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PROFILE OF FETAL OUTCOME IN RH POSITIVE MOTHERS WITH INDIRECT COOMB'S TEST POSITIVE – A REPORT OF 3 CASES.

Transfusion Medicine

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ABSTRACT

Introduction: In the majority of cases, routine antenatal antibody screening is done only for Rh(D)-negative mothers while Rh D positive mothers are often overlooked which may lead to a serious delay in diagnosing Hemolytic Disease of Fetus and newborn (HDFN) due to the rarity of antibodies like anti-c, C, e, E, or Kell, Kidd, Duffy, MNS, Lutheran, Diego, Xg. **Aims and objective:** This study was conducted to study the fetal outcome amongst RhD-positive mothers having irregular antibodies. **Materials and methods:** A total of 200 antenatal Rh-positive patients were screened over 10 months and were subjected to the Indirect Coomb's test (ICT). Patients who were ICT positive were further evaluated for ICT titres and the type of irregular antibodies by employing 11 cell antibody cell panel. These patients were then followed throughout the pregnancy to assess the fetal outcome. **Results:** Of 200 Rh-positive patients, 3 patients were ICT positive and were followed regularly during their Antenatal visits. One of the patients who was Gravida 5 with a previous history of transfusion and ICT titre of 1:128, had an Anti-Kell antibody and delivered preterm with massive fetal ascites and jaundice. The baby was Direct Coomb's Test (DCT) positive and underwent repeated exchange transfusion but ultimately baby succumbed. The other two patients who were ICT positive had a titre of 1:8 (Gravida 2) and 1:4 (Gravida 3) respectively. On screening, these patients had Anti-M and Anti-Kidd(Jka) antibodies respectively and underwent term delivery. Both the babies were healthy, but the baby of a patient with the Anti-M antibody had mild anaemia and prolonged jaundice **Conclusion:** Patients with Anti- kell antibodies have poor fetal outcomes compared to those who have anti-Kidd and anti-M antibodies. Thus, screening of maternal serum antibodies in Rh-positive mothers must be formulated as a protocol to prevent perinatal morbidity and mortality thus improving the foetal outcome.

KEYWORDS

Rh antigen, Indirect Coomb's Test (ICT), fetal hemolysis, Anti Kidd, Anti kell.

INTRODUCTION:

Alloimmunisation refers to the development of an immune response to a foreign antigen (1). Antibodies thus formed are called alloantibodies and are usually formed against Rh (D, C, E,c,e) and Kell (K) (2) Antibodies directed against other blood groups like Anti Duffy. Anti-Kidd and Anti MNS have also been implicated (3). The anti-D antibody is the most common antibody causing Hemolytic disease in newborns and other complications in 80% of the cases (4).The prevalence of irregular red cell antibodies in pregnant females is 0.89-5.98% worldwide while 1.21-1.48% amongst Indian pregnant female (5). All igG RBC antibodies are capable of causing HDN of mild to moderate severity and all pregnant women with such antibodies should be followed up closely (6).Pahuja et al stated that routine antenatal screening is done in India only for RhD-negative women currently (7). The most important risk factors determining the fetal outcome that have been studied are multiparity, mothers' age, and antenatal maternal serum IAT titre (8). Positive DAT test may be due to several reasons including antiantibodies to intrinsic red cell antigens, hemolytic reactions post-transfusion, hemolytic disease of the newborn, drug-induced antibodies, alloantibodies acquired passively, some non-specifically adsorbed proteins, complement activation following a bacterial infection, autoantibodies, alloantibodies and antibodies produced by passenger lymphocytes (9,10).

Case Series :

Case 1: A 26 years old pregnant woman presents with complaints of pain abdomen for 2 days and amenorrhoea for 9 months, gravida 3, para 2. There was no history of any blood derivatives transfusion. Her blood group type was A Rh(D) positive which on the Indirect antiglobulin test (IAT) showed antibody against Job (Anti Kidd)in a titer of 1:4 None of her previous children presented data of hemolytic disease. Her husband was healthy and unrelated. Her HCV/HIV/ Hbsag were non-reactive. Father's RBC phenotype was A, Rh(D) positive. Follow-up was continued and anti-Jkb titer remained low during the whole pregnancy. No data of anaemia were noted in the fetus, thus no intrauterine transfusion was required. after 39 weeks of gestation, she delivered a healthy male with a weight of 3.1 kg. The baby had no complications at birth and he was a normal full-term infant, without jaundice or data of hemolysis. Blood type A Rh(D) positive was confirmed in the cord blood sample, with DAT being negative. Forty-eight hours after birth total serum bilirubin was 9.4 mg/dL. Haemoglobin was 16.5 g/dl and reticulocyte count was 5.1%. Neither phototherapy nor exchange transfusion was needed, and the newborn as well as her mother were discharged 2 days after birth.

Case 2: A 30-year-old female presented with pain abdomen, fever and restlessness and 38 weeks of amenorrhoea was gravida 5, para 4 with 3 live births with her fourth child death 8 years ago after a day of delivery. At 36 weeks of gestation, her routine USG was done which revealed massive fetal ascites. Her blood group was AB Rh positive and her DCT was negative but her ICT was positive. She had a history of recent blood transfusions. Her blood sample was sent to the blood bank for an antibody screening test and was found to be Anti Kell positive (titre 1:128) along with anti-E and k. At 36 weeks 3 days, a preterm female fetus was delivered with ascites and kernicterus.

Case 3:A 26 -year old female presented for an antenatal check-up at the 34^{h} week of pregnancy. She gave a history of one previous pregnancy and delivered a healthy baby. She gave no history of transfusions in the past and had not received anti-D immunoprophylaxis in any of the previous pregnancies. Her blood group was found to be AB Rh(D) and an anti-M antibody was detected in the antibody panel with a titre of 1:4. AT 39 weeks a male newborn was delivered with mild anaemia. The neonate had mild jaundice at birth and so received phototherapy, but an exchange transfusion was not required.

MATERIALS AND METHODS:

A sample of 200 antenatal patients was evaluated over 2 years and were divided into positive and negative. RhD-positive mothers were tested for IAT and an 11-cell antibody panel was applied to screen irregular antibodies. Patients with positive antibodies were followed throughout pregnancy and the outcome of the fetus was studied.

DISCUSSION

For the prevention of alloimmunization due to the most common Rh D antigen, all rhesus-negative pregnancies are routinely screened for evidence of all immunisation by employing an indirect agglutination test and anti-D immunoglobulin is administered prophylactically during and after delivery abortion or ectopic in such females (10). Amongst the 200 rhesus D positive cases in our study, only 3 (1.5%)

were positive for alloantibodies. Pahuja et al described an isoimmunization rate of 0.12% in 3183 RhD-positive Indian antenatal women (7). This higher occurrence of alloimmunisation in our study may be due to variations in sample size, geographical variation in antigen expression and a variable quantity of pretransfusion practice and no antigen screening for patients requiring repeated transfusion. Of all the IAT-positive cases, Anti Kell antibody was found in 1 (0.5%) case. In the study done by Pahuja et al and Varghese et al, anti-Kell antibodies contributed to 0.02% and 0.01% of cases respectively (7,11). Similarly, the occurrence of anti-M and Anti Duffy antibodies was 0.5% (1 case). In a study done by Pahuja et al and Suresh et al Anti Kdd antibody showed no contribution while the Anti-M antibody showed an occurrence of 0.005 % and 0.04% respectively (6,10).This slightly higher occurrence of Anti Kell, anti-Kidd and anti-Duffy antibodies may be because the study place is a tertiary centre with most of the cases being high-risk referral cases and also may be due to possible concealed history of drug abuse and previous abortion (12). In our case study, the fetal outcome of a patient having an anti-Kell antibody with a titre of 1.128 was adverse with kernicterus, ascitis and ultimately the death of the foetus. The anti-Kell has been known to cause adverse fetal outcomes irrespective of titres (13). Thus the possibility of anti-Kell antibody-associated mortality cannot be ruled out as also documented by Wamalen et al in their study suggesting that in the event of Kell alloimmunisation, the safest approach should be close monitoring of pregnancy with a Kell titre of 1:2 or above. They also suggested that the severity of anaemia is more common in women with a history of previous Kell-positive children (14). The patient having Anti M antibody with titre 1: 8 had a baby with mild anaemia and prolonged jaundice. A review of the literature for anti-M antibodies suggested that patients have varied presentations (15). Duro et al studied that high titres of IgG and IgM antibodies against M antigens could cause neonatal red cell aplasia and hemolytic disease in newborns (16). Mother with anti-Kidd antibody in the titre 1:4 delivered a healthy term baby. It has been discussed by Rodriguez et al that pregnancies with anti-Kidd antibodies (Jka), can potentially lead to hemolytic disease in the newborn but the severity is usually less and the newborns have a good outcome (17). Schumacher et al have suggested that if the fetus carries the corresponding antigen for a maternal antibody which is capable of causing fetal anaemia and if the antibody titres rise beyond the level for risk then the pregnancy is to be monitored weekly by ultrasonography and specific assessment of the fetal middle cerebral artery peak systolic velocities (MCA PSV) must be done (18). The consideration of invasive treatment should be made if the MCA PSV has risen above 1.5 multiples of the median (MoM) threshold or if other signs suggest fetal anaemia (19).

CONCLUSION

In addition to the Rh-negative mothers, there is a need to screen the Rh-positive mothers due to irregular red cell antibodies, as these are associated with a significant risk of hemolytic disease in fetuses and newborns. Anti-Kell antibodies can cause adverse fetal outcomes even at low antibody titres hence their titration must always be done in correlation with Doppler assessment for fetal MCA flow for better assessment of fetal status. Also if possible the status of fetal antigen and paternal phenotype must be determined as this can predict the outcome of the pregnancy and the risk of development of hemolytic disease in newborns. All alloimmunization pregnancies must be classified as high risk and low risk depending on the antibody titer and requirement of transfusion. Moreover, antenatal women that require repeated transfusion for other associated conditions must be considered high risk even at low titres. Thus there is a need to formulate protocols for the screening of maternal serum antibodies to prevent perinatal morbidity and mortality.

REFERENCES

1. Hendrickson JE, Tormey CA. Understanding red blood cell alloimmunization triggers. Hematology Am Soc Hematol Educ Program.2016(1):446-451.
2. Zaman S, Chaurasia R, Chatterjee K, Thapliyal RM. Prevalence and Specificity of RBC Alloantibodies in Indian Patients Attending a Tertiary Care Hospital. Adv Hematol. 2014;2014:749218.
3. Hassan MN, Mohd Noor NH, Johan Noor SR, Sukri SA, Mustafa R, Luc Aster HV. Hemolytic disease of the fetus and newborn due to maternal red blood cell alloantibodies in the Malay population. Asian J Transfus Sci. 2014;8(2):113-7.
4. Bennardello F, Coluzzi S, Curciarello G et al.Recommendations for the prevention and treatment of haemolytic disease of the foetus and newborn. Blood Transfus. 2015 ;13(1):109-34.
5. Foudoulaki-Paparizos L, Valsami S, Bournas N, Tsantes A, Grapsas P, Mantzios G, Travlou A, Politou M. Alloimmunisation during pregnancy in Greece: the need for nationwide HDFN prevention programme. Transfus Med. 2013;23(4):254-9.
6. Harmening DM, Prihoda LA. The antiglobulin Test. In: Green REB, Hughes VC, Editors. Modern Blood Banking and transfusion Practices. 5th ed. New Delhi: Jaypee Brothers; 2008: 94-10 3.
7. Pahuja S, Gupta SK, Pujani M, Jain M. The prevalence of irregular erythrocyte antibodies among antenatal women in Delhi. Blood Transfus. 2011;9(4):388-93.
8. Philip J, Jain N. Antenatal Maternal Serum IAT Titer and Fetal Outcome in Rh Isoimmunized Pregnancies. Indian J Hematol Blood Transfus. 2015;31(1):137-41.
9. Fung MK, Grossman BJ, Hillyer CD, Westhoff CM. The positive Direct Antiglobulin Test and Immune mediated hemolysis. In:Leger RM Editor. AABB Technical manual. 18th ed. United States: Maryland ; 2014.p 425-445.
10. Sarkar RS, Philip J, Mallhi RS, Jain N. Drug-induced immune hemolytic anemia (Direct Antiglobulin Test positive). Med J Armed Forces India. 2013;69(2):190-2.
11. Varghese J, Chacko MP, Rajaiah M, Daniel D. Red cell alloimmunization among antenatal women attending a tertiary care hospital in south India. Indian J Med Res. 2013;138(1):68-71
12. Suresh, Balakrishnan et al. "Prevalence of "unexpected antibodies" in th antenatal women attending the Government Maternity Hospital, Tirupati." The Journal of Clinical and Scientific Research.2015;4(1): 22-30.
13. Slootweg YM, Lindenburg IT, Koelewijn JM, Van Kamp IL, Oepkes D, De Haas M. Predicting anti-Kell-mediated hemolytic disease of the fetus and newborn: diagnostic accuracy of laboratory management. Am J Obstet Gynecol. 2018 ;219(4):393.e1-393.e8.
14. Van Wamelen DJ, Klumper FJ, de Haas M, Meerman RH, van Kamp IL, Oepkes D. Obstetric history and antibody titer in estimating severity of Kell alloimmunization in pregnancy. Obstet Gynecol. 2007 ;109(5):1093-8. 13.
15. Tondon R, Kataria R, Chaudhry R. Anti-M: Report of two cases and review of literature. Asian J Transfus Sci. 2008;2(2):81-3
16. Duro EA, Desalvo L, Kuret S. Severe hemolytic disease of the newborn caused by anti-m antibodies. Iran J Pediatr. 2013;23(5):607-8
17. Velasco Rodríguez D, Pérez-Segura G, Jiménez-Ubieto A, Rodríguez MA, Montejano L. Hemolytic disease of the newborn due to anti-jkb: case report and review of the literature. Indian J Hematol Blood Transfus. 2014;30(2):135-8.
18. Schumacher B, Moise KJ Jr. Fetal transfusion for red blood cell alloimmunization in pregnancy. Obstet Gynecol. 1996;88(1):137-50.
19. Andrei C, Vladareanu R. The value of reference ranges for middle cerebral artery peak systolic velocity in the management of rhesus alloimmunized pregnancies. Maedica (Bucur). 2012;7(1):14-9.