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Effectiveness and Safety of Biologic Therapy in Hispanic Vs Non-Hispanic Patients With Inflammatory Bowel Diseases: A CA-IBD Cohort Study

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Unplanned healthcare utilization and safety of biologic therapy in Hispanic vs. non-Hispanic patients with IBD: A CA-IBD Cohort Study

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Abstract

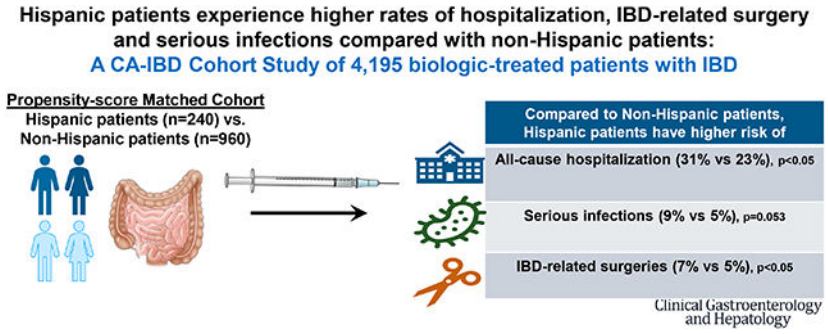
BACKGROUND: There is limited data on outcomes of biologic therapy in Hispanic patients with inflammatory bowel diseases (IBD). We compared risk of hospitalization, surgery and serious infections in Hispanic vs. non-Hispanic patients with IBD in a multi-center, electronic health record (EHR)-based cohort of biologic-treated patients.

METHODS: We identified adult patients with IBD who were new-users of biologic agents (TNFα antagonists, ustekinumab, vedolizumab) from five academic institutions in California between 2010-17. We compared the risk of all-cause hospitalization, IBD-related surgery, and serious infections in Hispanic vs. non-Hispanic patients using 1:4 propensity score matching and survival analysis.

RESULTS: We compared 240 Hispanic patients (53% male, 45% with ulcerative colitis [UC]; 73% TNFα antagonist-treated; 20% with prior biologic exposure) with 960 non-Hispanic patients (51 % male, 44% with UC; 67% TNFα antagonist-treated; 27% with prior biologic exposure). After propensity score matching, Hispanic patients were younger (37±15 vs. 40±16, p=0.02) and higher burden of comorbidities (Elixhauser index >0, 37% vs. 26%, p<0.01), without any differences in patterns of medication use, burden of inflammation and hospitalizations. Within 1y of biologic initiation, Hispanic patients had higher rates of hospitalizations (31% vs 23%; adjusted HR, 1.32 [95% CI, 1.01-1.74]) and IBD-related surgery (7.1% vs 4.6%; aHR, 2.00 [1.07-3.72]), with a trend towards higher risk of serious infections (8.8% vs 4.9%; aHR, 1.74 [0.99-3.05]).

CONCLUSION: In a multicenter, propensity score-matched cohort of biologic-treated patients with IBD, Hispanic patients experienced higher rates of hospitalization, surgery, and serious infections. Future studies are needed to investigate the biological, social, and environmental drivers of these differences.

Graphical Abstract



Keywords

Ethnic minorities; disparities; social determinants of health; Crohn’s disease; immunosuppressives

The incidence and prevalence of inflammatory bowel diseases (IBD) in Hispanic adults is rising rapidly.[1] Currently, 1.2% Hispanic adults in the United States (US) report having IBD,

and this number is expected to increase progressively over the next few years with global immigration patterns and changing demographics of the US.[2] There is significant paucity of evidence on comparative effectiveness and safety of biologic therapy in Hispanic patients, who represent <5% participants in clinical trials of biologic therapies.[3]

Prior studies have identified lower rates of utilization of biologics and immunomodulators (IMM) in Hispanic patients, despite no differences in disease phenotype and behavior between Hispanic and non-Hispanic Caucasians.[4-8] Studies in hospitalized patients with IBD suggest higher rates of inpatient mortality and healthcare costs in Hispanic patient. However, there are limited studies specifically comparing the effectiveness and safety of biologics in Hispanic patients with IBD. Understanding the impact of ethnicity on treatment outcomes and healthcare utilization is critical for improving IBD management in Hispanic patients.

Hence, to evaluate the impact of ethnicity on treatment outcomes and healthcare utilization in Hispanic patients, we compared the risk of all-cause hospitalization, IBD-related surgery, and serious infections in biologic-treated Hispanic vs. non-Hispanic patients with IBD, using 1:4 propensity score matching and Cox proportional hazard analysis in a large, multi-center, electronic health record (EHR)-based cohort.

METHODS

Data Source

Using the PCORnet Common Data Model, we created a multi-center EHR-based cohort of patients with IBD from five academic health systems in California (UC San Diego, UC Los Angeles, UC Irvine, UC San Francisco, and Cedars-Sinai Medical Center); these included safety net hospitals. This privacy, data-preserving infrastructure was based on pSCANNER (patient-centered SCAlable National Network for Effectiveness Research), one of 13 clinical data research networks funded by Patient Centered Outcomes Research Institute (PCORI).[9, 10] pSCANNER is a distributed clinical data network that utilizes a distributed, service-oriented architecture to integrate data from existing networks and designed to improve the capacity to conduct comparative effectiveness research using real-world data. To improve semantic interoperability and facilitate data harmonization, all data have already been transformed into the validated PCORnet common data model (version 3.1), which includes demographics, diagnosis and procedure codes, medications, laboratory data and vital parameters.

We used a set of strict inclusion criteria to identify patients with IBD from EHRs: (A) two disease diagnostic codes (Crohn's disease [CD]: ICD-9 555.x or ICD-10 K50; ulcerative colitis [UC]: ICD-9 556.x or ICD-10 K51; one of these codes may have come from the 'Problem List' field in the EHR) from an ambulatory visit encounter, (B) one disease diagnostic code from an inpatient hospitalization, or (C) one disease diagnostic code from an ambulatory visit encounter, along with a prescription for an IBD-related medication (mesalamine/sulfasalazine, azathioprine/6-mercaptopurine, methotrexate, infliximab, adalimumab, certolizumab pegol, golimumab, vedolizumab or ustekinumab). These validated criteria have been shown to have >80% sensitivity and >90% specificity, with a positive predictive value of >90%.[11, 12]

Study Population

Only adult patients (≥18 years) who were newly prescribed biologic agents (tumor necrosis factor [TNF]α antagonists, vedolizumab, and/or ustekinumab), without prior prescription for the same class of medication in the preceding 12 months, between January 1, 2010 to June 30, 2017, and had at least 1 year follow-up within the health system were included in our analysis. At initiation of biologic, patients were presumed to be adherent to their biologic continuously for 1 year, unless a prescription for a new biologic agent was identified in the EHR. Data on prescription refill claims was not available. On specifically examining frequency of infusions for infliximab and vedolizumab in the cohort, we confirmed high rate of adherence. Of 851 patients who received at least one infusion, 704 (83%) received a second infusion within 4 months; the median interval until second infusion was 15 days. Over the course of 1 year, patients who received at least one infliximab infusion, received a median 8 infusions. Similarly, of 274 patients who received at least one infusion of vedolizumab, 213 (78%) received a second infusion within 4 months; median interval until second infusion was 14 days. Over the course of 1 year, patients who received at least one vedolizumab infusion, received a median 5 infusions.

Exposure and Comparator

Primary exposure was being of Hispanic ethnicity, and comparator was non-Hispanic ethnicity. Data on ethnicity was based on self-reporting by the patient and recorded in the EHR. Ethnicity was missing for 46/4195 (1.1%) patients in our cohort.

Outcomes

The primary outcomes of interest were risk of: 1) all-cause hospitalization, 2) IBD-related surgery (based on common procedural terminology [CPT] codes), and 3) serious infections (defined as infections requiring hospitalization, based on ICD-9 or ICD-10 codes for discharge diagnosis of infections of the respiratory tract, skin and soft tissue, genitourinary tract, gastrointestinal tract, central nervous system, and septicemia/sepsis), within 1 year of biologic initiation.[13, 14]

Covariates

We collected baseline covariates (at time of biologic start or in the preceding 12 months) including demographic characteristics (age at time of biologic initiation, sex, race, ethnicity); disease and treatment characteristics including IBD phenotype (CD or UC), prior biologic prescription (12-month baseline period), prior and/or concomitant prescription for immunomodulators (including azathioprine, 6-mercaptopurine, or methotrexate), corticosteroids and opiates; elevated C-reactive protein [CRP] (>5mg/L) and low albumin (<3.5g/dl) at time of biologic initiation, and patterns of healthcare utilization in the preceding 12 months including comorbidity burden measured by Elixhauser index for EHRs, abdominal surgery, hospitalization and serious infection. We did not have access to patients' unstructured clinic notes and endoscopy reports.[15]

Statistical analysis

We used descriptive statistics to compare baseline demographic, disease and treatment characteristics between Hispanic and non-Hispanic patients. Categorial variables were expressed as percentages and continuous variables as means with standard deviation. We used chi-square test and student *t*-test for parametric categorical and continuous variables, respectively. For non-parametric categorical and continuous variables, we used Fisher's exact test and ANOVA, respectively.

To study the effect of ethnicity and risk of all-cause hospitalization, IBD-related surgery, and serious infection, we performed 1:4 propensity score matching, without replacement to adjust for differences in baseline covariates. The propensity score model included demographic variables (age, sex, race, institution, body mass index), disease characteristics (phenotype, abnormal baseline albumin and/or CRP, prior abdominal surgery, prior hospitalization and prior serious infection), treatment characteristics (current and prior biologic exposure, concomitant medication exposure including IMM, corticosteroids, and opioids) and comorbidity burden and healthcare utilization (abdominal imaging and/or endoscopy). We performed a paired t-test for continuous variables, a McNemar test for dichotomous variables, and a Bowker's test for categorical variables with more than two levels; then, we measured the standardized difference of each covariate in the propensity score model, and variables were considered to be different across treatment if after propensity score matching the standardized difference was greater than 10%. In order to correct for any remaining imbalance after propensity score analysis was performed, we included remaining covariates that were shown to be different across treatment groups into the final multivariate Cox proportional hazard models for assessment of the outcomes of interest.

We performed secondary analysis using the overall cohort prior to applying propensity score matching. To evaluate the association between ethnicity and risk of all-cause hospitalization, IBD-related surgery, and serious infection, we performed a Cox proportional hazard analysis adjusting for age, sex, ethnicity, IBD phenotype, Elixhauser index (≥2 vs. <2), abnormal baseline albumin and/or CRP, current and prior biologic exposure, concomitant medication exposure (immunomodulator, steroid, and opioids), prior abdominal surgery, prior hospitalization and prior serious infection. Stratified analysis to examine the effect of ethnicity in specific subgroups of patients was performed, based on IBD phenotype (patients with CD or UC) and biologic exposure type (patients treated with TNFα antagonists, vedolizumab, or ustekinumab).

All hypothesis testing was performed with a two-sided *p*-value with a statistical significance threshold <0.05. All statistical analyses were performed using R version 3.5.3 (Vienna, Austria).

RESULTS

Patient characteristics

Our cohort of biologic-treated patients included 4,195 patients with IBD, of whom 6.6% (n=278) were Hispanic (eTable 1). Prior to propensity score matching, Hispanic patients

were significantly younger, were more likely to be overweight and obese, more likely to have UC, had higher comorbidity burden, were more likely to have elevated CRP and low albumin, were more likely to be on concomitant IMM and opiates at time of biologic initiation, and were more likely to be hospitalized in the baseline 1 year prior to biologic initiation. After 1:4 propensity score matching, we included 240 Hispanic patients matched with 960 non-Hispanic patients for our primary analysis. Baseline characteristics in this matched cohort was more balanced (Table 1). In the propensity score-matched cohort, Hispanic patients were significantly younger (37±15y vs. 40±16y, p=0.02), had a higher burden of comorbidities (Elixhauser index >0, 37% vs. 26%, p<0.01), were less likely to have prior biologic exposure (20% vs. 26%, p=0.04) and corticosteroid exposure in preceding 1y (25% vs. 32%, p=0.04) with no significant differences in IBD subtype, burden of inflammation, prior hospitalization and IBD-related surgery and current biologic exposure, and concomitant exposure to IMM, corticosteroids and opiates. Standardized mean differences before and after matching, and propensity score distribution is shown in eFigures 1 and 2.

All-cause hospitalization

In the propensity score-matched cohort, within 1 year after biologic initiation, 30.8% Hispanic patients vs. 22.8% non-Hispanic patients (p=0.01) were hospitalized (Figure 1). After additionally adjusting for age, comorbidity burden, prior exposure to biologics and prior use of corticosteroids (variables unbalanced after propensity score matching), Hispanic patients were 32% more likely to be hospitalized than non-Hispanic patients (adjusted hazard ratio [aHR], 1.32; 95% confidence interval [CI], 1.01-1.74). No time trends in magnitude of this association was observed (eTable 2).

Similar results were observed in the full cohort (eFigure 3A), in patients with CD (eFigure 3B) and UC (eFigure 3C). In specifically examining outcomes with different biologic agents, Hispanic patients treated with TNFα antagonists had higher risk of hospitalization compared with non-Hispanics (32% vs. 21%, p<0.01), but not vedolizumab- (30% vs. 27%, p=0.88) and ustekinumab-treated patients (29% vs. 28%, p=1.00). On Cox proportional hazard analysis, after adjusting for demographic-, disease- and treatment-related characteristics and healthcare utilization, Hispanic patients were more likely to be hospitalized compared with non-Hispanic patients (aHR, 1.33; 95% CI, 1.05–1.70) (Table 2). Besides Hispanic ethnicity, higher burden of comorbidities (Elixhauser index ≥2) (aHR, 1.45; 95% CI, 1.23-1.70), prior hospitalization in the baseline 12m (aHR, 1.40; 95% CI, 1.18-1.65), and concomitant use of opiates (aHR, 3.37; 95% CI, 2.89-3.92) and corticosteroids (aHR, 1.43; 95% CI, 1.23-1.67) was associated with increased risk of hospitalization.

IBD-related surgery

In the propensity score-matched cohort, within 1 year after biologic initiation, 7.1% Hispanic patients vs. 4.6% non-Hispanic patients (p=0.16) underwent IBD-related surgery (Figure 1). After additionally adjusting for variables unbalanced after propensity score matching, Hispanic patients were two times more likely to undergo IBD-related surgery than

non-Hispanic patients (aHR, 2.00; 95% CI, 1.07-3.72). No time trends in magnitude of this association was observed (eTable 2).

In the full cohort, Hispanic patients were more likely to undergo surgery (7.6% vs. 3.3%, p<0.01) (eFigure 4A), with similar results observed in patients with CD (eFigure 4B) and UC (eFigure 4C). Hispanic patients treated with TNFα antagonists (7.3% vs. 3.0%, p<0.01) and vedolizumab (13.5% vs. 2.6%, p<0.01) had higher risk of IBD-related surgery compared with non-Hispanics, but not ustekinumab-treated patients (2.9% vs. 5.5%, p=0.77). On Cox proportional hazard analysis, after adjusting for demographic-, disease- and treatment-related characteristics and healthcare utilization, Hispanic patients were 71% more likely to undergo IBD-related surgery compared with non-Hispanic patients (aHR, 1.71; 95% CI, 1.01–1.92) (Table 2). Besides Hispanic ethnicity, elevated CRP at baseline (aHR, 2.83; 95% CI, 1.66-4.85), prior IBD-related surgery (aHR, 1.92; 95% CI, 1.01-3.64), prior biologic exposure (aHR, 1.77; 95% CI, 1.08-2.72) and concomitant use of opiates (aHR, 3.45; 95% CI, 2.25-5.29) was associated with increased risk of IBD-related surgery.

Serious infection

In the propensity score-matched cohort, within 1 year after biologic initiation, 8.8% Hispanic patients vs. 4.9% non-Hispanic patients (p=0.03) experienced serious infection (Figure 1). After additionally adjusting for variables unbalanced after propensity score matching, there was a trend towards higher risk of serious infections in Hispanic patients (aHR, 1.74; 95% CI, 0.99-3.05, p=0.053). No time trends in magnitude of this association was observed (eTable 2).

In the full cohort, Hispanic patients were more likely to experience serious infection within 1y of biologic initiation (eFigure 5A), with similar results observed in patients with UC (eFigure 5C) but not CD (eFigure 5B). No specific differences were observed in risk of serious infections was observed in Hispanic patients vs. non-Hispanics, by biologic type. On Cox proportional hazard analysis, after adjusting for demographic-, disease- and treatment-related characteristics and healthcare utilization, no significant increase in risk of serious infections was observed in Hispanic patients (aHR, 1.36; 95% CI, 0.86-2.16) (Table 2). Low albumin at baseline (aHR, 1.97; 95% CI, 1.12-3.45), prior serious infection (aHR, 2.68; 95% CI, 1.91-3.75), and concomitant use of opiates (aHR, 1.90; 95% CI, 1.40-2.58) was associated with increased risk of serious infections, whereas current use of ustekinumab (vs. TNFα antagonists) (aHR, 0.38; 95% CI, 0.21-0.69) and prior failure of biologics (aHR, 0.62; 95% CI, 0.40-0.98) was associated with lower risk of serious infection.

DISCUSSION

Using a large, multi-center EHR-based cohort study of over 4,000 patients with IBD starting new biologic therapy, we observed that Hispanic patients were more likely to have higher rates of unplanned healthcare utilization and IBD-related surgery, along with a trend towards higher risk of serious infections after adjusting for important confounding factors through propensity score matching. To the best of our knowledge, our study is the one of the largest to evaluate treatment outcomes and patterns of healthcare utilization in Hispanic patients with IBD treated with biologic therapies.

Prior studies have focused primarily on the epidemiology, natural history and treatment patterns in racio-ethnic minorities. In a systematic review of 193 studies, of which 27 were conducted in Hispanics (5 from North America), Shi and colleagues observed that Hispanic patients may have a slightly higher prevalence of ileum-dominant disease compared with non-Hispanic Caucasians and African-American patients, without any significant differences in disease behavior.[8] In patients with UC, Hispanic patients were more likely to have left-sided or extensive colitis. In contrast, in a review of 7 studies comparing disease phenotype in Hispanic Americans vs. non-Hispanic Caucasian Americans, Avalos and colleagues did not observe significant differences in disease phenotype and behavior.[5] In examining treatment patterns and outcomes, Shi and colleagues observed no significant differences in cumulative use of corticosteroids, immunomodulators and biologics in Hispanic vs. non-Hispanic Caucasians in CD or UC, but observed that Hispanic patients had significantly higher rates of surgery.

However, these studies have not specifically examined the impact of biologics in the Hispanic population.[4-8] Hispanic patients have been under-represented in clinical trials of biologic agents in IBD, and hence, there is limited data on effectiveness and safety of these agents in Hispanics. In our real-world study of new users of biologic agents, we observed that Hispanic patients have higher risk of hospitalization and IBD-related surgery after starting biologic agents, along with a trend towards higher risk of serious infections. These findings were observed in a propensity score-matched cohort, after accounting for differences in demographic, clinical and treatment-related factors, including inflammatory burden and prior medication exposure. In a contemporary cohort study of 5,987 biologic-treated patients with IBD using an administrative claims database, we have observed that Hispanic ethnicity was associated with 54% higher risk of serious infections, compared with non-Hispanic Caucasians, suggesting potential differences in treatment safety. Overall, these findings suggest that biologic agents may not be as effective or safe in Hispanic patients as they are in non-Hispanic Caucasians. These differences may be driven by biological or socio-economic differences in Hispanic and non-Hispanics. Lower effectiveness of biologic agents may be driven by unmeasured factors such as differences in disease duration due to potential delays in biologic initiation in Hispanic patients, endoscopic severity, etc. Though we observed higher risk of hospitalization and surgery in Hispanics treated with TNFα antagonists but not in ustekinumab-treated patients, this should be interpreted with caution due to small number of Hispanic patients treated with non-TNF biologics. Genetic determinants may also impact effectiveness of specific biologic agents, though this has not been well-studied in Hispanic patients. Studies in Hispanics from South Florida and Puerto Rico suggest a genetic risk score for IBD (based on NOD2 and IL23R) comparable to Europeans.[16, 17] Besides biological factors, socio-economic factors related to costs and access to care which contribute delayed initiation of biologics, and/or limited post-initiation monitoring leading to higher rates of unplanned healthcare utilization. In the National Health Interview Survey, we previously observed that patients with IBD report high prevalence of negative social determinants of health with one in four patients report financial hardship due to medical bills, one in six report cost-related medication non-adherence, one in seven report food insecurity and over 50% report inadequate social support.[18, 19] In this study, Hispanic patients with IBD had a higher prevalence of negative social determinants

of health, particularly food insecurity (27%) and lack of adequate social support (83%), compared with non-Hispanic Caucasians (unpublished data). In other studies on healthcare utilization, Hispanic patients were found to have limited access to appropriate specialist care and lack of insurance coverage.[20]

Our study has several strengths. This is one of the largest studies in Hispanics from multiple centers in California, the state with one of this highest number of Hispanic patients. We focused on a cohort of biologic-treated patients to examine treatment effectiveness and safety. We utilized propensity score methods to balance disease characteristics that may influence use of biologic agents. However, there are important limitations. First, we were unable to extract detailed information on disease duration, phenotype/behavior, clinical and endoscopic activity, which are important confounders that may influence treatment choice and outcomes. Similarly, we relied on hospitalization, surgery and serious infections as measures of treatment effectiveness and safety, and were unable to capture patient-reported outcomes and endoscopic outcomes. We could not identify primary reason for hospitalization since data on primary vs. secondary discharge diagnoses was not available. We were unable to robustly examine treatment effectiveness and safety of specific biologic agents in Hispanic patients. Second, since we relied on medication prescription in EHRs, we could not confirm dispension and adherence to medications. Third, by focusing only on biologic-treated patients, we were unable to examine potential impact of diagnostic and treatment delay on outcomes of these patients. Fourth, we do not have specific data on social determinants of health. There was selection bias since we focused only on biologic-treated patients and did not focus on outcomes in those who may have warranted biologic therapy but were unable to receive it. Fifth, most Hispanic patients in our cohort were presumptively from Mexico. It is unclear whether these findings would apply to Hispanics from other parts of Latin America or Cuba.

In conclusion, using a large, multi-center, EHR-based cohort of biologic treated patients with IBD, we observed that Hispanic patients experience higher rates of hospitalization, IBD-related surgery, and serious infections, suggesting ethnicity may drive potential differences in effectiveness of biologic agents. Future studies examining the role of how biological, social, genetic, behavioral and environmental determinants of health impact healthcare utilization and treatment outcomes in Hispanic patients with IBD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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WHAT YOU NEED TO KNOW

Background:

There is limited data on outcomes of biologic therapy in Hispanic patients with inflammatory bowel diseases (IBD).

Findings:

In a multi-center electronic health record-based cohort of biologic-treated patients with IBD in California, using 1:4 propensity score matching, Hispanic patients were significantly more likely to experience hospitalization and IBD-related surgery, and a trend towards higher risk of serious infection, within 1 year of biologic initiation.

Implications for patient care:

Hispanic patients with IBD experience disproportionately higher rates of unplanned healthcare utilization compared with non-Hispanic patients. Further evaluation of drivers of these healthcare disparities is warranted.

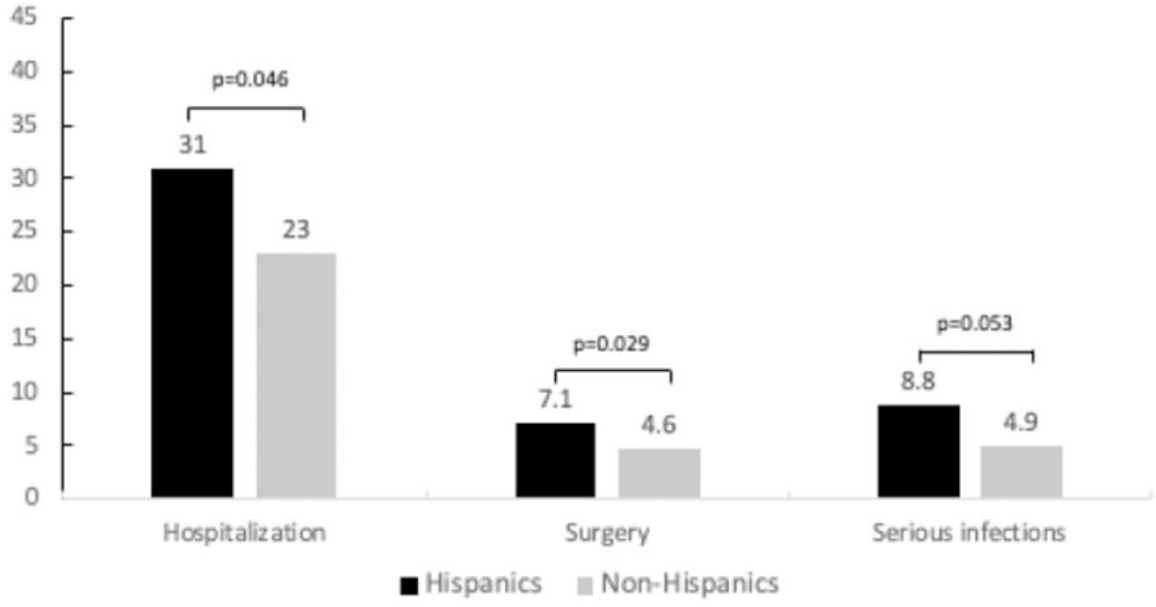

Figure 1.
Unplanned healthcare utilization and serious infections in Hispanic vs. non-Hispanic biologic-treated patients with IBD

Table 1.

Baseline characteristics of Hispanics vs non-Hispanics in the propensity score matched cohort

	Non-Hispanic (n = 960)	Hispanic (n = 240)	p-value
Age (SD) at start of biologic	40.1 (16.2)	37.3 (15.3)	0.02
Male (%)	50.6%	52.9%	0.57
Biologic			
• TNFα antagonists	67.4%	72.5%	0.31
• Ustekinumab	15.1%	12.9%	
• Vedolizumab	17.5%	14.6%	
Proportion with ulcerative colitis (%)	44.0%	45.4%	0.74
Body mass index (SD)	25.4 (9.4)	24.8 (5.2)	0.35
Elixhauser index (%)			
• 0	74.1%	62.9%	<0.01
• 1	12.5%	22.1%	
• 2	4.8%	6.7%	
• 3 and above	8.6%	8.3%	
Proportion of patients with abnormal baseline albumin (%)	6.7%	5.8%	0.75
Proportion of patients with abnormal baseline CRP (%)	16.4%	13.3%	0.29
Concomitant immunomodulator (%)	34.8%	30.0%	0.19
Concomitant opiate use (%)	36.2%	36.2%	1.0
Concomitant steroid use (%)	36.8%	35.0%	0.66
History of IBD surgery (%)	5.3%	5.0%	0.97
Hospitalized within 1 year (%)	30.8%	34.6%	0.30
Serious infection within 1 year (%)	8.0%	9.2%	0.66

Table 2.

Multivariable cox proportional hazard analysis for all-cause hospitalization, IBD-related surgery, and serious infection in patients with IBD within a year of starting a new biologic agent – overall cohort.

Variables	All-cause hospitalization Hazard Ratio (95%CI)	p-value	IBD-related surgery Hazard Ratio (95% CI)	p-value	Serious infection Hazard Ratio (95% CI)	p-value
Hispanic ethnicity	**1.33 (1.05 – 1.70)**	0.02	**1.71 (1.01 – 2.92)**	0.05	1.36 (0.86 – 2.16)	0.19
Biologic agent (vs. TNFα antagonists as reference)						
• Ustekinumab	1.09 (0.88 – 1.34)	0.44	0.62 (0.34 – 1.14)	0.12	0.38 (0.21 – 0.69)	<0.02
• Vedolizumab	0.96 (0.77 – 1.19)	0.70	0.70 (0.38 – 1.27)	0.24	0.86 (0.56 – 1.33)	0.50
Age at start of biologic	1.00 (0.99 – 1.01)	0.44	0.99 (0.98 – 1.00)	0.12	1.01 (0.99 – 1.01)	0.22
Male (vs female)	1.07 (0.93 – 1.22)	0.36	1.13 (0.78 – 1.64)	0.51	0.89 (0.68 – 1.17)	0.41
Ulcerative colitis (vs Crohn's disease)	0.86 (0.74 – 1.01)	0.06	0.66 (0.43 – 1.03)	0.06	1.05 (0.79 – 1.41)	0.72
Elixhauser index r≥2 (vs <2)	1.45 (1.23 – 1.7)	<0.01	1.14 (0.73 – 1.80)	0.56	1.78 (1.30 – 2.44)	<0.01
Abnormal baseline albumin	1.322 (0.95 – 1.84)	0.1	1.80 (0.93 – 3.47)	0.08	1.97 (1.12 – 3.45)	0.02
Abnormal baseline C-reactive protein	1.08 (0.83 – 1.40)	0.57	2.83 (1.66 – 4.85)	<0.01	0.922 (0.56 – 1.53)	0.75
Prior biologic exposure	0.84 (0.69 – 1.03)	0.09	1.71 (1.08 –2.72)	0.02	0.62 (0.40 – 0.98)	0.04
Concomitant immunomodulator use	0.87 (0.74 – 1.03)	0.10	1.04 (0.69 – 1.57)	0.85	1.31 (0.97 – 1.77)	0.08
Concomitant opiate use	3.37 (2.89 – 3.92)	<0.01	3.45 (2.25 – 5.29)	<0.01	1.90 (1.40 – 2.58)	<0.01
Concomitant corticosteroid use	1.43 (1.23 – 1.67)	<0.01	1.33 (0.89 – 2.01)	0.17	1.23 (0.90 – 1.67)	0.19
Prior IBD-related surgery	1.01 (0.73 – 1.39)	0.96	1.92 (1.01 – 3.64)	0.05	1.09 (0.58 – 2.05)	0.79
Hospitalization (in preceding 12mo)	1.40 (1.18 – 1.65)	<0.01	0.87 (0.55 – 1.36)	0.53	1.39 (0.99 – 1.94)	0.05
Serious infection (in preceding 12mo)	1.31 (1.08 – 1.60)	0.01	-	-	2.68 (1.91 – 3.75)	<0.01