Participant Research Consent Form

Title of Research Project:
Elucidating the Dynamics and Impact of the Gut Microbiome on Maternal Nutrition During Pregnancy (MMIP)

Principal Investigator:
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Purpose of the Research:
In your gut, there are different organisms called microbes or the gut microbiome. The gut microbiome is very important to your body's ability to function and good health, and it can help you digest food and absorb nutrients to affect your nutrition. Sometimes when we get sick or are exposed to different elements, this can cause the good microbes that promote good health to die, while helping the number of potentially harmful microbes to increase. Research has found that your microbiome can also affect whether someone has undernutrition. During pregnancy, it is very important that a mother consumes enough healthy foods to nourish the mother and the growing baby. The microbiome is important during pregnancy too, given its role in maintain good health and nutrition. At this time, few studies have examined the role of the microbiome on measures of health and nutrition of both the mother and the baby. In this study, we want to take measures to tell us about a mother's nutrition and her microbiome, so that we can learn more about the relationship between the two during pregnancy, and how they contribute to birth outcomes.

Description of the Research:
You are being invited to take part in this study because:

- You are 17-24 years old
- You are pregnant with a gestational age of <16 weeks.
- You have a BMI below 25
- You plan to stay in your area for the whole study (about two years)

- You are not participating in any interventional trials at this time.
- You are in good general health

Procedures:

There are two phases to this study, phase 1: post-conception and phase 2: post-partum. Overall, we will follow up with you and your baby over the course of your pregnancy and for a year after you give birth. These follow up visits will include different measures for you and your baby at different time points. Details of these activities are briefly given in table 1 and 2, separate for mothers and their infant separately.

Table 1: Maternal Study Overview and Summary of Activities

	Brief description of visit/assessment	Visit 1: 10-14 weeks post-conception	Visit 2: 30-34 weeks post-conception	Visit 3: 24-72 hours post-delivery	Visit 4: 3 months post-partum	Visit 5: 6 months post-partum	Visit 6 12 months post-partum
Screening and consent (20-30 minutes)	Eligibility screening and informed consent discussion and documentation.	X					
Anthropometrics (~10 minutes)	Collection of height, weight, mid upper arm circumference and triceps skinfold thickness.	X	X	X	X	X	X
Baseline demographics (~20-30 minutes)	Verbal data will be collected about individual and household/social demographics i.e. age, number of pregnancies, children, language, religion, ethnicity education, income, housing and marital relationship etc.	X					
Stool sample (10 minutes)	Stool sample collection. Instruction on methods and kits of stool collection will be provided at length.	X	X		X		X
Blood sample (10 minutes)	An intravenous blood sample of 3-5ml will be drawn. It will be examined for anemia, nutrient levels (minerals and vitamins) and general metabolites (protein components, fat components etc).	X	X				X
Health Assessment (5-10 minutes)	You will be asked questions about your health and medication use.	X	X	X	X	X	X
Dietary Recall (30 minutes)	You will be asked questions about what you eat over the past 24 hours.	X	X				X
Dietary Diversity (10 minutes)	You will be asked questions about the types of the food group consumed.				X		
Empowerment Questionnaire (20 minutes)	You will be asked questions around your perceived self-efficacy, perceived social support, decision making and perceived stress.	X			X		

Post-Partum Questionnaire (15 minutes)	You will be asked questions about your labor pains, type of delivery, place of delivery and GA at delivery.			X			
Approximate time in hours at each visit		2-3	1	0.5	1	0.3	1

Table 2: Infant Study Overview and Summary of Activities

	Brief description of visit/assessment	Visit 3: 24-72 hours post-delivery	Visit 4: 3 months post-partum	Visit 5: 6 months post-partum	Visit 6: 12 months post-partum
Anthropometrics (~10 minutes)	Collection of height, weight, mid upper arm circumference and triceps skinfold thickness.	X	X	X	X
Stool sample (10 minutes)	Stool sample collection. Instruction on methods and kits of stool collection will be provided at length. Small amount of stool will be collected from your kid at home.		X		X
Blood sample (10 minutes)	An intravenous blood sample of 2-3ml will be drawn to see anemia and nutrients status				X
Health Assessment (5 -10 minutes)	You will be asked questions about your infant's health, congenital morbidity assessment and use of medications.	X	X	X	X
Infant Feeding Assessment (15 minutes)	You will be asked questions about your infant's colostrum administration and feeding.		X	X	X
Approximate time in minutes at each visit		15-20	40-45	30-35	50-55

Optional Component: Future Genetic Research Consent

Optional means that you may refuse to consent to this part of the study without affecting your participation in the main study. Please take your time to make your decision.

This study will involve optional genetic research. In general, genetic research involves isolating your genes from your sample(s). Every person has their own unique set of genes, or "genome". Genes carry the information that helps to determine your characteristics. Genetic research is being done in this study to further investigate how the microbes in your gut interact with your genes and how they affect and interact with your infant's genes. We will store your and your infant's blood samples (Biobank) and in the future we will conduct whole genome sequencing. Conducting whole genome sequencing will allow the researchers to better understand how your genes and your gut microbiome interact and contribute to your nutritional status and the birth outcomes of your baby. To do this test it will not involve an additional blood sample.

Even with protections in place, there is a risk that your information and your infant's information could be released by accident. Advances in technology could also increase the risk that your genetic samples and results could be linked back to you or your blood relatives.

Reports about research tests done with your samples and your infant's samples will be given to the study researcher. If you would like to learn the results of this research, please let them know.

You should be aware that genetic information cannot be protected from disclosure by court order. The potential psychological and social risks of participating and receiving genomic information are not fully known at this time. It may be upsetting to learn about genetic causes and medically actionable findings. Because parent(s) and children can share genetic variants, the discovery of harmful variants in your genome may lead to identifying the same variants in your family members' genome. It may be upsetting to learn that other members of your family share harmful genetic variants with you.

What if the researchers discover something about me?

In genetic research, the researchers may learn something about you that they didn't expect. For example, the researchers may identify genes that may predispose to immune-related disorders such as inflammatory bowel disease This is called a secondary finding. **Secondary findings are information that was discovered unintentionally.**

Some secondary findings may be **medically actionable.** Medically actionable secondary findings mean there is a high chance of a health problem AND treatment and/or screening is available for this health problem.

If we discover medically actionable findings we will only talk to you about those medically actionable findings that we think are likely to have a major effect on health. Seeing a medical specialist could be helpful as there might be specific health recommendations for you and/or family member(s). We will work with you, your family and your doctor(s) during this process. Because many of these variants are passed from parent to child, identification of one of these variants in you could have implications for biological (blood) family members' (such as parent(s) and siblings) health as well. Any medically actionable secondary findings identified through this research study need to be validated in a clinical laboratory. This will be discussed with the doctor involved in your care.

Medically non-actionable findings:

There are also medically non-actionable findings. These findings may indicate there is a high chance for a disease but there is currently no treatment and or screening available (e.g., Alzheimer's or Huntington's Disease). We will not return these findings to you; we do not return information on incidental findings that are not medically actionable. We will not place this information into your medical records at AKU.

For this part of the study, participation is optional. Please initial your preference in the box below.

Optional Genetic Research Consent	
	Yes, I consent to whole genome sequencing of my blood samples.

Initials	
Initials	No, I do not consent to whole genome sequencing of my blood samples.

Optional Genetic Research Consent for your Infant	
Initials	Yes, I consent to whole genome sequencing of my infant's blood samples.
Initials	No, I do not consent to whole genome sequencing of my infant's blood samples.

Genomic Sequencing Data:

Genomic sequencing allows us to test a person's DNA and find variations in DNA sequence for thousands of their genes at the same time. Your genomic sequencing data is unique to you and will have important health information about you.

We would like your permission to use your de-identified and or anonymized genomic sequencing data in future research. Please initial next to your preference:

Future Research of Genomic Sequencings data about me:	
Initials	Yes, you can use my de-identified and or anonymized whole genome sequencing data for future research purposes.
Initials	No, you cannot use my de-identified and or anonymized whole genome sequencing data for future research purposes.

Future Research of Genomic Sequencings data about my infant:	
Initials	Yes, you can use my infant's de-identified and or anonymized whole genome sequencing data for future research purposes.
Initials	No, you cannot use my infant's de-identified and or anonymized whole genome sequencing data for future research purposes.

Possible risks or discomforts:
This is an observational study. Potential risks include the general risks of giving blood, including light-headedness, bruising, minor bleeding where the needle is inserted into the arm, pain, and a very low chance of infection. You may feel discomfort providing a stool sample, detailed instructions and research staff will be available to provide support. The stool samples are an essential component of the study, and as such it is a required component of participation.

You may also experience psychological and emotional distress when completing questionnaires and/ or answering questions about their socio-economic status, their health, their infants' health. In addition, some participants may go through postpartum depression that may impact their mental state during the study period. You will have the option leave questions blank/unanswered if they are uncomfortable, research staff members will be on hand if you experience's physiological and/ or emotional distress during a study visit/ during study procedures. If this occurs the study staff members will refer and transport you to the government health care facility.

Possible Benefits:

There are no direct benefits to participants in the study. However, you will be assessed for anemia, and ongoing interaction with the Lady Health Worker Program (LHWs) will be promoted. This provides a small benefit to the study population. You will benefit from receiving appropriate standard of care, which may be better than the average care received in the health system. If you are found to have severe anemia you will be referred to the nearest public health facility for further evaluation and treatment.

The societal benefits of the proposed study are that it is expected to yield insights into the relationships between prokaryotic and eukaryotic microbes in the gut and their association with maternal health and birth outcomes. The study results are expected to have an impact beyond the study setting. The actual risk of harm caused by a non- interventional trial is expected to be low, and the potential benefits in terms of knowledge generation outweigh the theoretical risks.

Confidentiality:
Your identity in this study will be treated as confidential, unless the law requires us to do so. The results of the study, including laboratory or any other data, may be published for scientific purposes but will not give your name or include any identifiable references to you. However, any records or data obtained as a result of your participation in this study may be inspected by the study team/ investigators or by AKU ERC members.

The documents and information from this study will be stored in a secure, locked location. The research team may also give permission to other people from Aga Khan University and The Hospital for Sick Children to look at the information. After the research study ends, the information will be kept for at least seven years after the study report is published. Published reports will not show your name or personal information. AKU and SickKids will share your de-identified data and samples with collaborating institutions to assist with analysis and interpretation of results and the subsequent animal studies.

Research data will be sent to central repositories:

It is expected that the microbiome data will be de-identified and uploaded on the National Centre for Biotechnology Information (NCBI). The NCBI facilitates the automated storage and analysis of databases for the research and medical community. In addition to publishing findings in open access journals, we will ensure all de-identified sequences and metabolomics datasets are deposited in appropriate public repositories. SOPs, pathogen samples and statistical methods developed through this project will be shared with the IMPACTT research core.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

Reimbursement:
There is no payment provided to you for joining this study. Visits will be made at your house and the study materials/ study supplies will be provided free of cost. However, to thank participants for their time and effort in the study, participants will be given a thank- you gift at three times during the study. 1) Non-food items i.e. suit for mother at enrollment 2) baby hygiene kit at birth 3) toys for baby at the end of participation.

Participation:
It is your choice to take part in this study voluntarily. You can stop at any time. Your contact with any health facilities will not be affected in any way by your choice to join or not to join this study.

If you become ill or are harmed specifically because of study participation, we will make sure that you get medical care, free of cost to you. Your signing this consent form does not interfere with your legal rights in any way. The staff of the study, any people who gave money to pay for the study, or Aga Khan University and The Hospital for Sick Children are still responsible, legally, and professionally, for what they do.

Sponsorship:
The sponsor of this study is the Canadian Institute of Health Research.

Conflict of Interest:
The Principal Investigator, Dr. Bhutta, and other research team members have no conflicts of interest to declare.

Consent:

By signing this form, I agree that:

1. You have explained this study to me. You have answered all my questions.
2. You have explained the possible harms and benefits (if any) of this study.
3. I know what I could do instead of taking part in this study. I understand that I have the right not to take part in the study and the right to stop at any time. My decision about taking part in the study will not affect my health care at associated organizations.
4. I am free now, and in the future, to ask questions about the study.
5. I have been told that my study records will be kept private except as described to me.
6. I understand that no information about who I am will be given to anyone or be published without first asking my permission.
8. I have read and understood pages 1 to 9 of this consent form. I agree, or consent, to take part in this study.

Name of participant and age	Participant's signature and date

	Ask the participant to mark a "left thumb impression" in this box if the participant is unable to provide a signature above.

Name of person who explained consent	Signature of person who explained consent and date

Name of witness (if the subject is unable to read)	Witness' signature and date

	Ask the witness to mark a "left thumb impression" in this box if the witness is unable to provide a signature above.

If you have questions, complaints, or get sick or injured as a result of being in this study, please contact the principal investigator Dr. Zulfiqar Bhutta Phone: 92 21 3493 0051 Ext: 1054