Prospective follow up of the natural history of Inflammatory Bowel Disease during pregnancy

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- to analyze the changes in the gut microbiome of IBD patients during pregnancy and try to find an association with disease activity - to analyze whether changes in the gut microbiome remain after post partum period of 3 months-to analyze gut...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal conditions NEC
Study type	Observational invasive

Summary

ID

NL-OMON50661

Source
ToetsingOnline

Brief title
PROPRE study

Condition

- Gastrointestinal conditions NEC
- Maternal complications of pregnancy

Synonym
Crohn's Disease, ulcerative colitis

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Inflammatory Bowel Disease, Microbiota, Pregnancy, Pregnancy outcomes

Outcome measures

Primary outcome

- Gut microbiome before pregnancy, in the first, second and third trimester,

and at least three months after delivery

- Gut microbiome changes in children from IBD mothers in terms of diversity,

taxonomic changes and richness compared to a historical cohort

- Clinical activity scores (Harvey Bradshaw Index for CD and Simplified

Clinical Colitis Activity Index for UC)

Secondary outcome

- Gestational term (weeks)

- Birth weight (grams)

- Small for gestational age (=birth weight < 10th percentile for that

gestational term) (yes/no)

- Congenital abnormalities

- Mode of delivery (vaginal or caesarean section)

- Child health data

o Number of infections that required antibiotics

o Hospital admissions

o Growth

o Reactions to vaccinations

o Allergies

Study description

Background summary

Crohn*s disease and ulcerative colitis, collectively referred to as inflammatory bowel disease (IBD), are chronic, relapsing diseases. The exact etiology remains unknown, however, it is currently believed to be a complex interaction between genetic susceptibility, gut microbiota, the host immune response and environmental factors(1). IBD typically arises at a young, fertile age, as 50% of patients will be younger than 35 years old when the diagnosis is established(2). Therefore, reproductive issues are of important concern for both the IBD patients and their treating physicians. Preconception counseling in these patients remains challenging, as many complex questions can only be answered with limited, mainly retrospective and sometimes conflicting data. In addition, most of the (registry based) cohorts are outdated(3-10), not including the most recent therapies for IBD like anti-TNF, which have become a mainstay in IBD treatment over the last decade(11). Obviously, the need for an up-to-date, properly conducted, prospective cohort is long overdue. We therefore propose to conduct a prospective cohort study in IBD females with a pregnancy wish and pregnant IBD females, to gather data on IBD characteristics during pregnancy and the effect of pregnancy on IBD. Furthermore, as a recent study has shown pregnancy to influence gut microbiota in non IBD patients(12), we also propose to investigate whether the gut microbiome in IBD patients changes during pregnancy and whether these changes have any clinical implications. Studies have described an altered bacterial diversity in the gut of women with IBD as compared to healthy controls.(13, 14) Infants born to mothers with IBD have shown to have lower diversity and altered gut microbiome at least until age 3 months. (13) This might be important since prenatal and early life microbiome is thought to influence the development of the immune system.(13) Whether this altered gut microbiome remains in women after pregnancy and in infants beyond age 3 months is unclear. We will perform follow up on the gut microbiome of women who previously in the study participated and their children beyond 3 months of age.

Study objective

- to analyze the changes in the gut microbiome of IBD patients during pregnancy and try to find an association with disease activity
- to analyze whether changes in the gut microbiome remain after post partum period of 3 months
-to analyze gut microbiome of children born to mothers with IBD and to analyze whether lower diversity remains beyond age 3 months

Study design

A cohort study will be performed at the Erasmus Medical Center, Rotterdam, the Netherlands. Since 2008, as part of standard clinical care this tertiary referral center has set up a specialized preconception outpatient clinic (POC) for IBD patients (both male and female). This study will focus on the women exclusively.
All women between 18 and 43 years of age, with a confirmed diagnosis of IBD (CD, UC or IBD unclassified (IBDU) who visited this special outpatient clinic from January 2008 to July 2013 will be included for the retrospective part of this study, and from the approval of this protocol until 2018 (approximately 5 years) eligible IBD females visiting the POC will be included for prospective follow up.
At the POC, IBD women receive counseling on fertility, heredity of IBD, pregnancy, IBD medication use during pregnancy, mode of delivery, lactation and other life style factors. The POC is meant as an addition to routine obstetric-gynecologic visits and has been part of standard clinical care since 2008. After a first preconception visit, the women will be prospectively followed every three months. If a pregnancy occurs, she will return to this clinic every two months during the entire pregnancy. Follow up ends three months after delivery.
Since 2008, all data from the pre-conception outpatient clinic has been collected. For the retrospective part of this study, we propose to conduct a chart review and questionnaire-based study in all patients who have visited the pre-conception outpatient clinic, to gather information on patient characteristics, life style factors, medication use, disease course during pregnancy and pregnancy outcomes.
For the prospective part of this study, all eligible women will be asked to sign an informed consent to be followed up during pregnancy every two months and to donate fecal and blood samples before pregnancy, at each trimester during pregnancy and 3 months after delivery. Clinical disease activity scores (Harvey Bradshaw Index (HBI) for CD and Simplified Clinical Colitis Activity Index (SCCAI) for UC) will be obtained every two months during pregnancy and every three months before pregnancy and three months after delivery.
For the follow up part of the study, concerning the gut microbiome, women who previously visited the POC and participated in the original cohort study will be contacted and asked to donate a fecal sample of themselves and their children and fill out a questionnaire concerning the diet, medication and lifestyle of themselves and their child.

Study burden and risks

Participants will experience no direct benefit from participating in this study. The burden associated with participation is the donation of fecal samples (4 x combined with routine visits), donating extra vials of blood (4x 20 ml with routine bloodwork) and filling out a food and lifestyle questionnaire (2 x 15 minutes).
Extra blood will be collected at routine blood control visits during pregnancy (each trimester). No adverse events from drawing extra blood (20 ml) is to be

expected.
For the follow up part of the study women will be asked to donate a fecal sample of themselves and their child once and to fill out a food and lifestyle questionnaire for themselves and their child (2 x 15 minutes). A control group of healthy women with healthy children at the same age will be asked to donate a faecal sample of themselves and their child and fill out the same questionnaire as the IBD women. No extra blood will have to be drawn for the follow up part of the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

female

age 18-43
pregnancy (wish)
confirmed diagnosis of crohn's disease, ulcerative colitis, or IBDU (endooscopic/histopathologic)

Exclusion criteria

incapacity to understand informed consent
Infection with HIV, HBV or HCV
Diabetes mellitus
Substance abuse (hard drug use or alcoholism, less than 2 years clean)
other auto immune disease

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-04-2014
Enrollment:	270
Type:	Actual

Ethics review

Approved WMO

Date:	23-04-2014

Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-05-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 26221
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL47357.078.13
Other	NTR NL8418
OMON	NL-OMON26221