

Prevalence of Rhesus Negative Status Amongst Antenatal Attendees in the University of Uyo Teaching Hospital, Uyo, Nigeria: A 5-Year Review

Emem Abasi Bassey^{1, *}, Matthias Gabriel Abah¹, Christopher Azubuiké Opone²,
Aniekan Linus Jackson²

¹Department of Obstetrics and Gynaecology, College of Health Sciences, University of Uyo, Uyo, Nigeria

²Department of Obstetrics and Gynaecology, University of Uyo Teaching Hospital, Uyo, Nigeria

Email address:

emembassey70@yahoo.com (E. A. Bassey)

*Corresponding author

To cite this article:

Emem Abasi Bassey, Matthias Gabriel Abah, Christopher Azubuiké Opone, Aniekan Linus Jackson. Prevalence of Rhesus Negative Status Amongst Antenatal Attendees in the University of Uyo Teaching Hospital, Uyo, Nigeria: A 5-Year Review. *Clinical Medicine Research*. Vol. 10, No. 1, 2021, pp. 26-30. doi: 10.11648/j.cm.20211001.15

Received: January 4, 2021; **Accepted:** January 22, 2021; **Published:** February 9, 2021

Abstract: Introduction: The Rhesus (Rh) antigen is the most polymorphic of human blood group systems second only to the ABO in transfusion and transplantation medicine with significance in iso-immunization which can cause haemolytic disease of the foetus and newborn. This study was carried out to determine the prevalence of Rhesus negativity amongst antenatal clinic attendees in the University of Uyo Teaching Hospital. Methodology: This was a 5-year retrospective study carried out between March 1st, 2012 and February 28th, 2017. Data containing the ABO and Rhesus blood group of all antenatal clinic attendees was collected from the Laboratory registers and analysed using Microsoft excel. Results: The prevalence rate of Rhesus D negative women was 4.40%. The average yearly attendance was 2861 women. The commonest blood group was O with 8232 (57.54%), followed by blood group A, 3416 (23.88%) and blood group B, 2388 (16.69%) while the least common blood group was AB, 271 (1.89%). Most Rhesus D-negative women were of blood group O; 382 (60.78%), followed by group A; 142 (22.58%), and blood group B was 94 (14.49%). AB blood group was the least; 11 (1.70%). Sensitization rate among the 629 Rhesus D-negative women was 1.11%. Conclusion: The prevalence of rhesus negativity is low in the population studied with an ABO distribution that mirrored the antenatal population, hence the overall need for immunoprophylaxis. It is however very necessary to educate and counsel all non-sensitized Rhesus negative women on the need for antenatal and post-partum immuno-prophylaxis as well as public enlightenment on the rationale for Rhesus typing, especially among women.

Keywords: Blood Group, Rhesus, Pregnancy, Haemolytic Disease

1. Introduction

The Rhesus (Rh) blood group system is the most polymorphic of the human blood groups, believed to consist of at least 45 independent antigens and, is next only to the ABO in clinical significance and transfusion medicine. [1] It is a product of Rh antigens (include D, C or c, and E or e) which are trans-membrane proteins expressed on the surface of erythrocytes apparently used for the transport of CO₂ and/or ammonia across the plasma membrane. [2]

Historically, following the description of the A, B, O blood types, a fourth, the Rhesus system was discovered by

Landsteiner and Weiner in 1940. [3-5] This followed experiments which made use of Rhesus monkeys, hence the statuses of Rhesus Positive or Rhesus negative depending on the presence or absence of the antigen respectively on the red blood cells of a person. [1, 3, 4]

The significance of the Rh status in pregnancy is the Rh D iso-immunization which can occur when a Rh D negative woman is pregnant with a Rh D Positive foetus and in-utero interaction between maternal and foetal blood from fetomaternal haemorrhage during the course of pregnancy. [6, 7] This may arise either from spontaneous or induced abortion, trauma, normal delivery and invasive obstetric procedure or

when an Rh-negative female receives an Rh-positive blood transfusion. [8, 9] Anti-Rh D Immunoglobulin antibodies which are generated as a result of the iso-immunisation can cross the placenta once present and attack the foetal red blood cells resulting in a range of complications termed Haemolytic Disease of the foetus and newborn which could range from hyperbilirubinaemia through severe anaemia to Hydrops fetalis. [7-9] The maternal Rh immunoglobulin G (IgG) antibodies produced following iso-immunisation persist for life and may undergo transplacental migration to the foetal circulation with resultant formation of antigen-antibody complexes with Rh-positive foetal red blood cells and subsequently resulting in the foetal alloimmune-induced haemolytic anaemia described. [8, 10, 11] Other causes of fetomaternal haemorrhage include amniocentesis, spontaneous or induced abortion, cordocentesis, chorionic villus sampling, and ruptured ectopic pregnancy. [1]

The D-antigen is the most immunogenic and most commonly involved antigen in Rhesus incompatibility and Rh Haemolytic disease of newborn (HDN) despite the existence of different Rh blood group antigen subtypes (D, C, c, E, e). [8] The ABO group incompatibility is however the commonest cause of HDN, followed by anti-Rh D, while anti-Kell is the least involved. [10, 12] Haemolytic disease of foetus and newborn following allo-immunization to Rh D is a major contributor to perinatal mortality and morbidity, hence impacting on a women's obstetric career. Sensitisation, anti D antibody formation and the sequelae of Haemolytic disease of foetus and newborn can be prevented by the administration of anti-D immunoglobulin G (IgG) prophylaxis soon after delivery in Rhesus negative women and is recommended by the World Health organization (WHO). [11, 13, 14]

Despite documented benefits, [9-11, 13, 14] uptake of anti-D immunoglobulins in Uyo, Nigeria is poor, largely due to prohibitive cost with a dose of Rhogam (Kedrion Biopharma, New Jersey, USA) costing N38,000 (\$124). A search for National data on the prevalence of Rh D Negative women and the incidence of allo-immunization yielded no results with only few single centre studies. This study was carried out to with the aim of determining the prevalence of Rh D Negative blood group among antenatal clinic attendees in the University of Uyo Teaching Hospital located in South south Nigeria. This we hope will not only add to the data on this study subset, but will assist management in planning for, sourcing and making available the needed Rh immunoglobulin-G for prevention of alloimmunisation with a view to eliminating Haemolytic disease in Fetuses and Erythroblastosis fetalis in neonates.

2. Materials and Methods

2.1. Study Location

The University of Uyo Teaching Hospital is located in Uyo the capital of Akwa Ibom State, Nigeria. It was established in 1996 as a state specialist hospital, but was later transformed to a Federal Medical Centre (FMC), in 1997. The hospital

was later upgraded to a Teaching Hospital in February, 2007 by the Federal Government of Nigeria. The Hospital is a 500-bed tertiary healthcare facility occupying about 43 hectares of land. The institution receives referrals from peripheral healthcare facilities in the state with a population of over 5.7million people in the South-South geopolitical zone of Nigeria.

The Hospital runs a busy Antenatal clinic all through the week and the results used for this study were those of pregnant women booked and attending the antenatal clinic of the University of Uyo Teaching Hospital (UUTH).

In the Obstetrics unit of the hospital, routine screening for the ABO blood group and Rhesus factor is carried out at the booking visit for all pregnant women attending antenatal clinics. Rhesus Negative pregnant women were requested to do the indirect Coomb's test to determine those that are sensitized to the Rhesus D antigen while sensitized pregnant women are managed according to established departmental protocols.

2.2. Data Collection

This was a retrospective cross-sectional study conducted at the University of Uyo Teaching Hospital, Uyo, Akwa-Ibom state in South-South Nigeria. The Laboratory registers containing the blood groups of women who attended antenatal clinic from March 2012 to February 2017 were retrieved for this study. Information on the total number of women who attended antenatal clinic, the total number of those who were Rh-Negative mothers, the numbers of those with blood groups A, AB, B and O and the distribution of the Rh status among them were extracted. The folders of the Rh-Negative women were retrieved and further analyzed for iso-immunisation (positive Indirect Coomb's test). The collated data were analysed using Microsoft excel for windows. Statistical comparison was done using percentages. The results were presented in tables and form the basis for the discussion.

3. Results

During the study duration, fourteen thousand, three hundred and seven (14,307) women registered for antenatal care at the University of Uyo Teaching Hospital, 629 of them had Rhesus D Negative blood group. This gave a prevalence of 4.40%. (Table 1)

The yearly blood group type distribution of all antenatal attendees at the booking clinic from from March 2012 through February 2017 showed an average of 2861 woman booked for antenatal care per year during the 5 year study period and had their blood group checked. (Table 2)

The commonest blood group was O with 8232 (57.54%), followed by blood group A, 3416 (23.88%) and blood group B, 2388 (16.69%) while the least common blood group was AB, 271 (1.89%) (Table 3).

Majority of pregnant women with Rhesus D-negative were of blood group O; 382 (60.78%), followed by group A; 142 (22.58%), and blood group B was 94 (14.49%). AB blood

group was the least; 11 (1.70%). (Table 4)

Out of the 629 Rhesus negative women, 7 (1.11%) had positive Rh D antibodies at the time of the booking visit while 622 (98.9%) were negative for antibodies. Of these 7 sensitised women, 5 were multigravida, with 2 having had intrauterine foetal deaths (IUFD) late in pregnancy.

Unfortunately, these IUFDs were not investigated because pregnancies and deliveries were managed by the traditional birth attendants (TBA). The other 2, while carrying their first pregnancies past viability, admitted to having terminated 'several' pregnancies without receiving Rh-anti D prophylaxis.

Table 1. Rhesus blood group distribution among Antenatal attendees 2012 to 2017.

S/N	RHESUS TYPE	FREQUENCY	PERCENTAGE
1	Positive	13678	95.60
2	Negative	629	4.40
3	Total	14307	100.00

Table 2. ABO Blood group Distribution by year.

YEAR	A	B	AB	O	TOTAL
2012 (Mar. 2012)	510	310	41	1175	2036
2013	706	502	68	1723	2999
2014	697	477	46	1764	2984
2015	705	559	49	1658	2971
2016	720	489	57	1705	2971
2017 (Feb. 2017)	78	51	10	207	346
TOTAL	3416	2388	271	8232	14307

Table 3. Frequency table for ABO blood groups over 5 years.

S/N	BLOOD GROUP	FREQUENCY	PERCENTAGE
1	A	3416	23.88
2	B	2388	16.69
3	AB	271	1.89
4	O	8232	57.54
TOTAL		14307	100.00

Table 4. Distribution of Rh Negativity Among different ABO groups.

S/N	ABO GROUP	RH-NEG	% RH-NEG
1	A	142	22.58
2	B	94	14.94
3	AB	11	1.70
4	O	382	60.78
Total		629	100.00%

4. Discussion

The knowledge of blood group and Rhesus factor is important not only in blood transfusion, organ transplantation, forensic pathology and prevention of complications related to Rhesus incompatibility, but in the management of disease conditions and has been found to be associated with dental malocclusion in some populations. [6-9, 15] The prevalence of Rh D negativity among the studied obstetric population was 4.4%. This compared to 4.5%, found in Enugu, South-East Nigeria by Okeke et al, [16] 5.4% by Adewale et al in Oyo, South-West Nigeria, [17] 4.3% by Ezhil et al in Telangana [18] and 4.6% by Kasturi et al in Karnataka [19] Indian provinces. The prevalence of Rh D in our study was however less than 7.1% found in a study carried out in Sokoto, North-West Nigeria, [20] 6.7% and 10% amongst males and females in an Indian study, [21] 19.4% found in an Ethiopian study [22] and 17% among white non-Hispanic donors in America. [23] The highest frequency of the Rh D negativity worldwide was found

among the Basques, Spain with a reported prevalence of 47.2%. [24]

Studies which showed lower prevalence of Rh negativity relative to ours included a study in the mid-80s which showed a prevalence of 3.3% in Ogbomosho, South-west Nigeria. [25] A lower prevalence of 0.7% was found in Kaduna, Northern Nigeria [26] and 0.3% in Thailand, South-East Asia, [27] while Rhesus negativity was almost non-existent in a study in Papua New Guinea. [28]

From the studies above, there seem to be regional/ethnic differences in the prevalence of the Rhesus gene in Nigeria. A study in Sokoto, north west Nigeria with a high Rhesus D prevalence of 7.1% which involved participants from the major different ethnic Nationalities in Nigeria showed that among the Rh D negative proportion, the Hausas contributed the highest (42.5%), while the Yorubas contributed nothing (0). [20] Another study in Kaduna which had a very low prevalence of 0.7% had the Yorubas contributing the highest proportion (44.73%) among ethnic groups to the Rh Negative population while the Southern minority ethnic groups had the least contributors (3.9%). [26] Even though some of the

studies on the prevalence of Rhesus negativity in Nigeria made no mention of the different ethnic groups that contributed to the study, [17] it may however be deduced that the Yoruba ethnic group of Nigeria seem to have the lowest prevalence of the Rhesus blood type against the Hausas who seem to have highest prevalence in Nigeria. [17, 20, 26] The participants of this study were mainly from the ethnic minorities in South south Nigeria. Apart from the spatial and ethnic/racial variations, the ABO-Rh blood group frequencies had been shown to temporally change in a single population and this may further explain variations in the prevalence of Rhesus negativity in studied populations over time. [29]

The yearly booking at the antenatal clinic in the University of Uyo teaching hospital, Uyo ranged between 2382 and 2999, with an average attendance of 2861. The commonest ABO blood group of the women was blood group O, followed by A and B in that order with AB being the least frequent. This pattern of distribution was also found in other studies in Nigeria and beyond. [30-32] The ABO group distribution of the Rhesus negative population found mirrored that of the entire antenatal attendees over the five-year study period. This was also found by other researchers. [16, 33]

The low percentage (4.40) of Rhesus negatives in the studied population is an advantage in the light of the prohibitive cost implication of immunoprophylaxis vis-à-vis the very high poverty rate in our population. An Indian study showed a rise in prevalence from 1.8 to 4.6% Rh D negative pregnancy when compared with its prevalence 10 years earlier.[34]. The researchers ascribed the change to possible increased antenatal testing Though, it is known that failure of prophylaxis does occur, most of the women that did not receive the immunoprophylaxis following the previous sensitizing event like delivery or the abortion within the study period had detectable Rh D antibody. It is possible therefore that individual genetic predisposition may be responsible for certain women coming down with iso-immunization even with prophylaxis while others do not despite not receiving immuno-prophylaxis in previous pregnancies/sensitising events. The patients with documented history of adverse effects (IUFD) were not managed in our facility in those pregnancies, hence the scanty details were available about them.

5. Conclusion

The prevalence of Rhesus negativity is low with an ABO distribution that mirrored that of the antenatal population, hence the overall need for immunoprophylaxis. It is however very necessary to educate and counsel all non-sensitized Rhesus negative women on the need for antenatal and post-partum immuno-prophylaxis as well as sensitised women for management of pregnancies in tertiary health facilities. This is more-so, that once Rhesus immunized mothers remain so for life. There is need for proper public education about this preventable possible sequele of being Rhesus negative.

Limitations of Study

Information was manually extracted and could be subject to error as laboratory data in the University of Uyo Teaching hospital during the study period was not computerised.

Funding

The research was not funded by any agency.

Conflict of Interests

The authors declare that they have no competing interests.

Acknowledgements

The Authors wish to acknowledge the cooperation of the staff of the Departments of Haematology and Health Information Records who assisted in the retrieval of Data for this work.

References

- [1] Avent, Neil D. Reid, Marion E. The Rh blood group system: a review. *Blood* 2000; 95 (2): 375–387. Available At: <https://doi.org/10.1182/BLOOD.V95.2.375> Accessed 21/07/2020.
- [2] Gonsorcik V. K. Rh. Typing. *Medscape Emecicine*. Available at: <https://emedicine.medscape.com/article/1731214-overview#a1> Accessed 21/07/2020.
- [3] Landsteiner K, Wiener AS. An agglutinable factor in human blood recognized by immune sera for Rhesus blood. *Proc Soc Exp Biol Med* 1940; 43: 223-4.
- [4] Farhud DD Zarif Yeganeh M A Brief History of Human Blood Groups *Iranian J Publ Health*, 2013; 42 (1): 1-6 Available at: <http://ijph.tums.ac.ir> Accessed 22/07/2020.
- [5] Alexander S. Wiener, History of the Rhesus Blood Types, *Journal of the History of Medicine and Allied Sciences*. 1952; 7 (4): 369–383, <https://doi.org/10.1093/jhmas/VII.4.369>.
- [6] Carter BloodCare. The significance of being Rh Negative or Rh Positive. May 2016. Available at: <https://www.carterbloodcare.org/the-significance-of-being-rh-negative-or-rh-positive/> Accessed: 16/08/2020.
- [7] Management of Rhesus Negative Mother. *SLCOG National guidelines*. Available at: <https://www.gfmer.ch/SRH-Course-2010/national-guidelines/pdf/Management-Rhesus-Negative-Mother-SLCOG.pdf>. Accessed 16/08/2020.
- [8] Salem L. Rh. Incompatibility. *Medscape Emecicine*. Available at: <https://emedicine.medscape.com/article/797150-overview> Accessed 16/08/2020.
- [9] Agarwal K, Rana A, Ravi AK. Treatment and Prevention of Rh. Isoimmunization. *J. Fetal Med*. June 2014; 1: 81–88. Available at: <https://link.springer.com/content/pdf/10.1007/s40556-014-0013-z.pdf>.
- [10] Delaney M, Matthews DC. Hemolytic disease of the fetus and newborn: managing the mother, fetus, and newborn. *Hematology Am Soc Hematol Educ Program*. 2015; (1): 146-51.

- [11] Elalfy MS, Elbarbary NS, Abaza HW. Early intravenous immunoglobulin (two-dose regimen) in the management of severe Rh hemolytic disease of newborn--a prospective randomized controlled trial. *Eur J Pediatr.* 2011; 170 (4): 461-7.
- [12] Das S. Hemolytic Disease of the Fetus and Newborn. Available at: <http://dx.doi.org/10.5772/intechopen.85316> Accessed 17/08/2020.
- [13] Brinc D, Lazarus AH. Mechanisms of anti-D action in the prevention of hemolytic disease of the fetus and newborn. *Hematology Am Soc Hematol Educ Program.* 2009; 185-191 <https://doi.org/10.1182/asheducation-2009.1.185>.
- [14] WHO Reproductive Health Library. WHO recommendation on antenatal anti-D immunoglobulin prophylaxis. (December 2016). The WHO Reproductive Health Library; Geneva: World Health Organization. Available at: <https://extranet.who.int/rhl/topics/preconception-pregnancy-childbirth-and-postpartum-care/antenatal-care/who-recommendation-antenatal-anti-d-immunoglobulin-prophylaxis>.
- [15] Al-Khatieeb MM, Al-Joubori SK, Taha SS. Association of ABO Blood Group and Rhesus Factor with Dental Malocclusion in a Population of Baghdad, Iraq. *Int J Med Res Health Sci* 2018; 7 (1): 165-169 Available online at www.ijmrhs.com Assessed 25/08/2020.
- [16] Okeke TC, Ocheni S, Nwagha UI, et al. The prevalence of Rhesus negativity among pregnant women in Enugu, South-East Nigeria. *Nigerian Journal of Clinical Practice.* 2012; 15 (4): 400-402.
- [17] Adewale SA, Hajara TB. Prevalence of Rhesus D negative blood type and the challenged of Rhesus D immunoprophylaxis among obstetric population in Ogbomoso, South-Western Nigeria. *Ann Trop Med Public Health* 2016; 9 (1): 12-15.
- [18] Ezhil AN, Padmavathy M, Pasupulati R, et al. Prevalence of Rhesus negativity among pregnant women. *International Journal of Research in Medical Sciences* 2016; 4 (8): 3305-09.
- [19] Kasturi BH, Pranita RV. A study on the prevalence of rhesus factor among at tertiary care center in North Karnataka. *Int J Curr Res.* 2015; 7 (01): 11556-8.
- [20] Erhabo O, Kabiru SA, Yakubu A, et al. Rhesus D phenotype among pregnant women in Sokoto, North-West Nigeria. Implication of Hemolytic disease of the newborn and hemolytic transfusion reaction. *Health Science Research* 2014; 1 (2): 19-24.
- [21] Makroo R, Gupta R, Bhatia A, Rosamma NL. Rh phenotype, allele and haplotype frequencies among 51,857 blood donors in North India. *Blood Transfus.* 2014; 12: 36-9.
- [22] 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. <https://doi.org/10.1186/s13104-017-2644-3>.
- [23] Garratty G, Glynn SA, McEntire R. ABO and Rh (D) phenotype frequencies of different racial/ethnic groups in the United States. *Transfus.* 2004; 44: 703-6.
- [24] Flores-Bello A, Mas-Ponte D, Rosu ME, Bosch E, Calafell F, Comas D. Sequence diversity of the Rh blood group system in Basques. *Eur J Hum Genet.* 2018 Dec; 26 (12): 1859-1866 Available at: doi: 10.1038/s41431-018-0232-1.
- [25] Kulkarni AG, Peter B, Ibazebo R, Dash B, Fleming AF. The ABO and Rhesus groups in the North of Nigeria. *Ann Trop Med Parasitol.* 1985; 79: 83-88.
- [26] Onwuhafua PI, Adze J. Pregnancy in Rhesus Negative women in Kaduna, Northern Nigeria. *Trop. J. Obstet. Gynaecol.* 2004; 21: 21-23.
- [27] Puangsricharn A, Suksawat S. (2007). Prevalence of Rh negative pregnant women who attended the antenatal clinic and delivered in Rajavithi Hospital: 2000-2005. *J Med Assoc Thai* 2007; 90 (8): 1491-4.
- [28] Salmon D, Godelier M, Halle L, et al. Blood groups in Papua New Guinea Eastern Highlands. *Gene Geography: a Computerized Bulletin on Human Gene Frequencies.* 1988 Aug-Dec; 2 (2-3): 89-98.
- [29] Pourfath EA, Oody A, Honarkaran N. Geographical distribution of ABO and Rh (D) blood groups among Iranian blood donors in the year 1361 (1982) as compared with that of the year 1380 (2001). *Blood (Khoo).* 2004; 1 (1): 11-7.
- [30] Bamidele O, Arokoyo DS, Akinbola AO. Distribution of ABO and rhesus blood groups among medical students in Bowen University, Iwo, Nigeria. *Ann. Biol. Res.* 2013; 4 (11): 1-6.
- [31] Adeyemo OA, Soboye JO, Omolade B, (2006). Frequency distribution of ABO, RH blood groups and blood genotype among cell biology and genetics students of University Lagos, Nigeria. *African J. Biotech.* 2006; 5: (22) 2062 - 2065.
- [32] Bakare AA, Azeze MA, Agbolade JO. Gene frequencies of ABO and rhesus blood groups and haemoglobin variants in Ogbomoso, South-West Nigeria. *African Journal of Biotechnology* 2006; 5 (3): 224-229 Available online at <http://www.academicjournals.org/AJB>.
- [33] Odokuma EI, Okolo AC, Aloamaka PC. Distribution of ABO and rhesus blood groups in Abraka, Delta State. *Niger J Physiol Sci* 2007; 22: 89-91.
- [34] Shoujanya Pinapothu, Triveni Guvvada, M. N. Sowjanya, Vasanthi, Anusha, Deepika. Prevalence of rhesus negative pregnancy and comparison to its prevalence in previous decade. *IAIM,* 2019; 6 (12): 10-14.