Cover page

The prevalence of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in patients suspected of hemorrhagic proctosigmoiditis (SOS Proctitis)

A quality improvement project in the Central Denmark Region

Clinical Trials Protocol

Version 1., April 1st, 2025

Background

Chlamydia trachomatis and *Neisseria gonorrhoeae* can cause infectious proctitis, which macroscopically cannot be distinguished from haemorrhagic proctosigmoiditis (HP) caused by chronic inflammatory bowel disease. In Denmark, general practitioners are advised to consider whether patients presenting with proctitis symptoms might have a sexually transmitted infection (STI). However, there is no requirement for STI testing before referring the patient to a specialised department. At specialised departments, it is not standard practice to systematically inquire about sexual risk behaviour or to test for *Chlamydia* and *Gonorrhoea*. As a result, there is no data on how many patients diagnosed with HP due to chronic inflammatory bowel disease who are also positive for an STI—either as the sole cause or as a contributing factor to their inflammation. *Chlamydia* and *Gonorrhoea* are the most common causes of symptomatic, sexually transmitted proctitis and are increasingly prevalent in Denmark.

Aims

We aim to investigate the proportion of patients with newly diagnosed proctosigmoiditis or treatment-refractory disease who have an underlying STI. Furthermore, we aim to determine whether the prevalence of STIs varies across sex or age groups while also investigating whether STIs are prevalent in both newly diagnosed patients and patients with refractory disease. We also aim to monitor the effect of antibiotic treatment on proctitis progression. The implications of these findings could help determine whether screening for these pathogens should be implemented as part of the standard diagnostic process for haemorrhagic proctosigmoiditis.

Materials and methods

Since diagnosing haemorrhagic proctosigmoiditis requires an endoscopy (sigmoidoscopy or colonoscopy), all newly diagnosed patients will undergo such an examination. Moreover, an endoscopy is often performed in individuals with refractory proctosigmoiditis. If inflammation is observed up to 35 cm from the anal opening, an additional swab will be taken during the procedure to test for *Chlamydia* and *Gonorrhoea* using standard PCR techniques. If the swab is not taken during the endoscopy, it will be collected during a follow-up outpatient visit. The tests will be analysed immediately at the Department of Microbiology, Aarhus University Hospital.

Over a 24-month period, we will examine all patients diagnosed with proctosigmoiditis at the Department of Liver, Digestive, and Gastrointestinal Diseases at Aarhus University Hospital (AUH), Viborg/Silkeborg Regional Hospital, Horsens Regional Hospital, Gødstrup Regional Hospital and Randers Regional Hospital. This includes patients with inflammation extending from the anal opening to 35 cm proximally, as well as those with treatment-refractory proctosigmoiditis. All patient data will be prospectively collected through Region Midt EPJ, Denmark's electronic medical record system, and registered in a REDCap database.

The tested patients will undergo standard follow-up at their respective departments. Supplementary, patients who test positive for *Chlamydia* or *Gonorrhoea* will be offered treatment at the Venereology Outpatient Clinic, Aarhus University Hospital. If they are only on 5-ASA treatment

and it is found reasonable to pause their treatment, their IBD treatment will be paused during treatment for STI.

The studied patients will form a prospective cohort, and their disease progression, including the extent of haemorrhagic proctitis and current medication, will be recorded.

Endpoints

Primary endpoint:

- Prevalence of Chlamydia and Gonorrhoea in our cohort of individuals with suspected haemorrhagic proctitis.

Secondary endpoints:

- Prevalence of Chlamydia and Gonorrhoea across gender
- Prevalence of Chlamydia and Gonorrhoea across age groups
- Prevalence of Chlamydia and Gonorrhoea depending on time for diagnosis
- Frequency of clinical remission of proctitis after treatment with STI-related antibiotics
- Differences in the frequency of clinical remission between those with a negative or positive STI test at inclusion

Statistical analysis

The statistical analyses will mainly be descriptive. For the primary and secondary outcomes, numbers with frequencies will be reported. Furthermore, appropriate statistical analyses will be applied to compare differences between those with a positive STI test and those with a negative test.
The data collection period runs from October 1, 2024 until September 30, 2026**.** We expect to include at least 100 patients in the cohort but aim towards at least 200 patients. After 100 patients have been tested, we will assess whether we should continue to screen patients. If no positive patients have been found, we will terminate the study prematurely. By September 2025, we will consider publishing the results if more than 5% of all patients examined are positive or if an isolated group has a more than 15% positivity percentage.

The results will be submitted for publication regardless of the outcome.

Ethical considerations

To assess whether screening for STI in patients suspected of HP should be mandatory, screening for STI in patients suspected of HP has become a recommended clinical procedure in Region Midt in the current study period. All patients will give oral consent to perform the swab during the endoscopy or in the outpatient ward. Local authorities have approved the collection of data for a quality improvement project.

Perspectives

If *Chlamydia* and *Gonorrhea* are found frequently, these results could indicate the necessity for integrating screening practices for all newly diagnosed HP patients and those with treatment-refractory disease.

If patients improve after pathogen-directed treatment and avoid treatment-refractory disease, there could be cost reduction if fewer biological therapies and ambulatory visits are required.