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Prediction of Risks in Early onset Pre-eclampsia (PREP)

Submission date	Recruitment status
08/02/2012	No longer recruiting
Registration date	**Overall study status**
13/02/2012	Completed
Last Edited	**Condition category**
22/09/2017	Pregnancy and Childbirth

✓ Retrospectively registered
? Protocol not yet added
? SAP not yet added
✓ Results added
? Raw data not yet added
✓ Study completed

Plain English Summary
Background and study aims
Pre-eclampsia is a disorder in pregnancy, characterised by raised blood pressure and abnormal levels of protein in the urine, beyond 20 weeks of pregnancy. Pre-eclampsia can affect different parts of the body such as liver, kidneys, lungs, brain and clotting systems. In 1% of pregnant women it occurs before 34 weeks of pregnancy called early onset pre-eclampsia and causes more serious complications for mother and baby compared to later onset pre-eclampsia. The only known cure is delivery of the baby. Delivery before 34 weeks of pregnancy is premature, so the decision about when is the best time to deliver involves a difficult balance between the risks to the woman of continuing the pregnancy and the risks to the baby of being born too soon. One third of women develop complications and need care in specialist units. About £1 billion in extra costs per year in the NHS are linked to neonatal care due to extreme prematurity. Presently women with early onset pre-eclampsia are playing 'Russian Roulette'. They are either admitted on a 'let's play safe' ticket which may unnecessarily disrupt family life with husbands leaving their jobs for extended periods during a highly anxious several months ensues or they are at home living normally with the unknown potential of a major medical crisis looming for which they are not prepared. The third possibility is that they are in and out of the day unit or clinic, which is tiring and expensive and dispiriting. More importantly they are often faced with making difficult decisions of early delivery of an extremely premature infant with a slim chance of survival and major neurological handicap in view of major concerns to their health. Mothers know that the decision on which of these happens is not based on a level of objective knowledge. Current tests on admission to mothers with early onset pre-eclampsia include clinical history, examination and laboratory investigations. Often the crucial decision of when to deliver is based on the personal clinical experience of the clinician. This is due to a lack of evidence regarding the ability of tests to correctly predict complications to the mother or baby. In this study we aim to develop a model that provides a score for individualised risk assessment for complications in the mother.

Who can participate?
Women admitted with early onset pre-eclampsia.

What does the study involve?
Your pregnancy will be managed in the normal way and you will not have to do anything extra if you take part in the study. Information about you and your baby's health will be collected from your medical notes until you and your baby are discharged from hospital. The data collected will be anonymised and not linked to your personal details. If you are confirmed to have pre-eclampsia, your clinical team will arrange regular follow ups as part of routine care. At each visit, you will be asked about any symptoms, such as headache, nausea, vomiting or upper tummy pain, your blood pressure and urine will be checked and blood samples will be sent to the lab. The clinical team will also check the wellbeing of your baby. This is the recommended care that is currently done in clinical practice. You may also be asked to collect 24-hour urine samples once a week, which is currently done in many units. If your hospital does not routinely ask for this test, we would like your permission to collect a 24-hour urine sample once a week for the study. If tests show that you do not have pre-eclampsia, you will be followed up by your clinical team according to routine care. We would like you to remain in the study and allow us to include information collected from your medical notes about you and your baby's health for the study.

What are the possible benefits and risks of participating?
The main benefit from the study is that the information gained will help to improve the management of women with pre-eclampsia in the future. Since the tests are done as part of routine practice, there are no additional risks due to participation.

Where is the study run from?
Barts and The London School of Medicine and Dentistry (UK).

When is the study starting and how long is it expected to run for?
From November 2011 to April 2014.

Who is funding the study?
NIHR Health Technology Assessment Programme - HTA (UK).

Who is the main contact?
Prof Khalid Khan

Contact information

Type(s)
Scientific

Contact name
Prof Khalid Khan

Contact details
Women's Health Research Unit
Centre for Primary Care and Public Health
Blizard Institute
Barts and The London School of Medicine and Dentistry
Yvonne Carter Building
58 Turner Street
London
United Kingdom
E1 2AB

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Protocol/serial number
09/22/163

Study information

Scientific Title
Development and validation of a Prediction model for Risk of complications in Early onset Pre-eclampsia (PREP)

Acronym
PREP

Study hypothesis
1. To develop and internally validate a prediction model in women admitted with early onset pre-eclampsia from 20+0 and 33+6 weeks of gestation for timely assessment of the risk of adverse maternal outcome at 48 hours and by discharge.
2. To externally validate and update the model through two external datasets of patients admitted with diagnosis of early onset pre-eclampsia.
3. To assess the risk of adverse fetal and neonatal outcomes at birth and by discharge.

More details can be found at http://www.nets.nihr.ac.uk/projects/hta/0922163
Protocol can be found at http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0015/54330/PRO-09-22-163.pdf

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Research Ethics Committee West Midlands, Edgbaston, 13/10/2011, ref: 11/WM/0248

Study design
Prospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Condition
Early onset pre-eclampsia

Interventions
Prospective cohort study of development and validation of prediction model for risk of adverse outcomes in women admitted with early onset pre-eclampsia.

Women will be recruited into the study between 20+0 and 33+6 weeks gestation and followed up until they are discharged from hospital following the birth of their baby. The results of routine clinical tests will be collected for the study; these will include:

1. History:
1.1. Symptoms of headache, epigastric pain , nausea or visual disturbance
1.2. Pre existing hypertension, renal disease, diabetes mellitus, autoimmune disease and other past relevant history of pre-eclampsia obtained at antenatal booking
2. Examination:
2.1. Blood pressure
2.2. Exaggerated tendon reflexes or clonus
2.3. Papilloedema
3. Investigations:
3.1. Serum uric acid
3.2. Urine dipstick, 24 hour urine protein, Protein Creatinine Ratio (PCR)
3.3. Renal and liver function tests
3.4. Pulse oximetry
3.5. Ultrasound (fetal growth, liquor volume, umbilical artery doppler, uetrine artery doppler at 20-24 weeks of gestation)

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Adverse maternal outcome at 48 hours and at discharge that includes maternal death
2. Other adverse effects:
2.1. Involvement of Central Nervous System - eclamptic seizures
2.2. Glasgow coma score of less than 13
2.3. Stroke or RIND (Reversible Ischaemic Neurological Deficit)
2.4. Cortical blindness
2.5. Retinal detachment]
2.6. Posterior reversible encephalopathy
2.7. Bell's palsy
2.8. Hepatic dysfunction

2.9. Hematoma, or rupture
2.10. Cardio respiratory - need for positive ionotrope support
2.11. Myocardial ischaemia or infarction
2.12. Infusion of any third parenteral antihypertensive
2.13. At least 50% FIO2 for greater than 1 hour
2.14. Intubation
2.15. Pulmonary oedema
2.16. Renal-acute renal insufficiency (creatinine >200uM)
2.17. Dialysis
2.18. Haematological-transfusion of any blood product

Added 27/02/2015:
2.19. Delivery at a gestational age less than 34 weeks

Secondary outcome measures
Adverse perinatal outcome at birth and by discharge that includes one or more of the following:
1. Perinatal or infant mortality
2. Bronchopulmonary dysplasia (defined as oxygen requirement at 36 weeks corrected gestation unrelated to an acute respiratory episode)
3. Necrotising enterocolitis (include only Bell's stage 2 or 3. Definition - evidence of pneumotosis intestinalis on abdominal x-ray and/or surgical intervention)
4. Grade III/IV intraventricular haemorrhage
5. Cystic periventricular leukomalacia
6. Stage 3-5 retinopathy of prematurity
7. Hypoxic ischaemic encephalopathy (Apgar score </= 5 at 10 mins and/or pH 7.00 in first 60 minutes of life and/or Base deficit >/= -16 in first 60 minutes associated with abnormal conscious level (lethargy, stupor or coma) and seizures and/or poor/weak suck and/or hypotonia and/or abnormal reflexes).

Overall study start date
01/11/2011

Overall study end date
30/04/2014

Eligibility

Participant inclusion criteria
1. Women admitted with diagnosis of 'superimposed pre-eclampsia': this was defined as new-onset proteinuria (as defined previously) in women with chronic hypertension and no proteinuria at base line. In women who had proteinuria at base line, the diagnosis of preeclampsia required an elevated serum alanine aminotransferase concentration (>70 U per litre) or worsening hypertension (either two diastolic BP of at least 110 mm Hg four hours apart or one diastolic measurement of at least 110 mm Hg if the woman had been treated with an antihypertensive drug), plus one of the following: increasing proteinuria, persistent severe headaches, or epigastric pain.
2. Women with diagnosis of HELLP syndrome with no proteinuria or hypertension
3. Women with one episode of eclamptic seizures with no hypertension or proteinuria
4.1. Gestational age between 20+0 weeks and 33+6 weeks
4.2. Pre-eclampsia defined as new onset hypertension (systolic BP ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg on 2 occasions 4 -6 hours apart in women) after 20 weeks of pregnancy and presence

of proteinuria (≥ 2+ in urine dipstick or PCR ratio of greater than 30mg/mmol or 300 mg of protein excretion in 24 hours)
4.3. Be capable of understanding the information provided, with use of an interpreter if required
4.4. Give written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
500

Participant exclusion criteria
1. There is occurrence of the outcome (including recurrent eclamptic seizures) prior to testing
2. There is insufficient time for gaining informed consent.
3. The mother does not comprehend spoken and written English adequately and a translator is not available.

Recruitment start date
16/01/2012

Recruitment end date
30/04/2014

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Women's Health Research Unit
Centre for Primary Care and Public Health
Blizard Institute
Barts and The London School of Medicine and Dentistry
Yvonne Carter Building
58 Turner Street
London
United Kingdom
E1 2AB

Study participating centre
50 other centres
United Kingdom
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Sponsor information

Organisation
Queen Mary University of London (UK)

Sponsor details
Queen Mary's Innovation Centre
Lower Ground Floor
5 Walden Street
London
England
United Kingdom
E1 2EF

Sponsor type
University/education

Website
http://www.bartsandthelondon.nhs.uk/our-services/research-and-development/

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Government

Funder Name
NIHR Health Technology Assessment Programme - HTA (UK) ref: 09/22/163

Results and Publications

Publication and dissemination plan
Funder: The findings will be provided as a detailed report to the NIHR. Any outputs as scientific publications, presentations and websites will highlight the support provided by the NIHR.

Scientific papers and presentations: Every effort will be made to ensure that the study is conducted and reported with the highest standard necessary for publication in high impact journals. This is one of the principal factors that determine incorporation of findings into clinical guidelines. The findings will be disseminated to peers and experts through presentations in relevant specialty conferences and Network meetings.

Patient and Public: A regular newsletter will be sent to the collaborators updating and highlighting the work. We will provide the details of the findings in the APEC website.

Websites: The details of the study and findings will be provided through the institutional websites of QMUL and the Blizard Institute.

Mainstream and Social media: QMUL has an active press department to facilitate the research findings to the public by staging press releases that are relevant, factual and informative. The increasing integration of social media in our day today lives will be exploited to effectively disseminate the findings through applications such as Twitter and LinkedIn.

Professional Societies: Through existing links, the findings will be disseminated to the Association of Medical Royal Colleges (AoMRC), Royal College of Obstetricians and Gynaecologists (RCOG), Royal College of Midwifery and Nursing (RCM), Royal College of General Practitioners (RCGP) and British Maternal Fetal Medicine Society (BMFMS).

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	30/03/2017		Yes	No
Results article	results	01/04/2017		Yes	No