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CONTENTS

Journal of Enterocolitis

Review

Inflammatory Bowel Disease in Africa: A Growing Public Health Challenge

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Abstract

Inflammatory bowel disease (IBD), once thought to be rare in Africa, is now increasingly recognized due to urbanization, dietary changes, and improved diagnostic awareness. However, significant challenges in diagnosis and management persist across the continent. This review explores current trends, risk factors, diagnostic barriers, and treatment gaps related to IBD in the African context, while suggesting strategic solutions. We conducted a narrative review of the published literature, focusing on epidemiology, environmental and genetic drivers, dietary influences, health system constraints, and policy gaps related to IBD in Africa. Rates of IBD are rising in sub-Saharan Africa, particularly among young adults. Ulcerative colitis is reported more frequently than Crohn's disease, though both are often misdiagnosed as infections. Contributing factors include dietary westernization, reduced microbial exposure, and air pollution. Delayed diagnosis, limited access to advanced treatments, malnutrition, and coexisting infections complicate care. Policy support and investment in research remain limited. IBD is emerging as a significant public health challenge in Africa. Addressing this issue requires coordinated efforts to raise awareness, improve diagnostics and treatment, and strengthen local research. Integrating IBD into broader non-communicable disease strategies and health system planning is essential to mitigate long-term health and economic impacts.

Keywords: Africa, Crohn's disease, diagnosis, diet, epidemiology, health systems, inflammatory bowel disease, public health, ulcerative colitis

INTRODUCTION

Inflammatory bowel disease (IBD), characterized by chronic inflammation of the gastrointestinal tract and including Crohn's Disease (CD) and Ulcerative Colitis (UC), was once considered rare in Africa. However, recent data indicate a rising incidence in Sub-Saharan Africa (SSA) amid rapid urbanization and lifestyle changes.[1,2] Historically, the burden of IBD in SSA has been low, likely due to under-diagnosis and underreporting, whereas North America and Europe saw sharp increases in the 20th century before plateauing.[3] Current estimates show that the prevalence in SSA remains modest—around 10 per 100,000 in 2017—compared to over 400 per 100,000 in North America.[1] This stark disparity highlights the "emerging" status of IBD in Africa's epidemiological transition, similar to patterns observed in parts of Asia and South America.[1,2] Notably, South Africa, the continent's most industrialized country, reports the highest IBD rates in the region, likely due to better diagnostic infrastructure and surveillance.[1] In contrast, many other African countries still report very low incidence and prevalence, which reflects, in part, limitations in healthcare access and data collection.

A severe lack of robust epidemiological studies from SSA means that the true burden of IBD remains uncertain.[3] Two systematic reviews from 2020 found fewer than 250 documented IBD cases in SSA (excluding South Africa) in the published literature,1 highlighting how underrepresented the region is in global data. The apparent rarity of IBD in Africa is believed to be largely an artifact of underreporting and misdiagnosis, rather than the absence of the disease.[1] Many cases likely go undetected due to low awareness and the tendency to attribute chronic gastrointestinal symptoms to infectious diseases, such as diarrheal illnesses or tuberculosis.[1,3] In endemic regions, distinguishing IBD from infections poses a diagnostic challenge that can mask the true incidence. For example, a South African cohort study found that about 12% of IBD patients had a tuberculosis infection either before or after their IBD diagnosis,[4] illustrating how a high TB burden complicates case identification. Overall, mounting evidence suggests that IBD incidence in Africa is genuinely on the rise.[3] As countries undergo socioeconomic development, the risk factors associated with IBD become more prevalent, and previously "hidden" cases are increasingly recognized. Improved awareness and surveillance are gradually revealing an emerging disease burden, moving Africa from the earliest stage of IBD epidemiological transition toward the "emerging epidemic" stage noted in Asia and Latin America.[2,3] Despite this progress, significant gaps remain in epidemiological data, and strengthening registries and reporting systems in Africa is crucial to understanding the true scope of IBD in the region.[5]

Methodology

This article presents a narrative review synthesizing current evidence on IBD in Africa, focusing on emerging epidemiology, environmental and genetic risk factors, dietary patterns, comorbidities, and health system responses.

Search Strategy: We conducted a targeted literature search across major databases, including PubMed, Scopus, Web of Science, and Google Scholar, from inception through March 2025. The search terms included combinations of: "Inflammatory Bowel Disease," "Crohn's Disease," "Ulcerative Colitis," "Africa," "epidemiology," "risk factors," "genetics," "diet," "nutrition," "comorbidities," "health systems," and "management." Boolean operators ("AND," "OR") and Medical Subject Headings (MeSH) were applied to improve precision. We also reviewed reference lists of relevant articles to identify additional sources not captured through the database searches.

Inclusion Criteria: Peer-reviewed articles, systematic reviews, and reports focused on IBD in Africa or African-ancestry populations. Publications in English. Studies reporting on epidemiological trends, risk factors (both genetic and environmental), diet, comorbidities, or health policy aspects relevant to IBD.

Exclusion Criteria: Articles focused exclusively on non-African populations without comparative or contextual relevance. Animal studies and basic science articles unrelated to population health or clinical management. Non-peer-reviewed opinion pieces, unless published by established global health organizations.

Data Extraction and Thematic Analysis: Relevant studies were screened and selected based on titles and abstracts, followed by full-text review. Key themes were identified and organized under predefined categories aligned with the review objectives. We synthesized the findings qualitatively, highlighting regional patterns, knowledge gaps, and areas needing further research.

Demographic and Clinical Characteristics

Across African studies, IBD tends to affect younger adults, with most patients diagnosed between 20 and 40 years of age.[6] This aligns with global patterns, where IBD often presents in early adulthood. For example, a South African cohort reported a median age of onset of 32 years,6 and Nigerian data also show that the majority of cases occur in the third and fourth decades of life.[7] Pediatric onset IBD (under 18 years) appears less common, accounting for approximately 10% or fewer of cases. In Cape Town, for instance, children under 19 represented about 9.7% of IBD cases—a proportion comparable to that observed in Western countries.2 Late-onset IBD (over 60 years) is reported but remains relatively rare in Africa,1 possibly due to the region's younger population demographics and shorter life expectancies. Gender distributions in African IBD cohorts are generally balanced or show a slight female predominance, similar to patterns seen elsewhere. Some reports from East and South Africa note a higher frequency of IBD in females,[8] while Nigerian studies show near-equal gender ratios.[7] These variations may reflect small sample sizes or regional differences, but overall, they mirror global trends, where UC tends to have a modest female preponderance, whereas CD affects males and females equally.[7]

In terms of disease phenotype, UC appears to be more common than CD in Africa.[3] Hospital registries in South Africa attribute roughly 60–70% of IBD cases to UC.6 By contrast, Western countries often have a more balanced or even CD-predominant case mix, making the skew toward UC in Africa a notable difference. Patients in Africa often present with long-standing, severe symptoms by the time IBD is recognized. Common clinical features include chronic diarrhea, abdominal pain, weight loss, and rectal bleeding in UC cases.[6,9–11] However, comprehensive data on the frequency of these manifestations in Africa are limited. One striking demographic observation is the historical ethnic pattern of IBD in Africa. In South Africa, which has the largest number of IBD cases on the continent, IBD was, until recently, far more common in the white population than in indigenous black Africans.[2] Despite black Africans comprising approximately 81% of South Africa's population, they represented only about 5% of IBD cases in older studies.[2] This disparity is narrowing as IBD diagnoses increase across all groups, but it raises questions about genetic susceptibility versus access to care. It is likely that socioeconomic differences and access to specialized care played a significant role in the underdiagnosis of IBD among indigenous Africans in the past.[2] More recent data from Ghana and other African countries confirm that IBD is being identified across diverse ethnic groups as awareness grows.[2] In summary, the profile of IBD patients in Africa—where UC is more common than CD, and the disease is often advanced at diagnosis—reflects both global commonalities and unique regional patterns influenced by healthcare access and possibly genetic factors.

Environmental and Genetic Factors

Environmental factors are central to the rise of IBD in Africa. As countries develop, changes in sanitation, lifestyle, and microbial exposure alter the immune environment. The hygiene hypothesis suggests that reduced early-life exposure to microbes increases the risk of autoimmune diseases like IBD by weakening immune regulation.[1,12] In Africa, rapid urbanization may be reducing these exposures.[12] A South African case-control study found that helminth infections in childhood protect against CD.[13] Helminths modulate the immune system, and their absence could heighten IBD susceptibility.[14] Immigrant data reinforce this: African-born individuals moving to the West have low IBD rates, but their children acquire local disease risks within a generation.[1] This highlights that early environmental exposure is more influential than genetic background.

Urbanization brings westernized lifestyles that further increase IBD risk. Smoking, though less prevalent in Africa, is rising in cities. It worsens CD but may protect against UC.[1,3,15] Air pollution, particularly nitrogen and sulfur oxides and fine particulate matter, has been linked to IBD in high-income countries.[7] African cities experiencing air quality decline may face similar risks. Psychosocial stress is another factor. The stress of urban life and shifting social dynamics may trigger IBD onset or flares.[7] Modern diets, rich in fat and sugar, along with increased antibiotic use and reduced exposure to farm environments, foster conditions that promote IBD.[16,17] Infectious disease burdens in Africa further complicate the IBD landscape. Chronic gastrointestinal infections, such as tuberculosis, Clostridioides difficile, and parasites, can trigger gut inflammation or disrupt the microbiome.[13] These infections mimic IBD symptoms, making diagnosis difficult. For instance, intestinal TB resembles CD. Misdiagnosis can delay proper treatment or lead to dangerous use of immunosuppressants in TB-positive patients.[13,18] High endemic rates of infections and frequent antibiotic exposure in Africa could shape gut immunity in ways not fully understood, potentially affecting IBD risk.

Genetic contributions to IBD in Africa differ from Western patterns.

Genes linked to IBD in European populations, such as NOD2, are rare among African patients.[6,8] A South African study confirmed low frequencies of classic NOD2 mutations in CD cases, suggesting that different pathways may drive disease.[3,16,19] African populations may carry unique risk alleles, but large-scale studies remain lacking. Few genome-wide association studies (GWAS) include African cohorts. However, multi-ethnic GWAS involving African-ancestry individuals have uncovered novel variants not found in Europeans.[9,12] These insights demonstrate the value of inclusive genetic research and reveal how current knowledge is limited.

Despite the research gap, some genetic patterns are emerging. Hereditary clustering occurs in 5-15% of African IBD cases-lower than the 20–30% in European populations but still notable.[12] This suggests heritability exists, though with possible differences in expression or variant types. The historically low incidence of IBD in Africa raises the question: Is it due to low genetic risk or a lack of exposure to environmental triggers? Data from migrants suggest the latter is more likely.[1] Africa may harbor distinct genetic predispositions, but their roles remain unclear due to underrepresentation in research.

In summary, environmental shifts are likely driving the increase in IBD across Africa. Urbanization, reduced microbial exposure, air pollution, dietary changes, and ongoing infections all interact with a genetic background that is poorly understood. The African IBD profile may reflect unique gene–environment interactions not yet captured by global research. To improve diagnosis, prevention, and treatment, more genomic studies must be conducted within African populations. Understanding these dynamics can inform tailored strategies and support the development of context-specific therapies in a region where IBD is rapidly emerging.

Dietary Patterns and Gut Health in African Inflammatory Bowel Disease

Urbanization in Africa is reshaping dietary habits in ways that may promote IBD. Traditional African diets—high in fiber, fruits, and unrefined carbohydrates, and low in saturated fats and processed sugars—are being replaced by Western-style diets that are energy-dense and low in fiber.[7,20-22] These changes correlate with rising IBD rates and are part of a broader nutrition transition linked to non-communicable diseases.[3,7,16,19,23] Western diets promote dysbiosis and gut inflammation, factors implicated in IBD pathogenesis.[24,25] Fiber is essential for gut health, as beneficial gut bacteria ferment fiber to produce short-chain fatty acids (SCFAs), such as butyrate, which support intestinal barrier integrity and modulate inflammation. When fiber intake drops, SCFA production declines, potentially weakening the gut barrier and increasing inflammation.[26-29] This shift, observed in populations adopting Western diets, may explain the growing burden of UC and colorectal cancer in industrializing countries. High intake of animal proteins, additives, and fats further disrupts the microbiota, potentially exacerbating IBD.[28-30] Some traditional African foods may be protective. Millet, sorghum, and cassava provide fermentable fibers that help maintain a diverse gut microbiome.[31] As these foods are displaced by ultra-processed foods and sugar-sweetened beverages, microbiome diversity declines. Experimental studies suggest that emulsifiers and food additives, common in processed foods, aggravate gut inflammation.[24,31,32] Increased consumption of red meat and saturated fats may also encourage bile-tolerant, pro-inflammatory bacteria.[20,33] Although African-specific data are limited, global findings indicate that dietary modernization is a key environmental factor in IBD.[7,16,20,21,34]

Diet also plays a crucial role in IBD management.[35] Even during remission, many African patients report persistent gastrointestinal symptoms such as bloating, pain, and diarrhea, often triggered by food.[16,36] Diets like low-FODMAP, which restrict certain fermentable carbohydrates, have shown promise in reducing these symptoms.[37-40] However, such interventions are based on Western diets and lack cultural adaptability. As a result, African patients often receive generalized dietary advice or rely on traditional beliefs, which may lack evidence-based support. Tailored dietary guidance remains scarce. The gap between available advice and local dietary practices makes it difficult for patients to follow nutritional recommendations. Culturally adapted interventions that reflect local ingredients and eating habits are needed. Without these, patients may continue to manage symptoms through trial and error or misinformation. Research exploring diet–IBD interactions in African populations is essential to inform practical and effective nutritional strategies.

Malnutrition and micronutrient deficiencies are common among IBD patients in Sub-Saharan Africa. These arise from poor intake, malabsorption, and existing food insecurity. Deficiencies in iron, zinc, magnesium, folate, vitamin B12, and vitamin D are frequent.[41,42] Pediatric patients often experience growth stunting or delayed puberty, which exacerbates disease severity.[2] Malnutrition worsens gut inflammation and delays healing, making it both a cause and consequence of IBD.[43] Improving nutritional status through enteral feeding or supplementation can help alleviate symptoms and potentially support the induction of remission.[43,44] Unfortunately, access to specialized nutrition support is limited.[35] Most facilities lack access to elemental or parenteral nutrition and have no clinical dietitians, leaving patients reliant on general practitioners for dietary guidance. Developing practical plans using local foods can enhance adherence and promote self-care. Diet plays a dual role as both a trigger and a management tool in IBD. The shift from traditional high-fiber diets to Western eating patterns may be driving the rise in cases. Preserving or adapting traditional diets with locally appropriate solutions could reduce risk and improve outcomes. Therefore, there is a pressing need for more African context-specific studies.

Diagnostic and Therapeutic Challenges

IBD, once considered rare in Africa, is now emerging as a significant health challenge amid rising cases and under-resourced health systems.[3,7,45] Accurate diagnosis remains difficult due to limited access to essential diagnostic tools, such as endoscopy with biopsies, histopathology services, and advanced imaging like CT or MRI enterography—especially outside major urban centers.[1,3,7,46] Many African countries also face critical shortages of trained specialists, including gastroenterologists, radiologists, and pathologists.[3,7] Consequently, patients often endure prolonged diagnostic journeys, marked by misdiagnoses involving infections like tuberculosis, dysentery, or cancer.[1,47] During these delays, the disease progresses, often resulting in severe complications, such as strictures, fistulas, abscesses, and malnutrition, by the time of a correct diagnosis.[1] These systemic gaps not only delay diagnosis but also hinder timely treatment. Access to effective IBD therapies, particularly biologic agents such as anti-TNF drugs, remains extremely limited due to high costs and unavailability in most public health systems in sub-Saharan Africa.[48] Together, these barriers exacerbate patient suffering and place added strain on already overstretched healthcare infrastructures.

A meta-analysis found that delays in diagnosis are associated with worse clinical outcomes and higher complication rates.[46] One study noted that the average time from symptom onset to IBD diagnosis in some African

settings exceeded one year.[46] Key reasons include a low index of suspicion among frontline healthcare workers and the paucity of diagnostic tools. Many physicians in primary care hospitals may never have seen a case of IBD and thus might not consider it until multiple treatments for infections have failed.[46] Underreporting and misdiagnosis remain persistent problems. The high prevalence of infectious diseases, including tuberculosis, amebiasis, and chronic dysentery, indicates that IBD is often diagnosed by exclusion.[1,3] This challenge is amplified in pediatric cases, where growth faltering from malnutrition can mask IBD, or chronic diarrhea is attributed to recurrent infections.44 After diagnosis, treatment poses major challenges. While standard IBD care includes drugs like aminosalicylates, corticosteroids, immunosuppressants, and biologics (including anti-TNF agents and IL-12/23 inhibitors), many African countries lack access to the full range due to high costs and limited insurance coverage.[15] These gaps in diagnostics and treatment highlight the need for systemic investment, innovation, and advocacy to improve care.

Tuberculosis (TB) complicates IBD diagnosis in Africa.[4,49] Crohn's disease and intestinal TB present with similar symptoms, often leading to misdiagnosis. In some South African studies, up to one-third of CD patients were initially treated for TB.[4] This misdiagnosis poses serious risks, as immunosuppressive therapy for IBD can exacerbate undetected TB. Clinicians face a common dilemma: whether to delay IBD treatment until TB is excluded or to begin anti-TB therapy without a confirmed diagnosis. The challenge is further complicated by overlapping gastrointestinal infections, such as schistosomiasis and chronic bacterial enteritis. Malnutrition is also prevalent among African IBD patients and worsens disease outcomes.[44] Chronic inflammation increases nutritional needs while impairing absorption. Many patients, particularly those with CD, present with anemia, stunted growth, and vitamin deficiencies.[2,43,44] Long-standing IBD, especially ulcerative colitis, increases the risk of colorectal cancer.[32,50] While high-income countries implement regular colonoscopy screening to detect precancerous lesions, such surveillance is largely unavailable in Africa. Effective IBD management in the region requires integrated care that considers the burden of local infections and nutritional deficiencies. Urgent, population-specific research is needed to guide context-appropriate treatment strategies.

Healthcare facilities in many African countries continue to rely on older, less effective treatments, such as steroids and sulfasalazine, because newer medications are often unregistered, uncovered by insurance, or unaffordable.[15] Biologic therapies, for example, remain largely inaccessible outside South Africa due to high costs and unstable supply chains.[15,48] Diagnostic procedures also pose a financial challenge. A Nigerian audit revealed that colonoscopy services are mostly confined to private facilities and come with steep out-of-pocket expenses, with little to no insurance support.[51] Many patients, especially those without insurance, must pay for diagnostics, medications, and hospital care entirely from their own pockets, worsening economic hardship. The long-term costs of managing IBD, including lifelong medication, repeated hospitalizations, and surgery, place a significant financial burden on both households and national health systems.[7,52] Chronic conditions like IBD often force families to choose between essential healthcare and basic needs, while under-resourced health systems struggle to provide specialized care without adequate funding or financial protection mechanisms.

Policy Gaps and Barriers to IBD Care

Improving IBD care in Africa requires both grassroots action and strong policy support. Encouraging efforts are already underway. Organizations like IBD Africa, established in 2019, are increasing public awareness and offering patient education programs across the continent.[15] Professional networks, such as the Gastroenterology and Hepatology Society of Sub-Saharan Africa (GHASSA), are also contributing by providing ongoing clinical training, including virtual sessions on IBD diagnosis and treatment.[15] These initiatives are patient-centered and aim to empower both healthcare providers and those living with IBD. They have strengthened patient advocacy, encouraged open discussions, and promoted partnerships, including with pharmaceutical companies, to improve access to more affordable treatments.[15] Public campaigns, such as World IBD Day, and community outreach activities are helping reduce stigma and promote early intervention.

However, IBD care still faces significant system and policy challenges. No African country has a national registry or control program, making it difficult to track disease trends or plan services effectively. Access to care is largely confined to a few urban centers, leaving rural areas underserved. Financial barriers are significant, as insurance rarely covers chronic conditions, forcing patients to pay for tests and medications out-of-pocket.[7] Many delay seeking care due to cost or low awareness, especially when symptoms appear mild. Most national health strategies exclude IBD, leading to a lack of funding, culturally appropriate dietary advice, and psychosocial support.[48] Clinical guidelines are often borrowed from Western contexts, which may not suit local realities.[52] The shortage of region-specific research on genetics, the microbiome, or treatment response further limits evidence-based care. Together, these gaps in planning, affordability, and local data contribute to delayed diagnoses and inadequate treatment.

Limitations/Strengths of the Study

This narrative review is limited by potential selection bias and the lack of large-scale studies from Africa. However, it provides timely and relevant insights into the growing IBD burden on the continent, where awareness and policy remain underdeveloped. By combining clinical, environmental, socioeconomic, and health system perspectives, the review offers a more comprehensive view of IBD in African settings. It critically applies global knowledge to local contexts, highlights evidence gaps, and calls for more region-specific research. By connecting grassroots advocacy with systemic barriers, it serves as a valuable resource for improving IBD care and informing policy in Africa.

CONCLUSION

IBD is becoming an increasingly important public health issue in Africa, though its true impact is often concealed by underdiagnosis and poor reporting. While some clinical features align with global patterns, African cases are influenced by unique factors such as changing diets and rapid urbanization. Limited access to diagnostics and modern treatments leads to delayed care, complications, and a reduced quality of life. There is an urgent need for region-specific research on genetics, nutrition, and care approaches to guide effective responses. Addressing policy gaps by including IBD in national health plans, improving healthcare infrastructure, and expanding access to affordable treatments is essential. Adapting proven global strategies, such as early diagnosis, team-based care, and patient education, to local settings could greatly improve outcomes. Progress will require coordinated action from governments, healthcare providers, researchers, and partners across the region.

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Original Article

Assessing Cardiovascular Risk in Inflammatory Bowel Disease Using Novel Inflammatory and Dyslipidemia Markers: An Evaluation of PAI, MHO, and SII

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Abstract

Objective: Inflammatory Bowel Disease (IBD), encompassing Crohn's Disease (CD) and Ulcerative Colitis (UC), is a chronic immune-mediated condition associated with systemic inflammation that may increase the risk of cardiovascular disease (CVD). This study aimed to investigate the utility of novel, accessible inflammatory and atherogenic biomarkers-Plasma Atherogenic Index (PAI), Monocyte-to-HDL Ratio (MHO), and Systemic Immune-Inflammation Index (SII)-in assessing cardiovascular risk and disease activity in IBD patients compared to healthy controls. We also evaluated the association of these markers with Abdominal Aortic Calcification (AAC), a surrogate for subclinical atherosclerosis.

Methods: This retrospective, single-center study included 99 IBD patients (40 with CD, 59 with UC) and 70 healthy controls evaluated between January 2017 and April 2023. Demographic, clinical, and laboratory data were collected from patient files. PAI (log[Triglycerides/HDL-C]), MHO (Monocyte/HDL-C), and SII ([Platelet × Neutrophil]/Lymphocyte) were calculated. Disease activity was assessed using the Crohn's Disease Activity Index (CDAI) for CD and the Mayo score for UC. AAC was assessed in patients with available abdominal computed tomography (CT) scans. Statistical analyses included group comparisons and Receiver Operating Characteristic (ROC) curve analyses.

Results: IBD patients demonstrated significantly higher levels of PAI, MHO, SII, and Neutrophil-to-Lymphocyte Ratio (NLR) compared to the healthy control group ($p < 0.05$ for all). Within the IBD cohort, patients with active disease exhibited significantly higher SII and NLR values compared to those in remission. However, PAI levels did not differ significantly between active and inactive disease states. Of the 63 patients evaluated with CT, 40 (63.5%) had AAC. Patients with AAC had significantly higher levels of CRP, NLR, SII, MHO, and PAI compared to those without AAC ($p < 0.01$ for all). ROC analysis identified PAI and MHO as strong predictors of AAC presence.

Conclusion: The novel, easily calculable biomarkers PAI, MHO, and SII are significantly elevated in patients with IBD, suggesting a heightened pro-inflammatory and pro-atherogenic state. The strong association of these markers with AAC reinforces their potential utility in identifying subclinical atherosclerosis and increased cardiovascular risk in this patient population. These findings suggest that routine calculation of these indices could aid in cardiovascular risk stratification for IBD patients, although further validation through large-scale, prospective studies is warranted.

Keywords: Abdominal aortic calcification, cardiovascular risk, inflammatory bowel disease, monocyte-to-hdl ratio, neutrophil-to-lymphocyte ratio, plasma atherogenic index, systemic immune-inflammation index.

INTRODUCTION

Inflammatory Bowel Disease (IBD) is a term for a group of chronic, immune-mediated disorders characterized by relapsing and remitting inflammation of the gastrointestinal tract, often accompanied by extraintestinal manifestations.[1] Its two primary forms are Ulcerative Colitis (UC) and Crohn's Disease (CD). While the etiology is not fully understood, IBD is believed to result from a complex interaction among genetic predisposition, environmental factors, microbial dysbiosis, and a dysregulated immune response.

Cardiovascular disease (CVD) is a leading cause of mortality worldwide, with atherosclerosis as its main underlying pathology. Systemic inflammation plays a critical role in the development of CVD, and its contribution to atherogenesis is well-documented in chronic inflammatory conditions such as rheumatoid arthritis.[2] Key mechanisms-including endothelial dysfunction, increased arterial stiffness, and pro-inflammatory cytokine production-are common to both IBD and atherogenesis.[2-8] The prevailing hypothesis suggests that immune dysregulation and inflammatory burden in IBD promote the formation of atherosclerotic plaques.[9,10] Consequently, large-scale studies and meta-analyses have shown that IBD patients have a significantly increased risk of coronary artery disease (CAD), myocardial infarction, and stroke.[4,11-14] Furthermore, disease activity itself has been identified as an independent risk factor for these acute arterial events.[15]

- Patients with Inflammatory Bowel Disease have significantly higher levels of Plasma Atherogenic Index, Monocyte-to-HDL Ratio, and Systemic Immune-Inflammation Index compared to healthy controls, indicating a heightened pro-inflammatory and pro-atherogenic state in IBD.
- PAI, MHO, and SII are strongly associated with Abdominal Aortic Calcification, a surrogate marker of subclinical atherosclerosis, suggesting their potential role in cardiovascular risk assessment in IBD patients.
- Active IBD is linked to higher levels of inflammatory markers, including CRP, NLR, and SII. However, PAI did not significantly correlate with disease activity, suggesting it may reflect a more chronic cardiovascular risk rather than acute inflammation.
- PAI and MHO were identified as strong predictors for the presence of AAC, highlighting their potential as cost-effective biomarkers for identifying subclinical atherosclerosis and enhancing cardiovascular risk stratification in IBD patients.
- Routine integration of PAI, MHO, and SII into clinical practice could help identify high-risk IBD patients for targeted cardiovascular risk management, though further prospective studies are needed to validate these biomarkers and their role in improving long-term cardiovascular outcomes.

Given this heightened risk, there is a need for improved risk stratification tools. Abdominal Aortic Calcification (AAC), detectable on CT scans, has been identified as a marker of early atherosclerosis. Data from the Framingham Heart Study demonstrated that AAC is an independent risk factor for the progression of coronary artery calcification and is predictive of future cardiovascular events.16 Concurrently, several simple, blood-based biomarkers have emerged. The Plasma Atherogenic Index (PAI), calculated as the logarithm of the Triglyceride/HDL-C ratio, is a novel biomarker that integrates two independent CVD risk factors.[17,18] PAI has been associated with cardiovascular disease in a variety of other clinical settings.[19-24]

The primary aim of this study was to investigate these inflammatory and atherogenic markers (PAI, MHO, SII, NLR) in IBD patients and compare them to healthy controls to assess their role in determining increased CVD risk. A secondary aim was to evaluate the relationship between these markers and AAC, thereby testing their utility as predictors of subclinical atherosclerosis.

METHODS

Study Design and Population

This retrospective, cross-sectional study was conducted at the Gastroenterology Clinic of Cemil Taşçıoğlu City Hospital in İstanbul, Türkiye. We reviewed the records of patients evaluated between January 2017 and April 2023. The study included 99 adult patients (≥18 years) with a confirmed diagnosis of IBD (40 with CD, 59 with UC) and a control group of 70 healthy individuals without known chronic diseases or chronic medication use. Exclusion criteria included age under 18, other chronic inflammatory diseases, recent surgery, known CVD, severe liver or kidney disease, pregnancy, malignancy, recent systemic infection, and current use of statin medications.

Ethical Approval

The study protocol was approved by the Cemil Taşçıoğlu City Hospital Clinical Research Ethics Committee (Approval Number: 119, Date: 31.07.2023). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Data Collection and Calculations

Demographic, clinical, and laboratory data were collected from patient files. The following indices were calculated from routine blood tests:

• NLR: Absolute Neutrophil Count / Absolute Lymphocyte Count
• SII: (Platelet Count × Absolute Neutrophil Count) / Absolute Lymphocyte Count
• MHO: Absolute Monocyte Count / HDL-C Level
• PAI: log (Triglyceride Level / HDL-C Level)

Assessment of Disease Activity and AAC

Disease activity was assessed using established scoring systems. For Ulcerative Colitis, the Mayo score was used, with a score >2 defining active disease. For Crohn's Disease, the Crohn's Disease Activity Index (CDAI) was used, with a score >150 indicating active disease.

For IBD patients who had undergone abdominal CT scans as part of their clinical care, the images were retrospectively analyzed by a single radiologist for the presence of visible AAC in the abdominal aorta.

Statistical Analysis

Analyses were performed using SPSS software (version 26.0, IBM Corp, Armonk, NY, USA). Group comparisons were made using Student's t-test, ANOVA, Mann-Whitney U test, or Kruskal-Wallis tests as appropriate. Kolmogorov-Smirnov analysis was used to assess normality. Categorical variables were compared using the Chi-square test. ROC curve analysis was used to evaluate the predictive capacity of the biomarkers. A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline Cohort Characteristics

A total of 169 individuals were enrolled in the study, comprising 99 patients with IBD (40 with CD and 59 with UC) and 70 healthy controls. A comprehensive summary of the cohort's baseline demographic and clinical characteristics is provided in Table 1. The three groups were well-matched, with no statistically significant differences in age, sex distribution, or Body Mass Index (BMI). Among the IBD patients, the most common disease location for CD was ileocolonic (57.5%), while UC was most frequently characterized by distal colitis or pancolitis (37.3% for each). Active disease was present in 32.5% of CD patients and 27.1% of UC patients at the time of data collection. Medication usage varied: 5-ASA preparations were the most common treatment in UC patients (91.5%), while azathioprine was most frequently used in the CD cohort (45.0%).

Comparison of Laboratory Biomarkers Across Groups

A detailed comparison of laboratory biomarkers across the CD, UC, and control groups is presented in Table 2. In the analysis of lipid parameters, IBD patients exhibited a significantly more atherogenic profile, characterized by lower HDL-C levels ($p = 0.01$ for both CD and UC vs. control) and consequently higher PAI values ($p = 0.003$ for CD, $p = 0.017$ for UC). No significant differences were observed in LDL-C or triglyceride levels. The vast majority of inflammatory markers and indices were significantly elevated in IBD patients. Compared to controls, both CD and UC patients had significantly higher neutrophil counts, CRP, ESR, platelet counts, Neutrophil-to-Lymphocyte Ratio (NLR), Systemic Immune-Inflammation Index (SII), and

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

Characteristic	Crohn's Disease (n=40)	Ulcerative Colitis (n=59)	Control (n=70)	p-value
Demographics				
Age (years, mean ± SD)	41.8 ± 10.4	44.4 ± 13.7	39.9 ± 9.2	0.09
Sex (Male, n (%))	17 (42.5%)	31 (52.5%)	28 (40.0%)	0.491
BMI (kg/m², mean ± SD)	25.66 ± 5.33	25.84 ± 4.35	24.66 ± 3.91	>0.05
Crohn's Disease Clinical Features				
Location: Colonic / Ileocolonic / Ileal (%)	5.0 / 57.5 / 37.5	-	-	-
Behavior: Inflammatory / Stricturing / Fistulizing (%)	57.5 / 17.5 / 25.0	-	-	-
Active Disease (CDAI > 150) (%)	32.5%	-	-	-
Perianal Involvement (%)	15.0%	-	-	-
Extraintestinal Manifestations (Arthralgia/Arthritis) (%)	30.0%	-	-	-
Ulcerative Colitis Clinical Features				
Location: Proctitis / Distal Colitis / Pancolitis (%)	-	25.4 / 37.3 / 37.3	-	-
Active Disease (Mayo > 2) (%)	-	27.1%	-	-
Perianal Involvement (%)	-	5.1%	-	-
Extraintestinal Manifestations (Arthralgia/Arthritis) (%)	-	22.0%	-	-
Medication Usage (n,%)				
5-ASA	15 (37.5%)	54 (91.5%)	-	-
Azathioprine (AZT)	18 (45.0%)	11 (18.6%)	-	-
Corticosteroids (CS)	11 (27.5%)	2 (3.4%)	-	-
Anti-TNF	5 (12.5%)	2 (3.4%)	-	-

Table 2. Comparison of Laboratory Biomarkers Across Study Groups

Parameter (mean ± SD or median [IQR])	Crohn's Disease (n=40)	Ulcerative Colitis (n=59)	Control (n=70)	p-value (IBD vs Control)
Lipid Parameters				
HDL-C (mg/dL)	46.4 ± 14.2	45.5 ± 12.9	53.0 ± 14.1	CD: 0.01, UC: 0.01
LDL-C (mg/dL)	107.05 ± 40.43	103.3 ± 39.48	126.15 ± 17.77	>0.05
Triglycerides (mg/dL)	126.65 ± 60.34	111.95 ± 59.44	99.77 ± 59.8	>0.05
PAI	0.41 ± 0.25	0.36 ± 0.23	0.22 ± 0.09	CD: 0.003, UC: 0.017
Inflammatory Parameters				
Neutrophil Count (10^3/mm³)	5.69 ± 2.5	5.01 ± 2.27	2.54 ± 0.76	<0.001 for both
Lymphocyte Count (10^3/mm³)	1.93 ± 0.82	2.00 ± 0.65	1.88 ± 0.57	>0.05
CRP (mg/L)	24.67 [0.33-284]	13.94 [0.42-137]	2.0 ± 1.41	CD: 0.002, UC: 0.008
ESR (mm/h)	19.9 [2-90]	21.6 [2-113]	5.4 ± 3.6	<0.001 for both
Inflammatory Indices				
Platelet Count (10^3/mm³)	318.4 ± 93.9	317.3 ± 112.1	257.6 ± 55.3	CD: 0.003, UC: 0.001
NLR	3.88 [1.1-29.0]	2.78 [0.71-17.4]	1.54 ± 0.82	CD: <0.001, UC: 0.023
SII	1367.6 [327-10678]	948.6 [105-7126]	229.9 ± 81.2	CD: <0.001, UC: 0.025
MHO	13.5 [3.9-46]	11.7 [3.4-40]	9.9 [3.7-10]	CD: 0.019, UC: 0.029
LMO	3.81 ± 1.59	4.6 ± 1.94	2.0 ± 1.21	>0.05

Monocyte-to-HDL Ratio (MHO). However, lymphocyte counts and the Lymphocyte-to-Monocyte Ratio (LMO) were not significantly different between the groups.

Subgroup Analyses

Subgroup analyses were performed to assess the relationship between biomarkers and disease activity or the presence of subclinical atherosclerosis. The results are summarized in Table 3.

• **Disease Activity:** In both CD and UC, active disease was associated with a significantly heightened inflammatory state, marked by higher levels of CRP, NLR, and SII, and a lower LMO ($p < 0.05$ for all). There were notable differences in lipid profiles: active CD was associated with significantly lower HDL-C and triglycerides, while active UC was associated with lower LDL-C. However, PAI was not significantly associated with disease activity in either group.

• **Abdominal Aortic Calcification:** AAC was identified in 40 of the 62 IBD patients with available imaging (63.5%). The presence of AAC was strongly associated with a pro-inflammatory and pro-atherogenic profile. As shown in Table 3, patients with AAC had significantly higher levels of CRP, NLR, SII, MHO, and PAI compared to those without AAC.

Specific Analyses of PAI and ROC Findings

Further analyses specific to PAI are detailed in Table 4. PAI was found to be significantly higher in males than females within the UC and con-

Table 3. Subgroup Analyses Based on Disease Activity and Presence of Aortic Calcification

Parameter	Inactive CD (n=27)	Active CD (n=13)	p	Inactive UC (n=43)	Active UC (n=16)	p	AAC Negative (n=22)	AAC Positive (n=40)	p
BMI (kg/m²)	27.01±5.01	22.96±5.07	.016	25.99±4.3	25.45±4.62	.732	26.67±5.17	25.1±4.5	.3
HDL-C (mg/dL)	50.2±12.8	38.5±14.3	.023	46.7±10.6	42.3±17.6	.098	-	-	-
LDL-C (mg/dL)	118.15±48.35	84±32.98	.123	109.91±35.75	85.56±44.58	.021	-	-	-
Triglycerides (mg/dL)	142±61.87	94.77±43.7	.011	118.74±65.22	93.69±35.51	.159	-	-	-
CRP (mg/L)	4.7	66.03	<.001	4.5	39.26	<.001	4.77	35.2	.001
NLR	2.53±1.42	4.43±1.27	<.001	2.69	6.01	<.001	2.32±1.1	4.48±1.3	<.001
SII	771.5	2605.8	.012	725.2	2555.3	<.001	662.9	1613.2	.002
LMO	4.43	2.53	<.001	4.85	2.74	<.001	3.83	4.2	.444
MHO	19.49±12.55	10.32±3.66	<.001	10.05±4.4	16.64±9.98	.001	10.15±4.11	17.96±11.12	.001
PAI	0.42±0.02	0.38±0.03	.696	0.37±0.02	0.35±0.02	.878	0.23±0.02		

Table 4. Specific Analyses of the Plasma Atherogenic Index

Analysis Type	Group	Detail / Compared Variable	Value	p-value
PAI Comparison by Gender	Crohn's Disease	Male vs Female	0.40 vs 0.42	0.512
	Ulcerative Colitis	Male vs Female	0.43 vs 0.29	0.020
	Control	Male vs Female	0.43 vs 0.08	<0.001
PAI Correlations (Pearson r)	Crohn's Disease	With Age	0.261	0.134
		With BMI	0.256	0.115
	Ulcerative Colitis	With Age	0.203	0.122
	57.5 / 17.5 / 25.0	With BMI	0.010	0.992
	Control	With Age	0.553	<0.01
		With BMI	0.475	<0.01

Table 5. ROC analysis of Ulcerative Colitis and Crohn's diseases patients for SII and NLR

Ulcerative colitis	Sensitivity	Specifity	Cut-off	AUC	p
NLO	84.6	72.7	2.69	0.7	0.00
SII	69.2	63.6	786	0.72	0.02
Crohn's Disease	**Sensitivity**	**Specifity**	**Cut-off**	**AUC**	**p**
NLO	93	74.4	2.82	0.86	0.00
SII	93	74	876	0.9	0.00

trol groups, but this was not the case in the CD group. Additionally, PAI showed a significant positive correlation with age and BMI in the healthy control group; however, this association was not observed in either of the IBD cohorts.

Receiver Operating Characteristic (ROC) curve analysis was used to assess the predictive value of these indices. NLR and SII were significant predictors of active disease in both CD (AUC 0.772 and 0.726, respectively) and UC (AUC 0.865 and 0.904, respectively) (Table 5). In contrast, PAI and MHO emerged as the strongest predictors of the presence of AAC (AUC 0.790 and 0.785) (Figure 1).

DISCUSSION

This study elucidates the clinical utility of novel, accessible biomarkers-PAI, MHO, and SII-in the context of IBD. Our principal findings demonstrate that patients with IBD have significantly elevated levels of PAI, MHO, and SII compared to healthy controls, strongly supporting the growing paradigm of IBD as a systemic condition characterized by atherogenic dyslipidemia and chronic inflammation. The most compelling aspect of our research is the robust association between these simple blood markers and the presence of AAC, a surrogate for subclinical atherosclerosis. These findings underscore the critical importance of proactive cardiovascular risk screening in the comprehensive management of IBD.

The significantly elevated PAI and MHO levels observed in our IBD cohort reflect a pathophysiological state known as "inflammatory dyslipidemia." It is well-established that chronic inflammation directly alters hepatic lipid metabolism, increasing triglyceride (TG) synthesis while impairing both the quantity and function of anti-atherogenic HDL

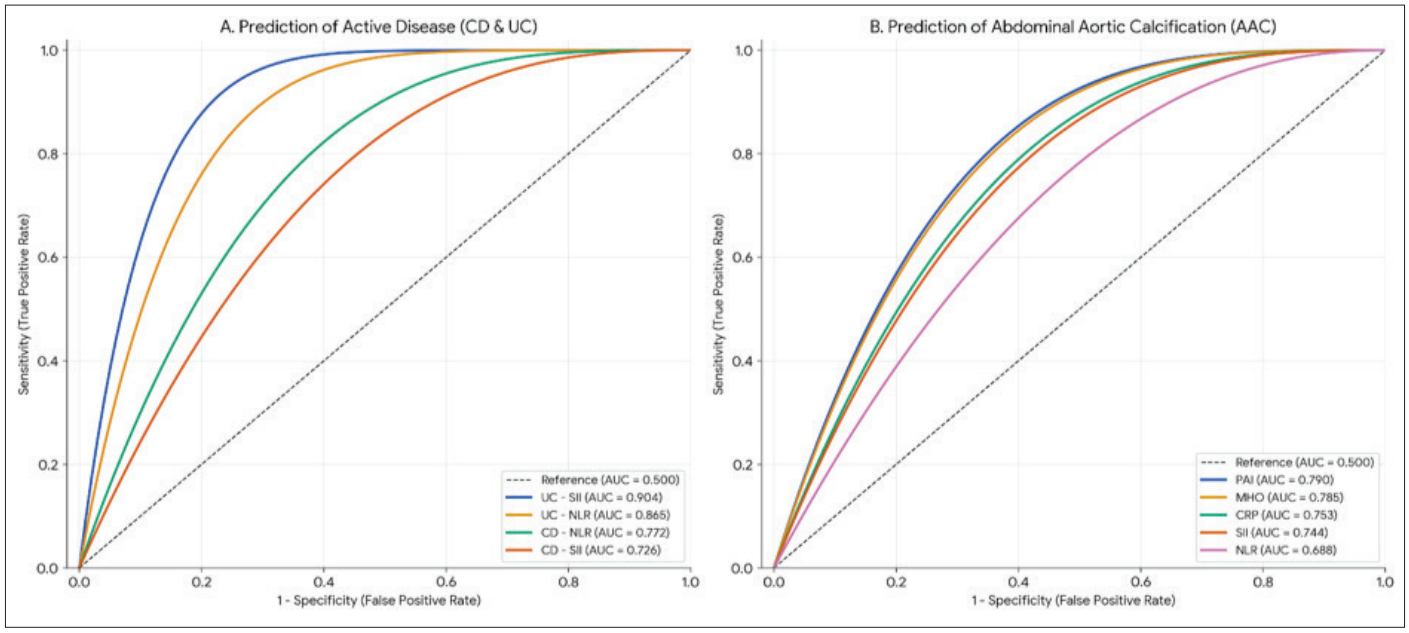

Figure 1. ROC analysis of parameters and prediction of active disease and AAC.

cholesterol (HDL-C). PAI, as the logarithmic ratio of TG to HDL-C, effectively captures this imbalance and serves as a strong proxy for the presence of small, dense LDL particles, which more readily penetrate the arterial wall to initiate atherosclerosis.[25] Concurrently, a high MHO reflects dual pathology: an increase in pro-inflammatory monocytes, the cellular precursors to foam cells in atheromatous plaques, and a decrease in protective HDL. Recent large-scale meta-analyses confirm that patients with IBD have a 20-30% higher risk of myocardial infarction and stroke-risks not fully explained by traditional factors but directly linked to the underlying inflammatory burden.[13,14]

In parallel, our study reaffirms the role of hematological inflammatory indices like the NLR and SII. The fact that both markers were elevated in IBD patients and correlated significantly with disease activity aligns with their known pathophysiology. Active inflammation stimulates the bone marrow to release neutrophils and platelets while promoting the migration of lymphocytes into inflamed gut tissue, resulting in the characteristic peripheral blood signature of elevated NLR and SII. Contemporary research suggests that these indices are not only useful for tracking disease activity but may also predict long-term complications and therapeutic response to biologics. This positions NLR and SII as valuable, cost-effective tools for both dynamic monitoring and prognostication in IBD care.

An intriguing finding from our study is the dissociation between markers of acute inflammation and PAI. While NLR and SII tracked well with disease activity, PAI levels did not differ significantly between active and remission states. This suggests that PAI may reflect a more chronic, established atherogenic state rather than fluctuating with acute inflammatory flares. This observation could be partially explained by the complex metabolic effects of active IBD, where malabsorption or the use of certain medications like corticosteroids might confound the lipid profile, masking the true relationship of PAI with an acute flare. This distinction highlights the complementary roles these biomarkers can play: NLR and SII can help answer, "How active is the disease right now?" while PAI can address, "What is the patient's long-term, cumulative cardiovascular risk?"

Perhaps the most clinically impactful contribution of our study is the powerful and consistent association demonstrated between all the investigated biomarkers and the presence of AAC. We found that patients with detectable aortic calcification had significantly higher levels of PAI, MHO, SII, NLR, and CRP. AAC is a well-established indicator of subclinical atherosclerosis and an independent predictor of future cardiovascular events. The high predictive performance of PAI (AUC = 0.790) and MHO (AUC = 0.785) for identifying patients with AAC provides tangible, anatomical evidence that these blood tests reflect a real-world atherosclerotic burden, not just a theoretical risk. Current literature confirms an increased prevalence of both AAC and coronary artery calcification (CAC) in IBD patients, findings directly linked to the cumulative inflammatory burden.[16] This strongly suggests that the incidental finding of AAC on CT scans performed for other indications should be diligently reported and integrated into the patient's cardiovascular risk profile.

These findings support modern mechanistic models linking IBD and atherosclerosis via the "gut-vascular axis." This concept moves beyond general systemic inflammation to include more specific pathways. Gut dysbiosis and increased intestinal permeability in IBD allow the translocation of microbial products (e.g., LPS) and pro-atherogenic metabolites (e.g., Trimethylamine N-oxide, or TMAO) into the systemic circulation. These molecules can directly promote endothelial dysfunction, monocyte activation, and foam cell formation, thereby accelerating atherosclerosis. From this perspective, the elevated biomarkers we observed, such as MHO and PAI, can be seen as downstream reflections of this complex interplay between gut-derived factors and systemic inflammation.

Finally, the limitations of this study must be acknowledged, including its retrospective, single-center design and relatively small cohort size, which may affect the generalizability of the results. Additionally, the potential confounding effects of IBD medications on these biomark-

ers were not fully analyzed, and AAC evaluation was not performed by multiple radiologists. Despite these limitations, our work provides strong evidence for the utility of simple biomarkers in IBD-related cardiovascular risk assessment. In clinical practice, the routine calculation of these indices, particularly PAI and MHO, could help identify high-risk patients for earlier, more aggressive management of modifiable cardiovascular risk factors. There is a pressing need for prospective, multi-center studies to validate these findings, incorporate these markers into new IBD-specific cardiovascular risk calculators, and investigate the impact of IBD therapies, especially biologics, on these markers and long-term cardiovascular outcomes.

CONCLUSION

This study confirms that the simple, cost-effective biomarkers PAI, MHO, and SII are significantly elevated in patients with Inflammatory Bowel Disease and are strongly predictive of subclinical atherosclerosis, as evidenced by their association with abdominal aortic calcification. These findings support the modern paradigm of IBD as a systemic disease that actively promotes atherogenesis through a complex interplay of systemic inflammation and gut-specific factors, such as microbial dysbiosis. Clinically, the routine integration of these indices into patient care could enhance cardiovascular risk stratification, enabling more targeted and timely preventive strategies. Future prospective, randomized controlled trials are warranted to validate the prognostic value of these markers and to elucidate how specific IBD therapies may modulate them to improve long-term cardiovascular outcomes.

Ethics Committee Approval: The study's protocol received approval from Prof. Dr. Cemil Taşcıoğlu City Hospital Clinical Research Ethics Committee (Approval Number: 119, Date: 31.07.2023).

Informed Consent: Written informed consent was obtained from the patients participating in this study.

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Author Contribution: Concept – B.A.Ç., Y.G.; Design – B.A.Ç., Y. G.; Supervision – B.A.Ç, Y.G.; Resource – B.A.Ç., Y.G.; Materials – B.A.Ç., Y.G.; Data Collection and/or Processing- B.A.Ç., H.E.; Analysis and/or Interpretation - B.A.Ç., H.E.; Literature Review – B.A.Ç., H.E.; Writing – B.A.Ç., H.E.; Critical Review – H.E., B.A.Ç.

Declaration of Interests: The authors declare that they have no competing interest.

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Journal of Enterocolitis

Case Report

Solitary Rectal Ulcer Diagnosed in a Malignancy-Mimicking Polypoid Rectal Lesion: A Case Report

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Abstract

Solitary rectal ulcer syndrome (SRUS) is a chronic anorectal disorder of unknown etiology, most commonly observed in young adults. The diagnosis is established through a combination of clinical, endoscopic, and histopathological findings. Its polypoid appearance, which may mimic malignancy, often leads to misdiagnosis. Herein, we present the case of a 64-year-old woman with a history of constipation and digital evacuation, who was found to have a polypoid rectal lesion resembling malignancy, which was subsequently diagnosed as SRUS.

Keywords: Biofeedback, mesalazine, polypoid rectal lesion, solitary rectal ulcer.

INTRODUCTION

Solitary rectal ulcer syndrome (SRUS) is an uncommon anorectal condition with an incompletely understood pathogenesis, predominantly affecting young adults. Clinical manifestations are often nonspecific and include rectal bleeding, mucous discharge, defecatory difficulty, tenesmus, a sensation of incomplete evacuation, and anorectal pain. Endoscopically, SRUS may present as a single ulcer, a polypoid mass, or erythematous mucosal patches, potentially being mistaken for malignancy.[1-3] Diagnosis is based on a high index of suspicion, endoscopic appearance, and confirmatory histopathology. We report a case of SRUS presenting with a malignancy-mimicking polypoid rectal lesion.

CASE PRESENTATION

A 64-year-old woman presented to the gastroenterology outpatient clinic with a one-year history of constipation, a sensation of incomplete evacuation after defecation, and occasional hematochezia. Her medical history was unremarkable. Upon further inquiry, she reported long-standing use of digital maneuvers to aid evacuation due to constipation.

Flexible sigmoidoscopy revealed a 3-cm ulcerovegetant polypoid lesion on the anterior wall of the rectum, located 5 cm from the anal verge, along with several smaller polyps, the largest measuring 0.5 cm (Figure 1). Multiple biopsies were obtained under suspicion of malignancy. Histopathologic examination revealed chronic inflammatory changes characterized by mononuclear cell infiltration of the lamina propria, ulceration, and inflammatory granulation tissue, with no evidence of malignancy. Pelvic magnetic resonance imaging showed no evidence of a mass lesion (Figures 2-3).

Anorectal manometry demonstrated findings consistent with rectoanal dyssynergia. Based on these findings, a diagnosis of SRUS was established. The patient was instructed in daily biofeedback therapy and advised to discontinue digital evacuation. Topical mesalazine suppositories (1 g/day) were prescribed. At a three-month follow-up colonoscopy, the lesion had regressed significantly, leaving only erythematous mucosal patches and superficial ulcerations (Figure 4). Her defecatory symptoms had also improved markedly.

Written informed consent was obtained from the patient for this case. No artificial intelligence–assisted technologies were used in the preparation of this work.

DISCUSSION

SRUS is a rare but diagnostically challenging chronic condition.[3,4] Its nonspecific clinical features can mimic both benign and malignant disorders. In our case, the endoscopic appearance initially raised suspicion of malignancy, which was subsequently excluded by histopathology in favor of SRUS. Literature reports indicate that SRUS can present with ulcerative, polypoid, or erythematous mucosal patterns.[3]

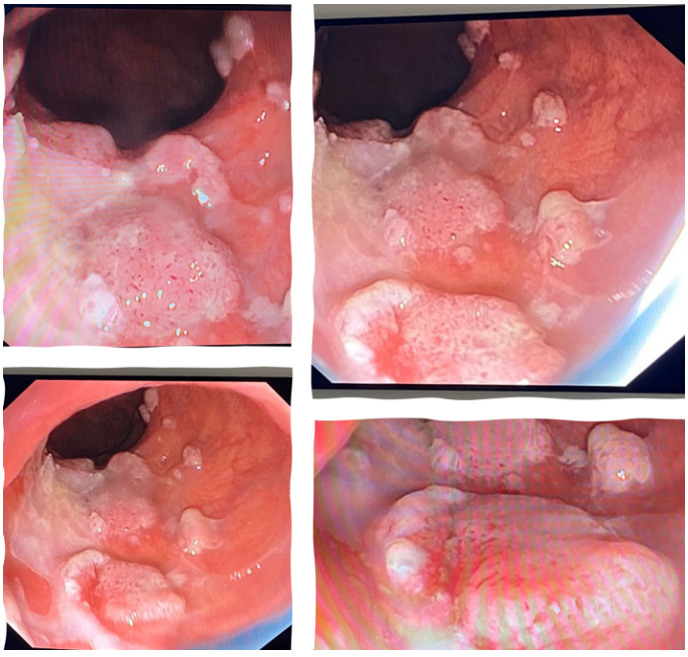

Figure 1. Polypoid ulcerovegetant lesion measuring approximately 3 cm, located on the anterior wall of the rectum, 5 cm from the anal verge, with additional smaller polyps—the largest measuring 0.5 cm.

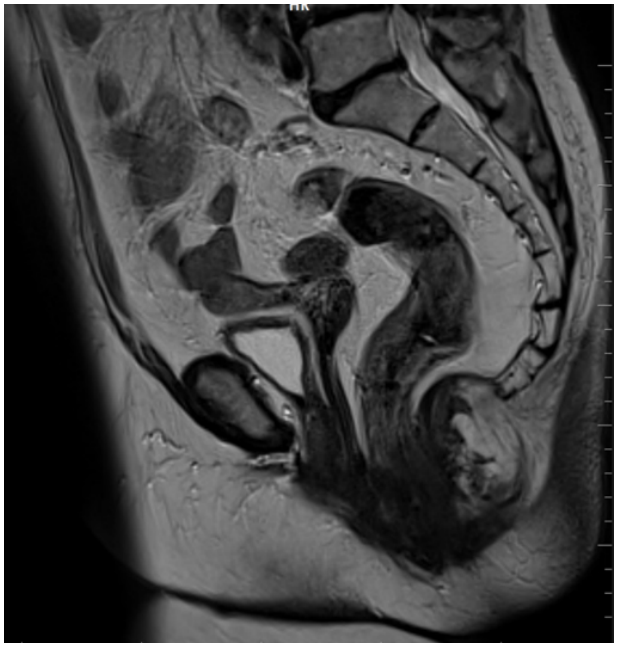

Figure 2. Thickening of the rectal wall, with the lesion located posteriorly and displaying a mildly polypoid intraluminal configuration. No evidence of diffuse inflammatory changes or infiltration into the surrounding fat tissue is observed, which is not suggestive of malignant infiltration.

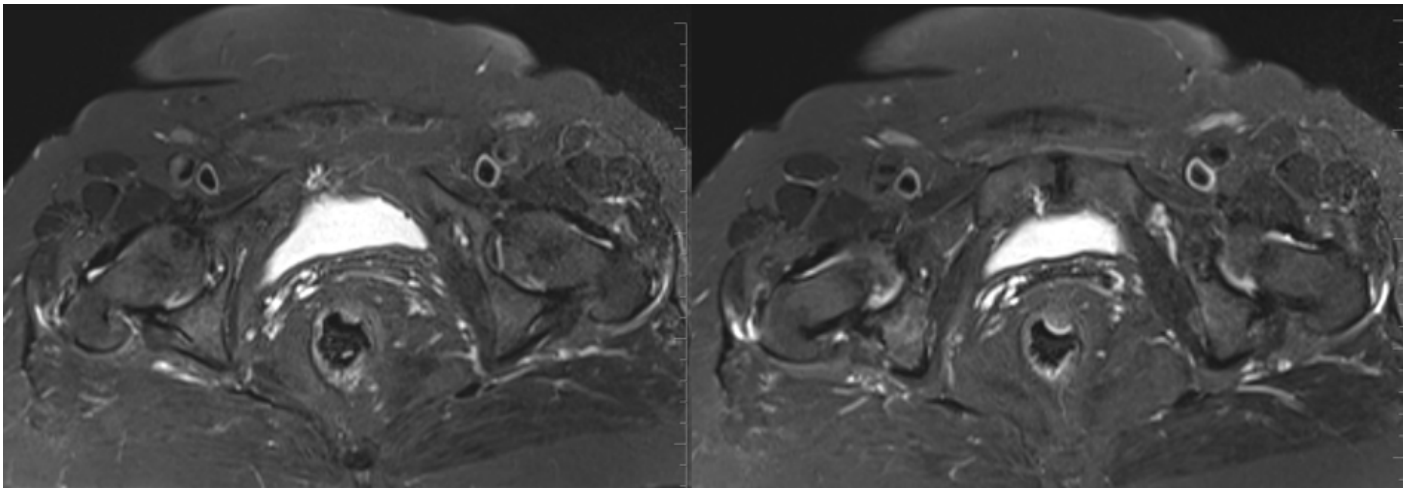

Figure 3. Axial T2-weighted sequences showing localized thickening of the posterior/lateral quadrant of the rectal wall. Signal intensity is pronounced at the submucosal level, with no significant infiltration into the surrounding fatty tissue. No diffuse inflammatory reaction or fistulous tract is observed. The mesorectal fat plane is preserved, and no significant perirectal pathological lymphadenopathy is noted.

The pathogenesis of SRUS is thought to involve rectal prolapse, pelvic floor dysfunction, and mucosal ischemia.[5,6] Habitual digital evacuation may exacerbate mucosal trauma, contributing to lesion development.[7] In our case, rectoanal dyssynergia, chronic constipation, and a history of digital maneuvers were all present.

Treatment options include behavioral modifications, biofeedback therapy, and topical mesalazine.[8,9] Biofeedback has been shown to improve pelvic floor coordination and alleviate symptoms.[9,10] Our patient experienced significant clinical and endoscopic improvement after three months of therapy.

CONCLUSION

SRUS should always be considered in the differential diagnosis of rectal lesions mimicking malignancy. A thorough history, including inquiry about digital evacuation, is essential. Anorectal manometry and defecography should be performed when indicated to evaluate pelvic floor dysfunction. Successful outcomes can be achieved with biofeedback therapy and topical mesalazine.

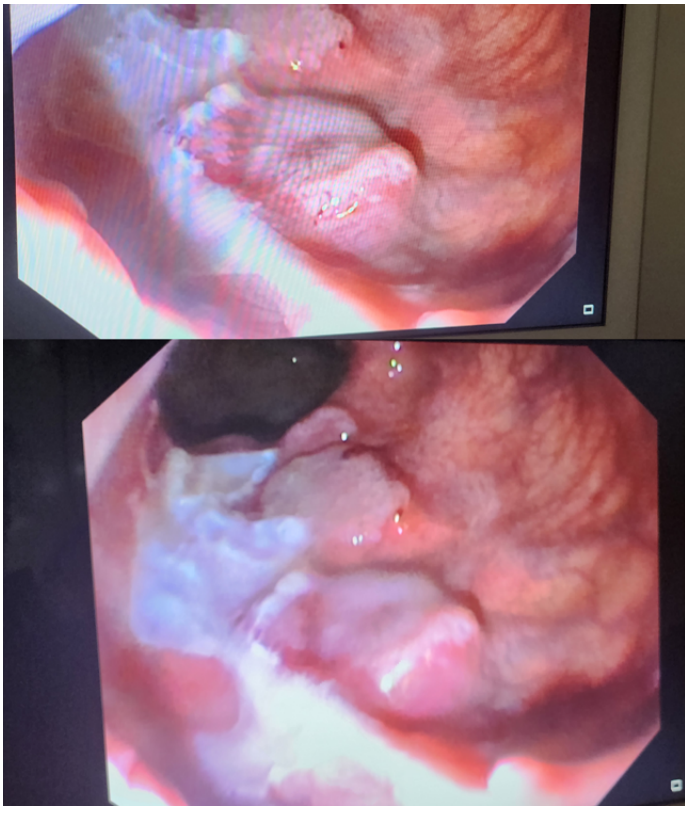

Figure 4. Polypoid lesion on the anterior wall of the rectum, 5 cm from the anal verge, displaying erythematous mucosal patches and superficial ulcerations.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consent was obtained from the patients participating in this study.

Peer-review: Externally peer-reviewed.

Author Contribution: Concept – R.E; Design – R.E.; Supervision – R.E., M.A.; Resource – R.E.; Materials – R.E., M.A.; Data Collection and/or Processing – R.E.; Analysis and/or Interpretation – R.E., M.A..; Literature Review – R.E., M.A.; Writing – R.E.; Critical Review –R.E., M.A.

Declaration of Interests: The authors declare that they have no competing interest.

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A Rare and Overlooked Cause of Chronic Diarrhea: Hereditary Transthyretin Amyloidosis

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Abstract

Hereditary transthyretin amyloidosis is a rare, rapidly progressive, and fatal disease caused by pathogenic variants in the transthyretin gene. It is inherited in an autosomal dominant manner. The disease is characterized by the accumulation of amyloid fibrils in various organs, particularly the peripheral nerves, heart, kidneys, eyes, and gastrointestinal tract. We present a rare case of transthyretin amyloidosis manifested by chronic diarrhea.
Keywords: Amyloidosis, diarrhea, hereditary

INTRODUCTION

Amyloidosis is a heterogeneous group of diseases caused by the extracellular deposition of insoluble fibrillar proteins, leading to multiple organ dysfunction and a shortened lifespan.[1] Various systems can be affected by amyloid deposition, with the digestive tract being one of the organs involved, potentially causing chronic diarrhea.[2] Gastrointestinal involvement in amyloidosis can present with a variety of clinical symptoms, including weight loss, fatigue, nausea, vomiting, bleeding, and abnormal bowel habits.[3] The onset of gastrointestinal tract involvement is often insidious, and the nonspecific nature of the symptoms makes diagnosis challenging, often resulting in diagnostic delays. Endoscopic biopsy plays a crucial role in diagnosing amyloidosis, determining the subtype, and ruling out other potential diagnoses. While many endoscopic findings have been described, they are generally nonspecific and include edema, erythema, submucosal hematoma, or even normal findings.[4] We present a rare case of transthyretin (TTR) amyloidosis manifesting as chronic diarrhea.

CASE REPORT

A 63-year-old woman presented with a 2-year history of watery diarrhea and a 30 kg weight loss over the same period. She had no significant medical history and was not on any medications. She did not smoke or consume alcohol. On physical examination, the patient appeared dehydrated. Stool tests were negative for polymorphonuclear leukocytes, starch, and fat. Microbiological cultures were also negative. The patient had normocytic anemia, while iron, vitamin B12, and folic acid levels were normal. Liver and kidney function tests were within normal limits, and celiac antibodies were negative. Protein electrophoresis revealed an M-band (Figure 1). Her IgG level was 1681 mg/dL (normal range: 700–1600 mg/dL), while IgA and IgM levels were normal. Serum and urine immunofixation electrophoresis showed IgG lambda and lambda light chain. Magnetic resonance enteroclysis revealed no significant intestinal pathology (Figure 2). Both gastroscopy and colonoscopy, including examination of the terminal ileum, were unremarkable, and biopsies were taken from all segments. Jejunal aspirate was negative. Biopsies from the antrum, corpus (Figure 3), duodenum (Figure 4), and transverse colon showed deposits consistent with amyloidosis. PET-CT imaging revealed several hypermetabolic lymph nodes (SUVmax: 10.4) with effaced fatty hilums in the left inguinal area, the largest measuring 16x14 mm (Figure 5). Lymph node excision was performed, and pathology confirmed lambda amyloid deposition in the vessel walls. A bone marrow biopsy revealed hypercellular bone marrow with a minimal plasma cell population and lambda light chain monopathy. Echocardiography showed concentrically increased cardiac wall thickness, with a normal ejection fraction. ProBNP levels were elevated at 2395 pg/mL (normal range: 0–125). Cardiac magnetic resonance imaging (Figure 6) revealed an interventricular septum thickness of 18 mm and an increased lateral wall thickness of 18 mm. Concentric hypertrophy of the left ventricle was observed, along with thickening of the interatrial septum. Subendocardial ring enhancement, more prominent in the basal segments, suggested cardiac amyloidosis. Genetic testing confirmed the presence of a transthyretin amyloidosis gene variant, and the patient was diagnosed with hereditary transthyretin amyloidosis.

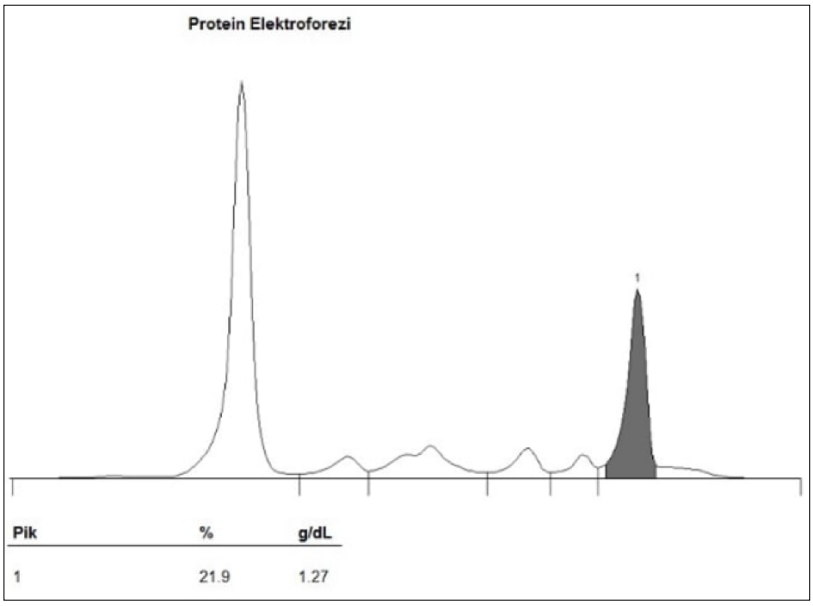

Figure 1. M-band in protein electrophoresis.

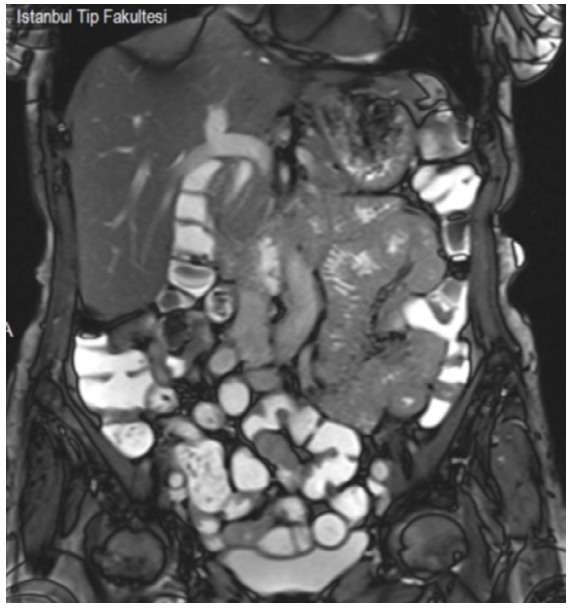

Figure 2. Magnetic resonance enteroclysis findings.

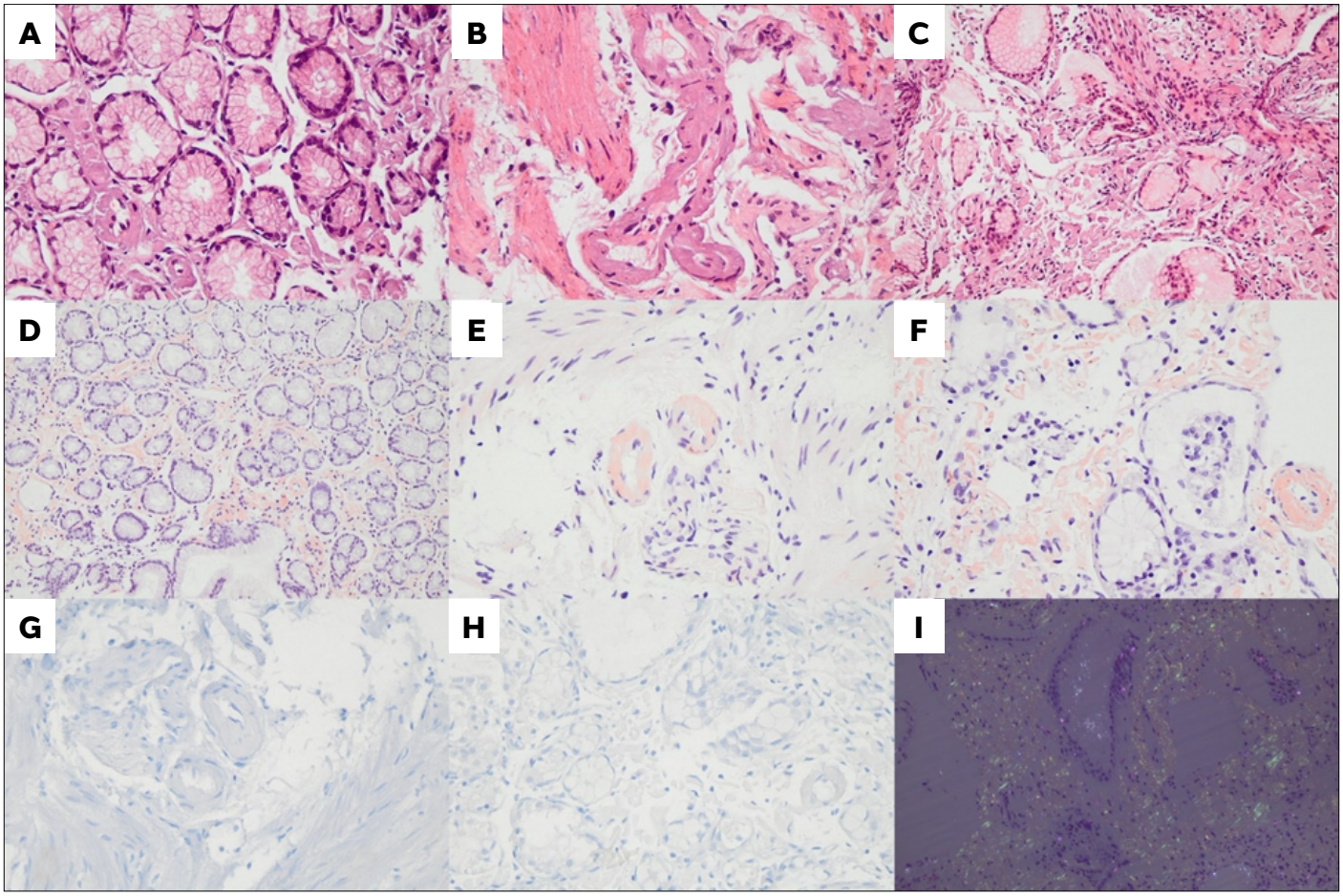

Figure 3. Amyloid deposition in gastric biopsies taken from the antrum and corpus: **(A)** Antrum mucosa showing homogeneous eosinophilic thickening of the vessel walls and eosinophilic droplets in the lamina propria, suspicious for amyloid deposition (H&E, ×400); **(B)** Antrum submucosal vessel walls with homogeneous eosinophilic thickening, suspicious for amyloid (H&E, ×400); **(C)** Corpus mucosa showing similar eosinophilic thickening of the vessel walls and droplets in the lamina propria (H&E, ×200); **(D-F)** Congo red staining showing amyloid deposition at ×200 **(D)** and ×400 **(E)** in the antrum, and at ×400 **(F)** in the corpus; **(G-H)** Negative immunostaining with the anti–Amyloid-A antibody at ×400 in the antrum **(G)** and corpus **(H)**; **(I)** Congo red stain under polarized light demonstrating apple-green birefringence in the corpus (×200).

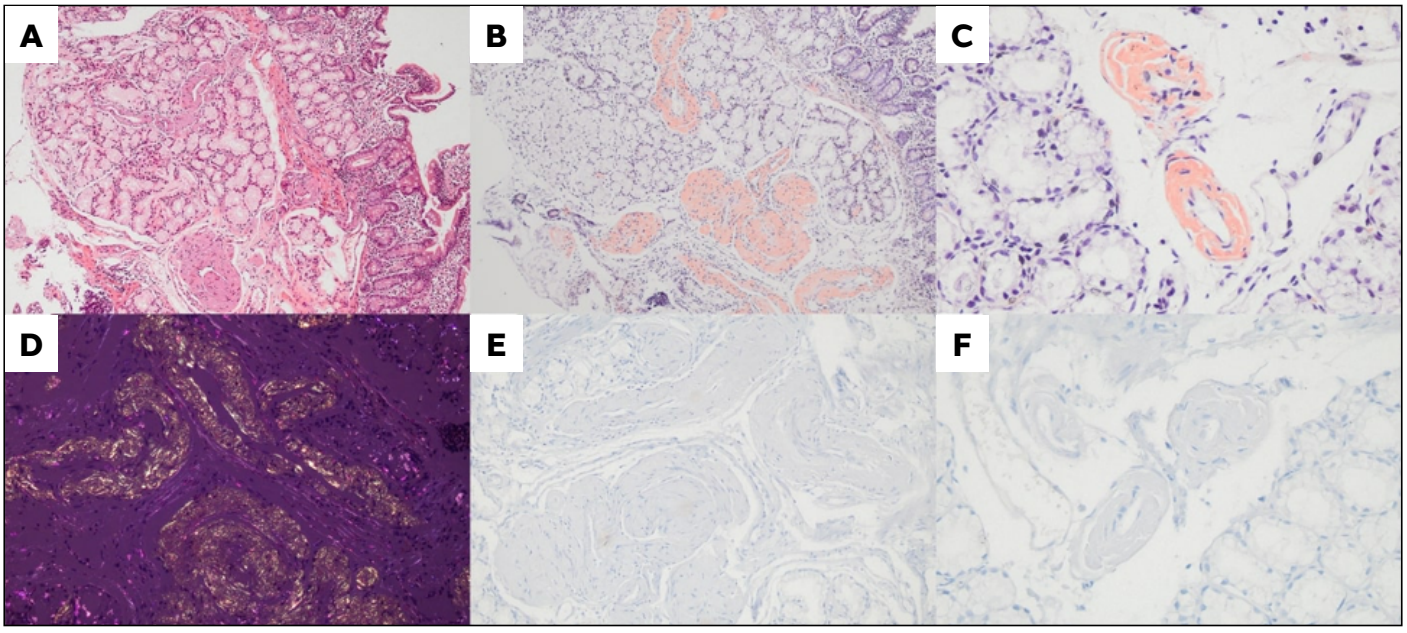

Figure 4. Amyloid deposition in the duodenum endoscopic biopsy specimen: **(A)** Submucosal vessel walls with homogeneous eosinophilic thickening, suspicious for amyloid (H&E, ×100); **(B-C)** Congo red staining showing amyloid deposition at ×100 **(B)** and ×400 **(C)**; **(D)** Congo red stain under polarized light demonstrating apple-green birefringence (×200); **(E-F)** Negative immunostaining with the anti–Amyloid-A antibody at ×200 **(E)** and ×400 **(F)**.

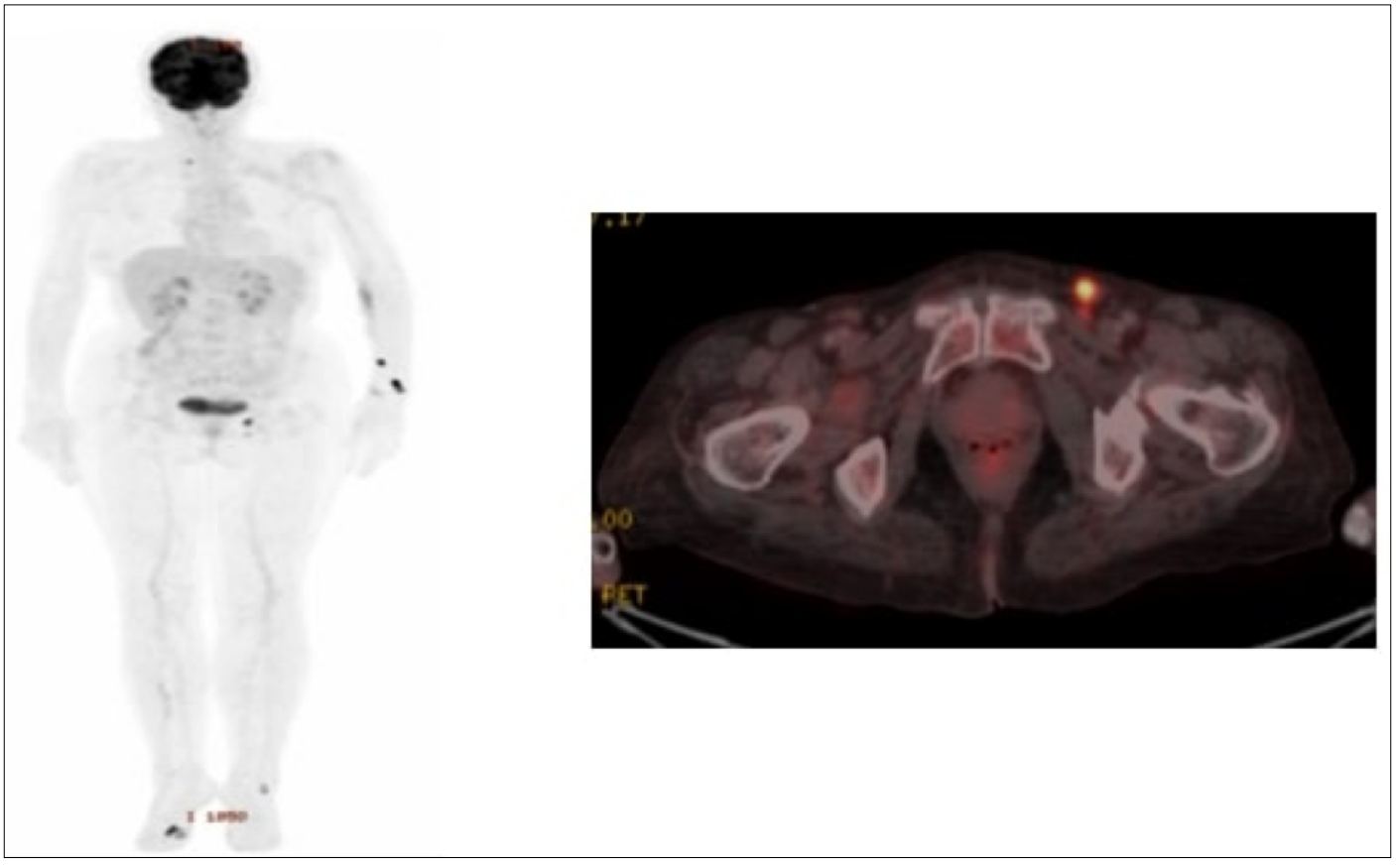

Figure 5. PET-CT findings.

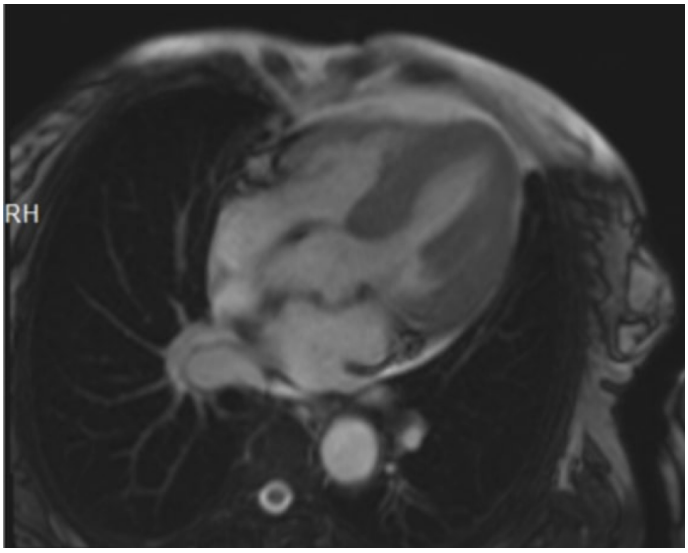

Figure 6. Cardiac magnetic resonance imaging findings.

DISCUSSION

Amyloidosis refers to a heterogeneous group of disorders, which can be classified into two main subtypes: systemic and localized amyloidosis.[5] The most common subtype is systemic amyloidosis, which can be due to either acquired or hereditary conditions. The most well-known hereditary condition is caused by mutations in the TTR gene.[6]

Hereditary TTR amyloidosis is a rare, systemic, autosomal dominant disease caused by mutations in the gene encoding the transthyretin transport protein.[7,8] It is characterized by progressive peripheral sensorimotor and/or autonomic neuropathy, typically beginning in the 3rd to 5th decades of life. The disease often involves the heart, central nervous system, eyes, and kidneys.[9] Hereditary transthyretin amyloidosis should be suspected in adults with cardiac conduction blocks, restrictive cardiomyopathy, and nephropathy. Gastrointestinal manifestations can significantly impact a patient's quality of life, primarily due to damage to the autonomic nervous system, which affects motility and secretory functions in the gastrointestinal tract. Nearly 70% of individuals with transthyretin amyloidosis report gastrointestinal manifestations.[10] In some cases, gastrointestinal symptoms, especially diarrhea, may be the first symptom to appear.[11]

The most common gastrointestinal symptoms, in order of frequency, include unintentional weight loss, early satiety, alternating constipation and diarrhea, constipation, chronic diarrhea, nausea, vomiting, and fecal incontinence.[12] Changes in bowel habits may be the only symptom in some patients, and if not considered in the differential diagnosis, these patients may undergo multiple endoscopic examinations.[13]

Gastrointestinal manifestations in hereditary TTR amyloidosis often present insidiously and nonspecifically. These symptoms are poorly specific, leading to misdiagnosis with more common conditions such as irritable bowel syndrome and functional dyspepsia. Gastroenterologists play a critical role in both the diagnosis and management of this disease. Early diagnosis and treatment are essential for improving the patient's quality of life. Therefore, hereditary TTR amyloidosis should be considered in the differential diagnosis, especially as a rare cause of chronic diarrhea.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written informed consent was obtained from the patients participating in this study.

Peer-review: Externally peer-reviewed.

Author Contribution: Concept – Z.İ., A.O.Ç.; Design – Z.İ., A.O.Ç.; Supervision – B.Ç., F.A.; Materials – Z.İ., A.O.Ç., B.Ç., F.A.; Data Collection and/or Processing - Z.İ., A.O.Ç., B.Ç., F.A.; Analysis and/or Interpretation - Z.İ., B.Ç., F.A.; Literature Review – Z.İ., A.O.Ç., N.B., B.Ç., F.A.; Writing – Z.İ., B.Ç., F.A.; Critical Review – Z.İ., B.Ç., F.A.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: Authors declare that this study have not received any financial support.

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