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

Submission date
22/06/2024

Recruitment status
Recruiting

Registration date
03/07/2024

Overall study status
Ongoing

Last Edited
26/11/2025

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
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 the clinical trial, while the health facilities will be purposively selected, to account for health systems-based organisation factor, in the 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 in addition to the usual care provided in the health facility (such as handwashing, use of hand gloves, and aseptic techniques).
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: Deployment of Plan, Do, Study, Act (PDSA) cycles by the healthcare

personnel to generate context-specific implementation strategies (bottom-up approaches). Control group: The usual strategy of 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?
March 2025 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

Protocol serial number
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)
1. 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; oysofola@yahoo.com), ref: ADM/DSCST /HREC/APP/6325

2. approved 17/12/2024, National Health Research Ethics Committee (NHREC) (Department of Health Planning, Research & Statistics, Federal Ministry of Health, 11th Floor, Federal Secretariat Complex Phase III, Ahmadu Bello Way, Abuja, 900211, Nigeria; +234 09 523 8367; deskofficer@nhrec.net), ref: NHREC Protocol Number NHREC/01/01/2007- 10/09/2024

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

Primary study design
Interventional

Study type(s)
Efficacy, Prevention, Safety, Treatment

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 use 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

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Azithromycin

Primary outcome(s)
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.

Key secondary outcome(s))
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

Completion date
30/08/2026

Eligibility

Key inclusion criteria

Current key inclusion criteria as of 26/11/2025:

1. Pregnant women with a live or stillborn singleton or twin pregnancy of at least 24+0 weeks gestation in the active phase of the first stage of labour (cervical dilatation of 4cm or more) or early (non-pushing) phase of the second stage of labour.
2. Pregnant women admitted in labour to the selected health facilities following spontaneous or induced labour with a planned vaginal birth.

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Previous 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

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
16 years

Upper age limit
50 years

Sex
Female

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 26/11/2025:

1. Pregnant women of gestational age <24 weeks.
2. Pregnant women not admitted to the facility with a plan to deliver vaginally.
3. Pregnant women in threatened preterm labour and no immediate plan for birth.
4. Pregnant women with fever >38°C.
5. Pregnant women with history of use of a macrolide antibiotic in the previous three days.
6. Pregnant women with known allergy to azithromycin, its excipients, or other macrolide antibiotics.
7. Pregnant women with known history of cardiac disease (such as cardiac arrhythmia or

cardiomyopathy).
8. Pregnant women with planned caesarean birth.

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Previous 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°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
17/03/2025

Date of final enrolment
28/04/2026

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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Sponsor information

Organisation
University of Lagos

ROR
https://ror.org/05rk03822

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. 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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes