

# Vaginal microbiome in late pregnancy and parturition

<b>Submission date</b> 14/06/2018	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 18/09/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 30/01/2023	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> 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:

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 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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## Contact information

### Type(s)

Scientific

### Contact name

Dr Pekka Nieminen

### Contact details

Helsinki University Central Hospital (HUCH) Women's Hospital

Haartmaninkatu 2

PL 140

Helsinki

Finland

00029

### Type(s)

Public

### Contact name

Dr Kaisa Kervinen

### Contact details

Helsinki University Central Hospital (HUCH) Womens Hospital

Haartmaninkatu 2

PL 140

Helsinki

Finland

00029

## Additional identifiers

### Protocol serial number

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

## **Study type(s)**

Diagnostic

## **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(s)

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.

## Key secondary outcome(s)

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.

## 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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

Female

**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

**ROR**

<https://ror.org/02e8hzhf44>

## Funder(s)

**Funder type**

Government

**Funder Name**

Helsingin ja Uudenmaan Sairaanhoidopiiri

**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

**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