Article

Not peer-reviewed version

Comparative Analysis of Management Strategies and Demographics in Older-Onset vs. Younger-Onset Inflammatory Bowel Disease

Fatih Kıvrakoğlu *, Vedat Kılıç, Mustafa Ergin, Harun Küçük, Çağdaş Erdoğan, Ilhami Yuksel

Posted Date: 31 December 2024

doi: 10.20944/preprints202412.2642.v1

Keywords: Ulcerative Colitis; Crohn's Disease; Older-onset

Article

Comparative Analysis of Management Strategies and Demographics in Older-Onset vs. Younger-Onset Inflammatory Bowel Disease

Fatih Kıvrakoğlu [1,*], Vedat Kılıç [2], Mustafa Ergin [3], Harun Küçük [4], Çağdaş Erdoğan [5] and İlhami Yüksel [6,7]

[1] Department of Gastroenterology, Adana Seyhan State Hospital, Adana 01150, Turkey
[2] Department of Gastroenterology, Balıkesir City Hospital, Balıkesir 10100, Turkey
[3] Department of Gastroenterology, Aksaray Education and Research Hospital, Aksaray 68200, Turkey
[4] Department of Gastroenterology, Mardin Education and Research Hospital, Mardin 47100, Turkey
[5] Department of Gastroenterology, Ankara Etlik City Hospital, Ankara 06170, Turkey
[6] Department of Gastroenterology, Ankara Yildirim Beyazit University School of Medicine, Ankara 06700, Turkey
[7] Department of Gastroenterology, Ankara Bilkent City Hospital, Ankara 06800, Turkey
* Correspondence: dr.fkivrakoglu@gmail.com; Tel.: +90-54-4664-5628

Abstract: Background/Objectives: This study examines how demographics and treatment approaches differ between adults with Ulcerative Colitis (UC) and Crohn's Disease (CD) in two age groups: those diagnosed at 60 years or older and those diagnosed between 18 and 60 years. **Methods**: A retrospective study was performed to examine and contrast the clinical profiles and therapeutic approaches of patients diagnosed within the period spanning June 1993 to February 2023. Demographic, clinical, and therapeutic data were evaluated for both UC and CD groups across the two age categories. Patients were categorized into older-onset (≥60 years) and younger-onset (18-60 years) groups. **Results**: The study cohort comprised 1245 patients, including 56 older-onset adults (4.5%, 73% male) and 1189 younger-onset adults (95.5%, 58% male). The median duration of follow-up was 11 years. Ulcerative colitis was significantly more prevalent among the older-onset group, with a rate of 69.6% (p=0.002). Active smokers were more frequent in the younger-onset group (23%, p=0.003). A family history of IBD was less common in the older-onset group (4% vs. %13, p=0.037). Thiopurine usage was more frequent in the younger-onset group (32.9% vs. 16.1%, p=0.008). Biological experience was less common in the older-onset group (26.8% vs. %49.3, p=0.001). No notable differences were observed between the older-onset and younger-onset groups regarding UC extension, CD location, disease behavior, or perianal involvement. **Conclusions**: Older-onset patients differ significantly from younger-onset patients in terms of clinical presentation and therapeutic approaches. The lower use of thiopurines and biological agents in older-onset patients may reflect concerns about drug-related risks. Customized therapeutic approaches are essential to enhance outcomes for this patient population.

Keywords: ulcerative colitis; Crohn's disease; older-onset

1. Introduction

Inflammatory bowel disease (IBD), comprising Crohn's disease (CD) and ulcerative colitis (UC), represents a chronic inflammatory condition of the gastrointestinal tract with an uncertain etiology, often linked to genetic predispositions, environmental influences, and irregular immune responses to gut microbiota [1]. As global populations age, the incidence of older-onset IBD is expected to rise significantly, alongside increases observed across all age groups, including both children and the elderly [2].

The phenotype and progression of IBD appear to vary based on the age at disease onset. Early in the disease course, severe episodes are more common, indicating that older-onset patients might necessitate tailored management approaches to account for age-associated physiological alterations

 doi:10.20944/preprints202412.2642.v1

and differences in treatment tolerance [3]. However, many existing studies fail to clearly delineate between these age groups, with conflicting findings regarding the severity of disease progression in later-onset IBD patients [4,5]. While some suggest milder disease progression in older individuals, others highlight worse outcomes or more aggressive complications [6].

With increasing reliance on early therapeutic interventions such as biologics or combination therapies, understanding age-specific disease progression is critical. Older patients often exhibit reduced tolerance to immunosuppressive regimens due to heightened vulnerability to infections and malignancies, necessitating a balance between the potential risks of aggressive treatment and the benefits of disease control [7,8]. Further investigations into the demographic, clinical, and therapeutic characteristics of older-onset IBD are essential to develop tailored treatment protocols that align with their unique needs.

This study seeks to address these knowledge gaps by analyzing critical differences in demographics and management strategies between older-onset and younger-onset IBD patients, offering essential insights to guide age-specific clinical practices.

2. Materials and Methods

2.1. Study Population

This retrospective analysis includes data from patients diagnosed with UC or CD at a tertiary referral center between June 1993 and February 2023. Patients were eligible for inclusion if they had a confirmed diagnosis of UC or CD and were 18 years or older at the time of diagnosis. Patients with indeterminate colitis or those who were unable to provide written informed consent were excluded from the study due to the limited number in these groups

2.2. Variables

The study collected demographic and IBD characteristics from electronic medical records, including age, sex, weight, height, prodromal time, type of disease, disease duration, extraintestinal manifestations, current and previous IBD medications, IBD-related hospitalization, and previous IBD-related surgery. Disease behavior and location were classified according to the Montreal Classification to ensure consistency across data points. Clinical disease activity was measured using the partial Mayo score for UC and the Crohn's Disease Activity Index (CDAI) for CD. Laboratory values (hemoglobin, albumin, and C-reactive protein [CRP]) were extracted from the electronic medical record if tests had been performed within three months of baseline.

2.3. Outcomes

The aim of this study was to investigate the differences between UC and CD in terms of disease behavior, site of involvement, prodromal period, change in disease type according to gender, need for hospitalization, history of surgery, extraintestinal manifestations, choice of medical treatment, and use of biological agents in older and younger patients. The study did not include patients under the age of 18. Patient age was categorized into two groups: younger-onset (18-60 years) and older-onset (≥60 years).

2.4. Ethical Considerations

This retrospective study was approved by the Ethical Committee of Ankara City Hospital (E2-24-6116) and there were no conflicts of interest or sponsors of this analysis.

2.5. Statistical Analysis

Descriptive statistics are shown as number (n) and percentage (%) for qualitative data. For quantitative data, mean and standard deviation were given for normally distributed data, and median and minimum-maximum values (Inter Quantile Range [IQR]) were given for non-normally

 doi:10.20944/preprints202412.2642.v1

distributed data. Intergroup comparisons of categorical variables were made by Pearson Chi-square or Fischer's exact test. Mann-Whitney U test was used for the comparison of continuous variables in two independent groups because the assumption of normal distribution was not fulfilled. Type 1 margin of error (alpha) was accepted as 0.05 for all statistics. SPSS version 29.0 was used for data analysis.

3. Results

3.1. Patient Characteristics

A total of 1245 adult patients diagnosed with IBD between June 1993 and February 2023 were included in this study. The study included 618 (49.7%) patients with UC and 627 (50.3%) patients with CD. 39 of 618 (6.3%) patients with UC and 17 of 627 (2.7%) patients with CD were diagnosed with older-onset IBD. The prevalence of UC was higher in the older-onset group compared to the younger-onset group (69.6% vs. 48.7%) (p=0.002). The mean age at diagnosis for all patients with older-onset IBD was 71.5 years (range 61-95 years) and 46 years (range 18-84 years) for all younger-onset IBD. The mean ages at diagnosis in patients with older-onset UC and CD were 72 and 71 years, respectively. The mean ages at diagnosis in the younger-onset UC and CD groups were 49 and 43 years, respectively.

Disease duration was lower in the older-onset groups of total IBD, UC, and CD (6 vs. 11 years, 6 vs. 12 years, and 6 vs. 11 years, respectively; p<0.001, p<0.001, p=0.02). The time between the first symptoms of IBD and IBD diagnosis, defined as prodromal time, was similar in all groups and there was no statistically significant difference. The proportion of male patients was higher than that of female patients with IBD (766, 61.5% vs. 479, 38.5%), UC (395, 64% vs. 223, 36%), and CD (371, 59% vs. 256, 41%). A higher proportion of male patients was similar in the subgroups of older-onset patients (73%, 79%, and 59%) and younger-onset patients (58%, 63%, and 59%) for total IBD, UC, and CD, respectively.

The number of cigarette smokers was significantly lower in the older-onset CD group (2, 12%) than in the younger-onset CD group (202, 33%) (p=0.04). There was no statistically significant difference in cigarette smokers/nonsmokers between older-onset and younger-onset IBD and UC patients. A family history of IBD was significantly lower in the older-onset group of patients with IBD and UC (p=0.03, p=0.04). The BMI was significantly higher in the older-onset CD group than in the younger-onset CD group (p=0.02). Previous major abdominal surgeries were reported in 484 of 1245 (38.9%) patients with IBD, 97 of 618 (15.7%) patients with UC, and 387 of 627 (61.7%) patients with CD. There was no statistically significant difference in prior major abdominal surgery between the older-onset and younger-onset groups of total IBD, UC, and CD patients.

3.2. Disease Extent, Localization, and Behavior

Of the 618 patients with UC, 59 (9.5%) had proctitis, 305 (49.4%) had left-sided colitis, and 254 (41.1%) had extensive colitis. Six of the 39 patients with older-onset UC were diagnosed with proctitis (15.4%), 17 had left-sided colitis (43.6%), and 16 had extensive colitis (41%). Among the younger-onset UC patients, 53 of 579 (9.2%) had proctitis, 288 (49.7%) had left-sided colitis, and 238 (41.1%) had extensive colitis. There was no statistically significant difference in disease extension between older- and younger-onset UC patients.

Crohn's disease was diagnosed in 627 patients, with ileal (269, 43%), colonic (82, 13%), ileo-colonic (272, 43.4%), and upper GI involvement (4, 0.6%). Among the CD patients, non-stenosing non-penetrating disease was found in 469 (75%), stenosing disease in 54 (9%), penetrating disease in 105 (16%), and perianal disease in 205 (32.7%) patients. Nine of the 17 patients with older-onset CD had ileal disease (52.9%), one had colonic CD (5.9%), five had ileo-colonic CD (29.4%), and two had upper gastrointestinal (GI) involvement (11.8%). Twelve of the 17 patients with older-onset CD had non-stenosing non-penetrating disease (70.6%), stenosis in 4 (23.5%), penetrating disease in 1 (5.9%), and perianal disease in 3 (17.6%). Of the 610 younger-onset CD patients, 260 had ileal disease (42.9%), 81 had colonic CD (13.1%), 267 had ileo-colonic CD (43.4%), and two had upper GI involvement (0.6%).

 doi:10.20944/preprints202412.2642.v1

Of the 610 younger-onset CD cases, 457 had non-stenosing non-penetrating disease (74.8%), 49 had stenosis (8.5%), 104 had penetrating disease (16.7%), and 202 had perianal disease (32.7%). There was no statistically significant difference in disease location and behavior among older- and younger-onset CD patients.

3.3. Extra-Intestinal Manifestations

Extra-intestinal manifestations were observed in 624 of the 1245 IBD patients (50%). Peripheral arthralgia was the most common extra-intestinal manifestation (390, 62.5%). Aphthous ulcer (242, 38.7%), back pain (210, 33.7%), peripheral arthritis (107, 17.1%), ankylosing spondylitis (69, 11%), sacroiliitis (31, 5%), thromboembolism (31, 5%), erythema nodosum (27, 4%), primary sclerosing cholangitis (21, 3%), osteoporosis (21, 3%), uveitis (16, 2.5%), pyoderma gangrenosum (9, 1.4%), and episcleritis (5, 0.8%) were other extra-intestinal manifestations detected in IBD patients.

Twelve of 39 (30.8%) older-onset UC patients had at least one extra-intestinal manifestation, with peripheral arthralgia being the most common (6, 15%). Among the younger-onset UC patients, 272 of 579 (47%) had at least one extra-intestinal manifestation, with peripheral arthralgia being the most common (168, 29%). Extra-intestinal manifestations and aphthous ulcers were significantly lower in the older-onset UC group (p=0.04, p=0.02 respectively).

Six of 17 (35.3%) older-onset CD patients had at least one extra-intestinal manifestation, with peripheral arthralgia and back pain being the most common (4, 24%). Among the younger-onset CD patients, 334 of 610 (54.8%) had at least one extra-intestinal manifestation, with peripheral arthralgia being the most common (212, 34.7%). There was no statistically significant difference between the older- and younger-onset CD patients with respect to extra-intestinal manifestations and subgroups.

3.4. Medical Treatments

Thiopurine and mesalamine treatments were the most preferred treatment in all IBD patients (400, 32%; 417, 33.5% respectively). Other conventional treatments included budesonide (335, 27%), corticosteroids (75, 6%), sulfasalazine (53, 4%), and methotrexate (51, 4%) in descending order. Thiopurine usage was higher in younger-onset patients (391, 32.9%) compared to older-onset patients (9, 16.1%) (p=0.008). There was no difference between the older- and younger-onset groups in terms of other conventional medications for all patients with IBD. In patients with UC, mesalamine was the most used treatment (130, 21%). Other conventional treatments included corticosteroids (125, 20%), thiopurine (107, 17.3%), sulfasalazine (10, 1.6%), and methotrexate (5, 0.8%). Thiopurine and mesalamine treatments were the most preferred in CD patients (293, 46.7%; 287, 45.7% respectively). Other conventional treatments included budesonide (212, 33.8%), corticosteroids (73, 11.6%), methotrexate (46, 7%), and sulfasalazine (27, 4.3%) in descending order. Thiopurine and mesalamine treatments were significantly lower in the older-onset CD group (p=0.003, p=0.004). There was no difference between the older-onset and younger-onset groups in terms of the use of other conventional medications for UC and CD.

Biological treatment was administered to 601 of the 1245 (48.2%) patients with IBD: 390 (31.3%) were treated with adalimumab, 374 (30%) with infliximab, 117 (9.3%) with vedolizumab, 82 (6.5%) with ustekinumab, and 31 (2.4%) with certolizumab. At least one biological experience was less common in the older-onset group (15, 26.8%) compared to the younger-onset group (586, 49.3%) (p=0.001). The two most frequently used biological therapies were adalimumab (older-onset 6, 10.7%; younger-onset 384, 32.8%) (p=0.001) and infliximab (older-onset 15, 26.8%; younger-onset 586, 49.3%) (p=0.02).

Of the 618 patients with UC, 168 (27.1%) were treated with biological agents. Infliximab was the most used agent (105, 17%). Other biological agents included adalimumab (97, 15.7%), vedolizumab (42, 6.8%), ustekinumab (14, 2.2%), and certolizumab (3, 0.5%). Vedolizumab treatment was significantly higher in the older-onset UC group (older-onset 6, 15.4%; younger-onset 36, 6.2%) (p=0.04).

Of the 627 patients with CD, 433 (69%) were treated with biological agents. Adalimumab was the most used agent (293, 46.7%). Other biological agents included infliximab (269, 43%), vedolizumab (75, 12%), ustekinumab (69, 11%), and certolizumab (28, 4.5%) in descending order. The

 doi:10.20944/preprints202412.2642.v1

total biological treatments (older-onset 4, 23.5%; younger-onset 429, 70.3%), infliximab (older-onset 3, 17.6%; younger-onset 266, 43.6%), and adalimumab (older-onset 62, 11.8%; younger-onset 291, 47.7%) treatments were lower in the older-onset group (p<0.001, p=0.03, p=0.003 respectively).

Steroid dependence was detected in 553 of 1245 (44.4%) IBD patients, 7 of 618 (1.1%) UC patients, and 311 of 627 (49.6%) CD patients. There was no difference in steroid dependence between the older-onset and younger-onset groups. Steroid resistance was detected in 34 of 1245 (2.7%) patients with IBD, 20 of 618 (3.2%) patients with UC, and 14 of 627 (2.2%) patients with CD. Steroid resistance was significantly higher in the older-onset UC group (older-onset 4, 10.3%; younger-onset 16, 2.8%) (p=0.03).

Immunomodulator (IM) resistance was detected in 417 of 1245 (33.5%) IBD patients, 103 of 618 (16.6%) UC patients, and 314 of 627 (50%) CD patients. IM resistance was lower in the older-onset CD group (older-onset 4, 23.5%; younger-onset 310, 50.8%) (p=0.03). IM side effects were detected in 194 of 1245 (15.6%) patients with IBD (148 thiopurine, 46 methotrexate), 49 of 618 UC (8%) patients (47 thiopurine, 2 methotrexate), and 143 of 627 (22.8%) CD patients (101 thiopurine, 42 methotrexate). There was no difference between older-onset and younger-onset groups for IM side effects

3.5. Disease Severity and Baseline Laboratory Tests

The baseline Crohn's Disease Activity Index (CDAI) for CD was 302 in the older-onset group and 297 in the younger-onset group. The baseline MAYO total score was 9 in both older-onset and younger-onset groups. Baseline partial MAYO scores were 7 in both older-onset and younger-onset groups. There was no difference in disease severity scores between the older-onset and younger-onset groups.

Baseline hemoglobin (Hb) levels were 12.6 mg/dL in the older-onset group and 13 mg/dL in the younger-onset group of IBD patients. Baseline Hb levels were 13 mg/dL in the older-onset group and 12.9 mg/dL in the younger-onset group of UC patients. Baseline Hb levels were 12.4 mg/dL in the older-onset group and 13 mg/dL in the younger-onset group of CD patients. There was no difference between the older-onset and younger-onset groups in laboratory tests.

All results summarized in Table 1.

Table 1. Demographic characteristics of adult non-geriatric and geriatric patients with IBD.

	Total, n=1245 (100%)		**UC, n= 618(50.7%)**		**CD, n= 627 (50.3%)**	
	Older-onset n=56 (4.5%)	Younger-onset n=1189 (95.5%)	Older-onset UC n= 39(6.3%)	Younger-onset UC n=579(93.7%)	Older-onset CD n=17(2.7%)	Younger-onset CD n=610(97.3%)
Age at onset of IBD (median years)	71.5	46	72	49	71	43
Total disease duration (median years)	6	11[a]	6	12[b]	6	11[c]
Prodrom (median months)	3	4	2	1	7	11
Female / Male	15 (27%) / 41 (73%)	464 (42%) / 725 (58%)	8(21%)/ 31(%79)	215(%37)/ 364(%63)[b]	7(41%)/ 10(59%)	249(%41)/ 361(59%)
Smokers						
Current smoker	6 (10%)	277 (23%)	4(10%)	75(13%)	2(12%)	202(33%)
Ex-smoker	29 (52%)	368 (31%)	20(51%)	206(%36)	9(53%)	162(27%)
Non-smoker	21 (38%)	544 (46%)	15(39%)	298(%51)	6(35%)	246(40%)[j]
Family history of IBD	2 (4%)	155 (13%)[d]	1 (2.6%)	80 (13.8%)[e]	1 (5.9%)	75 (12.3%)
Prior major abdominal surgery n (%)	20 (35. 7%)	464 (39%)	8 (20.5%)	89 (15.4%)	12 (70.6%)	375 (61.5%)
Hospitalization at the time of diagnosis n (%)	13 (23.2%)	422 (35.5%)	5 (12.8%)	142 (24.5%)	8 (47.1%)	280 (45.9%)
Hospitalization for related to IBD n (%)	23 (41.1%)	571 (48%)	14 (35.9%)	184 (31.8%)	9 (52.9%)	387 (63.4%)
Body Mass Index (BMI)	25	24	24.5	25	29	23[k]
UC/Crohn	39 (69.6%) / 17 (30.4%)	579 (48.7%) / 610 (51.3%)				
UC (Disease extension)						
Proctitis	6 (15.4%)	53 (9.2%)	6 (15.4%)	53 (9.2%)		
Left Site	17 (43.6%)	288 (49.7%)	17 (43.6%)	288 (49.7%)		
Extensive	16 (41%)	238 (41.1%)	16 (41%)	238 (41.1%)		
CD (Disease location)						

 doi:10.20944/preprints202412.2642.v1

Ileal (L1)	9 (52.9%)	260 (42.9%)			9 (52.9%)	260 (42.9%)
Colonic (L2)	1 (5.9%)	81 (13.1%)			1 (5.9%)	81 (13.1%)
Ileo-colonic (L3)	5 (29.4%)	267 (43.4%)			5 (29.4%)	267 (43.4%)
Upper GI disease (L4)	2(11.8%)	2 (0.6%)			2(11.8%)	2 (0.6%)
CD (Disease behavior)						
Inflammatory disease (B1)	12 (70.6%)	457 (74.8%)			12 (70.6%)	457 (74.8%)
Stenosing (B2)	4 (23.5%)	49 (8.5%)			4 (23.5%)	49 (8.5%)
Penetrating (B3)	1 (5.9%)	104 (16.7%)			1 (5.9%)	104 (16.7%)
CD P (Perianal disease)	3 (17.6%)	202 (32.7%)			3 (17.6%)	202 (32.7%)
Extra-intestinal manifestations	18 (32.1%)	606 (51%)	12 (30.8%)	272 (47%) [f]	6 (35.3%)	334 (54.8%)
Erythema nodosum	0	27	0	11	0	16
Pyoderma gangrenous	0	9	0	3	0	6
Peripheral arthralgia	10	380	6	168	4	212
Peripheral arthritis	0	107	0	36	0	71
Back pain	9	201	5	82	4	119
Ankylosing spondylitis	1	68	1	27	0	41
Sacroiliitis	0	31	0	10	0	21
Aphthous ulcer	4	238	2	122 [g]	2	116
Thromboembolism	0	31	0	15	0	16
Osteoporosis	2	19	2	7	0	12
Primary Sclerosing Cholangitis	2	19	2	7	0	12
Uveitis	0	16	0	6	0	10
Episcleritis	0	5	0	2	0	3
Medication (Conventional)						
Thiopurine	9 (16.1%)	391 (%32.9)	7 (17.9%)	100 (17.3%)	2 (11.8%)	291 (47.7%) [m]
Methotrexate	0	51 (4.3%)	0	5 (0.9%)	0	46 (7.5%)
Sulfasalazine	0	53 (4.5%)	0	10 (1.7%)	0	43 (7%)
Mesalazine	10 (17.9%)	407 (34.2%)	8 (20.5%)	122 (21.1%)	2 (11.8%)	285 (46.7%) [n]
Budesonide	11 (19.6%)	324 (27.2%)	9 (23.1%)	114 (19.7%)	2 (11.8%)	210 (34.4%)
Steroids	0	75 (6.3%)	0	2 (0.3%)	0	73 (12%)
Cyclosporin	1 (1.8%)	1(0.1%)	0	0	0	0
Biological therapy	15 (26.8%)	586 (49.3%)	11 (28.2%)	157 (27.1%)	4 (23.5%)	429 (70.3%) [o]
Infliximab	9 (16.1%)	365 (30.7%)	6 (15.4%)	99 (17.1%)	3 (17.6%)	266 (43.6%) [p]
Adalimumab	6 (10.7%)	384 (32.8%)	4 (10.3%)	93 (16.1%)	2 (11.8%)	291 (47.7%) [r]
Vedolizumab	6 (10.7%)	111 (9.3%)	6 (15.4%)	36 (6.2%) [h]	0	75 (12.3%)
Ustekinumab	1 (1.8%)	81 (6.8%)	1 (2.6%)	13 (2.2%)	0	69 (11.1%)
Sertolizumab	0	31 (2.6%)	0	3 (0.5%)	0	28 (4.6%)
Steroid dependence	21 (37.5%)	532 (44.7%)	1 (2.6%)	6 (1%%)	5 (29.4%)	306 (50.2%)
Steroid resistance	4 (7.1%)	30 (2.5%)	4 (10.3%)	16 (2.8%) [i]	0	14 (2.3%)
IM resistance, n (%)	8 (14.3%)	409 (34.4%)	4 (10.3%)	99 (17.1%)	4 (23.5%)	310 (50.8%) [s]
Thiopurine side effect	7 (12.5%)	141 (11.9%)	4 (10.3%)	43 (7.4%)	3 (17.6%)	98 (16.1%)
Methotrexate side effect	2 (3.6%)	44 (3.7%)	0	2 (0.3%)	0	42 (6.9%)
Biologic resistance/intolerance n (%)	0	15 (3%)	0	6 (1%)	0	9 (1.5%)
Baseline Hb (mg/L), mean (IQR)	12.6	13	13	12.9	12.4	13
Baseline Albumin (g/L), median (IQR)	41 (8.75)	42 (9)	41 (11)	43 (8)	42 (10)	41(-)
Baseline CRP (mg/L), median (IQR)	11.4 (28.7)	10.2 (26.9)	4.8 (30.6)	9.1 (24.3)	17.3 (23)	11.7 (31)
Baseline CDAI (CD), median (IQR)	302 (277)	297 (179)			302 (277)	297 (178)
Baseline MAYO Total score, mean (SD)	9	9	9	9		
Baseline MAYO Partial score, mean (SD)	7	7	7	7		

Duration of disease was significantly lower in older-onset groups of total patients, UC and CD ($p^a<0.001$, $p^b<0.001$, $p^c=0.02$). Family history of IBD were significantly lower in older-onset groups of total patients and UC ($p^d=0.03$, $p^e=0.04$). Extra-intestinal manifestations and aphthous ulcer were significantly lower in older-onset group of UC ($p^f=0.04$, $p^g=0.02$). Vedolizumab treatment was significantly higher in older-onset groups of UC ($p^h=0.04$). Steroid resistance was significantly higher in older-onset groups of UC ($p^i=0.03$). Cigaratte smokers was significantly lower in older-onset group of CD ($p^j=0.04$). BMI was significantly higher in older-onset groups of CD ($p^k=0.02$). Thiopurine and mesalazine treatment was significantly lower in older-onset groups of CD ($p^m=0.003$, $p^n=0.004$). Total biological treatments, Infliximab and Adalimumab treatments were lower in older-onset group of CD ($p^o<0.001$, $p^p=0.03$, $p^r=0.003$). Immunmodulator resistance was lower in older-onset group of CD ($p^s=0.03$).

 doi:10.20944/preprints202412.2642.v1

4. Discussion

This study provides valuable insights into the demographic and management differences between older-onset and younger-onset IBD patients, emphasizing the need for age-specific treatment strategies. The findings reveal significant variations in disease characteristics, treatment patterns, and clinical outcomes between these groups, highlighting the need for tailored approaches to manage older-onset IBD patients effectively.

The literature reveals variations in the epidemiology of IBD, with some studies finding no significant differences in incidence, while others report that either UC or CD is more prevalent among the elderly population [9,10]. Our study found a higher prevalence of UC among older-onset patients compared to younger-onset patients. This aligns with existing literature indicating that UC is more common in older adults [11], possibly due to the cumulative effects of environmental factors and improved diagnostic techniques over time. The gender distribution showed a higher proportion of male patients in both older-onset and younger-onset groups, consistent with global patterns in IBD epidemiology. The higher prevalence of UC in older-onset patients may reflect cumulative environmental exposures, diagnostic delays, or age-related immune changes.

The relationship between smoking and IBD has been studied for a long time, and it has been found to have different effects on both CD and UC [12–14]. A significantly lower prevalence of active smokers was observed among older-onset CD patients compared to their younger counterparts. This difference may reflect age-related cessation trends or a protective effect against CD development in older individuals who quit smoking. Additionally, the study noted a significantly lower family history of IBD in older-onset patients. The reduced family history of IBD in older-onset patients suggests that environmental factors might play a more dominant role in disease onset compared to genetic [15].

Older-onset IBD patients exhibited distinct clinical presentations and complications [16,17]. Our study demonstrated that there were no significant differences in disease extension between patients with older-onset and younger-onset UC. Conversely, patients with older-onset CD were more likely to exhibit ileal disease and a non-penetrating, non-stenosing disease behavior. These findings emphasize the need for tailored diagnostic and therapeutic approaches based on the age of onset.

Extra-intestinal manifestations (EIMs) are common in patients with IBD, affecting a significant portion of those with both CD and UC. These manifestations often involve systems such as the musculoskeletal, dermatological, hepatobiliary, and ocular systems, leading to complications that can impact patients' quality of life even beyond their intestinal symptoms. The prevalence and presentation of EIMs can vary based on age at onset, disease type, and geographical factors.

In younger IBD patients, EIMs are more frequently observed, with peripheral arthritis, ankylosing spondylitis, and primary sclerosing cholangitis (PSC) being relatively common. However, studies suggest that older-onset IBD patients generally exhibit a lower frequency of EIMs. This reduction could be attributed to age-related immune changes, such as immunosenescence, which potentially leads to a less active systemic immune response in older patients. Additionally, different disease courses and treatment approaches for older individuals may influence the occurrence of these manifestations [18]. The study found that while EIMs remain a notable aspect of IBD, their frequency is somewhat reduced in older-onset patients compared to their younger counterparts. This observation aligns with other research suggesting that the immune response in older adults may lead to fewer systemic complications, thus reducing the risk of developing EIMs.

This data underlines the importance of a tailored clinical approach for older IBD patients, considering not only intestinal symptoms but also the lower risk and different profile of EIMs. Recognizing these age-related differences can aid clinicians in better managing older patients by prioritizing intestinal health while carefully monitoring for potential but less frequent EIMs.

The treatment landscape for older-onset IBD patients revealed significant variations compared to younger-onset patients. The lower use of thiopurines and biologics among older-onset patients may reflect concerns about the increased risk of infections and malignancies, necessitating a cautious therapeutic approach [7]. Despite these differences, mesalamine remained the most prescribed

 doi:10.20944/preprints202412.2642.v1

medication across all age groups for UC, underscoring its established role in maintaining remission with a favorable safety profile [19]. The widespread use of mesalamine across all age groups underscores its safety profile and established role in maintaining remission, particularly in UC.

These findings indicate that older-onset IBD patients require different clinical approaches to balance the benefits of aggressive treatment against the risks of adverse effects. The necessity for age-specific guidelines and more extensive clinical trials, including older patients, is paramount to better understand the safety and efficacy of various treatment modalities in this group. Future research should focus on longitudinal studies to assess the long-term impact of different treatment approaches in older adults with IBD.

In conclusion, our findings highlight the importance of personalized treatment strategies and age-specific guidelines to enhance the quality of care and outcomes for the growing population of older-onset IBD patients. Further research and inclusion of older patients in clinical trials are essential to develop effective treatment strategies and improve the quality of life for this population. By understanding and addressing the unique needs of older-onset IBD patients, healthcare providers can ensure comprehensive and effective management of this increasingly prevalent group.

5. Conclusions

This study highlights significant differences in the demographics, disease characteristics, and treatment patterns between older-onset and younger-onset IBD patients. Older-onset patients present unique challenges, including a higher prevalence of UC, lower rates of family history and smoking, distinct disease behavior, and reduced usage of aggressive treatments such as thiopurines and biologics. These findings emphasize the need for tailored clinical approaches and age-specific guidelines to optimize the care and outcomes for older-onset IBD patients.

Author Contributions: Conceptualization, I.Y and F.K.; methodology, Ç.E.; formal analysis, M.E. and H.K.; writing—original draft preparation, F.K. and V.K.; supervision, I.Y. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This retrospective study was approved by the Ethical Committee of Ankara City Hospital (E2-24-6116) and there were no conflicts of interest or sponsors of this analysis. The study was conducted in accordance with the Declaration of Helsinki.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data underlying this article are available within the article. Any additional information will be shared on reasonable request to the corresponding author.

Acknowledgments: No administrative, technical, or material support that falls outside the scope of author contributions or funding was received during the preparation of this manuscript.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

UC	Ulcerative Colitis
CD	Crohn's Disease
IBD	Inflammatory bowel disease
GI	Gastrointestinal
CDAI	Crohn's Disease Activity Index
BMI	Body Mass Index
PSC	Primary Sclerosing Cholangitis

 doi:10.20944/preprints202412.2642.v1

IM	Immunomodulator
Hb	Hemoglobin
IQR	Inter Quantile Range
CRP	C-reactive protein
EIMs	Extra-intestinal manifestations

References

1. Abraham C, Cho JH. Inflammatory Bowel Disease. N Engl J Med. 2009 Nov 19;361(21):2066–78.
2. Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, et al. Increasing Incidence and Prevalence of the Inflammatory Bowel Diseases With Time, Based on Systematic Review. Gastroenterology. 2012 Jan 1;142(1):46-54.e42.
3. Ruel J, Ruane D, Mehandru S, Gower-Rousseau C, Colombel JF. IBD across the age spectrum: is it the same disease? Nat Rev Gastroenterol Hepatol. 2014 Feb;11(2):88–98.
4. Banerjee R, Pal P, Nabi Z, Shava U, Ganesh G, Reddy DN. Very early onset inflammatory bowel disease in a South Asian country where inflammatory bowel disease is emerging: a distinct clinical phenotype from later onset disease. Intest Res. 2021 Oct;19(4):398–407.
5. Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A, Barreiro-de Acosta M, et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagnosis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery, and Ileo-anal Pouch Disorders. J Crohns Colitis. 2017 Jun 1;11(6):649–70.
6. Shim JO. Recent Advance in Very Early Onset Inflammatory Bowel Disease. Pediatr Gastroenterol Hepatol Nutr. 2019 Jan 10;22(1):41.
7. LeBlanc JF, Wiseman D, Lakatos PL, Bessissow T. Elderly patients with inflammatory bowel disease: Updated review of the therapeutic landscape. World J Gastroenterol. 2019 Aug 14;25(30):4158.
8. Ingrasciotta Y. Insight into Real-world use and Benefit-risk Profile of Biologics and Frequently Prescribed Drugs in Aging Populations.
9. Everhov ÅH, Halfvarson J, Myrelid P, Sachs MC, Nordenvall C, Söderling J, et al. Incidence and Treatment of Patients Diagnosed With Inflammatory Bowel Diseases at 60 Years or Older in Sweden. Gastroenterology. 2018 Feb 1;154(3):518-528.e15.
10. Mak JWY, Lok Tung Ho C, Wong K, Cheng TY, Yip TCF, Leung WK, et al. Epidemiology and Natural History of Elderly-onset Inflammatory Bowel Disease: Results From a Territory-wide Hong Kong IBD Registry. J Crohns Colitis. 2021 Mar 1;15(3):401–8.
11. Shrestha MP, Taleban S. Management of Ulcerative Colitis in the Elderly. Drugs Aging. 2019 Jan 1;36(1):13–27.
12. Georgiou AN, Ntritsos G, Papadimitriou N, Dimou N, Evangelou E. Cigarette Smoking, Coffee Consumption, Alcohol Intake, and Risk of Crohn's Disease and Ulcerative Colitis: A Mendelian Randomization Study. Inflamm Bowel Dis. 2021 Feb 1;27(2):162–8.
13. Rozich JJ, Holmer A, Singh S. Effect of Lifestyle Factors on Outcomes in Patients With Inflammatory Bowel Diseases. Off J Am Coll Gastroenterol ACG [Internet]. 2020;115(6).
14. Papoutsopoulou S, Satsangi J, Campbell BJ, Probert CS. Review article: impact of cigarette smoking on intestinal inflammation—direct and indirect mechanisms. Aliment Pharmacol Ther. 2020;51(12):1268–85.
15. Gupta YK, Singh A, Narang V, Midha V, Mahajan R, Mehta V, et al. Clinical spectrum of elderly-onset inflammatory bowel disease in India. Intest Res. 2022 Aug 8;21(2):216.
16. Fries W, Demarzo MG, Navarra G, Viola A. Ulcerative Colitis in Adulthood and in Older Patients: Same Disease, Same Outcome, Same Risks? Drugs Aging. 2022 Jun 1;39(6):441–52.
17. Rozich JJ, Dulai PS, Fumery M, Sandborn WJ, Singh S. Progression of Elderly Onset Inflammatory Bowel Diseases: A Systematic Review and Meta-Analysis of Population-Based Cohort Studies. Clin Gastroenterol Hepatol. 2020 Oct 1;18(11):2437-2447.e6.

 doi:10.20944/preprints202412.2642.v1

18. Ng WK, Wong SH, Ng SC. Changing epidemiological trends of inflammatory bowel disease in Asia. Intest Res. 2016 Apr 27;14(2):111.
19. Zheng X, Zhang Z, Wang B, Li J, Qiu C, Zhang Q, et al. Efficacy and safety of once daily versus twice daily mesalazine for mild-to-moderate ulcerative colitis: A meta-analysis of randomized controlled trials. Medicine (Baltimore) [Internet]. 2019;98(14).