2022 Annual SHOT Report – Supplementary information

Chapter 26: Anti-D immunisation in pregnancy

No previous pregnancy (NPP) n= 16

There were 16 new cases in 2022 (no cases excluded), cumulative to date 132 cases**.**

Summary of 2022 NPP data

Whilst in the majority of NPP cases, alloimmune anti-D is detected at delivery, there continues to be an increase in cases detected prior to 28 weeks, although the cause remains unclear.

We would encourage reporters to try and obtain booking weight as it is important in providing evidence for the role of obesity as a risk factor for immunisation.

Of the cases that were eligible for RAADP (n=12), 8 received RAADP between 28-30 weeks. Of the four remaining eligible cases: 2 case RADDP was missed, 1 case the maternal D group (variant) was incorrectly assigned to a D positive pathway, 1 case stated there was no local policy for RAADP, anti-D Ig only provided for potential sensitising events. A business case for RAADP was submitted in 2021 however pending outcome and implementation.

Case 26.7: RAADP implementation and local policy

A D-negative primiparous woman in her 20s was booked in at 10 weeks. No RAADP was administered. No PSE were recorded. Alloimmune anti-D was detected on admission prior to delivery, quantification 1.9IU/mL; routine antenatal samples did not detect any red cell atypical antibodies. The woman delivered a D-positive infant at 39^{+4}. The department had a policy to administer anti-D Ig following a PSE, but no policy regarding RAADP.

All D-negative pregnant women who have not been previously sensitised should be offered RAADP. RAADP has been shown to reduce antenatal sensitisation from 1% to 0.35% of pregnancies. The NICE guidelines (TA156) cover RAADP for women who are D-negative (NICE 2008, BCSH Qureshi et al.2014).

The number of documented cases where the fetal D screening test has been performed when gestation appropriate prior to the subsequent detection of alloimmune anti-D has improved but remains lower than expected (n=5).

There were no documented cases of fetal genotyping from maternal blood subsequent to the detection of maternal antibodies. Documentation of testing since its introduction in 2018 continues to improve and hopefully reflects uptake of cffDNA fetal D screening and fetal genotyping from maternal blood and access to the results. At least 1 infant were subsequently detected to be D negative at delivery, highlighting the missed opportunity regarding cffDNA testing uptake which may have reduced maternal concern regarding the risk of haemolytic disease of the fetus or newborn (HDFN) and resulted in less antenatal appointments and maternal anti-D quantification testing.

There was 1 case of a potential sensitising events: PV bleeding at 14 weeks gestation, no anti-D Ig was administered.

In 4 cases alloimmune anti-D was first detected at or beyond 40 weeks, at the time of delivery, all had RAADP, no sensitising events, data regarding weight was missing for 1 of the cases, 1 was obese, 1 neonate required phototherapy.

Pregnancy outcomes were reported in all cases including 15 live births and 1 termination of pregnancy. With regards to neonatal intervention for haemolytic disease of the fetus and newborn (HDFN) 2 required phototherapy.

When was the alloimmune anti-D detected?

The cumulative data shows that in the majority of cases immune anti-D is first detected at delivery.

Table 24.1: Time of detection of alloimmune anti-D

	Number of new cases 2022	Number of cases cumulative to 2022
Before 28 weeks	1	19
At or after 28 weeks, before delivery	5	45
At delivery	7	61
Other	0	2*
No information	3	5
Total	**16**	**132**

**Alloimmune anti-D was detected 6 months postpartum after large FMH of 12.7mL at delivery managed correctly, Alloimmune anti-D was detected 3 months postpartum prior to a surgical procedure, twin pregnancy managed correctly.*

What was the booking weight?

Weight is used in place of body mass index (BMI) as weight is more fully reported than BMI. Using average female height in the United Kingdom (UK), 80kg would equate to obesity in most women.

Table 24.2: Booking weight

Weight at booking in kg	Number of new cases 2022	Number of cases cumulative to 2022
<68	4	48
68-80	3	16
>80 (obese)	1	18
No information	8	50
Total	**16**	**132**

Cumulatively, of the 82 women where booking weight was provided, 18 (21.9 %) were obese. National data (NHS digital 2019) report 22% incidence of obesity in pregnant women in England. https://files.digital.nhs.uk/58/FFD7B1/msms-mar19-exp-rep.pdf

Did the women receive appropriate RAADP?

Alloimmune anti-D was detected in 1 case prior to 28 weeks and in 2 case at 28 week weeks. One pregnancy was terminated prior to 28 weeks. The remaining 12 were eligible for RAADP, 8 received RAADP between 28-30 weeks. Of the four remaining eligible cases: 2 case RADDP was missed, 1 case the maternal D group (variant) was incorrectly assigned to a D-positive pathway, 1 case stated there was no local policy for RAADP (Case 26.7 above).

Table 24.3: Details of RAADP for eligible cases

RAADP regimen	Number of new cases 2022	Number of cases cumulative to 2022
Single dose 1500IU at 28-30 weeks	8	87
Single dose 1500IU after 30 weeks (delayed)	0	2
Two dose regimen 500IU	0	1
Not given	4	20
Unknown	0	2
Total eligible cases	**12**	**112**

The route was intramuscular (IM) in all cases, in 4 cases deltoid was specified.

cffDNA testing

Table 24.4: cffDNA testing

cffDNA test	Number of cases 2021	Details
Not performed	9	5 cffDNA not available or routinely performed 1 termination of pregnancy 1 maternal D group (variant) was incorrectly assigned to a D-positive pathway
Performed	5	5 Fetal RHD screening test
No information	2	
Total	**16**	

The number of documented cases where the Fetal RHD screening test has been performed when gestation appropriate prior to the subsequent detection of alloimmune anti-D has improved but remains lower than expected (n=5).

There were no documented cases of fetal genotyping from maternal blood subsequent to the detection of maternal antibodies. At least 1 infants were subsequently detected to be D negative at

delivery, cffDNA testing may have reduced maternal concern regarding the anti D detected and resulted in less antenatal appointments and maternal interval anti-D testing.

Details of potentially sensitising events (PSE)

There was 1 case of a potential sensitising event: PV bleeding at 14 weeks gestation, no anti-D Ig was administered.

Table 24.5: Details of potentially sensitising events

Number of PSE	Details	Management
1 case PSE reported	PV bleeding 14 weeks	No anti-D Ig received
13 cases	No PSE reported	
2 cases	No information given	

Pregnancy outcomes in NPP case

In the 2022 dataset pregnancy outcome was reported in all 16 cases. There were 15 that resulted in a live birth, and 1 termination of pregnancy. In 4 cases alloimmune anti-D was detected at or after 40 weeks.

With regards to neonatal intervention for haemolytic disease of the fetus and newborn (HDFN) 2 required phototherapy.

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.

Summary of 2022 PP data

There were 36 new PP cases in 2022, including 13 cases where alloimmune anti-D was found in the first trimester. Review of the cumulative cases identifies 133/353 (37.7%) cases were detected in the first trimester. Where alloimmune anti-D is detected at booking in the index (current) pregnancy, only the events in the preceding pregnancy are relevant to the sensitisation (assuming no other exposure to the D antigen occurred e.g. transfusion, an unlikely event in this demographic). Where anti-D is detected later in the index pregnancy, the relative contribution of events in the previous and index pregnancy is less certain.

In 4 cases where alloimmune anti-D was detected for the first time at delivery of index pregnancy, 1 had a gestation of more than 40 weeks ($41+^{3}$). The cumulative data show that of 52 pregnancies where alloimmune anti-D was first detected at delivery in the index pregnancy, 18 cases (34.6%) were delivered after 40 weeks gestation.

National Health Service (NHS) maternity statistics 2019-2020 indicate 15.9% pregnancies extended beyond 40 weeks. *https://www.gov.uk/government/statistics/nhs-maternity-statistics-england-2019-20.*

With regards to the data of the pregnancy preceding the index pregnancy, there were 27 live births, 3 terminations, 5 miscarriages and in 1 cases no outcome detail was provided.

Cumulatively, of the 153 women where booking weight was provided, 38 (24.8%) were obese. National data (NHS digital 2019) report 22% incidence of obesity in pregnant women in England. https://files.digital.nhs.uk/58/FFD7B1/msms-mar19-exp-rep.pdf.

The RAADP data in preceding pregnancies suggests a developed, embedded process, with the majority receiving appropriate RAADP where reported, however there are still missed opportunities to get this right. Of the 2 cases where RAADP was not provided 1 woman declined, the second case was a D variant incorrectly assigned to treat according to a D-positive pathway.

As with the NPP cases, very few cases report cffDNA testing. In only one preceding pregnancy cffDNA testing was performed and predicted the fetus to be D-positive. The responses suggests a number of hospitals have still not implemented the cffDNA Fetal RHD screening test.

There were 11 PSE's in preceding pregnancies; 2 appropriately managed, 1 error in management where anti-D was omitted following a surgical termination of pregnancy at 11 weeks. Management of 7 PSE's in inconclusive due missing data. Since reporting began in 2013, a total of 93 PSE's have been reported in the preceding pregnancies of which 55 (59.1%) were managed correctly. It is encouraging to see the antepartum haemorrhages reported have been managed appropriately.

Five of the preceding pregnancies delivered beyond 40 weeks gestation. Cumulatively (data collected from 2015 onwards), 54 out of 300 previous pregnancies (18%) lasted longer than 40 weeks. National Health Service (NHS) maternity statistics 2019-2020 indicate 15.9% pregnancies extended beyond 40 week.*https://www.gov.uk/government/statistics/nhs-maternity-statistics-england-2019-20.*

Where alloimmune anti-D was identified in the first trimester in the index case (n=13), review of the preceding pregnancies highlights cases where 'ideal' management with no risk factors still resulted in immunisation. Gaps in data in these cases make analysis difficult, however there are at least 3 cases where apparently 'ideal' management still resulted in immunisation. 47 had a potential sensitising event: One 4 appears to be treated according to current guidelines, a surgical termination of pregnancy at 11+6 weeks did not receive anti-D Ig, there data is missing regarding the remaining 2 events.in 2 cases there were undisclosed miscarriages identified in retrospect and in 1 case there is inadequate data to conclude. The management of two fetal maternal haemorrhages may not have been ideal – both are potentially undertreated.

There were 23 cases of immune anti-D detected beyond the first trimester. Cumulatively, 35 out of 157(22.2%) women where booking weight was provided, and who developed alloimmune anti-D in the index pregnancy, were clinically obese. National data (NHS digital 2019) report 22% incidence of obesity in pregnant women in England. https://files.digital.nhs.uk/58/FFD7B1/msms-mar19-exp-rep.pdf. Further research is required to determine if obesity is truly associated with increased alloimmunisation risk.

In keeping with the data regarding NPP cases and PP cases where alloimmune anti D detected in the first trimester; reported use of cffDNA testing is still limited.

There were 4 PSE's prior to detection of immune anti-D beyond the first trimester, all were managed appropriately.

Of the 36 PP cases there were 32 live births, outcome data was missing for 4 cases. Interventions were required in 10 cases, intervention data is missing in 7 cases. Interventions included phototherapy, immunoglobulin and one exchange blood transfusion.

When was alloimmune anti-D detected in index (current) pregnancy?

Table 24.6: When alloimmune anti-D was detected

Time of anti-D detection	Number of new cases 2022	Number of cases cumulative to 2022
At booking (if first trimester)	13	133
After booking to 28 weeks (includes late booking)	8	46
At or after 28 weeks	9	109
At delivery	4	52
Other	2	13*
Total	**36**	**353**

***** *3 preoperative assessment following pregnancy, 3 at planned follow up of large FMH at delivery where correct dose of anti-D Ig had been given, 7 unknown.*

Where alloimmune anti-D was detected at booking in the index (current) pregnancy, only the events in the preceding pregnancy are relevant to the sensitisation (assuming no other exposure to the D antigen occurred e.g. transfusion, an unlikely event in healthy fertile women). Where anti-D is detected later in the index pregnancy, the relative contribution of events in the previous and index pregnancy is less certain.

In the 4 women who had alloimmune anti-D detected for the first time at delivery of index pregnancy, 1 had gestation of more than 40 weeks (41^{+3}).

The cumulative data show that of 52 pregnancies where alloimmune anti-D was first detected at delivery in the index pregnancy, 18 cases (34.6%) were delivered after 40 weeks gestation.

Information about the pregnancy immediately preceding index (current) pregnancy

Table 24.7: Outcome of the preceding pregnancy

Outcome of preceding pregnancy	Number	Details
Live birth	27	• 16 D-positive neonates • 3 D-negative neonates • 8 D-type unknown
Other	9	• 3 termination of pregnancy • 5 miscarriages • 1 no detail provided

What was the booking weight of preceding pregnancy? (Includes only cases where previous pregnancy resulted in live birth)

Table 24.8: Booking weight of preceding pregnancy

Weight at booking in kg	Number of new cases 2022	Number of cases cumulative to 2022
<68	8	89
68-80	2	26
>80 (obese)	3	38
No information	14	147
Total	**27**	**300**

3 TOP and 5 miscarriages 1 unknown outcome not included

Cumulatively, of the 153 women where booking weight was provided, 38 (24.8 %) were obese. National data (NHS digital 2019) report 22% incidence of obesity in pregnant women in England. https://files.digital.nhs.uk/58/FFD7B1/msms-mar19-exp-rep.pdf

RAADP in preceding pregnancy (for women who carried to a live birth in preceding pregnancy)

Table 24.9: Details of RAADP in preceding pregnancy

RAADP	Number of new cases 2022	Number of cases cumulative to 2022
Single dose	21	191
Two doses	1	13
Given (no details on dose)	0	2
Not given	2*	35**
No information	3	59
Total	**27**	**300**

3 TOP and 5 miscarriages 1 unknown outcome not included

*****1 declined needle phobic, D variant treated as D positive.*
***Reasons include: learning difficulties, concealed pregnancy, needle phobic, prior to RAADP introduction, delivered abroad, declined, typed incorrectly, midwife error, typed incorrectly as D-positive, 1 transcription error maternal D group to electronic health record, notes stated not required.*

In 9 cases the route was specified as deltoid, no cases were given anti-D Ig intravenously.

Details of cffDNA testing in preceding pregnancy (for women who carried to a live birth in preceding pregnancy)

As with the NPP cases, very few cases report cffDNA testing. In only one preceding pregnancy cffDNA testing was performed and predicted the fetus to be D-positive. The responses suggests a number of hospitals have still not implemented the cffDNA Fetal RHD screening test.

Table 24.10: cffDNA preceding pregnancy

cffDNA test	Number of new cases 2022	Details
Not performed	23	19 commented cffDNA not available or routinely performed 2 no comment 1 D variant treated as D positive 1 no consent
Performed	1	Predicted D positive fetus n=1
No information	3	3 missing data
Total	**27**	

3 TOP and 5 miscarriages 1 unknown outcome not included

Details of PSE in preceding pregnancy reported in 2022

Table 24.11: Details of PSE

Number of PSE	Details
11 PSE reported	**Appropriate management** • Fall/Abdominal trauma, 30+1 weeks, kleihauer < 2ml, received 500IU anti-D Ig <24 hours • Antepartum haemorrhage, 11+6 weeks, received 1500IU anti-D Ig <24 hours **Error in management** • Surgical termination of pregnancy 11 weeks omitted anti-D Ig prior to discharge **Inconclusive management** • Miscarriage 6 weeks no management detailed • Miscarriage • Surgical management miscarriage 9 weeks • Termination of pregnancy • Miscarriage 5 weeks • Termination of pregnancy • Miscarriage **Treatment declined** • Antepartum haemorrhage/ PV bleeding 17/40, Needle phobic – no anti-D Ig
25 cases had no PSE reported	

Since reporting began in 2013, a total of 93 PSE have been reported in the preceding pregnancies of which 55 (59.1%) were managed correctly. It is encouraging to see the antepartum haemorrhages reported have been managed appropriately.

Method of delivery of preceding pregnancy

Table 24.12: Delivery details

Type	Number of new cases 2022	Number of cases cumulative to 2022
No information	2	67
Vaginal	13	140
Instrumental	3	17
Elective caesarean section (El CS)	5	37
Emergency CS (Em CS)	3	39
Total	**27**	**300**

3 TOP and 5 miscarriages 1 unknown outcome not included

Gestation at delivery of preceding pregnancy

Table 24.13: Gestation at delivery of preceding pregnancy

Gestation at delivery (weeks)	Number of new cases 2022
40 weeks or less	19
More than 40 weeks	5
No information	3
Total	**27**

3 TOP and 5 miscarriages 1 unknown outcome not included

Cumulatively (data collected from 2015 onwards), 54 out of 300 previous pregnancies (18%) lasted longer than 40 weeks. National Health Service (NHS) maternity statistics 2019-2020 indicate 15.9% pregnancies extended beyond 40 week.*https://www.gov.uk/government/statistics/nhs-maternity-statistics-england-2019-20.*

Postpartum management in preceding pregnancy

Table 24.14a: Test for postpartum FMH

FMH test performed postpartum	Kleihauer test (K)	Flow cytometry (F)	K+F	Method not specified	No	Notes on cases where FMH test not done	Unknown
16	14	0	2	0	**4**	1 D variant treated as D-positive 1 needle phobia 2 cord D-positive	**7**

3 TOP and 5 miscarriages 1 unknown outcome not included

Table 24.14b: Postpartum anti-D Ig prophylaxis

What happened?	Number of new cases 2022	Number of cases cumulative to 2022
FMH test and appropriate dose of anti-D Ig	14	168
No prophylaxis	0	18**
Incorrect dose/timing of anti-D Ig	1	8**
No information	9	84*
D-negative baby	3	23
Total	**27**	**301**

TOP and 5 miscarriages 1 unknown outcome not included
**No consent for FMH test given 500IU (1), not able to determine if correct dose in absence FMH test, no FMH test detail so not able to determine if correct dose in absence FMH (2)*
***Reasons included: immune anti-D detected at time of delivery, typed in error as D-positive, refused, from abroad, learning difficulties, needle phobic, declined, missed anti-D Ig in error, dose 250IU, dose given late, transcription error maternal D group to electronic health record*

Anti-D detected at first trimester booking of index pregnancy n=13

The details of the preceding pregnancy may provide information on the cause of immunisation in these cases.

Table 24.14: Details of management in previous pregnancy (- =no information/unknown)

Case	Obese (booking weight >80kg)	RAADP	PSE	Delivery gestation (weeks)	Delivery route	PPP	Risk factors identified
1	71	Yes	No	39^{+6}	Elective C-section	D-positive neonate FMH data missing anti-D Ig data missing	None although no data postpartum management
2	84	Yes	No	42	Data missing	D-positive neonate FMH (K) no fetal cells 1500IU anti-D Ig	Obese 42 week delivery
3	Data missing	Yes	No	39^{+1}	Vaginal	D-positive neonate FMH (K&F)>4ml, Flow 63.1ml, 4500iu anti-D Ig; FU KH <2ml, no further anti-D Ig	Large fetal maternal haemorrhage ? Adequate dose anti-D Ig ? documented route administration
4	Data missing	Yes	No	39^{+2}	Vaginal	D-positive neonate FMH (K) <2ml, 1500IU Anti-D Ig	8 previous pregnancies (6 miscarriages, 1 TOP, 1 live birth)
5	Data missing	Yes	No	39^{+3}	Vaginal	D-positive neonate FMH (K) no fetal cells, 500IU Anti-D Ig	None
6	Data missing	No	Yes surgical termination 11^{+0}, no anti-D Ig	-	-	-	Surgical Termination 11^{+0} no anti-D Ig
7	Data missing	Data missing	Data missing	Data missing	Data missing	Data missing	Prior pregnancy managed in Eritrea missing data
8	Data missing	Data missing	Postpartum haemorrhage	40	Vaginal	Data missing	Prior pregnancy managed in Pakistan missing data Postpartum haemorrhage

9	55	No	No-	42	Vaginal	No neonate D Group No FMH No Anti-D Ig	D variant treated as D positive : No RAADP, No PPP, 42 week delivery
10	47	Yes	Yes Antepartum haemorrhage/ PV bleeding 11^{+6}, anti-D Ig 1500IU	40^{+3}	Vaginal	D positive neonate FMH (K) no fetal cells detected, anti-D Ig 1500IU	PSE-managed appropriately
11	Data missing	Data missing	Yes – Termination of pregnancy no detail management provided	-	-	-	PSE – no management detail provided
12	Data missing	Yes – 31^{+0}	No	40^{+5}	Elective C-Section	Data missing	RAADP 31^{+0}, no detail PPP
13	Data missing	Yes	No	Data missing	Vaginal	D-positive neonate FMH (K&F)>4ml, Flow 6ml, 1500iu anti-D Ig; no follow up kleihauer or flow	No follow up kleihauer

Gaps in data in these cases make analysis difficult, however there are at least 3 cases where apparently 'ideal' management still resulted in immunisation. One cases did not receive RAADP (maternal D variant treated as D positive). 2 delivered beyond 40 weeks, 4 had a potential sensitising event: One appears to be treated according to current guidelines, a surgical termination of pregnancy at 11^{+6} weeks did not receive anti-D Ig, and the data is missing regarding the remaining 2 events. The management of two fetal maternal haemorrhages may not have been ideal – both are potentially undertreated.

Alloimmune anti-D detected after first trimester in index (current) pregnancy n=23

Further information is requested on the index pregnancy when alloimmune anti-D is detected after the booking (first trimester) sample, as it may be that the sensitisation occurred in the index pregnancy rather than in the preceding pregnancy.

What was the booking weight of index pregnancy?

Table 24.16: Booking weight

Weight at booking in kg	Number of new cases 2022	Number of cases cumulative to 2022
<68	9	77
68-80	5	45
>80	2	35
No information	7	54
Total	**23**	**211**

Cumulatively, 35 out of 157 (22.2%) women where booking weight was provided, and who developed alloimmune anti-D in the index pregnancy, were clinically obese. National data (NHS digital 2019) report 22% incidence of obesity in pregnant women in England. https://files.digital.nhs.uk/58/FFD7B1/msms-mar19-exp-rep.pdf. Further research is required to determine if obesity is truly associated with increased alloimmunisation risk.

RAADP in index pregnancy

Table 24.17: Details of RAADP

RAADP given or not	Number
Single dose 1500IU	12
Two dose 500IU	0
Not given	11
Alloimmune anti-D present prior to RAADP	*4*
Declined	*3*
Did not attend	1
Missing data	0

cffDNA testing

Table 24.18: cffDNA testing

cffDNA test	Number of cases	Details
Not performed	10	5 test not available/ not routinely performed 1 sample not suitable to process 2 declined (1 needle phobic) 2 reason unknown
Performed	11	Test performed by international blood group reference laboratory (IBGRL) 10 D-positive, 0 D-negative, 1 inconclusive
No information	2	

In keeping with the data regarding NPP cases and PP cases where alloimmune anti D detected in the first trimester; reported use of cffDNA testing is still limited.

Details of potentially sensitising events in index pregnancy

Table 24.19: Details of potentially sensitising events

Number of women	Details
4 cases PSE reported prior to detection alloimmune anti-D	• APH 27^{+0}, KH < 2ml,500IU anti-D Ig administered • Amniocentesis 21^{+6}, KH <2ml, 1500IU anti-D Ig administered • APH/ PV bleeding 16^{+4}, 1500IU anti-D Ig administered • Fall/ trauma 22^{+1}, KH no fetal cells detected, 1500IU anti-D Ig administered
19 cases no PSE reported	

Outcomes of pregnancies reported in 2022

Table 24.20: Outcome of pregnancies reported in 2022

Number of cases	Outcome
32	Live births
0	Miscarriage
0	Stillbirth
0	Termination of pregnancy
4	Outcome data missing
19	No treatment
10	Treatment
8	Phototherapy
1	Phototherapy and Immunoglobulin
1	Phototherapy, Immunoglobulin and exchange transfusion
7	Data missing

References

BSH Qureshi H, Massey E, Kirwan D, et al. (2014) Guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. Transfusion Medicine 2014;24(1):8–20. https://onlinelibrary.wiley.com/doi/epdf/10.1111/tme.12091 [accessed 06 March 2022].