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A study for investigating organ complications in preeclampsia

Submission date
10/06/2020

Recruitment status
Recruiting

Registration date
16/07/2020

Overall study status
Ongoing

Last Edited
04/08/2025

Condition category
Pregnancy and Childbirth

[_] 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
Pre-eclampsia, one of the most serious complications of pregnancy, is associated with severe morbidity and mortality for the mother and baby. There is an urgent need to better understand this devastating disease.
Pre-eclampsia affects 3-8 % of pregnancies worldwide. It is a multi-system disorder involving maternal blood vessels, the kidneys, the liver, the lungs, and the fetus. In its most severe form, it affects the brain, causing seizures (eclampsia), cerebrovascular events and even death. It is a leading cause of maternal and fetal/neonatal morbidity.
Globally, pre-eclampsia is responsible for > 60,000 maternal deaths annually, and in South Africa the hypertensive disorders of pregnancy are responsible for 14% of maternal deaths. The pathophysiology of pre-eclampsia is not completely understood but the leading hypothesis is based on placental dysfunction.
Unfortunately, pre-eclampsia is a disease that is seen only in humans and there are no convincing animal models of pre-eclampsia. This makes it imperative that critical laboratory observations are made on human tissues.

Study aims
We propose establishing an ethically responsible biobank to facilitate quicker access to clinical information, special investigations and biological samples to undertake research in the field of pre-eclampsia. It is modelled on many tissue banks currently in existence.

Who can participate?
Women with pre-eclampsia (cases) and women with healthy pregnancies (controls) between the ages of 16-45 and in gestational week 20-42 will be eligible. As this is a biobank there will be no limit to the number of participants included.

What does the study involve?
Our research team will be notified by attending clinicians when there is a possible candidate for the biobank. A member of the research team will then see the candidate and will give them an information and consent sheet and explain the project. If they decide to participate and after consent has been obtained, clinical information will be collected, samples may be collected, and special investigations may be done. The participants will be seen daily and will be contacted

again after discharge. All information will be kept confidential and the participants may withdraw at any stage.

Possible risks and benefits of participating
The risk of adverse events is unlikely. There are no added risks associated with being involved in the study. Any publications arising from projects that utilised the biobank will need to acknowledge the participants.
All information collected will be stored in a locked office in the principal researcher or research midwife's office. The medical data will be recorded in a REDCap database and only the biobank investigators and research midwives will have access to the identification codes. All information used for follow-up projects will be pseudonymised. Samples stored in the biobank will be given an identifying code and will not contain any identifying information.
Samples will not be used for a genetic register.

Where is the study run from?
The study is run from Tygerberg Hospital, Cape Town, South Africa

When is the study starting and how long is it expected to run for?
The study started in April 2018 and is expected to run until December 2030

Who is funding the study?
This study is supported by STINT; The Swedish foundation of International Cooperation in Research and Higher Education, Preeclampsia foundation, Märta Lundqvist's foundation, Ester Åsberg's foundation, Jane and Dan Olsson's foundation, Center for Clinical research Dalarna and the Swedish Society of Medicine.

Who is the main contact?
Dr Catherine Cluver, cathycluver@hotmail.com
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Study website
http://www.preeclampsiaresearch.com

Contact information

Type(s)
Scientific

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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
PROVE: PReeclampsia Obstetric adVerse Events

Acronym
PROVE

Study objectives
To set up a preeclampsia biobank at Tygerberg Hospital, Stellenbosch University, to facilitate clinical and laboratory based research in preeclampsia.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/02/2018, Regional ethical board at Stellenbosch University (PO Box 241, Cape Town 8000, South Africa; +27 (0)21 9389677; no email provided), ref: N17/05/048

Study design
Single center prospectively collected database and biobank of women with severe preeclampsia

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Preeclampsia

Interventions
Our research team will be notified by attending clinicians when there is a possible candidate for the biobank. A member of the research team will then see the candidate and will give them an information and consent sheet and explain the project. If they decide to participate and after consent has been obtained, clinical information will be collected, samples may be collected, and special investigations may be done. The participants will be seen daily and will be contacted again after discharge. All information will be kept confidential and the participants may withdraw at any stage.
When a project arises that involves the use of information or samples from the biobank, an independent proposal to HREC will be obtained and approval from the Preeclampsia biobank will be requested. Once this is done, deidentified information and samples will be released. The outcomes of updates will be reported annually to the ethics committee. We will collect information on the pregnancy and outcomes of the pregnancy. We may perform cognitive function assessments and questionaries on symptoms and signs of preeclampsia.
Special investigations could include MRI examinations of the brain, studies using ultrasound, ophthalmological examinations and non-invasive endothelial function assessment.

The sample collection includes the following
• Specimens usually discarded during clinical care: E.g. placenta, placental membranes, umbilical cord, cord blood, urine, stool and cerebrospinal fluid (CSF). The CSF (maximum volume of 0.5 ml) will only be collected in women who are having spinal anaesthesia. We will collect the fluid that is usually discarded before the anaesthetic is injected.
• Blood samples: maximum of 12 ml at each collection time (usually only a single test tube of 5

ml). We will only collect samples if the patient is having blood taken for a clinical indication. We will collect blood up to a maximum of 6 times per participant.
• Saliva: This will be collected once in a 3 cc cup, 1-2 ml for freezing.

Intervention Type
Other

Primary outcome measure
The items collected for the biobank include:
1. Specimens usually discarded during clinical care: E.g. placenta, placental membranes, umbilical cord, cord blood, urine, stool and cerebrospinal fluid (CSF). The CSF (maximum volume of 0.5 ml) will only be collected in women who are having spinal anaesthesia. We will collect the fluid that is usually discarded before the anaesthetic is injected
2. Blood samples: maximum of 12 ml at each collection time (usually only a single test tube of 5 ml). We will only collect samples if the patient is having blood taken for a clinical indication. We will collect blood up to a maximum of 6 times per participant
3. Saliva: This will be collected once in a 3 cc cup, 1-2 ml for freezing

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/07/2017

Completion date
31/12/2030

Eligibility

Key inclusion criteria
1. Cases:
1.1. Women with a diagnosis of preeclampsia or severe preeclampsia in gestational week 20-42
1.2. Admitted to Tygerberg hospital
Severe preeclampsia is defined as preeclampsia with an organ complication such as renal failure, pulmonary oedema, eclampsia, intracerebral hemorrhage, cerebral oedema, heart failure or disseminated intravascular coagulation

2. Controls:
2.1. Women with healthy pregnancies matched for gestational age admitted for delivery at Tygerberg hospital

Both primiparous and parous women are included

Participant type(s)
Patient

Age group
All

Sex

Female

Target number of participants
100 women with eclampsia, 100 women with pulmonary edema, 50 women with preeclampsia without end organ complications and 50 women with normal pregnancies

Key exclusion criteria
1. Cases: If the woman is not able to give informed consent
1.1. For women with pulmonary edema: Existing cardiac disease
1.2. For women with eclampsia: Existing neurological disease
2. Normotensive controls:
2.1. Pre-exisiting hypertension
2.2. Diabetes mellitus before or during pregnancy
2.3. Pre-exisiting cardiovascular, renal or cerebral disease
2.4. Chronic medication

Date of first enrolment
12/04/2018

Date of final enrolment
31/12/2029

Locations

Countries of recruitment
South Africa

Study participating centre
Tygerberg Hospital
Stellenbosch University
Francie van Zijl Drive
Cape Town
South Africa
7505

Sponsor information

Organisation
Stellenbosch University

Sponsor details
Faculty of MEdicine and Health Sciences
Francie van Zyl Drive
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Sponsor type
University/education

Website
http://www.sun.ac.za/english/faculty/healthsciences

ROR
https://ror.org/05bk57929

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Mercy Perinatal

Funder Name
Svenska Läkaresällskapet

Alternative Name(s)
Swedish Society of Medicine, Swedish Medical Society, SLS

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Sweden

Funder Name
Märta Lundqvists Stiftelse

Alternative Name(s)
Märta Lundqvists Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Sweden

Funder Name
Swedish Foundation for International Cooperation in Research and Higher Education

Alternative Name(s)
Stiftelsen för internationalisering av högre utbildning och forskning, STINT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Sweden

Funder Name
Preeclampsia Foundation

Alternative Name(s)
The Preeclampsia Foundation, Preeclampsia Fndn, PF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Funder Name
Ester Åsbergs Stiftelse

Funder Name
Center for Clinical research, Dalarna, Sweden

Funder Name
Jane och Dan Olssons Stiftelse

Alternative Name(s)
Jane and Dan Olssons Foundation

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Sweden

Results and Publications

Publication and dissemination plan
Planned publications in high impact peer reviewed journals.

Intention to publish date
31/12/2031

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.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	Blood pressure as a risk factor for eclampsia and pulmonary oedema in pre-eclampsia	23/07/2021	22/10/2021	Yes	No
Other publications	Cerebral perfusion pressure and autoregulation in eclampsia-a case control study	17/03/2021	22/10/2021	Yes	No
Other publications	Cognitive impairment in preeclampsia complicated by eclampsia and pulmonary edema after delivery	16/02/2021	22/10/2021	Yes	No
Protocol article	PROVE-Pre-Eclampsia Obstetric Adverse Events: Establishment of a Biobank and Database for Pre-Eclampsia	20/04/2021	22/10/2021	Yes	No

Other publications	Associations Between Soluble fms-Like Tyrosine Kinase-1 and Placental Growth Factor and Disease Severity Among Women With Preterm Eclampsia and Preeclampsia	16/08/2022	02/11/2023	Yes	No
Other publications	Cardiac magnetic resonance imaging in preeclampsia complicated by pulmonary edema shows myocardial edema with normal left ventricular systolic function	01/08/2022	02/11/2023	Yes	No
Other publications	Cerebral biomarkers in neurologic complications of preeclampsia	01/08/2022	02/11/2023	Yes	No
Other publications	Circulating Chemerin Is Elevated in Women With Preeclampsia	13/03/2023	02/11/2023	Yes	No
Other publications	Circulating Growth Differentiation Factor 15 Is Increased Preceding Preeclampsia Diagnosis: Implications as a Disease Biomarker	17/08/2021	02/11/2023	Yes	No
Other publications	Circulating concentrations of glycocalyx degradation products in preeclampsia	13/10/2022	02/11/2023	Yes	No
Other publications	Correlation between cognitive assessment scores and circulating cerebral biomarkers in women with pre-eclampsia and eclampsia	01/03/2023	02/11/2023	Yes	No
Other publications	Evidence of Neuroinflammation and Blood-Brain Barrier Disruption in Women with Preeclampsia and Eclampsia	05/11/2021	02/11/2023	Yes	No
Other publications	PSG7 and 9 (Pregnancy-Specific β-1 Glycoproteins 7 and 9): Novel Biomarkers for Preeclampsia	05/04/2022	02/11/2023	Yes	No
Other publications	Blood-brain barrier injury and neuroinflammation in pre-eclampsia and eclampsia	01/06/2025	04/08/2025	Yes	No
Other publications	Cerebral infarcts, edema, hypoperfusion, and vasospasm in preeclampsia and eclampsia	01/06/2025	04/08/2025	Yes	No
Other publications	Reduced circulating NrCAM as a biomarker for fetal growth restriction	21/07/2021	04/08/2025	Yes	No
Other publications	The association between circulating SIGLEC6 and preeclampsia: observational studies of seven cohorts	29/07/2025	04/08/2025	Yes	No