ISRCTN12380898 https://doi.org/10.1186/ISRCTN12380898

Can lactate testing improve maternal sepsis identification? A multi-country, test accuracy study

Submission date
17/03/2022

Recruitment status
No longer recruiting

Registration date
21/03/2022

Overall study status
Completed

Last Edited
24/09/2024

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Maternal sepsis is a severe bacterial infection, usually of the uterus (womb), which can occur in pregnant women or more commonly, in the days following childbirth.
Maternal sepsis can develop in pregnant women and women who have recently experienced pregnancy and is a life-threatening condition that develops as a result of an infection which develops during pregnancy, childbirth, post-abortion, or the post-partum period. The results of the WHO Global Maternal Sepsis Study (GLOSS) suggest infection contributes to up to half of all maternal deaths and is also a major cause of maternal morbidity. Leaving many who survive sepsis with life-changing effects, such as post-traumatic stress disorder (PTSD), chronic pain and fatigue, and persistent problems or disability. Failure to rapidly recognise and treat maternal sepsis is a common factor identified in those women who die.

Research in high income countries has shown that groups of key treatments given together at the same time can help reduce poor outcomes and deaths from sepsis. These groups of treatments collectively referred to as care bundles and usually consist of small sets of evidence-based, interventions that together result in significantly improved outcomes compared to when they are implemented individually. Care bundles have been a cornerstone of sepsis improvement initiatives in high-income settings and shown to reduce mortality in adult, high income populations.

Measurement of blood lactate forms a key part of sepsis management and risk stratification in current international guidelines from both National Institute for Healthcare Excellence (NICE) in the United Kingdom (UK) and the Surviving Sepsis Campaign. However, these guidelines were developed for non-pregnant populations in high income countries. In the substantially different population of pregnant women, in low-resource settings, it is anticipated that the test may perform differently. Additionally, pregnancy itself induces profound cardiovascular, physical and immunological changes that affect baseline physiology and the response to infection. The infections in pregnancy causing sepsis are also different to those in a typical adult medical population, and the co-morbidities are also different.

We propose in this study to investigate if a lactate measurement has an incremental benefit over conventional maternal vital sign assessment in the diagnosis of sepsis and identification of women at risk of severe morbidity or mortality in low resource settings. We will determine the diagnostic and prognostic accuracy of venous lactate measurement in the maternity populations, in low resource settings, which is unknown. If lactate testing in this population then this has the potential to improve maternal sepsis outcomes.

Who can participate?
Women aged 16 years or above who are pregnant or within 6 weeks of the end of the pregnancy with a suspected or confirmed infection requiring in-patient care

What does the study involve?
Participants will provide two blood samples whilst they are hospital inpatients. Research Staff will visit women at their bedside to collect information until they are sent home

What are the possible benefits and risks of participating?
We hope that the results from the study will help women in the future when doctors are making decisions about treatment. All women who agree to participate in the study will have other bloods taken by their doctor to monitor their infection. These are done on day 0 and day 1 and may be of benefit as they are not always available as an option in Low-income settings. The results will be provided to staff to support the best treatment for participants. The only results not shared are the extra samples taken to measure Lactate. The risks to participants of providing two blood samples are very low, however, any blood samples taken can result in some localised bruising.

Where is the study run from?
Malawi Liverpool Wellcome (Malawi)

When is the study starting and how long is it expected to run for?
January 2021 to September 2025

Who is funding the study?
UKRI Global Maternal and Neonatal Health 2019 (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
UoL001655

Study information

Scientific Title
Using lactate testing to improve maternal sepsis identification: a multi-country test accuracy study: LACTate in mATernal sEpsis

Acronym
LACTATE

Study objectives
To determine the diagnostic accuracy of maternal venous lactate measurement in addition to maternal vital sign thresholds, in maternal sepsis in low-resource health facility settings in Malawi, Uganda and Pakistan

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 25/02/2022, Aga Khan University Ethics Review Committee, ref: 2022-7066-20701
2. Approved 10/03/2022, National Institutes of Health Health Research Institute National Bioethics Committee (NBC) (Health Research Institute, Shahrah-e-Jamhuriat, Off Constitution Avenue, Sector G-5/2, Islamabad, Pakistan; +92 (0)51 9224325, 9216793; nbcpakistan@nih.org.pk), ref: No.4-87/NBC-744/22/1647
3. Approved 26/04/2022, University of Liverpool Central University Research Ethics Committee D, ref: 10737
4. Approved 21/02/2023, Aga Khan University Ethics Review Committee, ref: 2023-7066-24108
5. Approved 21/03/2023, National Institutes of Health Health Research Institute National Bioethics Committee (NBC) (Health Research Institute, Shahrah-e-Jamhuriat, Off Constitution Avenue, Sector G-5/2, Islamabad, Pakistan; +92 (0)51 9224325, 9216793; nbcpakistan@nih.org.pk), ref: No.4-87/NBC-744/23/1478
6. Approved 16/03/2022, College of Medicine Research and Ethics Committee (COMREC) University of Malawi, ref: P.01/22/3553
7. Approved 15/11/2022, Mbale Regional Referral Hospital Research and Ethics Committee (MRRH-REC) (Ministry of Health Mbale Regional Hospital, PO Box 921, Mbale — Uganda; +256 (0) 39 3280584; +256 (0)41 4671162; mrrhrec@gmail.com), ref: BUFHTS-2022-23
8. Approved 03/11/2022, Busitema University Faculty of Health Sciences REC, ref: BUFHS-2022-23
9. Approved 12/12/2022, Uganda National Council for Science and Technology (UNCST), ref: HS2589ES
10. Approved 30/01/2023, University of Liverpool Central University Research Ethics Committee D, ref: 10737

Study design
Prospective multi-site phase III test accuracy study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Maternal sepsis

Interventions
Day 0: We will obtain consent from individuals who meet the inclusion criteria to participate. After which we will collect the participants' medical and obstetric history; details about the current or most recent pregnancy; Vital signs such as blood pressure, pulse, temperature, oxygen levels, urine output. We will collect one extra blood sample (ideally at the same time as

routine samples) approximately 2.5ml to test for lactate. The sample is sent to the Laboratory for processing and the results blinded to clinical staff.
Day 1: Approximately 24 hours later the second blood sample will be taken for lactate along with other routine bloods. We will also take some vital signs, collect information about the pregnancy including any delivery or birth outcomes and record the result of any other blood tests conducted by the clinical team. The second lactate sample will be sent to the laboratory for processing.
Day 2 to Day 14: We will collect vital signs and information about the pregnancy including any delivery or birth outcomes. We will also collect near miss and death details as they occur.
Study End: The study ends when the woman is discharged, dies, or on Day 14, no further follow up information is collected.

Intervention Type
Other

Primary outcome(s)
Maternal sepsis will be assessed using venous lactate measurement in addition to maternal vital sign thresholds at two time points following inclusion: Day 0 (blood sample 1) and Day 1 (blood sample 2) taken 22 -36 hours after sample 1.

Key secondary outcome(s))
1. Immediate diagnostic value of lactate testing by comparing the baseline index test with baseline reference standard. Maternal venous blood lactate will be measured at baseline using the blood sample collected (day 0) at the same timepoint that maternal sepsis will be assessed.
2. Short-term predictive value of lactate testing, by comparing the baseline index test with 24-hour reference standard, in those without sepsis at baseline. Maternal venous blood lactate will be measured at baseline (day 0 blood sample), and in those without sepsis at baseline the index test will be assessed against the reference standard at day 1.
3. Severe morbidity and mortality from infection. This will be assessed daily until day 14 or discharge or death if sooner: Day 0-14.
4. Pregnancy status (pregnant or post-delivery/post miscarriage/post-abortion) and country of recruitment

Completion date
30/09/2025

Eligibility

Key inclusion criteria
1. Be pregnant or within 6 weeks of the end of the pregnancy.
2. Women with a suspected or confirmed infection requiring in-patient care:
2.1. Any suspected or confirmed infection with or without organ-dysfunction.
2.2. Any clinical signs suggestive of infection (e.g., fever).
2.3. Request for any bodily fluid culture (blood, urine, cerebrospinal fluid, etc.) or swab specimens (nasopharyngeal, oropharyngeal, vaginal, endocervical) for the diagnosis of suspected infection (not routine sampling e.g., routine COVID-19 screening).
2.4. Non-prophylactic use of antibiotics or other antimicrobial drugs at admission or during hospital stay.
2.5. Any procedure for treatment of a suspected infection (e.g., wound exploration, evacuation of the uterus, laparotomy, etc.)
2.6. Any unexplained organ-dysfunction (i.e., organ dysfunction not attributable to an underlying

cause).
3. Estimated age ≥16 years.
4. Willing to provide a signed (and witnessed, if applicable) informed consent form.
5. Willing to be contacted, if necessary.
6. Willing to have additional blood samples taken.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Sex
Female

Total final enrolment
567

Key exclusion criteria
1. Women in active labour or within 2 hours of delivery are excluded as lactate is expected to be elevated by labour and childbirth.
2. Women with any non-severe, localised, or chronic infection (TB, HIV) or colonization (GBS)
3. Women undergoing only treatment with prophylactic antibiotics (for procedures, GBS)

Date of first enrolment
20/07/2022

Date of final enrolment
22/06/2023

Locations

Countries of recruitment
Malawi

Pakistan

Uganda

Study participating centre
Queen Elizabeth Hospital
Chipatala Avenue
Box 95

Blantyre
Malawi
-

Study participating centre
Mbale regional referral Hospital
Pallisa road
P.O Box 921
Mbale City
Uganda
-

Study participating centre
Liaquat University of Medical and Health Sciences (LUMHS)
Department Unit 2
Hyderbad
Pakistan
-

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
UKRI Global Maternal and Neonatal Health 2019

Results and Publications

Individual participant data (IPD) sharing plan

At the end of the study, after the primary results have been published, and the separate country teams have completed any desired secondary analysis of country specific data, the anonymised individual participant data (IPD) and associated documentation (e.g., protocol, statistical analysis plan, annotated blank CRF) will be prepared to be shared with external researchers. All requests for access to the IPD will be reviewed by an internal committee at the Liverpool Clinical Trials Center (LCTC) and discussed with the Chief Investigator in accordance with the LCTC policy on data sharing.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Statistical Analysis Plan	version 1.0	07/02/2023	10/03/2023	No	No
Statistical Analysis Plan	version 2.0	14/06/2023	04/09/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes