Immune Anti-D in Pregnancy n=52

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Definition:

Cases of D-negative pregnant women who become sensitised and are found to have developed immune anti-D, which is detected during pregnancy, either at booking or later in the index pregnancy.

Abbreviations used in this chapter

BSH	British Society for Haematology	**IU**	International units
CffDNA	Cell-free fetal deoxyribonucleic acid	**IV**	Intravenous
DAT	Direct antiglobulin test	**NPP**	No previous pregnancies
FMH	Fetomaternal haemorrhage	**PP**	Previous pregnancies
HDFN	Haemolytic disease of the fetus and newborn	**PSE**	Potentially sensitising event
Ig	Immunoglobulin	**PV**	Per vaginal
IM	Intramuscular	**RAADP**	Routine antenatal anti-D Ig prophylaxis
IT	Information technology	**UK**	United Kingdom

Key SHOT messages

- Cases of immunisation are still occurring even where current best practice is being followed
- Obesity and delivery beyond 40 weeks remain potential risk factors for sensitisation in cases which are otherwise ideally managed
- There are ongoing missed opportunities where pregnancy management is not ideal
- Where a maternal D variant is detected, women should be assigned to a D-negative treatment pathway to ensure appropriate treatment and monitoring
- UK hospital uptake of maternal cffDNA fetal D screening is limited

Recommendations

- Cases of alloimmune anti-D found for the first time in pregnancy should be reported to SHOT, aiming to provide a complete data set after delivery
- Hospital transfusion teams and women's services to review current training to avoid missed opportunities where pregnancy management is not ideal e.g., patient stories
- All UK hospitals should check that they have implemented a maternal cffDNA fetal D screening programme and that a local policy is available and consider audit to determine the barriers to uptake
- Hospital transfusion teams and women's services to check the advice in guidelines, policies and reflex pathways regarding women typed D variant is to assign a D-negative treatment pathway

Action: Transfusion laboratory management, maternity services, hospital IT departments

Introduction

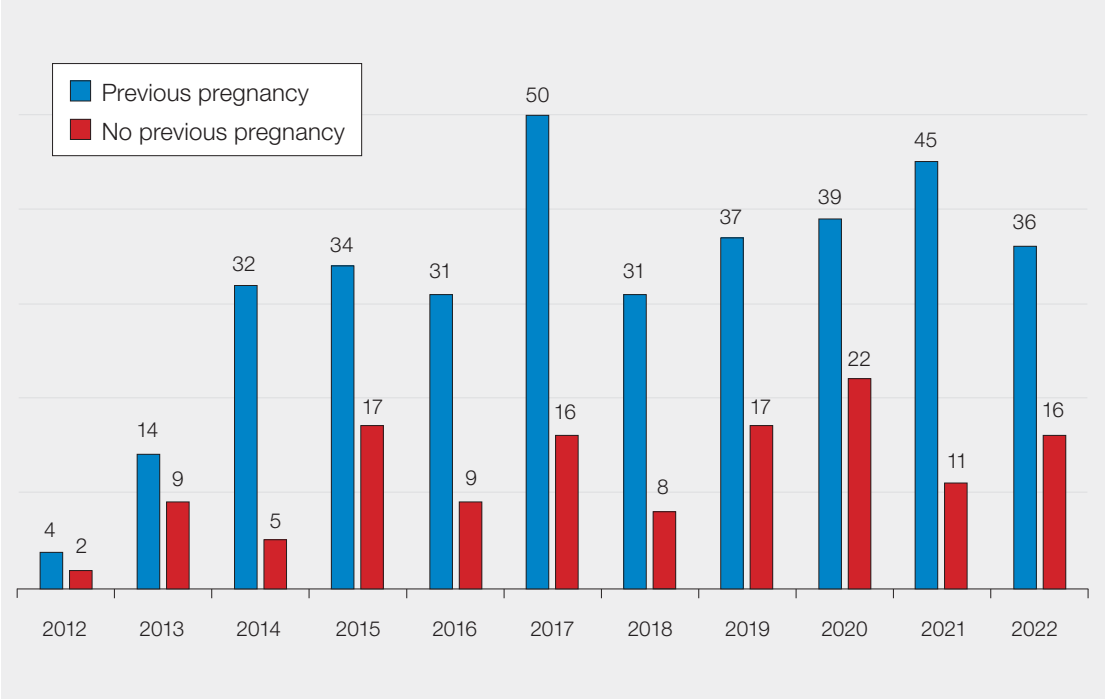
Since 2012 SHOT has been reviewing cases where immune anti-D has been detected for the first time in the current (index) pregnancy to improve understanding of the causes of continuing anti-D immunisations. Reporters are requested to provide data on booking weight, management of sensitising events during pregnancy and the administration of RAADP, both in the index pregnancy and the pregnancy immediately before the index pregnancy (if applicable).

Results

In 2022 a total of 52 cases were reported, 16 cases occurred in women with NPP, and 36 in women with PP. Reporting is fairly consistent however the available data would suggest that anti-D immunisation in pregnancy remains under-reported (see the assumptions and calculation provided in the 2018 Annual SHOT Report (Narayan et al. 2019)).

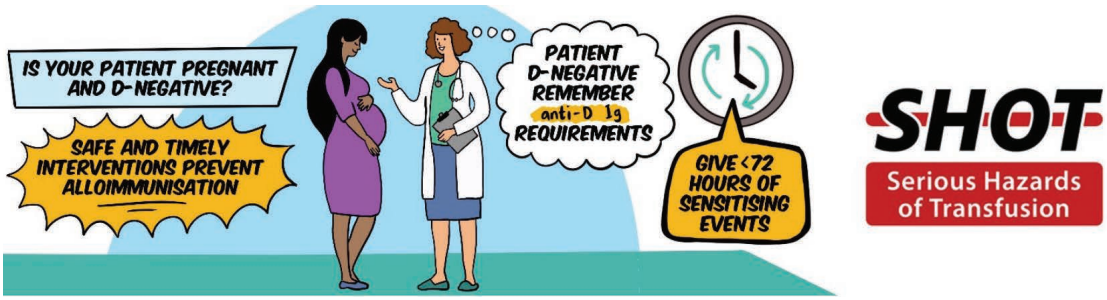
Cumulatively SHOT now has useful data on 132 women with NPP and 353 women with PP.

Figure 26.1: Number of reports of anti-D immunisation in pregnancy by year, 2012-2022



No previous pregnancy (NPP) n=16

For a detailed discussion of the NPP cases, and tables containing similar details to those published in previous Annual SHOT Reports, please see the supplementary information on the SHOT website (https://www.shotuk.org/report-summary-and-supplement-2022/).



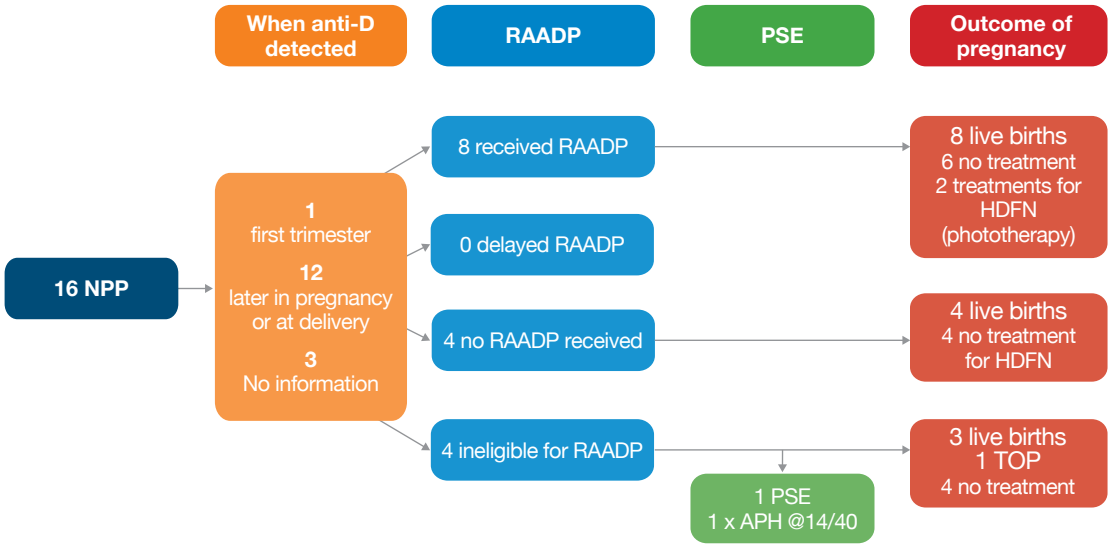


Figure 26.2: Summary of 2022 NPP data (n=16)

APH=antepartum haemorrhage; HDFN=haemolytic disease of the fetus and newborn; NPP=no previous pregnancy; PSE=potentially sensitising event; RAADP=routine antenatal anti-D Ig prophylaxis; TOP=termination of pregnancy

Illustrative cases

Case 26.1: Misinterpretation of the maternal blood group resulted in omission of anti-D Ig

A primiparous woman in her 20s booked in at 8 weeks. The maternal blood group was misinterpreted as D-positive. No RAADP was given at 28 weeks, and there were no PSE reported. Peripartum maternal anti-D was detected. A review of the maternal blood group report confirmed a D variant.

Women in whom the blood group is D variant must be treated the same as when blood group is D-negative.

Case 26.2: Immune or prophylactic anti-D 28-week sample

A primiparous woman in her early 30s was booked in at 9 weeks. The group and antibody screen detected the mother to be D-negative, and no alloantibodies were detected. The maternal sample for cffDNA at 16 weeks predicted the fetus to be D-positive. No PSE were reported. The maternal blood sample at 28 weeks was taken prior to RAADP administration which detected anti-D and was misinterpreted as prophylactic anti-D Ig. After a live birth at 40 weeks; the maternal antibody panel was 4+ anti-D, cord DAT 3+, maternal anti-D quantification was 156.7IU/mL. The neonate required phototherapy.

Case 26.3: Route of administration

A D-negative primiparous woman in her 20s of average weight, received 1500IU IM gluteal RAADP at 28 weeks gestation based on the cffDNA test which predicted the fetus to be D-positive. There were no PSE reported. Following delivery at 40 weeks a maternal blood sample detected anti-D, with a quantification of 27.7IU/mL.

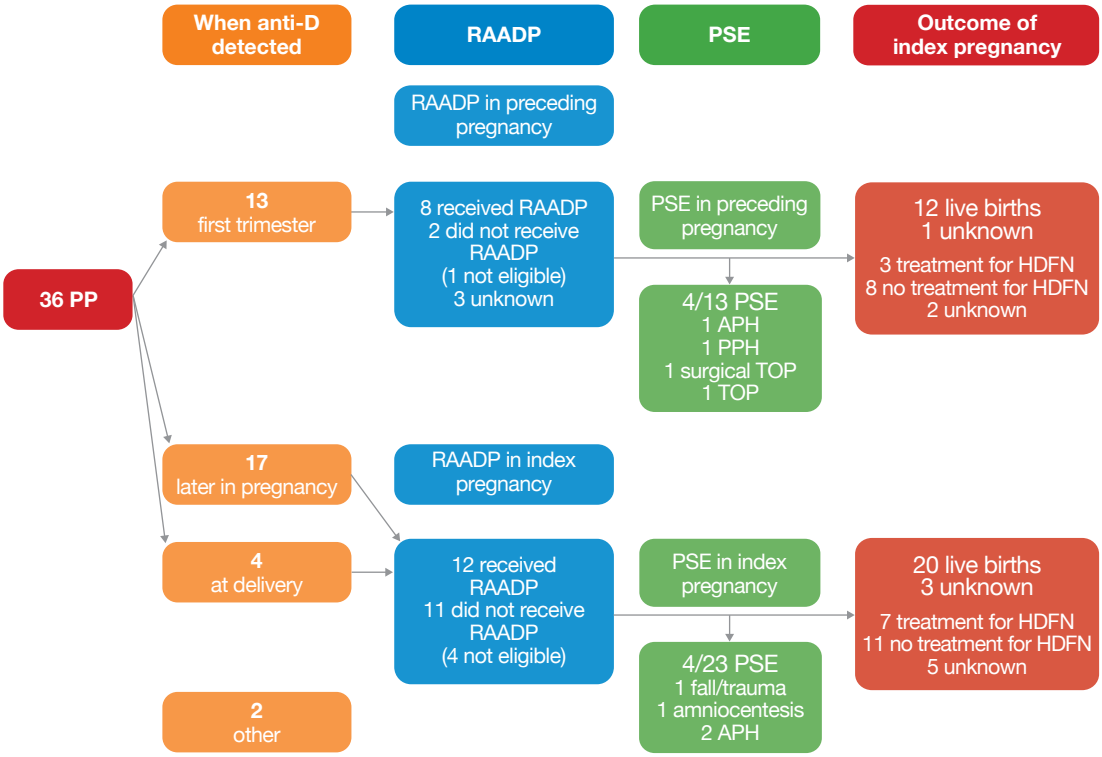
The management in this case was according to guidelines. It is important to note when IM gluteal injections are given, particular care should be taken to ensure that the injection is given into muscle as absorption may be delayed if it only reaches the subcutaneous tissues (BCSH Qureshi et al. 2014).

Previous pregnancies (PP) n=36

The index pregnancy in these cases refers to the current pregnancy – the pregnancy in which alloimmune anti-D was first detected.

For a detailed discussion of the PP cases, and tables containing similar details to those published in previous Annual SHOT Reports, please see the supplementary information on the SHOT website (https://www.shotuk.org/report-summary-and-supplement-2022/).

Figure 26.3: Summary of 2022 PP data (n=36)



APH=antepartum haemorrhage; HDFN=haemolytic disease of the fetus and newborn; PP=previous pregnancy; PPH=postpartum haemorrhage; PSE=potentially sensitising event; RAADP=routine antenatal anti-D immunoglobulin prophylaxis; TOP=termination of pregnancy

Illustrative cases

Case 26.4: Large fetomaternal haemorrhage

A D-negative woman in her late 20s, was booked in at 11 weeks. Her weight was 79kg, and she was gravida 2 para 1. Immune anti-D was detected at booking, and a D-negative baby was born at 36 weeks.

In the previous pregnancy RAADP was administered and from the details provided it appears that a suboptimal dose was given post delivery. Further details are provided here. Following an elective cesarean section at 39^{+1} a significant FMH of 63.1mL was recorded. If the anti-D Ig was administered IM the anti-D Ig dose required was calculated to be 8000IU (63.1x125=7887.5). Advice was provided that the dose required if the anti-D Ig was given IV. was equivalent to 50% of the IM dose. The calculation of anti-D Ig to be given IV should have been 100IU per mL (6310IU). This suggests the dose provided of 4500IU was not adequate. A Kleihauer at 72 hours reported a FMH of less than 4mL, no further anti-D Ig was provided and no further Kleihauer was performed.

As noted by the local reporting team 'The calculation of anti-D Ig to be given IV should have been 100IU per mL (6310IU)'. Healthcare professionals should refer to manufacturer's guidance depending on the product used (BCSH Qureshi et al. 2014). In addition, there was a delay in the repeat Kleihauer and an absence of further doses of anti-D Ig to clear the remaining FMH. Follow-up samples are required at 48 hours following an IV dose of anti-D Ig or 72 hours following an IM dose to check for clearance of fetal cells (BCSH Qureshi et al. 2014). Management of a FMH often spans a number of healthcare professionals and care should be taken to ensure local process provides continuity of care and management in accordance with guidelines.

Case 26.5: Prophylactic or immune anti-D, antenatal monitoring

A woman in her 20s, gravida 4 para 1 (2 miscarriages) booked at 8 weeks, with a booking weight of 66.5kg. Booking bloods did not detect any anti-D. A group and antibody screen at 28 weeks detected anti-D and the report noted probable prophylactic anti-D Ig and requested a further sample. A repeat sample was not sent. RAADP was provided at 28 weeks. At 35 weeks following a fall, prophylactic anti-D Ig was administered, however no Kleihauer was performed. A group and antibody screen detected alloimmune anti-D, quantification 5.2IU/mL. Following a scan at 36^{+6} weeks a decision was made to bring the planned elective caesarean section forward to 38 weeks. The prior live birth was a caesarean section. The mother delivered a D-positive baby, Hb130g/L, DAT 4+. The baby was monitored and re-admitted with evidence of ongoing haemolysis; Hb68g/L and the baby required red cell transfusion.

The management of this case highlights the complexity of the pathway with multiple points at which intervention and decision making according to guidelines may have increased awareness of the risk of haemolysis in pregnancy.

Case 26.6: Sensitisation in what appears to be ideal management

A D-negative woman, gravida 2 para 1 in her 30s was booked in at 9 weeks, booking bloods did not detect anti-D, booking weight 78.8kg. Maternal cffDNA at 16 weeks predicted the baby to be D-positive. The mother attended at 27 weeks following PV bleeding, a group and antibody screen was taken and the women was provided with 500IU anti-D Ig. The Kleihauer was negative however alloimmune anti-D, quantification 9.5IU/mL was detected. The highest level recorded in the pregnancy was 35.2IU/mL at 35 weeks. In the prior pregnancy the woman booked in at 9 weeks, received RAADP, no sensitising events had been identified, and the baby was born by vaginal delivery at 40^{+4} days. The previous baby was D-positive, postpartum anti-D Ig was provided and the Kleihauer was less than 2mL.

The mother and baby were monitored by the fetal maternal unit in the index pregnancy, the pregnancy resulted in a live birth at 37^{+3}. The baby was D-positive and received phototherapy.

Ideal management does not prevent all cases of HDFN, aside from the prior delivery at 40^{+4} and the PSE at 27 weeks which was adequately treated. No other factors were identified that would have potentially contributed to sensitisation.

Conclusions

The data this year detailed in the supplementary information on the SHOT website (https://www.shotuk.org/report-summary-and-supplement-2022/) demonstrate residual issues around ideal management of D-negative women during pregnancy to prevent immunisation. The 2022 data continue to illustrate missed opportunities where pregnancy management is not ideal. This is demonstrated in the NPP and PP RAADP and PSE data.

Two cases are described where women who are D variant have been incorrectly managed according to a D-positive pathway.

It is evident that the uptake of maternal cffDNA remains limited.

Further work needed

Hospital transfusion teams and women's services should review current training to avoid missed opportunities where pregnancy management is not ideal examples of training material include SHOT patient stories.

References

BCSH Qureshi H, Massey E, Kirwan D, et al. BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. *Transfus Med*. 2014;**24(1)**:8-20. https://doi.org/10.1111/tme.12091 [accessed 02 May 2023].

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