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Lifestyle interventions to prevent diabetes in pregnant mothers

Submission date
19/11/2018

Recruitment status
No longer recruiting

Registration date
21/12/2018

Overall study status
Completed

Last Edited
09/07/2024

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Diabetes during pregnancy or gestational diabetes mellitus (GDM) is associated with significant pregnancy-related complications, morbidity in newborns, and a long-term risk of developing type 2 diabetes, obesity and cardiovascular disease in both the mother and the offspring. In pregnant women with GDM, blood sugar usually returns to normal levels after delivery. However, about 50-70% of GDM mothers develop type 2 diabetes within 5-10 years after the birth of the child. Simple lifestyle interventions such as dietary modification and regular physical activity have shown to improve blood sugar levels and constitute potentially attractive options to reduce the risk of GDM. The current study aims to investigate if diet and/or physical activity intervention from earlier than 18 weeks of pregnancy helps reduce the risk of developing diabetes during pregnancy.

Who can participate?
Pregnant women aged 18 years or older and over and pregnancy for 16 weeks or less duration with at least one risk factor for developing diabetes during pregnancy.

What does the study involve?
Eligible women will be randomly allocated to one of the four treatment groups – diet, physical activity, diet and physical activity or standard care. In the dietary intervention, women will have to consume 200 g of fermented yoghurt daily. Women randomized to the physical activity (PA) group will have to undertake daily walking calculated as 40% more than their baseline activity monitored by device and the diet and PA group will have both interventions as above. All interventions will last for a minimum duration 14 weeks from randomization. Women allocated to standard care arm will serve as controls and will not be subjected to any active intervention, but will receive routine care by their treating physician. Participants will be studied for development of diabetes at 26 - 28 weeks and 32 weeks of pregnancy. Women who are diagnosed to have diabetes at 26-28 weeks could voluntarily withdraw from interventions or continue to 32 weeks on active interventions along with appropriate diabetes management as per local clinical practice. At 32 weeks of pregnancy final assessment of diabetes status will be done and all study procedures will be completed. Data of the mother and the newborn's health will be collected at delivery.

What are the possible benefits and risks of participating?
The possible benefit for participants is better pregnancy care and early screening for diabetes. The current study provides women with experience of specific healthy lifestyles during pregnancy. The opportunity to bring about behavioural changes during early pregnancy by changing mother's nutrition and increasing physical activity to prevent GDM can have immediate and lifelong health impacts on the mother, as well as the newborn, with possible positive consequences into adulthood. There are no known risks to participants taking part in the study. Both yoghurt and physical activity are generally considered safe during pregnancy.

Where is the study run from?
The study is run from the Oxford Centre for Diabetes, Endocrinology and Metabolism (UK) and will take place in a centre in India and a centre in The Gambia

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

Who is funding the study?
1. Medical Research Council (UK)
2. Director of Biotechnology (India)
3. Global Challenges Research Fund (UK)

Who is the main contact?
Dr Senthil Vasan
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MR/R020345/1

Study information

Scientific Title
Pregnancy-Related Interventions in Mothers at Risk for gestational Diabetes in Asian India and Low and middle income countries (PRIMORDIAL Study)

Acronym
PRIMORDIAL

Study objectives
Daily yoghurt and/or daily walking for at least 14 weeks will reduce the risk of developing gestational diabetes in ‘high-risk’ pregnant women

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Oxford Tropical Research Ethics Committee (OxTREC), 01/11/2018, 44-18
2. Christian Medical College, Vellore, 27/06/2018, IRB:11367
3. Scientific Co-ordinating Committee, MRC Unit The Gambia at the London School of Hygiene & Tropical Medicine, 13/11/2018, SCC 1645v1.1

Study design
Interventional 2x2 factorial randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

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
Gestational diabetes mellitus

Interventions
Current interventions as of 17/06/2020:

Participants will be randomly allocated to either the intervention or the control group.
Participants in the intervention group will be further randomised to receive either 200 g/day yoghurt, a physical activity intervention or both. This physical activity intervention will involve daily walking to a step count 40% higher than their baseline physical activity recorded during run-in-phase.
Participants in the control group will receive standard care with no specific intervention
Randomisation will be centre specific and stratified based on age and body mass index within each randomisation block.
The total duration of the intervention is 14 weeks. Participants will be randomised within 2 weeks of screening and active intervention will continue till 32 weeks as per protocol. However, if any participant develops diabetes prior to 32 weeks, further continuation in the intervention will depend on safety, the effect of continuing interventions on pregnancy and subject to the investigator. GDM will be managed according to local guidelines in these participants.

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Previous interventions from 07/05/2020 to 16/06/2020:

Participants will be randomly allocated to either the intervention or the control group.
Participants in the intervention group will be further randomised to receive either 200 g/day yoghurt, a physical activity intervention or both. This physical activity intervention will involve daily walking to a step count 40% higher than their baseline physical activity.
Participants in the control group will receive standard care with no specific intervention.
Randomisation will be centre specific and stratified based on age and body mass index within each randomisation block.
The total duration of intervention is 14 weeks. Participants will be randomised at ≤ 18 weeks gestation and the intervention will continue till 32 weeks as per protocol. However, if any participant develops diabetes prior to 32 weeks, active trial interventions will be stopped.

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Previous interventions:

Participants will be randomly allocated to either the intervention or the control group.
Participants in the intervention group will be further randomised to receive either 200 g/day

yoghurt, a physical activity intervention or both. This physical activity intervention will involve daily walking to a step count 40% higher than their baseline physical activity, or walking daily to a step count of 11,000 steps (whichever is the greatest).
Participants in the control group will receive standard care with no specific intervention.
Randomisation will be centre specific and stratified based on age, body mass index and history of gestational diabetes during previous pregnancy within each randomisation block.
The total duration of intervention is 14 weeks. Participants will be randomised at 18 weeks gestation and the intervention will continue till 32 weeks as per protocol. However, if any participant develops diabetes prior to 32 weeks, active trial interventions will be stopped.

Intervention Type
Mixed

Primary outcome measure
Current primary outcome measure as of 07/05/2020:

Incidence of gestational diabetes mellitus diagnosed based on IADPSG criteria at 26-28 weeks or fasting plasma glucose ≥5.1 mmol/l at week 32 (plasma glucose analysed using a Roche Cobas 800 Enzymic autoanalyser)

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Previous primary outcome measure:

Incidence of gestational diabetes mellitus according to IADPSG criteria, assessed by the following during weeks 26-28 of gestation and at 32 weeks of gestation:
1. Fasting plasma glucose, analysed using a Roche Cobas 800 Enzymic autoanalyser
2. Glucose at 1 and 2 hours post 75 g oral glucose tolerance test (OGTT), analysed using a Roche Cobas 800 Enzymic autoanalyser

Secondary outcome measures
Current secondary outcome measures as of 07/05/2020:

1. Absolute values of fasting blood glucose concentration at 32 weeks gestational age
2. Gestational weight gain using a Digital Tanita scale (in The Gambia) and a stadiometer (in India) from randomisation to week 32
3. Blood pressure from randomisation to week 32
4. Proportion of women undergoing instrumental/caesarean delivery, assessed using the study proforma
5. Post-partum haemorrhage,assessed using the amount of blood loss after child birth from the study proforma at delivery
6. Pre-eclampsia and eclampsia, assessed using clinical diagnosis of hypertension and proteinuria (with or without seizures) from the study proforma after 28 weeks of gestation
7. Blood loss at delivery, assessed using the amount of blood loss during the delivery from the study proforma at delivery
8. Pre-term births (less than 37 weeks of gestation), determined by calculating gestational age from dating the ultrasound scan at delivery
9. Foetal macrosomia (defined as birth weight >2 standard deviations above the population-specific mean in each setting), assessed from birth weight measured using an infantometer at delivery
10. Birth weight, assessed using an infantometer at delivery

11. Physical condition of newborn infant, assessed using the clinically recorded APGAR score at 1 and 5 minutes of birth
12. Length of newborn, assessed by measuring length from the head to the heel using a non-stretchable tape within 48 hours of birth.
13. Barriers to interventions in pregnancy, assessed using a questionnaire at screening and at 32 weeks of gestation

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Previous secondary outcome measures:

1. Gestational weight gain, assessed using a Digital Tanita scale (in The Gambia) and a stadiometer (in India) at screening, the run-in phase, the point of randomisation, visits 1, 2 and 3, and at delivery (prior to birth)
2. Requirement of insulin/metformin post-OGTT, assessed through a review of patient notes from the diagnosis of GDM to delivery
3. Proportion of women undergoing instrumental/caesarean delivery, assessed using the study proforma after delivery
4. Gestational age at delivery, determined by dating the ultrasound scan at delivery
5. Post-partum haemorrhage, assessed using the amount of blood loss after child birth from the study proforma at delivery
6. Pre-eclampsia and eclampsia, assessed using clinical diagnosis of hypertension and proteinuria (with or without seizures) from the study proforma after 28 weeks of gestation
7. Blood less at delivery, assessed using the amount of blood loss during the delivery from the study proforma at delivery
8. Pre-term births (less than 37 weeks of gestation), determined by calculating gestational age from dating the ultrasound scan at delivery
9. Foetal macrosomia (defined as birth weight >2 standard deviations above the population-specific mean in each setting), assessed from birth weight measured using an infantometer at delivery
10. Low birth weight (defined as birth weight <2.5 kg), assessed using an infantometer at delivery
11. Physical condition of newborn infant, assessed using the clinically recorded APGAR score at 1 and 5 minutes of birth
12. Length of newborn, assessed by measuring length from the head to the heel using a non-stretchable tape within 48 hours of birth
13. Ponderal index, assessed using the formula (birth weight (kg)/birth length (m))^3 within 48 hours of birth
14. Abdominal circumference of the newborn, assessed by measuring the circumference at the level of the xiphisternum and just above/below the level of the umbilicus using non-stretchable tape within 48 hours of birth
15. Barriers to interventions in pregnancy, assessed using a questionnaire at screening and at 32 weeks of gestation

Overall study start date
01/09/2018

Completion date
16/09/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/05/2020:

1. Aged 18 years or older
2. Gestational age ≤ 16 weeks
3. Meeting at least one of the following criteria for high-risk gestational diabetes mellitus (GDM):
3.1. Booking BMI ≥ 25kg/m²
3.2. Age ≥ 25 years
3.3. First-degree relative with diabetes
3.4. Previous pregnancy with GDM
3.5. Previous pregnancy with large baby (≥ 3.5kg)
3.6. Previous pregnancy with pre-eclampsia/eclampsia
3.7. History of PCOD/impaired fasting glucose)
4. Not currently on any medications (except iron, calcium or folic acid supplements, thyroxine supplement for hypothyroidism, low dose aspirin for pre-eclampsia)

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Previous inclusion criteria:

1. Aged 18 years or older
2. Pregnant females
3. Gestational age >16 weeks
4. Meeting at least one of the following criteria for high-risk gestational diabetes mellitus (GDM):
4.1. BMI ≥25 kg/m² (for Indian women, BMI ≥23 kg/m²
4.2. First-degree relative with diabetes
4.3. Previous pregnancy with GDM
4.4. Previous pregnancy with a large baby (≥3.5 kg)
4.5. Previous pregnancy with pre-eclampsia/eclampsia
4.6. History of polycystic ovary disease (PCOD) or impaired fasting glucose
5. Not currently on any medications (excluding iron or folic acid supplements)

Participant type(s)
Other

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
1,856 pregnant women (928 from each site)

Total final enrolment
1870

Key exclusion criteria

Current inclusion criteria as of 07/05/2020:

1. GDM diagnosed prior to screening visit based on IADPSG criteria or documented raised HbA1C, i.e., either fasting glucose ≥ 5.1 mmol/L or 1h glucose ≥ 10.0 mmol/L or 2h glucose ≥ 8.5 mmol/L, or a documented HbA1c of ≥ 6.5% at first booking
2. History of pre-gestational diabetes
3. Multiple gestations in the current pregnancy
4. History of severe hyperemesis in the first trimester
5. Uncontrolled pre-gestational or gestational hypertension (BP > 150/100 mmHg) on treatment
6. History of recurrent (≥ 2) first-trimester spontaneous abortions or stillbirths
7. Previous child born with congenital anomalies
8. History of significant ante- or post-partum haemorrhage in the previous pregnancy
9. Pregnancy following in-vitro fertilization or any assisted reproductive technology
10. Previous or current psychiatric illness on medication, epileptic seizures or on antiepileptic medication
11. Women meeting absolute contraindications for physical activity during pregnancy as recommended by the ACOG
11.1. Heart disease
11.2. Restrictive lung disease
11.3. incompetent cervix/cerclage
11.4. Pregnancies at risk for premature labour
11.5. gestational hypertension (BP > 150/100 mmHg)
11.6. Severe anaemia

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Previous exclusion criteria:

1. Diagnosis of pre-gestational diabetes, previous GDM based on The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria, or raised blood glucose at blooding - any of the following at first booking:
1.1. Fasting glucose ≥5.1 mmol/L
1.2. 1 hour glucose ≥10.0 mmol/L
1.3. 2 hour glucose ≥8.5 mmol/L
1.4. Documented HbA1c of ≥6.5%
2. Multiple gestation
3. History of severe hyperemesis in first trimester
4. History of hypertension (pre-gestational or gestational)
5. History or recurrent (more than two) first trimester abortions
6. History of ante- or post-partum haemorrhage in the previous pregnancy
7. Previous child born with congenital anomalies
8. Previous stillbirth or miscarriage
9. Pregnancy following in-vitro fertilisation or any assisted reproductive technology
10. Unwilling to adhere to the study protocol
11. History of or current psychiatric illness
12. History of or current neurological condition (i.e. epilepsy)
13. Meeting absolute contraindications for physical activity during preganncy as recommend by the American College of Obstetricians and Gynecologists (ACOG), including:
13.1. Heart disease
13.2. Restrictive lung disease
13.3. Incompetent cervix/cerclage
13.4. At risk for premature labour

13.5. Gestational hypertension
13.6. Severe anaemia

Date of first enrolment
01/02/2019

Date of final enrolment
16/06/2022

Locations

Countries of recruitment
Gambia

India

Study participating centre
Christian Medical College
Ida Scudder Road
Vellore
India
632001

Study participating centre
MRC Unit The Gambia at London School of Hygiene & Tropical Medicine
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Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Medical Research Council

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Department of Biotechnology , Ministry of Science and Technology

Alternative Name(s)
Dept. of Biotechnology, Govt of India, , , Department of Biotechnology, Department of Biotechnology, Ministry of Science & Technology, India, Department of Biotechnology, GOI, Dept. of Biotechnology, Govt. of India, Department of Biotechnology, Ministry of Sc & Tech, Govt of India, DBT

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
India

Funder Name
Global Challenges Research Fund, Oxford

Results and Publications

Publication and dissemination plan
The research findings will be disseminated in national and international platforms and through our network and collaborations. We anticipate publications in high impact international journals and presentation in relevant scientific meetings to inform researchers, clinicians and policy makers. The findings of general linterest will be publicised with the help of the Public Relations Office at the University of Oxford, which is well recognised for being an active communicant of research findings to the public through media. This includes an extensive open website and a full range of events organized during the National Science Week. Furthermore, the School of Medicine runs a very successful engagement programme, in which are its Science in Health, Public Lecture series and Science in Health LIVE event.

Intention to publish date
15/10/2024

Individual participant data (IPD) sharing plan
Fully anonymized data will be available on written request from Dr. Senthil Vasan (senthil.vasan@ocdem.ox.ac.uk) after the completion of the study and publication of the primary research findings. All data meant for sharing will be anonymised/de-identified by removing all individual-level participant data and will be archived on the servers of the Archives department of Medical Research Council (MRC) at The Gambia indefinitely. Personally identifiable data will not be shared outside the research team. Data sharing will be in agreement with the MRC, The Gambia as outlined and governed by the Data Sharing Policies and MRC Policy and Guidance on Sharing of Research Data from Population & Patient Studies. The regulations will also adhere to the University of Oxford data policy guidelines. Informed consent for sharing research data with interested collaborators will be obtained from all participants.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	17/02/2021	22/02/2021	Yes	No