

Oral azithromycin use during childbirth to prevent severe maternal infection among Nigerian women giving birth vaginally

Submission date 22/06/2024	Recruitment status Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 03/07/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 02/08/2024	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Maternal sepsis is a severe infection that occurs during or after childbirth and is a significant cause of maternal deaths worldwide, particularly in Nigeria. This study aims to investigate whether giving a single 2 g dose of azithromycin, an antibiotic medication, to women during labour can reduce the risk of sepsis and related infections and its complications. This study will also evaluate how best to implement this intervention in the Nigerian healthcare system.

Who can participate?

The study will involve pregnant women who plan to give birth vaginally. There are no specific age restrictions mentioned, but all participants will be women in labour at the selected health facilities. Health workers involved in the implementation aspect of the study will also participate in study.

What does the study involve?

The study will be conducted in 60 sites in Nigeria. The health facilities will be randomly assigned to either the intervention or control group for both the clinical trial and implementation study. The study will compare two groups of participants:

For the clinical study,

Intervention group: Women will receive a single 2-g oral dose of azithromycin during labour.

Control group: Women will receive the usual care without azithromycin.

The study participants will be scheduled for follow-up visits at 3 days, 2 weeks, 4 weeks, and 6 weeks after childbirth to assess for any symptom or sign of maternal infection and/or sepsis.

The study will also collect data on the cost-effectiveness of the intervention.

For the implementation study,

Intervention group: Implementation strategies will be generated through Plan, Do, Study, Act (PDSA) cycles by the healthcare personnel (bottom-up approaches).

Control group: One-off training workshops and distribution of guidelines for administering azithromycin (top-down approach).

What are the possible benefits and risks of participating?

Participants in the intervention group may benefit from a reduced risk of sepsis and related complications. However, as with any antibiotic treatment, there may be potential side effects such as nausea, diarrhoea, or allergic reactions. The control group will continue to receive the standard care currently provided at the selected health facility.

Where is the study run from?

The College of Medicine of the University of Lagos (Nigeria)

When is the study starting and how long is it expected to run for?

September 2023 to August 2026

Who is funding the study?

Bill & Melinda Gates Foundation (USA)

Who is the main contact?

Prof. Bosede B. Afolabi, bbafolabi@unilag.edu.ng

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Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

INV-056490

Study information

Scientific Title

Azithromycin use in labour to prevent maternal sepsis among pregnant women undergoing vaginal birth in Nigeria (AZIN-V): a cluster-randomised hybrid type-2 effectiveness implementation trial

Acronym

AZIN-V

Study objectives

Azithromycin use in labour reduces maternal sepsis among pregnant women undergoing vaginal birth in Nigerian when compared to usual care.

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 30/11/2023, Lagos University Teaching Hospital Health Research Ethics Committee (Room 107, 1st Floor, LUTH Administrative Block, Lagos University Teaching Hospital (LUTH) Idi-Araba, Lagos, 100254, Nigeria; +234 (0)8023305199; oyofole@yahoo.com), ref: ADM/DSCST/HREC/APP/6325

Study design

Hybrid type-2 effectiveness-implementation national multicenter parallel-group open-label cluster randomized controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Prevention, Treatment, Safety, Efficacy

Participant information sheet

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

Health condition(s) or problem(s) studied

Prevention of maternal sepsis among pregnant women undergoing vaginal birth

Interventions

The AZIN-V study will be a cluster-randomized controlled trial with parallel assignment using a 1:1 allocation ratio for both the clinical trial and implementation study.

A total of 60 study sites will be selected and randomised based on a minimisation algorithm, with factors to be considered including state (geographical location of the study site), level of care provided at the selected health facility (primary, secondary, or tertiary), and historical data on the empirical use of postpartum antibiotics. Randomisation may occur in several waves, with at least 8 participating study sites per randomisation wave, based on the timing of signing the site-level agreement and commitment to stay in study group allocation. Study sites will be informed of their random allocation before any participant eligibility assessments. This randomisation approach ensures that prognostic factors are evenly distributed between the intervention and control groups, thereby enhancing the validity and reliability of the study results.

For the clinical trial, a total of 48 study sites will be randomly assigned in a 1:1 ratio, with 24 sites randomised to intrapartum administration of a single 2-g oral dose of azithromycin (intervention group), and 24 study sites randomised to usual care without azithromycin (control group). For the implementation study, a total of 12 study sites will be randomised using a 1:1 ratio, with 6 sites randomised to adaptive Plan, Do, Study, Act (PDSA) cycles (bottom-up approach), and 6 sites randomised to the usual top-down approach.

Clinical trial:

Participants in intervention sites: A single 2 g oral dose of azithromycin will be administered to all eligible women in active labour who give consent in the randomised intervention sites.

Participants in control sites: Eligible women recruited in control sites will receive the usual care such as handwashing, use of hand gloves, antisepsis and aseptic techniques. Azithromycin will not be provided at the control sites, and the sites will be strongly counselled to ensure that azithromycin is not made available for use.

All participants (intervention and control sites) will be followed up until discharge and surveillance maintained (in-person), with visits at 3 days, then 2, 4 and 6 weeks, after delivery.

Implementation study:

Interventional group:

The PDSA cycle is the implementation strategy to improve the adoption and implementation of azithromycin during vaginal birth in the intervention healthcare facilities. For the implementation study, the researchers will establish a multidisciplinary team comprising obstetricians and gynaecologists, nurses, midwives, pharmacists, administrators (including data managers or clerks), participant representatives, and any other stakeholders that may be conscripted as necessary at the health facility level to ensure the integration of equity-informed methodologies into all research strategies of this study, ownership, and sustainability. The team will oversee the generation and testing of strategies and record and review data to determine if strategies lead to improvement and if improvements are being sustained.

Control group:

In the control sites, the usual strategy of one-off training workshops and distributing guidelines for administering the new treatment will be instituted. Afterwards, the new intervention is introduced. This approach is usually top-down with minimal involvement of the SHP, who will deliver the intervention to the pregnant women.

Intervention Type

Drug

Pharmaceutical study type(s)

Not Applicable

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Azithromycin

Primary outcome measure

Primary outcome measures for the clinical trial:

1. Incidence of maternal sepsis is measured using clinical and laboratory parameters at four timepoints after childbirth: day 3, 2 weeks, 4 weeks, and 6 weeks post-delivery.
2. Cost-effectiveness is measured using Incremental Cost-Effectiveness Ratio (ICER) at baseline

and 6 weeks post-delivery: additional cost per unit of health gain with azithromycin compared to the usual care for individual participants as a component of the sepsis prevention protocol in healthcare facilities.

Primary outcome measure for the implementation study:

1. Fidelity is measured using health facility records and observation checklist during implementation and endline.

Secondary outcome measures

Secondary outcome measures for the clinical trial:

1. Incidence of culture-confirmed maternal sepsis is measured using microbiological positive culture results at timepoints within 6 weeks of childbirth
2. Number of new prescriptions of antibiotics for a specific maternal infection (including bacterial vaginosis, chorioamnionitis, endometritis, abdominal or pelvic abscess, mastitis or breast abscess, pneumonia, or pyelonephritis or acute cystitis) measured using medical records and questionnaire at 6 weeks of childbirth
3. Incidence of neonatal sepsis within 28 days of birth is measured using clinical and laboratory parameters at time points within 28 days of birth
4. Incidence of stillbirth measured using questionnaire at baseline
5. Incidence of neonatal death measured using questionnaire at day 29 of birth
6. Duration of initial hospital stay for neonate, defined as the time of delivery until the time of hospital discharge, measured using medical records and questionnaire at day 29 of birth
7. Incidence of neonatal readmission is measured using medical records and questionnaire at day 29 of birth
8. Duration of hospital stay for mother is measured using medical records and questionnaire at 6 weeks after childbirth
9. Incidence of maternal readmission is measured using medical records and questionnaire at 6 weeks after childbirth
10. Incidence of adverse drug events (fainting or dizziness, nausea, vomiting, diarrhoea, and dyspepsia) and other reported side effects measured using medical records and questionnaire at 2 weeks after childbirth
11. Incidence of secondary post-partum haemorrhage, defined as excessive bleeding requiring surgical intervention or blood transfusion from 24 hours after delivery till 6 weeks postpartum, measured using medical records and questionnaire at 6 weeks after childbirth

Secondary outcome measures for the implementation study:

1. Reach is measured using health facility records and observation checklist during implementation and endline
2. Adoption is measured using the Organizational Readiness for Implementing Change (ORIC) tool, key informant interviews (KIIs), and focused group discussions (FGDs) at baseline and endline
3. Feasibility is measured using in-depth interviews (IDIs) and focused group discussions (FGDs) at baseline and endline
4. Acceptability is measured using KIIs and FGDs at baseline and endline
5. Sustainability acceptability is measured using KIIs at endline

Overall study start date

30/09/2023

Completion date

30/08/2026

Eligibility

Key inclusion criteria

1. Pregnant women with singleton or multiple pregnancies of at least 24+0 weeks GA in labour including those in the first stage with cervical dilatation of ≥ 7 cm or in the second stage of labour
2. Admitted in labour to the participating health facilities for spontaneous or induced vaginal birth
3. Women presenting with stillbirth will also be eligible since they are at risk of postpartum sepsis

Participant type(s)

Patient

Age group

Mixed

Lower age limit

16 Years

Upper age limit

50 Years

Sex

Female

Target number of participants

5040

Key exclusion criteria

1. Gestational age <24 weeks at screening
2. Not admitted to the facility with a plan to deliver vaginally
3. In preterm contraction and no immediate plan for delivery
4. Has fever $>38^{\circ}\text{C}$ with no other explanation
5. Has evidence of macrolide antibiotic use in the previous three days
6. Known allergy to azithromycin or its excipients or other macrolides
7. Known to have an arrhythmia or a known history of cardiomyopathy
8. Planned caesarean delivery

Date of first enrolment

30/06/2024

Date of final enrolment

30/03/2026

Locations

Countries of recruitment

Nigeria

Study participating centre
College of Medicine University of Lagos
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Study participating centre
Centre for Clinical Trials, Research, and Implementation Science (CCTRIS)
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Funder(s)

Funder type
Charity

Funder Name

Bill and Melinda Gates Foundation

Alternative Name(s)

Bill & Melinda Gates Foundation, Gates Foundation, BMGF, B&MGF, GF

Funding Body Type

Government organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location

United States of America

Results and Publications

Publication and dissemination plan

Planned publication in peer-reviewed journal

Intention to publish date

30/08/2027

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available on request from Prof. Bosede B. Afolabi (bbafolabi@unilag.edu.ng)

IPD sharing plan summary

Available on request