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Analysis of pregnancy and neonatal outcomes in 100 pregnant women with Rh-negative blood type

Bing-Cai Bi[1†], Hong-Yan Yang[2†], Jun-You Su[2*] and Li Deng[2*]

Abstract

Background This study aimed to explore variations in prenatal care, delivery methods, influencing factors, and neonatal outcomes among Rh-negative pregnant women, so as to improve pregnancy healthcare for this demographic, raise the quality of maternal–fetal management, and safeguard the health of both mother and infant.

Methods This study included 200 women who received routine prenatal care, exhibited no other pregnancy complications, and were admitted for delivery. They were divided into an observation group (100 Rh-negative blood type) and a control group (100 Rh-positive blood type). The study examined differences in pregnancy management, clinical characteristics and pregnancy outcomes between the two groups.

Results The results indicated that singleton pregnancies in Rh-negative mothers are associated with significantly higher rates of postpartum blood loss (305.1 ± 183.8 *vs.* 246.1 ± 84.9 mL, $P = 0.004$), neonatal hyperbilirubinemia (39% *vs.* 23%, $P = 0.014$), low birth weight (11% *vs.* 2%, $P = 0.01$), and NICU admission (30% *vs.* 18%, $P = 0.046$) compared to the control group. Among Rh-negative mothers, subgroup analysis by ethnicity revealed a higher incidence of fetal distress in the other ethnic groups compared to the Han and Zhuang groups (16.7%, 0, 6.5%, respectively, $P = 0.025$). Subgroup analysis based on ABO blood type within Rh-negative mothers did not show any statistical significance in various outcomes (all $P > 0.05$). Infants with neonatal hyperbilirubinemia born to Rh-negative mothers experienced a quicker resolution of hyperbilirubinemia compared to those whose mothers did not receive intramuscular anti-D immunoglobulin [1.0 (1.0, 1.5) *vs.* 5.0 (1.5, 10.0), $P = 0.002$].

Conclusions The Rh-negative blood type is linked to higher risks of neonatal hyperbilirubinemia, low birth weight, and increased postpartum hemorrhage, resulting in detrimental pregnancy outcomes. Administering anti-D immunoglobulin speeds up the resolution of neonatal hyperbilirubinemia. Thus, prudent and efficient use of anti-D immunoglobulin can mitigate adverse outcomes for both mothers and newborns.

Keywords Rh-negative, Pregnancy outcome, Hemolytic disease of newborn, Neonatal hyperbilirubinemia, Anti-RhD immunoglobulin

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Background

The rhesus (Rh) blood group system is the second most important blood group system after the ABO blood group system, and its genes are located on the short arm of chromosome 1 [1]. The Rh system currently contains 110 antigens, of which the Rh (D) antigen is the most immunogenic [2]. In routine laboratory tests, the Rh blood group is determined by the presence or absence of the Rh (D) antigen on the surface of red blood cells. Rh positive (+) denotes the presence of the Rh (D) antigen on red blood cells, while Rh negative (-) denotes the absence of the Rh (D) antigen [3].

Blood groups are important for pregnancy management because there is a high risk of hemolytic disease of newborns (HDN) when maternal and newborn blood groups are incompatible, and Rh-related HDN is more serious [4, 5]. This can result in localized and systemic edema for the fetus and, in severe cases, fetal heart failure or even fetal death [6]. Newborns born under these circumstances are at risk of developing neonatal jaundice, anemia, and other serious complications, which pose a significant threat to the safety of the perinatal infant [7]. According to statistics, rhesus incompatibility affects 3–8 out of every 100,000 patients annually, and before the development of anti-D prophylaxis, it resulted in fetal abortion in 1% of pregnancies [8]. The rational and practical application of anti-D immunoglobulin can substantially lower the frequency of hemolytic diseases in fetuses or newborns [9]. The prevalence of Rh-negative blood type is low, and the population of pregnant and postpartum women with this blood type is even smaller, resulting in restricted blood reserves. In situations involving complications, like postpartum hemorrhage (PH) that demands urgent blood transfusions, the shortage of blood supply greatly complicates the rescue process [10].

This study analyzed the clinical records of 100 singleton pregnant women with Rh-negative blood type hospitalized at Maternity and Child Health Care of Guangxi Zhuang Autonomous Region over the past five years. The study aimed to investigate the impact of Rh-negative blood type on pregnancy status, delivery outcomes and provide valuable data regarding the management of Rh-negative blood type pregnancies and prenatal care.

Methods

Subjects

From October 2018 to October 2023, 100 cases (38 primiparas and 62 multiparas) of 193 Rh-negative pregnant women who received regular prenatal care and were hospitalized for delivery at Maternity and Child Health Care of Guangxi Zhuang Autonomous Region were selected as the observation group based on the following criteria: all pregnant women had no other pregnancy complications. Furthermore, according to the principle of statistical equivalence and the following criteria, we randomly selected 100 cases (45 primiparas and 55 multiparas) with uncomplicated pregnancies from 51,204 Rh-positive pregnant women as the control group.

The inclusion criteria included regular and standardized prenatal checkups at outpatient clinics throughout pregnancy, complete prenatal examination data, singleton pregnancy, and a husband with an Rh-positive blood group. The exclusion criteria included pregnant women with blood system diseases, hypertension, diabetes, chronic kidney disease, thyroid dysfunction, immune disease, heart disease, infectious disease, or other ailments. Additionally, women with multiple gestation, husbands with Rh-negative blood group, maternal and fetal thalassemia, recent history of trauma and blood transfusion treatment, and significantly incomplete clinical data were also excluded. The cases were categorized into two groups: the observation group consisting of 100 single pregnant women with Rh-negative blood type, and the control group comprising 100 single pregnant women with Rh-positive blood type. For pregnant women with confirmed Rh-negative blood type, 1500 IU of anti-D immunoglobulin is injected intramurally at 28 weeks of gestation if no sensitization occurs. The study received approval from the Ethics Committee of Guangxi Maternal and Child Health Hospital (Research Review Report Number: GXMCHH-Ethics-2018–2-1). All participants provided informed consent by signing the consent form.

Screening of Rh-negative pregnant women and monitoring of postpartum newborns.

Prenatal testing for ABO and Rh blood types on a routine basis is essential. Upon diagnosing a Rh-negative blood type in pregnant women, it is imperative to promptly notify the neonatologist and maintain continuous monitoring of the newborn postpartum for timely intervention. The newborn should be promptly transferred to the neonatology department for further care if needed. Furthermore, if the newborn is Rh-positive, the mother should be given postpartum immunoprophylaxis within 24 h of delivery.

Observational indexes.

A retrospective analysis was performed on clinical data from two groups of parturients, including their demographic details [age, admission Body Mass Index (BMI), gravidity, parity, and gestational age at delivery] and pregnancy outcomes [PH, mode of delivery, stillbirth, preterm birth (PB), meconium-stained amniotic fluid (MSAF), neonatal asphyxia (NA), neonatal hyperbilirubinemia (NH; defined as elevated serum total bilirubin (TSB) levels, clinically manifested as jaundice, affecting most newborn infants [11]), and low birth weight (LBW; birth weight < 2,500 g [12])]. Moreover, this study also

analyzed the potential sensitizing events, including villi puncture, amniotic fluid puncture, placental abruption, stillbirth during current pregnancy, and previous pregnancy abortion or ectopic pregnancy history, as well as the results of indirect coombs of the two groups.

Statistical analysis

The analysis utilized SPSS 26.0 (IBM, Armonk, New York). The normality of the econometric data was assessed using the Shapiro–Wilk method. Data adhering to a normal distribution were presented as mean ± standard deviation (SD) and analyzed using independent sample *t*-tests or analysis of variance. For non-normally distributed data, comparisons were conducted using the median [Q1, Q3] and the Mann–Whitney U test or Kruskal–Wallis H test, with intergroup comparisons performed using the Bonferroni method. Categorical data was expressed as frequency (percentage) and analyzed using the Chi-square or Fisher's exact test. A P-value < 0.05 was defined as statistically significant.

Results

Subject information

In our study, 200 subjects were enrolled, with 100 in each control and observation group. According to general data, the average ages of the control and observation groups were 30.2 ± 4.8 years and 30.1 ± 5.2 years, respectively. No statistically significant differences were observed in age, BMI, gravidity, parity, and gestational age at delivery between the two groups (all $P > 0.05$) (Table 1). Additionally, the data showed that there were only 2 cases of amniotic fluid puncture and 1 case of previous ectopic pregnancy history, which were not statistically significant.

Comparisons of pregnancy and neonatal outcomes

In the observation group, postpartum bleeding volume was significantly higher compared to the control group [305.1 ± 183.8 *vs.* 246.1 ± 84.9 mL, $P = 0.004$]. However, the 50 mL difference between the two groups for postpartum bleeding is highly unlikely to have any clinical significance. The observation group also demonstrated elevated incidence of neonatal hyperbilirubinemia (39.0% *vs.* 23.0%, $P = 0.014$), low birth weight (11.0% *vs.* 2.0%, $P = 0.01$) and NICU admission (30.0% *vs.* 18%, $P = 0.046$) in contrast to the control group. However, ICU admission rate for pregnant women, rates of postpartum bleeding, cesarean section, stillbirth, preterm birth, fetal distress, neonatal asphyxia and days to recovery-exit from NICU did not display statistically significant differences between the two groups (all $P > 0.05$) (Table 2). Furthermore, the positive rate of indirect coombs for pregnant women in the observation group was higher than that in the control group ($P = 0.001$), but further verification showed that indirect coombs positive results had no statistical significance on pregnancy and neonatal outcomes.

Table 2 Comparisons of pregnancy and neonatal outcomes between the control and observation groups

Outcomes	Control group ($n = 100$)	Observation group ($n = 100$)	P
PH, n (%)	4 (4.0)	0 (0.0)	0.130
PBL (mL)	246.1 ± 84.9	305.1 ± 183.8	0.004
CS, n (%)	17 (17.0)	26 (26.0)	0.214
Stillbirth, n (%)	0 (0.0)	2 (2.0)	0.477
PB, n (%)	3 (3.0)	6 (6.0)	0.495
FD, n (%)	3 (3.0)	4 (4.0)	> 0.999
NA, n (%)	0 (0.0)	2 (2.0)	0.477
NH, n (%)	23 (23.0)	39 (39.0)	0.014
LBW, n (%)	2 (2.0)	11 (11.0)	0.010
ICU admission, n (%)	0 (0.0)	2 (2.0)	0.249
NICU admission, n (%)	18 (18.0)	30 (30.0)	0.046
Recovery-exit from NICU (days)	5.0 (4.0, 7.0)	5 (3.0, 8.0)	0.279
Indirect coombs	0 (0.0)	10 (10.0)	0.001

PBL were compared using independent samples *t*-tests, while the other variables were analyzed using either the chi-square test or Fisher's exact test

CS Cesarean section, *NA* Neonatal asphyxia, *NH* Neonatal hyperbilirubinemia, *FD* Fetal distress, *LBW* Low birth weight, *PB* Premature birth, *PH* Postpartum hemorrhage, *PBL* Postpartum blood loss

Table 1 Comparisons of general information between the control and observation groups

General information	Control group ($n = 100$)	Observation group ($n = 100$)	P
Age (year)	30.2 ± 4.8	30.1 ± 5.2	0.876
BMI (kg/m^2)	20.7 ± 2.1	20.7 ± 2.3	0.929
Number of gravidities	2.0 (1.0, 3.0)	2.0 (1.5, 3.0)	0.595
Number of parities	2.0 (1.0, 2.0)	2.0 (1.0, 2.0)	0.292
Gestational age at delivery (weeks)	39.3 (38.7, 40.0)	39.4 (38.5, 40.3)	0.445

Age and BMI were compared using independent samples *t*-tests, while the other variables were analyzed using the Mann–Whitney U test

The impact of ethnicity on pregnancy and neonatal outcomes in Rh-negative pregnant women.

In this investigation, 100 Rh-negative pregnant women in the Guangxi region were divided into three groups according to the predominant ethnicities: 63 Han, 31 Zhuang, and 6 other ethnicities. Analysis of hospitalization duration, neonatal hyperbilirubinemia, preterm birth, low birth weight, and neonatal asphyxia across the three groups revealed no statistically significant differences (all $P>0.05$). Nevertheless, the prevalence of fetal distress in the "other" ethnic category exhibited a notably higher rate compared to the Han and Zhuang groups (16.7%, 0, 6.5%, $P=0.025$) (Table 3).

The impact of ABO blood type on neonatal outcomes in Rh-negative pregnant women.

In this study, one hundred Rh-negative pregnant women were segregated into four groups based on their ABO blood types: 44 with blood type O, 24 with blood type A, 24 with blood type B, and 8 with blood type AB. Analysis of factors such as hospital stay duration, fetal distress, neonatal hyperbilirubinemia, preterm birth, low birth weight, and neonatal asphyxia incidence across these groups indicated no statistically significant differences (all $P>0.05$) (Table 4).

Table 3 The impact of ethnicity on pregnancy and neonatal outcomes in Rh-negative pregnant women

Outcomes	Han ($n=63$)	Zhuang ($n=31$)	Others ($n=6$)	P
LOHS	3.0 (2.0, 4.0)	3.0 (2.5, 4.0)	4.0 (3.0, 4.0)	0.321
FD, n (%)	0 (0.0)	2 (6.5)	1 (16.7)[a]	0.025
NH, n (%)	22 (34.9)	14 (45.2)	3 (50.0)	0.523
PB, n (%)	4 (6.3)	2 (6.5)	0 (0.0)	>0.999
LBW, n (%)	5 (7.9)	6 (19.4)	0 (0.0)	0.272
NA, n (%)	1 (1.6)	0 (0.0)	1 (16.7)	0.113

NH Neonatal hyperbilirubinemia, *FD* Fetal distress, *LOHS* Length of hospital stay, *PB* Premature birth, *LBW* Low birth weight, *NA* Neonatal asphyxia

[a] indicates a significant difference from the Han ethnic group, with a *p*-value less than 0.05. LOHS was evaluated using the Kruskal–Wallis H test, while other comparisons were conducted using either the chi-square test or Fisher's exact test

The impact of intramuscular injection of anti-D immunoglobulin on neonatal outcomes in Rh-negative pregnant women.

Among 100 Rh-negative pregnant women, 37 received anti-D immunoglobulin during pregnancy and 63 did not receive anti-D immunoglobulin. Among 39 neonates with hyperbilirubinemia born to Rh-negative mothers, 28 were hospitalized in the neonatal department for treatment. They were divided into two groups based on whether the mother received intramuscular anti-D immunoglobulin. Neonates born to mothers who received this immunoglobulin showed a significantly shorter time for hyperbilirubinemia resolution than those born to mothers who did not receive it [1.0 (1.0, 1.5) *vs.* 5.0 (1.5, 10.0), $P=0.002$]. There were no statistically significant differences (all $P>0.05$) between the two groups in terms of hyperbilirubinemia onset, NICU admission, hemoglobin levels at admission, total bilirubin levels, need for neonatal blood transfusion, incidence of neonatal ABO hemolysis, and incidence of neonatal Rh hemolysis, as detailed in Table 5.

Discussion

Numerous studies have shown that Rh-negative pregnant women face an elevated risk of developing hemolytic disease of the fetus and newborn (HDFN), which can lead to various complications such as fetal anemia, edema, jaundice, intrauterine growth restriction, premature birth, or stillbirth. Offspring born to Rh-negative mothers are also at risk of neonatal jaundice, anemia, and mortality, posing a significant threat to neonatal well-being [9, 13]. Maternal–fetal blood type incompatibility can result in fetal anemia, hypoxia, and growth impairments, leading to the birth of low birth-weight infants. Our investigation revealed significantly higher incidences of neonatal jaundice and low birth weight infants among Rh-negative mothers compared to the control group ($P<0.05$), consistent with existing literature. These differences are attributable to Rh-negative blood type, but rational and effective use of anti-D immunoglobulin can reduce these

Table 4 The impact of ABO blood type on neonatal outcomes in Rh-negative pregnant women

Neonatal outcomes	Type O ($n=44$)	Type A ($n=24$)	Type B ($n=24$)	Type AB ($n=8$)	P
LOHS	3.0 (2.0, 4.0)	3.0 (2.0, 3.5)	4.0 (2.0, 4.0)	2.5 (2.0, 4.5)	0.238
FD, n (%)	1 (2.3)	0 (0.0)	2 (8.3)	0 (0.0)	0.480
NH, n (%)	19 (43.2)	6 (25.0)	10 (41.7)	4 (50.0)	0.413
PB, n (%)	5 (11.4)	0 (0.0)	0 (0.0)	1 (12.5)	0.096
LBW, n (%)	8 (18.2)	0 (0.0)	2 (8.3)	1 (12.5)	0.116
NA, n (%)	2 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0.570

LOHS was evaluated using the Kruskal–Wallis H test, while other comparisons were conducted using either the chi-square test or Fisher's exact test

NH neonatal hyperbilirubinemia, *FD* fetal distress, *LOHS* Length of hospital stay, *PB* premature birth, *LBW* Low birth weight, *NA* Neonatal asphyxia

Table 5 The outcomes for neonates with hyperbilirubinemia based on maternal administration of anti-D immunoglobulin during pregnancy

Neonatal outcomes	Maternal anti-D immunoglobulin (*n* = 16)	Non-maternal anti-D immunoglobulin (*n* = 12)	P
OTNH (days)	2.0 (1.0, 2.0)	1.0 (1.0, 1.5)	0.119
RTNH (days)	1.0 (1.0, 1.5)	5.0 (1.5, 10.0)	0.002
Admitted to NICU, n (%)	3 (18.8)	4 (33.3)	0.659
Admission hemoglobin (g/L)	161.5 (152.0, 174.5)	149.0 (140.5, 162.5)	0.114
TB (umol/L)	201.0 ± 68.4	194.4 ± 53.0	0.784
ABO haemolysis, n (%)	1 (6.3)	1 (8.3)	> 0.999
NBT, n (%)	1 (6.3)	2 (16.7)	0.791
Rh haemolysis, n (%)	1 (6.7)	2 (16.7)	0.837

Mann–Whitney U tests were conducted for OTNH, RTNH, and Admission hemoglobin. TB was analyzed using an independent samples *t*-test, while the other variables were evaluated through chi-square tests or Fisher's exact tests

NBT Neonatal blood transfusion, *OTNH* Onset time of neonatal hyperbilirubinemia, *RTNH* Resolution time of neonatal hyperbilirubinemia, *TB* Total bilirubin

adverse outcomes. Prior research by Daniel Rosenkrans and colleagues indicated that before the introduction of anti-D immunoglobulin, 1% of pregnancies ended in fetal demise due to HDFN [14]. Present data suggests that 3 to 8 cases of HDFN occur per 100,000 pregnancies. Untreated neonatal jaundice can have long-lasting adverse effects, including deafness, disabilities, blindness, brain damage, and developmental challenges [14, 15]. A meta-analysis conducted by Mary Cannon and collaborators in 2002 established a strong link between Rh immune hemolysis and schizophrenia in adulthood, with neonatal jaundice identified as a risk factor for future mental health disorders [16]. It is evident that Rh-negative pregnant women face specific risks during pregnancy, underscoring the critical importance of timely medical interventions and thorough prenatal monitoring to detect and prevent HDFN, thereby ensuring favorable pregnancy outcomes.

According to statistics, the proportion of Rh-negative blood type in the population of European and American countries is about 15%, while the Rh-negative blood type in the Uighur population in China is about 5%, and the Rh-negative blood type in the Han population is only 0.2%-0.5% [17]. The Rh-negative blood type, often known as "panda blood", is rare in the general population, particularly among pregnant women. Postpartum hemorrhage, a prevalent and severe complication in obstetrics, frequently leads to maternal mortality, emphasizing the critical need for an adequate blood supply for effective treatment [18, 19]. The scarcity of Rh-negative blood presents challenges for blood centers and hospital transfusion services across various regions, complicating rescue efforts during cases of postpartum hemorrhage. This study identified a significant increase in postpartum blood loss among Rh-negative pregnant women with singleton pregnancies compared to the control group ($P = 0.006$). While the causes of postpartum hemorrhage are typically multifaceted and may not directly correlate with a woman's Rh blood type, the limited availability of Rh-negative blood creates barriers in situations necessitating extensive and immediate blood transfusions during emergency interventions. This scarcity could hinder the effectiveness and timeliness of treatment, thereby impacting the incidence of postpartum hemorrhage cases. A poignant case study illustrates the critical importance of blood, as a Rh-negative pregnant woman tragically succumbed to excessive bleeding during a miscarriage surgery due to the unavailability of pre-prepared blood resources [20]. Some scholars recommend the use of autologous blood transfusion as an effective strategy for managing deliveries involving Rh-negative pregnant individuals. This approach helps address blood supply shortages and reduces the risks associated with allogeneic blood transfusions, thereby improving transfusion safety and appropriateness [21]. Importantly, autologous blood transfusion poses no risks to the mother or fetus [22]. Long-term observations indicate that healthy pregnant individuals with normal prenatal examinations can safely store their own blood before delivery without experiencing adverse effects, as long as the amount collected does not exceed 400ml or 10% of their total blood volume. Therefore, advocating for autologous blood transfusion in Rh-negative pregnant individuals during delivery is justified [23]. A comprehensive peri-delivery management approach for Rh-negative pregnant individuals should include preventive measures and effective protocols for managing postpartum hemorrhage to ensure a stable blood supply and protect the well-being of these individuals.

The distribution of Rh-negative blood type exhibits significant variation among races, regions, and ethnicities. Sun et al. [24] reported a substantial influence of population migration on the distribution of blood types from 1998 to 2018. The prevalence of hemolytic disease of the newborn is closely associated with the differing frequencies of Rh-negative blood types among various ethnic groups. A comprehensive understanding of Rh blood type distribution within diverse ethnic populations is crucial for preventing Rh hemolytic disease in neonates [25]. Our study conducted a subgroup analysis based on maternal ethnicity, revealing a notable discrepancy, with a significantly higher occurrence of fetal distress among other ethnic groups compared to the Han and Zhuang groups (16.7%, 0, 6.5%, respectively, $P=0.025$). This variation may be linked to the socio-economic obstacles faced by individuals from non-Han ethnicities, particularly those residing in remote and disadvantaged regions, which could impede their access to adequate medical services and contribute to adverse pregnancy outcomes. The relationship between ethnicity and Rh pregnancy outcomes is debated due to variations in cultural, population, and clinical settings. Limited research exists on the impact of different ethnicities on perinatal outcomes in Rh-negative pregnant women, both nationally and globally. It is imperative to conduct future prospective cohort studies and establish multicenter research initiatives to increase sample sizes for validation.

The ABO and Rh, blood group systems, are recognized as highly significant in the human body, operating independently without direct correlation. Our subgroup analysis, based on maternal and neonatal ABO blood types, did not reveal significant differences in adverse pregnancy outcomes, such as fetal distress, neonatal hyperbilirubinemia, preterm birth, low birth weight, and neonatal asphyxia. According to Practical Obstetrics and Gynecology, Third Edition, ABO incompatibility between the mother and baby may provide some protection against Rh isoimmunization by preventing the stimulation of Rh antigens in the mother's body and subsequent fetal hemolysis. Further research is needed to explore the potential influence of ABO blood type on pregnancy outcomes in Rh-negative pregnant women.

The effectiveness of anti-D immunoglobulin prophylaxis in preventing RhD immunization and HDFN has been well-documented in various studies [26, 27]. Since its introduction in the late 1960s, anti-D immunoglobulin prophylaxis has substantially reduced the risk of sensitization from 13% to approximately 1% [28]. A meta-analysis conducted by Turner et al. [29], accounting for bias, robustly advocates the efficacy of anti-D immunoglobulin in averting sensitization in Rh-negative pregnant women, endorsing its utilization in all unsensitized Rh-negative pregnant women. The research proposes that the most efficacious dosage is 1250 IU of intramuscular anti-D immunoglobulin at 28 and 34 weeks of pregnancy, while a singular dose of 1500 IU at 28–30 weeks is less effective. These outcomes are consistent with the recommendations outlined in the latest clinical guidelines issued in March 2023 in Queensland [30]. The likelihood of maternal–fetal Rh blood type incompatibility stands at approximately 1% during the initial pregnancy or shortly thereafter. HDFN can result from Rh blood type incompatibility during pregnancy, studies found that administration of 500 IU of anti-D immunoglobulin to primigravid women can diminish this probability to roughly 0.2%, with no notable adverse reactions documented [31]. This underscores the safety of anti-D immunoglobulin administration for immunoprophylaxis. The administration of anti-D immunoglobulin within 72 h postpartum diminishes the likelihood of Rh-negative mothers birthing Rh-positive infants and developing Rh isoimmunization [32]. In a study involving 28 neonates with hyperbilirubinemia admitted to the neonatology department for treatment, we observed a faster resolution of hyperbilirubinemia ($P=0.002$) in neonates born to mothers who received anti-D immunoglobulin injections. However, no significant differences were found between the two groups in terms of the onset of neonatal hyperbilirubinemia, admission to the NICU, neonatal hemoglobin levels, total bilirubin levels, neonatal blood transfusions, neonatal ABO hemolysis, and neonatal Rh hemolysis. This observation can be attributed to the preventive role of anti-D immunoglobulin in inhibiting Rh-negative pregnant women from producing considerable quantities of anti-D antibodies. It can be seen that neonates born to mothers who received anti-D immunoglobulin demonstrate decreased hemolysis, reduced bilirubin levels, and expedited resolution of neonatal hyperbilirubinemia. Consequently, tailored management and surveillance of Rh-negative pregnant women are imperative. Discriminatory dispensation of anti-D immunoglobulin should be contemplated for unsensitized Rh-negative pregnant women to ensure appropriate usage and efficient management of neonatal hemolytic disease.

The study also has several limitations. Our study was a single-center study which was limited by region and lacked representative samples, and also the sample size of our study was small. Lastly, data concerning the occurrence of bleeding among patients in the first trimester and information regarding the management of such cases in previous pregnancies were ultimately unavailable. Additionally, the absence of data on the results of Kleihauer-Betke test were also missing, this issue limited the analysis. Therefore, in the future, multi-center, prospective cohort studies with a large

enough sample size and comprehensive and in-depth analysis of relevant data are needed to further provide more clinical evidence for pregnancy management and perinatal management of Rh-negative pregnant women.

Conclusions

In conclusion, healthcare providers must prioritize the management of high-risk pregnancies in Rh-negative women. Standardizing protocols for diagnosis, treatment, and follow-up is essential. Improving prenatal monitoring and management, maintaining an adequate blood supply, and administering anti-D immunoglobulin are vital steps to safeguarding the health of both the mother and the infant.

Abbreviations

BMI	Body Mass Index
HDFN	Hemolytic disease of the fetus and newborn
HDN	Hemolytic disease of newborn
LBW	Low birth weight
MSAF	Meconium-stained amniotic fluid
NA	Neonatal asphyxia
NH	Neonatal hyperbilirubinemia
PB	Preterm birth
PH	Postpartum hemorrhage
Rh	Rhesus
SD	Standard deviation

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Not applicable.

Authors' contributions

Conceptualization: Bingcai Bi, Hongyan Yang. Data curation: Bingcai Bi. Formal analysis: Hongyan Yang. Methodology: Bingcai Bi. Writing – original draft: Bingcai Bi, Hongyan Yang. Writing – review & editing: Junyou Su, Li Deng.

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Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The study received approval from the Ethics Committee of Guangxi Maternal and Child Health Hospital (Research Review Report Number: GXMCHH-Ethics-2018–2-1). All participants provided informed consent by signing the consent form.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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