



Human Development Index and Inflammatory Bowel Diseases

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Authors' contributions

This work was carried out in collaboration between all authors. Authors LART and DTC designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors ILA, LRRR, VNC and LFACCS managed the analyses of the study, the literature searches, and participated in the writing of the first draft of the study. Authors AOJ and SDFB managed the revision of the draft. All authors read and approved the final manuscript.

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ABSTRACT

Background: Inflammatory Bowel Disease has a growing incidence, especially in countries with increasing urbanization and increasing exposure to risk factors leading to inflammatory bowel disease. Such morbidity is still marked by the lack of epidemiological studies in the world.

Aims: To determine whether there is a correlation between the Human Development Index and Inflammatory Bowel Diseases in Brazil; and if there are variations between the different states of Brazil.

Methods: The Ecological study on secondary data analysis of Brazilian population diagnosed according to ICD-10 with Crohn's Disease and Ulcerative Colitis, from 2010 to 2014. The Ministry of Health provided data collection. We used mean and standard deviation for quantitative variables with normal distribution, and Pearson Test for the correlation between hospitalization for inflammatory bowel disease, type of hospitalization and Human Development Index for each year studied.

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Results: The correlation between the Human Development Index in Brazil and the total number of hospitalizations for inflammatory bowel diseases each year was shown to be moderate positive ($p < 0.01$). In the descriptive analysis per year, the mean hospitalization and the Human Development Index remained constant, and the standard deviation was relatively high.
Conclusion: There is a correlation between inflammatory bowel disease and Human Development Index in Brazil.

Keywords: Inflammatory bowel disease; epidemiology.

1. INTRODUCTION

Inflammatory bowel disease (IBD) corresponds to a chronic inflammation in the intestine, represented by Crohn's Disease (CD) and Ulcerative Colitis (UC). The pathophysiological mechanisms of IBD have not yet been fully elucidated, but it is known that there is a relationship with an immunological imbalance of the intestinal mucosa, in which adaptive immunity results in injury to the body's own antigens, resulting in chronic inflammation in patients [1].

The frequency of IBD may be related to the development of the countries, measured annually by the United Nations, through the Human Development Index (HDI). The HDI is obtained by the geometric mean of the following normalized indices: Education, health and income per capita [2].

The prevalence of IBD varies, especially in countries with different levels of development. In North America, prevalence ranges from 400 to 600 cases per 100,000 people (0.4–0.6% of the population). In the United States, the prevalence of Crohn's and ulcerative colitis is respectively 201 and 238 per 100,000 inhabitants [3]. In Korea, the incidence is approximately 3 cases per 100,000 person-years, values similar to countries like India, Japan and China [4] that still are in development. In Africa, continent with the lowest HDI, Crohn's prevalence in 2016 was 16.5 per 100,000 population, and Ulcerative Colitis was 7.6 per 100,000 population [5].

In Brazil, a 2009 study in São Paulo including 115 patients found an incidence of 4.48 cases / 100,000 inhabitants of ulcerative colitis and 3.50 cases / 100,000 inhabitants of Crohn's disease [6]. It must be highlighted that there are few epidemiological studies on IBD in underdeveloped and developing countries. Still, a significant increase in the incidence of IBD is observed worldwide, affecting countries previously considered low risk, such as India and other less developed countries [7,8].

Despite presenting little-known pathogenesis, some risk factors are recognized to predispose IBD. One of the main predisposing factors corresponds to the Westernized lifestyle, considering that urban and industrialized areas present a higher prevalence of IBD when compared to less developed areas.

Hence, environmental factors are fundamental in the development of inflammatory bowel diseases [8,9]. Other risk factors include diet rich in saturated fat; smoking; stress; family history; depression; low amounts of vitamin D; age under 30 years; white breed; and medications (such as nonsteroidal anti-inflammatory drugs and isotretinoin) [8,9,10].

The clinical panorama of IBD includes intestinal symptoms such as diarrhea, constipation, rectal bleeding, fecal urgency, tenesmus, abdominal pain, nausea and vomiting; And extra-intestinal symptoms such as arthropathy, pyoderma gangrenosum, erythema nodosum, uveitis, among others. Adequate management is essential to avoid possible complications, which are more common in children and include hemorrhagic ulcer, intestinal perforation, and intra-abdominal abscess, among others [7,11]. Symptomatology may also be due to the treatment of the disease, such as the use of corticosteroids, which favors arthropathy, glaucoma, cataract and other clinical manifestations of the patient with pelvic inflammatory disease [7].

Thus, studies show a growing incidence of IBD, especially in countries that have an increasing urbanization and, consequently, increasing exposure to risk factors leading to IBD, such as in Brazil [12]. Still, there are few epidemiological studies on inflammatory bowel disease in the Brazilian literature [6], and the patients with this disease present great symptomatology and frequency of complications [7,11]. There is no record of any study that seeks to correlate IBD with human development indicators, in Brazil or the world today.

Also, it is known that Brazil is a country with great socio-economic inequalities among its regions [13]. Although inflammatory bowel disease is more common in countries with a high degree of development, it is not known whether there is a difference between the incidences of the disease in different regions of the same country. Therefore, this study aims to correlate the IBD in Brazil with the Human Development Index (HDI) and determine if there are variations between the different states of Brazil.

2. MATERIALS AND METHODS

This is an ecological study based on the Brazilian population, admitted in the public hospitals, accredited by the Brazilian National Health System (SUS), diagnosed with Intestinal Bowel Disease (Crohn's Disease or Ulcerative Colitis) classified according to the International Classification of Diseases (ICD-10) of: Crohn's disease (K-50) and Ulcerative Colitis (K-51).

The territory of the research covers the Federative Units of Brazil. The chosen period of the analysis was between January 1, 2010 and December 31, 2014. The reliability of these data is due to the fact that from the 70's Brazilian censuses became more organized and complete; and the legitimacy of these data is becoming more and more consolidated because they are updated every year, adapting to the country's circumstances. In addition, the federative units have a legal obligation to provide the data to compose the census [14]. The data available from January 2015 to March 2016 were not used in this analysis since they were subject to rectification, according to the Ministry of Health, by the Hospital Information System of SUS (SIH / SUS) at the time of the structuring and analysis of the study.

Considering the prevalence of the disease, all inpatients admitted in public or private hospitals accredited to the SUS and diagnosed with Crohn's Disease or Ulcerative Colitis, regardless of length of stay, severity, and / or evolution were included in the study.

The study variables were: year (2010 to 2014); the Brazilian Federation Units (Rondonia – RO; Acre – AC; Amazonia – AM; Roraima - RR; Amapa – AP; Tocantins – TO; Maranhao – MA; Piaui – PI; Ceara – CE; Rio Grande do Norte – RN; Paraíba – PB; Pernambuco – PE; Alagoas – AL; Sergipe – SE; Bahia - BA; Minas Gerais – MG; Espírito Santo – ES; Rio de Janeiro – RJ;

Sao Paulo – SP; Parana – PR; Santa Catarina – SC; Rio Grande do Sul – RS; Mato Grosso do Sul – MS; Mato Grosso – MT; Goias – GO; Distrito Federal – DF); character of service (elective and urgent); and Human Development Index (HDI) for each Federal Unit according to the Brazilian Institute of Geography and Statistics (IBGE).

The information source used was the Hospital Information System of SUS (SIH / SUS), which presents data that has been digitized since 1984. The instrument of data collection provided by the Ministry of Health was: the Hospital Inpatient Authorization (AIH). The provider's database sends the information to the Department of Information Technology of SUS (DATASUS) available by the website www.datasus.gov.br. The SIH / SUS also provides the number of hospitalizations that occurred in each Unit of the Federation and the nature of attendance if the surgical treatment was required (urgency or elective).

For the statistical analysis, we made descriptive analysis of the HDI and the prevalence of IBD by State of the Federation. Data was assumed normal considering the Central Limit Theorem [15]. Quantitative data was analyzed by the mean and standard deviation.

Also, the Central Limit Theorem was used to validate the use of Pearson Correlation, verifying the association between the Brazilian HDI (mean of the federative units HDI) and the annual prevalence of IBD from 2010 to 2014.

Data analysis was performed in statistical software Stata version 11.0.

3. RESULTS

In the descriptive analysis per year, the average hospitalization and the HDI of all states of the federation remained practically constant. In 2010, Brazil's average HDI was 0.70 and in 2014, 0.74, growing 0.1 per year in this period. The mean incidence of Inflammatory Bowel Disease declined in the period, ranging from 155 in 2010 to 144.8 in 2014. However, the standard deviation remained relatively high (ranging from 207.46 to 224.76) (Table 1).

The correlation between the HDI and the total number of hospitalizations for inflammatory bowel diseases in each year was shown to be moderate positive, with a significant p ($P < 0.01$). From 2010 to 2014, the Pearson coefficient (r)

was, respectively, $r = 0.523$ ($p = 0.05$); $R = 0.534$ ($p = 0.004$); $R = 0.476$ ($p = 0.011$); $R = 0.467$ ($p = 0.014$) and $r = 0.479$ ($p = 0.011$) (Fig. 1).

The total prevalence of hospitalization for IBD (both Crohn's and Ulcerative Colitis) between 2010 and 2014, inclusive, varied in accordance with the Federative Units of Brazil. In AL, region with the lowest HDI (0.646), had 65 cases in total adding all the cases in the 5 years mentioned. The lowest cumulative prevalence, though, was from RR (HDI= 0.723, therefore, the 16th lowest HDI, from the 27 units), with 22 cases. The highest prevalence of IBD was in SP, the 26th highest HDI of Brazil (HDI = 0.805), with 5405 cases (Chart 1).

4. DISCUSSION

Inflammatory bowel diseases, including Ulcerative Colitis and Crohn's Disease, are chronic inflammatory disorders of the gastrointestinal tract that start most commonly in adolescence and young adulthood [16].

Traditionally, Ulcerative Colitis and Crohn's disease are more prevalent in developed countries, in regions such as Northern Europe, United States and Canada, which have the higher rates of Human Development Index. However, in recent years, the incidence of IBD has been increasing in developing countries, including Brazil. Still, as evidenced by this study, even in Brazil the IBD are more prevalent in regions where the HDI is higher, thus following the same global logic in a national proportion.

It is possible to associate a higher prevalence of IBD in areas of more advanced HDI due to the

elevated rate of diagnosis of the disease. Considering the absence of curative treatment, most patients need lifelong treatment and many will undergo surgery at some point. As a result, IBD is associated with a high economic burden for society, where hospitalization and surgery account for more than half of health costs [17].

Although the reasons for such increase in Developing Countries have not been convincingly described, the process of industrialization and pollution seems to have some influence in the incidence, since environmental factors have already been shown to be important risk factors for inflammatory bowel diseases. Along with the environmental factors, it is important to highlight the role of the genetic predisposition. It is proven that there is a higher prevalence of IBD in Caucasians and Ashkenazic Jews [18].

The Inflammatory Bowel Disease still does not have its pathophysiological mechanisms clarified, however it has been shown to be closely related to environmental modifiable factors that may aggravate or reduce the inflammatory process of the intestinal mucosa, such as tobacco, diet, vitamins, stress, sleep, drugs, surgical procedures and obesity [19]. People in developed countries usually have a larger use of industrialized foods, which leads to significant increase in incidence and prevalence of IBD, and higher morbidity in patients already diagnosed with Colitis and Crohn's Disease. In addition, the ingestion of fresh, high-fiber foods, is related to the reduction of the inflammatory bowel process. In underdeveloped countries, the supply is higher of fiber-rich and lower-industrialized foods, which can explain the lower incidence [13].

Table 1. Sample description

Year	Variable	Mean	Standard deviation	Min	Max
2010	HDI	0,70	0,05	0,63	0,82
	IBD	155,00	224,76	5,00	1.105
2011	HDI	0,71	0,05	0,63	0,82
	IBD	145,71	219,08	4,0	1.123
2012	HDI	0,72	0,04	0,64	0,83
	IBD	145,70	207,46	1,00	1.043
2013	HDI	0,73	0,04	0,65	0,83
	IBD	150,82	213,19	5,0	1.073
2014	HDI	0,74	0,04	0,67	0,84
	IBD	144,8	210,50	2,00	1.061

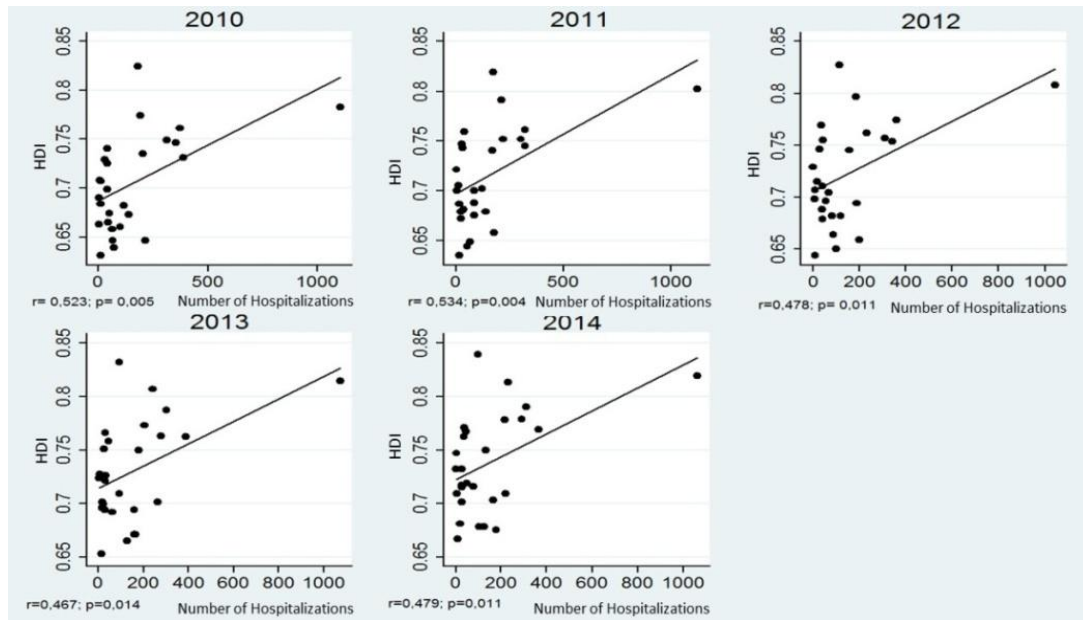


Fig. 1. Correlation between hospitalization for inflammatory bowel disease and HDI for each year studied

Stress is another very prevalent risk factor in developed and developing countries whose populations are increasingly busy with services that require them to perform repetitive functions, high professional billing and for long periods of time [13].

Though the incidence of IBD is increasing in the world, it is believed that its numbers are still underestimated due to the lack of epidemiological studies in underdeveloped and developing countries. A study in China by Li et al showed that the incidence of IBD in the country increased, although it is statistically smaller when compared to developed countries, due to its large population. This change of the epidemiology of IBD is attributed to the intense and rapid urbanization process experienced by the country in recent years, exposing the population to previously unprecedented risk factors [20].

Even though there are currently well-established guidelines for diagnosis and treatment of IBD, it is not commonly studied from an epidemiological point of view, justifying this study, which aims to demonstrate an association between human development index and prevalence of Ulcerative Colitis and Crohn's disease.

There are articles that show the incidence and prevalence of UC and CD, yet these studies are

only descriptive and do not correlate the HDI with inflammatory bowel diseases. In a study carried out in Piauí, which has one of the lowest Socioeconomic Indicators in Brazil, it has been found that IBD is still a rare disease in relation to more developed countries [21].

The present study demonstrated that there is a positive correlation between HDI and number of hospitalizations for IBD. The correlation found was moderate, since DATASUS only provides hospitalization data for IBD, not the actual prevalence of the disease, considering that not all patients are hospitalized during the course of the disease. To determine the total correlation between HDI and incidence of IBD, it would be essential to seek the actual number of patients who take high-cost drugs from the SUS. Unfortunately, the treatment of this disease is not highly specific, being common to other diseases. It consists basically of symptomatic drugs, corticosteroids, enteral nutrition therapy, immunomodulators, TNF-alpha, and aminosalicylates. Therefore, it hampers finding the real incidence of these diseases [16]. Also, this study only considered the relationship between HDI and BDI, not discriminating other confounders that may impact in the frequency of CD and UR such as lifestyle and diet.

Van Der Valk [17] found that of the patients with Crohn's disease, 23% were on anti-TNFα

Chart 1. Prevalence of hospitalization by IBD in the federative units, and mean HDI from 2010 to 2014

Federative unit abbreviation	Total prevalence of hospitalization for IBD (2010 to 2014)	Mean of HDI (2010-2014)
AL	65	0.646
MA	471	0.656
PI	498	0.661
PA	933	0.662
PB	270	0.682
SE	153	0.682
BA	629	0.683
AM	147	0.687
PE	952	0.691
AC	224	0.692
RO	74	0.697
CE	442	0.702
RN	107	0.709
TO	266	0.713
AP	36	0.718
RR	22	0.723
MS	155	0.742
GO	845	0.744
MT	212	0.750
MG	1807	0.752
RS	1537	0.759
ES	190	0.761
RJ	1250	0.765
PR	1608	0.772
SC	1067	0.796
SP	5405	0.805
DF	665	0.828

therapy, accounting for 64% of health costs. Hospitalization and surgery accounted for 19% and less than 1% of health costs, respectively. In ulcerative colitis, mesalazine and anti-TNF α therapy accounted for more than half of health costs (54%). Until the 2000s, hospitalization and surgery were the major cost drivers in IBD. Thus, today, the use of drugs, anti-TNF α in particular, is the main source of health costs, while costs related to hospitalization and surgery are substantially reduced compared to previous studies.

Surgery is an important therapeutic option in the management of ulcerative colitis and Crohn's disease in children. Total colectomy with anal anastomosis of the ileal pouch is indicated in children with ulcerative colitis refractory to clinical therapy. In this procedure, the diseased colon is removed and a pouch reservoir is constructed from the distal ileum and anastomosed into a short cuff of the remaining rectum to preserve

continuity and prevent a permanent ileostomy. Children have excellent long-term outcomes after this procedure, with a quality of life similar to that of the general population. Because of the transmural nature of inflammation in Crohn's disease, complications such as fistulas, abscesses, and intestinal stenosis that require surgery may arise. Surgery may also be indicated when the disease is refractory to medical therapy [16].

5. CONCLUSION

There is a positive and moderate correlation between IBD and HDI in Brazil. IBD frequency is usually higher in developed countries. However, it has been increasing in the developing ones. The rise of HDI - which measures income, health and education - leads to the expansion of IBD's diagnosis and exposition to risk factors (industrialization and habits).

CONSENT

It is not applicable.

ETHICAL APPROVAL

This is an analysis of secondary data of DATASUS, not requiring the consideration of the ethics committee due to the resolution of the National Health Council 510/2016, article 1, sole paragraph.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. De Mattos BRR, Garcia MPG, Nogueira JB, et al. Inflammatory bowel disease: An overview of immune mechanisms and biological treatments. *Mediators of Inflammation*. 2015;2015:493012. DOI: 10.1155/2015/493012
2. United Nations Development Programme. Human Development Index (HDI). Available:<http://hdr.undp.org/en/content/human-development-index-hdi> (Accessed in 09th April of 2017)
3. Centers for Disease Control and Prevention. Inflammatory bowel disease (IBD). Available:www.cdc.gov/ibd/data-statistics.htm (Accessed in 10th December of 2017)
4. Loftus, Edward V. Update on the incidence and prevalence of inflammatory bowel disease in the United States. *Gastroenterology & Hepatology*. 2016; 12(11):704–707.
5. Molodecky, Natalie A, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology*. 2012;142(1):46-54.
6. Victoria CR, Sassak LY, Nunes HR de C. Incidence and prevalence rates of inflammatory bowel diseases, in Midwestern Part of Sao Paulo State, Brazil. *Arq Gastroenterol*. 2009;46:20–5.
7. Bernstein CN, Eliakim A, Fedail S. World Gastroenterology Organisation global guidelines inflammatory bowel disease: Update August 2015. *J Clin Gastroenterol*. 2016;50(10):803-818.
8. Ashwin N. Ananthakrishnan. Epidemiology and risk factors for IBD. *Nature Reviews Gastroenterology & Hepatology*. 2015;12: 205–217.
9. Ye Y, Pang Z, Chen W, Ju S, Zhou C. The epidemiology and risk factors of inflammatory bowel disease. *International Journal of Clinical and Experimental Medicine*. 2015;8(12):22529-22542.
10. Peppercorn MA, et al. Definition, epidemiology, and risk factors in inflammatory bowel disease. Available:<http://www.uptodate.com/home> (Accessed June 16, 2014)
11. Hendrickson BA, Gokhale R, Cho JH. Clinical aspects and pathophysiology of inflammatory bowel disease. *Clinical Microbiology Reviews*. 2002;15(1):79-94. DOI: 10.1128/CMR.15.1.79-94.2002
12. Cyrla Zaltman. Doença inflamatória intestinal: Qual a relevância da doença no Brasil? *Cad. Saúde Pública*, Rio de Janeiro. 2007;23(5):992-993.
13. Neri M, Soares W. Desigualdade social e saúde no Brasil. *Cad. Saúde Pública*, Rio de Janeiro. 2002;18(Suplemento):77-87.
14. Oliveira LAP, Simões CCS. O IBGE e as pesquisas populacionais. *R. Bras. Est. Pop.* 2005;22(2):291-302.
15. Hazra A, Gogtay N. Biostatistics series module 1: Basics of biostatistics. *Indian Journal of Dermatology*. 2016; 61(1):10-20. DOI: 10.4103/0019-5154.173988
16. Rosen, Michael J, Ashish Dhawan, Shehzad A. Saeed. Inflammatory bowel disease in children and adolescents. *JAMA Pediatrics*. 2015;169(11):1053–1060. (PMC. Web. 4 July 2017)
17. Van Der Valk, Mirthe Emilie, et al. Healthcare costs of inflammatory bowel disease have shifted from hospitalisation and surgery towards anti-TNF α therapy: Results from the COIN study. *Gut*, p. [gutjnl-2012-303376](https://doi.org/10.1136/gutjnl-2012-303376); 2012.
18. Hanauer SB. Inflammatory bowel disease: Epidemiology, pathogenesis, and therapeutic opportunities. *Inflamm Bowel Dis*. 2006;12(1):S3-9. DOI:10.1097/01.MIB.0000195385.19268.68
19. Burke Kristin E, Boumitri Christine, Ananthakrishnan Ashwin N. Modifiable environmental factors in inflammatory bowel disease. *Current Gastroenterology Reports*. 2017;5(19):1-12.
20. Xue LI, et al. The disease burden and clinical characteristics of inflammatory

- bowel disease in the Chinese population: A systematic review and meta-analysis. International Journal of Environmental Research and Public Health. 2017;14(3): 238.
21. Parente José Miguel Luz, et al. Inflammatory bowel disease in an underdeveloped region of Northeastern Brazil. World Journal of Gastroenterology: WJG. 2015;21(4):1197–1206.

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