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Maternal glucose in pregnancy

Submission date
02/02/2023

Recruitment status
No longer recruiting

Registration date
13/03/2023

Overall study status
Completed

Last Edited
04/08/2023

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
The UK has one of the highest rates of stillbirth and early infant death in Europe. Abnormal growth of the baby in the womb (a baby that grows too big or too small) has been found to be a major factor leading to this. Many factors affect the way babies grow in the womb, but one of the most important and easiest to modify is the amount of glucose that they get from their mother. Too much glucose in their mother's blood during pregnancy usually leads to a large baby which increases the chance of serious problems during pregnancy, labour, and immediately after birth. Being born too big, or too small, is also not good for babies' long-term health as it markedly increases the chances of becoming obese and getting type 2 diabetes.
Pregnant women are offered a test (called a glucose tolerance test) to look for high glucose levels developing in pregnancy, but it is done late in pregnancy and relies on taking just two blood glucose readings 2 hours apart after taking a sugary drink. Many women already have signs of abnormal growth of the baby by this stage, so it's not a good enough test, but we don't have a better one yet. A mother's blood glucose changes constantly across the 24-hour day, affected by her daily lifestyle and the pregnancy. It is this daily variation in glucose that affects a baby's growth but the current glucose tolerance test does not measure this.
A new way of measuring glucose called 'continuous glucose monitoring' might help. It involves wearing a small sticky patch on the arm (the size of a £1 coin) whilst going about ordinary everyday life. The patch measures glucose levels every few minutes, day and night for up to two weeks, storing this information. It gives more than 4000 glucose readings over this time, which provides far more detail about what is happening with real-life 24-hour glucose levels than the current test. However, we do not currently know how 24-hour glucose levels alter from the beginning to the end of a pregnancy, or how changes in 24-hour glucose levels are related to the way babies grow.
The aim of this study is to find out how 24-hour glucose levels change across pregnancy and how they relate to the way babies grow and their pregnancy outcomes.

Who can participate?
Healthy pregnant women aged 18-45 years in the first trimester of (single) pregnancy with one or more of the following risk factors for developing gestational diabetes:
1. BMI >30 kg/m²
2. Previous unexplained stillbirth or baby >4.5 kg
3. First-degree relative with diabetes
4. Ethnic minority group (South Asian, Middle-Eastern, Afro-Caribbean)

What does the study involve?
Participants wear a continuous glucose monitoring patch on five occasions across their pregnancy. On each occasion the participants will have some basic details about themselves recorded and a blood sample taken. They will wear the patch at home while they go about their ordinary everyday activities.
At the end of a fortnight they will simply peel off the patch, put it into a stamped addressed envelope and send it back to the research team, who will download and save the data. The data from continuous glucose monitoring will be looked at in detail using three different analysis techniques.
At the end of the pregnancy the baby's birthweight will be recorded, as well as information on the results of the glucose tolerance test, measurements of the baby's growth from the ultrasound scans, and any pregnancy complications.

What are the possible benefits and risks of participating?
As this is an observational study, the risks to the participants are minimal. All of the study visits will be planned to coincide with their routine pregnancy visit to the midwives or hospital clinics. If for some reason this is inconvenient for the participant a separate visit will be arranged between them and the research team. The blood sampling will predominantly coincide with their routine blood testing but they will be required to provide an additional 10-15 ml of blood. As this is an observational study, there are no direct benefits to the mothers participating.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
July 2018 to October 2023

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Professor Eleanor Scott

Contact information

Type(s)
Scientific

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
271768

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 44424, IRAS 271768

Study information

Scientific Title
Understanding the glycemic profile of pregnancy: intensive continuous glucose monitoring glucose profiling and its relationship to fetal growth

Acronym
MAGiC

Study objectives
It is hypothesised that intensive glucose profiling of continuous glucose monitoring (CGM) will be able to detect maternal glucose dysregulation early in pregnancy that current clinical testing does not detect and that this will be associated closely with the development of Large for Gestational Age (LGA) and adverse pregnancy outcomes. This has the potential to lead to improved approaches for screening for dysglycemia in relation to excess fetal growth, and inform the timing and approach for future clinical trials to reduce adverse short and long-term outcomes related to abnormal fetal growth.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/03/2020, Yorkshire & The Humber - Leeds East Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 1048171, +44 (0)207 104 8141; leedseast.rec@hra.nhs.uk), ref: 20/YH/0011

Study design
Observational; Design type: Cohort study

Primary study design
Observational

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Glycemic profile of pregnancy

Interventions
CGM (masked - which means the participant can't see the data) will be performed for a 14-day period on five occasions across pregnancy. These five occasions will occur during routine hospital visits, when the participant:
1. Has their first ultrasound scan (dating scan) at 10-12 weeks of pregnancy
2. Has their second ultrasound scan (anatomy scan) at 18-20 weeks of pregnancy
3. Attends for their glucose tolerance test at 26-28 weeks of pregnancy
4. Is planning labour at 34-36 weeks of pregnancy
5. Is in hospital after giving birth

These times have been chosen to minimise burden and to maximise participation/concordance where possible. The research midwife will place the CGM sensor and the participant will return it after a fortnight via stamped addressed envelope for data download.

Routinely collected anthropometric and socio-demographic information will be recorded at each visit including: weight, height, blood pressure, current medication. Age, parity, ethnicity, and smoking will be recorded at the first visit.

Blood samples will be taken at each visit for a research HbA1c (a diabetes-related blood test) and a sample stored. A rectal swab will be requested (optional) at 26-28 weeks gestation and stored for later microbiome analysis.

Post-delivery, placenta and cord blood samples will be collected and stored in designated Human Tissue Act approved and compliant facilities for later analysis.

Infant birthweight and anthropometry measures will be taken (skin fold thickness - measured by callipers by gently pinching the skin on the arm, leg and tummy to measure how thick it is). Maternal and neonatal outcomes will be collected.

Details on fetal growth from routine clinical ultrasound scans and the oral glucose tolerance test (OGTT) results will be recorded.

CGM glucose profiling is the exposure of interest and will be performed using standard summary statistics, functional data analysis and glucotyping.
The primary outcome is large for gestational age (LGA) (>90th centile defined by customised birthweight centile) given its established relationship to maternal, neonatal and perinatal morbidity, adolescent obesity and type 2 diabetes.

The relationship of glucose to key secondary outcomes will be explored. This will establish:
1. The prevalence of dysglycemia detected by CGM in pregnancy
2. When it occurs and whether it resolves postnatally
3. Which glucose profiling technique is best at detecting it and how reproducible this is
4. The relationship of maternal dysglycemia to fetal growth and outcomes in healthy 'normal' women, as well as those who go on to have diagnosis and treatment of gestational diabetes mellitus (GDM)
5. Whether CGM glucose profiling can detect GDM before the OGTT
6. Whether CGM glucose profiling may be potentially more useful than the OGTT or HbA1c at detecting LGA and other perinatal outcomes

The data on CGM and HbA1c will be analysed at the end of the study, and will not be used to inform clinical care. All participants will have standard clinical care as per NICE guidance during their pregnancy.

Observational Methods and Researcher Bias:
Since this is a prospective observational study, researcher bias will be minimal. The primary outcome measures are based largely on laboratory measurements and predetermined cut-off values for the diagnosis of LGA and GDM, which the researchers will not be able to influence.

The researchers do not foresee any significant researcher bias in collecting perinatal outcome data because these will again be observational data obtained predominantly from the participants' medical notes (eg maternity records) and the baby's neonatal notes. The data which will be collected at this point includes maternal and foetal complications of labour, baby's birth weight/head and abdominal circumference, perinatal morbidity and mortality rates, and if the baby was admitted to the Special Care Baby Unit or Neonatal Intensive Care Unit. A potential source of researcher bias may occur when carrying out anthropometric measurements on babies (skinfold thickness). The researchers will ensure that all research staff receive standardised training and clear instructions on how to conduct these measurements. In addition, the quality of data collection will be independently reviewed every 3 months by the Clinical Study Coordinator to identify any inconsistencies or researcher bias.

Interim analysis/reports:
There is no formal interim analysis planned except for the ongoing evaluation of the recruitment numbers.

Study management:
A steering group comprised of the PI, CoIs, study coordinator and a patient representative from our PPI pregnancy group, will oversee the study. They will meet in person at the start and yearly, with quarterly teleconferences in between. Monthly meetings will be scheduled at each site between the respective clinical investigator and study employees. Project management responsibilities will be shared by all investigators. The clinical study coordinator will liaise with and regularly visit all sites to ensure timely overall recruitment, clinical data collection, data fidelity, and training of the research midwives in protocol-based study activity.

Patient involvement:
Patients have been involved in the design of the study and the Participant Information Sheet. This had a particular bearing on ensuring the visits for CGM coincide with routine clinical appointments to minimise participant burden. The PPI pregnancy group will meet throughout the study and a member from that group will sit on the steering group.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 16/03/2023:

The primary maternal outcome is a clinical diagnosis of GDM, and the primary neonatal outcome is Large for Gestational Age (LGA) at birth (>90th centile defined by customised birthweight centile).

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Previous primary outcome measure:

Large for gestational age (>90th centile defined by customised GROW birthweight centile) at birth

Key secondary outcome(s))
1. Gestational diabetes diagnosed by oral glucose tolerance test at 26-28 weeks gestation
2. Fetal growth (measured by birthweight; customised growth centiles; neonatal adiposity at birth measured by skin thickness; ultrasound measures of abdominal circumference and estimated fetal weight at 28, 32 and 36 weeks gestation)

Additional outcomes collected:
1. Maternal outcomes at end of pregnancy: hypertensive disorders (chronic; gestational; pre-eclampsia); mode of delivery inc. caesarean section; maternal weight gain; maternal length of stay in hospital after delivery, measured using clinical records
2. Neonatal outcomes at end of pregnancy: pregnancy loss <20 weeks; stillbirth; termination; congenital anomaly; preterm births (<37 weeks; <34 weeks) gestational age at delivery; neonatal hypoglycaemia, neonatal ICU admission, birth injury, shoulder dystocia, hyperbilirubinemia, respiratory distress; infant length of stay in hospital after delivery; composite neonatal outcome, measured using clinical records

Completion date
04/10/2023

Eligibility

Key inclusion criteria
1. Women aged 18-45 years
2. Pregnant women in the first trimester of pregnancy
3. Singleton pregnancy
4. Have one or more of the following risk factors for developing hyperglycaemia in pregnancy:
4.1. BMI >30 kg/m²
4.2. Previous unexplained stillbirth or baby >4.5 kg

4.3. First degree relative with diabetes
4.4. Ethnic minority group (South Asian, Middle-Eastern, Afro-Caribbean)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
Female

Key exclusion criteria
1. Women presenting after 14 weeks gestation
2. Type 1 or Type 2 diabetes
3. A previous history of gestational diabetes
4. On metformin therapy for infertility
5. Multiple pregnancy
6. Fetal congenital abnormality
7. Significant co-existent medical or psychiatric conditions
8. Unable to understand English and no translator available

Date of first enrolment
15/03/2021

Date of final enrolment
04/10/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
George Eliot Hospital
Lewes House
College Street
Nuneaton

United Kingdom
CV10 7DJ

Study participating centre
St Mary's Hospital
Oxford Rd
Manchester
United Kingdom
M13 9WL

Study participating centre
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council; Grant Codes: MR/T001828/1

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 will be available upon request from Prof. Eleanor Scott (e.m.scott@leeds.ac.uk). Anonymised data will be available 3 months after the study findings are published in a journal. Short description and variable metadata catalogues will be published through the MRC research data gateway. The PI will formally review access requests for proposals. All significant decisions (approval, referral back for further information, and decline) are documented for subsequent independent review.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		03/08/2023	04/08/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes