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Detecting Group B Streptococcus bacterial infection in the womb before labour

Submission date
08/09/2022

Recruitment status
No longer recruiting

Registration date
06/10/2022

Overall study status
Ongoing

Last Edited
10/12/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
A bug (bacterium) known as GBS (Group B Streptococcus) is present in the birth canal in about 1 in 5 pregnant women. In 2019, we demonstrated that GBS can get into the womb before labour starts and we can find it in the placenta. We now want to study a large number of women being delivered by planned caesarean section. Studying samples from women attending a planned caesarean section means we can be sure that any bugs we find invaded the womb before labour starts. We will ascertain how many women have GBS in the placenta before labour. We will ascertain how the placenta and the baby respond to the presence of GBS. We will ascertain whether anything about the specific type of GBS present in the mother determines whether or not it can invade the womb. During the study, we will provide anonymous patient samples of umbilical cord blood and placenta to biobanks that can be accessed by researchers in other fields who also want to study tissues obtained at the time of planned caesarean birth.

Who can participate?
Women undergoing an elective caesarean section prior to the onset of labour or membrane rupture

What does the study involve?
In the operating theatre, the treatment will be exactly the same as normal, but with the following additions. First, we will obtain a maternal blood sample prior to the caesarean section. If possible, this will be obtained by the anaesthetist when they insert an intravenous line (cannula). However, the woman can decline to have this sample taken. Second, a midwife always passes a catheter into the bladder before a caesarean section. If consent is provided to the study, they will also briefly (seconds) insert a swab into the lower vagina and a swab into the back passage (rectum) to check for the presence of the GBS bug. This is usually done after the anaesthetic (usually a regional block) hence the woman should not feel any discomfort. Women have the option to check a box on the consent form stating that they want to opt-out of those procedures. Third, when the surgeon is about to deliver the baby they will obtain a sample of the fluid from around the baby and we will check this for the presence of the GBS bug. Finally, when the surgeon delivers the placenta, it will be passed on to the research team who will obtain further samples.

What are the possible benefits and risks of participating?
There are no potential benefits for the participant personally. But if we can understand more about how GBS affects the baby it may help other women and their babies in the future. There are no risks to the mother or baby from participating.

Where is the study run from?
The Rosie Hospital, Cambridge (United Kingdom)

When is the study starting and how long is it expected to run for?
September 2021 to November 2026

Who is funding the study?
Medical Research Council (United Kingdom)

Who is the main contact?
Prof GCS Smith (United Kingdom)
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Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
316414

ClinicalTrials.gov (NCT)

Nil known

Central Portfolio Management System (CPMS)
53745

Study information

Scientific Title
Pre-labour invasion of the human uterus by Streptococcus agalactiae

Acronym
DIGS

Study objectives
Vertical transmission of Group B Streptococcus (GBS) during labour and delivery is the major determinant of early neonatal death due to sepsis. We previously reported that GBS was the only bacterial DNA signal detectable in the placenta prior to labour onset.

We hypothesise that:
1. Invasion of the uterus by group B Streptococcus (GBS):
The risk of GBS being present in the intra-uterine tissues prior to membrane rupture and labour onset is increased among women with GBS genital tract colonisation
2. GBS and fetal inflammatory response syndrome:
Pre-labour invasion of the uterus by GBS is associated with a fetal inflammatory response and predisposes the infant to neonatal morbidity
3. GBS genomics
The genome of GBS colonising the mother determines the risk of intrauterine invasion

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/11/2022, East of England - Essex Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 1048106; NRESCommittee.EastofEngland-Essex@nhs.net), ref: 22/EE/0175

Study design
Single-centre cohort observational study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Group B Steptococcus agalactiae infection

Interventions

We will quantify GBS DNA in the placenta, fetal membranes, amniotic fluid, and fetal blood from ~1,800 women being delivered by pre-labour caesarean section and compare the proportion of GBS-positive samples in women with and without GBS colonisation. We will then compare levels of inflammatory mediators in all four sample types in relation to the presence or absence of GBS DNA, and the risk of neonatal morbidity in those with and without GBS DNA in the intra-uterine tissues. Among women colonised by GBS, we will test associations between intra-uterine invasion by GBS and whole genome sequencing (WGS) of the isolates cultured from the mother. Specifically, we will compare previously described virulence factors (e.g. hyper-virulent adhesin) and we will perform discovery-based, hypothesis-generating analyses of the WGS data. Finally, we will perform Bayesian network analysis to determine causal associations and interactions between maternal, pathogen, and inflammatory factors, and to adjust associations for the effects of potential maternal confounders.

Intervention Type
Other

Primary outcome(s)
1. Admission of the neonate for special or intensive care since delivery due to the main diagnosis of confirmed or suspected sepsis measured using electronic medical records at the time of hospital discharge following delivery
2. Presence of group B Streptococcus (GBS) in fresh intra-uterine tissue samples (placenta, placental membranes, amniotic fluid, umbilical cord blood) and rectal and vaginal swabs detected by culture following delivery. Using current practices, samples will be incubated in Todd-Hewitt broth supplemented with antibiotics to select for GBS. After culture, identification of GBS will be confirmed using matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) mass spectrometry. Antibiotic disc susceptibility testing will be performed according to EUCAST guidelines. The presence of GBS DNA will be identified using PCR-qPCR for the bacterial 16S rRNA gene on frozen samples of the placenta, fetal membranes, fetal blood and amniotic fluid.
3. Presence of inflammation in the placenta and umbilical cord will be determined in frozen samples obtained at the time of delivery. Pro-inflammatory cytokines (IL-6, IL-8, TNF-α and IL-1β) will be measured using the R&D Systems Ella Automated Immunoassay platform. The levels of inflammatory cytokines will be compared between cases where GBS was detected with GBS-negative controls.

Key secondary outcome(s))
Neonate outcome:
1. Apgar score measured according to APGAR scoring system at 1,5 and 10 minutes after delivery. Data obtained from electronic medical records.
2. Hypoxic ischaemic encephalopathy, defined as any diagnosis of hypoxic-ischaemic encephalopathy prior to discharge. Data obtained from electronic medical records following discharge.
3. Any invasive or non-invasive ventilation that was required prior to discharge from the hospital. Data obtained from electronic medical records following discharge
4. Any use of inotropes prior to discharge from the hospital. Data obtained from electronic medical records following discharge.
5. Length of stay in neonatal intensive care unit or special care baby unit. Determined following discharge by reviewing electronic medical records.

Maternal outcome:
1. Maternal post-delivery haemorrhage, defined as a blood loss greater than 500 ml during their Caesarean section. Data obtained from electronic medical records.
2. Infection (e.g. endometritis). Defined as a temperature > 38oC or clinically treated for infection following caesarean section, determined by review of electronic medical records following discharge
3. Positive microbiology cultures for GBS (urine, high vaginal swab, placenta) during or after pregnancy. Determined by review of electronic medical records following discharge from hospital.

Completion date
01/11/2026

Eligibility

Key inclusion criteria
Patients planned for caesarean delivery at the Rosie Hospital Cambridge, prior to the onset of labour or membrane rupture

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
17 years

Upper age limit
100 years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Unable to consent
2. Aged 16 years old and under
3. Antibiotic treatment within the preceding week
4. An infectious condition which could represent a hazard (e.g. high-risk carrier of viral hepatitis B)

Date of first enrolment
15/12/2022

Date of final enrolment
30/01/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Rosie Hospital
Robinson Way
Cambridge
England
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Organisation
University of Cambridge

ROR
https://ror.org/013meh722

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Data will be available in relation to the studies described above (i.e. demographic, clinical and laboratory). Data will be available for sharing 4 years after the first recruitment of a patient (approximately November 2026) and should continue to be available until August 2032. Requests should be sent to Prof GCS Smith and reasonable requests with an acceptable scientific case will be considered. Transfer of data will require a Data Transfer Agreement (DTA), with the signature of the requester and a legal representative of the institution. The DTA will specify all conditions of the agreement and the scope of the work and will be negotiated by the Research Operations Office of the University of Cambridge. Participant identifiers will not be included in the data sent and researchers will be required to provide a commitment to refrain from using the data to try and identify participants. All participants have provided their written informed consent for their data to be used in this way.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2	21/09/2022	13/12/2022	No	No