AFRICAN JOURNAL OF FETOMATERNAL MEDICINE

Original Article

Prevalence and Foetal Outcomes of Rhesus Negative Pregnancies in A Tertiary Healthcare Institution in Abuja, Nigeria

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Abstract

Objectives: To determine the prevalence and fetal outcomes of Rhesus negative pregnancies in a tertiary healthcare institution in Abuja, Nigeria. **Methodology:** This was a retrospective cross-sectional review of the outcome of 141 cases of Rhesus negative pregnancies managed within the study period of January 1st to 31st December 2021. Available data of cases managed were entered into and analyzed using IBM SPPSS version 23. Descriptive statistics such as percentage were calculated for sociodemographic and obstetric variables. Tests of association between categorical variables were done using the Chi-square or Fisher's exact test where appropriate. Significance level was set at P<0.05. **Results:** The prevalence of Rhesus negative pregnancies during the period was 0.8%. There was 1/141 (0.7%) case of Rhesus-isoimmunization. The majority, 93/141 (66.0%) were multiparous, booked for antenatal care;128/141 (90.8%), had term deliveries; 124/141 (87.9%), and had spontaneous vaginal delivery; 119/141(84.4%). Outcome of delivery were live births in 134/141(95.0%) of cases while the remaining 7/141(5.0%) were still births. Majority of the newborn at discharge were alive and well 127/134 (94.8%). Increasing age of parturient (P=0.034), unbooked status (P<0.001). and preterm births (P < 0.001) were associated with poor foetal outcome. **Conclusion:** The prevalence of Rhesus negativity amongst pregnant women was low. However, the pregnancies were associated with high still birth rate and poor perinatal outcome which were unrelated to Rhesus Isoimmunization. Increased awareness about Rhesus negativity in pregnancy and attendance of antenatal care will help improve foetal outcome for this high-risk obstetric population.

Key words: Rhesus Negative, Pregnancy, Prevalence, Foetal, Nigeria

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Introduction

Rhesus negative mothers constitute a high-risk cohort of the obstetric population with elevated risk for poor perinatal outcomes particularly when Rhesus Isoimmunization which is an immunologic reaction against foreign antigens that are distinct from antigens on an individual's cells occurs.[1]

The prevalence of Rhesus D negative blood group in the general population have been known to have some regional variations being higher in white populations than other ethnic groups.[2] This variation in prevalence is also apparent amongst Nigerian pregnant populations with a prevalence rate of 2.6-4.5% reported in Southeast Nigeria,[3,4] 5-8.9% in Southwest Nigeria,[5,6,7] and 0.7% in Kaduna, North Central Nigeria.[8]

Antenatal care for Rhesus-negative pregnancies involves investigating for sensitization from the first visit.[1,9] Rhesus blood typing, indirect Coombs test is used to detect unbound antibodies in maternal serum.[9] If antibodies are detected the woman is managed as a Rhesus-D alloimmunized mother.[9,10] If antibodies are not detected, she is managed as a Rhesus D non-sensitized mother.[1,9] For the Rhesus D non-sensitized woman, management is geared towards prevention of alloimmunization which is achievable through the use of Anti-D immunoglobulin. A protocol of administering anti-D immunoglobulin routinely at 28 weeks, after delivery (if indicated by a Rhesus (D)-positive infant), and for other indications as they arise, was noted to drastically reduce the rate of sensitization from 16% to 0.1-0.3%.[1,9,10].

Despite the proven benefits of administration of Anti-D immunoglobulin prophylaxis, cases of Rhesus isoimmunization still exist among the Rhesus-negative pregnant populations in Nigeria[3,4,5,6] with rates as high as 28.2% recorded among babies delivered to Rhesus negative mothers in Enugu State.[4] The reasons for the poor perinatal outcome include but are not limited to: inadequate antenatal practices that often fails to identify Rhesus negative women, the high cost of procuring anti-D immunoglobulin, failure to recognize potentially sensitizing events in pregnancy and treating them appropriately, and noncompliance with postpartum prophylaxis guidelines to offer anti-D immunoglobulin to all Rhesus negative women delivered of Rhesus-positive babies within 72 hours of delivery.[3,5,6].
Hitherto, there has not been any published literature regarding Rhesus negativity in pregnancy from Nigeria's Federal Capital Territory, Abuja. The objective of this study was therefore to determine the prevalence and perinatal outcome of Rhesus-negative pregnant women managed in a tertiary health care institution in Abuja, Nigeria.

Materials and Methods

This was an 11-year retrospective cross-sectional study of Rhesus negative women who presented for management during labour/delivery at the University of Abuja Teaching Hospital between 1st January 2010 to 31st December 2021. Data was obtained from the labour and delivery registers of the hospital and supplemented by data from the maternity wards and theatre. Only 141 out of 174 case folders of Rhesus negative women managed during the period was retrievable and used for analysis. The folder retrieval rate was 81%.

The ABO blood group as well as the Rhesus D factors are part of the routine investigations done during the antenatal booking, and during delivery for unbooked patients. Indirect Coombs test is requested for all Rhesus negative women at booking visits. If the result is negative, follow-up testing is done at 28 weeks gestation. If the result is positive, the patient is managed as Rhesus sensitized pregnancy. Rhesus sensitized women with history of no previous foetus affected by Rhesus isoimmunization are usually followed up with antibody titres at booking, 20 weeks of gestation and then every 2-4 weeks intervals. Rhesus sensitized women with history of previous foetus affected by Rhesus isoimmunization are followed up with Doppler ultrasound of the middle cerebral artery (MCA). Parameters such as the peak systolic volume is compared with appropriate charts to ascertain the level of fetal anaemia and patients managed accordingly.

The relevant information including phone number, biodata, booking status, parity, approximate gestational age at delivery, whether baby was born alive or as stillbirth, neonatal jaundice, and admission of neonate in the special care baby unit were collected using a semi-structured data collection tool. The phone number was used to contact the women to ascertain some of the outcome parameters (whether baby was jaundiced at birth, state of baby at discharge, whether the mother received anti-D immunoglobulin and why it was not given if the records suggested that baby was Rhesus positive) when not available in the folder. The study was approved by the hospital's research and ethics committee.

Data were entered and analysed using the IBM Statistical Package for Social Sciences (SPSS

Statistics) version 23. The categorical variables were summarized and presented as frequency distribution tables, while continuous variables were presented as mean (standard deviation). Test of association for categorical variables was done with Chi-square and Fishers exact where majority of the cells were < 5 or contained zero. P-value was set at < 0.05 to be statistically significant. Missing data were treated using pair wise deletion.

Results

There were 22,478 deliveries during the period out of which 174 were Rhesus negative pregnancies. The prevalence of Rhesus negative pregnancies was therefore 0.8%. Only one (0.7%) case of Rhesus D alloimmunization occurred amongst the study cohort.

Table 1 Sociodemographic and obstetric characteristics

Variables	Frequency(N=141)	Percent
Age Group (Years)		
<20	3	2.1
20-29	83	58.9
≥30	55	39.0
Marital Status		
Single	1	0.7
Married	140	99.3
Religion		
Islam	50	35.5
Christianity	91	64.5
Educational Level		
None	4	2.8
Primary	10	7.1
Secondary	55	39.0
Tertiary	72	51.1
Employment Status		
Unemployed	70	49.6
Employed	71	50.4
Booking Status		
Booked	128	90.8
Unbooked	13	9.2
Parity		
1	48	34.0
2-4	86	61.0
≥5	7	5.0
Approximate Gestational age at delivery		
Preterm	15	10.6
Term	124	87.9
Post Term	2	1.4
Mode of delivery		
Instrumental	5	3.5
Caesarean Section	17	12.1
Vaginal	119	84.4

Table 2: Foetal outcome

Variables	Frequency(N=141)	Percent
Fetal outcome		
Live birth	134	95.0
Fresh still birth	7	5.0
Blood group of babies	n=90	
O +	56	62.2
A+	8	8.9
O -	14	15.6
B+	2	2.2
B-	5	5.6
A-	3	3.3
AB+	2	2.2
Did baby develop jaundice?	n=134	
Yes	13	9.7
No	121	90.3
Was baby admitted to SCBU?	n=134	
Yes	14	10.4
No	120	89.6
State of baby at discharge	n=134	
Alive and well	127	94.8
Alive but sick	3	2.2
Dead	4	3.0

Socio-Demographic and Obstetrics Characteristics

The age of the participants ranged from 19 to 40 years with a mean age of 28.2±4.6 years. Most of the participants were married, 140 (99.3%), had at least secondary level of education,127 (90.1%), and were multiparous, 93 (66.0%). Majority were booked for antenatal care, 128 (90.8%) and carried the pregnancy to term 124 (87.9%) with mean age at delivery being 38.9 ±1.78 weeks. The mode of delivery for most of them were vaginal occurring in 119 (84.4%). These are shown in Tables 1

Perinatal Outcome and Use of Anti-D Immune Prophylaxis

Live births occurred in 134 (95.0%) of cases while the remaining 7 (5.0%) were fresh still births. Thirteen (9.7%) of the live births had neonatal jaundice while 14 (10.4%) were admitted into the Special Care Baby Unit (SCBU). Majority of the neonates at discharge were alive and well 127 (94.8%). Evidence of confirmation and record of the blood group of the new-borns was seen only in 90 out of the 134 live births. Of these 90 recorded blood

groups, 68 (75.6%) were Rhesus Positive with O+ being the predominant in 56(62.2%). These are shown in Table 2.

Table 3: Association Between Foetal Outcome And Sociodemographic Variables

	Foetal outcome			
Variables	Live birth n=134 n (%)	Fresh still birth n=7 n (%)	χ^2	P-value
Age Group (Years)			6.763	0.034*
<20	3(2.2)	0(0.0)		
20-29	82(61.2)	1(14.3)		
≥30	49(36.6)	6(85.7)		
Marital Status			0.053	0.819^f
Single	1(0.7)	0(0.0)		
Married	133(99.3)	7(100.0)		
Religion			0.176	0.699^f
Islam	47(35.1)	3(42.9)		
Christianity	87(64.9)	4(57.1)		
Educational Level			1.450	0.694
None	4(3.0)	0(0.0)		
Primary	10(7.5)	0(0.0)		
Secondary	51(38.1)	4(57.1)		
Tertiary	69(51.4)	3(42.9)		
Employment Status			1.398	0.275^f
Unemployed	65(48.5)	5(71.4)		
Employed	69(51.5)	2(28.6)		

^{f}-Fisher's Exact test*-significant at 95%

Table 4: Association Between Obstetrics Characteristic and Foetal Outcome

	Foetal outcome			
Variables	Live birth n=134 n(%)	Fresh still birth n=7 n(%)	χ^2	P-value
Booking Status			20.211	0.001^f
Booked	125(93.3)	3(42.9)		
Un booked	9(6.7)	4(57.1)		
Gestational Age at Booking	n=125	n=3	1.969	0.374
First Trimester	12(9.6)	0(0.0)		
Second Trimester	75(60.0)	3(100.0)		
Third Trimester	38(30.4)	0(0.0)		
Parity			0.552	0.759
1	45(33.6)	3(42.9)		
2-4	82(61.2)	4(57.1)		
≥5	7(5.2)	0(0.0)		
Approximate Gestational age at delivery			16.781	<0.001*
Preterm	11(8.2)	4(57.1)		
Term	121(90.3)	3(42.9)		
Post Term	2(1.5)	0(0.0)		
Mode of delivery			3.285	0.193
Vaginal	113(84.3)	6(85.7)		
Instrumental	4(3.0)	1(14.3)		
Caesarean Section	17(12.7)	0(0.0)		

^{f}-Fisher's Exact test*-significant at 95%

When contacted on phone, out of 127 mothers reached, 71 (55.9%) confirmed that they received anti-D immune globulin in the postpartum period while 56(44.1%) didn't receive. When the latter group were asked why they didn't receive anti D immune globulin, 26 (46.4%) said that they were not aware if they were supposed to receive the injection, 8 (14.3%) complained of financial constraints, 8 (14.3%) mentioned that they had completed their family size, 12 (21.4%) reported that their babies were Rhesus Negative. The remaining 2(3.6%) didn't have any reason.

Association Between Some Sociodemographic Variables with Foetal Outcome and Neonatal Admissions

The age of the Rhesus negative parturient showed a significant association with fetal outcome as most of the still born occurred in the older parturient (P=0.034). Other socio-demographic variables among this cohort of women did not reveal any significant association as seen in Table 3.

Association Between Obstetric Characteristics and Foetal Outcome

Booking status showed a statistically significant association with fetal outcome with poor fetal outcome being greater among the unbooked parturient when compared to booked parturient (P=0.001). Approximate gestational age at delivery also showed significant association with fetal outcome (P < 0.001). Other variables had no significant association with fetal outcome. This is shown in table 4.

Discussions

The main purpose of this study was to ascertain the prevalence of Rhesus D negative phenotype, fetal outcomes, and practice of routine administration of Rhesus anti-D immune prophylaxis when indicated amongst pregnant women who received maternity services and delivered at a tertiary facility in Abuja, Nigeria.

The prevalence of Rhesus-negative pregnancies at the hospital between the years 2010 to 2021 was 0.8%. This was very much lower than the prevalence rates reported from other institutional based studies across the country; South-east:2.1-4.5%[3,4], South-west:5.0-8.9%[5,6,7], South-south:4.4-4.44%[11,12] and North-west:3.8%.[13] The low prevalence rate obtained in this study was however comparable to 0.7% reported amongst pregnant women in Kaduna, North-central Nigeria which is in the same region where our study was conducted. From the foregoing trends, it may be

reasonable to infer that different catchment areas of the country may have different rates of Rhesus D negative phenotypes in pregnancy. There may therefore be a need for a prospective national study to investigate this phenomenon. On the other hand, the lower prevalence rates obtained in our study may have been due to the retrospective study design which involved 22,478 pregnant women making the denominator large when compared to prospective studies quoted above which recruited sample sizes that ranged from 180 [12] to 700[7] pregnant women. The fact that our study only considered women who delivered at UATH meant that those who had miscarriages or didn't deliver in the hospital were omitted. Additionally, the study from Lagos[7] which reported the highest prevalence of 8-9% also included women from gynaecology clinics and blood donors. These may have contributed to the high prevalence as these group of women may have higher recurrence pregnancy losses necessitating visit to gynaecological clinics or may want to donate blood due to the rare nature and high premium placed on Rhesus negative blood at the blood banks. There was only one case of Rhesus isoimmunization in this study and is comparable to previous studies in Nnewi, Abeokuta and Enugu that had one[3,14] and two[4] cases respectively amongst their study participants. This is surprising as one would have expected a higher prevalence going by the fact that these previous studies[3,14] and in similarity to this study, there was poor adherence to the policy of routine administration of prophylactic anti-D immune globulin to women at risk of Rhesus isoimmunization in their subsequent pregnancies. It may also be that the women who developed Rhesus isoimmunization may have miscarried the pregnancy and therefore didn't present for delivery and were not captured.

The increased utilization of ANC observed in this study may have been due to the fact that they were mainly multiparous and may have been told of the need for attendance at ANC in subsequent pregnancies for close monitoring of the foetus due the risk associated with Rhesus negative status in pregnancy. High ANC attendance amongst Rhesus negative pregnant women have also been previously documented.[8,15]

Rhesus negative status is usually not an indication for caesarean section or instrumental delivery, and this was affirmed in this study where majority had normal vaginal delivery. Those that had caesarean section or instrumental delivery were for obstetric indications. Also, Rhesus negative status is not known to affect timing of delivery except in the setting of alloimmunization. Thus, majority of the participants delivered at term with only about one tenth of the women including the single case of isoimmunization delivering before term.

Although the still birth rate was high, it was comparable to 5.2% reported by researchers in Abeokuta[14] but lower than 9.9% (99/1000 total births) reported from Nnewi.[3] The causes of stillbirths were unlikely to be related to Rhesus isoimmunization as the only case in which there was isoimmunization was delivered alive. Just like for still birth, development of neonatal jaundice amongst the new-borns were mainly due to prematurity or sepsis and unrelated to Rhesus isoimmunization except for the previously discussed case which resolved following phototherapy. Previous studies from other institutions also showed that neonatal jaundice amongst new-borns of Rhesus negative pregnant mothers in Nigeria were rarely due to Rhesus isoimmunization. [3,4]

The departmental protocol is to obtain cord blood sample from which fetal blood group and Rhesus factor, packed cell volume, serum bilirubin, direct coomb's test and reticulocyte count are assessed. Documentation on whether the babies blood group and Rhesus factor were done postpartum was seen in only 90(63.8) of folders reviewed. Out these, as much as 24.4% where Rhesus negative babies with the remaining 75.6% being Rhesus positive necessitating the need for administration of anti-D immune globulin to the mothers.

Findings from this study showed that a high percentage of women received anti-D immunoglobulin prophylaxis when compared with some other studies,[3,6,7,14] The higher utilization of anti-D immune prophylaxis observed in this study may have been due to the multiparous nature of majority which meant that they may have received prior education on the benefits. Additionally, the high ANC attendance and high literacy level amongst the study population may have provided opportunity for counseling and comprehension on the risk of isoimmunization and benefits of the anti-D immune prophylaxis. Despite this positive finding of high anti-D immune prophylaxis

administration, some women were not aware if they needed to take the injections while others who needed the medications could not afford it. These findings suggest an obvious gap in the knowledge regarding pathophysiology of Rhesus isoimmunization and the role of anti-D immune prophylaxis in its prevention among some of the parturient. Topics related to Rhesus disease should be routinely discussed during antenatal health talks while health care providers should spend time during consultations to educate patients about benefits of anti-D immune prophylaxis.

It was also observed that patients who had completed family size where assured that they didn't need anti-D immune prophylaxis. This is in contrast with the recommendation of the American College of Obstetricians and Gynaecologists that supports administration of anti-D immune globulin even to women undergoing postpartum tubal sterilization as there are still slight chances of them getting pregnant in the future and the fact that alloimmunization complicates crossmatching of blood products in the future.[1]

One notable mention of a strategy that improved uptake of anti-D immune prophylaxis in a previous study was the "save-in-bits" strategy where pregnant Rhesus negative mothers are encouraged to save little amounts of money with the Pharmacy from booking till term.[15] In our hospital also, pregnant Rhesus negative mothers are encouraged to make their anti-D immunoglobulin available in the Pharmacy long before delivery. It is therefore not surprising that majority of the mothers who could not afford the anti-D prophylaxis were unbooked Rhesus mothers.

The study was limited by its retrospective design which is associated with incomplete documentation and data for some variables. However, this was resolved for most of the variables by using the labour, maternity ward and theatre registers. Additionally, information regarding administration of anti- D immune prophylaxis and status of baby at discharge was validated by phone calls made to the participants.

Conclusion

The prevalence of Rhesus negativity amongst pregnant women was low but the pregnancies were associated with high still birth rate and poor perinatal outcome which were unrelated to Rhesus Isoimmunization.

Although, the uptake of anti-D immune prophylaxis was reasonable high there were still many women who were unaware of the benefits. Cost was a constraint to its use by those who had indication for it.

Increased awareness about Rhesus negativity in pregnancy and attendance of antenatal care will help improve fetal outcome for this high-risk pregnant population.

Conflict of Interest: The authors report no conflict of interest.

Funding: None

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