ISRCTN13060768 https://doi.org/10.1186/ISRCTN13060768

A study for investigating effects on the brain, heart, clotting system during and after pregnancy and the pregnant woman's and partner's health in the postpartum period in pregnancies complicated by preeclampsia

Submission date
14/06/2020

Recruitment status
Recruiting

Registration date
27/07/2020

Overall study status
Ongoing

Last Edited
04/08/2025

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Current plain English summary as of 04/01/2021:

Background and study aims
Preeclampsia is one of the most serious complications of pregnancy affecting between 3% and 8 % of pregnancies worldwide. Preeclampsia leads to over 60,000 maternal deaths annually and for every preeclampsia related death, there are probably 50 to 100 other women who experience significant morbidity.

Preeclampsia is a multi-system disorder involving the blood vessels, kidneys, liver, brain, lungs, and heart of the mother, and the fetus and placenta. In severe cases, preeclampsia might cause heart failure, kidney failure, blood clotting disorders, seizures (eclampsia), stroke, and restriction of the fetus's ability to grow.

The causes of preeclampsia are not completely known but it is suggested that it is based on problems with the function of the placenta. Factors associated with pre-existing problems with the function of the blood vessels, such as diabetes, cardiac disease, and obesity, can also predisposing mothers to preeclampsia. The only cure is delivery.

Currently, there is a lack of evidence on how to assess organ failure due to severe preeclampsia. There are only a few tests available to evaluate the function of the liver, kidney, and blood clotting. Currently, there are no systems for predicting or assessing the function of the brain, heart, and blood vessels.

A better understanding of the causes and underlying changes that take place leading to organ failure would allow the development of more accurate prediction and assessment tools which would allow for faster, more accurate, and/or preventative treatment in these cases. This would lead to better outcomes for the mother and the child.

The overall aim of this study is to set up the Preeclampsia project and biobank at Sahlgrenska University Hospital, Gothenburg, Sweden and Uppsala University Hospital, Uppsala, Sweden, to facilitate laboratory-based research on preeclampsia and to contribute to a safer and more patient-centered management of women with preeclampsia. Specifically, this study aims to follow a group of women with preeclampsia, and women without. Blood samples, brain and heart scans, cognitive function tests, and measurements of blood flow, blood pressure and blood clotting will be collected. These will be compared to the outcomes of these pregnant women to see which of these measurements serve as an accurate marker for worse outcomes, to allow for better future treatment.

There is also a lack of data regarding women's and their partners experiences of preeclampsia during pregnancy and postpartum in a Swedish setting. Interviews with women with preeclampsia from other settings have described preeclampsia as a fearful, powerless, painful and/or life threatening event and inadequate clinical management and care, although many women felt lucky to survive. By increasing the knowledge about how women and their partners experience preeclampsia and the consequences regarding health-related quality of life, general self-efficacy, anxiety and depression levels, childbirth experiences and breastfeeding, improvements could be made to personalized management and when following up after a pregnancy complicated by preeclampsia.

Who can participate?
Women over 18 years of age, either diagnosed with preeclampsia or with healthy pregnancies (to serve as a comparison).

What does the study involve?
The study will collect characteristics and lifestyle data, blood samples, brain and heart scans, cognitive function tests, and measurements of blood flow, blood pressure and blood clotting, as well as information on the women and their partner's perspective of preeclampsia, rating of their health and wellbeing, and childbirth experiences, through interviews. This information will be collected during the pregnancy and 8-12 weeks and one year after the delivery has taken place.

What are the possible benefits and risks of participating?
This study is an observational study and so the risks associated with participating are low. Beyond the additional measurements taken, participants will be receiving standard care. After a blood sample is drawn the participant might have a small bruise. When the participants are examined in the MRI camera or undergoing heart ultrasound, there might be unexpected findings. If this happens they will be referred to a specialist for further management. The results from the study will be processed on a group level and individual results of the investigations will not be revealed for the individual research participant.

Where is the study run from?
Sahlgrenska University Hospital, Gothenburg and Uppsala University Hospital, Uppsala (Sweden).

When is the study starting and how long is it expected to run for?
March 2018 to December 2032

Who is funding the study?
The Swedish Brain Fund, Gothenburg Medical Society, Jane and Dan Olsson's foundation, Märta Lundqvist foundation, and Regional Research Funds, Västra Götaland (Sweden).

Who is the main contact?
1. Lina Bergman (Sahlgrenska University Hospital)
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2. Anna Karin Wikström (Uppsala University Hospital)
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Previous plain English summary:

Background and study aims
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Preeclampsia is a multi-system disorder involving the blood vessels, kidneys, liver, brain, lungs, and heart of the mother, and the fetus and placenta. In severe cases, preeclampsia might cause heart failure, kidney failure, blood clotting disorders, seizures (eclampsia), stroke, and restriction of the fetus's ability to grow.

The causes of preeclampsia are not completely known but it is suggested that it is based on problems with the function of the placenta. Factors associated with pre-existing problems with the function of the blood vessels, such as diabetes, cardiac disease, and obesity, can also predisposing mothers to preeclampsia. The only cure is delivery.

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The overall aim of this study is to set up the Preeclampsia project and biobank at Sahlgrenska University Hospital, Gothenburg, Sweden and Uppsala University Hospital, Uppsala, Sweden, to facilitate laboratory-based research on preeclampsia and to contribute to a safer and more patient-centered management of women with preeclampsia. Specifically, this study aims to follow a group of women with preeclampsia, and women without. Blood samples, brain and heart scans, cognitive function tests, and measurements of blood flow, blood pressure and blood clotting will be collected. These will be compared to the outcomes of these pregnant women to see which of these measurements serve as an accurate marker for worse outcomes, to allow for better future treatment.

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Where is the study run from?
Sahlgrenska University Hospital, Gothenburg and Uppsala University Hospital, Uppsala (Sweden).

When is the study starting and how long is it expected to run for?
From March 2018 to January 2023. Recruitment started in May 2019 at Sahlgrenska and in December 2019 at Uppsala.

Who is funding the study?
The Swedish Brain Fund, Gothenburg Medical Society, Jane and Dan Olsson's foundation, Märta Lundqvist foundation, and Regional Research Funds, Västra Götaland (Sweden).

Who is the main contact?
1. Lina Bergman (Sahlgrenska University Hospital)
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2. Anna Karin Wikström (Uppsala University Hospital)
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Investigating organ complications in preeclampsia during and after pregnancy and the pregnant woman's and partner's health in the postpartum period: An observational cohort study involving the GO PROVE - Gothenburg Preeclampsia Obstetric Adverse Events and UPMOST - Uppsala Pregnancy Complication Study

Acronym
GO PROVE and UPMOST

Study objectives
Women with preeclampsia demonstrate subclinical impaired organ function including endothelial dysfunction, cardiac dysfunction, and cerebral dysfunction.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 10/12/2018, Regional ethics committee Gothenburg (Box 2110, 75002 Uppsala, Sweden; +46 104750800; registrator@etikprovning.se), ref: 955-18
2. Approved 27/02/2019, Etikprövningsmyndigheten (Box 2110, 75002 Uppsala, Sweden; +46 104750800; registrator@etikprovning.se), ref: 2019-00309

Study design
Prospective cohort study with control group

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Organ impairment in preeclampsia

Interventions
Women are included at the time of diagnosis of preeclampsia or at the corresponding gestational age for women with normotensive pregnancies. At inclusion, blood samples are drawn and women are asked to answer questions about background characteristics and current signs and symptoms of preeclampsia. Additional information is retrieved from the medical charts. Subgroups of women are then asked to participate in organ specific evaluations including ultrasound of the heart, measurement of peripheral vascular resistance, cognitive function scoring, cerebral blood flow measurement through doppler technique and magnetic resonance imaging of the brain. At delivery, additional biological samples are drawn and for some deliveries, placental biopsies are collected. All biological samples are stored in a biobank provided by the respective hospital. Women are followed up after delivery with questionnaires about their health and the experience of childbirth together with their partner. At one year postpartum, organ specific evaluations are repeated together with an additional blood sample and some background characteristics and symptom scores are repeated.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measures as of 11/09/2024:
Organ dysfunction is measured using the following at inclusion in the study and after delivery:
1. Cognitive function is measured by magnetic resonance imaging (resting state) and a series of validated objective tests such as WAIS, SRB1, and Deary test, and, in addition, a subjective test called cognitive failure questionnaire
2. Cerebral blood flow regulation is measured by the Doppler technique and magnetic resonance imaging

3. Cerebral biomarkers are measured in cerebrospinal fluid and plasma by ELISA and SIMOA technique
4. Cardiac biomarkers are measured in plasma by automated laboratory-based instruments used in clinical care.
5. Coagulation is measured by thrombelastogram - ROTEM and Multiplate
6. Cardiac function is measured by transthoracic echocardiography
7. Cardiovascular indicators in women with preeclampsia and normotensive pregnancies at time of inclusion, at three and 12 months after birth
8. Complications related to preeclampsia at the time of enrolment, before delivery and before discharge from the hospital.

Previous primary outcome measures:
Organ dysfunction is measured using the following at inclusion in the study and after delivery:
1. Cognitive function is measured by magnetic resonance imaging (resting state) and a series of validated objective tests such as WAIS, SRB1, and Deary test, and, in addition, a subjective test called cognitive failure questionnaire
2. Cerebral blood flow regulation is measured by doppler technique and magnetic resonance imaging
3. Cerebral biomarkers are measured in cerebrospinal fluid and plasma by ELISA and SIMOA technique
4. Cardiac biomarkers are measured in plasma by automated laboratory based instruments used in clinical care.
5. Coagulation is measured by thrombelastogram - ROTEM and Multiplate
6. Cardiac function is measured by transthoracic echocardiography

Key secondary outcome(s))

Current secondary outcome measures as of 04/01/2021:
1. Patient reported outcomes are measured by General Self-Efficacy scale, (GES) Hospital Anxiety and Depression Scale, (HADS), Edinburgh Postnatal Depression Scale, (EPDS) EuroQol—5 Dimensions (EQ-5D), EuroQol- Visual Analogue Scale (EQ-VAS), Post Traumatic Stress Disorder Checklist for DSM-5 (PCL-5) at diagnosis of preeclampsia and compared with healthy controls. The GES, HADS, EPDS, EQ-5D, EQ-VAS, Childbirth experience questionnaire,2 (CEC2), PCL-5 and the Breastfeeding self-efficacy scale short form (BSE) are re-evaluated 8-12 weeks after birth. The GES, HADS, EPDS, EQ-5D, EQ-VAS, CEQ2, PCL-5 and BES are again re-evaluated 1 year after birth.
2. Qualitative interviews will be performed six months after birth. The aims of the qualitative research in the project are to describe the women's and their partner’s lifeworld experiences of severe preeclampsia during pregnancy, childbirth and postnatal care. The target number of participants for the qualitative study are 15 to 20 women and partners. Open-ended questions will be used to collect the data. The women will be asked to describe their experiences of severe preeclampsia during pregnancy, childbirth and postnatal care. The interviews will last about 60 minutes and will be audio-recorded. All interviews will be transcribed verbatim. The data will be analyzed using thematic or phenomenological analysis.

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Previous secondary outcome measures:

Patient reported outcomes are measured by General Self-Efficacy scale, Hospital Anxiety and Depression Scale, Edinburgh Postnatal Depression Scale, E-Q-5D visual analogue scale, Post Traumatic Stress Disorder Checklist for DSM-5, Childbirth experience questionnaire, and the Breastfeeding self-efficacy scale short form after delivery

Completion date
31/12/2032

Eligibility

Key inclusion criteria
Preeclampsia cohort:
1. Primiparous and parous pregnant women
2. Aged ≥18 years
3. Diagnosis of preeclampsia after gestational week 20

Control cohort:
1. Primiparous and parous women
2. Aged ≥18 years
3. Healthy pregnancies matched for gestational age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Female

Key exclusion criteria
Current participant exclusion criteria as of 10/01/2022:
1. Unable to give written informed consent
2. Magnetic resonance imaging (MRI) contraindications, including claustrophobia, for MR group only
3. Diabetes Mellitus before or during pregnancy, pre-existing cardiovascular, renal, or cerebral disease, or pre-existing hypertension for special investigations including MRI, echocardiography, cerebral doppler measurements, and cognitive function assessment

Previous participant exclusion criteria:
1. Unable to give written informed consent
2. Pre-existing hypertension
3. Diabetes Mellitus before or during pregnancy
4. Pre-existing cardiovascular, renal, or cerebral disease
5. Magnetic resonance imaging (MRI) contraindications, including claustrophobia, for MR group only

Date of first enrolment

01/05/2019

Date of final enrolment
31/12/2031

Locations

Countries of recruitment
Sweden

Study participating centre
Sahlgrenska Academy
Department of obstetrics and gynecology
Diagnosvägen 15
Gothenburg
Sweden
41650

Study participating centre
Uppsala University
Department of women's and children's health
Akademiska sjukhuset
Uppsala
Sweden
75185

Sponsor information

Organisation
Sahlgrenska University Hospital

ROR
https://ror.org/04vgqjj36

Organisation
Uppsala University Hospital

ROR
https://ror.org/01apvbh93

Funder(s)

Funder type
Charity

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
Göteborgs Läkaresällskap

Alternative Name(s)
Göteborg Medical Society, Gothenburg Medical Society, Medical Society of Göteborg

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
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

Funder Name
Hjärnfonden

Alternative Name(s)
Brain Foundation

Funding Body Type
Private sector organisation

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

Location
Sweden

Funder Name
Västra Götalandsregionen

Alternative Name(s)
Region Västra Götaland, Västra Götaland Regional Council, Västra Götaland region, Västra Götalandsregiona, VGR

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Sweden

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?
Results article		18/04/2023	17/08/2023	Yes	No
Results article		01/02/2025	04/08/2025	Yes	No
Protocol article		24/11/2021	26/11/2021	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes