Decoding personalized nutritional, microbiome and host patterns impacting clinical and prognostic features in Crohn*s disease

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

Summary

ID

NL-OMON50993

Source
ToetsingOnline

Brief title
Nutri-IBD

Condition

- Gastrointestinal inflammatory conditions

Synonym
Crohns disease, inflammatory bowel disease

Research involving
Human

Sponsors and support

Primary sponsor: Weizzmann Institute of Science

Source(s) of monetary or material Support: Helmsley Charitable Trust foundation

Intervention

Keyword: Crohns disease, pediatric IBD

Outcome measures

Primary outcome

1. Collect an unprecedented number of clinical, microbiome, barrier function-related, inflammatory and metabolic measurements from a cohort of newly diagnosed pediatric CD patients followed for a period of 12 months.

2. Analyze this *big data* with an aim to utilize advanced artificial intelligence and machine-learning techniques to correlate multiple dietary, environmental, and microbiome features to disease severity scores, and metabolic (glycemic control) features in these patients.

3. Devise individualized machine learning algorithms aimed at harnessing personalized nutritional recommendations to improve individual inflammatory and metabolic features.

4. Validate these algorithms in a sub-cohort of newly diagnosed CD patients not involved in the initial machine learning *training* process.

Secondary outcome

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Study description

Background summary

Crohn's disease (CD) presents during childhood in 10-20% of cases and manifests in chronic relapsing debilitating symptoms. Compared with adults, pediatric CD

is more extensive and aggressive. It is believed to arise in genetically susceptible individuals via excessive intestinal immune-activation. The factors responsible for this uncontrolled immune-mediated inflammation are only partially understood, but perturbations of the gut microbiome are believed to be critically important. While the intestinal microbiota is specific to each individual and remains stable for long periods of time, systematic shifts in its composition and function have been observed in patients with CD, compared with healthy individuals1. Dietary and nutritional shifts have been convincingly shown to impact the composition and function of the microbiome. However a clear actionable link between nutrition, gut microbiome composition and function, features related to clinical manifestations and the severity of CD has not been comprehensively investigated. Of note, CD is often responsive to dietary intervention, namely exclusive enteral nutrition (EEN), which is considered the first-line therapy in pediatric CD flares2. EEN seems to be less efficacious in adults compared to children3. Although the mechanism of this response is unclear, changes in gut microbiota seem to parallel the clinical response4.

We have recently shown in the largest human cohort to date5,6 that utilizing advanced computational pipelines, such as machine learning techniques, enables us to correlate personalized dietary habits, the gut microbiome and individualized host outcomes, to post-prandial glycemic responses. Moreover, interventional trials utilizing these person-specific algorithms enabled to tailor unexpected dietary interventions that normalized glucose levels in pre-diabetic individuals, providing a proof of concept for the utility of unbiased integration of *big data* in reaching translational clinical applications.

In this large-scale multi-national study, we propose to utilize similar approaches to study nutritional responses in a cohort of newly diagnosed pediatric CD patients, with an aim to reach new levels of understanding on features related to individualized inflammatory and metabolic responses of CD patients to nutritional compounds. Moreover, we intend to collect multi-omic datasets to devise patient and/or patient subset-specific machine learning algorithms, enabling to individually employ defined and measurable nutritional interventions with an aim to integrate them into the therapeutic scheme as means of improving inflammatory and metabolic profiles in CD patients.

A key success criterion is to evaluate the likelihood to predict, based on modeling, why disease activity responds to a given dietary intervention in some individuals, whereas in others it does not. As such, we will (1) develop a dedicated bioinformatics pipeline that enables primary analysis and visualization of the data. (2) Correlates metagenomics data with dietary patterns to quantitatively describe how disease severity parameters respond to diet. (3) Uses integrative analysis to identify microbial species interactions and thereby identifies stable consortia of gut symbionts. (4) Develops a kinetic modelling framework that allows for the simulation of how different gut symbionts interact with each other, and with host immunity. Specifically, we will correlate metagenomics data with dietary patterns.

The dynamic nature of our model is capable of identifying nutrients and

subsequent diet-microbiome interactions that may favourably affect CD behavior and integrating multiple substrates in a complex environment, which is thus suitable for the investigation of the colon milieu.

Study objective

By means of this study we want to find out whether there are certain characteristics that can influence or predict the course of Crohn's disease. We want to do this by collecting data on diet, inflammation levels in the blood, complaints and the microbiome of children who have recently been diagnosed with Crohn's disease. With the use of artificial intelligence techniques, computers will be able to establish links between dietary patterns and inflammation levels in patients with Crohn's disease.

Study design

This is an international multi-center 3 arm study. The study will include 250 newly diagnosed pediatric CD patients. All of the 250 CD patients will be recruited in parallel. However part of the data collected will be used for the primary construction of the algorithmic setup while the other part will be used for corroboration of the personalized algorithms. We will also recruit 20 healthy controls, undergoing colonoscopy for non-specific abdominal pain and 30 non-invasively characterized healthy controls to enable the machine learning process to differentiate between normal and pathological signals.
Patients will be allocated, recruited and followed at several leading pediatric IBD centers around the world headed by the project leads.

Study burden and risks

The risk involved with drawing blood is minimal, and involves only mild discomfort. There are well-known risks associated with endoscopy, due to insertion and maneuvering of the endoscope. However, endoscopies will only be performed for medical indications and per recommendation of the patients' physician. No endoscopies will be performed solely for research purposes. We estimate the risk of additional biopsies for this study to be negligible, in light of the large body of research that has found no increased risk of significant bleeding or perforation. In addition, intestinal biopsies do not cause any discomfort or pain.
No risks to participants are involved in taking samples of stool.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Children with clinical suspicion for CD.
2. Between 6 and 18 years of age.
3. Naïve to any medical or nutritional intervention.

Exclusion criteria

1. Chronic treatment with any drug upon enrolment and the se of systemic antibiotics, probiotics or proton pump inhibitors during 30 days prior to enrollment.
2. Pregnancy in the last 6 months, breastfeeding.
3. Morbid obesity (BMI > 95th percentile for their age and gender).
4. Following particular dietary regimen/dietitian consultation/participation in another study.
5. Chronic use of steroids or immunomodulatory medications prior to CD diagnosis.
6. Any other chronic disease (e.g. HIV, Cushing disease, acromegaly,

hyperthyroidism, etc.), cancer and recent anti-cancer therapy, neuro-psychiatric disorders, coagulation disorders, celiac disease or any other chronic GI disorder.
7. Gut-related surgery, including bariatric surgery.
8. Inability of the participant and nuclear family to follow and utilize the smartphone application.

Study design

Design

Study type:	Observational non 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):	06-07-2023
Enrollment:	38
Type:	Actual

Ethics review

Approved WMO Date:	27-05-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam)

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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL77446.018.21