



Original Article

Hospital Cost of Inflammatory Bowel Disease and Its Determinants in a Multicenter Study From Iran

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Abstract

Background: In the current era of monitoring healthcare costs for patients with inflammatory bowel disease (IBD), there has been a shift in the pattern of such costs. In this cross-sectional study conducted in three hospitals in Iran from 2015 to 2021, we aimed to assess the in-hospital costs of IBD and identify predictors of higher total hospital costs in hospitalized patients with IBD.

Methods: This cross-sectional study was conducted at three hospitals in Iran. For the purpose of this study, we collected demographic and clinical information, as well as cost data for patients with IBD. Two non-parametric statistical procedures, classification and regression trees (CARTs) and quantile regression forests (QRFs), were employed to identify the main factors related to hospital costs of IBD, which served as the dependent variable in our analysis.

Results: During 7 years, 930 admissions occurred in these three hospitals. 22.3% of patients (138 of 619) were readmitted, and 306 (49.4%) were male. The mean age of the patients was 33 (SD=18.9) years. A total of 454 patients (73.3%) had ulcerative colitis (UC), and 165 patients (26.7%) had Crohn's disease (CD). Hotelling and medication costs accounted for the largest share of the total hospital costs, with percentages of 30.61% and 23.40%, respectively. Length of stay (LOS) was found to be the most important variable related to hospital costs of IBD in both QRF and CART models, followed by age and year of hospital admission in QRF. Additionally, in the CART model, hospital type and year of hospital admission were also significant predictors of hospital costs for patients with IBD.

Conclusion: The present study showed that LOS, age, year of admission, and the hospital where the patient is admitted are all important factors that determine hospital costs for patients with IBD. Patients admitted for 20.5 days or longer had the highest hospital costs. These findings can be used as thresholds for future DRG policies.

Keywords: Hospital cost, Inflammatory bowel disease, Determinants, Iran

Cite this article as: Ghahramani S, Shojaadini H, Akbarzade A, Sadeghi F, Hajianpour V, Nozaie F, et al. Hospital cost of inflammatory bowel disease and its determinants in a multicenter study from Iran. *Middle East J Dig Dis* 2023;15(3):167-174. doi: 10.34172/mejdd.2023.339.

Received: February 8, 2023, Accepted: June 9, 2023, ePublished: July 30, 2023

Introduction

Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a chronic condition that affects the gastrointestinal tract.¹ IBD imposes a lifelong burden on individuals, caregivers, and societies, with direct costs mainly incurred by medication, hospitalizations, and surgeries, and indirect costs including lost productivity, premature retirement, and death.²

The prevalence of IBD is on the rise globally, particularly in Asia and the Middle East.³ In Iran, the prevalence of UC and CD was 35.5 and 5 per 100 000 people, respectively, in 2012, indicating that these rates will continue to increase in the coming years.^{1,4,5} As a result of the chronic nature of IBD and its associated complications, along with its increasing prevalence, the rate of hospitalization and related costs are also increasing worldwide.⁶

According to estimates, IBD imposes a significant economic burden on healthcare systems worldwide. In the US, the cost of IBD was around US\$ 6.3 billion in

2004, while in Canada, the annual direct healthcare costs for over 200 000 IBD patients were estimated to exceed CDN\$ 1.2 billion in 2012.^{7,8} Limited data are available on the cost of IBD in developing nations, but this is expected to increase over the next decade.^{9,10} In Iran, the total annual cost for IBD patients in 2017 was 4 588 631 Purchasing Power Parity Dollar (PPP\$).¹¹ A recent study found that the costs of illness for UC and CD in Iran were US\$ 22 331 079 and US\$ 15 183 678, respectively, with hospitalization accounting for 6% and 10% of the total costs.¹² A 2019 study conducted in a referral hospital in Shiraz, Iran, revealed that the total hospital cost for IBD patients was 640 843 PPP\$, with a daily hospital cost of more than 700 PPP\$.¹³

The direct medical costs of IBD are largely driven by hospitalization, surgery, ambulatory care (such as office visits and procedures), and medication. The cost of illness is further influenced by factors such as hospitalization rates and the severity and extent of the disease.¹⁴⁻¹⁶

Studies have shown that hospitalization is a significant



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part of the direct medical costs of IBD, with a significant proportion of IBD patients requiring hospitalization throughout their lifetime (ranging from 24% to 83%).¹⁷ Although IBD patients may constitute a minority of hospital admissions, hospitalization costs are still a major economic burden and a significant component of their direct medical costs.^{16,18} In the Netherlands, hospitalization accounts for one-fifth of the total healthcare costs, with surgery accounting for approximately one percent.¹⁹ Surgery is a high-cost service, particularly for CD, but its costs have decreased over time.^{8,20-23}

As the cost of treating IBD patients continues to be monitored, a shift in healthcare costs from hospitalization to medication is observed due to the emergence of new therapies, such as anti-TNF.^{19,24}

Nonetheless, monitoring hospital costs remains crucial for health policy planning, resource allocation, and cost-effectiveness. In a previous study,¹³ the authors analyzed the in-hospital costs of IBD over a short period in a single center with a limited sample size, which highlights the need for more comprehensive research. Therefore, we conducted a multicenter study spanning seven years to identify the hospital costs associated with IBD patients and the main factors contributing to higher costs using a more robust model.

Materials and Methods

Population and Clinical Data

This cross-sectional study was conducted in three hospitals in Iran. One hospital was affiliated with the Tehran University of Medical Science in the capital, and two hospitals were affiliated with the Shiraz University of Medical Sciences in the south of Iran. All three hospitals are tertiary referral hospitals for IBD patients and serve IBD patients from Tehran, Shiraz, and neighboring cities. Data on hospital costs for the hospital affiliated with the Tehran University of Medical Science was only available from September 2015 to September 2018. To address confidentiality issues, we named hospitals A, B, and C.

The study subjects included all patients with a confirmed diagnosis of IBD who were admitted at least once between September 2015 and September 2021 for an IBD-related reason. The diagnosis was based on clinical, endoscopic, and/or radiological imaging, along with pathological confirmation. The diagnosis was confirmed through clinical, endoscopic, and/or radiological imaging along with pathological confirmation.²⁵

We only included records of patients with confirmed IBD, specifically those with UC or CD, and conducted a review of their medical records to confirm that their hospitalization was related to IBD. Hospitalizations for the treatment of IBD flare-ups, associated illnesses, extra-intestinal complications, and complications related to IBD medical and surgical therapy were considered to be IBD-related. Patients without a definitive IBD diagnosis and those who were hospitalized for issues unrelated to IBD or who received total parenteral nutrition were

excluded. The year of hospitalization was recorded based on the date of discharge.

For the study purpose, the patient's demographic and clinical information including the dates of admission and discharge, length of stay (LOS) (days), status on discharge (alive/deceased), insurance status (have insurance/No insurance), type of disease (UC/CD), recorded site of gastrointestinal (GI) involvement, surgical intervention, and final diagnosis were collected. Disease severity indexes at admission and discharge naming Crohn's Disease Activity Index (CDAI)²⁶ for patients with CD and Mayo Score²⁷ for patients with UC were calculated. The Mayo scores ranged from 0 to 12, with higher scores indicating more severe disease. CDAI values ranging between 150 and 450 and values of 150 and below are associated with a quiescent disease, values above that indicate active disease, and values above 450 are seen in extremely severe disease.

The extent of disease in patients with UC and the site(s) of GI involvement in patients with CD were determined according to endoscopic and/or imaging studies with the most extensive involvement in each patient.

Determination and Predictors of Hospitalization Costs

Hospitalization costs were obtained using the Hospital Information Systems of each hospital based on the record numbers of IBD patients. Cost data included medication, examination, hoteling, surgery, visits, and consultations. The costs of biological agents were included in the medications. The cost of the laboratory tests was included in the examination costs. Consultation costs included visit costs. The hoteling cost included intensive care unit and ward costs. The cost of endoscopy was included in the examination costs. Surgery costs included surgical consumables, medications, anesthetic fees, and operation fees.

This study considered all costs associated with direct patient care but did not include administrative overhead, facility maintenance, or any other non-patient care costs. Additionally, the reported costs did not consider any reimbursements from public or complementary medical insurance, charities, or other forms of reimbursements. Costs in Iranian Rials were converted to PPP-adjusted US Dollars using the World Bank's data (World Economic Outlook Database, 2014). The cost was averaged by the number of hospitalizations, number of patients, and LOS.

The "annual hospitalization cost per patient" was defined as the annual hospitalization costs averaged by the annual number of individual patients, reflecting the real burden for every patient with IBD.

"Cost per hospitalization" was defined as the average hospitalization costs per hospital admission during a certain period, while "Daily cost during hospitalization" was defined as the average hospitalization cost per LOS during a certain period.⁶

These parameters were used for a more comprehensive understanding of hospital costs and to ensure consistency in future studies.

Statistical Analysis

This study utilized a two-stage procedure to identify the primary factors associated with hospital costs for IBD. In the first stage, quantile regression forests (QRF) were used to determine significant variables.²⁸ In the second stage, the top ten most significant variables were entered into the classification and regression tree (CART) model.²⁹ An independent t-test was employed to assess the hypothesis of no difference across groups, with a significance level set at 0.05.

Classification and Regression Trees

As a data-mining procedure, CARTs based on the nature of the dependent variable can be used for classification and regression. This tree-based method partitions the dataset into homogeneous subsets (i.e., terminal nodes) of the dependent variable.²⁹

Quantile Regression Forests

Random forests (RFs) are a modification of CARTs.²⁸ RFs generate an ensemble of trees using bootstrap sampling and average them to model the conditional mean. Contrary to RFs, QRFs approximate the full conditional distribution function, which enables the estimation of conditional quantiles.³⁰

Results

The Data Set

All hospitals recorded 930 IBD admissions during these seven years. This was for 619 patients. The disease severity levels of CD and UC are presented in Table 1. The difference between hospital readmissions and disease characteristics was not statistically significant (Supplementary file 1: Table S1). The subgroups of qualitative variables, their frequencies, and common descriptive statistics for the quantitative variables are presented in Table 2. As shown in Table 2, 22.3 percent of patients (138 of 619) were readmitted. A total of 306 patients (49.4%) were male, and 313 patients (50.6%) were female. The mean age was 33 (SD = 18.9) years, with a range of 1 to 88 years. 454 patients (73.3%) had UC, and 165 patients (26.7%) had CD. Most of the patients had basic insurance (93.5%). The disease severity criteria categorized 228 patients (44.9%) as moderate and 278

Table 1. Disease severity levels of Crohn's disease and ulcerative colitis

Levels	Disease characteristic	Disease severity indexes
Normal	Ulcerative colitis	0 ≤ Mayo ≤ 2
	Crohn's disease	CDAI < 150
Mild	Ulcerative colitis	3 ≤ Mayo ≤ 5
	Crohn's disease	150 ≤ CDAI < 220
Moderate	Ulcerative colitis	6 ≤ Mayo ≤ 10
	Crohn's disease	220 ≤ CDAI < 450
Severe	Ulcerative colitis	11 ≤ Mayo ≤ 12
	Crohn's disease	450 ≤ CDAI < 1100

Table 2. The frequency of qualitative variables and common descriptive statistics for quantitative variables (N = 619)

Variable	Subgroups	Frequency	Percent
Qualitative variables			
Hospital readmission	patients without readmission	481	77.7
	patients with readmission	138	22.3
Living status	dead	24	3.9
	alive	595	96.1
Surgery in hospital	don't have	524	84.7
	have	95	15.3
Corticosteroids	don't use	214	34.6
	use	405	65.4
Hospital code	A	308	49.8
	B	92	14.9
	C	219	35.4
Disease characteristic	Crohn's disease	165	26.7
	Ulcerative colitis	454	73.3
Gender	Male	306	49.4
	Female	313	50.6
Disease severity	Normal	85	13.7
	Mild	228	36.8
	Moderate	278	44.9
	Severe	28	4.5
Basic insurance	don't have	40	6.5
	have	579	93.5
5-ASA	don't use	368	59.5
	use	251	40.5
Immunomodulator	don't use	449	72.5
	use	170	27.5
Anti-TNF-α	don't use	516	83.4
	use	103	16.6
Patients per year (Admissions per year)	2015	63 (106)	10.2 (11.4)
	2016	154 (263)	24.9 (28.3)
	2017	175 (259)	28.3 (27.8)
	2018	67 (90)	10.8 (9.7)
	2019	74 (101)	12 (10.9)
	2020	52 (69)	8.4 (7.4)
	2021	34 (42)	5.5 (4.5)
Quantitative variables			
Hospital costs (dependent variable)	1.64-35766.29	1624.92	3070.57
Length of stay	1.00-48.00	7.73	7.43
Age	1.00-88.00	33.22	18.90
Admission time	1.00-13.00	1.50	1.34

patients (36.8%) as mild. Annual hospitalization costs per patient in different years, cost per hospitalization, and daily costs during hospitalization are presented in Table 3.

Table S2 (Supplementary file 1) illustrates the descriptive statistics of the total hospital costs, which include costs related to medication, examinations, hoteling, surgeries, visits, and consultations, along with their respective shares of total costs. Hoteling and medication costs accounted for the largest share of the total hospital costs, with percentages of 30.61% and 23.40%, respectively.

Quantile regression forests

The R package “*quantregForest*” was used for the QRF procedure. The *nree* parameter (number of trees) was set to 100 because the model performance did not change for values greater than 100. The *mtry* parameter (the number of variables for each split) was set to its default value (the number of independent variables divided by three). Considering that this study aimed to identify hospital costs and predictors of higher hospital costs in patients with IBD, the QRF results were computed for quantile 0.75. The variable importance measure is a useful output from the QRF model and reflects the effect of the predictor variables on the model. Figure 1 shows the variable importance computed for the top ten independent variables. It can be seen that LOS is the most important variable in the model, followed by age. The full result of variable importance in terms of an increase in node purity measure is displayed in Tables S3 of Supplementary file 1.

Table 3. Hospital cost indices for patients with inflammatory bowel disease

	Year	Number of patients	Mean
Annual hospitalization cost per patient ^a	2015	63	1203.36
	2016	154	1068.13
	2017	175	957.16
	2018	67	4118.17
	2019	74	2059.19
	2020	52	2401.14
Cost per hospitalization ^b	2021	34	1319.54
	Name of hospital	Number of hospital admissions	Mean
	A	444	1720.64
	B	135	340.37
	C	351	558.15
Total	930	1081.53	
Daily cost during hospitalization ^c	Name of hospital	Number of lengths of stay	Mean
	A	2268	336.85
	B	499	92.08
	C	2018	97.08
	Total	4785	210.20

^a The annual hospitalization costs averaged by the annual number of individual patients

^b Hospitalization costs were averaged by the number of hospital admissions during the study period.

^c Hospitalization costs averaged by LOS during the study period. All costs are presented as PPP\$.

Classification and Regression Trees

The CARTs analysis was performed using the “*rpart*” package in R. The top 10 most important variables listed in Figure 1 were entered into the CARTs model. The result of the CARTs is a tree with five non-terminal nodes and six terminal nodes (Figure 2). From the ten independent variables, CARTs used LOS, hospital, and years to build the optimal model. As shown in Figure 2, higher LOS was associated with higher hospital costs. The rules and the mean hospital costs from the final tree are provided in Tables S4 of Supplementary file 1.

Discussion

Hospitalization is one of the largest components of the direct medical costs of IBD.¹⁸ In this study, we aimed to assess the in-hospital costs of IBD over a period of time (2015-2021). Comparing our results to a previous report by the authors from 2013 to 2015,¹³ we observed a decrease in both costs per hospitalization (from 5339 PPP\$ in the previous report to 1081 in the present) and also daily costs during hospitalization (from 712 PPP\$ to 210). The predictors of higher patient payment and total hospital costs in hospitalized IBD patients based on quantile regression were LOS, age, and year of study, while the main component for higher hospital costs was the LOS, followed by hospital and year using CART. A previous study by the authors used quantile regression to find the predictors of hospital costs from 2013 to 2015 and found that predictors for all three quartiles of total hospital cost for UC were LOS, living status on checkout, year of study, and LOS for CD.¹³ However, in the previous study model, the level of variable significance and validation was not performed.

In the present study, we updated our study timeline and included data from another referral center for better validation and a larger sample size. We also utilized CART analysis to obtain an optimal model; 10-fold cross-validation was also carried out with LOS, hospital, and age to build the optimal model. In the period of the healthcare system’s shift away from fee-for-service reimbursement and toward more value-based reimbursement systems, recognizing possible cost-cutting and quality improvement opportunities is critical. Surveillance of IBD patients’ healthcare expenses, active identification, and the development of predictive algorithms for high-cost IBD patients, as well as cost monitoring for early warning, may help to avoid potentially needless unplanned care.³¹

To the best of our knowledge, this is the first study to display a cut-off for the duration of admission related to hospital costs in our region that could be used by insurance organizations as well as diagnostic reference groups (DRGs).³² We also used the QRF for quantile 0.75, considering that this study aimed to identify the hospital costs and predictors of higher hospital costs in patients with IBD. As demonstrated, LOS was the most important variable in the models, followed by year and age. This result is consistent with the previous model. However,

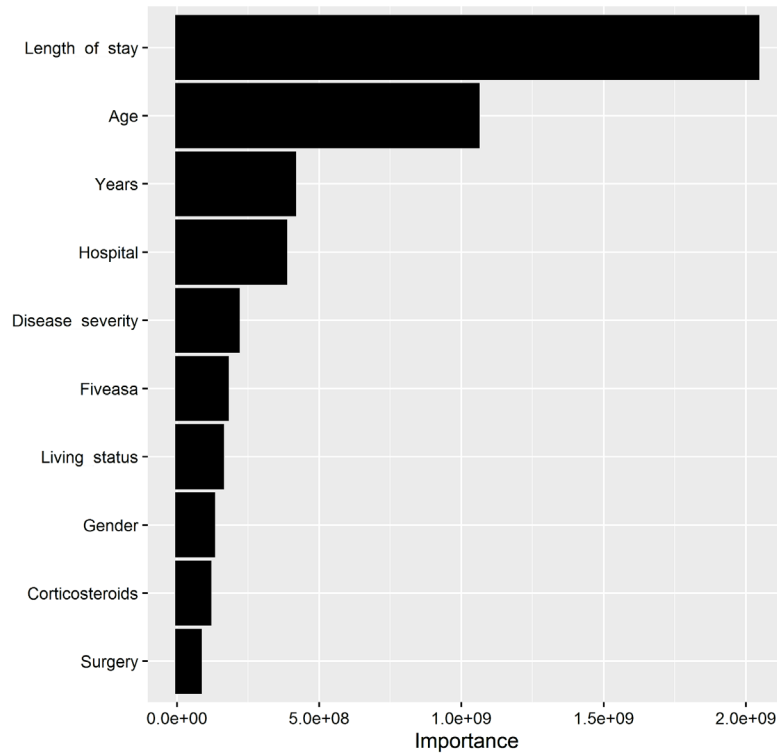


Figure 1. Importance of variables in the quantile regression forest model

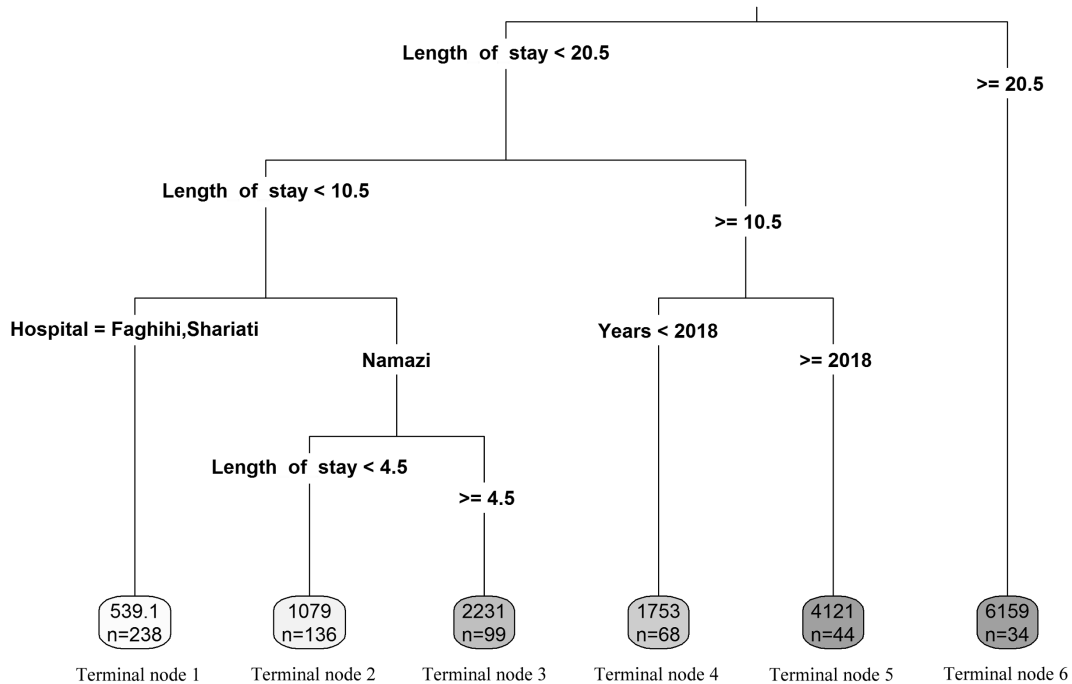


Figure 2. Optimal tree created using CARTs. The number of patients and their associated mean hospital costs as PPP\$ is shown at each terminal node

CART can better categorize patients based on LOS and age.

The in-hospital costs for patients with IBD in the three hospitals studied differed. A hospital is a referral hospital for IBD patients as well as the other two hospitals, but it has a higher annual hospitalization cost per patient, a higher cost per hospitalization, and a higher daily

cost during hospitalization. The effect of the hospital environment on procrastination and the use of hospital resources cannot be neglected,³³ however, it may also be because patients who are admitted to this hospital are more severe cases, requiring a higher LOS. Meanwhile, patients' resource utilization and, as a result, the best treatment for IBD, which necessitates specialized health

care, can be affected by patients traveling long distances to obtain this specialized health care.³⁴ As previously stated, the incidence of IBD is increasing in Iran, and since the majority of treatment services are located in tertiary care centers, many patients are referred to our study centers for treatment.⁵ As a result, we can consider the negative impact of a long waiting list on patients and resource utilization, as also reported by Bernstein et al in a Canadian population-based study regarding the direct medical cost of managing IBD³⁵ and, given the higher medical costs for IBD township patients compared to local residents, the same is likely to be true for our participants. As a result, implementing population health management strategies can be beneficial and cost-effective, as multiple studies have confirmed.^{36,37}

Several studies have examined the extent of the IBD costs in other countries.^{16,38,39,40} The annual direct medical costs of patients with CD (\$6561) were four times higher than the annual direct medical costs of patients with UC (\$1488), according to an analysis of IBD direct medical costs in the United States in 1990.^{38,41} Other cost estimates in the United States were, on average, lower, indicating that the costs associated with CD were only three times higher than those associated with UC. Our current study found no significant differences in the annual mean medical costs for disease characteristics. Although our previous study reported disease severity as a predictor of higher hospital costs, we also justified that this may be due to the smaller sample size in the CD group, which was amended in our study.¹³

The most prominent factor associated with hospital costs was the LOS, and hoteling costs accounted for the largest share of the total hospital costs. Petryszyn and Witczak¹⁸ reported that in surgical patients, the average LOS was longer than in medical patients: 9.6 and 8 days for CD and 13.2 and 7.3 days for UC, respectively. Surgical treatment accounts for 50% of all admissions, 58% of hospital days, and 61% of the total costs.^{42,43} In addition, Bewtra et al⁴⁴ observed that the increase in CD hospitalizations was counterbalanced by a decrease in the average LOS in their study on IBD hospitalization trends. In contrast, a study by Nguyen et al in the United States discovered that the average LOS for both CD and UC patients remained steady after 1998.⁴⁵

One of the factors associated with hospital costs in this study was the year. As reported in our previous study,¹³ one possibility for predicting a higher total cost by year is due to the overall increase in the cost of patients with IBD over time.⁶ Increased total hospital costs following healthcare reform have previously been documented.^{46,47} Although an increase in total hospital costs may increase as a result of rising healthcare inflation (31.7% in 2014 and 23.8% in 2015¹³ and the implementation of updated relative value units of healthcare services to align public and private service providers' payments, which began on September 29, 2014, at the third phase of the Health System Transformation Plan,⁴⁸ our results demonstrated

lower annual hospitalization costs per patient compared to our previous report.¹³

Age was the second most important factor associated with higher hospital costs. IBD incidence peaks in the second and third decades of life,⁴⁹ however, Nguyen et al⁴⁵ reported that hospitalization rates for UC peaked in the 20–30-year-old age group, but there was a second, larger peak after 60 years of age. Hospitalizations in this age range, which account for a share of the labor force, could result in indirect IBD costs due to lost productivity.

Our study's timeframe included a period when the COVID-19 pandemic led to massive healthcare center policy changes.^{50,51} This resulted in the closure of many outpatient centers, limited the hospitalization of IBD cases, and can also account for the lower annual costs per patient in the last study year. On the other hand, many healthcare professionals aimed to decrease the duration of hospitalization as much as possible to reduce the chance of hospital-acquired COVID-19 infection.⁵²

In this multicenter study, we used two models to predict the hospital costs of patients with IBD. However, prospective trials from different centers may validate our results. Studies that have assessed further potential factors that may influence the total hospital cost, such as admission due to an emergency versus an elective situation, are suggested.

Conclusion

The present study has shown that LOS, age, year of admission, and the hospital where the patient is admitted are all important factors that determine hospital costs for patients with IBD. Patients admitted for 20.5 days or longer had the highest hospital costs. These findings can be used as thresholds for future DRG policies.

Acknowledgements

Authors would like to acknowledge Dre Homayoun Vahedi and the Digestive Disease Research Institute, Tehran University of Medical Sciences, Shariati Hospital, Tehran, for their cooperation in the study.

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Competing Interests

The authors declare no conflict of interest related to this work.

Ethical Approval

The present study was approved and supervised by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran.

Supplementary Files

Supplementary file 1 contains Tables S1-S4.

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