Treatment of Nigerian women with Iron by drip or iron tablets taken by mouth, for low blood level, hours after delivery

Submission date	Recruitment status	[X] Prospectively registered		
22/09/2022	No longer recruiting Overall study status	[X] Protocol		
Registration date		[X] Statistical analysis plan		
03/10/2022	Completed Condition category	Results		
Last Edited		Individual participant data		
04/04/2025	Pregnancy and Childbirth	[X] Record updated in last year		

Plain English summary of protocol

Background and study aims

Iron deficiency anaemia is a condition where a lack of iron in the body leads to fewer red blood cells. Anaemia is a public health burden with a high incidence in Africa. Iron deficiency anaemia is often treated with high-dose iron tablets taken by mouth if it is mild or moderate in severity, while blood transfusion is give in severe cases of anaemia. Some women do not tolerate the tablets well as they may develop side effects like constipation, stomach pain, nausea or vomiting. Others forget to use the oral iron tablets and hence the blood levels still remain low. There are iron preparations in existence that can be given in infusion (drip) form and have been found to be safe, and their use for the treatment of iron deficiency anaemia after delivery is currently being studied. The aim of this study is to compare the effectiveness of ferric carboxymaltose (FCM) given as an infusion through a vein and oral ferrous sulphate (FS) taken by mouth for treating iron-deficiency anaemia in women after delivery, and to compare the acceptability of these two forms of iron preparation in Nigerian women with moderate or severe iron deficiency anaemia after delivery.

Who can participate?

Women aged between 15 and 49 who are anaemic (haemoglobin concentration <10 g/dL), and within 6-48 hours of delivery.

What does the study involve?

Information will be collected about the participants' health and delivery, after which blood samples will be taken for some tests which include iron studies, serum phosphate, and complete blood count. Participants will be randomly allocated to one of two drug treatment arms (FCM or FS group). Women in the FCM arm will be given ferric carboxymaltose in 200 ml of normal saline infusion (drip) and this will be given through the woman's vein over 20 minutes. Women in the FS arm will be started on ferrous sulphate tablets which will be given as one 200 mg tablet (containing 65 mg of elemental iron) twice a day until 6 weeks after delivery. They will be checked on the postnatal wards until discharge from hospital, and then followed up at the hospital or home at 2 weeks, 6 weeks, 3 months, and 6 months after delivery. During the followups, questions about her health and that of their newborn will be asked, vital signs will be

checked, specimens will be collected for investigation, and they will be assessed for depression, fatigue, maternal-to-infant bonding and quality of life at various intervals.

What are the possible benefits and risks of participating?

The study drugs to be used have been found to be safe in women after delivery and while breastfeeding. They may reduce the need for blood transfusion in women with low blood levels. Although, it is still possible to suffer some side effects from any of the medications like nausea, vomiting, and diarrhoea to any of the two study drugs. Participants will be monitored closely to identify any side effects and will be treated at no cost. All the study drugs will be given free of charge and all the tests relating to this research will also be done for free. Participants will be given contacts of their caregivers and will be sent regular reminders about their appointments. The findings of this study will improve the knowledge about the treatment of anaemia in women after delivery. This is planned to lead to the possible change of existing treatments, with improvement in the well-being of women after delivery and their newborns.

Where is the study run from? University of Lagos (Nigeria)

When is the study starting and how long is it expected to run for? February 2022 to December 2024

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?

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Contact information

Type(s)

Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

2021-002867-23

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

01/2.0

Study information

Scientific Title

Intravenous ferric carboxymaltose versus oral ferrous sulphate for the treatment of moderate to severe postpartum anaemia in Nigerian women

Acronym

IVON-PP

Study objectives

Hypothesis 1: Intravenous ferric carboxymaltose is effective, tolerable and safe in treating iron deficiency anaemia in postpartum women compared with oral ferrous sulphate. Hypothesis 2: Intravenous ferric carboxymaltose is acceptable and feasible for use in treating postpartum iron deficiency anaemia in Nigeria compared with oral ferrous sulphate.

Ethics approval required

Old ethics approval format

Ethics approval(s)

- 1. Approved 01/03/2022, Lagos University Teaching Hospital Health Research and Ethics Committee (Room 107, 1st Floor, LUTH administrative block, Surulere, Lagos, Nigeria; +234 (0) 15850737, +234 (0) 15852187, +234(0) 15852209, +234(0) 15852158, +234(0) 15852111; luthethics@yahoo.com), ref: ADM/DCST/HREC/APP/4908
- 2. Approved 07/09/2022, National Health Research and Ethics Committee (11th Floor, Federal Secretariat Complex Phase III, Amadu Bello Way, Abuja, Nigeria; +234 (0)9 523-8367; chairman@nhrec.net), ref: NHREC/01/01/2007
- 3. Approved 08/09/2022, National Agency for Food Drug Administration and Control (NAFDAC) (Plot 1, Isolo Industrial Scheme, Oshodi-Apapa Expressway, Isolo, Lagos, Nigeria; +234 (0)9 523-8367; der.headquarters@nafdac.gov.ng), ref: NAFDAC/DER/VCTD/IVON-PP/2022/01
- 4. Approved 26/07/2022, Lagos State Ministry of Health (LSMH) (Block 4, The Secretariat, Alausa, Ikeja, P.M.B 21007, Ikeja; no telephone number provided; health.lagosstate.gov.ng) ref: LSMH /6649/I/120
- 5. Approved 30/06/2022, Rivers State Health Research Ethics Committee (26 Okoroma street, Port Harcourt, Nigeria; +234 (0)84230828; rshmbph@yahoo.com), ref: RSHMB/RSHREC/2022/021 6. Approved 08/07/2022, Kano State of Nigeria Ministry of Health, Health Research Ethics Committee (2nd & 3rd floor, Post Office road, Kano State, Nigeria; +234 (0)8039472476; moh. kano2019@gmail.com), ref: NHREC/17/03//2018
- 7. Approved 20/07/2022, University of Port Harcourt Teaching Hospital Research Ethics Committee (P.M.B 6176, Port Harcourt, Nigeria; no telephone number provided; no email provided), ref: UPTH/ADM/90/S.II/VOL.XI/1394)
- 8. Approved 04/08/2022, Kwara State Ministry of Health Ethical Research Committee (ERC) (P.M. B 1386, Fate road, Ilorin, Kwara state, Nigeria; no telephone number provided; no email provided) ref: ERC/MOH/2022/08/068

Study design

Multicenter interventional parallel open-label individually randomized controlled trial with an implementation study

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Iron deficiency anaemia in postpartum women

Interventions

Postpartum women during 6-48 hours of delivery will be screened. Eligible women on the ward will be individually randomized in a 1:1 ratio to receive either intravenous ferric carboxymaltose or oral iron. The baseline biodata of the participant will be entered into "REDCap" and "Sealed envelope" will generate the randomisation code for each participant. The drugs have been presupplied and stored according to the manufacturer's standard on site. Research staff depending on the arm the participant is randomised into will administer the drug. The intervention group will receive ferric carboxymaltose, a single dose of 20 mg/kg up to a maximum of 1000 mg. This dose will be administered as an infusion in 200 ml 0.9% sodium chloride and infused over a minimum of 15 - 20 minutes. Thereafter, they will be observed closely for a minimum of 30 minutes after infusion. The control group will receive oral ferrous sulphate 200 mg (65 mg

elemental iron), to be taken two times daily; 1 hour before meals or 2 hours after meals with a full glass of water till 6 weeks postpartum. All participants will be followed up subsequently till 6 months postpartum.

Intervention Type

Drug

Phase

Phase III

Drug/device/biological/vaccine name(s)

Intravenous ferric carboxymaltose, oral ferrous sulphate

Primary outcome(s)

Current primary outcome measure as of 31/07/2024:

Proportion of participants who are anemic at six weeks postpartum. An anemic state is defined as hemoglobin level of < 11.0 g/dL, measured using haemoglobin levels at 6weeks postpartum

Previous primary outcome measure:

Proportion of participants who are non-anaemic at six weeks postpartum. Non-anaemic state is defined as haemoglobin level ≥ 11.0g/dl, measured using haemoglobin levels at 6weeks postpartum

Key secondary outcome(s))

- 1. Proportion of women with postpartum depression, measured using the Edinburgh Postnatal Depression Scale at six weeks and six months postpartum.
- 2. Change in mean postpartum haemoglobin levels at two weeks and six weeks postpartum, measured using haemoglobin levels at two weeks and six weeks.
- 3. Achievement of a non-anaemic state (Hb≥11.0g/dl) at six months postpartum, measured using haemoglobin levels at six months.
- 4. Prevalence of moderate/severe anaemia at six weeks and six months postpartum, measured using haemoglobin levels at six weeks and six months. Moderate anaemia is defined as haemoglobin level 7.0-9.9 g/dl and severe anaemia as haemoglobin level
- 5. Change in mean serum ferritin, serum transferrin, serum iron and % transferrin saturation at two weeks and six weeks postpartum.
- 6. Need for blood transfusion after iron treatment during the first 6 weeks postpartum.
- 7. Prevalence of fatigue at six weeks and six months postpartum, measured using the Fatigue Severity Scale (revised FSS-5R version).
- 8. Proportion of women with secondary postpartum haemorrhage after treatment. This will be defined as excessive bleeding requiring surgical intervention or blood transfusion from 24 hours after delivery till 12 weeks postpartum.
- 9. Proportion of infants being breastfed (exclusive and any) at six weeks and six months postpartum.
- 10. Prevalence of impaired maternal-infant bonding at six weeks and six months postpartum measured using the Mother-to-Infant Bonding Scale at six weeks and six months postpartum.
- 11. Incidence confirmed or suspected maternal infection within 6 weeks of birth, as defined by a new prescription of antibiotics for presumed perineal wound-related infection, endometritis or

uterine infection, urinary tract infection or other systemic infection (clinical sepsis).

- 12. Incidence of hypophosphatemia at two weeks and six weeks postpartum. Measurement of vitamin D, alkaline phosphatase, P1NP, FGF23, Ca, PO4, which are biomarkers of phosphorus homeostasis and bone turnover at two weeks and six weeks postpartum. Hypophosphatemia is defined as serum phosphate level < 1 mg/dL (0.32 mmol/L).
- 13. Incidence of early neonatal death, defined as death of new-born from enrolment of the mother to before 7 completed days.
- 14. Incidence of late neonatal death, defined as death of the new-born from enrolment of the mother to before 28 completed days.
- 15. Incidence of infant death, defined as death from enrolment before the age of six months.
- 16. Incidence of post-natal maternal death from enrolment up to 6 weeks and at 6 months postpartum.
- 17. Incidence of adverse drug events.
- 18. Quality of life measured using the WHOQOL BREF at enrolment, 6 weeks, and 6 months postpartum.

Completion date

18/12/2024

Eligibility

Key inclusion criteria

- 1. Women aged between 15 and 49 years
- 2. Between 6 and 48 hours after delivery
- 3. Baseline (enrollment) moderate or severe anemia (Hb \leq 9.9g/dl), confirmed by Hemocue haemoglobinometer
- 4. Able and willing to give written informed consent

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

15 years

Upper age limit

49 years

Sex

Female

Total final enrolment

1400

Key exclusion criteria

- 1. Having received a blood transfusion, for any indication, within the last 3 months
- 2. Symptomatic anemia and a need for urgent correction
- 3. Known haemoglobinopathy such as sickle cell disease, HbCC disease
- 4. Clinically confirmed malabsorption syndrome
- 5. Known hypersensitivity or contraindication to any form of iron treatment, study drug or any of its excipients
- 6. Self-reported pre-existing maternal depression or other psychiatric illness and as evidenced by a YES response to any past history of psychiatry ward hospitalization, psychiatry medications, behavioral changes, or past consultation with psychiatry services
- 7. Severe allergic conditions such as severe asthma, eczema or other atopic condition
- 8. Known autoimmune conditions e.g., systemic lupus erythematosus, rheumatoid arthritis or known severe drug allergies.
- 9. Planning to move or reside outside the research area

Date of first enrolment 28/11/2022

Date of final enrolment 03/07/2024

Locations

Countries of recruitment Nigeria

Study participating centre Lagos University Teaching Hospital Idi-Araba Lagos Nigeria 100254

Study participating centre Mother and Child Centre

1st Avenue 1st Gate Festac Town Amuwo-Odofin Lagos Nigeria 102102

Study participating centre Mother and Child CentreGbaja St
Surulere

Lagos Nigeria 101283

Study participating centre General Hospital

14 College Road Iju Road Ifako-Ijaye Lagos Nigeria 101232

Study participating centre Ipaja Primary Health Centre

Alimosho L.G.A. Idimu Lagos Nigeria 100278

Study participating centre University of Port Harcourt Teaching Hospital (UPTH)

East-West Rd Port Harcourt Rivers Nigeria 500102

Study participating centre Okrika General Hospital

Abuloma Port Harcourt Rivers Nigeria 501101

Study participating centre Bori General Hospital

Hospital Road Bori Notem Rivers Nigeria 502101

Study participating centre Ahoada General Hospital

Omoku-Obrikom Rd Omoku Rivers Nigeria 510101

Study participating centre Model Primary Health Centre

Ede Okia Community Road Abuloma Port Harcourt Rivers Nigeria 500102

Study participating centre Aminu Kano Teaching Hospital

Zaria Road Kano Nigeria 700233

Study participating centre Waziri Gidado General Hospital

Rijiyar Lemo Kano, Nigeria 700252

Study participating centre Nuhu Bammali General Hospital

Emir Palace Rd Kofar Nassarawa Kano Nigeria 700224

Study participating centre Sheik Jeddah General Hospital

Murtala Mohammed Road Kano Nigeria 700271

Study participating centre Kabuga Primary Health Care Center

Gwarzo Road Kofar Dukayuwa Kano Nigeria 700282

Study participating centre University of Ilorin Teaching Hospital (UITH)

Old Jebba Road Oke Ose Ilorin Kwara Nigeria 241102

Study participating centre General Hospital Ilorin

5 Unity Rd Ilorin Kwara Nigeria 240101

Study participating centre Adewole Cottage Hospital

Adewole Road Along Yebmot Hotel Ilorin Kwara Nigeria 240101

Study participating centre Civil Service Hospital

Ilofa Road GRA Ilorin Kwara Nigeria 240101

Study participating centre Okelele Health Center

Abayawo Road Ilorin Kwara Nigeria 240101

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 researchers will deposit the research data in the Open Science Framework. The data will be deidentified to maintain participants' confidentiality. The data will be shared at the time of publication of the first manuscript. This will likely be done within 6 months of study completion. The duration of IPD sharing will be 2 years.

IPD sharing plan summary

Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.1		03/10/2022	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 1.3	26/09/2022	03/10/2022	No	No
Protocol file	version 1.4	30/11/2022	09/02/2023	No	No
Protocol file	version 2.0	18/01/2024	12/03/2024	No	No
Statistical Analysis Plan		13/03/2025	04/04/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes