the associated risk factor is antenatal care and no antenatal anti-D. In a study by Yadav M, et al. has shown that frequency of caesarean section was 53.6%, fetal distress 17.7%, Neonatal anemia 7.3% and Stillbirth was 6.3% in rhesus negative mothers.¹⁴ There is a requirement for carrying out this research work at Dera Ismail Khan because there is a lack of information available in respect of pregnancy outcomes in Rh-negative women in that area. The hospitals in that area are often faced with resource and late antenatal booking problems; as a result, there may be increased rates of sensitization. By carrying out this research work, accurate rates for caesarean sections, fetal distress, neonatal anemia, and stillbirths can now accurately be ascertained.

METHODOLOGY

The study was carried out at the Department of Obstetrics and Gynecology DHQ Dera Ismail Khan over a period from 01-08-2023 to 01-02-2024. Approval for the study was taken from the institutional ethical committee (No. 50/GJMS, Dated June 22, 2023). All ethical standards related to patient safety, confidentiality and voluntary participation were maintained throughout the study period. A total sample size of 252 participants was included. The sample size was calculated using WHO sample size calculator by taking confidence level of 95%, margin of error of 3% and expected frequency of stillbirth as 6.3% among rhesus negative mothers.¹⁴ The participants were enrolled through non-probability consecutive sampling technique. Women aged between 18 and 40 years having singleton pregnancy confirmed on ultrasonography, gestational age more than 30 weeks calculated from last menstrual period and identified as rhesus negative on Rh screening test were included in the study. Women having history of caesarean section, diabetes mellitus or those with rhesus negative newborn were excluded from the study. Before initiation of data collection, informed consent was taken from each eligible participant after explaining the purpose of the study ensuring privacy and clarifying that there was no additional risk involved by participation.

The study recorded the base-line demographic variables of age, gestational age, and parity. All the enrolled patients were managed according to the Department's guidelines and followed up until delivery. A detailed obstetric history was also gathered. Routine clinical examinations were also carried out during the hospital stay of the patient. The end-points considered for the study were Cesarean delivery, Fetal distress, Neonatal anemia, and Stillbirth. Cesarean delivery was considered to be delivery of the fetus by abdominal route. Fetal distress was considered to be the presence of an abnormal fetal heart rate of more than 160 beats per minute or less than 120 beats per minute, determined by intermittent auscultation or continuous electronic fetal heart rate monitoring. Neonatal anemia was considered to be the venous hemoglobin of less than 13g/dl or capillary hemoglobin of less than 14.5g/dl, analyzed by laboratory tests. Stillbirth was considered to be the fetus of 37 weeks or more, without the heartbeat, confirmed by ultrasonography. All collected data was entered and analyzed using Statistical Package for Social

Sciences version 26. Quantitative variables such as age, gestational age and parity were expressed as mean and standard deviation. Categorical variables including caesarean section, fetal distress, neonatal anemia and stillbirth were presented as frequencies and percentages. Stratification was done with respect to age, gestational age and parity. Post-stratification chi-square test was applied and p-value less than or equal to 0.05 was taken as significant.

RESULTS

The study included total 252 rhesus negative mothers, the mean age of participants was 28.83 ± 4.78 years, mean gestational age was recorded as 36.77 ± 2.22 weeks and mean parity was 1.83 ± 1.18 (as shown in Table 1).

Table 1

Patient Demographics

Demographics	Mean \pm SD
Age (years)	28.83 \pm 4.78
Gestational Age (weeks)	36.77 \pm 2.22
Parity	1.83 \pm 1.18

Regarding pregnancy outcomes in rhesus negative mothers, caesarean section was performed in 151 (59.90%) cases while 101 (40.10%) had normal delivery, fetal distress was observed in 63 (25.00%) cases whereas 189 (75.00%) did not experienced fetal distress, neonatal anemia was found in 25 (9.90%) neonates and 227 (90.10%) neonates were not having anemia, stillbirth was occurred in 13 (5.20%) cases while 239 (94.80%) had live births (as shown in Table 2).

Table 2

Frequency of Pregnancy Outcomes in Rhesus Negative Mothers

Outcomes		Frequency	%age
Caesarean Section	Yes	151	59.90%
	No	101	40.10%
Fetal Distress	Yes	63	25.00%
	No	189	75.00%
Neonatal Anemia	Yes	25	9.90%
	No	227	90.10%
Stillbirth	Yes	13	5.20%
	No	239	94.80%

When association of pregnancy outcomes with demographic factors was analyzed, for caesarean section among mothers aged ≤ 30 years 97 (60.6%) had caesarean section and 63 (39.4%) did not had, while in mothers aged > 30 years 54 (58.7%) underwent caesarean section and 38 (41.3%) did not, the difference was not statistically significant ($p=0.763$). For gestational age ≤ 36 weeks, 71 (64.5%) had caesarean section versus 39 (35.5%) who did not, while for gestational age > 36 weeks 80 (56.3%) had caesarean section and 62 (43.7%) did not, this difference was also not significant ($p=0.187$). Regarding parity, mothers with parity ≤ 2 had 105 (56.8%) caesarean sections and 80 (43.2%) did not, whereas mothers with parity > 2 showed 46 (68.7%) caesarean sections and 21 (31.3%) did not, the p-value was 0.089 showing no significant association (as shown in Table III). For fetal distress, in age group ≤ 30 years 46 (28.7%) experienced

fetal distress while 114 (71.3%) did not, in age group >30 years 17 (18.5%) had fetal distress and 75 (81.5%) did not ($p=0.070$). Among gestational age ≤ 36 weeks, 23 (20.9%) had fetal distress versus 87 (79.1%) who did not, while in gestational age >36 weeks 40 (28.2%) experienced fetal distress and 102 (71.8%) did not ($p=0.187$). For parity ≤ 2 , fetal distress was present in 45 (24.3%) and absent in 140 (75.7%), while for parity >2, it was present in 18 (26.9%) and absent in 49 (73.1%) with p-value of 0.681 (as shown in Table III). Neonatal anemia was observed in 18 (11.3%) neonates born to mothers aged ≤ 30 years while 142 (88.8%) did not had anemia, in mothers aged >30 years 7 (7.6%) neonates had anemia and 85 (92.4%) did not ($p=0.352$). For gestational age ≤ 36 weeks, 11 (10.0%) had neonatal anemia and 99 (90.0%) did not, while for gestational age >36 weeks 14 (9.9%) had anemia and 128

(90.1%) did not ($p=0.970$). In parity ≤ 2 group, 19 (10.3%) neonates had anemia and 166 (89.7%) did not, whereas in parity >2 group 6 (9.0%) had anemia and 61 (91.0%) did not ($p=0.758$) (as shown in Table 3). Stillbirth was reported in 9 (5.6%) cases among mothers aged ≤ 30 years and 151 (94.4%) had live births, while in mothers aged >30 years 4 (4.3%) had stillbirths and 88 (95.7%) had live births ($p=0.774$). Among gestational age ≤ 36 weeks group, 3 (2.7%) had stillbirths and 107 (97.3%) had live births, while in gestational age >36 weeks group 10 (7.0%) had stillbirths and 132 (93.0%) had live births ($p=0.157$). For parity ≤ 2 , stillbirths occurred in 11 (5.9%) cases and live births in 174 (94.1%), whereas for parity >2, stillbirths were 2 (3.0%) and live births were 65 (97.0%) with p-value of 0.523 (as shown in Table 3).

Table 3

Association of Pregnancy Outcomes with Demographic Factors in Rhesus Negative Mothers

Demographic Factors	Caesarean Section		p-value	Fetal Distress		p-value	Neonatal Anemia		p-value	Stillbirth		p-value	
	Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		Yes n(%)	No n(%)		
Age (years)	≤ 30	97 (60.6%)	63 (39.4%)	0.763	46 (28.7%)	114 (71.3%)	0.070	18 (11.3%)	142 (88.8%)	0.352	9 (5.6%)	151 (94.4%)	0.774
	>30	54 (58.7%)	38 (41.3%)		17 (18.5%)	75 (81.5%)		7 (7.6%)	85 (92.4%)		4 (4.3%)	88 (95.7%)	
Gestational Age (weeks)	≤ 36	71 (64.5%)	39 (35.5%)	0.187	23 (20.9%)	87 (79.1%)	0.187	11 (10.0%)	99 (90.0%)	0.970	3 (2.7%)	107 (97.3%)	0.157
	>36	80 (56.3%)	62 (43.7%)		40 (28.2%)	102 (71.8%)		14 (9.9%)	128 (90.1%)		10 (7.0%)	132 (93.0%)	
Parity	≤ 2	105 (56.8%)	80 (43.2%)	0.089	45 (24.3%)	140 (75.7%)	0.681	19 (10.3%)	166 (89.7%)	0.758	11 (5.9%)	174 (94.1%)	0.523
	>2	46 (68.7%)	21 (31.3%)		18 (26.9%)	49 (73.1%)		6 (9.0%)	61 (91.0%)		2 (3.0%)	65 (97.0%)	

*Chi-square Test

DISCUSSION

The mean maternal age of the patients was calculated to be 28.83 ± 4.78 years and showed that most of the Rh-negative mothers were of childbearing age. The mean gestational age of the deliveries was calculated to be 36.77 ± 2.22 weeks and indicated that most of the pregnancies ended up with term deliveries. The mean parity of the mothers was determined to be 1.83 ± 1.18 and showed that most of the mothers had given birth previously. There were 59.90% or a total of 151 C-sections performed in this study and can be considered relatively high in frequency. Such high C-section frequencies can be advocated due to the high-risk nature of the Rh-negative pregnancies and the preference of the obstetrician to perform the C-section rather than risking the negative effects of the hemolytic disease of the newborn. The incidence of fetal distress was found to be 25.00% ($n = 63$). The pathophysiology of Rh incompatibility can account for this event, where the mother's antibody passes into the placenta and causes hemolysis of fetal red blood cells, resulting in anemic and hypoxic conditions of the fetus, thus fetal distress. The compromised blood flow to the fetus can also result in abnormal heart rate patterns. Neonatal anemia occurred in 9.90% ($n=25$), resulting from immune-mediated hemolysis, where maternal IgG antibodies against Rh D antigen can diffuse across the placental barrier, binding to fetal red blood cells, resulting in their breakdown in the fetal spleen and liver. Severity is variably dependent on the serum levels of maternal antibody titers and fetomaternal hemorrhage. Stillbirth rate was 5.20% ($n=13$), a very alarming rate associated with hemolytic disease, when there is widespread destruction of fetal erythrocytes, resulting in severe fetal anemia, hydrops fetalis, congestive cardiac failure, culminating in fetal demise.

In present study, caesarean section rate was 59.90% ($n=151$) which is comparable to findings of Khalil S *et al.* who reported 56.4% caesarean rate in their study of 133 rhesus negative mothers, however this rate is considerably higher than reported by Yadav M *et al.* who found 53.6% caesarean rate and Sagar R *et al.* who observed only 36% caesarean deliveries.¹⁴⁻¹⁵ The higher caesarean rates in present study and Khalil S *et al.* study can be explained by clinician's preference for controlled delivery in rhesus negative mothers to minimize risk of fetomaternal hemorrhage and alloimmunization during labor process, while lower rates in other studies may reflect different institutional protocols and patient selection criteria where vaginal delivery was attempted more frequently in uncomplicated cases. Mean gestational age in current study was 36.77 ± 2.22 weeks which is slightly lower than reported by Puangsricharern A *et al.* who documented mean gestation of 38.8 ± 1.8 weeks and Khalil S *et al.* who found 36.5 ± 1.7 weeks.^{15,17} This difference suggests that present study cohort had more preterm deliveries possibly due to increased surveillance and early intervention in rhesus negative pregnancies when complications like fetal distress or isoimmunization was suspected, whereas other studies may had different criteria for timing of delivery. Fetal distress was observed in 25.00% ($n=63$) cases in present study which is relatively high finding, this rate of fetal compromise indicates significant burden of rhesus incompatibility complications in study population where maternal antibodies causes hemolysis leading to fetal hypoxia. However direct comparison with other studies is difficult as most studies did not specifically reported fetal distress rates as separate outcome parameter and focused more on neonatal complications after delivery. Neonatal anemia was present

in 9.90% (n=25) of neonates in current study which shows similarity with Yadav M *et al.* who reported 7.3% neonatal anemia and Sharma M *et al.* who found 10% neonatal anemia, but is lower than Khalil S *et al.* who documented 12% neonatal anemia rate.^{14,15,18} The comparable rates across these studies reflects similar pathophysiology of immune-mediated hemolysis in rhesus incompatibility where severity depends on maternal antibody titers and degree of sensitization, slight variations may be due to differences in antenatal prophylaxis coverage and timing of delivery in respective study populations. Stillbirth rate in present study was 5.20% (n=13) which is comparable to Khalil S *et al.* who reported 4.5% stillbirths but lower than Yadav M *et al.* who found 6.3% stillbirths and Vaishnavi VS *et al.* who documented 11.42% in retrospective arm and 25% in prospective arm.^{14,15,19} The higher stillbirth rates in some studies particularly Vaishnavi VS *et al.* can be attributed to lack of adequate antenatal anti-D prophylaxis and poor antenatal surveillance in unimmunized mothers leading to severe alloimmunization and hydrops fetalis resulting in intrauterine deaths, whereas relatively lower rates in present study suggests better monitoring and timely interventions.²⁰

There are various limitations associated with the current research, which should be recognized and acknowledged. The research was carried out at a single institution, which may influence its generalizability with respect to diverse demographic characteristics and healthcare settings. The research also had low statistical power with respect to the determination of significant associations with pregnancy outcomes, considering it only took into account 252 rhesus-negative women. The research did not provide data associated with the actual administration of antenatal anti-D prophylaxis, maternal antibody titers, which may have contributed to the evaluation of their relationship

with pregnancy outcomes. Long-term follow-up data of neonates was not available, which may have been helpful in addressing possible long-term outcomes associated with hemolytic disease in neonates caused by Rh D sensitization.

CONCLUSION

Our research reveals that rhesus-negative pregnancies are associated with marked obstetric complications, including high cesarean section rates and high risks of adverse fetal outcomes like fetal distress syndrome, newborn anemia, and stillbirth. The rhesus-negative pregnancy outcomes are likely due to predominantly immunological reasons of maternal alloimmunization against fetal antigens and are independent of maternal and gestational age as well as parity. Early identification of rhesus status in newborn and rhesus-negative pregnancies and following rigorous antenatal care practices along with universally adopting anti-D antenatal prophylaxis programs would go a long way in minimizing maternal and fetal mortality and morbidity related to rhesus incompatibility.

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Ethical Permission

Permission for this research was taken from the Ethical Committee. All procedure was carried out by following committee instructions and the Helsinki rules.

Patient Consent

Before joining the study all patient signed written permission. They were informed that their personal data will be kept confidential and they may withdraw from the study at any time.

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