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A decade of inflammatory bowel disease: Insights from a tertiary referral center in Bulgaria

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Abstract

Introduction: In Bulgaria, the absence of comprehensive national data poses challenges for both clinicians and healthcare authorities.

Objectives: The aim of this retrospective study was to analyze the epidemiological characteristics of inflammatory bowel disease (IBD) over a 10-year period at a leading university referral center serving the northeastern, north-central, and southeastern regions of Bulgaria.

Methods: A total of 722 adult patients aged 18–75 years were included in the cohort. All patients were treated over a 10-year period at the Referral IBD Center of the Clinic of Gastroenterology, University Multiprofile Hospital for Active Treatment "St. Marina," Varna, Bulgaria.

Results: In the northeastern region of Bulgaria, the mean annual crude incidence was 1.72 per 100,000 population, and the mean annual crude prevalence during 2013–2022 was 13.86 per 100,000. In the north-central region of Bulgaria, the mean annual crude incidence was estimated at 0.41 per 100,000 population, and the mean annual crude prevalence during 2013–2022 was 3.12 per 100,000 population. In the southeastern region of Bulgaria, the mean annual crude incidence was 0.15 per 100,000 population. During the 2013–2022 period, the annual prevalence in this region ranged from 0.95 to 1.90 per 100,000 population.

Conclusion: The results of the present study indicate a consistent trend of increasing incidence of IBD, which is likely due both to a genuine rise in disease prevalence and to advancements in diagnostic technologies. This study provides valuable data on the epidemiology of IBD for the first time in Bulgaria.

Keywords: Inflammatory bowel disease; Incidence; Prevalence; Bulgaria

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1. Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease and ulcerative colitis, refers to chronic, relapsing, and disabling gastrointestinal disorders of unknown etiology that profoundly affect every aspect of patients' lives.[1-3] Over the past decades, epidemiological studies have demonstrated a steady rise in the incidence and prevalence of IBD across Europe, with an estimated 2.5 to 3 million individuals currently affected.[4-8] This growing burden highlights the importance of understanding regional disease

patterns, as epidemiological trends often provide critical insights into environmental, genetic, and socioeconomic factors that may contribute to disease development.[7,8]

Geographically, IBD prevalence follows a well-recognized North–South gradient and, to a lesser extent, a West–East gradient across Europe.[9–14] These gradients suggest that environmental exposures, lifestyle factors, and healthcare system characteristics may play a substantial role in shaping disease distribution. In recent years, however, several Eastern European countries have reported a marked increase in newly diagnosed IBD cases, indicating that the region may be undergoing the "third epidemiological stage" of IBD evolution—transitioning from low to rapidly rising incidence.[11,13,14]

In Bulgaria, the absence of comprehensive national epidemiological data poses significant challenges for clinicians, researchers, and healthcare authorities. Current knowledge is limited to isolated single-center observations, which do not adequately reflect regional differences or national trends.

Understanding the epidemiology of IBD across diverse geographic regions is essential not only for identifying high-risk populations but also for uncovering key environmental and socioeconomic determinants that shape disease patterns.

Given the increasing incidence of IBD reported across Eastern Europe, more comprehensive and region-specific epidemiological research is needed to better understand disease trends, identify potential risk factors, and assess public health implications across the region.[5,11,12,15]

This study aims to retrospectively examine the epidemiological features of IBD over a 10-year period at a leading university referral center that provides specialized care for patients from the northeastern, north-central, and southeastern regions of Bulgaria. The study also seeks to identify potential regional differences in disease distribution that may reflect variations in environmental exposures, healthcare access, or diagnostic practices.

2. Patient data and methods

2.1. Study design and setting

This study was a descriptive, retrospective, hospital-based epidemiological analysis conducted at a tertiary IBD center in northeastern Bulgaria, which serves the northeastern, north-central, and southeastern regions of the country. Importantly, during the study period, this was the sole tertiary IBD center available for these regions, making it the primary referral point for all patients requiring specialized care.

2.2. Participants

All patients included in the study were diagnosed with either ulcerative colitis or Crohn's disease based on the 2006 Montreal classification system, and fulfilled clinical, endoscopic, radiological, and histopathological criteria in accordance with the European Crohn's and Colitis Organisation guidelines from 2008 and 2010, depending on the time of inclusion.

A total of 722 IBD patients (aged 18–75 years; 360 males and 362 females) were included in the cohort. All patients were treated over a 10-year period (2013–2022) at the Referral IBD Center of the Clinic of Gastroenterology, University Multiprofile Hospital for Active Treatment "St. Marina," Varna, Bulgaria.

Data on patients, medical history, number of hospitalizations, and demographic characteristics were retrieved from the hospital's electronic medical records system.

Demographic data for the adult population (aged ≥ 18 years) in the studied region between 2013 and 2022 were obtained from the Bulgarian National Statistical Institute, based on official national census data for the corresponding years.

Based on the available data, we determined the crude incidence and prevalence rates of IBD across three distinct geographic regions—northeastern, north-central, and southeastern Bulgaria—reflecting the catchment area of the referral center.

2.3. Inclusion criteria

Patients aged 18 years and older with a confirmed diagnosis of IBD, including both newly diagnosed and previously known cases.

2.4. Exclusion criteria

Patients younger than 18 years were excluded, as were patients diagnosed with irritable bowel syndrome or non-IBD colitis, including infectious, microscopic, ischemic, and radiation colitis.

2.5. Ethical considerations

The study was conducted in full compliance with the applicable ethical standards and regulatory requirements to ensure the safety, rights, and well-being of all participants. It adhered to the principles outlined in the Declaration of Helsinki. All data were collected in an anonymized format, without the inclusion of any personal or identifiable information. The study protocol was reviewed and approved by the Ethics Committee at the

Medical University of Varna, Bulgaria (approval number: 58/01.12.2016).

2.6. Statistical analysis

A combined statistical approach was employed in the present epidemiological study to assess changes in disease incidence over time. Both parametric and non-parametric methods were applied to ensure robust and reliable results. Core epidemiological indicators—including incidence and prevalence—were calculated to quantitatively evaluate the frequency and distribution of diseases within the studied region.

To compare mean values across years, a one-way analysis of variance was used. Due to deviations from normality in the data distribution, the non-parametric Kruskal–Wallis test was additionally applied. To identify specific year pairs with the most significant differences, a post-hoc analysis using Tukey's test was conducted. Furthermore, the chi-square test (χ^2) was used to assess the frequency distribution of cases across years, confirming statistically significant temporal changes.

To evaluate differences between specific time periods and population subgroups, additional inferential tests were applied, including the independent samples *Z*-test, Fisher's exact test, and Poisson regression modeling. For all inferential analyses, 95% confidence intervals (CIs) were calculated, and statistical significance was determined at a *p*-value threshold of <0.05. All analyses were performed at a significance level of $\alpha = 0.05$ using IBM SPSS Statistics (Version 21.0.2.3.2, United States of America).

3. Results

Over the course of the 10-year observation period, 722 individuals diagnosed with IBD received care at the Department of Gastroenterology, University Hospital for Active Treatment "St. Marina," Varna, Bulgaria.

The study population included residents from the north-central, northeastern, and southeastern regions of Bulgaria, offering a broad geographic representation. This diversity provides valuable insight into potential regional differences in disease incidence and prevalence.

3.1. Northeastern region of Bulgaria

Over the 10-year study period, a total of 558 individual IBD patients were identified and managed at our tertiary referral center serving northeastern Bulgaria. However, the cumulative number of recorded cases during this timeframe reached 1,280, as many patients required repeated hospitalizations across multiple years.

The annual distribution of cases demonstrated a gradual upward trend in the number of patients recorded each calendar year.

Over the 10-year study period, a total of 149 newly diagnosed IBD cases were registered, with annual crude incidence rates ranging from 0.94 cases per 100,000 population (95% CI: 0.33–1.55) in 2013 to 2.79 cases per 100,000 population (95% CI: 1.68–3.90) in 2022. This trend was statistically significant ($p < 0.01$) (Figure 1).

Across the study area, the mean annual crude incidence reached 1.72 cases per 100,000 population (95% CI: 0.87–2.57).

A gradual increase in incidence was observed, with the highest rates reported during the final years of the study period — particularly in 2019 and 2022.

The average annual number of new cases during the 2013–2022 period was 15.9. The year-by-year distribution of newly diagnosed cases is presented in Figure 2.

The mean annual crude prevalence for the period 2013–2022 was 13.86 cases per 100,000 population (95% CI: 13.62–14.10).

During the period 2013–2022, a statistically significant increase in IBD prevalence per 100,000 population was observed.

The annual crude prevalence ranged from 9.53 cases per 100,000 population (95% CI: 7.63–11.43) in 2013 to 22.59 cases per 100,000 population (95% CI: 19.62–26.14) in 2022 ($p < 0.001$) (Figure 1).

Over a 10-year period, there were 1,023 patient cases from urban areas—approximately four times more than the 257 cases from rural areas.

During the observation period, the mean annual crude prevalence was 15.08 cases per 100,000 population (95% CI: 12.17–17.99) in urban areas and 10.49 cases per 100,000 population (95% CI: 6.53–14.46) in rural areas. By 2022, prevalence increased to 23.26 per 100,000 (95% CI: 19.60–26.91) in urban populations and to 20.57 per 100,000 (95% CI: 14.58–26.55) in rural populations (Figure 3).

During the 2013–2022 period, the annual crude prevalence was higher in urban areas compared to rural ones, with a clear upward trend observed in both types of settlements.

Statistical analysis using the z-test revealed that the difference in the mean annual crude prevalence of the disease between urban (15.08/100,000) and rural (10.49/100,000) areas during the 2013–2022 period was statistically significant ($Z = 2.52$; $p = 0.012$). This finding supports the hypothesis that the urban population is at a higher risk of developing the disease compared to the rural

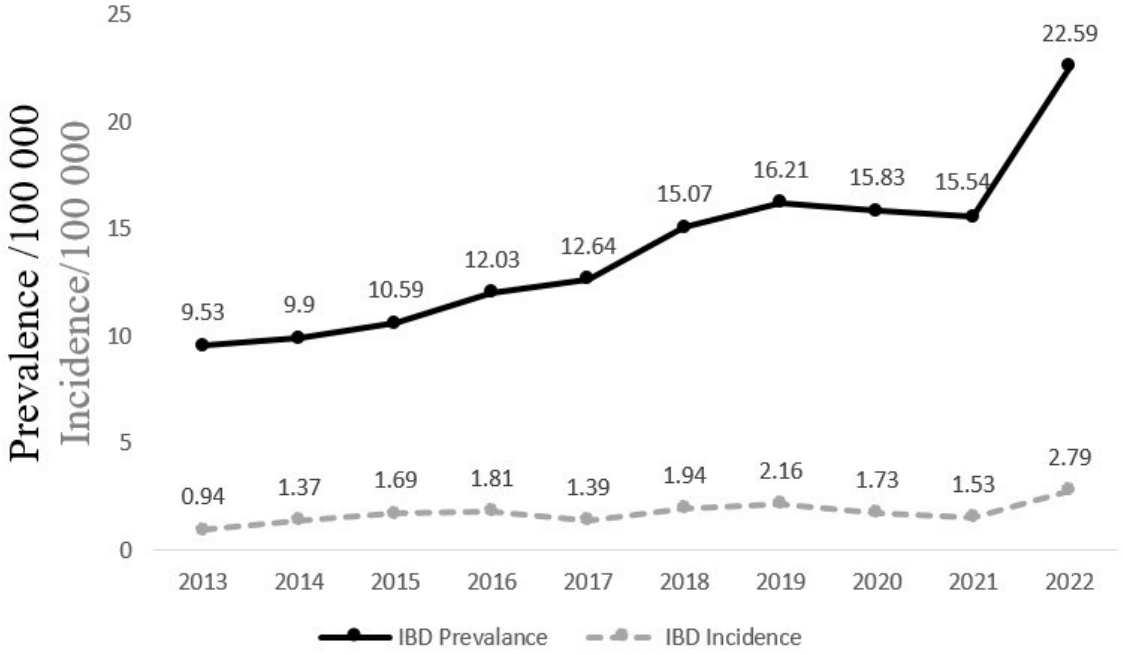

Figure 1. Crude incidence and prevalence of inflammatory bowel disease (IBD) for a 10-year period in the northeastern region of Bulgaria

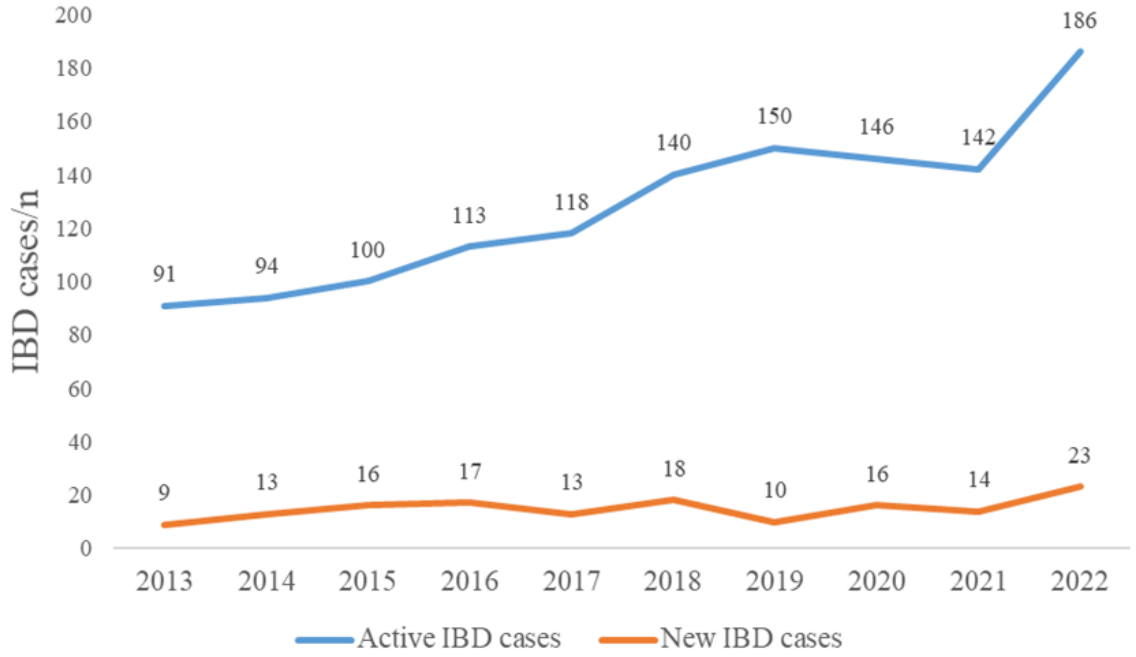

Figure 2. Annual number of active and newly diagnosed inflammatory bowel disease (IBD) cases during the 2013–2022 period in the northeastern region of Bulgaria

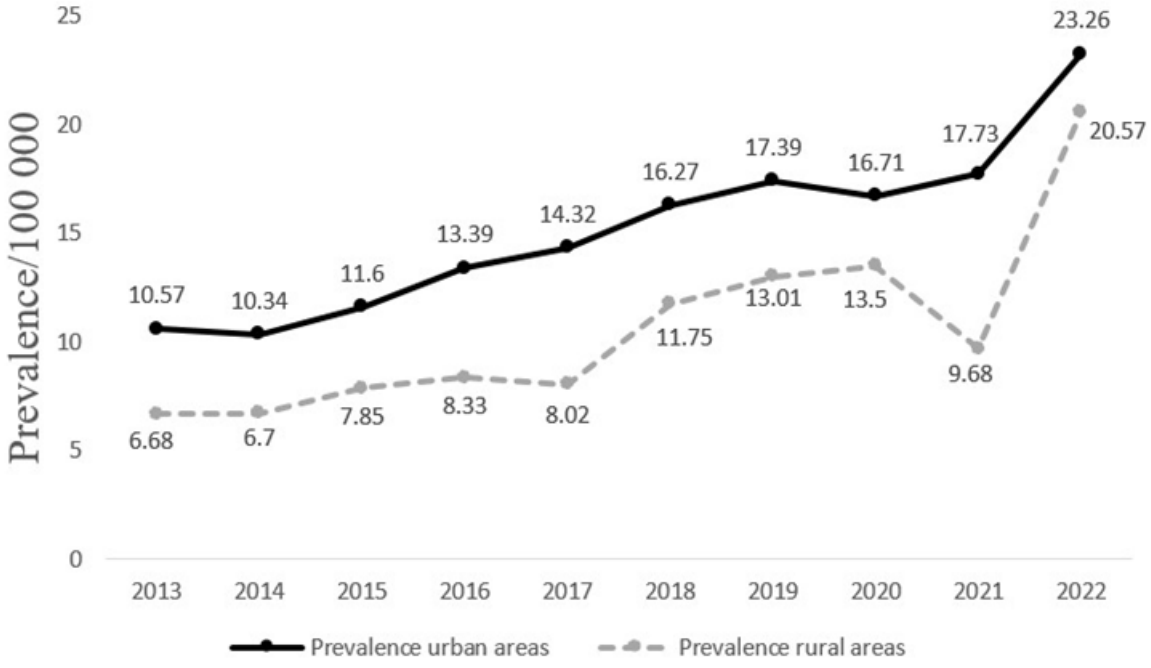

Figure 3. Annual trend of crude prevalence in urban and rural areas during the 2013–2022 period in the northeastern region of Bulgaria

population.

There was no statistically significant difference in the gender distribution among the study population ($p > 0.05$).

The mean annual crude prevalence among men during the 2013–2022 period was 13.71 cases per 100,000 population (95% CI: 12.70–14.75). Among women, the mean annual crude prevalence was 13.59 cases per 100,000 population (95% CI: 12.64–14.57), with no statistically significant difference observed ($p > 0.05$).

3.2. North-central region of Bulgaria

Between 2013 and 2022, 240 IBD-related records were identified among 96 individual patients treated at the Gastroenterology Clinic.

The mean annual crude incidence was estimated at 0.41 cases per 100,000 population (95% CI: 0.28–0.54), based on data from 32 newly diagnosed patients and a cumulative population of 7,690,373 individuals.

Year-by-year analysis of crude incidence using the χ^2 test did not reveal any statistically significant differences between individual years ($p > 0.05$), suggesting the presence of random fluctuations. A comparative analysis between the periods 2013–2017 and 2018–2022 indicated a slight increase in incidence (0.37 vs. 0.45 cases per 100,000 population); however, the results of the Z-test ($Z = -0.74$; $p = 0.459$) did not support the presence of a statistically significant difference.

Across the years 2013–2022, the mean yearly crude prevalence of IBD reached 3.12/ 100,000 (95% CI: 1.87–4.37). The data demonstrated a statistically significant rise over time, corresponding to an average annual growth of 0.24 cases per 100,000 population (Figure 4).

A comparative analysis between the periods 2013–2017 and 2018–2022 revealed a statistically significant difference in disease prevalence ($p < 0.05$). The second period showed a higher crude prevalence rate (3.65/100,000) than the first period (2.65/100,000), indicating an upward trend in recorded disease burden.

Of the 96 individual patients diagnosed with IBD, 142 cases were registered in urban areas and 98 in rural areas.

The mean annual crude incidence of IBD in urban areas was 0.43 cases per 100,000 population (95% CI: 0.25–0.61). No statistically significant temporal change was observed ($p > 0.05$), despite year-to-year fluctuations such as 0.00 in 2014 and a peak of 0.95 in 2018. A comparison of IBD incidence between the periods 2013–2017 and 2018–2022 in urban areas revealed a relative increase of 31%; however, the difference was not statistically significant ($p > 0.05$).

In rural areas, the mean annual crude incidence of IBD during the study period was 0.31 cases per 100,000 population (95% CI: 0.10–0.52). Although fluctuations were observed—including a peak of 1.18/100,000 in 2021—no statistically significant differences in incidence were detected across individual years ($p > 0.05$).

Furthermore, the crude incidence of IBD in rural areas showed a nearly 80% relative increase between the periods 2013–2017 and 2018–2022 (from 0.22 to 0.40 cases per 100,000). However, Poisson regression did not show a statistically significant difference between the two periods ($p > 0.05$).

The mean annual crude prevalence of IBD in urban areas was 3.02 cases per 100,000 population (95% CI: 1.50–4.54).

The lowest prevalence was observed in 2014 (1.45/100,000), while the highest was recorded in 2018 (3.79/100,000), representing more than a 2.5-fold increase. Statistical analysis revealed significant differences between certain years—particularly between the lowest (2013–2014), with prevalence rates of 1.97 and 1.45 cases per 100,000 population, respectively, and the highest (2018–2022), ranging from 3.79 (2018) to 3.28 (2022) cases per 100,000 population (Figure 5).

The average annual crude prevalence of IBD in rural areas was 3.83 cases per 100,000 population (95% CI: 1.46–6.20).

The lowest prevalence was observed in 2014, at 1.83 cases per 100,000 population, while the highest was recorded in 2022, reaching 6.99 cases per 100,000 population. This represents more than a 3.8-fold increase compared to the lowest value during the period (Figure 5).

Statistically significant differences were identified between individual years, particularly between the early years with lower prevalence rates (2013–2014), recorded at 2.53 and 1.83 cases per 100,000 population, respectively, and the later years with higher rates (2019–2022), ranging from 4.34 to 6.99 cases per 100,000 population.

Rural areas demonstrated a significantly higher crude prevalence of IBD, with an average of 3.83 cases per 100,000 population, compared to 3.02 cases per 100,000 population in urban areas ($p < 0.05$) during the 2013–2022 period.

Of the 240 recorded IBD cases during the 10-year observation period, 133 were recorded among females and 107 among males.

Among males, the mean annual crude prevalence was 2.81 cases per 100,000 population (95% CI: 1.39–4.23), with annual variation ranging from 0.98 to 5.18 cases per 100,000 population. Although an upward trend was noted toward the end of the study period, this increase was not statistically significant ($p > 0.05$).

The mean annual crude prevalence of IBD among females was 3.64 cases per 100,000 population (95% CI: 1.69–5.59), with no statistically significant differences observed across individual years.

Annual data analysis revealed notable fluctuations in case numbers, including years with no reported diagnoses. Despite these fluctuations, no statistically significant differences were observed either across individual years or between gender groups, indicating stability in disease dynamics and gender-related distribution.

3.3. Southeastern region of Bulgaria

In the southeastern region of Bulgaria, 142 IBD-related records were identified among 68 individual patients.

The mean annual crude incidence was 0.15 cases per 100,000 population (95% CI: 0.012–0.288). Over the entire 10-year period, a total of 15 newly diagnosed cases were registered in the region, with cases recorded in only 3 out of the 10 years. The highest incidence was recorded in 2020—0.98 cases per 100,000 population—while values in the remaining years ranged from 0.00 to 0.29 cases per 100,000 population.

Regarding incidence, only two new cases were identified during the 2013–2017 period (0.038/100,000; 95% CI: 0.003–0.138), compared to 13 new cases registered in 2018–2022 (0.258/100,000; 95% CI: 0.074–0.451). Fisher's exact test indicated a statistically significant increase in incidence during the latter period ($p < 0.01$). These findings suggest that while IBD maintains a low overall frequency in the studied region, an upward epidemiological trend is evident—particularly with respect to incidence in the second half of the observation period.

During the 2013–2022 period, the observed annual prevalence in the study region ranged from 0.95 to 1.90 cases per 100,000 population. The mean annual value was 1.41 cases per 100,000 population (95% CI: 0.68–2.14). Although the crude prevalence showed a slight upward trend over the years, it was based on a low number of cases.

Statistical testing did not reveal a significant difference between individual years ($p > 0.05$), suggesting the absence of a convincing annual trend during the observed period, despite visually apparent fluctuations.

Statistical tests—including linear regression, the χ^2 test, and the Cochran–Armitage trend test—did not identify any significant annual association or consistent temporal trend ($p > 0.05$).

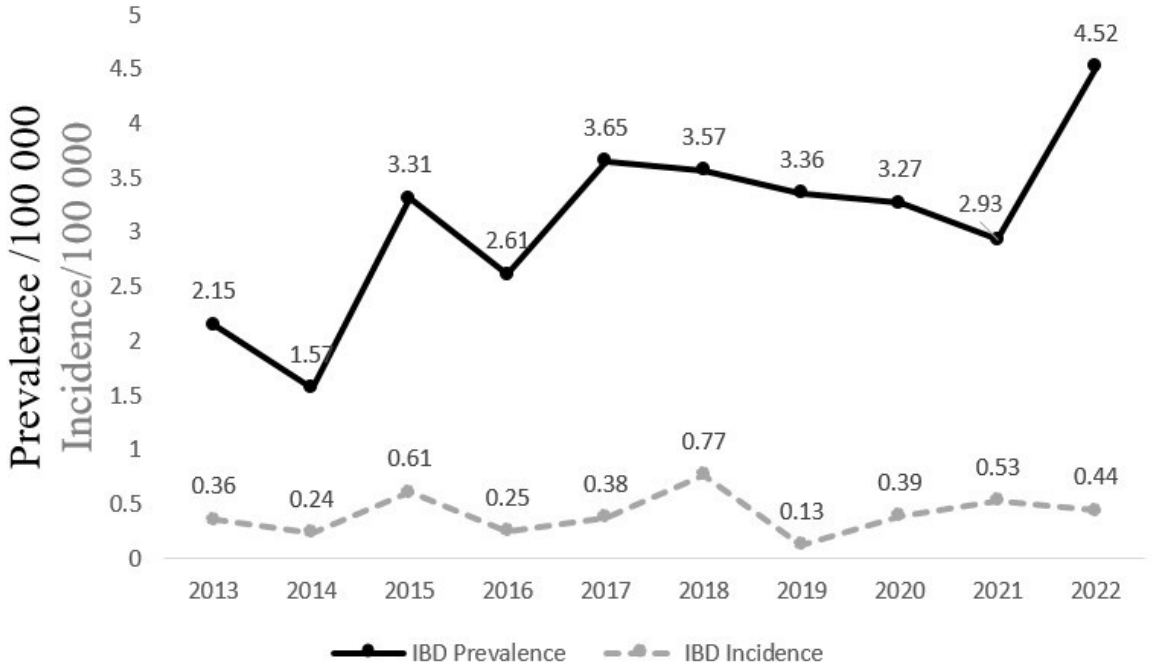

Figure 4. Crude incidence and prevalence of inflammatory bowel disease (IBD) for a 10-year period in the north-central region of Bulgaria

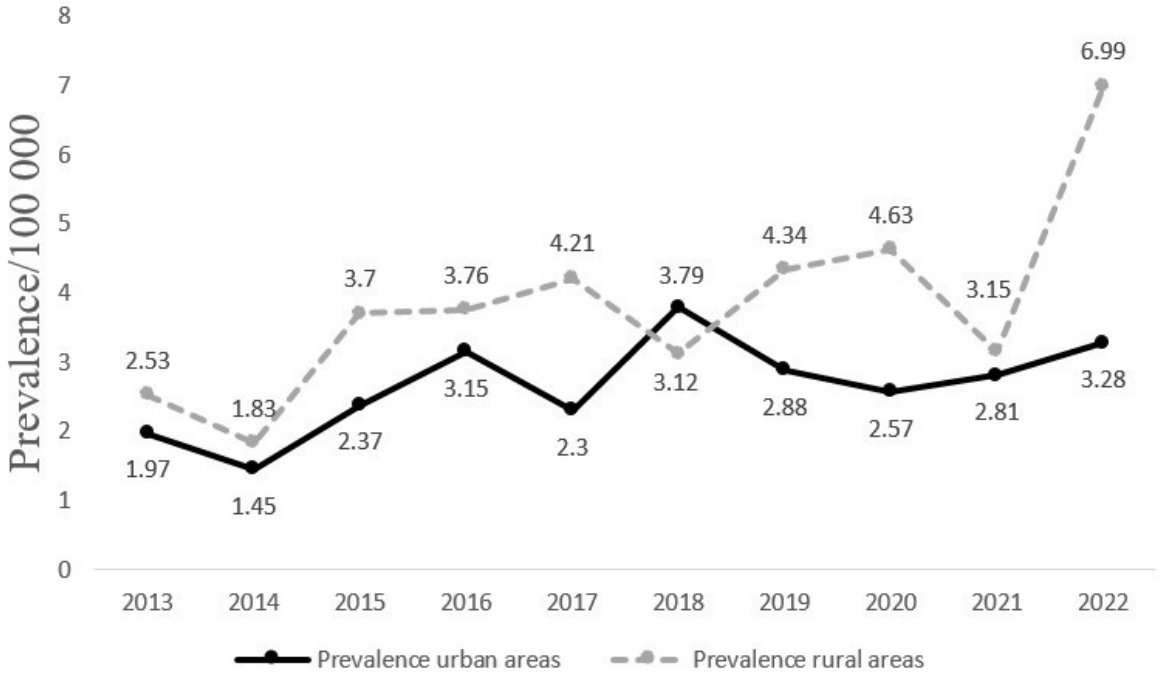

Figure 5. Annual crude prevalence of inflammatory bowel disease in urban and rural areas in the north-central region of Bulgaria

A comparative analysis between two 5-year periods—2013–2017 and 2018–2022—revealed that 65 cases were registered during the first period, while 80 cases were observed in the latter. The difference did not reach statistical significance ($p = 0.06$), although the direction of change suggested a possible upward trend.

The crude prevalence of IBD in the urban population during the period 2013–2022 demonstrated a clear upward trend, with a mean annual rate of 1.85 cases per 100,000 population (95% CI: 1.71–2.37).

Annual crude prevalence ranged from 1.19 cases per 100,000 population (95% CI: 0.54–2.26) in 2017 to 2.49 cases per 100,000 population (95% CI: 1.45–3.94) in 2022, with a noticeable increase observed after 2018.

Despite the apparent difference between certain years (e.g., 2022: 2.49 vs. 2017: 1.19/ 100,000), statistical tests did not confirm a significant difference across individual years ($p > 0.05$). An upward trend was observed, particularly after 2018, but it was not statistically significant when analyzed year by year.

A comparison of prevalence across periods reveals an increase from 1.61 (2013–2017) to 2.10 cases per 100,000 population (2018–2022), which is statistically significant ($p = 0.03$). This suggests either a rising disease burden or improved diagnostic practices among the urban population in recent years.

The crude prevalence of IBD among the rural population in this region remained extremely low throughout the entire study period. In most years, only one or no cases were registered, with annual rates ranging from 0.00 to 0.70 cases per 100,000 population. The highest annual crude prevalence was recorded in 2017 (0.70/100,000; 95% CI: 0.008–1.84) and in 2021 (0.69/100,000; 95% CI: 0.08–5.21). The wide CIs reflect the low statistical precision of these estimates.

A comparison of IBD crude prevalence among the rural population across two consecutive five-year periods—2013–2017 and 2018–2022—revealed no substantial change. During 2013–2017, four cases were registered in rural areas, with a total population of 1,467,243, corresponding to a prevalence of 0.27 cases per 100,000 population (95% CI: 0.07–0.69). In 2018–2022, the number of cases remained the same ($n = 4$), with a slightly smaller population of 1,407,698, resulting in a nearly identical prevalence of 0.28 cases per 100,000 population (95% CI: 0.08–0.72). Statistical analysis did not indicate a significant difference between the two intervals ($p > 0.05$).

Overall, IBD among the rural population in the studied region demonstrates extremely low and unstable prevalence over the past decade, with no clear trend. Year-to-year fluctuations appear random, lacking statistical significance or a consistent pattern. This may reflect both genuinely lower disease burden and limited access to diagnostic services and medical care in rural areas.

The mean annual crude prevalence of IBD among males during the study period was 1.31 cases per 100,000 men (95% CI: 0.99–1.63). The lowest annual prevalence was recorded in 2015 and 2016 (both 0.98/100,000), while the highest was observed in 2020 (1.82/100,000), resulting in a range of 0.84 cases per 100,000 men. Despite these fluctuations, no statistically significant difference in IBD prevalence among males was identified for the given period and region ($p > 0.05$). A moderate annual variation was observed, without a clear upward or downward trend (Figure 6).

During the period 2013–2017, 29 cases of IBD were registered among a male population of 2,560,994, resulting in a mean prevalence of 1.13 cases per 100,000 men (95% CI: 0.72–1.54). In comparison, the period 2018–2022 saw 36 cases among 2,435,007 males, corresponding to a higher mean prevalence of 1.48 cases per 100,000 men (95% CI: 1.08–1.88).

The statistical comparison between the two periods yielded a p-value of approximately 0.08, which did not reach the conventional threshold for statistical significance ($p < 0.05$). A moderate increase in prevalence was observed during the second period, consistent with global trends reported in recent epidemiological studies.

The mean annual crude prevalence of IBD among females in the region was 1.46 cases per 100,000 women ($n = 77$, $N = 5{,}254{,}517$; 95% CI: 1.14–1.79). No statistically significant differences in prevalence were observed across individual years ($p > 0.05$) (Figure 6).

A slight upward trend was noted, particularly after 2018, although this increase was not confirmed as statistically significant based on the applied tests.

Between 2013 and 2017, a total of 33 cases were registered among a female population of 2,699,460, resulting in a mean crude prevalence of 1.22 cases per 100,000 women (95% CI: 0.83–1.68). In the subsequent period, 2018–2022, the number of cases increased to 44, with a female population of 2,555,047, corresponding to a mean crude prevalence of 1.72 cases per 100,000 women (95% CI: 1.28–2.15).

The comparison between periods showed a statistically significant increase in IBD prevalence among females during 2018–2022 ($p = 0.04$), which falls below the conventional threshold for significance ($\alpha = 0.05$).

This indicates a statistically significant increase in IBD prevalence among females during the second period.

4. Discussion

Bulgaria is an Eastern European country located on the Balkan Peninsula. According to the 2022 national census, the population stands at 6,447,710 inhabitants. Administratively, the country is divided into six planning regions and 28 districts, encompassing a diverse mix of urban and rural settlements. It shares borders with Romania to the north, Serbia and North Macedonia to the west, Greece and Turkey to the south, and has a coastline along the Black Sea to the east.

Between 2013 and 2022, the number of patients with IBD treated at the referral center increased by 85.6%, with IBD remaining more prevalent in urban areas. The rise in newly diagnosed cases during the final three years of the study period may be attributed to improved access to gastroenterologists and the widespread availability of medical information. The incidence of IBD in the general Bulgarian population could not be assessed, as the database includes only patients from a university center covering the northeastern, north-central, and southeastern regions of Bulgaria. Although this is the first study of its kind conducted in Bulgaria, it provides valuable insights into the epidemiology of IBD.

Our sample size was limited, and results should therefore be interpreted with caution. However, these data remain valuable for identifying trends and generating hypotheses.

Across the three studied regions of Bulgaria—northeastern, north-central, and southeastern—a heterogeneous but coherent epidemiological pattern of IBD emerges, reflecting different stages of the epidemiologic transition described for Eastern Europe.[16] The northeastern region shows the highest burden, with a mean annual incidence of 1.72 cases per 100,000 population and prevalence increasing from 9.53 to 22.59 cases per 100,000 population. The north-central region has a much lower incidence (0.41/100,000) and moderate prevalence (3.12/100,000), while the southeastern region reports the lowest rates (incidence 0.15/100,000; prevalence 1.41/100,000). These gradients indicate that IBD in Bulgaria is unevenly distributed and shaped by demographic, environmental, and healthcare-related factors.

The northeastern region appears most advanced in the epidemiologic transition, with a significant rise in both incidence and prevalence. These results align with patterns in Romania, where incidence ranges 1–3/100,000 and prevalence 3–4/100,000.[17] Compared with other Eastern European countries, northeastern Bulgaria still shows lower rates than high-incidence areas such as Hungary and Croatia, where ulcerative colitis has exceeded 10 cases per 100,000 population and Crohn's disease 4 cases per 100,000 population.[18]

The north-central region, while demonstrating a significant increase in prevalence over time, maintains a low and statistically stable incidence. Its epidemiological profile resembles early-stage IBD emergence, similar to earlier Romanian reports and to the lower end of incidence ranges described in Serbia, where incidence is estimated at 2–3/100,000.[17,19]

The southeastern region shows the lowest IBD burden, with sporadic incident cases and extremely low prevalence, especially in rural areas where many years have recorded zero cases. Although incidence rose significantly in the second half of the study period, absolute numbers remain very small, and wide CIs indicate that stochastic variation and under-ascertainment are substantial factors. The increase in incidence and urban prevalence between the two 5-year periods aligns with the early acceleration phase of the epidemiologic transition, where incidence rises from a very low baseline and prevalence slowly accumulates.

When viewed in a regional context, Bulgaria's IBD burden remains lower than that of most neighboring countries. Romania and Serbia already report higher incidence and prevalence, while Greece and Turkey show substantially higher rates, with incidence of 3–8/100,000 and prevalence > 20/100,000.[20–22]

Even larger differences appear when compared with central European countries such as Hungary and Croatia, where ulcerative colitis reaches 8–10/100,000, Crohn's disease 3–4/100,000, and prevalence often exceeds 50–100/100,000.[23–25]

More recent Romanian studies confirm rising IBD numbers and strong regional heterogeneity, with higher case concentrations in more urbanized areas.[20]

This parallels the northeastern Bulgarian pattern, which also shows a clear urban–rural gradient and higher urban prevalence, consistent with European evidence linking urbanization to increased IBD risk through lifestyle factors, Westernized diets, reduced microbial exposure, and better diagnostic access.[9]

The north-central region shows an atypical pattern, with higher crude prevalence in rural areas—unlike northeastern Bulgaria and international data, including Romanian studies, where cases are mainly urban.[17] This likely reflects referral pathways, mobility, or urban

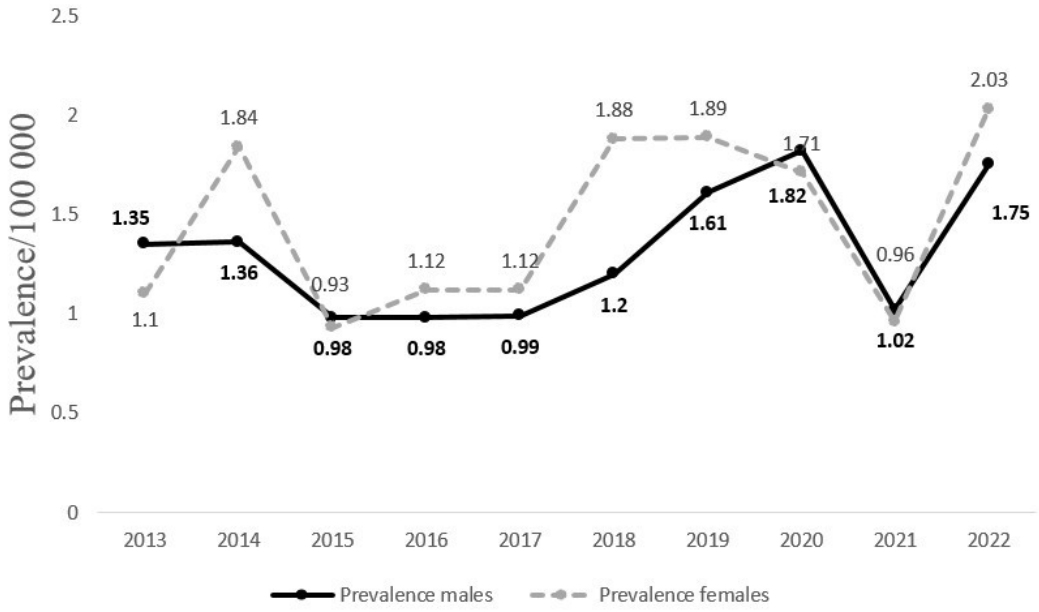

Figure 6. Distribution of annual crude prevalence of inflammatory bowel disease in males and females in the southeastern region of Bulgaria

underdiagnosis rather than a true reversal of expected trends. Overall, the region resembles early-stage IBD emergence, similar to earlier Romanian findings and Serbia's lower incidence of 2–3/100,000.[19] Thus, the north-central region aligns with Romania's low-incidence profile but with even lower absolute rates, possibly due to differences in healthcare access or diagnostic capacity.[26] The southeastern region shows the most pronounced urban–rural disparity. Urban prevalence has risen sharply, while rural prevalence remains extremely low and unstable, with some years showing no cases. This pattern strongly indicates underdiagnosis and limited access to specialized care in rural areas. The absence of a clear rural trend likely reflects incomplete case capture rather than the true absence of disease.

The distribution of IBD between urban and rural populations reveals important epidemiological insights. The higher number of registered cases in urban areas may be influenced by improved access to specialized medical care, greater health awareness, and more frequent diagnostic evaluations. However, this does not necessarily indicate a higher true incidence of IBD in urban settings. It is plausible that the actual disease burden is comparable across both urban and rural populations, but underdiagnosis in rural areas—due to limited healthcare infrastructure and access—may contribute to the observed disparity.

Regarding gender distribution, the analysis shows an almost equal representation of male and female patients (49.9% vs. 50.1%) across all three Bulgarian regions—northeastern, north-central, and southeastern, suggesting no significant gender-related predisposition to IBD.

This contrasts with other autoimmune diseases, such as systemic lupus erythematosus, which exhibit marked gender differences.[27] The balanced gender ratio in IBD may reflect a multifactorial etiology, where genetic, environmental, and immunological factors interact in a way that does not favor one gender over the other.[28-33]

In the northeastern region, prevalence was nearly identical in both genders (13.71/100,000 in men vs. 13.59/100,000 in women), with overlapping CIs and non-significant *p*-values, indicating a balanced distribution. This aligns with European studies reporting minimal or no gender variation in overall IBD occurrence, suggesting that environmental and healthcare-related factors may play a larger role than biological gender differences in this region.[34]

In the southeastern region, a small but statistically significant increase among women appeared in later years, but the numbers were too limited to indicate a meaningful difference.

These findings are consistent with data from neighboring Eastern European countries. Romanian and Serbian studies report similarly equal gender ratios, with only slight, non-significant male predominance in some

subgroups.

5. Limitations

This study presents several inherent limitations that should be considered when interpreting the findings. As a retrospective, hospital-based investigation, the results may not fully capture the broader epidemiological landscape of IBD in Bulgaria.

Additionally, the calculation of incidence and prevalence rates was based on the population served by a single tertiary center. This may not reflect the true burden of disease across the entire country, especially considering potential differences in healthcare access, referral patterns, and disease awareness between urban and rural areas.

Furthermore, the interpretation of our results is constrained by the absence of other published epidemiological data on IBD in Bulgaria, which prevents direct comparison and limits the ability to contextualize our findings within national trends. This lack of comparable datasets underscores the need for broader, population-based studies to more accurately define the epidemiology of IBD in the country.

6. Conclusion

The results of the present study indicate an increase in recorded IBD incidence and prevalence in the studied region. This pattern may reflect a true rise in disease occurrence and improved diagnostic capacity. This aligns with observed patterns in other European countries, where similar factors—including increased public awareness and potential environmental changes—also contribute to the growing incidence of the condition.[15,35,36]

The limitations of the study, related to the scope of the included patient population, suggest the need for broader epidemiological analyses. Such efforts would enable a more comprehensive assessment of the distribution and characteristics of IBD on a national scale.

This study provides valuable data on the epidemiology of IBD for the first time in Bulgaria and may serve as a foundation for future scientific research and strategic health policies. It emphasizes the importance of systematic monitoring of IBD patients, as well as the need to adapt the healthcare system to improve early diagnosis, access to specialized treatment, and effective disease management.

Overall, the combined findings from the three regions show that IBD in Bulgaria is increasing but remains at an early stage of epidemiologic development, with substantial regional disparities. The marked regional differences highlight the need for improved diagnostics, better access to specialized gastroenterology services, and the establishment of a national IBD registry. Strengthening provider awareness and ensuring consistent disease detection and long-term monitoring across the country are essential as Bulgaria moves through the early phases of IBD emergence.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

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Ethics approval and consent to participate

The study protocol was reviewed and approved by the Ethics Committee at the Medical University of Varna, Bulgaria (approval number: 58/01.12.2016). The requirement for written informed consent was waived by the institutional ethics committee. No identifiable personal data were collected.

Consent for publication

No individual patient-identifying information is included in this article, and therefore specific patient consent for publication was not required.

Availability of data

Data is available from the corresponding author upon reasonable request.

Further disclosure

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