25 Immune Anti-D in Pregnancy n=56

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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

APH	Antepartum haemorrhage
BMI	Body mass index
BSH	British Society for Haematology
CffDNA	Cell-free fetal deoxyribonucleic acid
FMH	Fetomaternal haemorrhage
HDFN	Haemolytic disease of the fetus and newborn
Ig	Immunoglobulin
IT	Information technology
IUD	Intrauterine death
NHS	National Health Service
NHSBT	NHS Blood and Transplant
NICE	National Institute for Health and Care Excellence
NIPT	Non-invasive prenatal testing
NPP	No previous pregnancies
PP	Previous pregnancies
PPP	Postpartum prophylaxis
PSE	Potentially sensitising event
RAADP	Routine antenatal anti-D Ig prophylaxis
UK	United Kingdom

Key SHOT messages

- 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
- 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 missed opportunities where pregnancy management is not ideal
- Interoperability of IT systems to improve the pathway and outcome for D-negative women in pregnancy and postpartum remains a challenge

Recommendations

- All UK hospitals should check that they have signed up to share results access in Sp-ICE
- Electronic health record providers and hospitals who plan to implement or continue to develop an electronic health record should map the pathway for D-negative women in pregnancy and post-partum and jointly develop intelligent pathways that support decision making
- All blood transfusion IT solutions must ensure appropriate IT interfaces between the laboratory information management system and electronic health record to remove the requirement of healthcare professionals to manually enter a blood group or D-type to reduce the risk of a transcription error that may prevent appropriate management

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

Introduction

SHOT has been reviewing cases where immune anti-D has been detected for the first time in the current (index) pregnancy since 2012 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 2021 a total of 56 cases were reported, 11 cases occurred in women with NPP, and 45 in women with PP. While there is a steady increase in the number of cases reported, available data suggests 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 116 women with NPP and 317 women with PP.

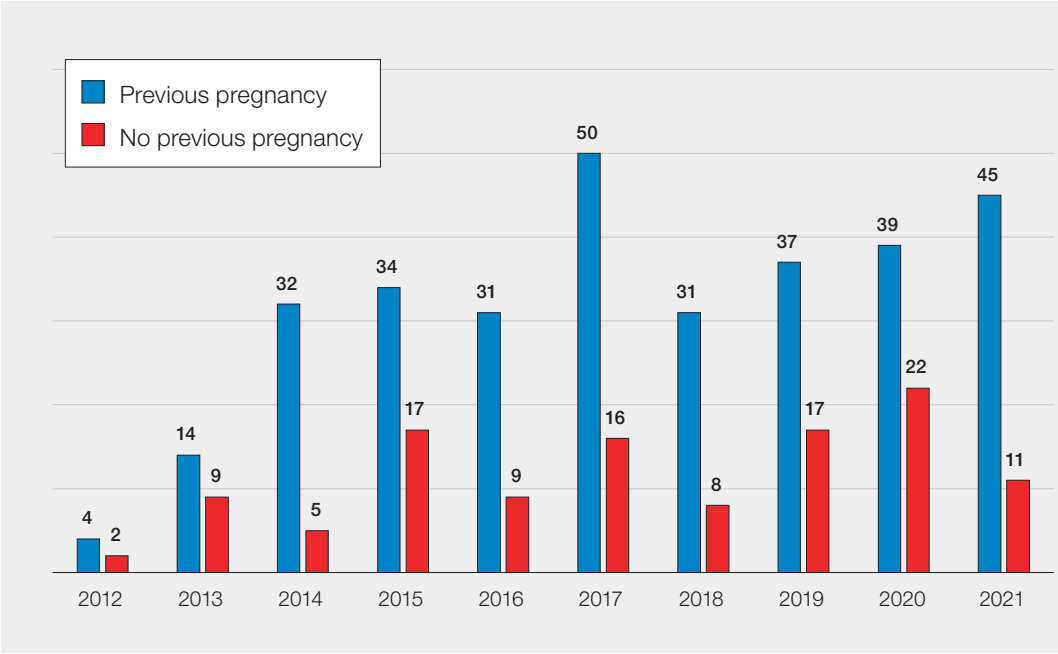
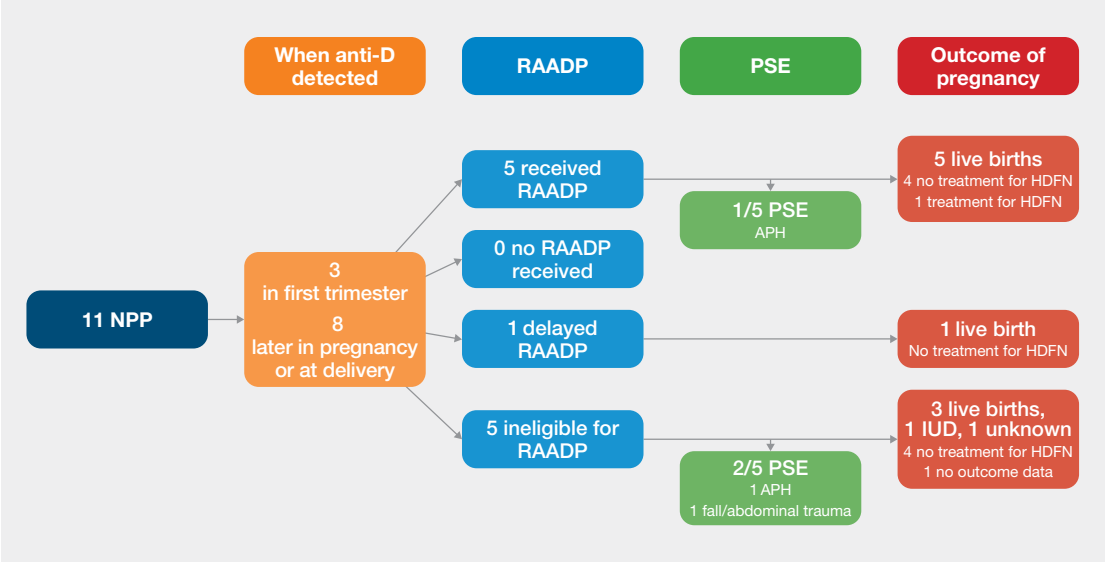


Figure 25.1: Number of reports of anti-D immunisation in pregnancy by year, 2012-2021

No previous pregnancy (NPP) n=11

For a detailed discussion of the NPP cases, and tables containing similar details to those published in previous Annual SHOT Reports, see the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2021/).

Figure 25.2: Summary of 2021 NPP data (n=11)



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

Illustrative cases

Case 25.1: Missed PSE

A primiparous woman in her 30s booked at 8 weeks, no alloantibodies were detected. The woman had a fall at 9 weeks but no medical attention was sought at the time. Maternal blood sampling for cffDNA predicted a D-positive fetus at 17 weeks. At 28^{+3} the woman attended for a scan following concern regarding reduced movements which identified an IUD. Anti-D was detected however there was no quantification. No postmortem was performed according to communications with the SHOT team.

In the absence of a postmortem it is not possible to conclude the cause of the IUD.

The PSE occurred the week after the booking and it is not known whether the maternal D-type and risk of sensitisation had been conveyed to the woman at booking. Where systems enable patient portal access to the electronic health record, this provides the advantage of real-time access for patients to blood results prior to the next appointment. Such a system could have triggered the provision of relevant information regarding the risk of sensitisation, when and how to seek medical advice to the patient.

Case 25.2: Detection of anti-D in early pregnancy

A primiparous woman in her 30s, BMI 46 booked at 8 weeks. Alloimmune anti-D was detected at booking, quantification 13.38IU/mL, highest quantification 15.5IU/mL. The woman delivered a D-negative infant at 37^{+3}.

There were no details provided with this case to determine whether there were definitively no prior sensitising events including transfusion or biochemical pregnancies. It is not clear if a maternal blood sample was sent for fetal genotyping following detection of alloimmune anti-D, potentially a missed opportunity to provide parental reassurance and limit repeat blood sampling and appointments for quantification during pregnancy.

Case 25.3: Sensitisation despite ideal management

A primiparous woman in her early 20s booked at 8 weeks, group and antibody screen detected the mother to be D-negative, no alloantibodies detected. She presented with abdominal pain at 12 weeks, no associated bleeding, scan did not detect any abnormality, she was reassured and discharged. Maternal sample for cffDNA at 13 weeks predicted the fetus to be D-positive. The maternal blood sample at 28 weeks prior to RAADP detected alloimmune anti-D, quantification 0.7IU/mL, the highest recorded quantification at 36 weeks was 3IU/mL. The pregnancy resulted in a live birth at 38/40, the baby showed no signs of jaundice, no treatment required.

In this case, there were no prior unidentified sensitisation events reported. This highlights the potential risk that some pregnant women may still be sensitised with a risk of HDFN, despite the recommended mitigating measures being implemented.

Case 25.4: Ideal management, gestation 41^{+5}

A primiparous woman, D-negative, 66kg in her late 30s, received ideal management throughout pregnancy receiving RAADP, no PSE. Following delivery at 41^{+5} a maternal blood sample detected anti-D, quantification 2.7IU/mL.

This is an example of sensitisation despite ideal management with the only risk factor identified to be a gestation beyond 40 weeks.

Previous pregnancies (PP) n=45

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/shot-reports/report-summary-and-supplement-2021/).

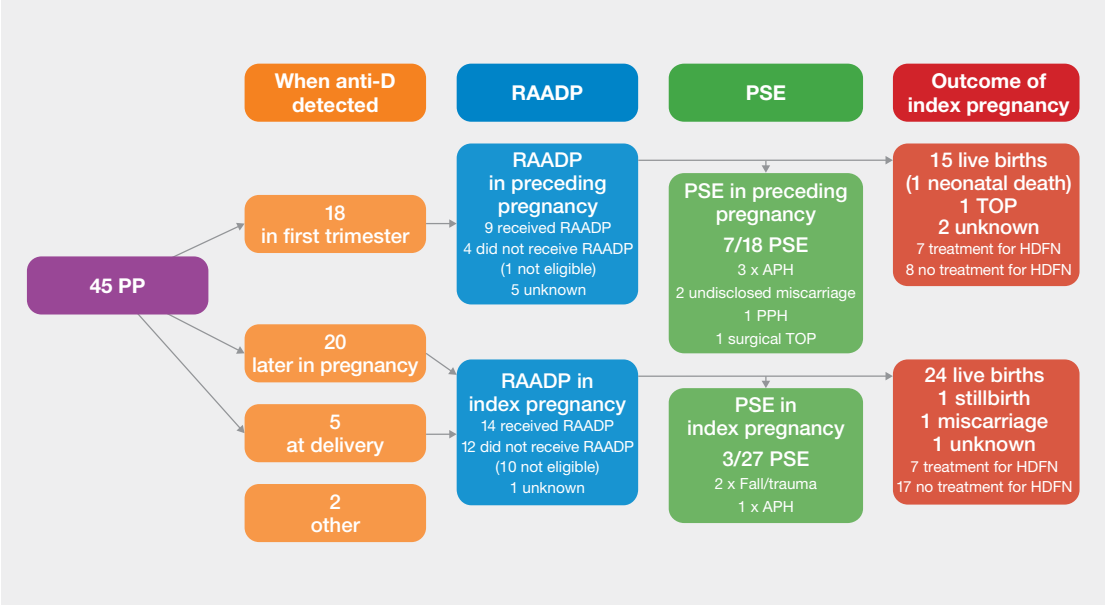


Figure 25.3: Summary of 2021 PP data (n=45)

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

Illustrative cases

Case 25.5: HDFN treatment

A D-negative woman in her 20s who weighed 87kg, gravida 2 para 1 was booked at 11 weeks. The previous pregnancy was managed at a different healthcare provider and details of the prior pregnancy were limited. In the previous pregnancy this woman received four doses of anti-D Ig, timing and dose not provided and she delivered a D-positive baby. She suffered a postpartum haemorrhage. In the index pregnancy, alloimmune anti-D was detected at booking. The highest quantification of anti-D was 330IU/mL at 36 weeks. The mother delivered a D-positive baby at 37^{+1}, the baby required phototherapy and due to increasing bilirubin levels was transferred to the neonatal unit and received immunoglobulin and an exchange blood transfusion.

It is not possible to determine if the woman received ideal management in the previous pregnancy. These cases are much less common since implementation of RAADP reduced the risk of HDFN. This case demonstrates the intense management that neonates with HDFN can require and the importance of prevention wherever possible.

Case 25.6: Baby D-positive, cffDNA predicted D-negative fetus

A D-negative female in her 20s, gravida 3 para 2, weight 77kg, booking bloods did not detect alloimmune anti-D and cffDNA in the index pregnancy at 13 weeks predicted a D-negative fetus. The woman as such did not receive RAADP. Maternal transfusion sample at delivery 37^{+1} detected alloimmune anti-D and anti-E, anti-D quantification 14.2IU/mL. Following delivery, the baby was identified to be jaundiced, D-positive and DAT 3+, phototherapy was required. The preceding pregnancy management was appropriate.

When the baby D-type is disconcordant with the cffDNA fetal D-screening test, it is important to notify the laboratory as further samples are required to enable further investigation. Whilst the test is highly accurate and can be performed from 11^{+2} weeks' gestation owing to the sensitivity of the test, there is a small chance (0.1%) that a fetus predicted to be D-negative will be D-positive at birth.

Case 25.7 Maternal blood group transcription error

A D-negative woman gravida 2 para 1 presented in her second pregnancy. In her first pregnancy due to the method of the test request the maternal blood group was not automatically transmitted to the maternity IT system. The maternal blood group was incorrectly transcribed A D-positive. In the subsequent pregnancy the error was detected when the woman's booking bloods were resulted and identified her to be A D-negative with alloimmune anti-D, quantification 0.1IU/mL. In the prior pregnancy no RAADP nor treatment for a PSE was provided. The pregnancy resulted in a live birth, baby was A D-negative.

The maternal D-type transcription error resulted in the failure to provide appropriate RAADP and treatment of a PSE. Appropriate IT interfaces between laboratory information management systems and the electronic health record must remove the requirement for healthcare professionals to manually enter a blood group or D-type as they may be referenced regarding future management.

Conclusions

The data this year (detailed in the supplementary information on the SHOT website) demonstrate residual issues around ideal management of D-negative women during pregnancy to prevent immunisation. The 2021 data continue to illustrate missed opportunities where pregnancy management is not ideal. This is demonstrated in the NPP RAADP and PSE data by delay in treatment and in the PP data by failure to provide RAADP and PSE anti-D Ig due to an electronic health record transcription error regarding documentation of maternal D-type. Cumulative data includes a total of 82 PSE in the preceding pregnancies of which 53 (64.6%) were managed correctly. It is encouraging to see the antepartum haemorrhages reported have been managed appropriately, however, the need for a focused approach to ensure the correct pathway and decision making for D-negative women in pregnancy is necessary.

The maternal D-type transcription error results in failure to provide appropriate RAADP and treatment of a PSE. Appropriate IT interfaces between LIMS and the electronic health record must remove the requirement for healthcare professionals to manually enter a blood group or D-type as they may be referenced regarding future management.

The emerging questions on ideal management from the cumulative data including the increased risk in obesity and particularly the increased risk of gestation beyond 40 weeks remain supported by the additional 2021 data. However, the differential between the 18 PP preceding pregnancy obesity rate of 25% and 27 PP cases of immune anti-D Ig detected beyond the first trimester index pregnancy obesity rate of 23.4% versus the national data (NHS Digital 2019) report 22% incidence of obesity in pregnant women in England is narrowing. The cumulative data with regards to gestation beyond 40 weeks is perhaps more convincing demonstrating 48 pregnancies where alloimmune anti-D was first detected at delivery in the index pregnancy, 17 cases (35.4%) were delivered after 40 weeks gestation. NHS maternity statistics 2019-2020 indicate 15.9% pregnancies extended beyond 40 weeks (NHS Digital 2020). All cases reported should endeavor to provide gestation in weeks and days and provide booking weight and BMI to enable direct comparison to national data sets.

The data collection on cffDNA highlights ongoing barriers to implementation. IBGRL are currently testing >4,000 samples per month. These samples come from NHS Trusts, private service providers (a minority) and 3 Republic of Ireland Trusts. The Trusts, which were on hold during the COVID-19 pandemic, were invited to implement the fetal D-screening test from September 2021. Although 60% of maternity hospitals in England send samples for fetal D-screening, staff shortages in obstetrics and pathology departments have slowed progress, not only for the Trusts which were on hold but also for Trusts who have not implemented this test. (personal communication International Blood Grouping Reference Laboratory).

The 2021 data suggest:

- Ideal management does not equal no sensitisation
- Delivery beyond 40 weeks may be a risk factor for sensitisation even when managed appropriately
- Women who are obese may not be adequately 'protected' by standard doses of anti-D Ig, however the cumulative data is less convincing
- There are missed opportunities where pregnancy management is not ideal

Further work needed

A review of the cumulative data with regards to obesity, delivery beyond 40 weeks and FMH >4mL should be undertaken to see if the data provide enough evidence to modify current guidelines.

A focused approach to ensure treatment decisions are right for D-negative women is necessary to prevent sensitisation.

Appropriate IT interfaces between laboratory information management systems and the electronic health record must remove the requirement for healthcare professionals to manually enter a blood group or D-type as they may be referenced regarding future management.

A review of the material available and the possibility of an electronic application to support decision making should be considered. Electronic health record providers and hospitals who plan to implement or continue to develop an electronic health record should map the pathway for D-negative women in pregnancy and post-partum developing intelligent pathways that support pathway management and decision making.

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Serious Hazards of Transfusion

References

Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2020 Annual SHOT Report (2021). https://www.shotuk.org/shot-reports/ [accessed 06 May 2022].

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