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Does placental growth factor testing improve outcomes for women with suspected preterm pre-eclampsia in low- and middle-income countries?

Submission date
27/04/2025

Recruitment status
Recruiting

Registration date
01/05/2025

Overall study status
Ongoing

Last Edited
01/05/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Preeclampsia is a serious pregnancy complication that can cause high blood pressure and organ damage in the mother, and poor growth or death of the baby. Globally, preeclampsia is one of the leading causes of death for pregnant women and their babies, especially in low- and middle-income countries (LMICs) such as those in Sub-Saharan Africa and South Asia. Each year, around 30,000 women and 500,000 babies die due to this condition—most of these deaths could be prevented with earlier diagnosis and timely delivery. Diagnosing preeclampsia in LMICs can be challenging due to limited access to tests like blood pressure monitoring, urine testing, and scans. This can lead to missed or late diagnoses with serious consequences. Placental growth factor (PlGF) is a substance in the blood that is low in women with preeclampsia. Testing for PlGF has been shown to help diagnose the condition earlier and reduce complications in high-income countries like the UK, where it is now used routinely. PlGF testing may be especially useful in low-resource settings where the need is greatest, however, its benefits have not yet been fully studied in this setting. Point-of-care PlGF tests are now available that can be done with minimal equipment or training. This study aims to test whether using point-of-care PlGF testing in LMICs improves outcomes for mothers and babies. It will also examine whether PlGF testing is cost-effective and how it affects the use of health resources.

Who can participate?
Women with suspected preeclampsia between 20 and 37 weeks of gestation, with a live, singleton pregnancy, will be able to take part in the study.

What does the study involve?
Half of the women will receive a PlGF test and care based on the results; the other half will receive the usual care available in their hospital, without a test. The outcomes of the mothers and babies will be followed until they are discharged from the hospital.

What are the possible risks and benefits of participating?
By taking part in the study, those who are allocated to receive a PlGF test will have additional information available to their medical team that may help inform their diagnosis. There may be slight discomfort associated with taking the blood test, however, no risks are expected from participation.

Where is the study run from?
The study is being run by King's College London. It will take place in sites in Brazil, India, Sierra Leone and Zambia.

When is the study starting and how long is it expected to run for?
July 2024 to June 2027. Recruitment for the study will start in May 2025 and will continue for one year, the data analysis and report writing is expected to take another year.

Who is funding the study?
The National Institute for Health and Care Research (NIHR), UK

Who is the main contact?
The trial coordinator is Louisa Samuels, louisa.samuels@kcl.ac.uk

Contact information

Type(s)
Principal investigator

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Type(s)
Public, 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
Placental Growth fActor testing for diagnosis of preterm preeclampsia and reductIon of adverse Outcomes in low- and middle-income countries: a pragmatic, international, open-label, randomised controlled trial

Acronym
PAPAGAIO Diagnosis

Study objectives
The use of placental growth factor testing for diagnosis of pre-term preeclampsia, implemented alongside a clinical management algorithm, improves maternal and neonatal outcomes in low- and middle-income countries.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 05/03/2025, King's College London Research Ethics Committee (5-11 Lavington Street, London, SE1 0NZ, United Kingdom; +44 (0) 20 7836 5454; rec@kcl.ac.uk), ref: HR/DP-24 /25-46560

2. approved 03/02/2025, University of Zambia Biomedical Research Ethics Committee (Ridgeway Campus, Lusaka, P.O. Box 50110, Zambia; +260 977925304; unzarec@unza.zm), ref: 6222-2024

3. approved 24/02/2025, Sierra Leone Ethics and Scientific Review Committee (Directorate of Training and Research, Youyi Building, Brookfields, Freetown, FQG2+CP5, Sierra Leone; +23278366493; efoday@mohs.gov.sl), ref: 004/02/2025

4. approved 20/01/2025, Institutional Ethics Committee of KLE Academy of Higher Education and Research (KLES Dr Prabhakar Kore Hospital, Nehru Nagar, Belagavi, 590010, India; +91-831-255 1876; kleclinicalresearch@gmail.com), ref: KAHER/EC/2025-26/D-21012501

Study design
Multicenter interventional open-label individual randomized controlled trial

Primary study design
Interventional

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diagnosis of pre-term preeclampsia

Interventions
Participants with suspected preeclampsia will be randomised to receive either a placental growth factor test, implemented alongside a clinical management algorithm (intervention), or usual care (control). The allocation ratio will be 1:1. Randomisation will be managed by a secure web-based randomisation facility hosted by OMDA. A minimisation algorithm will ensure balance between the intervention and control group, with respect to the country, site, gestational age at randomisation (20+0 to 27+6, 28+0 to 31+6, 32+0 to 33+6, 34+0 to 36+6 weeks' gestation), primary indication for testing (hypertension, other) and severity of hypertension (≥160mmHg, <160mmHg). Following randomisation, the participant will either receive a PlGF test, or ongoing usual care as the randomisation indicates.

In the intervention (PlGF test) group, a point-of-care PlGF test will be performed on whole blood collected as soon as feasible after randomisation. The clinical teams caring for the participant will be informed of the PlGF test result. All clinicians at the trial sites will be trained in interpretation of PlGF results. A 'normal' test result will indicate that preeclampsia can be ruled out, an 'abnormal' test will indicate that preeclampsia cannot be ruled out and ongoing follow-up is required, a 'very abnormal' test will indicate a confirmed diagnosis of preeclampsia (in accordance with the International Society for the Study of Hypertension in Pregnancy guidelines). Participants will be treated in accordance with local guidelines and at the discretion of the treating clinician.

The control group will receive routine clinical management according to local guidelines and clinician discretion.

Participants will be followed up until postnatal discharge of both mother and baby.

Intervention Type
Other

Primary outcome(s)
The following primary outcome measures will be assessed from data collected from medical records at discharge, using data collected between recruitment and primary hospital discharge:
1. Primary maternal outcome: A composite of maternal mortality and morbidity (based on the miniPIERS composite of adverse maternal outcomes) during pregnancy and delivery until primary hospital discharge

2. Primary perinatal outcome: Composite of stillbirth and early neonatal death (<7 days) until primary hospital discharge

Key secondary outcome(s))

The following secondary outcome measures will be assessed from data collected from medical records at discharge, using data collected between recruitment and primary hospital discharge:

Tested Maternal Outcomes:
1. Maternal mortality according to clinical diagnosis
2. Eclampsia according to clinical diagnosis
3. Placental abruption according to clinical diagnosis
4. Termination pre-viability for maternal preeclampsia according to clinical diagnosis
5. Time to diagnosis of pre-eclampsia according to the International Society for the Study of Hypertension in Pregnancy definition
6. Proportion of women diagnosed with preeclampsia according to the International Society for the Study of Hypertension (ISSHP) in pregnancy definition
7. Time to delivery
8. Mode of birth (vaginal, assisted vaginal, caesarean section)

Descriptive Maternal Outcomes:
1. Stroke
2. Cortical blindness
3. Retinal detachment
4. Pulmonary oedema
5. Acute Kidney Injury and using laboratory creatinine measurements, definition according to the KIDIGO definitions
6. Liver capsule haematoma/rupture
7. Major post-partum haemorrhage
8. Hepatic dysfunction measured according to the hospital medical records and using laboratory AST/ALT measurements, definition according to ISSHP definitions
9. Low platelets measured according to the hospital medical records and using laboratory platelet measurements, definition according to ISSHP definitions
10. ICU admission
11. Intubation and ventilation (other than for delivery)
12. Glasgow coma score <13
13. Transient ischaemic attack
14. Posterior reversible encephalopathy
15. Positive inotropic support
16. Myocardial infarction/ischaemia
17. Blood oxygen saturation <90%
18. Requirement of ≥50% FiO2 for over one hour
19. Supplemental oxygen >50% for more than one hour
20. Dialysis required
21. HDU admission
22. Labour onset (spontaneous, induced or pre-labour caesarean section)
23. Indication for delivery
24. Use of MgSO4
25. Use of steroids
26. Use of antihypertensives
27. Parenteral infusion of third-line antihypertensives required

Perinatal Outcomes
Tested Perinatal Outcomes
1. Stillbirth
2. Early neonatal death (within 7 days of life)
3. Neonatal unit admission
4. Neonatal unit admission for more than 48 hours
5. Gestational age at delivery
6. Preterm birth before 37 weeks' gestation
7. Preterm birth before 34 weeks' gestation
8. Birthweight <10th centile (Intergrowth-21)

Descriptive Perinatal Outcomes
1. Late neonatal death (after 7 days of life, up to primary hospital discharge)
2. Respiratory support
3. Sepsis
4. Neonatal seizures
5. Birthweight
6. Birthweight <3rd centile (Intergrowth-21)
7. Antibiotics given
8. APGARs at 1 and 5 minutes
9. Hypoxic Ischaemic Encephalopathy and grade
10. Respiratory distress syndrome
11. Supplementary oxygen and duration
12. Administration of surfactant
13. Hypoglycaemia requiring intervention
14. Hypothermia (temperature < 35.6 °c)
15. Neonatal jaundice requiring phototherapy
16. Necrotising enterocolitis
17. Nasogastric feeding required
18. Umbilical artery and venous pH
19. Abnormal cerebral ultrasound
20. Fetal sex

Adherence Measures
Among the intervention group:
1. Valid PlGF test result obtained, measured using a point-of-care PlGF test
2. PlGF test result documented in patient notes

Among the control group:
3. PlGF test performed at any point

Health resource use outcomes for budget impact analysis:
1. Number of test cartridges used measured by the research team audit
2. Number of test cartridges wasted measured by the research team audit
3. Number of failed tests measured by the research team audit

Maternal:
1. Antenatal outpatient attendances
2. Formal ultrasound scans
3. Inpatient days
4. Intensive care unit days

Perinatal:
1. Total days in hospital
2. Total days in each level of care (intensive care, high dependency and special care unit days)

Completion date
30/06/2027

Eligibility

Key inclusion criteria
1. Hypertension or other clinical suspicion of preeclampsia [such as proteinuria, abnormal blood test results suggestive of preeclampsia, small for gestational age with suspicion of preeclampsia, symptoms of preeclampsia (including headache, visual disturbances, right upper quadrant pain)]
2. Between 20- and 36+6-weeks' gestation
3. Singleton pregnancy
4. Live pregnancy
5. Able to give informed written or thumbprint consent (or assent if aged less than 18 years with parental or guardian consent)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
Female

Key exclusion criteria
1. In active labour (cervix dilated more than 4cm)

Date of first enrolment
26/05/2025

Date of final enrolment
29/05/2026

Locations

Countries of recruitment
Brazil

India

Sierra Leone

Zambia

Study participating centre
Women and Newborn Hospital of University Teaching Hospitals
Nationalist Road
Lusaka
Zambia
50001

Study participating centre
Ndola Teaching Hospital
Broadway Road
Ndola
Zambia
10101

Study participating centre
Kitwe Teaching Hospital
Kuomboka
Kitwe
Zambia
6625+VHM

Study participating centre
Kabwe General Hospital
Kabwe
Zambia
HC8H+5QP

Study participating centre
Princess Christian Maternity Hospital
Fourah Bay Road
Freetown
Sierra Leone
FQRJ+2CP

Study participating centre
S M S Medical College and Hospital
Jawahar Lal Nehru Marg, Ashok Nagar

Jaipur
India
302001

Study participating centre
Postgraduate Institute of Medical Education & Research and Capital Hospital
Unit 6, Ganga Nagar
Bhubaneswar
India
751025

Study participating centre
BLDE (Deemed to be University), Shri B M Patil Medical College Hospital & Research Centre
B.M. Patil Rd, Smt, Bangaramma Sajjan Campus
Vijayapura
India
586103

Study participating centre
Karnataka Medical College and Research Institute
PB Rd, Vidya Nagar
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580022

Study participating centre
Jawaharlal Nehru Medical College
Old Pune Bangalore Road, Nehru Nagar
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590010

Study participating centre
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Setor de Grandes Áreas Norte 605 - Asa Norte
Brasília
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70840-901

Study participating centre
Hospital das Clínicas da Unicamp
R. Vital Brasil, 251 - Cidade Universitária
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Study participating centre
Hospital das Clínicas da UFMG
Av. Prof. Alfredo Balena, 110 - Santa Efigênia
Belo Horizonte
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30130-100

Study participating centre
Hospital das Clínicas da Faculdade de Medicina de Botucatu da Universidade Estadual Paulista
UNESP Campus de Botucatu Avenida Professor Mário Rubens Guimarães Montenegro, S/N - Jardim Sao Jose
Botucatu
Brazil
18618-970

Study participating centre
Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto
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Ribeirão Preto
Brazil
14015-010

Study participating centre
Hospital das Clínicas Universidade Federal de Pernambuco
Av. Prof. Moraes Rego, 1235 - Cidade Universitária
Recife
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50670-901

Sponsor information

Organisation

King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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 Louisa Samuels louisa.samuels@kcl.ac.uk.

Type of data that will be shared: quantitative.
When the data will become available and for how long: 25/05/2027
By what access criteria data will be shared including with whom: to be determined at a later date.
For what types of analyses, and by what mechanism: to be determined at a later date.
Whether consent from participants was obtained: Consent will be gained for the research team to use participants data for future research if ethical approval from a research committee is gained.
Comments on data anonymisation: Data would only be supplied in fully anonymised format.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes