Original Article

Prevalence of Rhesus C and D Alloantibodies among Rhesus-Negative Women of Child Bearing Age at a Tertiary Hospital in South-West Nigeria

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Abstract

Background: A major cause of hemolytic disease of the fetus and newborn (HDFN) is an incompatibility of the Rhesus (Rh) blood group between the mother and fetus. **Aim:** To determine the prevalence of Rh c and D alloantibodies among Rh-negative women of childbearing age (18–49 years). We conducted a cross-sectional study among women who attended the antenatal, gynecology and blood donor clinics at a Tertiary Hospital in South-West Nigeria from January to August 2019. Serological typing of Rh c and D was done manually with the tube test using anti-c and anti-D antisera, while indirect antiglobulin test was then performed to screen for Rh antibodies. **Subjects and Methods:** Data was analyzed using Stata 16.1 software; Categorical data was summarized using frequency and percentages while continuous variables were described using the mean and standard deviation or median and interquartile range. Pearson's Chi-square (or Fisher's exact) test was used to test for association between categorical variables and Rh status. *P* values of ≤0.05 were assumed to be statistically significant. **Results:** A total of 700 consenting women, comprising 505 pregnant (72.1%) and 195 non-pregnant (27.9%) women were recruited into this study. The mean age was 30.7 ± 4.9 years. All (100%) participants were Rhc positive while 641 (91.6%) were RhD positive and 59 (8.4%) were RhD negative. All 59 RhD negative subjects tested negative for anti-D. There was no statistically significant difference between proportion of RhD-negative women who had a jaundiced baby and the proportion of RhD-positive women who had a jaundiced baby (15.6% vs. 18.6%, *P* = 0.540). **Conclusions:** This study did not identify any Rhc and D alloantibodies in the study population suggesting there is a low risk of alloimmunization and HDFN due to anti-Rhc and D in this population.

Keywords: *Hemolytic disease of the foetus and new born, Rhesus phenotype*

Introduction

Hemolytic disease of the fetus and newborn (HDFN) is still a serious complication in pregnancy. [1] It is triggered by red blood cell (RBC) antibodies that can cross the placental barrier and attack fetal RBCs. In particular, maternal alloimmunization to Rhesus-D antigen is recognized as a major contributor to fetal morbidity and mortality.[2] To date, the focus of antibody screening has been on determining the presence of anti-D antibody, with over 50 RBC antigens other antibodies including anti-c have been implicated in HDFN.[3-6]

In severe cases, HDFN can manifest as fresh stillbirth or as hydrops fetalis,[4,5] and despite adequate anti-D

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prophylaxis, 1.8% of RhD-negative women still go ahead to produce anti-D due to small transplacental hemorrhages during pregnancy.[7-10]

In Nigeria, the prevalence of HDFN due to RhD is between 2.5% and 11.3%,[11-14] but there is paucity of data on the prevalence of HDFN due to Rhc. This study was aimed at determining the prevalence of anti-c and anti-D and their contribution to risks of HDFN, to provide epidemiological and clinical data that will be useful in reducing HDFN in our environment.

Methods

This was a cross-sectional study to determine the prevalence of Rhc antigen, anti-c, RhD antigen, and anti-D among women who attended the antenatal, gynecology, and blood donor clinics in Lagos University Teaching Hospital (LUTH) from January to August 2019. Study participants were selected using convenience sampling. Ethical approval was granted by the LUTH HREC (ADM/DCST/HREC/APP/2612).

This study was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Sociodemographic characteristics, awareness of risks of Rhesus antigen, blood transfusion history, and previous Rhogam administration was elicited from the participants using an interviewer administered structured proforma.

Rhesus typing

Three milliliters of venous blood was carefully collected from the antecubital vein using 5 ml syringes and dispensed into a plain bottle. Serological typing of Rhc and D was carried out manually in tubes using anti-c and anti-D antisera (Lorne laboratories, Berkshire, United Kingdom), Rhesus controls were added in all tests and all negative results were confirmed using indirect agglutination test method with 20% bovine albumin and anti-human globulin (AHG) tests at 37°C. The RBC was then spun for 20 s at 100 rpm and was gently resuspended and immediately observed macroscopically and confirmed microscopically before recording the result as positive or negative. RhD-negative samples were centrifuged within an hour after sample collection and the sera were separated and stored in anti-coagulant free eppendorf tubes and stored at -20°c until time for analysis.

Antibody screening

Indirect antiglobulin test was used to screen for alloantibodies by tube method in low ionic strength solution, albumin, and AHG phase according to the manufacturer's instructions. All the different laboratory procedures were assayed at the blood bank of Lagos University Teaching Hospital, Lagos with the appropriate reagents in line with the manufacturer's instructions.

Data was analyzed using Stata version 16.1 statistical software and presented in Tables. Categorical data was summarized using frequency and percentages while continuous variables were described using the mean and standard deviation or median and interquartile range. Prevalence (and 95% confidence interval) of each of the studied Rhesus antigens and antibodies were calculated. Prevalence of Rhesus antigen D-positive and negative status was further calculated by ethnicity, age-group, and pregnancy status. Pearson's Chi-square (or Fisher's exact) test was used to test for association between categorical variables and Rhesus status. Student's *t*-test and Mann–Whitney U test was respectively used to test for association between normally distributed continuous variable, non-normally distributed continuous variables, and the Rhesus antigen status. Sub-analysis of the association between Rhogam administration and pregnancy and clinical outcomes among Rh D-negative women was also conducted. Two tailed test of hypothesis was assumed and P values of < 0.05 were assumed to be statistically significant.

Result

Sociodemographic and clinical characteristics of the participants

A total of 700 women were enrolled in this study. Mean age was 30.7 ± 4.9 years.

Demographic characteristics are shown in Table 1.

Prevalence of Rhesus D and c antigen and antibodies with test for association between categorical variables and Rhesus status.

Out of 700 subjects tested for their Rhc and D phenotype, all (n = 700/700, 100%) were Rhc positive and none (0%) was Rhc negative, while 641 [91.6% (95% CI: 89.3–93.4%)] participants were RhD positive and 59 [8.4%, (95% CI: 6.6–10.7%)] were RhD negative. [Table 2A] The prevalence of Rhesus D negative status among pregnant women was 8.9% (95% –CI: 6.7–11.7%) [Table 2B]. The prevalence of RhD-negative phenotype was highest among the Hausa ethnic group [2/16, 12.5% (95% CI: 2.6–43.0%)]. and followed by the Yoruba ethnic group [(34/394, 8.6% (95% CI: 6.2–11.9%)], P value = 0.88). [Table 2B].

The 59 RhD-negative subjects were further screened for antibodies to the RhD antigen (anti-D). All tested negative for anti-D. Since all the participants were positive for Rhesus c antigen, antibody screening test for anti-c was not done.

Table 1: Socio-demographic and clinical characteristics of participants

Characteristics	Frequency *n*=700 (%)	95% Confidence interval (%)
Age (mean±SD) Years	30.7±4.9 years	
<25	56 (8.0)	6.2-10.3
25-29	277 (39.6)	36.0-43.3
30-34	197 (28.1)	24.9-31.6
35-39	138 (19.7)	16.9-22.8
40-44	32 (4.6)	3.2-6.4
Ethnicity		
Yoruba	394 (56.3)	5.6-9.5
Igbo	239 (34.1)	5.3-5.9
Hausa	16 (2.3)	3.1-3.8
Others	51 (7.3)	1.4-3.7
Religion		
Christianity	586 (83.7)	8.1-8.6
Islam	114 (16.3)	1.4-1.9
Educational status		
At most Primary education	32 (4.6)	3.2-6.4
Secondary	193 (27.6)	2.4-3.1
Tertiary	475 (67.9)	6.4-7.1
Marital status		
Single	177 (25.3)	2.2-2.9
Married	523 (74.7)	7.1-7.8
Pregnancy state		
Pregnant	195 (27.9)	2.5-3.1
Non-Pregnant	505 (72.1)	6.9-7.5
Trimester of pregnancy		
Not Pregnant	195 (27.9)	24.7-31.3
First trimester	186 (26.6)	23.4-29.9
Second trimester	217 (31.0)	27.7-34.5
Third trimester	102 (14.6)	12.1-17.4
Number of times pregnant (Gravidity) Median, IQR		0.97 (IQR 0-2)
0	52 (7.4)	
1-4	613 (87.6)	
≥5	35 (5.0)	
Number of livebirths, Median, IQR		0.94 (IQR 0-5)
0	291 (41.6)	
≥1	409 (58.4)	
History of Neonatal Jaundice (*n*=111)		
Yes	111 (15.9)	13.3-18.8
No	589 (84.1)	81.2-86.7
History of Caesarean section (*n*=86)		
Yes	86 (12.3)	10.0-14.9
No	614 (87.7)	85.1-89.9
History of Ectopic pregnancy (*n*=15)		
Yes	15 (2.1)	1.3-3.5
No	685 (97.9)	96.5-98.7
History of Prenatal diagnosis (*n*=43)		
Yes	43 (6.1)	4.6-8.2
No	657 (93.9)	91.8-95.4
History of Blood transfusion		
Yes	67 (9.6)	7.6-11.9
No	633 (90.4)	88.0-92.4
History of Blood transfusion reaction (*n*=12)		
Yes	12 (1.7)	0.9-2.9
No	688 (98.3)	97.0-99.0
History of use of Rhogam (*n*=22)		
Yes	22 3.14	2.1-4.7
No	678 96.86	95.3-97.9

Association between socio-demographic characteristics, pregnancy outcome and Rhesus status.

Table 3 shows the association between sociodemographic characteristics and Rhesus D status. Of the 59 RhD-negative women, more than half were of the Yoruba ethnic group (n = 34/59, 57.6%). There was no statistically significant association between ethnicity, age marital status, and educational status in relation to Rh D status of the participants.

Table 4 shows the association between pregnancy outcome, history of blood transfusion, and Rh D antigens. There was no statistically significant difference between proportion of RhD-negative women who had a jaundiced baby as compared to the proportion of RhD-positive women who had a jaundiced baby (15.6% vs. 18.6%, P value = 0.540). RhD-negative women had higher median live births as compared to the RhD positive women [0.98 (0–5), P = 0.0007)]. The prevalence of ectopic pregnancy [(20.3%

Table 2a: Prevalence of Rhesus antigen and antibodies

Rhesus antigen/ antibodies	Frequency (n=700)	Prevalence % (95% CI)
Rhesus D Positive	641	91.6 (89.3%-93.4%)
Rhesus D Negative	59	8.4 (6.6%-10.7%)
Rhesus c Positive	700	100.0
Anti-D (n=59)	0	0.0

Table 2b: Prevalence of Rhesus D antigen among age groups, ethnicity and pregnancy

Characteristics	Prevalence of Rhesus D positive % (95%CI)	Prevalence of Rhesus D negative status % (95%CI)
Age (Years)		
<25	87.5 (75.7%-94.0%)	12.5 (5.9%-24.3%)
25-29	89.9 (85.7%-92.9%)	10.1 (7.1%-14.3%)
30-34	91.9 (87.1%-94.9%)	8.1 (5.0%-12.9%)
35-39	94.2 (88.8%-97.1%)	5.8 (2.9%-11.2%)
40-44	1	0
Ethnicity		
Yoruba	91.4 (88.1%-93.8%)	8.6 (6.2%-11.9%)
Igbo	92.1 (87.8%-94.9%)	7.9 (5.1%-12.2%)
Hausa	87.5 (57.0%-97.4%)	12.5 (2.6%-43.0%)
Others	92.2 (80.3%-97.1%)	7.8 (2.9%-19.7%)
Pregnancy status		
Non pregnant	92.8 (88.2%-95.7%)	7.2 (4.3%-11.8%)
Pregnant	91.1 (88.3%-93.3%)	8.9 (6.7%-11.7%)

Table 3: Association between Socio demographic characteristics and Rhesus D antigens

Characteristics	Rhesus D Positive n=641, (%)	Rhesus D Negative n=59, (%)	P
Age (mean±SD) Years	30.9±5.0	29.3±4.4	0.0227
<25	49 (7.6)	7 (11.9)	0.151
25-29	249 (89.9)	28 (10.1)	
30-34	181 (28.2)	16 (27.1)	
35-39	130 (20.3)	8 (13.6)	
40-44	32 (4.9)	0 (0)	
Ethnicity			
Yoruba	360 (56.2)	34 (57.6)	0.876
IGBO	220 (34.3)	19 (32.2)	
HAUSA	14 (2.2)	2 (3.4)	
Others	4 (6.8)	47 (7.3)	
Religion			
Christianity	537 (83.8)	49 (83.1)	0.855
Islam	104 (16.2)	10 (16.9)	
Educational status			
At most Primary education	30 (4.7)	2 (3.4)	0.550
Secondary	180 (28.1)	13 (22.0)	
Tertiary	431 (67.2)	44 (74.6)	
Marital status			
Single	158 (24.7)	19 (32.2)	0.212
Married	483 (75.4)	40 (67.8)	

Table 4: Association between Pregnancy outcome, history of blood transfusion and Rhesus D antigens

	Rhesus D Positive	Rhesus D Negative	*P*
Awareness of Rhesus D complications in pregnancy			
Aware	135 (21.1)	48 (81.4)	0.00
Not aware	506 (78.9)	11 (18.6)	
Pregnancy state			
Pregnant	460 (71.8)	45 (76.3)	0.545
Non-Pregnant	181 (28.2)	14 (23.7)	
Trimester of pregnancy			
Not Pregnant	181 (28.2)	14 (23.7)	0.081
First trimester	174 (27.2)	12 (20.3)	
Second trimester	190 (29.6)	27 (45.8)	
Third trimester	96 (14.9)	6 (10.2)	
Number of times pregnant (Gravidity) Median, IQR	2 (1-3)	2 (2-3)	0.432
0	50 (7.8)	2 (3.4)	0.279
1-4	557 (86.9)	56 (94.9)	
≥5	34 (5.3)	1 (1.7)	
Number of livebirths, Median, IQR	0.53 (0-2)	0.98 (0-5)	0.0007
0	254 (39.6)	37 (62.7)	0.001
≥1	387 (60.4)	22 (37.3)	
History of Neonatal Jaundice (*n*=111)			
Yes	100 (15.6)	11 (18.6)	0.540
No	541 (84.4)	48 (81.4)	
History of Caesarean section (*n*=86)			
Yes	74 (11.5)	12 (20.3)	0.049
No	567 (88.5)	47 (79.7)	
History of Ectopic pregnancy (*n*=15)			
Yes	8 (1.3)	7 (11.9)	0.000
No	633 (98.8)	52 (88.1)	
History of Prenatal diagnosis (*n*=43)			
Yes	39 (6.1)	4 (6.8)	0.777
No	602 (93.9)	55 (93.2)	
History of Blood transfusion			
Yes	52 (8.1)	15 (25.4)	0.000
No	589 (91.9)	44 (74.6)	
History of Blood transfusion reaction (*n*=12)			
Yes	9 (1.4)	3 (5.1)	0.037
No	632 (98.6)	56 (94.9)	

vs. 11.5%, *P* value = 0.049), cesarean section [(11.9% vs. 1.3%, *P* value < 0.001)], blood transfusion [(25.4% vs. 8.1%, *P* value < 0.001), and blood transfusion reaction [(5.1% vs. 1.4%, *P* = 0.037)] was higher among Rh-negative participants than the prevalence among Rh-positive participants (*P*-value < 0.05). The level of awareness of Rhesus type among participants who had Rh-negative phenotype were about four-fold as compared to the Rhesus type awareness among participants who had Rh-positive phenotype. (81.4% vs. 21.1%, *P* value < 0.0001)

History of Rhogam administration and potentially sensitizing events

Of the 59 women who were RhD negative, Rhogam was previously administered to 22 of them giving a prevalence rate of Rhogam administration of 37.3% (95% CI: 25.7% - 50.6%). Nearly all or all the women who had Rhogam were previously pregnant (100%) or currently pregnant (99.9%). All the women who had history of neonatal jaundice (NNJ) (*n* = 11,100%) or cesarean section (*n* = 12, 100%) had Rhogam administration. In contrast, about 25% (*n* = 1/4), 57.1% (*n* = 4/7), and 100% (*n* = 3/3) of women who respectively had prenatal diagnosis procedure, ectopic pregnancy and blood transfusion reaction did not have Rhogam injection [Table 5].

Table 5: Association between history of blood transfusion and pregnancy and clinical outcome among Rhesus negative women

Events/Status	Rhogam administered	Rhogam not administered	*P*
Pregnancy status			
Pregnant	20 (90.9)	25 (67.6)	0.042
Non-Pregnant	2 (9.1)	12 (32.4)	
Trimester of pregnancy			
Not Pregnant	2 (9.1)	12 (32.4)	0.103
First trimester	4 (18.2)	8 (21.6)	
Second trimester	12 (54.6)	15 (40.5)	
Third trimester	4 (18.2)	2 (5.4)	
Number of times pregnant (Gravidity)			
0	0 (0)	2 (5.4)	0.238
1-4	21 (95.5)	35 (94.6)	
≥5	1 (4.6)	0 (0)	
Number of livebirths, Median, IQR			
0	0 (0)	37 (100)	0.000
≥1	22 (100)	0 (0)	
History of Neonatal Jaundice (*n*=11)			
Yes	11 (50)	0 (0)	0.000
No	11 (50)	37 (100)	
History of Caesarean section (*n*=12)			
Yes	12 (54.6)	0 (0)	0.000
No	10 (45.5)	37 (100)	
History of Ectopic pregnancy (*n*=7)			
Yes	3 (13.6)	4 (10.8)	0.746
No	19 (86.4)	33 (89.2)	
History of Prenatal diagnosis (*n*=4)			
Yes	3 (13.6)	1 (2.7)	0.106
No	19 (86.4)	36 (97.3)	
History of Blood transfusion (*n*=15)			
Yes	5 (22.7)	10 (27.0)	0.714
No	17 (77.3)	27 (72.9)	
History of Blood transfusion reaction (*n*=3)			
Yes	0 (0)	3 (8.1)	0.170
No	22 (100)	34 (91.9)	

Discussion

The Rh immune response in Rh-negative women is the primary etiology for hemolytic disease of the fetus and newborn.[15] The distribution of RhD antigen significantly varies with race,[16,17] with the prevalence of RhD antigen higher in Africans than Asians.[18] The prevalence of RhD and Rhesus c phenotypes in this study were 91.6% and 100%, respectively, which is in keeping with findings in previous studies done in Northern and Eastern parts of Nigeria.[19-22] As expected these are higher than what has been reported in the Caucasian population.[23]

In this study, we found the RhD-negative prevalence of 8.4% (95% CI 6.6–10.7%) which is consistent with some reports from various parts of the country[22,24,25] but slightly higher than prevalence studies carried out in the Northern region of the country.[26-32] The Yoruba ethnic group from the South western part of the country has been known to have the highest proportion of RhD-negative population.[31] Therefore, it was not surprising that a prevalence of 8.4% was obtained in this study whose population is predominantly of Yoruba ethnic group. This rate shows a slightly higher frequency in this environment which implies an increased risk of alloimmunization to the RhD antigen.

In this study, neither Rhc nor D alloantibodies were detected suggesting that Rhc and D alloimmunization are rare causes of NNJ among neonates in Lagos. This finding is in line with other previous studies which puts RhD alloimmunization rate to between 0% and 1.6%.[11,33-34] It has been postulated that RhD-negative Nigerians have a low isoimmunization potential, probably due to some genetic predisposition. Interestingly, as reported by previous studies the commonest causes of NNJ in our environment are sepsis

and preterm delivery.[35-37] This hypothesis has been corroborated by our study which reported no statistically significant difference between RhD-negative women and RhD-positive women who have had a baby with NNJ.

As revealed in this study, RhD-negative women had higher median live births as compared to the RhD-positive women despite the fact that there is still a challenge to Rhogam administration in the antenatal period, after a sensitizing episode or after delivery. We report a prevalence rate of Rhogam administration of 37.3% and only a quarter of the RhD-negative participants received Rhogam after a sensitizing episode. The major obstacle to Rhogam is cost and this finding underscores the need for government to subsidize the cost of Rhogam to reduce fetal morbidity and mortality.

Conclusion

Our study shows that whereas the risk of HDFN due to Rh c alloantibodies is negligible in this population, RhD alloimmunization still poses a risk of adverse pregnancy outcome especially without the use of anti-D prophylaxis.

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Conflicts of interest

There are no conflicts of interest.

References

1. Zwiers C, van Kamp I, Oepkes D, Enrico L. Intrauterine transfusion and non-invasive treatment options for haemolytic disease of the foetus and newborn-Review on current management and outcome. Expert Rev Hematol 2017;10:337-44.
2. Urbaniak SJ, Greiss MA. RhD haemolytic disease of the foetus and the newborn. Blood Rev 2000;14:44–61.
3. Hoffbrand A, Moss PAH. Essential Haematology. 6th ed. Sussex: Wiley Blackwell; 2012. p. 418-22.
4. Basu S, Kaur R, Kaur G. Haemolytic disease of the foetus and newborn: Current trends and perspectives. Asian J Transfus Sci 2011;5:3–7.
5. Akhtar K, Ray PS, Rab ZZ, Sherwani RK. Survival in haemolytic disease of newborn due to Rh-isoimmunisation: An unusual presentation. International journal of pregnancy and child birth 2017;2:115-7.
6. Chacham S, Reddy DS, Reddy UN, Khan W, Nandita S. Neonatal outcomes of Rh-negative pregnancies in a tertiary level neonatal intensive care unit: A prospective study. J Compr Ped 2016;7:e36573.
7. De Haas M, Koelewijn J, Thurik FF, Van der Schoot CE. Haemolytic disease of the foetus and newborn. Vox Sanguinis 2015;109:12265.
8. Strotmann F, Nocke C, Crummenerl N, Karnuth B, Kamp N, Hafner G. Inappropriate blood transfusion in neonatal haemolytic due to anti-C. Am J Med Case Rep 2018;5:56-8.
9. Kawthalkar SM. Essentials of Haematology. Second edition. New Delhi: JAYPEE Brothers Medical Publishers; 2013. p. 456.
10. Solves P, Gomez-Segui I, Guinot M, Saus A, Osorio J, Martinez F. "Prevalence of red blood cell alloantibodies in pregnant women and haemolytic disease of newborn in a tertiary care hospital". ARC J Gynecol Obstet 2017;2:18-22.
11. Jeremiah ZA, Mordi A, Buseri FI, Adias TC. Frequencies of maternal red blood cell alloantibodies in Port Harcourt, Nigeria. Asian J Transfusion Sci 2011;5:39-41.
12. Mina SS, Bhardwaj R, Gupta S. Haemolytic disease of newborn: Can think beyond Rh (D) and ABO incompatibilities. J Clin Neonatol 2017;6:37-9.
13. Erhabor O, Ati SR, Yakubu AY, Tambuwal BU. ABO and Rh D blood group and haemolytic disease among the new-born at Sokoto specialist hospital, Nigeria. J Blood Disord Transfus 2017;8:2.
14. Oyapero O, Disu AE, Njokanma FO. Clinical and sociodemographic correlates of neonatal jaundice at a tertiary health facility in Lagos, Nigeria. Adv Human Biol 2018;8:117-23.
15. Okeke TC, Ocheni S, Uwagha UI, Ibegbulam OG. The prevalence of Rhesus negativity among pregnant women in Enugu, South East, Nigeria. Niger J Clin Pract 2012;15:400-2.
16. Gundrajukuppam DK, Vijaya SBK, Rajendran A, Sarella JD. Prevalence of principal Rh blood group antigens in blood donors at the blood bank of a tertiary care hospital in Southern India. J Clin Diagn Res 2016;10:EC07-10.
17. Swelem O, Goubran F, Younis S, Kamel N. ABO, RH phenotypes and kell blood groups frequencies in an Egyptian population. Hematol Transfus Int J 2018;6:71-5.
18. Ogbenna AA, Oyedeji A, Onifade OO, Adewoyin AS. Knowledge of Rh (Rhesus) D blood group, risk factors and burden of Rh D alloimmunisation among female secondary school students in Ikorodu, Lagos, Nigeria. Int Blood Res Rev 2016;6:1-7.
19. Ngassaki-Yoka C, Mireille J, Ndong N, Bisseye C. ABO, Rhesus blood groups and transfusion-transmitted infections among blood donors in Gabon. SJMS 2017;13:1685.
20. Gwaram BA, Abdullahi S. Prevalence of Rh phenotype among blood donors in Kano, Nigeria. J Med Tropics 2013;15:1.
21. Erhabor O, Okwesili A, Aliyu BS, Onuigwe F, Buhari H, Bagudo A. Prevalence of Rhesus c and e phenotype among pregnant women attending antenatal clinic in Usmanu Danfodiyo University Teaching Hospital. J Gynecol Neonatal Biol 2016;2:13-16.
22. Jeremiah Z, Biribo A, Adias T, Uko E. Uncommon Rh phenotypes in a cross section of Nigerian antenatal women: Implications for molecular genotyping for blood groups. J Blood Disord Transfus 2012;10:001.
23. Golassa L, Tsegaye A, Erko B, Mamo H. High rhesus (Rh (D)) negative frequency and ethnic-group based ABO blood group distribution in Ethiopia. BMC Res Notes 2017;10:330.
24. Erhabor O, Kabiru SA, Yakubu A, Shehu CE, Hassan M, Singh S. Rh(D) phenotype among pregnant women in Sokoto, North Western Nigeria. Implications on haemolytic disease of the new-born and haemolytic transfusion reaction. Health Sci Res 2014;1:19-24.
25. Adienbo OM, Nwafor A, Egwurugwu JN, Okon UA. The distribution of ABO and Rhesus blood groups among indigenes of Ijaw ethnic group in Niger Delta region, Nigeria. Global J Pure Appl Sci 2010;16:345-8.
26. Chima OK, Mohammed TB, Aisha K, Alhaji SA, Muhammed BM. ABO and Rhesus blood groups among blood donors in Kano, North- Western, Nigeria. J Basic Clin Sci 2012;9:11-3.
27. Iyiola OA, Igunnugbemi OO, Anifowoshe AT, Raheem UA. Gene frequencies of ABO and Rh(D) blood group alleles in Ilorin, North-Central Nigeria. World J Biol Res 2011;4:6–14.

28. Erhabor O, Isaac IZ, Saidu A, Ahmed HM, Abdulrahman Y. The distribution of ABO and Rhesus blood groups among residents of Gusau, Zamfara state, North Western Nigeria. J Med Health Sci 2013;2:55-63.
29. Olaniyan TO, Ajibola BM, Rasong H, Dare BJ, Shafe MO. Blood group and rhesus factor pattern among indigenes of FCT, Abuja, Nigeria. J Community Med Health Educ 2013;3:208.
30. Anifowoshe AT, Owolodun OA, Akinseye KM, Iyiola OA, Oyeyemi BF. Gene frequencies of ABO and Rh blood groups in Nigeria; A review. Egypt J Med Hum Genet 2017;18:205-10.
31. Adeyemi AS, Bello-Ajao HT. Prevalence of Rhesus D-negative blood type and the challenges of Rhesus D immunoprophylaxis among obstetric population in Ogbomoso, Southwestern Nigeria. Ann Trop Med Public Health 2016;9:12-5.
32. Onuoha EC, Eledo BO, Young-Dede EU, Agoro ES. Distribution of ABO, Rhesus blood groups and haemoglobin variants among residents of Yenagoa and environs, Bayelsa state, Nigeria. Adv Life Sci Tech 2015;34:26-31.
33. Eleje GU, Ilika CP, Ezeama CO, Umeobika JC, Oguejiofor B. Feto-maternal outcomes of women with Rhesus iso-immunization in a Nigerian tertiary health care institution. J Preg Neonatal Med 2017;1:21-7.
34. Fawole AO, Sotiloye OS, Hunyinbo KI, Durodola A, Omisakin SI, Bale AO, *et al*. A review of Rhesus Iso-immunization in a nigerian obstetric population. Trop J Obstet Gynaecol 2001;18:69-72.
35. Olusanya BO, Osibanjo FB, Mabogunje CA, Slusher TM, Olowe SA. The burden and management of neonatal jaundice in Nigeria: A scoping review of the literature. Niger J Clin Pract 2016;19:1-17.
36. Eneh AU, Oruamabo RS Neonatal jaundice in a special care baby unit (SCBU) in Port Harcourt, Nigeria: A prospective study. PHMJ 2008;2:110-7.
37. Ekwochi U, Osuorah CD, Ndu IK. Determinants of delay in presentation and clinico-laboratory features of newborns admitted for neonatal jaundice in a tertiary hospital in south-east Nigeria. J Med Trop 2018;20:128-34.