

CASE REPORT**NON-INVASIVE MONITORING OF FOETAL ANAEMIA IN KELL SENSITIZED PREGNANCY****Zaibunnisa Memon, Sana Sadiq Sheikh**

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We report a case of Kell sensitized pregnancy with good neonatal outcome. Anti-K antibodies were detected in maternal serum in early pregnancy as a part of routine antibody screening test. The middle cerebral artery doppler monitoring and serial titers were carried out to screen for foetal anaemia. Despite of rising antibody titers, serial middle cerebral artery doppler was normal and did not showed foetal anaemia. The pregnancy was carried out till term and patient delivered at 37 weeks of pregnancy with no evidence of foetal anaemia. This case underlines the need of general screening on rare antibodies in all pregnant women and that non-invasive monitoring of foetal anaemia can be done with anti-k titers and middle cerebral artery Doppler.

Keywords: Kell, Blood group incompatibility, Irregular antibodies, Noninvasive monitoring

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INTRODUCTION

Minor red blood cell (RBC) antibodies are the rare immune-globulins associated with RBC antigens other than ABO and Rh (D). These antibodies develop by exposure to foreign RBC antigens, bacteria or viruses. In order to determine risk of haemolytic disease of the foetus or newborn and to facilitate cross matching of maternal blood if an emergency transfusion is required at the time of delivery it is important to perform antibody screening test in all pregnant women irrespective of rhesus status. These rare antibodies like Kell, Duffy, Kidd or other blood group antigens may give rise to foetal anaemia, hydrops foetalis and intrauterine death if not detected and monitored.¹ The type and frequency of RBC antibodies reported in the literature varies.²

Among the rare antibodies associated with severe hemolytic disease of the fetus include RhD, RhC and Kell (K1). The exact incidence of Kell sensitized pregnancies is unknown. In one of the series published in 1996, Kell alloimmunization was higher (3.2/1000) as compared to studies of US populations in both 1967 and 1969 (2.2 and 1.6/1000, respectively).^{3,4} This could be related to increase detection of antibodies due to improvement of blood banking techniques and increase awareness among the obstetricians. Another reason could be increasing maternal age and parity and higher likelihood of exposure to blood transfusions that leads to red-cell sensitization. The variation in geographic distribution is explained by gene frequency. Caine ME and Mueller-Heubach reported 9% of Caucasians and 2% of blacks show K antigen on the red cells.

CASE REPORT

Twenty eight years old female, second gravida, parity 0+1 presented for her 2nd pregnancy. There was past history of spontaneous miscarriage one year back at

some local hospital. No blood transfusions were done in the past and antibody screening was not performed during her first pregnancy.

In her second pregnancy she was booked at 9 weeks of gestation for antenatal care. Routine antenatal laboratory investigations along with antibody screening were carried out. Antibody screening was found positive for anti-k antibodies. Patient was counselled regarding anti-k antibodies effect on the foetus and was advised to get serial antibody titers with close monitoring for foetal anaemia. Figure-1. Her partner refused to get antibody screening test. Since there was no history of blood transfusion in the past we assumed her partner as Kell positive. Antibody titer initially revealed rising trend and reached to critical level (1:8). However, middle cerebral artery doppler showed no evidence of foetal anaemia. Follow-up titers showed falling trend until 35 weeks of pregnancy where antibodies titer again started to rise. Serial middle cerebral artery doppler and ultrasound growth were carried out for screening of foetal anaemia, all remained within normal range and foetus had shown normal interval growth with no signs of foetal anaemia or hydrops. Routine screening for gestational diabetes mellitus was performed and found to be positive. Gestational diabetes was managed successfully with diet control and metformin. At full term antibodies titer started to rise again so labour was induced because of rising titer and gestational diabetes. Patient delivered by caesarean section due to non-progress of labour. A baby boy of 2.9 kg delivered with Apgar score of 8 in one minute and 9 at five minute.

Neonatal examination was unremarkable and laboratory investigations did not show evidence of neonatal anaemia and direct coombs was negative. A review of the management of alloimmunization to Kell antibodies follows.

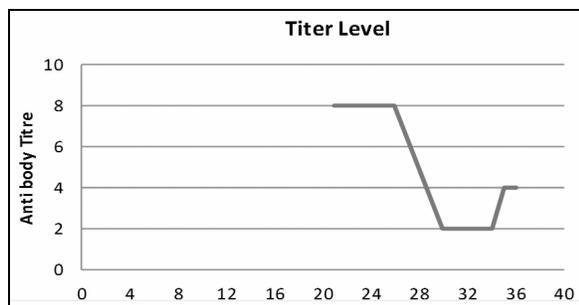


Figure-1: Showing serial titers of Kell antibodies

DISCUSSION

The Kell blood group is the most common of the minor RBC antibodies. The major antigen of the Kell group is K.⁵ Anti-Kell antibodies are responsible for approximately 10 percent of cases of severe antibody-mediated anaemia in foetuses and neonates.⁶ In one large series reported by Bowman, *et al* 20 affected foetuses and infants among 311 sensitized women, three foetuses required intrauterine foetal transfusions for severe anaemia or hydrops, one required an early delivery and multiple neonatal exchange transfusions, four required neonatal exchange transfusion and/or phototherapy, and 12 did well without any treatment for anaemia or hyperbilirubinemia. The literature search did not produce any data regarding degree of the haemolytic disease of the neonates due to anti-K.⁷ Blood transfusion may be the most common mode of Kell sensitization in childbearing age women, since Kell compatibility is not routinely checked when blood is cross matched. In one series 8 of 12 Kell-sensitized women with Kell-positive babies had a prior blood transfusion history.⁸

Therefore it is important to know history of blood transfusion and obstetrical history to assess possible modes and risk of sensitization. The risk of developing foetal anaemia will base on mode of sensitization. For woman who was sensitized after a transfusion, the chance of the baby's father would be Kell-positive (KK or Kk) is only 8.9 percent, thus there is only about a 4.5% chance the foetus will be Kell-positive and at risk from maternal antibodies. However, if patient has not been transfused and was sensitized from a previous pregnancy with the same partner, then the father must be Kell-positive (KK or Kk) and there is an approximately 51% chance the foetus will be Kell-positive and potentially affected by maternal antibody.

The predominant mechanism of foetal anaemia involves transplacental passage of a maternal IgG antibody directed against a foetal erythrocyte antigen but Kell alloimmunization involves an additional mechanism whereby erythropoiesis is suppressed at the level of the

progenitor cell and hence, at same level of foetal anaemia, the foetus with Kell alloimmunization has a lower number of circulating reticulocytes and normoblasts and relatively low levels of serum and amniotic fluid bilirubin compared with the foetus with Rh(D) alloimmunization.^{9,10}

The monitoring of Kell sensitized pregnancies is challenging as the titer of anti-Kell antibody in maternal serum and the amniotic fluid bilirubin level do not correlate well with the degree of foetal anaemia. In rhesus sensitized pregnancies 16 is taken as the critical titer but in Kell sensitized pregnancy experts recommend 8 as the critical titer because of the unique pathogenesis of this disorder. Others believe no threshold can be designated to accurately predict absence of severe foetal anaemia.^{11,12} Interpretation of delta OD450 is less accurate for assessing anaemia in the Kell-positive foetus due to suppression of erythropoiesis rather than haemolysis is the more prominent cause of anaemia in Kell antibody-mediated foetal anaemia compared to the Rh (D)-positive foetus where haemolysis causes generation of bilirubin which can be detected in amniotic fluid. So, for the monitor foetal anaemia Doppler assessment of the foetal middle cerebral artery peak systolic volume assessment is the most preferred tool for determination of foetal anaemia in Kell sensitized pregnancies.^{13,14} If middle cerebral artery peak systolic volume is above 1.5 MoMs, then cordocentesis for foetal haematocrit/haemoglobin and confirmation of blood type should be performed if available.

If a non-pregnant woman is found to have anti-red cell antibodies, she should be counselled regarding the potential effects of the antibody on a future pregnancy. If the biologic father of the future pregnancy is known, it is reasonable to determine his RBC antigen status and zygosity (if he carries the RBC antigen to which the patient is immunized). A low maternal pre-pregnancy titer is not predictive of foetal outcome since the titer can raise several-fold during pregnancy. However, a past history of HDFN or high maternal antibody titer is predictive of adverse foetal outcome.

There are only three interventions which can be used to prevent HDFN:

1. Donor insemination with sperm from a RBC-antigen compatible donor
2. If the biologic father is heterozygous for the relevant RBC antigen, in vitro fertilization with pre-implantation genetic diagnosis and implantation of only embryos with a compatible blood type, if any are produced, and
3. Surrogate pregnancy using the patient's ovum and her partner's sperm.¹⁵

CONCLUSION

With this case we want to emphasize on screening of rare antibodies during pregnancy and that the management of Kell (K1 and K2) allo-immunization is different from RhD due to ability of these antibodies to suppress the foetal erythropoiesis leading to foetal anaemia. Amniocentesis for foetal haemolysis assessment when a critical titer is reached has got limited value in Kell sensitized pregnancy. Non-invasive monitoring with middle cerebral artery PSV has got good predictive value of assessing foetal anaemia. All women of reproductive age should receive Kell negative blood transfusions to avoid such complication.

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