

Study Protocol and Statistical Analysis Plan

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A multicenter prospective observational study comparing the prevalence of renal dysfunction in adult patients with inflammatory bowel disease and the general population (NEPHRO-IBD Study)

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Background

Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, are chronic inflammatory disorders frequently associated with extraintestinal manifestations. Although musculoskeletal, dermatologic, and hepatobiliary manifestations are well recognized, renal involvement in IBD remains relatively underinvestigated.

Renal complications described in patients with IBD include nephrolithiasis, amyloidosis, tubulointerstitial nephritis, glomerulonephritis, and urothelial malignancies. Potential mechanisms include immune dysregulation, genetic susceptibility, environmental factors, and nephrotoxic effects of medications used in IBD treatment.

Recent studies indicate that patients with IBD may have an increased risk of chronic kidney disease (CKD) and acute kidney injury (AKI). However, prospective data evaluating the prevalence of renal dysfunction in this population remain limited.

Study Objectives

Primary Objective

- To determine the prevalence of renal dysfunction in adult patients with inflammatory bowel disease compared with individuals from the general population.

Secondary Objectives

- To evaluate the prevalence of albuminuria using urine albumin-to-creatinine ratio (ACR).
- To assess abnormal renal biochemical parameters.
- To evaluate structural abnormalities of the kidneys and urinary tract detected by ultrasound.
- To assess the association between renal dysfunction and inflammatory bowel disease activity.
- To evaluate the relationship between renal dysfunction and medications used in IBD treatment.

Study design

The NEPHRO-IBD study is a multicenter prospective observational cohort study conducted in gastroenterology centers in Poland.

The study will be conducted from October 15, 2025, to October 30, 2026.

Approximately 6,000 participants will be included:

3,000 patients with confirmed inflammatory bowel disease

3,000 individuals without IBD serving as a control group

Participants will undergo routine clinical evaluation at baseline and during follow-up visits performed at approximately three-month intervals, from baseline to six months.

The study has a multicenter design. In addition to our center, the following institutions will participate in the study:

- Department of Gastroenterology, Dietetics and Internal Medicine, Poznan University of Medical Sciences, Heliodor Świącicki University Hospital, Poznan, Poland
- Department of Gastroenterology and Eating Disorders, Nicolaus Copernicus University, Collegium Medicum, Bydgoszcz, Poland
- Department of General and Oncological Gastroenterology, N. Barlicki University Clinical Hospital, Lodz, Poland
- Department of Gastroenterology, Central Clinical Hospital, Medical University of Lodz, Lodz, Poland
- Department of Gastroenterology, Bielanski Hospital, Warsaw, Poland
- Department of Internal Medicine, Gastroenterology, Endocrinology and Diabetology, Cardinal Stefan Wyszyński Provincial Hospital, Lomza, Poland
- Department of Gastroenterology and Hepatology, Jagiellonian University Medical College, Krakow, Poland
- Department of Gastroenterology and Hepatology, Medical University of Silesia, Katowice, Poland
- Department of Gastroenterology, Endotherapy H-T Medical Center, Silesian Academy, Katowice, Poland
- Department of Gastroenterology and Internal Medicine, Military Institute of Medicine, Warsaw, Poland
- Department of Gastroenterology, Hepatology and Internal Medicine, University Clinical Hospital, Wroclaw, Poland

Study Procedures

The study will include the following assessments:

- demographic and clinical data collection
- medical history including comorbidities and medication use
- blood tests including biochemical and inflammatory markers
- urinalysis with measurement of urine albumin-to-creatinine ratio (ACR)
- abdominal ultrasound of the kidneys and urinary tract
- In patients with inflammatory bowel disease, disease activity will be assessed using validated clinical indices:
- Total Mayo Score for ulcerative colitis
- Crohn's Disease Activity Index (CDAI) for Crohn's disease
- Fecal calprotectin will also be measured as a marker of intestinal inflammation.

Statistical Analysis Plan

Statistical Methods

Statistical analyses will be performed using appropriate statistical software such as R, SPSS, or Stata. A two-sided p-value <0.05 will be considered statistically significant.

Descriptive Statistics

Baseline demographic and clinical characteristics will be summarized using descriptive statistics.

Continuous variables will be reported as mean \pm standard deviation or median with interquartile range depending on distribution.

Categorical variables will be presented as counts and percentages.

Primary Outcome Analysis

- The primary outcome is the prevalence of renal dysfunction in patients with inflammatory bowel disease compared with individuals without IBD.
- Renal dysfunction will be assessed using laboratory parameters including:
 - serum creatinine
 - urine albumin-to-creatinine ratio (ACR)
- Prevalence estimates will be presented with 95% confidence intervals.

Secondary Outcome Analysis

Secondary analyses will include:

- prevalence of albuminuria based on ACR values
- prevalence of abnormal renal biochemical parameters
- prevalence of structural abnormalities detected by abdominal ultrasound
- association between renal dysfunction and IBD disease activity
- association between renal dysfunction and medications used in IBD therapy

Comparative Analyses

- Comparisons between study groups will be performed using appropriate statistical tests:
 - Chi-square test or Fisher's exact test for categorical variables
 - Student's t-test for normally distributed continuous variables
 - Mann-Whitney U test for non-normally distributed variables
- Multivariable Analysis
 - Multivariable logistic regression may be performed to identify independent factors associated with renal dysfunction. Covariates may include age, sex, type of inflammatory bowel disease, disease activity, medication exposure, and comorbidities.

Data Management and Confidentiality

All study data will be anonymized before analysis. Data will be securely stored and used exclusively for scientific purposes.

Dissemination of Results

The results of the NEPHRO-IBD study will be published in peer-reviewed scientific journals and presented at international conferences related to gastroenterology and inflammatory bowel disease.

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