Recent Advances in Biology and Medicine

Original Research Article

Clinical and Demographic Characteristics of Older Inflammatory Bowel Disease Patients

Clinical and Demographic Characteristics of Older Inflammatory Bowel Disease Patients

Pamila Adikari*, Jesica Makanyanga, John Olynyk

Department of Gastroenterology, Fiona Stanley Hospital, 11 Robin Warren Dr, Murdoch WA 6150, Australia.

*Correspondence: Pamila.Adikari@health.wa.gov.au, m19604@pgim.cmb.ac.lk

Abstract

There is limited data describing management of older Australians with inflammatory bowel disease (IBD). The prevalence of IBD in the elderly is increasing due to an aging population and increasing overall incidence, which presents challenges in management due to comorbidities and polypharmacy. The aim of the study was to describe demographic and clinical characteristics, and management of IBD in older patients. Around 100 consecutive patients ($n = 100$) aged above 60 years and attending the IBD outpatient clinic of Fiona Stanley Hospital from January 2019 were selected. Demographic and clinical information were compiled from the digital medical record. Around 59 patients had Crohn's disease (CD), 39 had ulcerative colitis (UC) and 2 unclassified IBD (IBD-U). Around 75% of patients had a Montreal classification recorded, which is a recommended standard of care. For both CD and UC, no patients had onset of symptoms <17 years old, and the majority had symptom onset after 40 years of age (CD—56%, UC—52%). Around 39% of CD patients had undergone at least one surgery, and 5% a second operation. No UC patients had undergone surgery. 5'Aminosalicylates (59%), antitumor necrosis factor alpha (33%), thiopurines (22%), and vedolizumab (11%) were the most common current treatments. Around 9% of patients were currently taking steroids while 36% had previously taken corticosteroids. Immunosuppressive events were recorded, if they occurred, after treatment with steroids, immunomodulatory or biologic agents. Two patients had melanoma, 12 nonmelanoma skin cancer, 3 solid organ tumors (2 prostate adenocarcinoma and 1 bladder transitional cell carcinoma), 3 latent tuberculosis, 1 myelodysplasia, and 1 septic arthritis. Around 14% of the patients had osteoporosis or osteopenia; 43% of these had prior corticosteroid exposure; however, there was a low rate of bone densitometry. Most patients both with CD and UC were diagnosed over 40. Biologics were the most common treatment category in keeping with the aim of achieving deep remission.

1. INTRODUCTION

Inflammatory bowel disease (IBD) includes Crohn's Disease (CD) and ulcerative colitis (UC), which cause chronic inflammation of the gut. Both genetic and environmental factors are postulated as etiological factors. IBDs commonly present with chronic diarrhea and abdominal pain. The diagnosis is confirmed by endoscopy and biopsy. Males and females are equally affected by CD, while there is a slight male predominance in UC [1]. Approximately 10–30% of patients with IBD are over 60 years of age [2]. This group includes patients who were diagnosed and transitioned with the disease and late-onset IBD.

Both CD and UC have a wide spectrum of severity. Correct documentation of the Montreal classification of IBD patient counseling, assessment of disease prognosis, and decisions on the most appropriate therapy are important [3]. In CD, the age of onset (A), disease location (L), and disease behavior (B) are considered as predominant phenotypic elements, and UC considers an assessment of disease extent and severity of an individual relapse of disease as of critical relevance [3].

The main aim of pharmaceutical treatment is to induce and maintain remission. The choice of treatment depends on the severity of disease and response to medication. Glucocorticoids, immunomodulatory therapy, and biologic therapy are the main approaches to treatment. Glucocorticoids have effects on bone remodeling, placing patients at increased risk of reduced bone mineral density [4]. Immunomodulatory therapy is associated with myelosuppression and liver toxicity. Biologic agents have adverse effects, such as infusion site reactions, infectious complications, malignancy, and autoimmune phenomena. Azathioprine (AZA) and mercaptopurine (MP) are two commonly used thiopurine immunomodulators for over 50 years and are well known for their association with nonmelanoma skin cancer [5]. Immunosuppressive events are common among patients with IBD due to the disease itself and because of treatment. However, the clinician has to carefully assess the benefits and risks of immunosuppressive therapy when planning treatment [6]. Elderly patients suffer from multiple chronic disorders that increase the complexity of pharmaceutical management giving rise to numerous drug interactions. Polypharmacy is also associated with a heightened incidence of noncompliance. Deteriorating liver and kidney function affect drug clearance or metabolism, altering plasma concentration and further enhancing the adverse reactions. Cognitive and functional impairments in this population

further weaken therapeutic success [2]. Changes in body composition in the elderly also affect pharmacokinetics and drug metabolism. Cognitive and locomotor disturbance also influence the preference of treatment in this important group [7].

Although the mainstay of treatment is medical, surgery may be required in the management of IBD due to complications or refractory disease to treatment. Surgical intervention is more common in patients with CD. Half of the patients with CD are expected to have some kind of surgical intervention during the disease course [8]. Right hemicolectomy, small bowel resection, colectomy, and fistula operation are among the most common operations that these patients undergo.

Data on older patients with IBD is rare, and frequently they are excluded from research. Improved knowledge on IBD in patients over 60 years will help the physicians to widen their expertise and appropriately plan their care of this important group in a holistic manner [9].

1.1. Aims
The main aims of the study were to describe the demographic and clinical characteristics of the patients over 60 years with IBD managed at the outpatients' clinic of Fiona Stanley Hospital and to improve care and outcomes in patients with IBD through a systematic review of documentation and care against explicit criteria.

1.2. Standards
There were no internationally accepted guidelines for the care of older age IBD patients. The study team collaboratively designed an acceptable best practice standard drawn from IBD care guidelines for adults, scientific literature, and expert consensus. From the electronic medical records, patient demographic details, the Montreal classification, details of current and past treatment, concurrent treatment for comorbidities, details of surgical treatment the patient underwent, and any immunosuppressive events reported were obtained. Receipt of advice for immunization and skin cancer screening was also recorded. Furthermore, whether the patient was diagnosed with prednisolone induced osteoporosis/osteopenia and referral for bone densitometry was also noted.

2. METHOD(S)

The study aimed to describe demographic, clinical characteristics, and management of IBD in older patients. The study team decided to assess the quality of care provided to the older patients against implicit criteria as no endorsed guideline described ideal care for this important group. Key elements in the documentation and care were identified by the research team by literature review. These elements were further discussed among peers, and their validity was confirmed.

It was essential to collect demographic data of patients to describe the clinical characteristics. The study team decided to collect the Montreal classification of patients as it is an important treatment and prognosis determinant. Current and past medications and surgical history, concurrent treatment details, and immunosuppressive events and malignancies patients underwent were considered important because major drug interactions were considered common among this group. The literature further mentioned IBD treatment increases the susceptibility to certain vaccine-preventable illnesses and skin cancer. Therefore, it was considered that advising their primary care physicians on this regard is important. Data on whether the patient developed reduced mineral density of bone after the diagnosis of IBD was made and whether they were treated with prednisolone for IBD and their status of screening done for bone density within the last 5 years was also recorded.

Inclusion criteria for the study was: consecutive 100 patients with IBD, above 60 years of age attending the outpatients' clinic of Fiona Stanley Hospital within the 6 months from January 1, 2019, to June 31, 2019, selected by filtering through BOSSnet electronic medical records. Exclusion criteria were second visits of the same patient within the study period. A data entry sheet was created in MS Excel and patient data was manually extracted retrospectively going through the digital medical record. MS Excel data validation function was used to prevent errors while entering data. Pilot data collection was performed on 20 records and discussed with the research team to identify inherent or interpretation problems.

All data were extracted by the principal investigator. Data analysis was performed using MS Excel and presented in an easy-to-understand tabular format.

Administrative and ethical permission was obtained through GEKO application No: 33620. No sensitive information was collected from medical records. All stored data sheets were password protected.

2.1. Definitions
Presence of melanoma, nonmelanoma skin cancers, solid organ or hematological malignancy, and infections requiring hospital admissions were considered immunosuppressive events. Iatrogenic causes of immunosuppression were also included in this group, namely previous treatment with prednisolone exceeding 20 mg daily, thiopurine, methotrexate, or biologic medication.

If prednisolone has been used in the therapy of IBD and subsequently if the patient was diagnosed with osteoporosis or osteopenia, then that was counted as a case of prednisolone-induced reduced bone mineral density (rBMD).

3. RESULTS

Data were collected from 100 consecutive patients with IBD and over 60 years of age attending FSH during the first 6-month period of 2019. Fifty-nine of them had CD, 39 were diagnosed with UC, and 2 patients were unclassified. From the study

Table 1: Demographic characteristics of the patients with IBD over 60 years of age.

Age group	Gender	Diagnosis		
		CD	UC	Unclassified
60–69	Male	14	13	0
	Female	20	6	1
70–79	Male	11	5	1
	Female	9	8	0
80–89	Male	3	4	0
	Female	2	3	0
Total		59	39	2

Table 2: Characterization of patients with CD according to the Montreal classification.

Variable	Description of clinical factor	Frequency* $n = 50$	(%)
Age	A1 (<17 years)	0	0.0
	A2 (17–40 years)	22	44.0
	A3 (>40 years)	28	56.0
Disease location	L1 (ileal)	22	44.0
	L2 (colonic)	13	26.0
	L3 (ileocolonic)	15	30.0
Disease behavior	B1 (inflammatory)	20	40.0
	B2 (stricturing)	23	46.0
	B3 (penetrating)	7	14.0
Upper GI modifier	L4 (isolated upper disease)—yes	2	4.0
	L4 (isolated upper disease)—no	48	96.0
Peri-anal disease modifier	P yes	6	12.0
	P no	43	86.0

*Montreal classification not documented in nine records.

Table 3: Characterization of patients with UC according to the Montreal classification.

Variable		Frequency* $n = 25$	(%)
Age	A1 (<17 years)	0	0.0
	A2 (17–40 years)	12	48.0
	A3 (>40 years)	13	52.0
Extent	E1 (proctitis)	3	12.0
	E2 (left-sided colitis)	12	48.0
	E3 (pan-colitis)	10	40.0

*Montreal classification not documented in 14 records.

sample, 49 patients were females and 51 patients were males. Age group related to the distribution of cases follow age analogous survival patterns. Table 1 describes the demographic characteristics of the patients with IBD over 60 years of age.

Table 2 outlines the characterization of patients with CD according to the Montreal classification. About 25% of patient records did not carry documented Montreal classification. More than half of the cases with CD had onset after 40 years. More than 96% of the sample had no concomitant upper gastrointestinal (GI) disease and no perianal involvement. Less than 14% of patients had penetrating disease.

About an equal percentage of cases with UC presents between the 17-40 and >40 years age group. Approximately half of the study sample had left-sided or pancolitis. Table 3 describes the characterization of patients with UC according to the Montreal classification.

Table 4: Past surgical history of patients with CD.

Past surgical history	Frequency (*n* = 59)	(%)
Right hemicolectomy	13	22.0
Small bowel resection	11	18.6
Colectomy	0	0.0
Fistula operation	2	3.4

Table 5: Previous and current medication prescribed for patients over 60 years of age with IBD.

	Frequency (*n* = 100)	
Medication	**Previous medication**	**Present medication**
5-ASA	19	59
Adalimumab	3	18
Budesonide	13	5
Golimumab	0	1
Infliximab	6	15
Methotrexate	6	1
Prednisolone	23	4
Thiopurine (azathioprine and mercaptopurine)	24	22
Tofacitinib	0	0
Ustekinumab	0	5
Vedolizumab	1	11

Table 6: Concurrent medication prescribed for patients over 60 years with IBD.

Concurrent medication	Frequency (*n* = 100)
Antihypertensive	36
Proton pump inhibitor (PPI)	31
Inhalers for asthma or chronic obstructive pulmonary disease	13
Oral hypoglycemics	12
Aspirin	12
Non-vitamin K antagonist oral anticoagulants (NOAC)	10
Antiplatelet medication (other)	4
Parkinson's treatment	3
Warfarin	2
Insulin	2

Of the patients diagnosed with CD, almost 39% had undergone at least one surgery, and a further 5% had a second surgical intervention. No patient with UC has undergone surgery.

Table 4 describes the past surgical history of studied patients with CD.

Table 5 outlines the previous and current medication prescribed for patients over 60 years with IBD. An increase in use of 5-ASA and biologics is noted in present medication. Place of prednisolone in management of IBD has diminished.

Table 6 details the concurrent medication prescribed for patients over 60 years with IBD. Antihypertensives and proton pump inhibitors were the commonly prescribed medications in the group.

Table 7 specifies immunosuppression events that occurred and recommendations made on their clinical notes in the study population. A higher number of patients with CD have experienced immunosuppressive events (27.1%), been advised on immunization (37.3%), and screening for skin cancer (18.6%). All immunosuppressive events recorded in the study population are listed in Table 7. Nonmelanomatous skin cancers and basal and squamous cell carcinomas were the commonest. Active or latent tuberculosis infection occurred while the patient was being treated for IBD and was viewed as an immunosuppressive state. Similarly, recurrent *Clostridium difficile* infection, septic arthritis of knee joint, and shingles infection on a patient with myelodysplasia were combined into this group. Some patients had more than one immunosuppressive circumstance.

Table 7: Immunosuppression events and recommendations among patients over 60 years of age with IBD.

Clinical consideration		Diagnosis			
		CD		UC	
		Frequency	% (*n* = 59)	Frequency	% (*n* = 39)
The occurrence of an immunosuppressive event (specify)		13	22.0	7	17.9
1. Melanoma	2				
2. Nonmelanoma skin cancer	12				
3. Solid organ tumors	4				
4. Recurrent *Cl. difficile* infection	2				
5. Active or latent TB	3				
6. Pancytopenia (myelodysplasia)	1				
7. Other infections (in text septic arthritis and shingles)	2				
Advised on immunization with vaccine-preventable diseases		22	37.3	9	23.1
Advised on skin cancer screening		11	18.6	4	10.3

Table 8: Reduced bone mineral density (rBMD) in the patients with IBD >60 years.

Description	Frequency (*n* = 100)
Distribution of rBMD in the study sample	
Total patients with rBMD	14
Gender	
Male	3
Female	11
Age group	
60–69	4
70–79	6
80–89	4
Diagnosis	
CD	5
UC	8
Unclassified	1
Prednisolone usage in the treatment of IBD	
Prednisolone induced rBMD	6
Nonprednisolone-related rBMD	8

Table 8 summarizes the findings of rBMD in patients over 60 years of age in the study sample. The total 14 patients with IBD, who developed rBMD after the diagnosis, were predominantly females of the 70 to 79-year-old age group. Only 6 patients had documented evidence on request for dual-energy x-ray absorptiometry (DEXA) scan through their general practitioners.

4. DISCUSSION

A sample of 100 outpatients with IBD who attended the clinic from January 1st, 2019, at Fiona Stanley Hospital was included in the study. Their demographic details, Montreal classification, past surgical history, current, past, and concurrent medication history, immunosuppression events, presence of osteoporosis, prednisolone-induced osteoporosis, and counseling of patients for immunization and bone mineral density screening were collected from their digital medical records. Findings were analyzed and tabulated in a meaningful way based on literature review.

High burden of disease was from CD and followed age-specific survival patterns. Approximately two out of every five patients over the age of 60 with CD had undergone surgery due to disease complications or being refractory to treatment. Mesalazine was the most commonly used drug to treat IBD among this subgroup patient, and antihypertensives and PPIs were concurrently used in the treatment in about a third of patients. Immunosuppressive events were common among the patients

with CD, and the majority of patients/ primary care providers were not alerted on the importance of screening for skin cancer and receipt of immunization.

Among the UC patients in the present study, 56% were diagnosed after 40 years and penetrating disease complications account for a mere 14%. Freeman, Choi *et al.* suggest that age at diagnosis is an important factor in predicting the complications patients develop, especially penetrating disease complications [10, 11]. In the present study sample, the cohort with UC showed a lower percentage of ulcerative proctitis accounting for 12%. But, in the study done in Korea by Choi *et al.*, 2015, they reported the highest numbers in the E1 extent, ulcerative proctitis. The reason for this difference is not clear.

The Montreal classification is important to decide on therapy and prognosis [3], and also minimize interpersonal variation in interpretation [12]. Totally, 25% of the records in the study sample carried no Montreal classification noted. Granted that transcription of this is purely clinician-dependent, proper documentation of Montreal classification could enhance the quality and completeness of the medical record.

Most commonly prescribed medicines are aminosalicylates among the study sample, which rates at 60%. Only 9% of the patients were currently on steroid therapy (4% on prednisolone), a lower figure compared to 33% as described by Kedia. Around 23% of patients were on immunomodulatory therapy, lower than the latest reported figures (32%). A higher proportion of patients in the sample were on biologics, 50% in comparison to 15% in the study by Kedia *et al.* [7]. This is likely to reflect an increasing trend to using biologic therapies to achieve deep remission consistent with current guidelines.

Multiple, prescribed, and over-the-counter medications place older aged patients at enhanced risk of drug interactions. More than 10% of the study sample was on one in six categories or multiple categories of drugs. Antihypertensives were the commonest prescribed medicine category in the sample under study. Internationally, a third of patients had drug interaction reported, but the present study could not capture the figures due to a lack of this information in medical records.

Although it is mentioned that the elderly with UC have a 20–30% risk of surgery [9], none of the patients with UC had undergone the four major surgical procedures that were studied. Even among the diagnosed patients with CD, nearly 40% underwent at least one surgery compared to 70–80% as described by Arnott, indicating successful early diagnosis, optimum control of disease, and early intervention, if needed. This is a commendable finding as postoperative complexities are well known in the view of comorbidities in elderly patients [9].

Ali *et al.* described a higher risk of osteoporosis and osteopenia in IBD patients than the general population [4]. However, Tian *et al.* described prevalence of osteoporosis at 9.65% for postmenopausal women and 8.08% for elderly males, and an even higher rate of osteopenia, which was at 27.09% for postmenopausal women and 26.68% for elderly males [13]. The current study sample had only 14 cases of osteoporosis and osteopenia, which is a lower rate than reported by Tian *et al.*; however, this may be influenced by a low rate of DEXA scanning in the population.

5. CONCLUSION

The quality of care provided to the >60 years aged patients attending the IBD clinic of FSH was assessed by review of their digital medical record against an implicit criterion developed by review of international literature. CD had the most disease burden. None of the patients with UC had developed major surgical complications. 5-ASA and biologics have overridden the dominant role played by steroids in the past. Antihypertensives and PPIs are the predominant concomitant drugs used by the study sample. Referrals for the screening of skin cancer and reduced bone density and immunization for vaccine-preventable diseases were found to be low.

5.1. Recommendations
5.1.1. Improving Documentation of Montreal Classification
Availability of Montreal classification in medical records has shown to improve the determination of treatment and prognosis. The findings of this project suggest the implementation of a suitable intervention to improve documentation of the Montreal classification.

5.1.2. Vaccination and Documentation
Improved communication with primary care providers to promote the delivery of vaccination is needed. Documentation of vaccination status is stressed to facilitate calculation of vaccine coverage.

5.1.3. Routine Skin Cancer Screening
Push needed for periodic referring of patients for annual skin cancer-screening services through general practitioner (GP).

5.1.4. Consistent Screening for rBMD in Patients with Risk Factors for Osteoporosis and Osteopenia
Considering the low reported number of patients with rBMD, it is recommended to actively recognize risk factors and refer elderly patients with IBD for appropriate screening via their GPs.

Conflict of Interest
None.

References

1. Shandro B, Poullis A. BMJ best practice, ulcerative colitis- epidemiology. Ulcerative Colitis- Epidemiology. [Online]. Available at: https://bestpractice-bmj-com.smhslibresources.health.wa.gov.au/topics/en-gb/43/epidemiology [Accessed: December 26, 2019].
2. Taleban S, Colombel J-F, Mohler MJ, Fain MJ. Inflammatory bowel disease and the elderly: a review. J Crohns Colitis. 2015; 9(6):507-15. doi:10.1093/ecco-jcc/jjv059
3. Satsangi J, Silverberg MS, Vermeire S, Colombel J-F. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006; 55(6):749-53. doi:10.1136/gut.2005.082909
4. Ali T, Lam D, Bronze MS, Humphrey MB. Osteoporosis in inflammatory bowel disease. Am J Med. 2009; 122(7):599-604. doi:10.1016/j.amjmed.2009.01.022
5. Quezada SM, McLean LP, Cross RK. Adverse events in IBD therapy: the 2018 update. Expert Rev Gastroenterol Hepatol. 2018; 12(12):1183-91. doi:10.1080/17474124.2018.1545574
6. Beaugerie L, Kirchgesner J. Balancing benefit vs risk of immunosuppressive therapy for individual patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol. 2019; 17(3):370-79. doi:10.1016/j.cgh.2018.07.013
7. Kedia S, Limdi JK, Ahuja V. Management of inflammatory bowel disease in older persons: evolving paradigms. Intest Res. 2018; 16(2):194-208. doi:10.5217/ir.2018.16.2.194
8. Reese G, Woodfield G, Patel P. BMJ best practice, Crohn's disease - treatment algorithm. 2018. [Online]. Available at: https://bestpractice-bmj-com.smhslibresources.health.wa.gov.au/topics/en-gb/42/treatment-algorithm. [Accessed: December 26, 2019].
9. Arnott I, Rogler G, Halfvarson J. The management of inflammatory bowel disease in elderly: current evidence and future perspectives. Inflamm Intest Dis. 2018; 2(4):189-99. doi:10.1159/000490053
10. Freeman HJ. Application of the Montreal classification for Crohn's disease to a single clinician database of 1015 patients. Can J Gastroenterol. 2007; 21(6):363-66. doi:10.1155/2007/951526
11. Choi JH, Kim ES, Cho KB, Park KS, Lee YJ, *et al.* Old age at diagnosis is associated with favorable outcomes in Korean patients with inflammatory bowel disease. Intest Res. 2015; 13(1):60. doi:10.5217/ir.2015.13.1.60
12. Spekhorst LM, Visschedijk MC, Alberts R, Festen EA, van der Wouden E-J, *et al.* Performance of the Montreal classification for inflammatory bowel diseases. World J Gastroenterol. 2014; 20(41):15374-81. doi:10.3748/wjg.v20.i41.15374
13. Tian L, Yang R, Wei L, Liu J, Yang Y, *et al.* Prevalence of osteoporosis and related lifestyle and metabolic factors of postmenopausal women and elderly men: a cross-sectional study in Gansu province, Northwestern of China. Medicine (Baltimore). 2017; 96(43):e8294. doi:10.1097/MD.0000000000008294