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Fecal Calprotectin, Serum Ferritin, and C-Reactive Protein Levels in Individuals with Inflammatory Bowel Disease Concomitant with Type 2 Diabetes: A Retrospective Study

ABSTRACT

Objective: The current study aims to conduct comparative analysis of C-reactive protein (CRP), serum ferritin (SF), and fecal calprotectin (CALP) levels in individuals presenting with both inflammatory bowel disease (IBD) and type 2 diabetes (T2D) in contrast to those with IBD without T2D.

Materials and methods: This retrospective analysis of a laboratory database included 2274 unique individuals diagnosed with IBD categorized into two cohorts: 2125 IBD patients without T2D, and 149 IBD patients with T2D. The differences between groups on a continuous measure were determined using non-parametric Mann-Whitney U test.

Results: The study involved 925 male and 1200 female IBD patients without T2D, with mean ages of 41.6 ± ± 15.1 years for males and 47.1 ± 17.4 years for females. The second cohort involved 51 males and 98 females with IBD and T2D, with mean ages of 58.1 ± ± 13.9 years for males and 64.2 ± 12.1 years for females. Individuals with comorbid IBD and T2D demonstrated elevated levels of CRP and SF compared to those affected by IBD without T2D, with statistical significance observed ($p < 0.05$). An increase in CALP values was found in females afflicted with both IBD and T2D when compared to individuals with IBD without comorbid T2D ($p < 0.01$); however, such an increase was not noted in males.

Conclusions: These findings underscore the need for further research on gender-specific differences and the potential presence of additional inflammatory conditions in individuals with IBD and T2D. (Clin Diabetol 2024; 13, 2: 106–115)

Keywords: type 2 diabetes (T2D), inflammatory bowel disease (IBD), comorbidities, C-reactive protein (CRP), ferritin, fecal calprotectin

Introduction

A recent Danish population-based cohort study revealed an increased risk of type 2 diabetes (T2D) development in individuals with both subtypes of inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), linked to prolonged intestinal inflammation [1]. It has also been suggested that there is a coexistence of IBD and T2D and that a potential link between these two conditions may arise due to dysbiosis of the gut microbiota, disruption of the epithelial barrier and inflammatory processes [2]. Another large IBD cohort study indicates a potential link between T2D in IBD and heightened severity of the disease, elevated utilization of 5-aminosalicylic

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acid (5-ASA), and increased instances of IBD-related hospitalizations [3].

Fecal calprotectin (CALP) is frequently employed to identify disease activity in IBD [4–6]; its elevated levels have also been seen in individuals with insulin resistance, as well as in individuals with other low-grade chronic inflammatory conditions such as obesity and T2D [7]. Nevertheless, to the best of our knowledge, a comparative analysis of CALP levels in patients with IBD, both with and without T2D, has not been conducted to date.

Routine monitoring of inflammatory biomarkers is recommended for the aforementioned health conditions, as their elevated levels may signal the activity and progression of disease in IBD [4, 9–10], along with potential complications linked to T2D [11]. CRP, a sensitive marker of inflammation, and ferritin, functioning as an iron storage protein and acute phase reactant during inflammation, are frequently elevated in both IBD and T2D [8, 12–14]. Serum ferritin (SF) has been noted as serving as an early indicator of atherosclerosis in a cohort of hypertensive patients with diverse levels of glucose tolerance [15]. An association was observed also between HbA1c and the levels of SF and CRP in individuals with T2D [16].

In light of the fact, that IBD occurs in episodes of inflammation in the gastrointestinal tract, varying in intensity and duration, interspersed with periods of remission [17, 18], whereas in T2D, inflammation tends to persist chronically and systemically, contributing to the development of lasting complications associated with diabetes [19]. Uncertainties persist regarding whether differences in the values of inflammatory biomarkers are discernible among individuals with IBD, with or without concomitant T2D.

Thus, the objective of this retrospective investigation was to conduct comparative analysis of CRP, SF, and CALP levels in individuals presenting with both IBD and T2D in contrast to those with IBD without T2D.

Materials and methods

Study design and participants

This retrospective analysis of a database contrasts laboratory findings between individuals diagnosed with IBD and comorbid T2D against those with IBD without T2D. The studied dataset, comprising laboratory tests and disease records, comes from Latvia's clinical laboratory, "E. Gulbis Laboratory" (EGL), situated in Riga, Latvia. EGL holds accreditation in accordance with international standards LVS EN ISO/IEC 17025 and LVS EN ISO 15189:2013, thereby ensuring the international recognition of their test results. Adherence to rigorous quality control protocols guarantees precise medical test results, mitigating measurement bias and ensuring measurement accuracy. All laboratory tests included in this study adhered to the respective analysis and reagent manufacturers' guidelines.

The laboratory has established branches and offers its services to healthcare providers and patients throughout all areas of Latvia, thereby mitigating the potential bias arising from patients selected from specific regions.

Data generation relied on the EGL database, which documents and stores clinical data obtained during patient laboratory visits. All patient data used in this study were subjected to de-identified measures to protect privacy.

Inclusion criteria

The study enrolled individuals aged 18 years and older who had been registered at the EGL laboratory over a five-year period, from January 1, 2015, to December 31, 2019, and who had been diagnosed with IBD. Diagnoses were identified using the International Classification of Diseases 10 (ICD-10) codes for Ulcerative Colitis (UC) (K51.XX) and Crohn's Disease (CD) (K50.XX). From the cohort of individuals diagnosed with IBD, a subset was identified comprising individuals concurrently diagnosed with T2D, as determined by the ICD-10 code E.11.XX. Accordingly, patients suffering from IBD were divided into two subgroups depending on the presence or absence of T2D.

To ensure the distinctiveness of each patient, a unique identification number was assigned to them during their initial visit to the EGL laboratory. This identifier remained unchanged for all subsequent analyses, facilitating the accurate tracking and differentiation of individual patients within the study.

Ethical approval

The study was designed in accordance with the principles enshrined in the Declaration of Helsinki and was approved by the Research Ethics Committee of the Institute of Cardiology and Regenerative Medicine of the University of Latvia. Patient consent was waived due to all patient data used in this study was anonymized before its use.

Data collection

Laboratory data [20] was extracted from database using specific criteria and filters. Initially, individuals aged 18 and above with IBD were identified within a 5-year timeframe, based on their registration and completion of laboratory blood tests. Each patient in the database was assigned a unique identifier during

their initial visit, ensuring anonymity while enabling continuous tracking across subsequent visits. The investigation focused on analyzing patient demographics (age, gender) and laboratory parameters CRP, SF, CALP. All specified laboratory tests conducted on these subgroups during the specified period were considered.

Statistical data analysis

The age of patient was expressed as a mean of ages recorded at the date of laboratory analysis and assigned to the determined age groups.

Descriptive statistics were described as number of patients for categorical parameters and mean (standard deviation; SD), 95% confidential intervals (95% CI) for distributed continuous parameters.

The Lilliefors test (a modified Kolmogorov-Smirnov test), an empirical distribution function (EDF) omnibus test for the composite hypothesis of normality [21], as well as visual informal assessment of normality methods (quantile-quantile plots, QQplot) were used to test for normality. Measurement data distributed in a non – normal manner was expressed as the median, Inter Quartile Range (IQR). Minimum required sample size to test difference between two groups was calculated by "pwrss" package for R [22]. The differences between two independent groups on a continuous measure were determined using non-parametric Mann-Whitney U test. A p-value of below 0.05 was considered statistically significant.

Tests wherein the outliers were detected and eliminated comprised values which lied outside the boxplot 25^{th} and 75^{th} percentiles multiplied by 1.5 range IQR (from 25^{th} percentile – 1.5* IQR to 75^{th} percentile + 1.5* IQR [23]. Data sets wherein outliers were eliminated did not pass any further modification and proceeded directly in tests.

The outcome of the Mann-Whitney test encompasses a standardized Z-score. Subsequently to the execution of the Mann-Whitney U test on the dataset, the Z-score was utilized for the computation of the correlation coefficient denoted as 'r.' The explication of the derived 'r' value aligns with the interpretation conventions applied to Pearson's correlation coefficient ('r') [24]. The r values were interpreted as follows 0.10–0.29 (small effect), 0.30–0.49 (moderate effect) and ≥ 0.50 (large effect).

Statistical analysis was conducted in R [25]. Figures and data were processed using R packages [26–28]. RStudio [29] was used for Integrated Development Environment for R.

Results

Subject characteristics

Among the 2274 unique individuals diagnosed with IBD, 149 had concomitant T2D. The average age varied between genders in the study, with female patients (n = 1298) having an average age of 48 years, while male patients (n = 976) had an average age of 42 years. A comprehensive delineation of age groups among enrolled patients with IBD, classified according to the presence or absence of T2D, is illustrated in Figure 1.

The study comprised 925 male and 1200 female IBD patients without T2D, with mean ages of 41.6 ± 15.1 years (95% CI, 40.60–42.55) for males and 47.1 ± 17.4 years (95% CI, 46.10–48.10) for females.

For IBD patients with T2D, 51 males and 98 females were included, with mean ages of 58.1 ± 13.9 years (95% CI, 54.21–62.06) for males and 64.2 ± 12.1 years (95% CI, 61.80–66.70) for females.

Comparison of serum C-reactive protein values between IBD patients with and without T2D

Regular CRP aids in identifying high-risk individuals and guiding appropriate interventions in IBD and T2D.

In this study, 27,102 CRP analyses were performed on a cohort of 2,126 unique patients diagnosed with IBD without T2D, and 2,862 CRP analyses were carried out on a subgroup of 149 unique IBD patients with concomitant T2D. Graphical representation of the statistics and detailed processed data is plotted in Figure 2.

Our study revealed a statistically significant difference in all CRP values between cohorts ($p < 0.05$), indicating higher CRP levels in patients with IBD and comorbid T2D compared to those with IBD without T2D, median [IQR] CRP 3.10 [1.00–8.88] and 1.50 [0.40–5.70] respectively. The difference persisted after adjusting for outliers, emphasizing higher CRP levels in IBD patients with T2D compared to those without T2D ($p < 0.01$).

A more detailed examination based on gender indicated that within a group of 1200 female patients diagnosed with IBD and without T2D, a total of 15,718 CRP analyses were conducted, yielding a median [IQR] of 1.50 [0.40–5.90]. In a distinct cohort of 98 females diagnosed with both IBD and T2D, a total of 1,797 CRP analyses were carried out, revealing a median [IQR] of 3.70 [1.50–9.20]. Despite small (0.16) effect size, there were significant differences in CRP values in females between IBD subgroups with and without T2D, with a p-value of < 0.01; 95% CI (–1.50; –1.20).

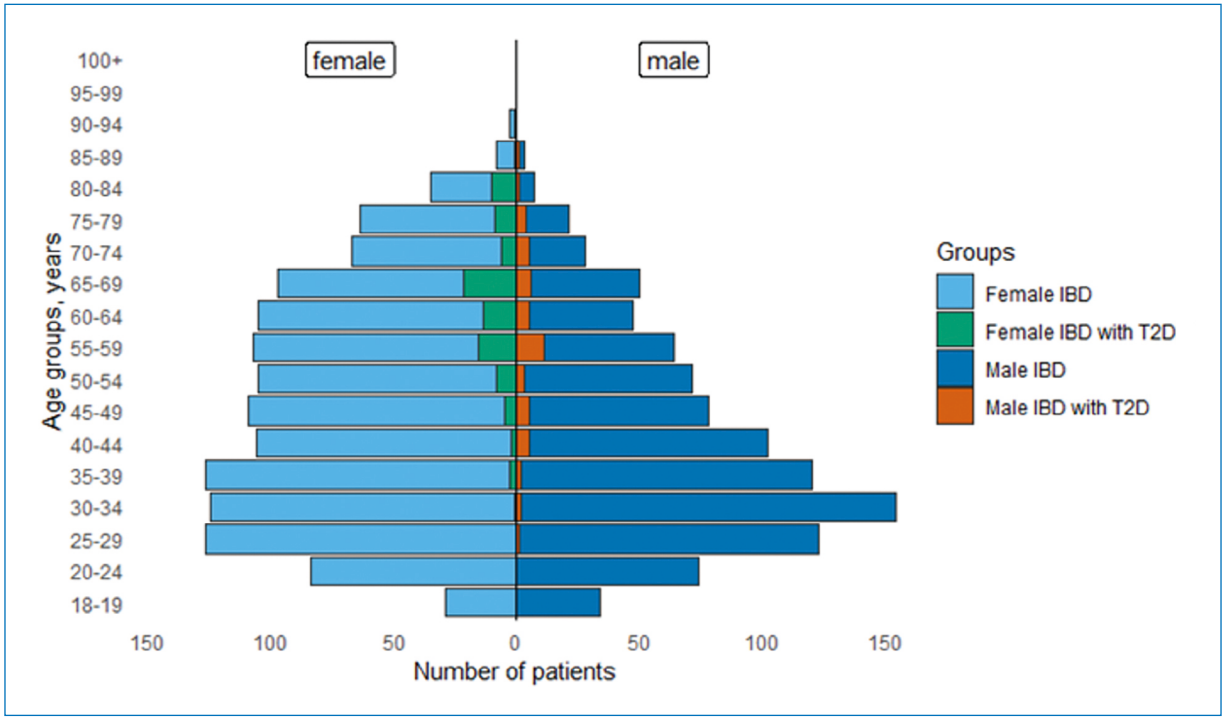

Figure 1. The Total Count of IBD Patients Included in the Study, Categorized Based on Age Groups (Years) and the Presence or Absence of T2D as a Comorbidity
IBD — inflammatory bowel disease; T2D — type 2 diabetes

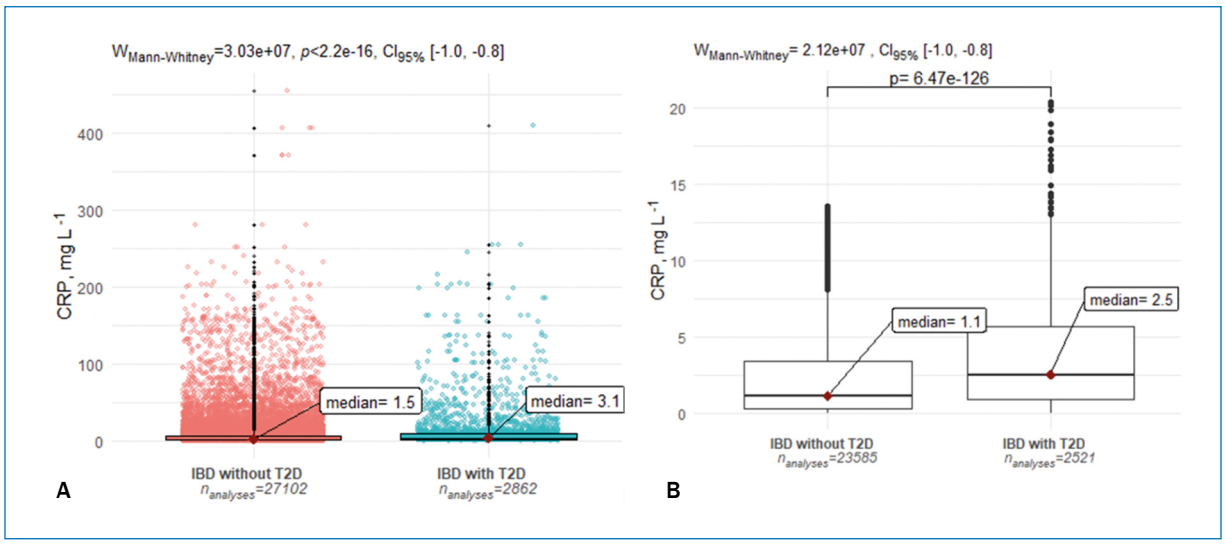

Figure 2. Comparison of Serum CRP Values in Patients with IBD Performed over 5-Year Period
The analysis compares two groups: IBD patients without T2D and IBD patients with T2D. The complete set of obtained CRP values, as shown in the color figure and the subset that underwent adjustment to exclude outliers, as shown in the black and white figure
CRP — C-reactive protein; CI — confidence interval; IBD — inflammatory bowel disease; T2D — type 2 diabetes

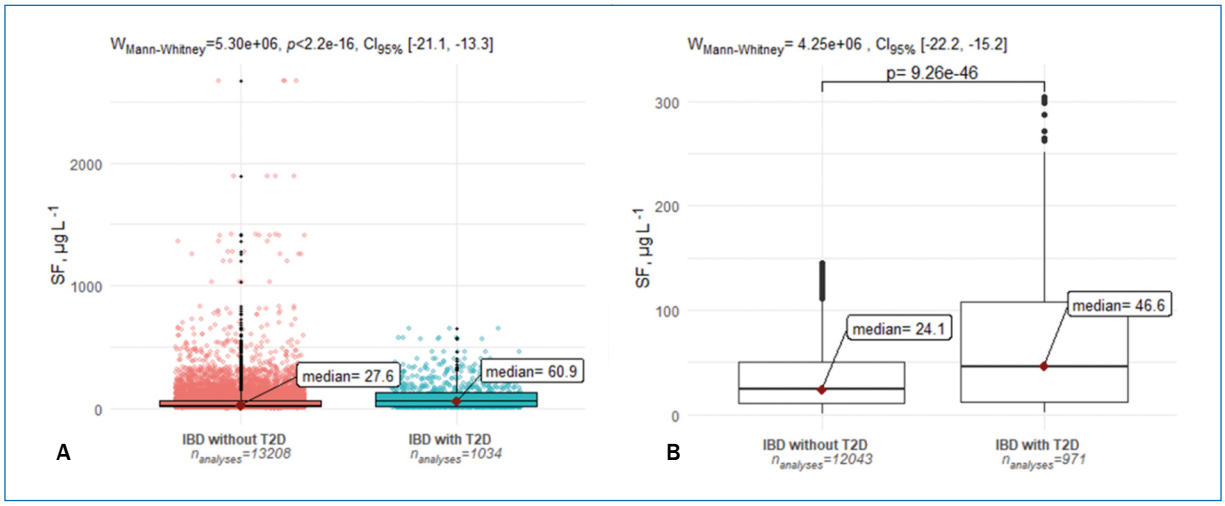

Figure 3. Comparison of SF Values in Patients with IBD Performed over 5-Year Period
The analysis compares two groups: IBD patients without T2D and IBD patients with T2D. The complete set of obtained CRP values, as shown in the color figure and the subset that underwent adjustment to exclude outliers, as shown in the black and white figure
CRP — C-reactive protein; CI — confidence interval; IBD — inflammatory bowel disease; SF —serum ferritin; T2D — type 2 diabetes

Similarly, in 925 male patients with IBD and without T2D, a total of 11 384 CRP analyses were conducted, with a median [IQR] of 1.50 [0.40–5.90]. Among 51 males with IBD and T2D, a total of 1065 CRP analyses were performed, yielding a median [IQR] of 2.00 [0.70–7.40]. Analogously to the observations in females, noteworthy distinctions in CRP values among males across IBD groups with and without T2D were identified, with a p-value of < 0.01 and a 95% CI of (–0.40; –0.10). The effect size was calculated to be 0.04, indicating a small magnitude of impact.

Comparison of serum ferritin values between IBD patients with and without T2D

Similar to the CRP analysis, an elevation in SF levels was observed among patients with IBD and comorbid T2D. The conducted investigation encompassed 13 208 observations within the cohort of 2125 distinct IBD patients without T2D, median [IQR] 27.60 [11.80–65.30]. In the subset of 149 unique patients with IBD and comorbid T2D, there were 1034 observations of SF, median [IQR] 60.90 [12.50–130.00]. Graphical representation of the statistics and detailed processed data is plotted in Figure 3.

Our investigation unveiled a statistically significant differences in all SF values across cohorts ($p < 0.01$), signifying elevated SF levels in individuals with both IBD and comorbid T2D in comparison to those diagnosed with IBD without T2D. This finding persisted after adjusting for outliers, emphasizing higher SF levels in IBD patients with T2D compared to those without T2D ($p < 0.005$).

A more thorough analysis focused on gender revealed that among a cohort of 1200 female IBD patients without T2D, a total of 9105 SF analyses were carried out, resulting in a median [IQR] of 22.40 [10.30–49.50]. In a distinct cohort of 98 females diagnosed with both IBD and T2D, 710 SF analyses were carried out, revealing a median [IQR] of 71.60 [15.43–142.75]. Despite small (0.15) effect size, there were significant differences in SF values in females between IBD subgroups with and without T2D, with a $p < 0.01$; 95% CI (–30.30; –21.20).

Similarly, within a subset of 925 male patients diagnosed with IBD without T2D, a comprehensive 4103 SF analyses were undertaken, revealing a median [IQR] of 47.30 [18.20–108.00]. Among 51 males with IBD and T2D, 324 SF analyses were performed, yielding a median [IQR] of 56.00 [11.40–107.00]. Analogously to the observations in females, noteworthy distinctions in SF values among males across IBD groups with and without T2D were identified, with a *p*-value of < 0.01 and a 95% CI of (–3.10; –5.40). The effect size was calculated to be 0.01, indicating a small magnitude of impact.

Comparison of fecal calprotectin values between IBD patients with and without T2D

For a more comprehensive examination of the inflammatory state among the studied IBD subgroups,

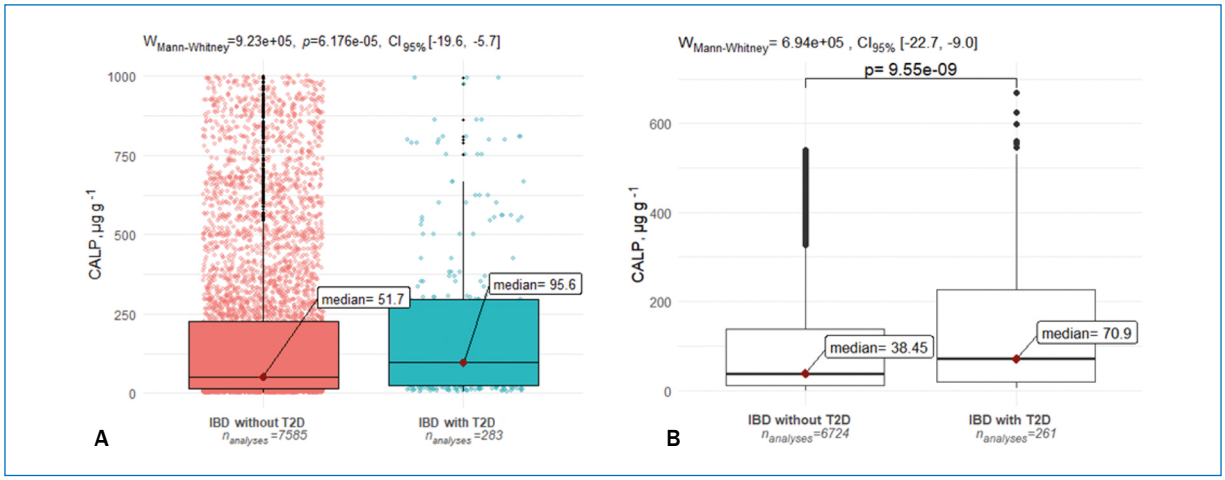

Figure 4. Comparison of Fecal Calprotectin (CALP) Values in Patients with IBD Performed over 5-Year Period
The analysis compares two groups: one comprising individuals diagnosed with IBD without T2D and the other consisting of individuals with IBD alongside T2D as a comorbidity. The complete set of obtained CALP values, as shown in the color figure and the subset that underwent adjustment to exclude outliers, as shown in the black and white figure
CI — confidence interval; IBD — inflammatory bowel disease; T2D — type 2 diabetes

we incorporated fecal CALP, a commonly utilized marker for assessing disease activity in individuals with IBD [5, 7].

In our investigation, elevated CALP levels were noted in individuals with IBD and comorbid T2D. The conducted investigation encompassed 7585 observations within the cohort of 2125 unique IBD patients without T2D, median [IQR] 51.70 [14.20–225.10] µg/g. In the subset of 149 unique patients with IBD and comorbid T2D, there were 283 observations of CALP, median [IQR] 95.60 [23.70–296.00] µg/g.

Graphical representation of the statistics and detailed processed data is plotted in Figure 4.

Our study revealed a statistically significant difference in CALP values between cohorts ($p < 0.005$), indicating higher CALP levels in patients with IBD and comorbid T2D compared to those with IBD alone. This finding persisted after adjusting for outliers, emphasizing higher CALP levels in IBD patients with T2D compared to those without T2D ($p < 0.05$).

A more detailed examination based on gender indicated that within a group of 1200 female patients diagnosed with IBD and without T2D, a total of 4103 CALP analyses were conducted, yielding a median [IQR] of 48.90 [13.90–233.00] µg/g. In a distinct cohort of 98 females diagnosed with IBD and T2D, 185 CALP analyses were carried out, revealing a median [IQR] of 167.30 [27.10–301.30] µg/g. Despite small (0.08) effect size, there were significant differences in CALP values in females between IBD subgroups with and without T2D, with a p-value of < 0.01; 95% CI (–56.50; –12.90).

Similarly, in 925 male patients with IBD and without T2D, 3482 CALP analyses were conducted, with a median [IQR] of 53.40 [14.63–220.00] µg/g. Among 51 males with IBD and T2D, a total of 98 CALP analyses were performed, yielding a median [IQR] of 36.90 [16.80–134.00] µg/g. Small effect size (0.003) was observed, and no statistically significant differences in CALP values among males were found between IBD subgroups with and without T2D, with a p-value of 0.85 and a 95% CI of (–6.30; 11.70).

Discussion

According to Latvian health statistics for 2022 [30], 92 187 residents, representing 4.9% of the population, were diagnosed with T2D. In our study, 6.6 % of patients with IBD had T2D as co-morbidity, which is 33% higher than the prevalence of T2D in the general population.

Although a recent study indicates that genetic predisposition to T2D is linked to a reduced likelihood of IBD [31], findings from a Danish nationwide cohort population study suggest an elevated susceptibility to T2D among individuals afflicted with both forms of IBD [1]. It is imperative not to overlook the potential negative impacts of T2D on IBD, as T2D in IBD may be associated with worse disease severity [3]. Hence, despite the absence of a genetic links between the two conditions, further investigations should delve into lifestyle factors, the impact of medications, the composition of intestinal microbiota, and other pertinent variables to elucidate their interplay in comorbid conditions.

The findings from our investigation indicate that 81% of females with IBD and comorbid T2D fall within the age range of 55–94 years, in contrast to only 34% of IBD females without T2D within the same age group. Likewise, among male individuals diagnosed with IBD and comorbid T2D, 65% were situated in the age category exceeding 55 years, contrasting with the inclusion of only 20% of IBD-afflicted female without T2D in the same age bracket. These results are consistent with the official statistical information reported by The Centre for Disease Prevention and Control of Latvia [30], where the prevalence data for T2D in 2022 revealed that 89% of T2D patients fall within the age category of 55 and older [30].

Our cohort of IBD patients with T2D had a limited representation of individuals below the age of 55. However, an alternative study indicates that in younger individuals with a relatively low risk of metabolic diseases, IBD significantly contributes to the pathogenesis of T2D, which underscores the importance of healthcare practitioners being vigilant for potential diabetes development in this population [32].

Our investigation provided a thorough comparative analysis of inflammatory biomarkers, including CRP, SF, and CALP, conducted over a 5-year period in patients with IBD.

Fecal CALP is commonly employed to assess disease activity in individuals with IBD [5]. An elevated CALP level surpassing 250 μg/g is associated with mucosal disease activity, while a threshold of 150 μg/g may prove beneficial in identifying individuals undergoing mucosal healing; conversely, a negative CALP value below 100 μg/g may suggest histological healing [6].

To our knowledge, there are no previous studies comparing the differences in CALP values between IBD people with and without T2D. Although the study results showed statistical differences in CALP values among study groups, a more detailed analysis by gender showed increased CALP values among female subjects with comorbid IBD and T2D, while no such increase was observed in male subgroup. The increased CALP levels in females with concurrent IBD and T2D may suggest a multifaceted origin related to intestinal inflammation and microbiota dysbiosis. A recent study [33], using a novel ex vivo assay demonstrated microbiome-dependent variations in calprotectin metabolism sensitive to amino acid levels. Further exploration into intestinal microbiota composition, its relationship with CALP levels, and the potential impact of gut microbiome on calprotectin metabolism could enhance our comprehension of these interconnections.

Furthermore, there is a need for scientific focus and additional investigations into CALP levels in females with T2D, particularly within the context of gynecological conditions like polycystic ovary syndrome (PCOS), which is recognized for its higher prevalence in individuals with T2D [34]. Consistent with earlier research, a strong correlation was observed between serum calprotectin and fecal calprotectin in individuals with IBD [35]. Studies on females with PCOS suggested that serum calprotectin might be a valuable diagnostic indicator, especially in cases linked to insulin resistance [36]. However, the relationship to fecal calprotectin remains uncertain, requiring additional investigations for a comprehensive understanding.

Our study findings indicated heightened CRP and SF values in IBD patients with comorbid T2D, $p < 0.05$. These results align with those of another large cohort study on IBD [3], wherein individuals with IBD and T2D exhibited increased occurrences of elevated C-reactive protein levels. In people diagnosed with T2D, CRP concentrations typically vary from 4.49 to 16.48 mg/L [37, 38]. In the context of our investigation, the median [IQR] CRP values in IBD patients with T2D were observed to be 3.10 [1.00–8.88] mg/L. CRP levels above 100 mg/L may suggest the presence of infection, rheumatologic diseases, malignancy and various inflammatory conditions, and multiple diagnoses [39]. For those experiencing acute systemic inflammatory response syndromes, the CRP levels can range much higher, reaching from 31.08 to 226.1 mg/L [37]. The latest cross-sectional analysis, conducted among adults aged 50 and above, revealed that individuals diagnosed with Metabolic Syndrome (MetS) exhibited a 34% higher probability of developing atherosclerotic cardiovascular disease (CVD) for every 1 mg/L increase in serum high sensitivity C-reactive protein levels [40]. MetS results from imbalances in calorie intake, energy expenditure, genetic/epigenetic factors, sedentary behavior, diet quality, and gut microbiome composition [41]. Thus, these factors might play a role in the increased CRP levels detected in our study's participants with both IBD and T2D, indicating a potential link with CVD. Consequently, further research investigating the concurrent factors that worsen the condition of IBD is warranted.

In our study, the SF median [IQR] values in patients with IBD, both with and without T2D, were observed to be 60.90 [12.50–130.00] and 27.60 [11.80–65.30] μg/L, respectively. Elevated levels of SF were observed in both male and female patients with IBD who also had comorbid T2D when compared to the IBD group without T2D. SF is a recognized acute-phase reactant, indicative of both acute and chronic inflammation in various systemic diseases [15]. Serving as a biomarker for disease progression, SF independently predicts

diverse clinical outcomes in different patient settings [15]. Moreover, an elevated SF levels, stemming from inflammation, may lead to misleading false-negative outcomes in the diagnosis of iron deficiency (ID), emphasizing the utility of incorporating CRP levels to discern individuals with concurrent inflammation [42].

Therefore, in patients with IBD, the diagnosis of ID is advised through the application of specific thresholds for SF and CRP, including SF threshold of < 30 μg/L in the absence of inflammation (CRP < 5mg/L), and SF threshold of < 100 μg/L in the presence of inflammation (CRP > 5mg/L) [4, 43]. However, SF thresholds to identify ID, iron overload, or low-grade inflammation in distinct subgroups of individuals with T2D remain uncertain [44].

Further research is warranted to explore the potential impact of probiotics, prebiotics, and synbiotics in regulating gut microbiota and their potential implications for inflammation, particularly in comorbid conditions such as IBD and T2D.

Clinical implications and future research directions

The clinical implications derived from the findings of this preliminary investigation suggest that individuals concurrently affected by IBD and T2D tend to exhibit elevated levels of inflammatory biomarkers compared to those solely affected by IBD without comorbid T2D. These findings underscore the necessity for additional prospective studies aimed at investigating gender-specific variances and potential concurrent inflammatory conditions that could exacerbate IBD. Furthermore, the findings underscore the necessity for developing inflammation management strategies tailored to individuals with concurrent conditions such as IBD and T2D. Such strategies should consider the unique physiological and inflammatory profiles of patients with comorbidities to optimize their clinical care and outcomes.

Study limitations

Our study has its limitations, mostly due its retrospective character of analysis. This study was conducted in a single medical laboratory, so analyzes of general data and laboratory tests specific to hospitalized patients with severe illness, complications such as blood loss, or recent surgeries are not available.

There was no possibility to obtain some missing information, such as duration of illness or medications used. The assignment of IBD and T2D diagnoses in the laboratory database was based on ICD-10 codes provided by referring physicians for laboratory tests, but the confirmation of IBD diagnoses through endoscopies or radiological examinations is unknown.

The study findings indicate small effect sizes, which, for clinical significance, warrant validation through additional prospective studies before strong definitive conclusions can be drawn regarding their application in clinical practice.

Despite the retrospective design limitations, our study's strengths lie in the robustness of the biomedical test data sourced from Latvia's largest accredited laboratory, which maintains branches across all regions of the country. Adherence to stringent quality control measures makes it possible to compare this laboratory data with results from other tests and laboratories.

Further studies, employing precise patient selection and subgrouping individuals into categories such as those with Crohn's disease and ulcerative colitis, along with a separate group of patients with T2D without IBD, would be beneficial for understanding baseline variations in biomarkers attributable to each condition independently.

Conclusions

The results obtained from the present preliminary investigation indicate that individuals with comorbidities, such as IBD and T2D exhibit heightened levels of CRP, SF, when compared to individuals affected by IBD without comorbid T2D. An increase in CALP values was identified in females afflicted with both IBD and T2D when compared to individuals with IBD without comorbid T2D; however, such an increase was not noted in males. The potential for worsening inflammatory status in IBD when coexisting with T2D requires consideration, and individualized approach. These findings underscore the need for further prospective studies on gender-specific differences and the potential presence of additional inflammatory conditions, as well as the development of inflammation management strategies for individuals with comorbidities such as IBD and T2D.

Article information

Data availability statement

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Research Ethics Committee of the Institute of Cardiology and Regenerative Medicine of the University of Latvia (LU KRMI ZP sēde 17.11.2020). Ethical review and approval were waived for this study because all patient data used in this study were subjected to pseudo-depersonalization measures to protect privacy. Patient consent

was waived because all patient data used in this study were subjected to pseudo-depersonalization measures to protect privacy.

Author contributions

Conceptualization, V.S and D.G.; methodology, V.S.; software, V.S. and D.G. validation, V.S., D.G. and R.L.; formal analysis, V.S.; investigation, V.S.; data curation, D.G.; writing — original draft preparation, V.S.; writing — review and editing, D.G.,R.L.; visualization, V.S.; supervision, D.G.,R.L. All authors have read and agreed to the published version of the manuscript.

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Conflicts of interest

The authors declare no conflict of interest.

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