

**BEYOND THE D: WHEN ANTI-D PROPHYLAXIS ISN'T ENOUGH; A CASE OF ANTI-C AND ANTI-E NEONATAL HEMOLYSIS****Obstetrics & Gynaecology****Dr. Aakanksha Padma Naik\***

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**ABSTRACT**

RhD-negative pregnancies complicated by clinically significant maternal red cell antibodies require close antenatal surveillance and coordinated perinatal care to prevent hemolytic disease of the fetus and newborn (HDFN). Anti-D prophylaxis does not protect against alloimmunization to other red cell antigens, and anti-c and anti-e antibodies can cause neonatal hemolysis even when the maternal course is uncomplicated. Case presentation: A G3P1L1A1 woman with blood group B, Rh-negative, had strongly positive (4+) anti-c and anti-e antibodies. She had received anti-D immunoglobulin on day 2 after her previous delivery and first booked at 34+2 weeks. She underwent lower segment cesarean section at 37+2 weeks for a previous cesarean scar. The baby weighed 2.7 kg, had Apgar scores of 8, 9 and 9 at 1, 5 and 10 minutes, was blood group B positive, and had a strongly positive (4+) direct antiglobulin test. The neonate required monitoring and treatment for hemolysis, including intravenous immunoglobulin (IVIG) on day 1 of life, and was discharged on day 13 with a phototherapy blanket. Live vaccines (BCG and OPV) were deferred until after 6 weeks. The maternal postpartum period was uneventful. Conclusion: Antenatal detection of non-D antibodies in Rh-negative pregnancy is essential. Even with an uncomplicated maternal course, anti-c and anti-e alloimmunization can cause clinically significant neonatal hemolysis requiring prolonged postnatal care and follow-up, underscoring the need for multidisciplinary maternal- neonatal management.

**KEYWORDS**

Alloimmunization; Anti-c; Anti-e; Hemolytic Disease Of The Newborn

**INTRODUCTION**

Hemolytic disease of the fetus and newborn (HDFN) results from transplacental passage of maternal IgG alloantibodies directed against fetal red cell antigens inherited from the father. Routine anti-D immunoglobulin prophylaxis has sharply reduced anti-D-mediated disease, but it offers no protection against alloimmunization to other red cell antigens (Hall et al., 2025). Anti-D remains the most frequent culprit, followed by anti-K and anti-c (Wagle & Aslam, 2024). We report a woman with concurrent anti-c and anti-e alloimmunization whose newborn developed significant hemolysis despite an uncomplicated maternal course.

**Case Report**

A woman, G3P1L1A1, with blood group B Rh (D) negative, presented for her first antenatal booking at 34+2 weeks of gestation. Antibody screening showed strongly positive (4+) anti-c and anti-e antibodies. She had one living child and one abortion, and had received anti-D immunoglobulin on day 2 after her previous delivery. No history of any transfusion of any blood products. Antenatal Doppler findings: in Biophysical Profile scan at 36 weeks: MCA of 1.2 MoM. Her antenatal course was otherwise clinically uncomplicated.

Because of a previous cesarean scar, she underwent lower segment cesarean section at 37+2 weeks. The baby weighed 2.7 kg and had Apgar scores of 8, 9 and 9 at 1, 5 and 10 minutes. The neonatal blood group was B positive, and the direct antiglobulin test (DAT) was strongly positive (4+), consistent with antibody-mediated hemolysis. The neonate required monitoring and treatment for hemolysis, including intravenous immunoglobulin (IVIG) on day 1 of life. Baby received Phototherapy (initially continuous and later intermittently) for total of 8 days from DOL-1 to DOL-8. BIND score was noted to be ZERO throughout the stay. The phototherapy was stopped on DOL-9 at 10:30am for 24hrs after which the rebound bilirubin level on DOL-10 was noted to be: 17.3MG/DL. Hence single surface phototherapy was started with bili blanket and continued. repeat Sr bilirubin was sent on DOL 12 was noted to be 17.6mg/dl, hence double surface phototherapy was started and continued for 24 hours. The baby was discharged on day 13 with a phototherapy blanket. Live vaccines (BCG and OPV) were deferred at discharge and planned after 6 weeks. The maternal postpartum period was uneventful. Table 1 summarizes the key findings.

**Table 1. Key maternal and neonatal findings**

| Parameter                  | Finding            |
|----------------------------|--------------------|
| Maternal obstetric formula | G3P1L1A1           |
| Maternal blood group       | B, Rh (D) negative |

|                                    |                                           |
|------------------------------------|-------------------------------------------|
| Maternal antibodies                | Anti-c and anti-e, strongly positive (4+) |
| Booking gestation                  | 34+2 weeks                                |
| Previous anti-D prophylaxis        | Day 2 after previous delivery             |
| Delivery                           | LSCS at 37+2 weeks (previous scar)        |
| Birth weight; Apgar (1, 5, 10 min) | 2.7 kg; 8, 9, 9                           |
| Neonatal blood group; DAT          | B positive; strongly positive (4+)        |
| Neonatal treatment                 | IVIG on day 1 of life                     |
| Discharge                          | Day 13, phototherapy blanket              |

**DISCUSSION**

Since the introduction of anti-D prophylaxis, antibodies to non-D antigens account for a growing share of clinically significant HDFN. Anti-c is among the most important of these, whereas anti-e usually causes milder disease; anti-D, anti-K and anti-c have been reported to account for roughly 85%, 10% and 3.5% of cases requiring intrauterine transfusion, respectively (Wagle & Aslam, 2024). The IgG antibodies cross the placenta, coat fetal red cells and promote their extravascular destruction, causing anemia and hyperbilirubinemia, with a positive neonatal DAT as the laboratory hallmark (Hall et al., 2025). In this case, the strongly positive DAT and the maternal antibody specificities explained the neonatal course.

Several points merit emphasis. First, prior anti-D prophylaxis was irrelevant to this sensitization, because no immunoprophylaxis exists for anti-c or anti-e; prevention rests on comprehensive antenatal antibody screening and, where relevant, antigen-matched transfusion. Second, the combination of anti-c and anti-e in an RhD-negative woman implies an uncommon Rh phenotype lacking both antigens, or variant antigen expression. Rh phenotyping or genotyping, including paternal testing, would clarify this and help predict recurrence risk.

Third, booking at 34+2 weeks left little time for surveillance. Current guidance recommends serial antibody titration and middle cerebral artery Doppler assessment once critical titers are reached, with delivery planned in a center equipped for neonatal care (American College of Obstetricians and Gynecologists, 2018; Mustafa et al., 2025). Early booking is therefore a modifiable determinant of outcome.

Fourth, neonatal management follows the HDFN pathway: phototherapy, with IVIG as an adjunct in selected infants to limit the need for exchange transfusion, although evidence for its benefit is still evolving (Hall et al., 2025; Mustafa et al., 2025). Infants should be

followed after discharge for late anemia, and decisions on live vaccines after immunoglobulin or blood products should be individualized, as in our patient.

Published neonatal reports of anti-C with anti-e, all in RhD-positive mothers, are few (Jung et al., 2023). In these, jaundice typically appeared between days 3 and 5, bilirubin was moderately high, and most infants recovered with phototherapy with or without IVIG; exchange transfusion was needed in only one (Table 2). Our infant required IVIG on day 1 and a 13-day stay, longer than the 5-day admission reported by Jung et al. (2023), although missing bilirubin and hemoglobin data limit this comparison. Unlike the Korean mother, who had no prenatal screen, our patient's antibodies were identified before delivery. Indian series highlight the ongoing debate on routine screening: a tertiary-centre study found alloimmunization in 3.1% of antenatal women and questioned universal screening (Gothwal et al., 2023), whereas others argue that minor-group HDFN justifies it (Agrawal et al., 2020). Antibody titers also correlate poorly with severity, so clinical vigilance is needed even at low titers.

Table 2. Comparison with published neonatal anti-C/anti-e cases

| Report                      | Antibodies; mother             | Onset; bilirubin      | Treatment                                | Outcome                 |
|-----------------------------|--------------------------------|-----------------------|------------------------------------------|-------------------------|
| Wagner et al., 2000         | Anti-C + e                     | 13 h; 28.6 mg/dL      | IVIG, phototherapy, exchange transfusion | Severe                  |
| Sharma et al., 2015         | Anti-C + e; preterm            | 29.6 mg/dL            | IVIG, phototherapy                       | No exchange transfusion |
| Sharma & Farahbakhs h, 2019 | Anti-C + e                     | 48 h; 17.1 mg/dL      | Phototherapy                             | Recovered               |
| Jung et al., 2023           | Anti-C + e; no prenatal screen | Day 3; 28.9 mg/dL     | Intensive phototherapy, IVIG             | Discharged day 5        |
| Present case                | Anti-c + e; RhD-negative       | IVIG on day 1; DAT 4+ | IVIG, phototherapy                       | Discharged day 13       |

Finally, a positive maternal antibody screen attributable to non-D antibodies should not by itself lead to withholding anti-D immunoglobulin. Prophylaxis remains indicated for an RhD-negative woman who has not formed anti-D after delivering an RhD-positive baby (Royal College of Obstetricians and Gynaecologists, 2011), which requires that the antibody specificity be identified rather than reported simply as "positive." The limitations of this report are its single-patient design and the incomplete laboratory data noted above.

CONCLUSION

Antenatal detection of non-D antibodies in an RhD-negative pregnancy is essential. Even with an uncomplicated maternal course, anti-c and anti-e alloimmunization can cause clinically significant neonatal hemolysis requiring IVIG, prolonged postnatal care and follow-up. Comprehensive antibody screening, early booking and multidisciplinary obstetric-neonatal planning are the cornerstones of management.

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