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Biofortification with zinc and iron for eliminating deficiency in Pakistan

Submission date
13/08/2019

Recruitment status
No longer recruiting

Registration date
14/08/2019

Overall study status
Completed

Last Edited
17/09/2024

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Zinc and iron deficiencies are a global public health problem, with the greatest burden occurring in low and middle-income countries. In Pakistan, around 1 in 5 women of reproductive age is zinc deficient, and the level is similar for iron deficiency (National Nutrition Survey 2018). These conditions have negative consequences for maternal and child health, and it is imperative that sustainable and cost-effective solutions are found. The aim of this study is to investigate the potential of biofortification to reduce zinc and iron deficiencies in Pakistan. Biofortification is a process by which the nutritional quality of food crops is improved through conventional plant breeding techniques and the addition of nutrient-rich fertilisers. HarvestPlus has developed a variety of wheat with significantly greater zinc and iron concentrations compared to standard varieties. Wheat is the staple crop in Pakistan and most families consume chapatis (made from wheat flour) with every meal. Therefore, biofortified flour may benefit communities who cannot afford to consume a diverse range of foods.

Who can participate?
Households including an adolescent girl (aged 10-16 years) and a child (aged 1-5 years)

What does the study involve?
The study is conducted in two phases of six months. In phase 1, families consume their usual locally purchased flour. In phase 2, they consume either biofortified flour (intervention group) or standard flour (control group). Households are randomly allocated to the intervention or control group and they do not know which flour they are consuming (nor do the research team). Tests are carried out to assess the impact of consuming biofortified flour on zinc and iron status. The researchers also record the incidence of diarrhoea and upper respiratory tract infections (in children), which are known to be associated with zinc deficiency.

What are the possible benefits and risks of participating?
There are no direct benefits to the participants for taking part in this study. However, it is hoped the information from this study will help to increase understanding of the potential for biofortified wheat to improve zinc and iron status in Pakistan. There is a risk of temporary bruising at the site of blood sampling.

Where is the study run from?
Baghbanan Health Centre (Pakistan)

When is the study starting and how long is it expected to run for?
April 2019 to March 2021

Who is funding the study?
Biotechnology and Biological Sciences Research Council (UK)

Who is the main contact?
Prof. Nicola Lowe
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Study website
https://www.uclan.ac.uk/research/explore/projects/bizifed-project.php

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
BB/S013989/1

Study information

Scientific Title
A randomised controlled trial to investigate the effect of biofortification on zinc and iron status in adolescent girls in a low resource community in Pakistan

Acronym
BIZIFED2

Study objectives
Consumption of flour made from biofortified wheat improves zinc and iron status in adolescent girls with low dietary intakes.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 30/08/2019, University of Central Lancashire STEMH Ethics Committee (University of Central Lancashire, Preston, PR1 2HE, UK; Tel: +44 (0)1772 201 201; Email: EthicsInfo@uclan.ac.uk), Reference # STEMH 1014

Study design
Double-blind cluster-randomised controlled trial

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
Community

Study type(s)
Prevention

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Zinc and iron deficiencies

Interventions
Phase 1 (November 2019 to April 2020): Families will continue to consume their usual, locally purchased flour. The cost of the flour will be reimbursed in the form of coupons to use at the local market. The coupons will be distributed fortnightly to mirror the distribution of flour in phase 2. This represents a substantial saving in the household budget, which is evenly distributed throughout the study. Samples of flour will be collected on a monthly basis to monitor the zinc and iron content.

Phase 2 (June 2020 to November 2020): Families will be provided with either biofortified flour (intervention group) or control flour (control group). Households will be randomly allocated to the intervention or control group and they will not know which flour they are consuming (nor will the research team). The flour will be provided free of charge, with enough flour for the entire household. Grain will be milled locally and flour will be distributed fortnightly. A range of biochemical measures will be taken to assess the impact of consuming biofortified flour on zinc and iron status. The researchers will also record the incidence of diarrhoea and upper respiratory tract infections (in children), which are known to be associated with zinc deficiency.

The duration of the intervention and follow-up will be 6 months for each phase.

Intervention Type
Other

Primary outcome measure
Plasma zinc concentration measured by inductively coupled plasma mass spectrometry (ICP-MS) at start of phase 1 (T1), middle of phase 1 (T2), end of phase 1 (T3), middle of phase 2 (T4), end of phase 2 (T5)

Secondary outcome measures
Measured at the start of phase 1 (T1), middle of phase 1 (T2), end of phase 1 (T3), middle of phase 2 (T4), end of phase 2 (T5):
1. Biochemical indicators of zinc and iron status (adolescents only):
1.1. Serum iron concentration measured by ICP-MS
1.2. Serum transferrin receptor protein and serum ferritin measured by sandwich ELISA
1.3. Haemoglobin, haematocrit and complete blood count (CBC) estimated using clinical haematology methods
1.4. Inflammatory markers (CRP and AGP) measured by sandwich ELISA
1.5. DNA damage measured by comet assay and histone H2A phosphorylation
1.6. Hair zinc concentration measured by mass spectroscopy
1.7. Natural zinc stable isotope composition measured by ICP-MS
2. Anthropometric measures (adolescents and children):
2.1. Height/length measured using stadiometer or infant measuring board
2.2. Weight measured using digital weighing scale
2.3. Mid upper arm circumference (MUAC), waist circumference, hip circumference and head circumference measured using standard techniques and measuring tape
3. Dietary intake of energy and nutrients (adolescents only) assessed by 24-hour recall method
4. Diarrhoeal episodes: frequency and duration (children only) assessed by interview with mother
5. Upper respiratory tract infections (adolescents and children) assessed by clinical staff

Overall study start date
01/04/2019

Completion date
31/03/2021

Eligibility

Key inclusion criteria
Households will be invited to participate in this study if they include an unmarried adolescent girl (aged 10-16 years) who is not pregnant or lactating AND a child (aged 1–5 years)

Participant type(s)
Mixed

Age group
Mixed

Sex
Both

Target number of participants
500 households

Total final enrolment
483

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
01/09/2019

Date of final enrolment
31/01/2020

Locations

Countries of recruitment
Pakistan

Study participating centre
Baghbanan Health Centre
Peshawar
Pakistan
-

Sponsor information

Organisation
University of Central Lancashire

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Sponsor type
University/education

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ROR
https://ror.org/010jbqd54

Funder(s)

Funder type
Government

Funder Name
Biotechnology and Biological Sciences Research Council

Alternative Name(s)
UKRI - Biotechnology And Biological Sciences Research Council, BBSRC UK, BBSRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trialists are planning to publish the results of this study in high-impact peer reviewed journals. Papers will be submitted for publication within two years of the completion of the overall study, of which this intervention forms a part. The anticipated date for submission of papers is May 2023.

Additional documents (such as study protocol, statistical analysis plan, other) will be available in accordance with the UCLan open access policy which can be found here: https://www.uclan.ac.uk/research/environment/assets/rdm-policy-approved-online.pdf

Intention to publish date
01/05/2023

Individual participant data (IPD) sharing plan
The University adheres to an Open Data policy and has an open data repository. Metadata will be collected in the form of “read me” files using basic Dublin Core. Scientific publications will serve to release data into the public domain, and non-confidential data will be available from public data repositories https://uclandata.uclan.ac.uk/. Public release of non-commercially-sensitive material will be concurrent with publication, or prior to this when publication is not compromised, with the agreement of all partners. Data release will be under a “cc-By” licence. The data that will be made available will be anonymised in accordance with the participant consent form. The types of data that will be made available include biochemical data, physiological data and dietary data. Final datasets will be made available in the form of Excel spreadsheets. All data will be anonymised using unique ID numbers. Informed consent will be obtained from adolescent girls, mothers of children and heads of household.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	18/11/2020	08/03/2021	Yes	No
Results article	Effects on haematological concentrations	15/04/2022	20/04/2022	Yes	No
Results article	Effects on hair concentrations	24/03/2023	11/04/2023	Yes	No
Participant information sheet	Consent		17/09/2024	No	Yes