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Enhancing nutrition and infection treatment during pregnancy for maternal and child health in Ethiopia (ENAT)

Submission date
17/07/2020

Recruitment status
No longer recruiting

Registration date
29/07/2020

Overall study status
Completed

Last Edited
25/06/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary as of 12/08/2021:
Background and study aims
Maternal undernutrition and infections in pregnancy are important causes of poor birth outcomes, including low birth weight (less than 2,500 grams at birth) and preterm birth (less than 37 weeks). In Ethiopia, one in three mothers are malnourished and infections in pregnancy are common, but screening and treatment for such conditions are limited. Each year, an estimated 635,000 (20%) babies are born with a low birth weight, and 320,000 (10%) are born prematurely.

The ENAT Study (Enhancing Nutrition and Antenatal infection Treatment for maternal and child health) aims to determine the effectiveness of a program to enhance the delivery of antenatal interventions that improve maternal nutritional status and management of infections in pregnancy. The ENAT study will assess the impact of this program on maternal and infant health outcomes in West Gojjam and South Gondar Zones of the Amhara regional state of Ethiopia.

Who can participate?
Pregnant women presenting for antenatal care in 12 health facilities who are <= 24 weeks pregnant.

What does the study involve?
All health centers undergo health systems strengthening for the provision of antenatal care (ANC). Study health centers and staff are provided training, equipment, and supplies for routine ANC services, including obstetric ultrasonography, blood pressure monitoring, anemia screening, and medication supply chain. Health centers have been randomly assigned either to routine care or to a strengthened nutrition activity model. The health centers assigned to the strengthened nutrition activity model are providing Ethiopian FMOH and WHO recommended nutritional interventions to pregnant women, including adequately iodized salt and a balanced energy protein supplement (local corn soya blend) for undernourished women. Pregnant women presenting for antenatal care at all health centers are randomly assigned to receive routine management of pregnancy infections or an enhanced program to test and treat for

genitourinary tract infections. Women, and their infants, are assessed at several time points during antenatal care, birth, and up to 1 month postpartum.

What are the possible benefits and risks of participating?
All women will have an ultrasound at enrollment that will date the pregnancy and help identify any major problems. Some women will receive iodized salt and a corn soya blend, which may improve the nutritional status of the mother and the growth and development of the baby. For women who receive infection screening and treatment, the treatment of infections in pregnancy may prevent maternal and newborn infections. Additionally, treatment of these infections may reduce risk of inflammation, which may help prevent the baby being born too small (low birth weight) or too soon (premature).

Where is the study run from?
This study is being run by the Addis Continental Institute of Public Health (Addis Ababa, Ethiopia) and the Brigham and Women's Hospital (Boston, MA, USA).

When is the study starting and how long is it expected to run for?
January 2018 to April 2022.

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

Who is the main contact?
In Ethiopia:
Professor Yemane Berhane: Addis Continental Institute of Public Health, yemaneberhane@addiscontinental.edu.et
In the US:
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Previous plain English summary:
Background and study aims
Maternal undernutrition and infections in pregnancy are important causes of poor birth outcomes, including low birth weight (less than 2,500 grams at birth) and preterm birth (less than 37 weeks). In Ethiopia, one in three mothers are malnourished and infections in pregnancy are common, but screening and treatment for such conditions are limited. Each year, an estimated 635,000 (20%) babies are born with a low birth weight, and 320,000 (10%) are born prematurely.

The ENAT Study (Enhancing Nutrition and Antenatal infection Treatment for maternal and child health) aims to determine the effectiveness of a program to enhance the delivery of antenatal interventions that improve maternal nutritional status and management of infections in pregnancy. The ENAT study will assess the impact of this program on maternal and infant health outcomes in West Gojjam and South Gondar Zones of the Amhara regional state of Ethiopia.

Who can participate?
Pregnant women presenting for antenatal care in 12 health facilities who are <= 24 weeks pregnant.

What does the study involve?
Health centers will be randomly assigned either to routine care or to a strengthened capacity care model. The health centers assigned to the strengthened capacity model will provide Ethiopian FMOH and WHO recommended nutritional interventions to pregnant women,

including adequately iodized salt and a balanced energy protein supplement (local corn soya blend) for undernourished women. Pregnant women presenting for antenatal care at all health centers will be randomly assigned to receive routine management of pregnancy infections or an enhanced program to test and treat for genitourinary tract infections. Women, and their infants, will be assessed at several time points during antenatal care, birth, and up to 6 months postpartum.

What are the possible benefits and risks of participating?
All women will have an ultrasound at enrollment that will date the pregnancy and help identify any major problems. Some women will receive iodized salt and a corn soya blend, which may improve the nutritional status of the mother and the growth and development of the baby. For women who receive infection screening and treatment, the treatment of infections in pregnancy may prevent maternal and newborn infections. Additionally, treatment of these infections may reduce risk of inflammation, which may help prevent the baby being born too small (low birth weight) or too soon (premature).

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When is the study starting and how long is it expected to run for?
January 2018 to June 2022.

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

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Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
2018P002479

Study information

Scientific Title
Effect of antentatal interventions to improve maternal nutritional status and infection control on birth outcomes and infant growth in rural Ethiopia

Acronym
ENAT

Study objectives
1. Increasing coverage of a package of WHO-recommended interventions to enhance antenatal screening and treatment of genitourinary tract infections during pregnancy (urinary tract infections/asymptomatic bacteriuria, sexually/reproductive transmitted infections) will increase birth weight by at least 58 grams and birth length by at least 3.0 mm, compared to newborns of pregnant women receiving routine care
2. Increasing coverage of a package of WHO-recommended interventions to enhance maternal nutritional status (iron-folate in pregnancy/lactation, use of adequately iodized salt, and balanced energy protein supplement to women with MUAC <23 cm) will increase birth weight by at least 80.3 gm and birth length by 7.8 mm
3. Increasing coverage of BOTH packages of interventions to enhance maternal nutrition AND antenatal infection management will increase birth weight by at least 78.9 grams and birth length by at least 4.2 mm, compared to newborns of women receiving routine care (neither of these packages).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 04/03/2019, Partners Human Research Committee/IRB (Partners Healthcare, 399 Revolution Drive, Suite # 710, Somerville MA, 02145, USA; +1-857-282-1900; no email provided), ref: none provided
2. Approved 18/02/2019, Addis Continental Institute of Public Health (ACIPH) IRB (ACIPH Head Office, Ayat Zone 8, Addis Ababa, Ethiopia; +251 116 390 039; aciph@addiscontinental.edu.et), ref: none provided

Study design
Open-label pragmatic comparative study cluster-randomized and individually randomized

Primary study design
Interventional

Secondary study design
Pragmatic comparative effectiveness study

Study setting(s)
GP practice

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied
Low Birthweight; Preterm Birth; Maternal Malnutrition, Affecting Fetus; Sexually Transmitted Diseases; Urinary Tract Infections; Pregnancy and Infectious Disease

Interventions
Current interventions as of 12/08/2021:
RANDOMIZATION
After a participant has consented, a study nurse will open a sequential, numbered sealed opaque envelope containing the allocation, and the participant will be assigned to that study arm.

STUDY ARMS
Arm 1: Enhanced Nutrition Package (ENP) health center, Enhanced Infection Management Package (EIMP) participant.
ENP: The health centers are strengthened to provide WHO/FMOH-recommended nutrition interventions in pregnancy. Pregnant women receive a supply of adequately iodized salt for household use and iron-folate tablets from enrollment to 6 months postpartum. Women with undernutrition (mid-upper arm circumference <23 cm), also receive a daily balanced energy protein supplement (SuperCereal, local corn soya blend, Faffa Food Products).
EIMP: At the study enrollment visit, pregnant women receive screening for bacteriuria with urine culture and antimicrobial susceptibility testing and presumptive deworming with mebendazole 500mg. From August 3, 2020, to April 1, 2021, women also received screening for chlamydia and gonorrhea (Cepheid GeneXpert), and symptomatic women were also tested for bacterial vaginosis and trichomonas. For women with chlamydia or gonorrhea, the participant (and partner) was treated per FMOH guidelines with recommended antibiotics. STI/RTI screening was discontinued on April 1, 2021, due to supply shortage and the low prevalence of STI. At ANC follow-up visits, women with identified urinary tract infection or asymptomatic bacteriuria were treated with antibiotics based on antimicrobial susceptibility patterns. Test of cure samples were obtained, and persistent infection was retreated.
In the 3rd trimester, a test of cure stool specimen is obtained to screen for persistent ova and parasites. If positive, women are provided treatment per MOH guidelines.

Arm 2: ENP health center, standard care infection management participant.
ENP: The health centers are strengthened to provide WHO/FMOH-recommended nutrition interventions in pregnancy. Pregnant women receive a supply of adequately iodized salt for household use and iron-folate tablets from enrollment to 6 months postpartum. Women with undernutrition (mid-upper arm circumference <23 cm), also receive a daily balanced energy protein supplement (SuperCereal, local corn soya blend, Faffa Food Products).
Standard infection care: Maternal genitourinary tract infections is managed as per standard FMOH health center guidelines that utilize a syndromic management approach.

Arm 3: Standard nutrition care health center, EIMP participant.
Standard nutrition care: Maternal nutrition is managed as per standard FMOH health center guidelines.
EIMP: At the study enrollment visit, pregnant women receive screening for bacteriuria with urine

culture and antimicrobial susceptibility testing and presumptive deworming with mebendazole 500mg. From August 3, 2020, to April 1, 2021, women also received screening for chlamydia and gonorrhea (Cepheid GeneXpert), and symptomatic women were also tested for bacterial vaginosis and trichomonas. For women with chlamydia or gonorrhea, the participant (and partner) was treated per FMOH guidelines with recommended antibiotics. STI/RTI screening was discontinued on April 1, 2021, due to supply shortage and the low prevalence of STI. At ANC follow-up visits, women with identified urinary tract infection or asymptomatic bacteriuria were treated with antibiotics based on antimicrobial susceptibility patterns. Test of cure samples were obtained, and persistent infection was retreated.
In the 3rd trimester, a test of cure stool specimen is obtained to screen for persistent ova and parasites. If positive, women are provided treatment per MOH guidelines.

Arm 4: Standard of care nutrition and infection management.Pregnant women will receive routine strengthened antenatal care services at the health center per Ethiopian Federal Ministry of Health (FMoH) guidelines. Maternal genitourinary tract infections will be managed as per standard FMOH health center guidelines that utilize a syndromic management approach.

FOLLOW UP:
All pregnant women and infants will be followed up until 1 month post-partum in all four study arms.

Previous interventions:
RANDOMIZATION
After a participant has consented, a study nurse will open a sequential, numbered sealed opaque envelope containing the allocation, and the participant will be assigned to that study arm.

STUDY ARMS
Arm 1: Enhanced Nutrition Package (ENP) health center, Enhanced Infection Management Package (EIMP) participant.
The health center will be strengthened to provide WHO/FMOH-recommended nutrition interventions in pregnancy. Pregnant women will receive a supply of adequately iodized salt for household use and iron-folate tablets from enrollment to 6 months postpartum. Women with undernutrition (mid-upper arm circumference <23 cm), will also receive a daily balanced energy protein supplement (SuperCereal, local corn soya blend, Faffa Food Products).
At the study enrollment visit, pregnant women will receive screening for bacteriuria with urine culture, and antimicrobial susceptibility testing; screening for chlamydia and gonorrhea (Cepheid GeneXpert); and presumptive deworming with mebendazole 500mg. Symptomatic women will also be tested for bacterial vaginosis and trichomonas.

At a follow-up visit, women with identified urinary tract infection or asymptomatic bacteriuria will be treated with antibiotics based on antimicrobial susceptibility patterns. For women with chlamydia or gonorrhea, the participant (and partner) will be treated per FMOH guidelines with recommended antibiotics. Test of cure samples will be obtained, and persistent infection will be retreated. A second deworming dose will be provided in the 3rd trimester ANC visit.

Arm 2: ENP health center, standard care infection management participant.
The health center will be strengthened to provide WHO/FMOH-recommended nutrition interventions in pregnancy. Pregnant women will receive a supply of adequately iodized salt for household use and iron-folate tablets from enrollment to 6 months postpartum. Women with undernutrition (mid-upper arm circumference <23 cm), will also receive a daily balanced energy

protein supplement (SuperCereal, local corn soya blend, Faffa Food Products).
Maternal genitourinary tract infections will be managed as per standard FMOH health center guidelines that utilize a syndromic management approach.

Arm 3: Standard nutrition care health center, EIMP participant.
At the study enrollment visit, pregnant women will receive screening for bacteriuria with urine culture, and antimicrobial susceptibility testing; screening for chlamydia and gonorrhea (Cepheid GeneXpert); and presumptive deworming with mebendazole 500mg. Symptomatic women will also be tested for bacterial vaginosis and trichomonas.

At a follow-up visit, women with identified urinary tract infection or asymptomatic bacteriuria will be treated with antibiotics based on antimicrobial susceptibility patterns. For women with chlamydia or gonorrhea, the participant (and partner) will be treated per FMOH guidelines with recommended antibiotics. Test of cure samples will be obtained, and persistent infection will be retreated. A second deworming dose will be provided in the 3rd trimester ANC visit.

Arm 4: Standard of care nutrition and infection management.
Pregnant women will receive routine antenatal care services at the health center per Ethiopian Federal Ministry of Health (FMoH) guidelines. Maternal genitourinary tract infections will be managed as per standard FMOH health center guidelines that utilize a syndromic management approach.

FOLLOW UP:
All pregnant women and infants will be followed up until 6 months post-partum in all four study arms.

Intervention Type
Mixed

Primary outcome measure
1. Birth weight: Mean infant weight (g) among live born infants measured <72 hour of delivery
2. Birth length: Mean infant length (cm) among live born infants measured <72 hours of delivery

Secondary outcome measures
1. Gestational age: Mean gestational age, measured using ultrasound, at delivery
2. Preterm birth: Proportion of pregnancies resulting in spontaneous birth <37 weeks' gestation among all births, measured using birth assessment, at birth
3. Small-for-gestational age (SGA): Proportions of newborns born SGA (<10% birthweight for gestational age and sex) among live born infants whose birthweight if measured within 72 hours of delivery, measured using digital infant scales, at birth
4. Low birthweight: Proportion of newborns born with weight <2500 g among liveborn infants whose weight is measured within 72 hours of delivery, measured using digital infant scales, at birth
5. Length-for-age: Mean Length-for-age Z scores at birth and 6 months of age among live born infants based on the WHO growth reference standards, measured using infant length boards, at birth
6. Weight-for-age: Mean Weight-for-age Z scores at birth and 6 months of age among live born infants based on the WHO growth reference standards, measured using digital infant scales, at birth
7. Rate of weight gain in pregnancy: Maternal weight gain (kg) per week gestation in the 2nd and 3rd trimester, measured using digital maternal scales, from date of first 2nd trimester antenatal

care (ANC) visit until date of last ANC visit before birth, assessed up to 6 months
8. Maternal anemia: Mean hemoglobin concentration, using Mission Hb or similar hemoglobin devices, at the third trimester antenatal care visit (28-40 weeks' gestation)
9. Stillbirth: Rate of stillbirths per 1000 births, measured using maternal assessment, throughout the study period
10. UTI: Maternal clinically diagnosed urinary tract infection (cystitis, pyelonephritis) reported in medical records in 3rd trimester
11. Maternal endometritis or puerperal sepsis measured by clinical diagnosis in medical records at or within 42 days after birth

Overall study start date
01/01/2018

Completion date
07/06/2022

Eligibility

Key inclusion criteria
1. Pregnant women < = 24 weeks gestation with a viable pregnancy based on a best clinical algorithm (LMP and/or symphysis fundal height)

Participant type(s)
Healthy volunteer

Age group
All

Sex
Female

Target number of participants
3,600 participants in 12 clusters (health centers) across 4 study arms (300 per health center)

Total final enrolment
2403

Key exclusion criteria
1. Pregnant women presenting with non-viable fetus
2. Women who do not intend to deliver in the study catchment area
3. Women who refuse to provide consent

Date of first enrolment
01/08/2020

Date of final enrolment
01/12/2021

Locations

Countries of recruitment
Ethiopia

Study participating centre
Addis Continental Institute of Public Health
Ayat Zone 8
Addis Ababa
Ethiopia
-

Sponsor information

Organisation
Brigham and Women's Hospital

Sponsor details
75 Francis St.
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+1-617-732-5500
bwhmediarelations@partners.org

Sponsor type
Research organisation

Website
http://www.brighamandwomens.org/

ROR
https://ror.org/04b6nzv94

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
Study findings will be disseminated to stakeholders and publications planned for peer-reviewed journals.

Intention to publish date
01/06/2023

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	version 3	13/01/2022	15/08/2022	Yes	No
Statistical Analysis Plan		01/02/2023	06/12/2023	No	No
Protocol article		28/04/2025	29/04/2025	Yes	No
Results article		18/06/2025	25/06/2025	Yes	No