Assessing the potential of GBS maternal immunisation in preventing maternal infection and foetal harm

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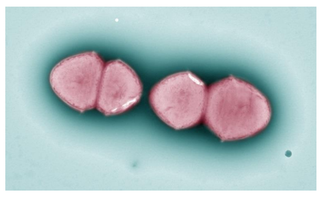
Protecting and improving the nation's health

INTRODUCTION

Despite wide recognition as a complication of pregnancy and childbirth, few studies have quantified the burden of maternal sepsis due to group B *Streptococcus* (GBS) infection. Recent studies in the UK have measured the incidence and impact of severe maternal sepsis due to GBS, 0.037 per 1000 maternities[1], but a wider enumeration of the burden of infection has not been undertaken.



Streptococcus agalactiae. Negatively stained TEM image, PHE 2017

With encouraging progress in the development of a GBS vaccine, attention is increasingly focusing on identifying the breadth of potential target groups for immunisation. Quantifying the incidence and impact of maternal infection, along with infant disease, is essential to the estimation of cost-effectiveness of any maternal immunisation programme as this has the potential to not only provide protection for the neonate but to also to the mother. In the context of marked increases in adult GBS disease, [2]
quantifying the attributable disease burden associated with pregnancy and childbirth is essential as a means to identify potential interventions.

Our study aimed to quantify the incidence of GBS sepsis associated with pregnancy and childbirth.

METHODS

Case definition

Laboratory-confirmed infection diagnosed by isolation of GBS from normally sterile sites (invasive GBS disease, iGBS) in women identified as being pregnant or within 6 weeks of delivery at the time of diagnosis.

Data sources

Laboratory surveillance: laboratory records for patients in England diagnosed in 2014 captured through PHE's Second Generation Surveillance System (SGSS)

Hospital admissions: NHS records in England (Hospital Episode Statistics, HES©) for admissions from Jan 2013 to July 2015

Capsular serotype distribution: national reference laboratory data on isolates submitted in 2014 for women 15-44y were extracted to assess serotype distribution.

Data analysis

Data were extracted from SGSS, submitted to NHS tracing service to complete/check NHS numbers (unique patient ID) and linked to HES. Hospital admission records were analysed to identify pregnancy or childbirth using the following fields:

- maternity data fields
- clinical coding fields (ICD-10)
- admission method and medical speciality
- operative procedure codes (OPCS)

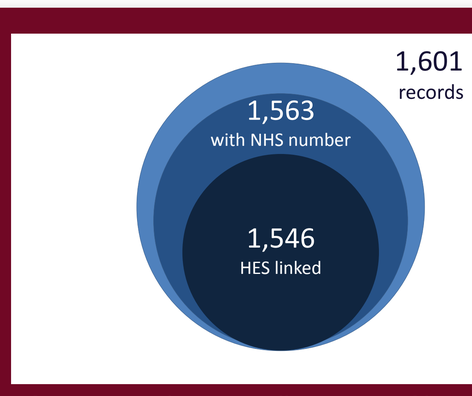


Figure 1. Laboratory diagnoses of iGBS infection linked to hospital admission data, England 2014

Cases were compared to normative maternity data from Office for National Statistics (ONS) and NHS Digital and rates calculated using ONS maternity denominators.

Hospital Episode Statistics. Copyright © 2016. Re-used with the permission of NHS Digital. All rights reserved

RESULTS

Overall results

- of 1601 records for patients diagnosed with iGBS infection in England in 2014, 1546 (97%) were successfully linked to a hospital admission record (Figure 1).
- 185 were identified as maternal infections, and comprised 12% of iGBS infections across all age groups and 83% amongst women aged 18-44y, accounting for the excess number of cases in women vs men (222 vs 47) in this age group (Figure 2a).
- median age of maternal cases was 30y (18-44y), similar to all maternities in England (Figure 2b).
- incidence of maternal iGBS infection was 0.29 (95% CI: 0.25-0.33) per 1000 maternities.

Onset of GBS maternal infection

- 74% of maternal GBS infections were diagnosed on the day or within 1 day of delivery (93%); 1 infection was diagnosed 4 days prior to delivery and 10 diagnosed 2 or more days postpartum (Figure 3a; Table).
- 96% of infections arose during the third trimester, 4% in first or second trimester.

Duration of admission

- analysis of hospital admissions closest to time identified GBS diagnosis during the childbirth admission for 171 cases; for 13 cases, diagnosis was in a distinct admission.
- of admissions associated with childbirth, length of stay was typically long (median 7 days; Table); of the admissions not associated with childbirth, median stay was 4 days.

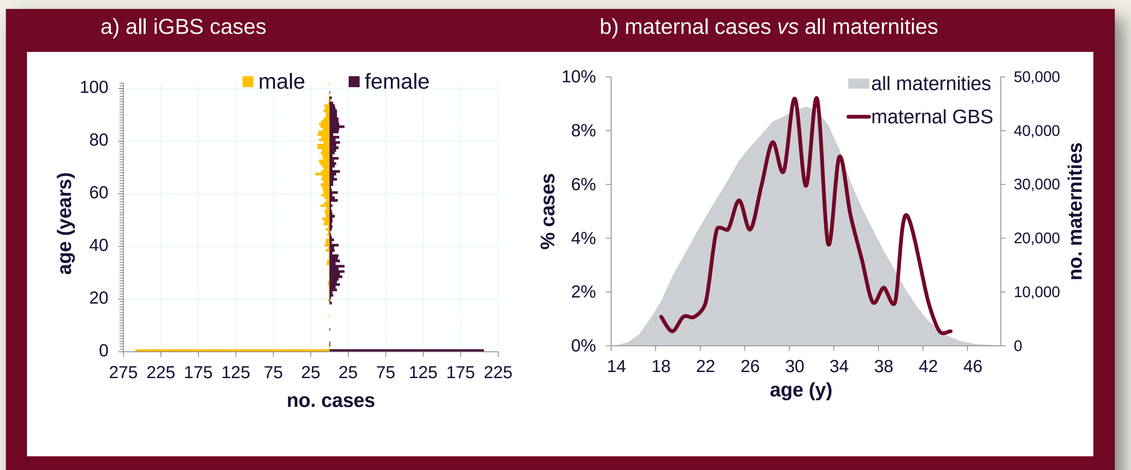


Figure 2. Age distribution of a) all iGBS cases and b) maternal iGBS cases vs all maternities in England, 2014

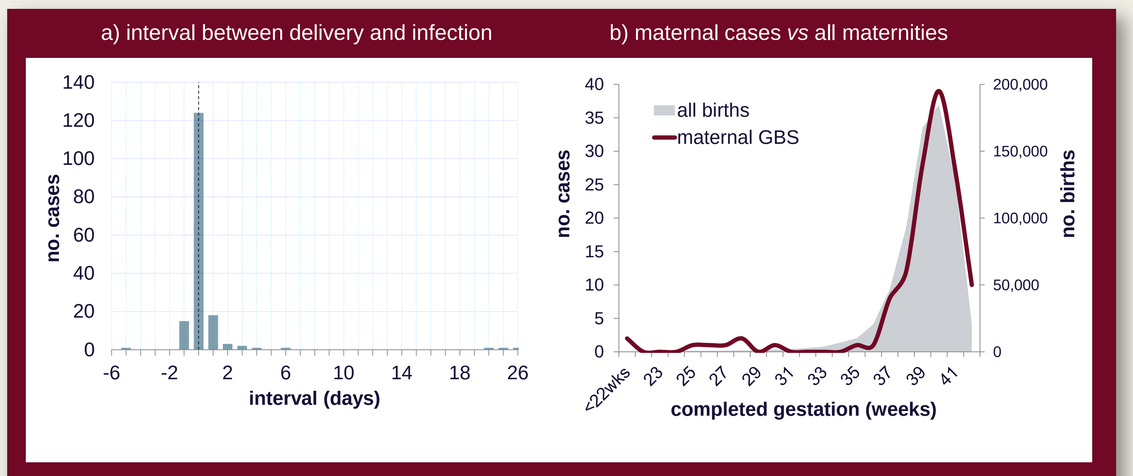


Figure 3. Distribution of maternal GBS cases according to a) timing of onset in relation to delivery and b) gestational age of infant vs all births in England, 2014

Capsular serotype distribution

- 49 GBS isolates from women aged 15-44y were submitted to the reference laboratory in 2014
- Of these, 45 were sterile site isolates, 3 placenta, 1 unknown
- Seven serotypes were identified with serotype III the most common (43%) followed by Ia (31%), V (10%), II (8%)

N=187	Number	(%)
trimester at diagnosis (n=134)		
first (0-12 weeks)	1	(0.7%)
second (13-27)	4	(3.0%)
third (28-40)	129	(96.3%)
diagnosis to delivery interval, days (n=168)		
antepartum (-4 to -2d)	1	(0.6%)
peripartum (-1 to 1d)	157	(93.5%)
postpartum (2 to 26d)	10	(6.0%)
delivery method (n=144)		
vaginal	79	(54.9%)
elective C-section	1	(0.7%)
emergency C-section	61	(42.4%)
pregnancy outcome (n=184)		
miscarriage	7	(3.8%)
live or stillborn	174	(94.6%)
foetal outcome (n=147)		
still-born	5	(3.4%)
live born	142	(96.6%)
pre-term live-born (<37 wk)	12	(9.0%)
duration of admission, days (n=184)		
admisson including childbirth (median, range)	7	1 – 20
admission not including childbirth (median, range)	4	2 – 7

Table. Clinical characteristics of maternal iGBS cases, England, 2014

Pregnancy outcome

- 7 cases were associated with miscarriage.
- 42% of cases delivered by emergency C-section, 55% vaginal.
- foetal outcome was provided for 147 cases of which 5 were stillborn (3%), considerably higher than national average of 0.47% ($\chi^2_{(1df)}$=27.22; p<0.001).
- 9% of infants were preterm (<37 week, Figure 3b), slightly higher than national rate (8%); rates of extreme prematurity (<28 weeks) were significantly higher in infants born to mothers with iGBS infection, 4% vs 1% ($\chi^2_{(1df)}$=25.10; p<0.001).
- no maternal deaths associated with GBS infection were identified.

DISCUSSION & CONCLUSIONS

Our study identified a substantial burden of maternal GBS infection with an incidence of 0.3 per 1000 maternities, ten times higher than the estimated incidence of severe maternal sepsis due to GBS but slightly below estimates using comparable case definitions from the USA.[1,3] Pregnancy outcomes were significantly poorer than background population rates, with excess rates of emergency C-section, stillbirth and extreme prematurity. Lengths of stay were also extended highlighting the additional impact of infection on these women, their families as well as the healthcare economy. Increased referral of maternal isolates to the national reference laboratory would further assist in our understanding of the epidemiology of these infections. Of the small sample assessed to date, serotype III and Ia were dominant with an overall distribution similar to early onset infant disease.[2]

In conclusion, our assessment captured valuable data on the burden of maternal GBS infection in England, indicating the potential of vaccination to prevent adverse maternal and foetal outcomes associated with GBS.

ACKNOWLEDGEMENTS

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