Immune Anti-D in Pregnancy n=61 25

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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.

Key SHOT messages

- Cases of alloimmune anti-D found for the first time in pregnancy should be reported to SHOT, and reporters should provide a complete data set after delivery
- Cases of immunisation are still occurring even where current best practice is being followed
- Delivery beyond 40 weeks and obesity continue to be potential risk factors for sensitisation in cases which are otherwise ideally managed
- There are missed opportunities for anti-D Ig prophylaxis where pregnancy management is not ideal
- Interoperability of information technology systems to improve the pathway and outcome for D-negative women in pregnancy and postpartum remains a challenge

Recommendations

- Hospitals should sign up to share access to results on Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment (Sp-ICE) where applicable
- Where an electronic health record is being planned or has been implemented, pathways to support decision-making should be incorporated for appropriate management of D-negative women in pregnancy and post-partum. Hospital staff should work collaboratively with electronic health record providers to support this

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

Abbreviations used in this chapter

APH	Antepartum haemorrhage	**NHSBT**	National Health Service Blood and Transplant
BMI	Body mass index	**NICE**	National Institute for Health and Care Excellence
BSH	British Society for Haematology	**NPP**	No previous pregnancies
cffDNA	Cell-free fetal deoxyribonucleic acid	**PCR**	Polymerase chain reaction
DAT	Direct antiglobulin test	**PP**	Previous pregnancies
FMH	Fetomaternal haemorrhage	**PSE**	Potentially sensitising event
HDFN	Haemolytic disease of the fetus and newborn	**RAADP**	Routine antenatal anti-D Ig prophylaxis

Ig	Immunoglobulin	**RTA**	Road traffic accident
IT	Information technology	**Sp-ICE**	Specialist Services electronic reporting using Sunquest's Integrated Clinical Environment
IUD	Intrauterine death	**UK**	United Kingdom
LIMS	Laboratory information management system		

Introduction

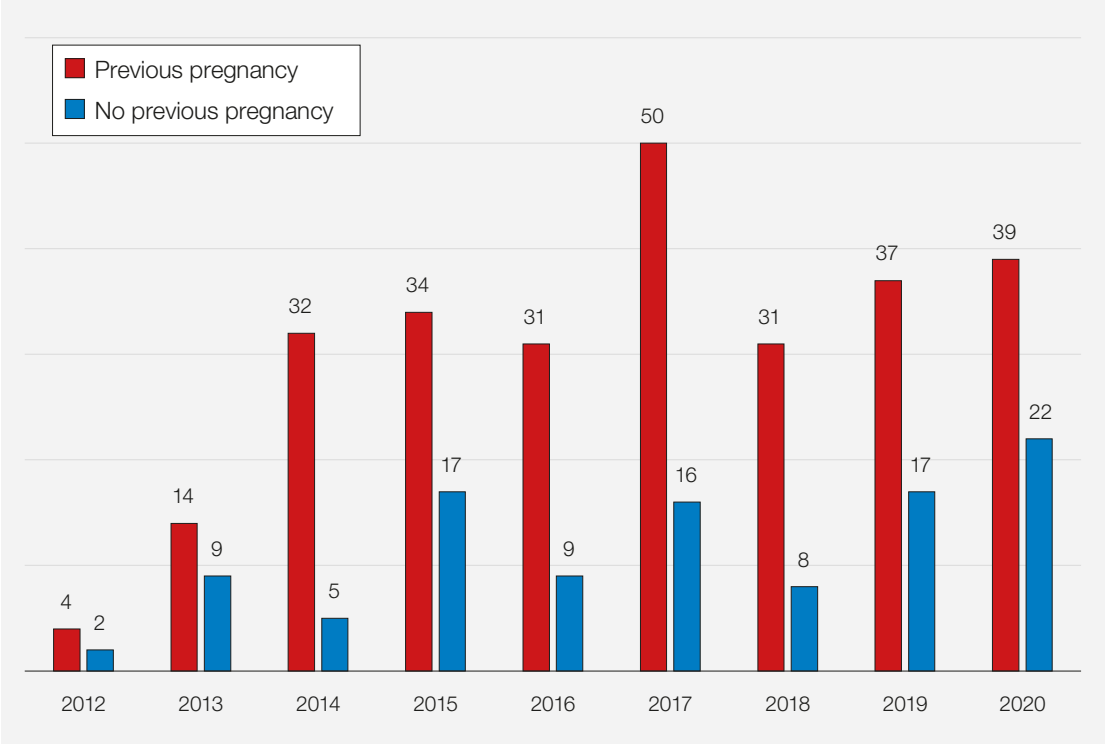
To improve understanding of the causes of continuing anti-D immunisations, SHOT has been reviewing cases where immune anti-D has been detected for the first time in the current (index) pregnancy since 2012. Reporters are requested to provide data on booking weight, management of sensitising events during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

Results

In 2020 a total of 61 cases were reported, 22 cases occurred in women with NPP, and 39 in women with PP. It is reassuring to note that the upturn in 2019 reporting continued in 2020, as 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 105 women with NPP and 272 women with PP.

Figure 25.1: Number of reports of anti-D immunisation in pregnancy by year, 2012-2020



No previous pregnancy (NPP) n=22

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/shot-reports/report-summary-and-supplement-2020/).

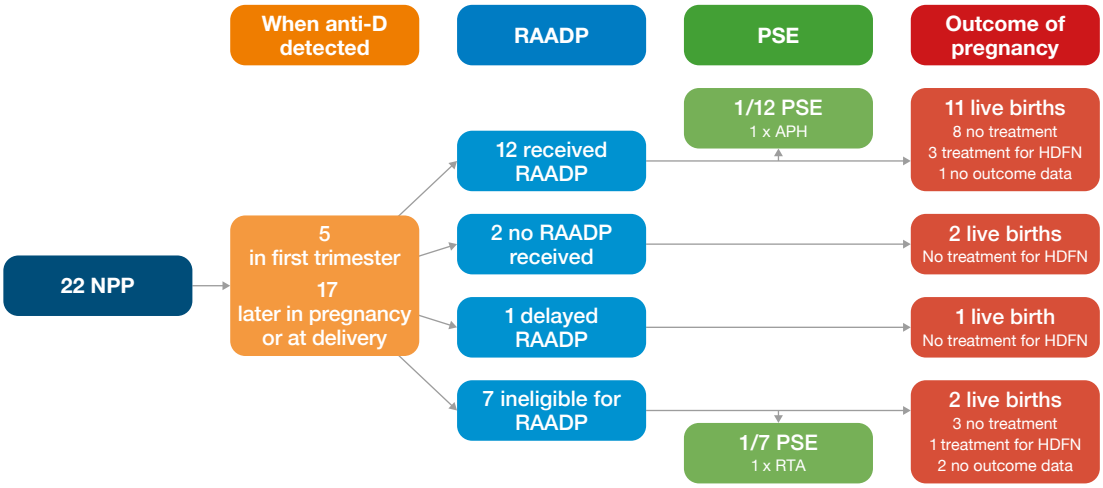


Figure 25.2: Summary of 2020 NPP data (n=22)

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

Illustrative cases

Case 25.1: Difficulty in determining whether anti-D detected was due to prophylaxis or alloimmune anti-D in pregnancy

A primiparous woman in her 30s, booked at 10-weeks gestation (booking weight 73kg) and no alloantibodies were detected. A group and antibody screen was taken at 28 weeks and then RAADP was given. The sample was rejected due to incorrect annotation of the label. A further sample was taken the following week, anti-D detected, quantification less than 0.1IU/mL. At the time this was considered most likely prophylaxis. A further sample was taken at 34 weeks, the quantification remained less than 0.1IU/mL and was again considered most likely prophylaxis. No PSE was reported. A D-positive baby was delivered at 41^{+1}. A group and screen sample taken at delivery demonstrated a strong antibody reaction, quantification 4IU/mL, confirming alloimmune anti-D.

The guidelines and pathways for D-negative women in pregnancy are complex and challenging and require close working of the multidisciplinary team. This case highlights issues with logistics in a time-dependent pathway and the need to continue to determine prophylaxis versus alloimmune anti-D. History of anti-D Ig administration, quantification and serial monitoring of antibody levels at increased frequency in ambiguous cases may be useful to help differentiate between passive and immune anti-D (BSH Qureshi et al. 2014).

Case 25.2: Ideal management of twin pregnancy

A primiparous woman in her late 30s, booked at 10-weeks gestation, booking weight of 61kg. She was D-negative, and no alloantibodies were detected. RAADP was given at 28 weeks. This was a twin dichorionic diamniotic pregnancy, delivered at 37^{+4}, both twins were D-positive and anti-D Ig was given post-delivery. Alloimmune anti-D was detected by chance following a preoperative assessment 3 months postpartum 0.8IU/mL and remained persistent after 6 months.

Ideal management may not always prevent sensitisation and further work is needed to explore this, in particular a review of twin pregnancy data in D-negative women is of interest.

Case 25.3: Omission of RAADP

A primiparous woman in her early 20s presented to triage at 37^{+5}, having not attended since booking at 18 weeks. A diagnosis of maternal preeclampsia was made, fetal tachycardia was detected, and a caesarean section performed. A D-positive baby was delivered, DAT positive, and the baby required no interventions for HDFN. This patient was lost to follow up and did not receive RAADP, no PSE were identified retrospectively.

Case 25.4: Presentation of severe HDFN during first pregnancy

A primiparous woman in her late 30s, booked at 12 weeks, booking weight 64kg. Maternal antibody screen at booking and 28 weeks was negative. The mother received RAADP, no evidence of PSE. She presented at 36 weeks with suspected abruption, underwent caesarean section and it was concluded that abruption was unlikely. The baby was D-positive with Hb 40g/L, and a strongly positive DAT. Maternal antibodies anti-D, C and S were detected, and anti-D quantified as 247.9IU/mL. The baby recovered following exchange transfusion for HDFN.

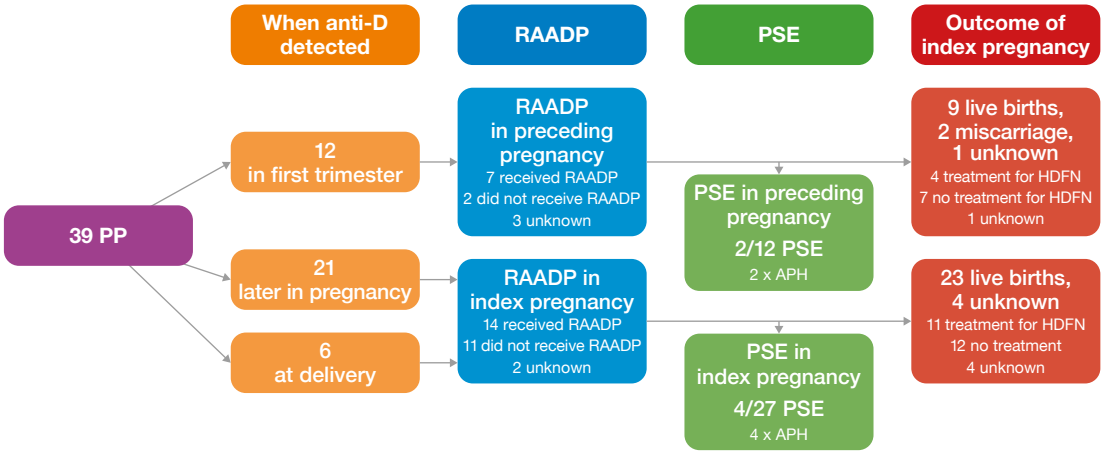
This case is a reminder that in the absence of identification of antibodies at 28 weeks, HDFN may still present in first pregnancies.

Previous pregnancies (PP) n=39

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-2020/).

Figure 25.3: Summary of 2020 PP data (n=39)



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

Illustrative cases

Case 25.5: Sensitisation associated with concealed pregnancy

A woman in her 20s, gravida 2 para 1 (booking weight 67kg) had anti-D detected at 11-weeks gestation with a quantification of 0.1IU/mL, which peaked at a quantification of 4.6IU/mL. A D-positive baby was delivered at 39^{+6}. No neonatal treatment was required. The preceding pregnancy was concealed, and no antenatal care was received. The woman had presented at 40 weeks, and a D-positive baby was delivered vaginally. The FMH estimation was less than 2mL, the woman received 500IU anti-D Ig.

When pregnancies are concealed and/or when patients are lost to follow up, opportunities to prevent sensitisation are missed, which can have deleterious effects on subsequent pregnancies.

Case 25.6: Sensitisation associated with obesity and multiple previous pregnancies

A woman in her 30s, gravida 5 para 1(live birth) +3 (miscarriages), booked at 13-weeks gestation, with a booking weight of 92kg. Anti-D was detected with a quantification of 0.1IU/mL. The peak quantification at 31-weeks gestation was 60.4IU/mL. Induction progressed at 36^{+5}, a D-positive baby was delivered and required phototherapy. In the preceding pregnancy the mother had been booked at 10 weeks, with a booking weight of 120kg. RAADP was given, no PSE were identified during the pregnancy, and postpartum FMH estimation was less than 2mL, for which she received 500IU anti-D Ig.

This case is an example where apparently 'ideal' management still resulted in immunisation. Cases in this category included 4 with 3 or more prior pregnancies, 2 of whom were obese in the PP cases where alloimmune anti-D was detected in the first trimester. Potential risk factors include obesity and the number of prior pregnancies. SHOT only collects information about management of the preceding pregnancy, therefore it is not possible to comment on management of the earlier pregnancies.

Case 25.7: Ineffective and sub-optimal clinical decision-making pathways

A woman in her 30s, gravida 3 para 2, booked at 8-weeks gestation, with a booking weight of 83kg. Maternal cffDNA screening test predicted the fetus to be D-positive at 16 weeks. Anti-D was detected at 20 weeks, quantification was not performed. This error was identified at the third trimester antenatal appointment, the fetus was scanned and demonstrated signs of hydrops. The mother was transferred to a fetal maternal unit. A D-positive baby was delivered at 34 weeks requiring exchange blood transfusion. In the preceding pregnancy the mother had been booked at 10 weeks with a booking weight of 63kg, RAADP was given, and there were no PSE identified. Delivery was at 39 weeks and postpartum prophylaxis was adequate (FMH less than 2mL, 1500IU anti-D Ig).

The pathway of D-negative women in pregnancy is complex, involving multi-professional teams, and failure to complete all steps in management risks poor fetal outcome. Electronic systems could be utilised to support good practice and ensure all relevant testing is performed. 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.

Conclusions

The data this year (detailed on the SHOT website https://www.shotuk.org/shot-reports/report-summary-and-supplement-2020/) demonstrate residual issues around ideal management of D-negative women during pregnancy to prevent immunisation. The 2020 data continue to illustrate missed opportunities where pregnancy management is not ideal. This is demonstrated in the NPP RAADP data by a delay, an insufficient treatment dose and an omission to treat. This is also reflected in the continuing anti-D Ig errors detailed in Chapter 9, Adverse Events Related to Anti-D Immunoglobulin (Ig). Case 25.7 highlights the need for robust processes to ensure steps are completed to ensure appropriate monitoring of antibody levels, to prevent poor fetal/neonatal outcomes. A focused approach to ensure the correct pathway and decision making for D-negative women in pregnancy is necessary.

There are unanswered questions on the ideal management of pregnancies with obesity and/or gestation beyond 40 weeks. These have been identified as potential risk factors previously and data from 2020 shows similar risks. More work needs to be done in this area to improve management and reduce risk.

The data collection on cffDNA highlights ongoing barriers to implementation. IBGRL are currently testing 3,400-3,600 samples per month. These samples come from NHS Trusts/Health Boards, private service providers (minority) and 3 Republic of Ireland Trusts. There are Trusts on hold, which would represent 16,000 samples per annum, due to COVID-19 and the knock-on effect for PCR consumables that resulted in a shortage.

The forecast is that 56% of NHS Trusts and Health Boards will have implemented cffDNA screening by April 2022 (personal communication from International Blood Grouping Reference Laboratory).

One case commented that the pregnancy was booked in another Health Board and no cffDNA data was provided. This highlights the need for more effective information sharing between healthcare organisations, to optimise patient outcomes and quality of care. NHSBT currently report cffDNA results via the online NHSBT database Sp-ICE. At present this is the only way to receive these results. Midwifes can be trained and added as users by the Sp-ICE laboratory administrator and can look up results in this system. Not all Trusts agree to share their data on Sp-ICE, which prevents other UK Trusts and Health Boards from being able to view these results. NHSBT are also developing an electronic data interchange between the NHSBT and hospital LIMS to enable interoperability. This is an example of work that will contribute to the digital transformation of care driven by NHSX, https://hospital.blood.co.uk/diagnostic-services/red-cell-immunohaematology/service-developments/.

The 2020 data suggest:

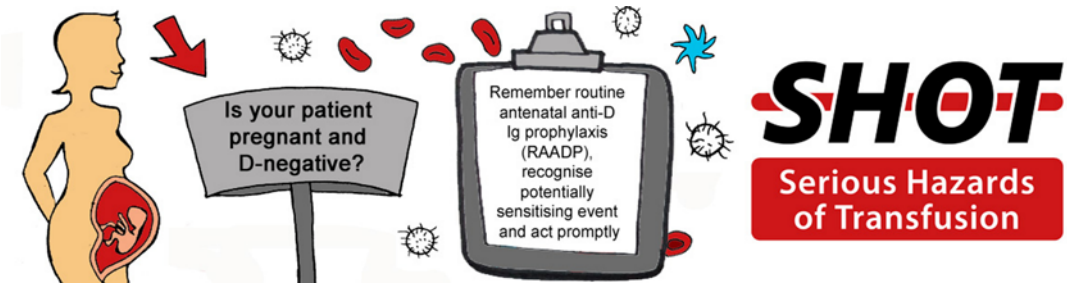
- Ideal management does not prevent sensitisation
- Delivery beyond 40 weeks may be a risk factor for sensitisation even when managed appropriately
- Women who are obese may not be adequately 'protected' by standard doses of anti-D Ig
- There are missed opportunities where pregnancy management is not ideal
- Interoperability of IT systems to improve the pathway and outcome for D-negative women in pregnancy and postpartum remains a challenge

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. The possibility of using electronic applications to support clinical decision making should be considered. Where an electronic health record is being planned or has been implemented, pathways to support decision-making should be incorporated for appropriate management of D-negative women in pregnancy and post-partum. Hospital staff should work collaboratively with electronic health record providers to support this. In the interim, hospitals should align local policies with the BSH addendum which signposts the more recent NICE Guidance 126 and 140 (2019).

The interoperability between Blood Services, reference laboratories, hospital IT systems and wider digital transformation in the NHS needs to progress.



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