# Disease activity and iron status in children with inflammatory bowel disease

No registrations found.

| | |
|---|---|
| **Ethical review** | Positive opinion |
| **Status** | Pending |
| **Health condition type** | - |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON22615

**Source**
NTR

**Brief title**
DISIRO-IBD study

**Health condition**

English: Inflammatory bowel disease, Disease activity, Iron, Children

Dutch: Chronisch inflammatoire darmziekten, Ziekteactiviteit, IJzer, Kinderen

### Sponsors and support

**Primary sponsor:** Haga Teaching Hospital/Juliana Children's Hospital, The Hague
Els Borst-Eilersplein 275, 2545 AA The Hague, The Netherlands
Tel nr.: +31 (0)70 2100000
**Source(s) of monetary or material Support:** Haga Wetenschapsfonds

### Intervention

### Outcome measures

**Primary outcome**

Iron deficiency (ID): a combination of absolute and functional ID. Absolute ID: serum ferritin

(SF) <12 µg/l in patients <5 years of age and <15 µg/l in patients ≥5 years of age. This definition will be used in the absence of acute infection (i.e. CRP <10 mg/l). Functional ID: zinc protoporphyrin/heme ratio (ZnPP/H) >61 mmol/mol heme in patients <5 years of age and >70 mmol/mol heme in patients >5 years of age and/or red blood cell distribution width (RDW) >14 %. Functional ID will be determined in patients without absolute ID. The presence of disease activity will be determined based on FC-level. Active disease: FC-levels ≥250 µg/g, and No active disease: FC-levels <250 µg/g.

### Secondary outcome

Anemia will be defined as hemoglobin >2 standard deviations below the mean of similarly aged children according to criteria of the World Health Organization. Iron deficiency anemia (IDA) will be defined as absolute ID in combination with anemia. Anemia of chronic disease (ACD) will be defined as functional ID in combination with anemia. Vitamin D status will be based on 25[OH]D measurements. Vitamin D deficiency (VDD) will be defined as 25[OH]D <50 nmol/l (20 ng/ml).

## Study description

### Background summary

Background of study:

Children with inflammatory bowel disease (IBD) have an increased risk of developing iron deficiency (ID). Studies in children with IBD report prevalence rates of ID between 20% and 88%. However, studies reporting on ID in children are difficult to compare since different definitions, iron indices and cut-off values are used. ID in children with IBD can be an absolute or a functional deficiency, or both. Both types of ID represent two different forms of impaired iron homeostasis. Absolute ID refers to depleted iron stores due to insufficient dietary intake, iron malabsorption and/or (chronic) blood loss from the gastrointestinal tract due to (chronic) inflammation of the intestinal epithelium. Iron deficiency anemia (IDA) occurs when iron stores are exhausted and iron availability to the erythropoiesis is compromised. In functional ID pro-inflammatory cytokines, especially interleukin-6 (IL-6), induce changes in iron homeostasis by upregulating hepcidin expression. Hepcidin is a 25-amino-acid peptide hormone, primarily synthesized in the liver, that reduces iron efflux from enterocytes and macrophages, and hereby causing an increased uptake and retention of iron in strorage sites of the reticuloendothelial system. This leads to a limitation of the availability of iron for erythroid progenitor cells (iron-restricted erythropoiesis). Ultimately, this can lead to the so-called anemia of chronic disease (ACD). Regarding the pathophysiology of ID in children with IBD, we hypothesize that increased disease activity (i.e. more inflammation) is associated with an increased risk of developing ID. Furthermore, patients with IBD are at increased risk of vitamin D deficiency (VDD) compared to the general population, because of decreased nutrient intake or absorption and/or increased losses in stool. Studies in children and adolescents with IBD report prevalence rates of VDD between 6% and 62%. The co-existence

of VDD and ID has been described in several populations other than children with IBD. Several possible mechanisms have been proposed in order to explain this co-existence. However, data regarding the relation between vitamin D status and iron status in children with IBD are practically non-existent.

Objective of the study:

Primary Objective: To investigate the relationship between disease activity and iron deficiency (i.e. absolute and functional ID combined) in children with IBD. Secondary Objectives: 1.To establish the prevalence of iron deficiency (both absolute and functional) and anemia (IDA and ACD) in children with IBD. 2.To assess whether the following factors contribute to iron deficiency (both absolute and functional) and anemia (IDA and ACD) in children with IBD: Sex, Ethnicity, Parental educational level, Socioeconomic status (SES), Dietary iron intake, Menstrual cycle, Disease related factors: use and type of medication, duration of disease, IBD related surgery 3.To investigate the relationship between FC-levels and different iron parameters reflecting different aspects of iron homeostasis in children with IBD. 4. To investigate whether change in disease activity over time effects iron status in children with IBD. In order to do so, we will measure various parameters (i.e. SF, RDW, ZnPP/H and hepcidin) at inclusion (t=0) and after six months (t=after 6 months). 5.To establish the prevalence of vitamin D deficiency in children with IBD, and to investigate the relation between vitamin D status and iron status in children with IBD.

Study design:

We will conduct a multi-center prospective observational study.

Study population:

Children with IBD, up to 18 years years of age, will be recruited from the Haga Teaching Hospital/Juliana Children's Hospital in The Hague and from the University Medical Center Utrecht (UMCU)/Wilhelmina Children's Hospital in Utrecht, both in the Netherlands.

Primary and secondary parameters of the study:

Primary:

Iron deficiency (ID): a combination of absolute and functional ID. Absolute ID: serum ferritin (SF) <12 µg/l in patients <5 years of age and <15 µg/l in patients ≥5 years of age. This definition will be used in the absence of acute infection (i.e. CRP <10 mg/l). Functional ID:

zinc protoporphyrin/heme ratio (ZnPP/H) >61 mmol/mol heme in patients <5 years of age and >70 mmol/mol heme in patients >5 years of age and/or red blood cell distribution width (RDW) >14 %. Functional ID will be determined in patients without absolute ID. The presence of disease activity will be determined based on FC-level. Active disease: FC-levels ≥250 µg/g, and No active disease: FC-levels <250 µg/g.

Secondary:

Anemia will be defined as hemoglobin >2 standard deviations below the mean of similarly aged children according to criteria of the World Health Organization. Iron deficiency anemia (IDA) will be defined as absolute ID in combination with anemia. Anemia of chronic disease (ACD) will be defined as functional ID in combination with anemia. Vitamin D status will be based on 25[OH]D measurements. Vitamin D deficiency (VDD) will be defined as 25[OH]D <50 nmol/l (20 ng/ml).

### Study objective

We hypothesize that increased disease activity (i.e. more inflammation) is associated with an increased risk of developing ID.

### Study design

T0 (at inclusion); T1 (after 6 months)

### Intervention

None

## Contacts

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# Eligibility criteria

## Inclusion criteria

- Children up to18 years of age

- Diagnosis of IBD based on conventional endoscopic, histological and radiological criteria in accordance with the Porto-criteria

- Written informed consent from parent(s)/
guardian and children themselves if ≥12 years who are capable of a reasonable valuation of their interests pertinent to the situation.

- Parent(s)/guardian and pediatric IBD-patients understand the Dutch language

## Exclusion criteria

- Oncologic disorder

- Known hemoglobinopathies

- Congenital malformations

- Iron supplementation during the last 8 weeks

- Blood transfusion during the last 6 months

- Known liver disease

- Monogenic IBD

# Study design

## Design

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| Study type: | Observational non invasive |
| Intervention model: | Other |
| Masking: | Open (masking not used) |
| Control: | N/A , unknown |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-06-2018 |
| Enrollment: | 133 |
| Type: | Anticipated |

# Ethics review

Positive opinion

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|---|---|
| Date: | 21-05-2018 |
| Application type: | First submission |

# 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 |
|---|---|
| NTR-new | NL6436 |
| NTR-old | NTR7227 |
| Other | METC Zuidwest Holland : 18-024 |

# Study results