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Vaginal microbiome in late pregnancy and parturition

Submission date	Recruitment status	[ ] Prospectively registered
14/06/2018	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
18/09/2018	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
30/01/2023	Pregnancy and Childbirth	[ ] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 20/09/2019:
Background and study aims
The vaginal microbiome (microorganisms) and its association with preterm birth have been studied extensively, but the changes in the vaginal microbiome during late pregnancy and childbirth have received much less attention. The ultimate factors behind the triggering of childbirth are, despite intensive research, still unknown. The possible associations between the vaginal microbiome in late pregnancy, just before childbirth and in the onset of labor is thus an intriguing field of research. The mode of delivery is known to affect the baby's future microbiome composition and the mother's vaginal microbiome also seems to change during childbirth and after the rupture of the membranes. However, the extent and related associations have remained largely unknown. The aim of this study is to assess the vaginal microbiome changes that occur during pregnancy and childbirth.

Who can participate?
Pregnant women aged 18 or older, early term, full term, late term and post-term, giving birth spontaneously, by cesarean section or whose labor is induced.

What does the study involve?
Brush samples are taken from the vagina to assess the vaginal microbiome and immune system at different times before and during labor, before and during induction of labor, and before cesarean section. The samples are taken by healthcare professionals from the wall of vagina.

What are the possible benefits and risks of participating?
This study is not expected to benefit the patients involved in the study but aims to improve the quality of treatment for future patients. Every patient in the study gives a written informed consent and can withdraw from the study at any point. The samples are collected from volunteers during normal diagnostic or treatment visits. No extra visits to the outpatient clinic or hospital are needed. The samples are taken with soft, cotton flocked swabs which are easy and quick to use and do not cause discomfort during sample taking. The method does not harm the mother or the baby. A discomfort for the patient would be the time spent filling out the

background questionnaire, which includes also sensitive questions. The same questionnaire is already being used in other studies. All data is analyzed with highest confidentiality and are coded so that the answers cannot be connected to an individual person during analysis.

Where is the study run from?
Helsinki University Central Hospital, Women's' Hospital (Finland)

When is the study starting and how long is it expected to run for?
January 2017 to December 2021

Who is funding the study?
1. Helsinki University Central Hospital (Finland)
2. University of Helsinki (Finland)

Who is the main contact?
1. Dr Pekka Nieminen
2. Dr Kaisa Kervinen

Previous plain English summary:
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Who can participate?
Pregnant women aged 18 to 45, early term, full term, late term and post-term, giving birth spontaneously, by cesarean section or whose labor is induced

What does the study involve?
Brush samples are taken from the vagina to assess the vaginal microbiome and immune system at different times before and during labor, before and during induction of labor, and before cesarean section. The samples are taken by healthcare professionals from the wall of vagina.

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1. Dr Pekka Nieminen
2. Dr Kaisa Kervinen

Contact information

Type(s)
Scientific

Contact name
Dr Pekka Nieminen

Contact details
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00029

Type(s)
Public

Contact name
Dr Kaisa Kervinen

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Haartmaninkatu 2
PL 140
Helsinki
Finland
00029

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HUS/42/2017

Study information

Scientific Title
Changes in vaginal microbiome and metabolome in late pregnancy and parturition among women with spontaneous or induced vaginal delivery and before elective cesarean section

Acronym
EMMI

Study objectives
The hypothesis is that the vaginal microbiome changes during pregnancy and alterations happen at the time of parturition.

Ethics approval required
Old ethics approval format

Ethics approval(s)
University of Helsinki Institutional Review Board, 16/03/2017, ref: HUS/907/2017

Study design
Observational single-center study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Pregnancy, spontaneous or induced vaginal delivery and elective cesarean section

Interventions
Current interventions as of 20/09/2019:
The aim is to recruit altogether 600 patients in the following three groups:
1. 200 late and post term gravidae (41+0 or more weeks of gestation) at their first over-term visit

2. 200 early and full term gravidae (37+0-40+6 weeks of gestation) admitted to the delivery room, whose labor has started with spontaneous contractions and without rupture of the membranes
3. 200 early and full term gravidae (37+0-40+6 weeks of gestation) scheduled for an elective cesarean section.

Brush samples are taken from the vagina to collect the vaginal microbiome and soluble vaginal immune mediators at different timepoints before and during labor, before and during induction of labor, and before elective cesarean section. The samples are taken by healthcare professionals from the lateral wall of vagina. The vaginal microbiome is analyzed by sequencing using Illumina Miseq or HiSeq technology targeting the V3-V4 region of 16S rRNA gene. To assess local immune response, inflammatory cytokines and other small proteins are analyzed with ELISA and/or Luminex. Bacterial metabolites are analyzed with NMR spectroscopy and larger proteins including mucins with tandem mass spectrometry. The overall observation and follow-up time per person for the analyses explained above can be up to 7 days.

Previous interventions:
The aim is to recruit altogether 250 patients in the following three groups:
1. 100 late and post term gravidae (41+0 or more weeks of gestation) at their first over-term visit
2. 100 early and full term gravidae (37+0-40+6 weeks of gestation) admitted to the delivery room, whose labor has started with spontaneous contractions and without rupture of the membranes
3. 50 early and full term gravidae (37+0-40+6 weeks of gestation) scheduled for an elective cesarean section

Brush samples are taken from the vagina to collect the vaginal microbiome and soluble vaginal immune mediators at different timepoints before and during labor, before and during induction of labor, and before elective cesarean section. The samples are taken by healthcare professionals from the lateral wall of vagina. The vaginal microbiome is analyzed by sequencing using Illumina Miseq or HiSeq technology targeting the V3-V4 region of 16S rRNA gene. To assess local immune response, inflammatory cytokines and other small proteins are analyzed with ELISA and/or Luminex. Bacterial metabolites are analyzed with NMR spectroscopy and larger proteins including mucins with tandem mass spectrometry. The overall observation and follow-up time per person for the analyses explained above can be up to 7 days.

Intervention Type
Other

Primary outcome measure
Vaginal microbiome composition assessed using Illumina Miseq or HiSeq technology targeting the V3-V4 region of 16S rRNA gene

All of the outcomes are measured at baseline. In the post term induction study group and early and full term study group the outcomes are also measured during the induction and parturition.

Secondary outcome measures
1. Vaginal cytokine profile measured using multiplex ELISA and/or Luminex
2. Vaginal proteomic profile measured using tandem mass spectrometry
3. Bacterial metabolites analyzed with NMR spectroscopy

All of the outcomes are measured at baseline. In the post term induction study group and early and full term study group the outcomes are also measured during the induction and parturition.

Overall study start date
01/01/2017

Completion date
31/12/2021

Eligibility

Key inclusion criteria
Current participant inclusion criteria 20/09/2019:
1. Female
2. Age 18 or older

Further inclusion criteria for different study arms:

Post-term induction study arm:
1. Patients have more than 41+0 pregnancy weeks
2. Intact membranes before the induction of labor

Early-term and full-term parturition study arm:
1. Patients come to the delivery ward with contractions and intact membranes
2. Patients have 37+0-40+6 pregnancy weeks

Cesarean section study arm:
1. Patients are scheduled for an elective cesarean section
2. Patients have 37+0-40+6 pregnancy weeks on the scheduled cesarean section date

Previous participant inclusion criteria:
1. Female
2. Age 18 to 45

Further inclusion criteria for different study arms:

Post-term induction study arm:
1. Patients have more than 41+0 pregnancy weeks
2. Intact membranes before the induction of labor

Early-term and full-term parturition study arm:
1. Patients come to the delivery ward with contractions and intact membranes
2. Patients have 37+0-40+6 pregnancy weeks

Cesarean section study arm:
1. Patients are scheduled for an elective cesarean section
2. Patients have 37+0-40+6 pregnancy weeks on the scheduled cesarean section date

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
600

Key exclusion criteria
1. Breech presentation in vaginal delivery
2. Non-singleton pregnancy

Date of first enrolment
01/05/2017

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
Finland

Study participating centre
Helsinki University Central Hospital, Womens' Hospital
Finland
00290

Sponsor information

Organisation
Helsinki University Central Hospital

Sponsor details
Helsinki University Central Hospital (HUCH) Women's Hospital
Haartmaninkatu 2, PL 140
Helsinki
Finland
00029

Sponsor type

Hospital/treatment centre

ROR
https://ror.org/02e8hzf44

Funder(s)

Funder type
Government

Funder Name
Helsingin ja Uudenmaan Sairaanhoitopiiri

Alternative Name(s)
Helsinki University Central Hospital, HUS

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Finland

Funder Name
Helsingin Yliopisto

Alternative Name(s)
University of Helsinki, Helsingfors Universitet, Universitas Helsingiensis, HY, UH

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Finland

Results and Publications

Publication and dissemination plan

Planned publication in a peer reviewed scientific journal, first publication by the end of 2019. Results will also be disseminated as abstracts in related scientific conferences. Additional documents such as study protocol and statistical analysis plan are available upon request from the principal investigator, Dr Pekka Nieminen.

Intention to publish date
31/12/2021

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

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