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Assessing the feasibility of testing for M2 haplotype in predicting adverse pregnancy outcomes: A feasibility study

Submission date
28/11/2024

Recruitment status
No longer recruiting

Registration date
19/12/2024

Overall study status
Completed

Last Edited
20/01/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Recent scientific research has shown that couples who are positive for the M2 haplotype gene may be at a higher risk of implantation failure/preclinical miscarriage if undergoing IVF; miscarriage in the first trimester and pregnancy complications such as high blood pressure in pregnancy (pre-eclampsia), preterm birth (baby delivering before 34 weeks of pregnancy) and fetal growth restriction (baby not growing as expected). Currently, there is no treatment for this condition. The first phase of this study, which will run until March 2025, will be testing couples to see whether they are positive for the M2 haplotype. The study aims to determine the proportion of screened individuals who test positive for the M2 haplotype gene in both males and females; assess the willingness of the source population to undergo screening; and, pilot procedures for obtaining informed consent. The study will involve test biosampling methods and laboratory analysis processes.

Who can take part?
Couples who meet one of the following conditions may be eligible to take part:
• Primary infertility (never been pregnant) or secondary infertility (been pregnant before but have been unable to conceive again)
• One or more failed embryo transfers during IVF
• One or more miscarriages including biochemical pregnancy loss (a very early pregnancy loss)
• Problems with the placenta during pregnancy, such as preeclampsia, a low birth weight baby or a spontaneous pre-term birth (less than 34 weeks gestation)

What does the study involve?
Both partners in the couple will need to undergo testing to confirm whether either (or both) of them are positive for the M2 haplotype gene. They will both need to give a blood sample which will be sent to a lab for M2 haplotype testing. They may also choose to give an optional saliva sample. Test results will be sent to the research teams at sites approximately one week after the sample is sent to the lab.

What are the possible risks and benefits of taking part?
Participants will not gain any personal benefit. It is hoped that their participation in this initial phase will help refine study procedures and gather preliminary data to inform future research. The main benefit of the LAMP study will be that information gained from the study will help improve the options available for women and couples in similar circumstances in the future.

Minimal risks are expected from involvement in LAMP. Participants may feel dizzy or faint during the blood test. Staff taking the blood sample will be trained to deal with this. After the test, there may be a small bruise where the needle went in. This should fade over the next few days.

Where is the study run from?
The University of Birmingham is the study sponsor and coordinating organisation.

When is the study starting and how long is it expected to run for?
April 2022 to March 2025

Who is funding the study?
Innovate UK (part of UK Research and Innovation), UK

Who is the main contact?
Please contact the trial mailbox: LAMP@trials.bham.ac.uk

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
340830

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 66451

Study information

Scientific Title
Level of Adverse pregnancy outcomes in M2 haPlotype (LAMP)

Acronym
LAMP

Study objectives
Feasibility
1. Determine the feasibility of testing eligible women and men for M2 gene haplotype using the gold standard of Sanger sequencing DNA from blood and saliva samples
2. Determine the proportion of women and men with M2 heterozygous and homozygous status
3. Obtain preliminary estimates to compare the performance of the test for DNA from Blood samples vs Saliva samples by Sanger sequencing in detecting the M2 gene haplotype

Prognostic
4. Explore factors which determine the risk of adverse pregnancy outcomes in women and men who test positive for M2 gene haplotype

Ethics approval required
Old ethics approval format

Ethics approval(s)
Pending submission

Study design
Multicentre feasibility study and an exploratory prognostic study

Primary study design
Observational

Study type(s)
Diagnostic, Screening

Health condition(s) or problem(s) studied
Couples trying to get pregnant who meet at least one of the following conditions:
- Primary or secondary infertility (primary infertility is when a pregnancy has never been achieved (when tried for), and secondary infertility is when at least one prior pregnancy has been achieved)
- One or more failed implantation post-embryo transfer
- One or more miscarriages including biochemical pregnancy loss
- Previous placenta-mediated pregnancy complications defined as pre-eclampsia, small for gestational age foetus (<10th centile), spontaneous preterm birth (<34 weeks) or a combination of these.

Interventions
Both partners in the couple will give a blood sample (+/- optional saliva sample) for M2 haplotype testing. The M2 haplotype, a genomic variant with four consecutive nucleotide substitutions in the ANXA5 promoter gene, reduces ANXA5 protein production and is linked to implantation failure, early pregnancy loss, and obstetric complications like pre-eclampsia and small for gestational age fetuses.

Intervention Type
Other

Primary outcome(s)
Feasibility outcome:
The proportion of eligible couples (men and women) who consent to be tested measured using data recorded in study records at one timepoint

Key secondary outcome(s))
Preliminary estimates of sensitivity (Sn), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) from the proportions of false positive, false negative, true

positive, and true negative rates will be calculated using binomial exact methods. This will be undertaken for salivary versus blood samples for M2 gene haplotype status measured using Sanger sequencing at one timepoint

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. Women planning a pregnancy or currently pregnant
2. Women aged 18-40 years old
3. Maternal BMI (body mass index) 18.5-34.9 kg/m2
AND
4. At least one of the following:
5. Primary or secondary infertility (primary infertility is when a pregnancy has never been achieved (when tried for), and secondary infertility is when at least one prior pregnancy has been achieved)
6. One or more failed implantation post-embryo transfer
7. One or more miscarriages including biochemical pregnancy loss
8. Previous placenta-mediated pregnancy complications defined as pre-eclampsia, small for gestational age foetus (<10th centile), spontaneous preterm birth (<34 weeks) or a combination of these.
9. Male partners of eligible women*
*The male partner needs to be the same partner as in previous pregnancies where a fertility /pregnancy complication occurred which deemed the woman eligible i.e. primary or secondary infertility, failed implantation post embryo transfer, previous miscarriage, previous placenta mediated pregnancy complication.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
40 years

Sex
All

Key exclusion criteria
1. Anti-phospholipid syndrome (APS)
2. Participation in a clinical Study of an investigational medicinal product in the last 90 days

3. Participation in any other open or blinded, placebocontrolled trials of investigational medicinal products (if currently pregnant)
4. Women found to have multiple pregnancies or who have had multiple embryos transferred in IVF (if currently pregnant)
5. Current pregnancy conceived using donor egg or sperm
6. Women who are known to be taking heroin, cocaine or other illegal substances
7. Paternity status not known for male partner
8. Female and/or male participants unwilling to give consent

Date of first enrolment
06/01/2025

Date of final enrolment
31/03/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Liverpool Women's NHS Foundation Trust
Liverpool Womens Hospital
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
Birmingham Women's NHS Foundation Trust
Birmingham Womens Hospital
Metchley Park Road
Birmingham
United Kingdom
B15 2TG

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Innovate UK

Alternative Name(s)
UK Research and Innovation Innovate UK, innovateuk

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes