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A randomised controlled trial testing the effect of counselling via Zoom upon intake of iron and folic acid supplements, diets, and antenatal care in pregnancy in the rural plains of Nepal

Submission date
12/01/2022

Recruitment status
No longer recruiting

Registration date
13/01/2022

Overall study status
Completed

Last Edited
22/11/2024

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims
Anaemia is a deficiency in the number or quality of red blood cells in your body. Red blood cells carry oxygen around your body using a particular protein called haemoglobin. Anaemia means that either the level of red blood cells or the level of haemoglobin is lower than normal. Anaemia in pregnancy is associated with low birth weight and maternal mortality, with 20% of maternal deaths directly related to anaemia. Over half of the world's maternal deaths caused by severe anaemia occur in South Asia. Despite the provision of routine supplementation with iron and folic acid (IFA) as per the government's protocol from 20 weeks of pregnancy in Nepal, uptake remains suboptimal and anaemia levels in pregnancy remain high. If compliance with daily IFA consumption could be improved anaemia levels in pregnant women could improve. The Virtual Antenatal Intervention for improved Diet and iron intake (VALID) trial aims to improve consumption of iron and folic acid (IFA) supplements and improve dietary intake to prevent and treat iron-deficiency anaemia in pregnancy.

Who can participate?
Any pregnant woman or girl aged 13 to 49 years, who is able to respond to questions and who lives permanently in one of the 54 selected population areas in Kapilbastu district can participate. If a woman has missed one or more periods and is up to 28 weeks since her last menstrual period she can enrol in the trial.

What does the study involve?
For any pregnant woman who agrees, the Female Community Health Volunteer for that village will link those women with the trial staff (data collectors) who confirm their eligibility, take consents (by signing or thumb-printing a consent form) and provide a unique identification number.
The data collectors will collect pregnant women's information on tablets using an electronic data collection system. Data collectors will visit the pregnant women twice to collect information, once at enrolment up to 28 weeks' gestation and again after 4 to 6 weeks to collect

primary outcome data. They will record personal details such as age, education, household details, medical and obstetric history as well as many details of the pregnancy.

Intervention: For pregnant women who are allocated to the intervention, a female HERD staff who is a qualified nurse (a 'nutrition assistant') will provide two virtual counselling sessions via Zoom link using a tablet, first shortly after enrolment (between 12 and 28 weeks of pregnancy) and next at least 2 weeks after the first session (at 14 to 32 weeks). At each session, the nutrition assistant discusses with the pregnant woman and her family members about her diet and health in pregnancy using a problem-solving approach. The family come up with an agreed action plan to improve the nutrition and health of the pregnant woman. She tells the woman the importance of antenatal care and consumption of iron and folic acid (IFA) supplements and an iron-rich diet for preventing or treating anaemia in pregnancy.

What are the possible benefits and risks of participating?
Benefits: All women in intervention and control arms will receive phone credit at the end of their participation in the study. In the intervention arm, pregnant women and their family members who attend the virtual counselling session will learn about nutrition in pregnancy and how to solve the problem of anaemia. For women who are identified early in pregnancy, the intervention may help them to plan their pregnancies, seek timely and appropriate health care and eat nutritious food required for the proper growth of the baby.
Risks: We do not think that any harm will come to participants from taking part, but it is possible that women might find sharing information about their periods or pregnancy uncomfortable or upsetting. They do not have to continue to take part if they don’t feel like it and can talk to someone working on the study whenever needed.

There is a risk that COVID-19 could be carried into participants households by project staff when they go for data collection. In order to mitigate this risk project staff will screen for covid symptoms before visiting pregnant women’s households. To prevent the spread of COVID-19 participants the data collectors will wear masks at all times during interactions, will wash hands with soap and water or use sanitiser before and at the end of interactions. They will offer the pregnant woman a mask and request her to wear it. If community infection rates become very high, data collection will also be conducted virtually depending on government guidelines.

Where is the study run from?
The study is being run by three organisations that are working together. These include a research organization based in Kathmandu called HERD International and two research organisations based in the United Kingdom called University College London (UCL) and London School of Hygiene and Tropical Medicine (LSHTM).
The location of the study is in Kapilbastu district Province 5, in central Nepal, near the border with Uttar Pradesh state of India. The selected study areas are in the southern part of the district below the Mahendra Highway, in rural areas, without any big markets, where most of the people are Madhesi ethnicity. The study concentrates on the Madhesi ethnic group because anaemia rates are higher in this population.

When is the study starting and how long is it expected to run for?
September 2021 to December 2022.

Who is funding the study?
The study is funded by UK Medical Research Council (MRC)/ Newton Fund (MR/R020485/1).

Who is the main contact?
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Virtual Antenatal Intervention for improved Diet and Iron intake (VALID): A randomized controlled trial in Kapilbastu district, Nepal

Acronym
VALID

Study objectives
An antenatal virtual counselling intervention delivered twice (in mid-pregnancy) imparting counselling on diet, IFA supplements, and ANC will increase compliance to IFA tablets compared with women who have access to usual government health services.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/11/2021, Nepal Health Research Council Ethics Committee (NHRC, Ramshah Path, PO Box: 7626, Kathmandu, Nepal; +977 1 4254220; nhrc@nhrc.gov.np), reference no: 570/2021

Study design
Non-blinded parallel-group two-arm randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of iron deficiency anaemia during pregnancy

Interventions

Tailored virtual counselling will be conducted with pregnant women and their families by nutrition assistants (NAs) using zoom (or similar) video conferencing on tablets containing SIM cards that have prepaid mobile data packages. NAs are trained auxiliary nurse midwives (ANMs) employed by HERD International to provide counselling services to pregnant women. Using stories and inductive questioning to trigger dialogue and reflection, the NAs will encourage pregnant women and their families to think critically about the causes of anaemia in pregnancy in their households and community.
Two virtual counselling sessions will be conducted with each pregnant woman, first at 12 to 28 weeks' gestation (shortly after enrolment) and second at a minimum of 2 weeks after the first session (at around 14 to 32 weeks' gestation). In each session, the NAs engage pregnant women and their families in a cycle of action and reflection in response to the stories and inductive questioning. Then, common issues and examples of actions that could be made will be discussed. These may include improving pregnant women's uptake of iron and folic acid supplementation (IFA), deworming tablets, antenatal care, and improving diet, especially intake of iron-rich foods and actions to enhance absorption of iron. Then, with the NA's support, the pregnant women and families will make specific action plans to address the issues that are relevant for their family drawing upon examples provided by the NA where needed. In the second visit, these action plans will be reviewed and further discussed in order to support pregnant women and their families to address the issues. Then a second action plan will be drawn up for the remainder of the pregnancy. NAs will encourage pregnant women and their families by praising them for any progress made. Where action plans have not been followed the NA will discuss with the family the barriers to following the action plan and what steps can be taken going forwards.

The method of allocating participants to study arms is as follows:
Sequence generation: A stratified block randomization process will be used to allocate the 300 pregnant women (PW) enrolled into the intervention or the control arms of the trial. To balance the trial arms by two strong pre-identified confounders, parity and Iron and folic acid (IFA) consumption status, randomization will be done within each of the four different strata. The four strata will be: (IFA yes/1st pregnancy); (IFA Yes/ other than 1st pregnancy); (IFA no/1st pregnancy) and (IFA no/ other than 1st pregnancy).
a. For each of the four strata, separate allocation sequences will be prepared.
b. To make the sequence unpredictable, random permutation of the allocations within blocks of sizes 8, 6 and 4 will be performed using "blockrand" package in R programming software. For e.g. for the first 8 participants the sequence may look like this ICCICIIC, where I=intervention C=control.

Allocation concealment: Within each stratum, the blockrand function will vary the number of blocks of sizes 8, 6 and 4, which will add up to 300 randomized allocations to either Intervention or Control. Based on the list of randomized allocations, Sequentially Numbered Opaque Sealed Envelopes (SNOSE) will be prepared, altogether 1,200 envelopes. The number of envelopes is higher than the total sample size because the number of PW that needs to be enrolled from each stratum is not known beforehand. This ensures the enrolment team won't run out of envelopes during the trial.

Implementation:
a. The HERD Data Management Officer (DMO) generates the list of randomized allocations.
b. The HERD Project Coordinator (PC) with help from Knowledge Management Officer (KMO) puts randomly generated sequence numbers and the allocations "Intervention" and "Control" in an opaque numbered envelope. The sequence number indicates the order in which allocations are taken across all blocks for the stratum, running from 1 to 300, e.g. S1001 through S1300 for the 300 allocations in strata 1, S2001 to S2300 for strata 2 and so on). The boxes for each strata

will be labelled in the following way for convenience:
Box A = IFA yes/1st pregnancy
Box B = IFA Yes/ other than 1st pregnancy
Box C = IFA no/1st pregnancy
Box C =IFA no/ other than 1st pregnancy
c. After completing the SNOSE preparation for all strata, the four boxes are closed and sealed so that envelopes do not move or reshuffle when transporting the box.
d. An excel sheet is used to keep a record of the strata (i.e., the box), envelope number and the random allocation assigned to that envelope. This is kept secure and not shared with the trial implementation team.
e. After transporting the envelopes from Kathmandu to Kapilvastu, the Project Manager (PM) keeps them in a locked cupboard. Only the PM and DMO who are not involved in recruiting and enrolling participants will have access to these boxes.

Random assignment during enrolment:
After collecting baseline data from each pregnant woman and taking her consent, the data assistant (DA) will call Kapilvastu office to give the PW's strata (parity and IFA consumption). One of the allocated staff will take out one sealed envelope from the front of box that matches the strata combination, open the envelope and reveal the allocation sequence to the data assistant. Based on this sequence, the DA will inform and assign the PW to the appropriate trial arm. Records of the envelope number, stratum and sequence number will be recorded by the data staff in the office and by the data collector using the CommCare form on their data collection tablet. The DA will inform the PW about her arm allocation and the envelope sequence number will also serve as the unique identifier in the CommCare database for each PW enrolled in the trial.

Intervention Type
Behavioural

Primary outcome(s)
The proportion of pregnant women consuming IFA on at least 80% of the days (i.e. on 12 or more days out of 14 days recalled) at endline interview which will be at least two weeks after the second virtual counselling session (17-36 weeks' gestation).

Key secondary outcome(s))
All secondary outcomes will be recalled by trial participants during face-to-face or telephone interviews and recorded in electronic questionnaires collected at endline:
1. Count of Antenatal (ANC) visits between enrolment and endline interview
2. 24 hour Women's Diet Diversity Score collected using the women's dietary diversity score updated 2021 tool collected at endline (mean per arm)
3. Consumption of intervention-promoted foods (green leafy veg with lemon, organ meat or and meat/fish) in the 24 hours preceding the endline interview.
4. Practicing ways to enhance bioavailability in the 7 days preceding the at endline questionnaire. This will be scored as 1 if the pregnant woman reports having done any of the following in the previous 7 days and will otherwise be scored as 0:
- using lemon or other vitamin C-rich foods with meals,
- eating sprouted grains or pulses,
- avoiding tea/coffee 1 hr either side of meals,
- spreading meat-eating over two eating occasions rather than one.
5. Knowledge of iron-rich foods: a count of the number of iron-rich food groups correctly recalled at the endline interview.

Exploratory outcomes on the impact pathway:
1. Timing of first ANC (in completed months' gestation) – collected at baseline if ANC has been initiated, otherwise collected at endline.
2. Timing of first IFA (in completed weeks' gestation) – collected at baseline if ANC has been initiated, otherwise collected at endline.
3. Quality of Antenatal care received between baseline and endline. This will comprise a score constructed from recall of advice received, measurement of height/ weight/ blood pressure/ fetal heartbeat, tetanus vaccination, deworming tablet receipt/intake, blood and urine tests, checking position of the baby). Data will be collected at endline.
4. Understanding of why blood tests are taken at antenatal check-ups. Measured as the proportion of women who had a blood test at their ANC visits who could correctly explain one or more reason for having a blood test taken at the endline questionnaire.

Process evaluation outcomes:
1. Acceptability and Appropriateness measured using:
1.1 Qualitative and quantitative interviews with trial participants in the intervention arm after the intervention is complete
1.2. Satisfaction (content, comfort, delivery, and credibility) with the antenatal virtual counselling Participation and engagement of the of the pregnant women (PW) and family members
1.3. Focus group discussions with project staff, nutrition assistants (NAs) and data assistants (DAs), 2 times during trial implementation
1.4. Satisfaction with the trainings/ orientation/ technical and monitoring support
2. Effectiveness measured using quantitative interview at endline:
2.1. Proportion of PW taking the required IFA doses in the 14 days preceding the endline interview
2.2. Proportion of PW reporting eating diverse diet (diet diversity score) in the 24 hours preceding the endline
2.3. Proportion of PW completing the required ANC visit for their gestation month
2.4. Proportion of PW whose family member attended one or both of the virtual counselling sessions
3. Feasibility
3.1. Quantitative data extracted from trial implementation (monitoring) data filled by NAs
3.1.1 Proportion of scheduled virtual counselling sessions not completed (cancelled/ not able to connect / not finished)
3.1.2 Number of attempts made to contact participant when intervention not possible
3.1.3 Proportion of PW completing 2 virtual counselling sessions
3.1.4 Reasons for cancellation of scheduled virtual counselling session (network, electricity, not charged, credit, difficulty in using tablets, not picking the phone)
3.2. Quantitative Interview at baseline
3.2.1 Proportion of women approached with direct access to a phone/device that DA can contact them on
3.3. Qualitative interviews with trial participants after intervention is complete
3.3.1 Factors affecting participation in the intervention
3.4. Focus group discussions with NAs (2 times during trial implementation) and monthly review meeting with intervention team
3.4.1 Factors (barrier and facilitators) affecting the delivery of the intervention and corrective actions taken
4. Fidelity measured using quantitative and qualitative observation of the virtual sessions:
4.1. Proportion of NAs adhering to the virtual counselling manual guidance
4.2. Proportion of NA's delivering the session competently

5. Implementation cost measured using quantitative data extracted from actual expenditure:
5.1. Total intervention cost from program provider perspective (including start up and design /adaptation, and implementation costs)
5.2. Total intervention costs by line items/inputs (e.g. human resource, materials, capital, admin /joint) and activities (e.g. trainings, preparation/planning, delivering virtual counselling)
5.3. Cost of intervention per PW
6. Coverage (reach and equity) measured using quantitative Interview with trial Participants at baseline/enrolment:
6.1. Proportion of PW enrolled out of those approached
6.2. Proportion of PW enrolled from different ethnic and socioeconomic groups out of those approached
6.3. Proportion primiparous women enrolled of those approached
6.4. Proportion of young (<18 years of age) enrolled of those approached
7. Sustainability:
7.1. Quantitative Interview with trial Participants at baseline/enrolment
7.1.1 Availability of devices among pregnant women
7.2. Quantitative post session forms filled by the attendees in the dissemination session
7.2.1 Proportion of organizations (government and non-governmental) attending the dissemination workshop willing to implement the intervention

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Pregnant girl/woman aged between 13 to 49 years
2. Able to respond to questions
3. Resident of study cluster (whether at husband's or parental home)
4. Less than or equal to 28 weeks' gestation estimated from recall of last menstrual period (or expected date of delivery given by a health worker)
5. Plans not to leave the country during the follow-up period 5 weeks since enrolment
6. Does not have another pregnant woman in her household already enrolled in the trial
7. Consents to participate in the trial

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
13 years

Upper age limit
49 years

Sex

Female

Total final enrolment
319

Key exclusion criteria
1. Aged <=12 years or >=50 years
2. Not-consenting to participate in the trial
3. Unable to respond to questions
4. ≥28 weeks' gestation at enrolment as estimated from LMP (or expected date of delivery given by a health worker)
5. Planning to leave the country during follow up period.
6. Has another pregnant woman in her household already enrolled in the trial

Date of first enrolment
14/01/2022

Date of final enrolment
31/05/2022

Locations

Countries of recruitment
Nepal

Study participating centre
HERD international
Kapilbastu district
Lumbini Province (no. 5)
Kapilbastu
Nepal
-

Sponsor information

Organisation
HERD International

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Newton Fund

Alternative Name(s)
The Newton Fund, NF

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from:
Name: Santosh Giri, HERD International. Email: santosh.giri@herdint.com or
Naomi Saville, Email: n.saville@ucl.ac.uk
Individual-level fully anonymised data with all locations and personal identifiers removed will become available 1 year after the publication of the study results for an indefinite period. The criteria for access will include any non-commercial use to answer research questions of scientific importance. Data will be shared with any scientist submitting a bona fide reason for analysis regardless of the type of analyses, so long as the proposed analysis is not already being undertaken by the investigators or another user of the data and providing the use of the data fit within any ethical or legal restrictions within the UK or Nepal. Only fully anonymised data will be shared using a secure data transfer mechanism. Consent from participants for sharing

anonymised data for secondary analyses is obtained in writing at the time of trial registration. The dataset analysed in the final trial paper may also accompany the publication of the trial results as supplementary material depending upon the journal requirements.

IPD sharing plan summary

Stored in publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		07/11/2024	22/11/2024	Yes	No
Protocol article		16/02/2023	17/02/2023	Yes	No
Dataset		23/09/2024	07/10/2024	No	No
Other publications	Process evaluation	06/07/2023	01/08/2023	Yes	No
Other publications	Health worker perspectives	24/04/2023	07/10/2024	Yes	No
Other publications	Mixed methods study	28/07/2023	07/10/2024	Yes	No
Participant information sheet		13/01/2022	13/01/2022	No	Yes
Preprint results		03/08/2023	15/02/2024	No	No
Statistical Analysis Plan	version 1.0	27/05/2022	01/08/2023	No	No