ISSN: 2469-5769

Bongurala et al. Int J Pediatr Res 2024, 10:133
DOI: 10.23937/2469-5769/1510133
Volume 10 | Issue 2
Open Access

International Journal of Pediatric Research

ORIGINAL ARTICLE

Clinical Manifestations of Inflammatory Bowel Disease in Minority Children: A Retrospective Study

Archana Reddy Bongurala[1], Moses O Evbuomwan[2], Oluwatoyin A Gbademu[3], Inaya Hajj Hussein[4*] and Ayesha Fatima[5]

[1]*Department of Pediatrics, Omni Family Health, Bakersfield, USA*

[2]*Department of Radiation Oncology, University of Iowa Hospitals and Clinics, Iowa City, USA*

[3]*Department of Anesthesiology, University of Michigan Hospital, Ann Arbor, USA*

[4]*Department of Foundational Medical Studies, Oakland University William Beaumont School of Medicine, Rochester, USA*

[5]*Department of Pediatrics, Corewell Health William Beaumont University Hospital, Royal Oaks, USA*

***Corresponding author:** *Inaya Hajj Hussein, PhD, Department of Foundational Medical Studies, Oakland University William Beaumont School of Medicine, 586 Pioneer Dr, Rochester, MI-48309, USA, Tel: +12488317230*

Abstract

Objective: The study aims to describe the prevalence of IBD types and clinical presentations in pediatric minority populations treated at a single healthcare institute.

Methods: This study presents a retrospective analysis of pediatric minority IBD patients aged 6-17 years, treated at Beaumont Hospital from 2009 to 2019. Patient demographics including gender, age at diagnosis, race, IBD-type, associated problems, disease location, family history and surgical intervention were documented. The study analyzed data using SAS software and the Pearson chi-square test.

Results: A total of 119 pediatric patients were included in the study. The sample composed of 49 African Americans (AA), 25 Asians (AS), 31 who identified as others and 14 with missing/preferred not to answer. The mean age of IBD diagnosis was 12.3 years for AA, 11.7 years for AS, and 12.6 years for others group. Most patients in both AA and other groups were diagnosed with Crohn's Disease (CD, 55.1% and 48.4%, respectively) whereas the majority of the AS patients were diagnosed with Ulcerative Colitis (UC, 44.0%). The mean CRP values for AA were higher than normal (15.28 mg/dl vs. 0-8 mg/dl), but the CRP values for AS and other groups were within normal limits (2.38 mg/dl, 3.28 mg/dl, respectively, vs. 0-8 mg/dl), with no significant statistical difference (p-value -0.146).

Conclusion: IBD in AA children presents more commonly with CD and at older ages when compared to Asians and other minority group. Racial/Ethnic differences of IBD among children require further investigations.

Keywords

IBD phenotypes, Pediatric IBD, Minorities health, Gastrointestinal health, Pediatric gastroenterology, American African IBD, Asian IBD, C-reactive protein

Abbreviations

IBD: Inflammatory Bowel Disease; GI: Gastrointestinal; CD: Crohn Disease; UC: Ulcerative Colitis; AA: African Americans; AS: Asians; HCT: Hematocrit; Hgb: Hemoglobin; CRP: C-Reactive Protein

Introduction

Inflammatory bowel disease (IBD) is a complex disorder involving the relapsing and remitting inflammation of the gastrointestinal (GI) tract [1,2] resulting in significant long-term morbidity [3]. IBD is frequently associated with the development of extraintestinal manifestations affecting approximately 6% to 47% of adult patients and around 25% to 29% of pediatric patients with IBD [4,5]. IBD is a lifelong incurable chronic inflammatory disease affecting close to 7 million people worldwide and becoming a global emerging disease with prevalence estimated to reach 1% of the western population by 2030 [6]. The prevalence and incidence among Africans, African Americans, Asians, and Hispanics have been reported

Citation: Bongurala AR, Evbuomwan MO, Gbademu OA, Hussein IH, Fatima A (2024) Clinical Manifestations of Inflammatory Bowel Disease in Minority Children: A Retrospective Study. Int J Pediatr Res 10:133. doi.org/10.23937/2469-5769/1510133

Accepted: December 03, 2024: **Published:** December 05, 2024

with increasing frequencies worldwide [3]. Though traditionally emerging economies have reported lower prevalence of IBD; however, the incidence is currently increasing in many of these countries as they become more industrialized [7,8], thus the need for appropriate diagnosis and treatment for patients, especially minority pediatric population, is paramount.

The most common IBD types are Crohn disease (CD) and Ulcerative Colitis (UC) which are frequently diagnosed in genetically susceptible individuals exposed to environmental factors that alter their GI microbiome [1,2]. In patients with a very early onset of IBD, defined by diagnosis before the age of 6, genetics plays a prominent role [9,10]. CD can affect any of the GI segments from the oral cavity to the anus and may involve all layers of the gut, while UC only affects the large intestine primarily confined to the mucosal and to a lesser degree, the submucosal compartment [3,11]. The colon is the most common site of UC and CD disease in the pediatric population and differentiation of colonic CD from UC may be difficult [12]. The age at which pediatric patients are diagnosed with IBD is decreasing and could likely be due to factors such as improved access to care, advanced diagnostic techniques, or earlier disease onset [2]. Nonetheless, age-specific trends in the incidence of IBD vary globally [3].

It is well documented that IBD can cause substantial morbidity among children globally [13]. Recent epidemiologic studies have described increasing incidence rates of IBD among African American (AA) adults and African Caribbean children approaching those in Caucasians [14]. Furthermore, numerous studies have described IBD symptomatic presentations in Caucasians and Ashkenazi Jews because of its relatively high prevalence in these ethnic groups [15] few studies have described the prevalent IBD-type diagnosed and the clinical presentations of IBD in minorities populations such as African Americans, American Indians, Asian Americans, Hispanic Americans, and other minorities [13,16].

On this basis, the current study aims to describe the prevalent IBD-type diagnosed and the clinical presentations of IBD in the minority pediatric populations using a single healthcare institute database. Thus, the rationale for this study is to obtain baseline information that will help to identify factors such as age at onset of IBD, IBD-type (CD vs. UC) clinical presentations, family history, and associated problems. Such parameters will be an asset in the early diagnosis of IBD in minority pediatric populations.

Methods

This is a single institution retrospective study. The study design was approved by Beaumont Hospital Institutional Review Board. The electronic charts from January 2009 to December 2019 were retrospectively reviewed with the following inclusion criteria: Individuals between the ages 6-17 years-old, diagnosed with inflammatory bowel disease, who did not identify themselves as Caucasian in their medical record chart and were seen and treated by the pediatric gastroenterologist at Beaumont Hospital, Royal Oak, Michigan. Patients less than 6-years-old and those greater than 17-years-old and individuals, aged 6-17 years, who were not diagnosed with IBD or identified as White non-Hispanic, and/or Caucasians on their medical record chart were excluded. Patients who were pregnant and within the age group were excluded as well. Selected patient's charts were reviewed to assess demographic information such as gender, age at diagnosis, race, IBD-type (CD vs. UC vs. indeterminate colitis), associated problems, and disease location in the GI tract, family history and surgical intervention. Data was recorded on an excel sheet and was analyzed with The SAS system for Windows version 9.4. Categorical data were recorded as numbers and percent; continuous data as mean and standard deviation; and association analyzed with Pearson's Chi-square test were recorded as p-value. Where $p < 0.05$ was considered statistically significant.

Results

Demographics and clinical presentation of inflammatory bowel disease in minority patients

One hundred and nineteen pediatric minority patients aged 6-17 years were included in the study. These patients were treated at the pediatric gastroenterology clinic of Beaumont Hospital, Royal Oak, Michigan, between 2009-2019 and were selected as minority because they self-identified as a non-Caucasian race. The sample comprised of 49 African Americans (AA), 25 Asians (AS), 31 who identified as others and 14 with missing/preferred not to answer. Individuals who specified "other", missing/preferred not to answer do not identify as Caucasian, black, or African American or as Asian; they do not necessarily explicitly identify as a minority. Asian and black/African American remain as distinct categories. The final data analysis was based on 105 pediatric minority populations excluding the 14-missing identity.

As shown in Table 1, in both the AA and AS groups, the majority of patients diagnosed with IBD were male, 57.1%, and 68.0%, respectively. In all groups, most patients were diagnosed with a type of IBD at age equal or greater than 12 years. Most patients in both AA and other groups were diagnosed with Crohn's Disease (CD, 55.1%, and 48.4%, respectively) whereas the majority of the AS patients were diagnosed with Ulcerative Colitis (UC, 44.0%). More so, most of the diagnosed patients in all groups did not have associated problems of abscess or fistula or both (75.5%, 84.0%, and 83.9% respectively). In all populations, the colonic

Table 1: Demographic of minority pediatric populations and the clinical presentation of IBD.

Variable	African American	Asian	Others	
	N (%)	N (%)	N (%)	p-value
Sex (n)	49	25	31	
• Female	21 (42.9)	8 (32.0)	16 (51.6)	0.337
• Male	28 (57.1)	17 (68.0)	15 (48.4)	
Age at Disease				
• ≤ 12 years	11 (22.4)	0 (0)	20 (64.5)	0.550
• ≥ 12 years	38 (77.6)	25 (100)	11 (35.5)	
Inflammatory Bowel Disease-Type				
• Crohn's Disease	27 (55.1)	9 (36.0)	15 (48.4)	
• Ulcerative Colitis	8 (16.3)	11 (44.0)	8 (25.8)	0.156
• Indeterminate IBD (IC)	14 (28.6)	5 (20.0)	8 (25.8)	
Associated Problem				
• Abscess	2 (4.10)	3 (12.0)	1 (3.20)	
• Fistula	6 (12.2)	1 (4.0)	3 (9.70)	0.397
• Abscess + Fistula	4 (8.20)	0 (0.0)	1 (3.20)	
• No	37 (75.5)	21 (84.0)	26 (83.9)	
Disease Location				
• Colonic	20 (40.8)	15 (60.0)	14 (45.2)	
• Terminal ileum	13 (26.5)	2 (8.0)	11 (35.5)	0.164
• Ileocolonic	4 (8.20)	3 (12.0)	2 (6.45)	
• Upper and Lower GI	2 (4.10)	4 (16.0)	1 (3.23)	
• Missing information	10 (20.4)	1 (4.0)	3 (9.68)	
Family History				
• Positive	4 (8.20)	0 (0.0)	4 (12.9)	0.177
• Negative	45 (91.8)	25 (100)	27 (87.1)	
Surgical Intervention				
• Yes	4 (8.20)	0 (0.0)	0 (0.0)	0.093
• No	45 (91.8)	25 (100)	31 (100)	

Table 2: Mean laboratory values of minority pediatric populations diagnosed with IBD.

Variable	African American	Asian	Others	
	Mean (SD)	Mean (SD)	Mean (SD)	p-value
Age (years)	13.43 (2.85)	12.76 (3.39)	13.19 (2.56)	0.647
Age at diagnosis (years)	12.30 (2.96)	11.70 (3.96)	12.63 (3.13)	0.587
HCT (%)	34.63 (4.36)	35.77 (4.67)	36.04 (4.89)	0.308
Hgb (gm/dl)	10.99 (1.78)	11.73 (2.05)	11.55 (1.97)	0.324
CRP (mg/dl)	15.28 (39.8)	2.38 (2.54)	3.28 (5.31)	0.146
Albumin (gm/dl)	3.82 (0.62)	3.98 (0.52)	4.01 (0.57)	0.371

portion of their gastrointestinal were identified as the prominent disease location (40.8%, 60.0%, and 45.2% respectively) and many of the patients in all groups had negative family history of IBD (91.8%, 100%, and 87.1%, respectively) and did not undergo surgical intervention (91.8%, 100%, and 100%, respectively) as a treatment option. Nonetheless, AA compared to other groups had surgical intervention of their disease (8.2%, 0%, and 0%, respectively).

Mean laboratory values of minority pediatric populations diagnosed with IBD

As shown in Table 2, laboratory values were recorded at either one month prior or one month after patients were diagnosed with IBD. The mean age of IBD diagnosis was 12.30 years for AA, 11.70 years for AS and 12.63 years for the other group, and within one standard deviation of 2.96 vs. 3.96 vs. 3.13, respectively. There

were no significant differences between the groups. Similarly, there were no significant differences between the hematocrit (HCT) and hemoglobin (Hgb) values even though the groups' mean values were lower than the normal ranges of 40.1-50.1% for HCT and 13.5-17.0 gm/dl for Hgb. However, the mean C-reactive protein (CRP) values for AA were higher than normal (15.28 mg/dl versus 0-8 mg/dl reference), but the CRP valves for AS and other groups were within normal limits (2.38 mg/dl, 3.28 mg/dl, respectively versus 0-8 mg/dl reference). Within one standard deviation of 39.8 in the AA group, 2.54 in the AS group and 5.31 in the other group, there were no significant statistical differences with p-value of 0.146. In all groups, the mean albumin values were within normal limits of 3.5-5.1 gm/dl (reference), with no significant statistical difference, p-value of 0.371.

Discussion

Inflammatory bowel disease (IBD) is a complex continuum of inflammatory disorders involving the gastrointestinal (GI) tract [2] and resulting in significant long-term morbidity [3]. Extraintestinal manifestations of IBD are so common that the disease should be regarded as a systemic disorder that could affect any organ system including joints [17] , kidneys [18] as well as others, thus contributing to the morbidity of patients with IBD [4,5,17]. The prevalence and incidence among Africans, African-Americans, Asians, and Hispanics have been reported with increasing frequencies suggesting that the trend is indeed increasing worldwide [3]. With the increasing trend, both adult and pediatric onset of IBD is likely to increase too. Nonetheless, the need for appropriate diagnosis and treatment for patients, especially minority pediatric populations, is vital [2].

Individuals with IBD experience and present with diverse symptoms including fever, nausea, anorexia, weight loss, abdominal pain, diarrhea, fatigue, and growth failure [19,20]. Our study examined clinical characteristics of IBD in a minority pediatric population, providing insights into diverse disease clinical presentations. We observed in our decade of single institute experience of treating pediatric population with IBD that minority pediatric populations also present with the same symptoms. More so, the AA pediatric population exhibited a higher prevalence and a later age of diagnosis for CD [21] compared to AS pediatric population. In our study, close to 70.5% of pediatric minority populations above 12 years were diagnosed with IBD and 29.5% were below 12 years. These results concur with the observations made by Odufalu, et al. and White, et al. who reported an increasing trend of CD incidence in non-Caucasian populations [16,21]. However, our findings, while similar to studies which concluded racial differences in IBD presentation [13], was in stark contrast to the findings of Smith, et al. who noted that IBD phenotype did not differ by race [22].

Meta-analysis conducted by Piovani, et al. revealed as much as 43 environmental exposures and lifestyle factors associated with IBD [23]. Some of the strongest associations to pediatric IBD include the followings: living in urban area with increased air pollution and decreased greenspace, exposure to cigarette smoking and antibiotic exposure, as well as, the mode of birth, type of infant feeding, type of diet among others [2,23]. Such environmental factors that affect the gut microbiome led to imbalance or dysbiosis that is linked to intestinal barrier dysfunction and inflammation [24,25]. Together, these manifestations are responsible for IBD pathophysiology. With barrier dysfunction, come nutritional deficiencies such as low calcium, iron, vitamins B6, B9, and B12, vitamin D, and others which are common in IBD patients [6]. In addition, the role of nutritional intake contributes significantly to an individual's gut microbiota, and it is documented to affect the pathogenesis and development of IBD [26]. Research has shown that nutrition is essential in maintaining immune homeostasis with the potential to shape the composition and function of gut microbiota that affects disease outcome [26].

In addition to the intestinal barrier dysfunction, persistent inflammation is associated with cytokine imbalance as well as increase of inflammatory markers such as C-reactive protein (CRP) which is being implicated in potentiating neurodegeneration [11]. Growing evidence suggests that gut microbiome shapes the pathogenesis of IBD as well as other diseases pathogenesis such as those of cardiovascular [27], Alzheimer's [26] and Parkinson's disease by influencing inflammatory mediators [28]. Furthermore, CRP which is chronically increased in both IBD and rheumatoid arthritis, as an inflammatory mediator, is a pentameric protein synthesized in the liver in response to interleukin-6 and plays a pivotal function in the inflammatory response [11]. The irreversible dissociation of CRP into its monomers is accompanied by its biological activation, and stimulation of inflammatory processes including aggravating cognitive decline [11]. Increased CRP values in peripheral blood has been assessed as an indication of chronic systemic inflammation and meta-analysis investigating levels of CRP and rates of dementia showed that the risk of developing dementia was statistically significantly higher with elevated serum levels of CRP [11]. In our study, we found CRP within normal limits in AS and other groups compared to mean elevated CRP levels in AA, which might suggest a different inflammatory profile or pathophysiology of IBD in AA population. This discrepancy highlights the need for further research into ethnic-specific inflammatory profiles, which could inform diagnosis and management approaches critical to the outcome of the disease in the minority pediatric population.

Nonetheless, our findings are in line with other studies, where CRP was more abnormal in children with CD than UC at diagnosis [29]. Based on laboratory findings, higher levels of inflammatory markers and lower albumin levels are found in CD patients than UC patients [29]. In our study, more AA had more CD diagnosis and higher CRP values. CRP like ESR (erythrocyte sedimentation rate) was more normal in UC than in CD patients at diagnosis and during follow up [30].

Another notable result in our study was the finding that anemia and albumin levels remained within normal limits across all groups. On the contrary, anemia and hypoalbuminemia were more prevalent in pediatric IBD due to malabsorption and inflammation [31]. While CRP is widely used in IBD screening and assessment of disease activity, clinical relapse, and treatment responsiveness, serving as a predictor for surgical outcomes for a subgroup of patients with UC or CD [11], the role of albumin levels has not been well established. Given the discrepancies in our findings to those found in literature, we recommend future research that could evaluate the role of albumin in both IBD screening and assessment of disease activity in minority pediatric populations.

While this study sheds light on diverse IBD presentations in minority pediatric populations, we acknowledge its limitations. One of the study limitations is inherent in the study design itself by being retrospective. Moreover, data from a single institution restricts generalizability, hence, multi-center studies are crucial to confirm and broaden our findings [13]. Similarly, the sample size might not be sufficient to capture subtle variations between groups or the full spectrum of IBD presentations within each population. Additionally, the focus on selected phenotypic characteristics and markers leaves potentially relevant factors unexplored, such as socioeconomic factors and healthcare access, which warrants further investigation. Recognizing these limitations emphasizes the need for future research with larger, diverse samples and broader approaches to fully understand the complexities of IBD in minority pediatric populations.

Nonetheless, this study adds relevant information about IBD presentation in minority pediatric populations, which could potentially help in improving diagnostic accuracy and treatment strategies for this underserved population. Utilizing quantifiable markers like CRP and serum albumin strengthens the analysis and facilitates comparisons with future studies. By highlighting potential disparities in IBD presentations, the study emphasizes the need for equity-driven research and clinical practice. Overall, the data from this study has the potential to help identify differences in IBD symptomatic presentations in minority pediatric populations and generate future research questions. Also, we hope this study will help clinicians understand IBD symptomatic presentations and physiopathology in minorities and help guide treatment management of IBD in minorities [8]. Early diagnosis is critical to the long-term outcomes of children with IBD, and treating minority pediatric populations as early as possible is vital [2]. The healthcare system in emerging and developed economies should prepare for the growing number of pediatric populations with IBD, providing adequate access to high-quality specialized care to help early diagnosis and management [3].

Conclusions

Our data shows that IBD in AA pediatric population presents more commonly with CD, which is diagnosed at an older age when compared to AS pediatric population. These epidemiological variations in IBD among pediatric populations require further investigations. Our data show that quantifiable inflammatory markers like CRP and serum albumin could highlight potential disparities in IBD symptomatic presentations. Such results point to the need for further research into ethnic-specific inflammatory profiles. Lastly, the role of nutrition in shaping the gut microbiome as well as its interplay in disease outcome should not be overlooked.

Acknowledgements

We are grateful to the patients who entrusted their care to us. We also are grateful to our colleagues, Elizabeth Kring, Mary Coffey and Lihua Qi for their hard work and personal support for this study.

Conflict of Interest Disclosure and Source of Funding

No conflict of interest and no financial support needed/used.

No funding was received for this work from any of the following organizations: National Institutes of Health (NIH); Welcome Trust; and others.

Authors Contributions

Archana Reddy Bongurala: Primary and corresponding author: As the primary author, I played a pivotal role in all aspects of this research project. I significantly contributed to the conception and design of the study, ensuring its focus and methodology aligned with the journal's scope. I undertook the primary responsibility for data collection and analysis, implementing rigorous methods to ensure data accuracy and integrity. Furthermore, I drafted the manuscript, meticulously presenting the findings and their significance. Throughout the revision process, I addressed reviewer comments thoughtfully, ensuring the final manuscript met the journal's high standards.

Moses O Evbuomwan: Co-author: Dr. Moses O Evbuomwan played a key role in data collection

and management. His meticulous attention to detail ensured the accuracy and completeness of the data set. Furthermore, Moses O Evbuomwan assisted with the preparation of figures and tables, contributing significantly to the clarity and visual impact of the manuscript.

Oluwatoyin A Gbademu: Co-author: Dr.Oluwatoyin A Gbademu provided invaluable assistance throughout this project. Her meticulous work in data collection ensured the accuracy and completeness of the data set, which formed the foundation of our research. Additionally, Dr.Oluwatoyin A Gbademu played a crucial role in crafting the introduction section of the manuscript.

Inaya Hajj Hussein: Co-author: Dr. Inaya Hajj Hussein provided invaluable expertise in Pediatrics and Research. Her guidance during the study design phase was instrumental in ensuring the methodological soundness of the research. Additionally, she offered critical feedback on the data analysis and interpretation, contributing to the robustness of the findings.

Ayesha Fatima: Senior author: Dr Ayesha Fatima our senior author provided us with invaluable guidance and mentorship throughout this research project. Her extensive experience in Pediatric Gastroenterology was instrumental in shaping the direction of the study. Dr Fatima offered critical insights during the design phase, ensuring the research question aligned with current trends in the field. Additionally, her oversight and leadership were crucial in maintaining the project's focus and ensuring its successful completion.

References

1. Hajj Hussein I, Dosh L, Al Qassab M, Jurjus R, El Masri J, et al. (2023) Highlights on two decades with microbiota and inflammatory bowel disease from etiology to therapy. Transpl Immunol 78: 101835.
2. Khan R, Kuenzig ME, Benchimol EI (2023) Epidemiology of pediatric inflammatory bowel disease. Gastroenterol Clin North Am 52: 483-496.
3. M'Koma AE (2013) Inflammatory bowel disease: An expanding global health problem. Clin Med Insights Gastroenterol 6: 33-47.
4. Chams S, Badran R, Sayegh SE, Chams N, Shams A, et al. (2019) Inflammatory bowel disease: Looking beyond the tract. Int J Immunopathol Pharmacol 33: 2058738419866567.
5. Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, et al. (2015) Extraintestinal manifestations of inflammatory bowel disease. Inflamm Bowel Dis 21: 1982-1992.
6. Maldonado-Contreras A (2022) Food as treatment of inflammatory bowel diseases. Infect Immun 90: e0058321.
7. Nakagawa M (2013) [Gene mutations; up date]. Rinsho Shinkeigaku 53: 903-906.
8. Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, et al. (2017) Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: A systematic review of population-based studies. Lancet 390: 2769-2778.
9. Jadoon NA, Munir W, Shahzad MA, Choudhry ZS (2010) Assessment of depression and anxiety in adult cancer outpatients: A cross-sectional study. BMC Cancer 10: 594.
10. Costi S, Germinario S, Pandolfi M, Pellico MR, Amati A, et al. (2023) Chronic nonbacterial osteomyelitis and inflammatory bowel disease: A literature review-based cohort. Children (Basel) 10: 502.
11. Cooper J, Pastorello Y, Slevin M (2023) A meta-analysis investigating the relationship between inflammation in autoimmune disease, elevated CRP, and the risk of dementia. Front Immunol 14: 1087571.
12. Liles E, Irving SA, Dandamudi P, Belongia EA, Daley MF, et al. (2021) Incidence of pediatric inflammatory bowel disease within the Vaccine Safety Datalink network and evaluation of association with rotavirus vaccination. Vaccine 39: 3614-3620.
13. Nguyen GC, Torres EA, Regueiro M, Bromfield G, Bitton A, et al. (2006) Inflammatory bowel disease characteristics among African Americans, Hispanics, and non-Hispanic Whites: characterization of a large North American cohort. Am J Gastroenterol 101: 1012-1023.
14. Loftus EV Jr (2004) Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. Gastroenterology 126: 1504-1517.
15. Olén O, Askling J, Sachs MC, Frumento P, Neovius M, et al. (2017) Childhood onset inflammatory bowel disease and risk of cancer: A Swedish nationwide cohort study 1964-2014. BMJ 358: j3951.
16. Odufalu FD, Aboubakr A, Anyane-Yeboa A (2022) Inflammatory bowel disease in underserved populations: Lessons for practice. Curr Opin Gastroenterol 38: 321-327.
17. Jurjus R, Dosh L, Farhat R, Daccache T, El Masri J, et al. (2024) Lack of Syndecan-1 promotes the pathogenesis of experimental rheumatoid arthritis. Immunogenetics 76: 145-154.
18. Braysh K, Geagea AG, Matar C, Rizzo M, Eid A, et al. (2018) Kidney manifestation of inflammatory bowel disease. Open J Gasroenterol 8: 172-191.
19. Collaborators GIBD (2020) The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990-2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol 5: 17-30.
20. Jang J, Lee SH, Jeong IS, Cho J, Kim HJ, et al. (2022) Clinical characteristics and long-term outcomes of pediatric ulcerative colitis: A single-center experience in Korea. Gut Liver 16: 236-245.
21. White JM, O'Connor S, Winter HS, Heyman MB, Kirschner BS, et al. (2008) Inflammatory bowel disease in African American children compared with other racial/ethnic groups in a multicenter registry. Clin Gastroenterol Hepatol 6: 1361-1319.
22. Smith J, Liu C, Beck A, Fei L, Brokamp C, et al. (2023) Racial disparities in pediatric inflammatory bowel disease care: Differences in outcomes and health service utilization between black and white children. J Pediatr 260: 113522.
23. Piovani D, Danese S, Peyrin-Biroulet L, Nikolopoulos GK, Lytras T, et al. (2019) Environmental risk factors for inflammatory bowel diseases: An umbrella review of meta-analyses. Gastroenterology 157: 647-659.e4.
24. Hochuli N, Kadyan S, Park G, Patoine C, Nagpal R (2023) Pathways linking microbiota-gut-brain axis

with neuroinflammatory mechanisms in Alzheimer's pathophysiology. Microbiome Res Rep 3: 9.

25. Liu JJ, Abraham BP, Adamson P, Barnes EL, Brister KA, et al. (2023) The current state of care for black and hispanic inflammatory bowel disease patients. Inflamm Bowel Dis 29: 297-307.

26. Tian QB, Chen SJ, Xiao LJ, Xie JQ, Zhao HB, et al. (2024) Potential effects of nutrition-induced alteration of gut microbiota on inflammatory bowel disease: A review. J Dig Dis 25: 78-90.

27. Dosh L, Ghazi M, Haddad K, El Masri J, Hawi J, et al. (2024) Probiotics, gut microbiome, and cardiovascular diseases: An update. Transpl Immunol 83: 102000.

28. Dutta SK, Verma S, Jain V, Surapaneni BK, Vinayek R, et al. (2019) Parkinson's Disease: The emerging role of gut dysbiosis, antibiotics, probiotics, and fecal microbiota transplantation. J Neurogastroenterol Motil 25: 363-376.

29. Jo S-Y, Bang K-S (2023) Clinical characteristics and nursing diagnoses of pediatric patients hospitalized with inflammatory bowel disease: A single-center retrospective study in South Korea. Child Health Nurs Res 29: 218-228.

30. Alper A, Zhang L, Pashankar DS (2017) Correlation of erythrocyte sedimentation rate and C-Reactive protein with pediatric inflammatory bowel disease activity. J Pediatr Gastroenterol Nutr 65: e25-e27.

31. Zerouga I, Valeur J, Sommer C, Cvancarova Småstuen M, Medhus AW, et al. (2024) Dietary intake and nutritional status in patients with newly diagnosed inflammatory bowel disease: Insights from the IBSEN III study. Scand J Gastroenterol 59: 652-660.