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Alimentary Tract

Hospitalization trends of the Inflammatory Bowel Disease landscape: A nationwide overview of 16 years

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ABSTRACT

Introduction: In this study, we aimed to determine the hospitalization rates of Inflammatory Bowel Disease (IBD) in a southern-european country and its associated charges over a period of 16 years.
Methods: We identified all discharges with a primary diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) between 2000 and 2015 in data provided by the Central Administration of Health Services (ACSS). National estimates of hospitalization rates were assessed and adjusted to gender, age, population, and hospitalizations. Hospitalization charges were also assessed.
Results: There were an estimated 31 358 and 16 669 discharges for CD and UC, respectively. From 2000 to 2015, hospitalization rates per 100000 habitants increased for CD (8.4–11.2) and remained stable for UC (4.4–4.9). The hospitalization rate for IBD increased slightly over time (12.8 per 100 000 habitants in 2000 and 16.1 in 2015). Annual total hospitalization charges amounted to 4.0M€ in 2000 and 5.7M€ in 2015. This increase was mainly due to a rise in the total expenses of CD-related hospitalizations.
Conclusion: CD hospitalization rates per 100000 inhabitants increased over time while remaining constant for UC. Hospitalization charges for IBD increased approximately 2.0M€ during the study period, representing an important burden in the national healthcare system.

1. Introduction

Inflammatory bowel diseases (IBD) are a group of chronic immunologically-mediated disorders of unknown etiology of which the two main manifestations are Crohn's disease (CD) and ulcerative colitis (UC). These diseases are characterized by an early onset and by a pattern of relapses and remission periods. As currently available medical and surgical therapies are not curative, IBD management is primarily focused on controlling the symptoms and improving patients' quality of life [1]. During the course of the disease, 15–20% and 70–80% of all patients with UC and CD, respectively, will eventually require surgery [2].

IBD are estimated to affect up to 0.5% of the general population of western nations [3] with increasing incidence in newly industrialized countries whose societies have become more westernized due to rapid socioeconomic development [4].

Interestingly, due to the chronicity, early onset and low mortality rates of IBD, prevalence has increased over time at a higher degree when compared to the incidence rate, which is also known as compounding prevalence [5–7].

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In the particular case of Portugal, IBD prevalence has increased from 86 to 146 patients per 100 000 persons between the years of 2003 and 2007[8]. As such, Portugal is currently part of the group of European countries with a highest IBD prevalence estimates. In Europe, the prevalence of CD varies from 1.51 to 322 cases per 100 000 persons, whereas the prevalence of UC ranges from 2.42 to 505 per 100 000 [4].

Given the nature of their disease, IBD patients require continuous medical assistance. Accordingly, both CD and UC are associated with a considerable economic burden [9]. In Europe, the annual healthcare burden related to IBD patients was estimated to be 4.5–5.6 billion euros; most of these costs were due to hospitalizations and surgical procedures. Moreover, unemployment, sick leave, and work disability are common in patients with IBD (when compared to unaffected individuals), and contribute to almost 50% of the total costs [10–12]. As for the United States of America, the annual total costs associated with IBD may amount to $6.3 billion ($3.6 billion for CD and $2.7 billion for UC) [13].

Albeit the growing concern related to the IBD incidence and its economic impact [7,9,14], there is little information on the annual burden related to IBD patients' hospitalization and surgical interventions in Portugal, with Pinho et al. [15] work on gastric diseases as an exception.

The main objective of this study was to analyze IBD-related hospitalizations, surgical procedures and associated charges on a national scale.

2. Material and methods

2.1. Data collection

This study consisted in a retrospective analysis of all IBD patients admitted to mainland Portuguese public hospitals between 2000 and 2015. Data was retrieved from the Central Administration of Health Services (ACSS), which is an administrative database that concerns all patients subject to hospital discharge. All hospital discharges of patients that had an IBD as their primary diagnosis were considered: these were identified by the Clinical Modification of the International Classification of Disease (ICD-9-CM) codes (555.x for CD and 556.x for UC). Hospital discharge will also be referred as hospitalization henceforth. We considered each hospital discharge as an independent episode and included patients of all ages. The unit of observation was the hospital discharge and not the patient.

2.2. Variables analyzed

For each hospital discharge, the following variables were analyzed: year (defined by hospital discharge date), age (at hospitalization), gender, area of residence, length of stay (LOS), primary and secondary diagnosis, medical procedures, and healthcare charges. Disease location, extension, anemia, malnutrition and medical procedures were identified by the ICD-9-CM codes listed in the Supplementary Table 1.

Since national registries do not collect or concede access to direct patient identifiers for ethical reasons, an estimate for the number of patients was made using age, gender, and residence as identification variables.

The total number of inhabitants in mainland Portugal in the years analyzed, considered for the computation of the ratios, was obtained from the National Institute of Statistics (INE) [16].

Healthcare charges were estimated according to the National Health Service hospital reimbursements' rates, defined by governmental ordinance [17]. Expenditures tables from 2009 were the ones considered for cost-analysis since they were the latest to contemplate the 3M^{TM} All-Patient Diagnosis-Related Group (DRG) version 21, the only version we had available which spanned the entire studied period. This reimbursement is performed using the budget allocation model based on DRGs, which includes primary and secondary diagnoses, procedures, age, sex, and discharge destination [18].

To evaluate the level of variation of the following variables: hospitalization rates, hospitalization charges, number of emergency surgeries, number of elective surgeries and number of patients with IBD; percentage change was assessed between 2001 and 2015. We used the year of 2000 as the index year for calculation purposes.

Additionally, to assess the difference in mean charges between CD and UC patients for anemia and malnutrition, we calculated the delta percentage.

2.3. Statistical analysis

Categorical variables were described as absolute frequencies (n) and relative frequencies (%), whereas continuous variables were characterized by their median and percentiles, namely Inter-Quartile Range (IQR).

Statistical analysis was performed using the software Statistical Package for the Social Sciences v. 24.0.

The formula used to compute the ratio was the following:

$$Hospitalization\ rate = \frac{number\ of\ hospitalizations}{total\ of\ population} \times 100\ 000,$$

where the denominator could be (1) total population or (2) total hospitalizations.

3. Results

3.1. Hospital discharges

A total of 48 027 discharges from Portuguese public hospitals between 2000 and 2015 had a primary or secondary diagnosis of IBD. Of those, 31 358 (65%) had CD and 16 669 (35%) had UC. Concerning only those patients for whom IBD was the primary diagnosis, a total of 25 732 discharges were reported in the considered time-period: 70% concerned CD patients and 30% concerned UC patients (Table 1). The absolute number of hospital discharges has increased from 1303 in 2000 to 1674 in 2015. The IBD-related hospitalization rates per 100 000 inhabitants (Fig. 1) and per 100 000 hospitalizations (Fig. 2) have also increased from 12.7 to 16.1 and from 113.4 to 144.8, respectively.

3.1.1. Crohn's disease

Throughout the time period considered in this study, 18 124 hospital discharges in Portuguese public hospitals concerned patients with CD as their primary diagnosis. Overall, 8238 patients were discharged, which means that 9886 (55%) hospitalizations may be considered readmissions (Table 1). The majority of hospital discharges concerned female patients (53%), young adults (49%), and patients with an ileal (31%) or ileocolic (30%) location of the disease. In 17% of all hospitalizations the discharged patient required a surgical intervention. Conditions such as anemia and malnutrition were observed in 12% and 1% of all cases, respectively. Overall, patients stayed in the hospital for a median of 7 days (IQR: 4–12).

Table 2 depicts the rates of IBD-related hospitalizations per 100 000 hospitalizations and 100 000 inhabitants; in the latter, the rate was stratified by gender and age group. On average, there were 95.0 and 10.8 CD-related hospital discharges per 100 000 overall hospital discharges and inhabitants, respectively. The absolute number of CD-related hospitalizations increased in the considered time period, from 856 in 2000 to 1167 in 2015. Accordingly, so did the CD-related hospitalizations rate per 100 000 hospitalizations (from 74.5 to 101.0) and per 100 000 inhabitants (from 8.4 to 11.2) — Table 2 and Figs. 1 and 2. Similar increases were also observed

Table 1
Characterization of hospital discharges.

Crohn's disease											
	2000–2015 N = 18124	2000 (n = 856)	2001 (n = 899)	2003 (n = 1004)	2005 (n = 1107)	2007 (n = 1218)	2009 (n = 1207)	2011 (n = 1290)	2013 (n = 1264)	2014 (n = 1176)	2015 (n = 1167)
Patients, n (%)	8238 (46)	463 (54)	463(54)	474 (47)	468 (42)	469 (39)	535 (42)	730 (57)	637 (50)	579 (49)	600 (51)
Gender, n (%)											
Male	8478 (47)	412 (48)	425 (47)	500 (50)	525 (47)	526 (43)	565 (47)	612 (47)	607 (48)	563 (48)	563 (48)
Female	9646 (53)	444 (52)	474 (53)	504 (50)	582 (53)	692 (57)	642 (53)	678 (53)	657 (52)	613 (52)	604 (52)
Age, mean (sd)	38 (17)	37 (16)	38 (17)	37 (17)	37 (16)	38 (16)	37 (17)	38 (17)	38 (18)	38 (18)	38 (18)
Age, n (%)											
0–19	2572 (14)	120 (14)	105 (12)	123 (12)	135 (12)	143 (12)	159 (13)	198 (15)	230 (18)	210 (18)	208 (18)
20–39	8938 (49)	414 (48)	463 (52)	561 (56)	581 (52)	652 (54)	619 (51)	581 (45)	553 (44)	524 (45)	498 (43)
40–59	4551 (25)	224 (26)	224 (25)	195 (19)	281 (25)	291 (24)	294 (24)	378 (29)	317 (25)	291 (25)	324 (28)
≥60	2063 (11)	98 (11)	107 (12)	125 (12)	110 (10)	132 (11)	135 (11)	133 (10)	164 (13)	151 (13)	137 (12)
Disease extent, n (%)											
Ileal	5532 (31)	176 (36)	211 (36)	220 (34)	312 (42)	368 (44)	399 (40)	432 (41)	472 (48)	446 (49)	406 (44)
Colonic	2447 (14)	140 (29)	147 (25)	151 (23)	135 (18)	142 (17)	180 (18)	148 (14)	144 (15)	134 (15)	141 (15)
Ileocolonic	5342 (30)	171 (35)	222 (38)	277 (43)	305 (40)	330 (39)	415 (42)	476 (45)	364 (17)	326 (36)	386 (41)
Surgery, n (%)	3032 (17)	133 (16)	152 (17)	159 (16)	166 (15)	172 (14)	200 (17)	221 (17)	219 (17)	188 (16)	224 (19)
LOS (days), median (IQR)	7 (4–12)	8 (3–14)	8 (4–14)	7 (3–13)	7 (3–13)	7 (3–12)	7 (4–12)	7 (3–11)	7 (4–11)	7 (4–11)	7 (4–11)
Anemia, n (%)	2221 (12)	96 (11)	132 (15)	125 (13)	151 (14)	138 (11)	127 (11)	126 (10)	178 (14)	175 (15)	187 (16)
Malnutrition, n (%)	256 (1)	5 (1)	10 (1)	8 (1)	19 (2)	12 (1)	13 (1)	16 (1)	27 (2)	28 (2)	26 (2)

Ulcerative colitis											
	2000–2015 N = 7608	2000 (n = 447)	2001 (n = 398)	2003 (n = 425)	2005 (n = 442)	2007 (n = 484)	2009 (n = 474)	2011 (n = 565)	2013 (n = 532)	2014 (n = 561)	2015 (n = 507)
Patients. n (%)	4423 (58)	309 (69)	253 (64)	274 (65)	248 (56)	250 (52)	295 (62)	349 (62)	333 (63)	325 (60)	302 (60)
Gender, n (%)											
Male	3619 (48)	192 (43)	182 (46)	200 (47)	191 (43)	228 (47)	219 (46)	268 (47)	237 (50)	287 (51)	264 (52)
Female	3989 (52)	255 (57)	216 (54)	225 (53)	251 (57)	256 (53)	255 (54)	297 (53)	265 (50)	274 (49)	243 (48)
Age, mean (sd)	46 (21)	47 (20)	44 (20)	44 (21)	45 (21)	46 (21)	48 (21)	44 (21)	47 (22)	46 (22)	43 (21)
Age, n (%)											
0–19	890 (12)	39 (9)	44 (11)	57 (13)	59 (13)	48 (10)	40 (12)	69 (12)	60 (11)	81 (14)	93 (18)
20–39	2616 (34)	152 (34)	149 (37)	158 (27)	148 (33)	162 (34)	162 (34)	207 (37)	159 (30)	179 (32)	164 (32)
40–59	2016 (26)	130 (29)	112 (28)	104 (24)	115 (26)	130 (27)	139 (29)	157 (28)	144 (27)	146 (26)	125 (25)
≥60	2086 (27)	126 (28)	93 (23)	106 (25)	120 (20)	142 (30)	135 (28)	132 (23)	169 (32)	155 (28)	125 (25)
Disease extent											
Proctitis	473 (15)	29 (16)	20 (16)	29 (19)	25 (15)	34 (18)	31 (18)	42 (14)	39 (16)	31 (14)	30 (14)
Proctosigmoiditis	728 (23)	44 (24)	34 (27)	44 (29)	47 (29)	52 (28)	44 (25)	57 (19)	48 (20)	46 (20)	40 (18)
Left side	470 (15)	53 (29)	21 (17)	26 (17)	14 (9)	21 (11)	25 (14)	52 (18)	36 (15)	43 (19)	29 (13)
Pancolitis	1443 (46)	58 (31)	49 (40)	54 (35)	77 (47)	81 (43)	76 (43)	144 (49)	120 (49)	110 (48)	120 (55)
Surgery	1044 (14)	55 (12)	63 (16)	52 (12)	56 (13)	71 (15)	84 (18)	81 (14)	77 (14)	81 (14)	67 (13)
LOS (days), median (IQR)	9 (5–15)	11 (6–18)	11 (6–18)	10 (6–19)	9 (5–16)	10 (6–17)	9 (6–15)	8 (4–14)	9 (5–16)	9 (5–14)	8 (5–13)
Anemia, n (%)	1727 (23)	85 (19)	84 (21)	94 (22)	97 (22)	104 (22)	93 (20)	129 (23)	135 (25)	154 (28)	126 (25)
Malnutrition, n (%)	103 (1)	4 (1)	0 (0)	6 (1)	5 (1)	4 (1)	5 (1)	10 (2)	12 (2)	8 (1)	14 (3)

Table 2
IBD-related hospitalization rates.

Crohn's disease

	2000–2015 N = 18 124 mean (min–max)	2000 (n = 856)	2001 (n = 899)	2003 (n = 1004)	2005 (n = 1107)	2007 (n = 1218)	2009 (n = 1207)	2011 (n = 1290)	2013 (n = 1264)	2014 (n = 1176)	2015 (n = 1167)
Hospitalizations (per 100 000 hospitalization)	95.0 (74.5–109.6)	74.5	75.6	82.5	91.2	98.2	100.1	109.6	108.7	101.9	101.0
Hospitalization rate (per 100 000 inhabitant)	10.8 (8.4–12.6)	8.4	8.7	9.6	10.5	11.6	11.4	12.2	12.1	11.3	11.2
Gender (per 100 000 inhabitant)											
Male	10.6 (8.3–12.2)	8.3	8.5	9.9	10.4	10.4	11.2	12.1	12.2	11.4	11.5
Female	11.2 (8.3–13.5)	8.3	8.8	9.3	10.7	12.6	11.7	12.3	12.0	11.2	11.1
Age (per 100 000 inhabitant)											
0–19	6.1 (3.7–9.2)	4.3	3.7	3.9	5.0	5.3	6.2	7.5	9.1	8.9	9.2
20–39	19.2 (13.1–23.7)	13.1	14.8	18.3	18.8	21.1	21.0	20.7	20.9	20.1	19.8
40–59	10.5 (7.7–13.4)	9.5	9.1	7.7	10.7	11.2	10.5	13.4	11.3	10.1	11.1
≥60	5.5 (4.6–6.6)	4.6	4.8	5.7	5.0	5.9	5.9	5.5	6.4	6.0	5.2

Ulcerative colitis

	2000–2015 N = 7608 mean (min–max)	2000 (n = 447)	2001 (n = 398)	2003 (n = 425)	2005 (n = 442)	2007 (n = 484)	2009 (n = 474)	2011 (n = 565)	2013 (n = 532)	2014 (n = 561)	2015 (n = 507)
Hospitalizations rate (per 100 000 hospitalization)	39.9 (33.5–48.6)	38.9	33.5	34.9	36.4	39.0	39.3	48.0	45.8	48.6	43.9
Hospitalization rate (per 100 000 inhabitant)	4.5 (3.9–5.4)	4.4	3.9	4.1	4.2	4.6	4.5	5.3	5.1	5.4	4.9
Gender (per 100 000 inhabitant)											
Male	4.3 (3.6–5.8)	3.9	3.6	4.0	3.8	4.5	4.3	5.3	5.4	5.8	5.4
Female	4.6 (3.7–5.4)	4.8	4.0	4.2	4.6	4.7	4.6	5.4	4.8	5.0	4.5
Age (per 100 000 inhabitant)											
0–19	2.3 (4.4–4.3)	1.6	1.6	1.9	2.4	1.8	1.5	3.0	2.6	3.6	4.3
20–39	5.5 (4.4–7.0)	4.9	4.8	5.3	4.7	5.3	5.6	7.0	5.7	6.7	6.4
40–59	4.5 (3.9–5.7)	4.8	4.3	3.9	4.3	5.1	4.5	5.7	4.9	5.1	4.3
≥60	5.4 (4.4–6.6)	6.1	4.4	4.8	5.3	5.7	5.8	5.1	6.6	5.9	4.6

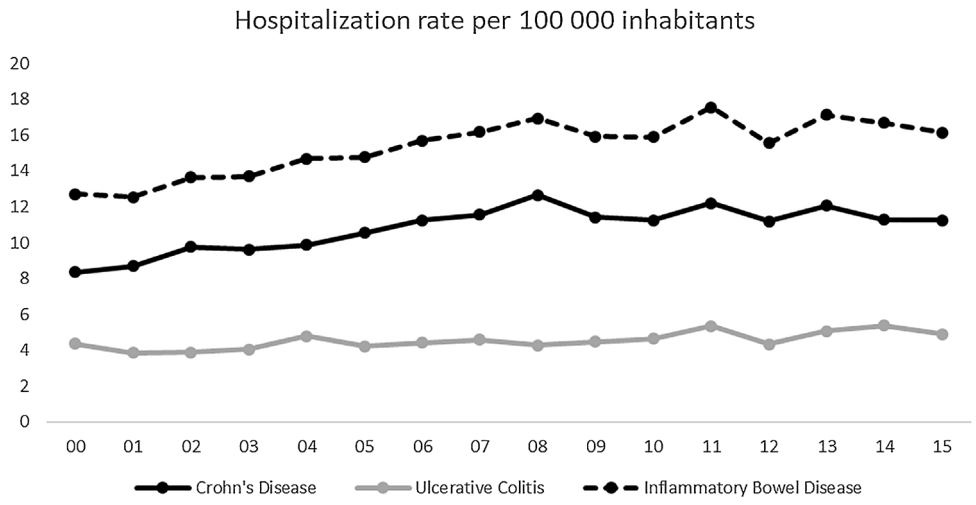

Fig. 1. IBD vs CD vs UC hospitalization rate per 100 000 inhabitants.

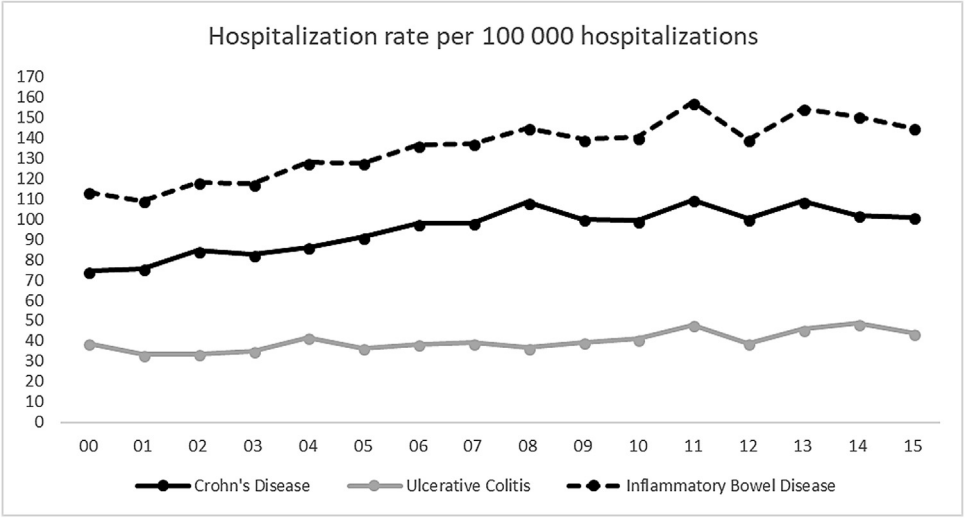

Fig. 2. IBD vs CD vs UC hospitalization rate per 100 000 hospitalizations.

for all categories when the hospital discharge rates were analyzed in an age-wise and gender-wise fashion (Table 2).

In Fig. 3A, by comparison to the index year of 2000, in 2015 there was an increase in percentage of hospitalization rate per 100 000 inhabitants (33%), hospitalization charges (55%), the number of discharges of CD patients (36%) and those submitted to surgery. Worthy of mention is the shift observed between the rates of elective (2001: 4%; 2015: 99%) and emergent surgeries (2001: 26%; 2015: 29%).

3.1.2. Ulcerative colitis

Over the 16 years analyzed in this study, 7 608 hospital discharges concerned 4 423 patients whose primary diagnosis was UC — 58% were first-time hospitalizations and 42% were re-hospitalizations (Table 1). The majority of hospitalizations concerned female patients (52%), patients who were over 19 years-old at the time of their discharge (88%), and those who had extensive disease (46%). In 14% of all cases, the admitted patients required surgical intervention. Throughout the study period, there was an increase of 50% in surgery-related hospitalizations (12% in 2000 and 18% in 2015) — Table 1. Conditions such as anemia and malnutrition were found in 23% and 1% of all hospitalizations, respectively. Globally, patients spent a median of 9 days in the hospital.

There was a slight increase in the absolute number of UC-related hospital discharges (from 447 to 507), also present in the UC-related hospital discharge rates per 100 000 hospitalizations and inhabitants (from 38.9 to 48.6 and from 4.4 to 4.9, respectively) — Table 2 and Figs. 1 and 2. For most cases, sex- and age-stratified rates shown a similar increase, with the exception of the categories female and age groups over 40, for which there was a decrease in the rate of hospitalizations per 100 000 inhabitants (Table 2).

When comparing to the base year of 2000, by 2015 there was an overall growth in percentage of hospitalization rate (13%) and charges (16%), number of UC patients that were discharged (13%) and those who were submitted to surgery. Interestingly, emergent surgery in 2015 was on par with the index year of 2000–a variation of 3%. On the other hand, elective surgery had risen over 50% by 2015 (Fig. 3B).

3.2. Healthcare charges

Fig. 4 depicts the fluctuation of the mean annual expenditure on healthcare in IBD patients throughout the analyzed period. Concerning the charge per patient-year (Fig. 4A), the values varied from 6215€/patient-year in 2000 and 6722€/patient-year in 2015. Conversely, the total charges related with IBD hospitalizations have

Fig. 3. Percentage variation from 2000 (index year) to 2015: DC patients (A) and UC patients (B).

increased from 4.0 million €/year in 2000 to 5.7 million € in 2015, mainly due to an increase in the total expenses of CD-related hospitalizations (Fig. 4B).

3.2.1. *Crohn's disease*

The mean charge of CD-related hospitalizations was 3162€/patient-year in 2000 and of 3582€/patient-year in 2015. Total cost was estimated to be 3.9 million (2000–2015: 2.7–4.2) million € per year. Additionally, when compared to the index year of 2000, by 2015 there was a rise in charges of 55% (Fig. 3A).

The mean charges of surgical interventions in CD patients were approximately 3-times higher than those related to medical interventions: 6 615 (2000–2015: 6086–7014) €/year and 2660 (2000–2015: 2532–2954) €/year, respectively. Notwithstanding, the overall annual charges of medical interventions was higher than that related to surgical interventions: 2.4 million (1.8–3.0) million € and 1.5 million (0.9–1.8) million €, respectively (Fig. S-1).

Additionally, we analyzed the delta percentage of mean charges of DC hospitalizations regarding conditions such as anemia and malnutrition. Mean charges were higher in patients hospitalized with anemia (by 10% in 2015) or malnutrition (by 42% in 2015) (Fig. S-3) when compared to hospitalizations not presenting these variables.

3.2.2. *Ulcerative colitis*

Mean cost expenditure regarding hospitalization of UC patients varied between 3 053€/patient-year in 2000 and 3139€ €/patient-year in 2015. Overall charges amounted to 1.4 million (2000–2015: 1.4–1.6) per year. When comparing charge variations between 2015 and 2000 (index year), an increase of 16% is observed (Fig. 3B).

As for UC patients, the mean charges of surgery-related discharges were approximately 3-fold higher than those of the medical interventions: 7194 (2000-2015: 6051–8 852)€/patient-year and 2667 (2000–2015: 2541–2837)€, respectively. Still,

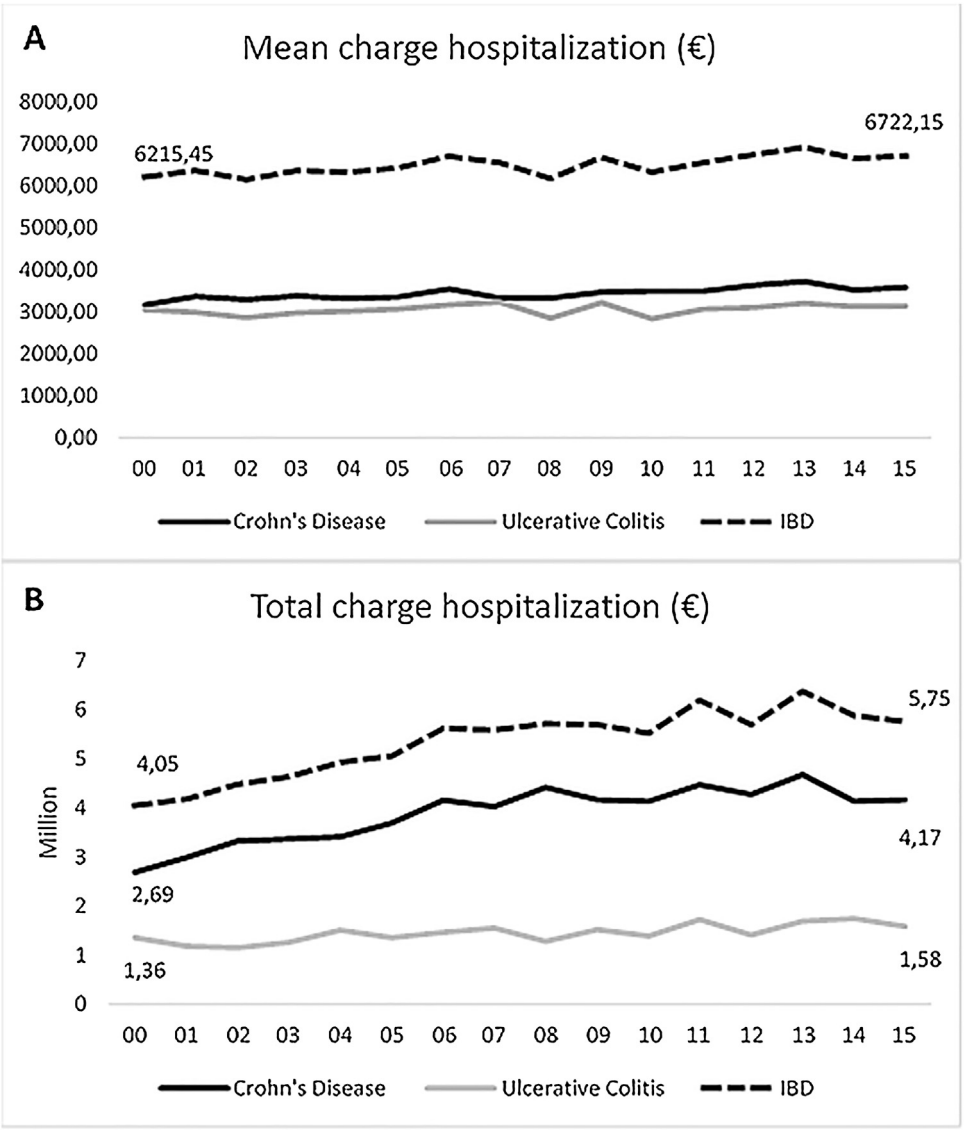

Fig. 4. Hospitalization charges: mean (A) and total (B).

the total annual charges related to medical interventions were higher than those related to surgical intervention: 1.2 million (2000–2015: 0.9–1.4)€ and 0.3 million (2000–2015: 0.2–0.4)€, respectively (Fig. S-2).

In addition, we calculated the delta percentage of the mean charges of UC hospitalizations presenting anemia or malnutrition. Mean charges were higher in patients hospitalized with anemia (by 8% in 2015) or malnutrition (by 10% in 2015) (Fig. S-3) when compared to those without these conditions. It should be noted that in the year of 2001, there were no hospitalizations coded for malnutrition thus the results found in Fig. S-3.

4. Discussion

Our analysis, based on a retrospective approach to a nationwide public hospital discharge database, allowed the clarification of the IBD-associated hospitalization trends in a European country throughout a period of 16 years.

Given the large sample size and considering the purpose of this study (to report observed fluctuations in hospitalization rates and associated charges), P-values are not presented.

Concerning CD patients, hospital discharges were more frequent among young adults (20–39 years old), which corresponds to what is considered to be the age of onset [19]. As for UC, hospitalization rates were higher for patients with more than 20 years of age. This is expected since UC is usually diagnosed at a later stage in life [20].

Interestingly, the absolute numbers of IBD-related hospitalizations and its rate per 100 000 inhabitants or 100 000 overall hospital discharges has increased. Additionally, when compared to the levels of 2000, in 2015 hospitalization rates per 100 000 inhabitants have increased by 33% and 13% regarding CD and UC patients, respectively.

With the introduction of biologic therapy in the year 1999 and biosimilars in 2003, achieving clinical response and remission in moderate-to-severe CD and UC has been effective in a substantial number of patients [21–24]. Hence, one would expect declining hospitalization and surgery rates as both are considered markers of IBD severity [25]. However, data on this matter has been heterogeneous with conflicting reports being published [26–31]

The increases seen in the absolute numbers of hospital discharges and hospitalizations rates may be partially explained by expected increases in prevalence, in addition to the aging of the Portuguese population.

The comparison between the two main IBDs also revealed that the hospitalization rates related with CD were approximately 2-fold higher than those related with UC as pictured in Figs. 1 and 3. This is consistent to what has been reported in other countries, such as Spain, Canada and the US [26–28].

The number of days an IBD patient is hospitalized varies from country to country [13,26,29–32]. Although our data is comparable to what was reported by Bähler et al. [30] in Switzerland (median LOS of 7 days), this study did not differentiate between the two forms of IBD.

The decrease in LOS observed over the 16-year period (CD: 8 days in 2000, 7 days in 2015; UC: 11 days in 2000, 8 days in 2015) may reflect improvements in the approach to IBD, however confirmation studies are required.

Although the paradigm on cost profiles may be shifting from surgery and hospitalizations towards biologic therapy [30,33,34], several studies have shown that hospitalization is one of the leading contributors to direct costs in IBD [11,13,35,36].

When compared with other European countries, national mean charges for IBD fall among countries such as Spain (CD: 4442€ and UC: 3930€), Denmark (mean total cost of 3705€) and the UK (CD: £3416 and UC: £3021) [26,37,38]. Moreover, mean total costs were lower in Norway (888€), Greece (1195€) and Italy (1539€) [37]. The differences in expenditure may be the result of variations in the management of these diseases in terms of diagnostics, medication, and dissimilarities in local pricing.

Mean expenditure for CD and UC hospitalizations revealed stable trends over 16 years (3435€ and 3055€, respectively), although one must not forget that hospitalizations have increased in number in the same period. This is of utter importance since it may be due to the decrease seen in LOS or to a lower consumption of healthcare resources by each patient.

Moreover, conditions such as anemia and malnutrition, seem to have great impact on the course and management of IBD as they relate to an increase in disease activity, higher number of hospitalizations and, consequently, higher healthcare usage [39,40]. Such was observed in our results, as hospitalization of patients with anemia or malnutrition were associated with higher mean charges for both CD and UC (Fig. S-3).

Regarding the comparison between surgical and medical procedures, the overall charges of medical hospitalizations in both CD and UC surmount to higher values than surgery-related ones, which has also been reported by Odes et al. [37]. One reason might be that surgical treatment is considered a therapeutic option for patients affected with severe CD or those with UC non-responsive to medical treatment [11].

In consequence, the evolution of surgical-related hospitalizations goes towards elective surgeries (as depicted in Fig. 3) in lieu of a reactive emergency management of the disease which reflects proactive surveillance as well as an achievement in the care of patients of IBD, in accordance to previous studies [41,42].

5. Limitations and strengths

Our study has a few strengths that should be highlighted: the utilization of an administrative database with national coverage granted the representativeness of the data to a nationwide scale. On the other hand, a few limitations should also be acknowledged: one of them is inherent to the utilization of any database and is related with the possibility of misclassification by inaccurate coding and validation, as well as by occasional underreporting. On this regard, and although this limitation cannot be overlooked, our experience in analyzing this type of data [15,43–45] helps in overcoming its shortcomings. Additionally, one should observe that several studies have validated the suitability of using the ICD-9-CM coding system in the IBD context [46,47]. Unfortunately, and unlike the ICD-10-CM classification, ICD-9-CM does not allow the codification of biological treatment, and therefore we could not possibly consider this factor in our analysis. Furthermore, ICD-9-CM does not classify CD into upper disease thus the lack of patients with said classification in our dataset.

Another limitation is related to the fact that private hospitals were not included in the analysed database, and therefore private hospital discharges were not considered in our study. Moreover, using only the expenditure tables from 2009 with the 3M™ All-Patient DRG version 21, underappreciates any price fluctuations regarding IBD-related charges that may have occurred afterwards. Any DRG changes were also not taken into account.

6. Conclusions

To the best of our knowledge, no recent studies have reported hospitalization rates and respective charges of IBD in Portugal, hence the relevance of the present study.

In summary, hospitalization rate for Crohn's disease has increased within a 16-year period in Portugal, while the hospitalization rate for ulcerative colitis remained stable.

Regarding hospitalization charges, overall estimates appear to mirror the rate patterns for CD and UC. On the other hand, mean charges have remained stable over the years which when compared to the increasing numbers of hospitalizations, lower health care consumption or a decrease in the length of stay might be the cause.

Due to a shift in the epidemiology of IBD, changes in hospitalization rates and cost of care should be monitored to ensure the distribution balance of healthcare resources, so that timely decisions can be made and to, ultimately, raise awareness on the impending burden of the disease.

Guarantor of the article

Fernando Magro

Conflict of interest

Fernando Magro received a fee for presenting from: AbbVie, Ferring, Falk, Hospira, PharmaKern, MSD, Schering, Lab. Vitoria, Vifor, OmPharma. All other authors: nothing to declare.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.dld.2019.01.016.

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