Coexisting psoriasis is associated with an increased risk of hospitalization for patients with inflammatory bowel disease: an analysis of the National Inpatient Sample database

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ABSTRACT

This study compares the odds of being admitted for inflammatory bowel disease (IBD) in patients with psoriasis compared with those without psoriasis alone. We also compared hospital outcomes of patients admitted primarily for IBD with and without a secondary diagnosis of psoriasis. Data were abstracted from the National Inpatient Sample (NIS) 2016 and 2017 database to search for hospitalizations of interest using International Classification of Diseases, 10th Revision codes. Multivariate logistic regression model was used to calculate the adjusted OR (AOR) of IBD being the principal diagnosis for hospitalizations with and without a secondary diagnosis of psoriasis. Multivariate logistic and linear regression analyses were used accordingly to compare outcomes of hospitalizations for IBD with and without secondary diagnosis of psoriasis. There were over 71 million discharges included in the combined 2016 and 2017 NIS database. Hospitalizations with a secondary diagnosis of psoriasis have an AOR of 2.66 (95% CI 2.40 to 2.96, p<0.0001) of IBD being the principal reason for hospitalization compared with hospitalizations without psoriasis as a secondary diagnosis. IBD hospitalizations with coexisting psoriasis have similar lengths of stay, hospital charges, need for blood transfusion, and similar likelihood of having a secondary discharge diagnosis of deep venous thrombosis, gastrointestinal bleed, sepsis, and acute kidney injury compared with those without coexisting psoriasis. Patients with coexisting psoriasis have almost three times the odds of being admitted for IBD compared with patients without psoriasis. Hospitalizations for IBD with coexisting psoriasis have similar hospital outcomes compared with those without coexisting psoriasis.

Significance of this study

What is already known about this subject?

- Patients with coexisting psoriasis have almost three times the odds of being admitted for inflammatory bowel disease (IBD) compared with patients without psoriasis with only primary diagnosis of IBD.
- Patients with IBD and psoriasis have common inflammatory pathways.
- IBD coexists in about 1%–2% of patients with psoriasis compared with 0.4% in the general population.
- Increased incidence of psoriasis in patients with IBD and vice versa in patients with psoriasis.

What are the new findings?

- Patients with coexisting psoriasis have almost three times the odds of being admitted for IBD compared with patients without psoriasis.
- IBD hospitalizations with coexisting psoriasis have similar lengths of stay and total hospital charges.
- IBD hospitalizations with coexisting psoriasis have similar likelihood of having a secondary discharge diagnosis of deep venous thrombus/pulmonary embolus, gastrointestinal bleed, sepsis, and acute kidney injury compared with those without coexisting psoriasis.

INTRODUCTION

Psoriasis is a chronic immune-mediated systemic inflammatory disorder that most commonly affects the skin and is reported to affect approximately 0.5%–11.4% of adults worldwide.[1] About a third of psoriatic patients have a family history of psoriasis.[2] Patients with psoriasis have been postulated to have a onefold to fourfold increased risk of developing inflammatory bowel disease (IBD).[3] It is also associated with various other comorbidities like metabolic syndrome, uveitis, cardiovascular diseases, chronic kidney diseases and psychiatric disturbances.[1 4]

IBD is a chronic inflammatory immune-mediated gastrointestinal (GI) tract disease.

Significance of this study

How might these results change the focus of research or clinical practice?

- Patients with coexisting psoriasis have almost three times the odds of being admitted for IBD compared to patients without psoriasis. Also the IBD and coexisting psoriasis cohort had a higher prevalence of hypothyroidism compared to the IBD-only cohort. Our study also showed increased prevalence of obesity in the IBD and coexisting psoriasis cohort compared to the IBD-only cohort. This in a clinical setting is important as a multidisciplinary approach can lead to better patient care with this understanding.

It has also been shown that genetics plays a role in the development of IBD.[1 5] The incidence of IBD in developing countries has increased exponentially in the past two decades with a reported annual incidence increase of 11.1% for Crohn's disease (CD) and 14.9% for ulcerative colitis (UC).[1 6] Because of the chronicity, debilitating nature and need for expensive medical and surgical management of IBD, it presents a significant burden to the average patient and the US healthcare system.[5] Patients with IBD are at increased risk of developing other immune-mediated inflammatory conditions like psoriasis, ankylosing spondylitis, and primary sclerosing cholangitis.[5]

There have been reports since the early 1960s about the association between psoriasis and IBD.[7–9] Skin manifestations in the form of psoriasis has been reported in 5%–10% of patients with UC and 20%–30% of patients with CD.[10] It has been postulated that these two conditions can either appear as concomitant disease in the same patient or sometimes can occur as treatment-related adverse effects in patients with IBD.[11]

Several other studies have reported common genotypes, shared pathogenic mechanisms of inflammation, a common clinical course and common biological drug use for both conditions.[1 2] Previous studies have also reported increased incidence and prevalence of IBD in psoriatic patients.[12–14] However, there is a scarcity of studies on incidence of IBD hospitalizations in psoriatic patients. To the best of our knowledge, however, no study until now, has compared clinical outcomes of IBD hospitalizations in patients with coexisting psoriasis to those without coexisting psoriasis using national population-level data. This study aimed to fill the knowledge gap.

We carried out a retrospective study of a large national inpatient database comparing odds of IBD hospitalizations in coexisting psoriatic versus non-psoriatic patients, and comparing clinical outcomes of IBD hospitalizations in psoriatic versus non-psoriatic patients.

METHODS

Data source

We conducted a retrospective cross-sectional study of hospitalizations in 2016 and 2017 with principal diagnosis of IBD with and without a secondary diagnosis of psoriasis. Hospitalizations were obtained from the National Inpatient Sample (NIS) database. It is the largest hospitalization database in the USA. The NIS is designed as a stratified probability sample to be nationally representative of all non-federal acute care hospitals across the USA. Hospitals are stratified in different strata. A 20% probability sample of hospitals within each stratum is then obtained. Hospitalizations are then weighted to ensure national representation is maintained. Diagnoses recorded for each hospitalization are either the principal diagnosis or secondary diagnoses. The principal diagnosis is the chief reason for the hospitalization. Secondary diagnoses are all other diagnoses excluding the principal diagnosis. The NIS data source description is similar to previously published NIS paper.[15]

Inclusion criteria and study variables

The study population encompasses all hospital admissions in the 2016 and 2017 NIS. Study variables included sociodemographic characteristics, medical comorbidities, hospital characteristics, and primary and secondary outcomes (highlighted further). ICD-10 codes were used to identify the principal and secondary diagnoses (see online supplemental table). We studied baseline characteristics of hospitalization for IBD with and without a secondary diagnosis of psoriasis.

Outcomes

Primary objective

Compare the odds of IBD being the principal diagnosis for hospitalizations with and without a secondary diagnosis of Psoriasis.

Secondary objective

Compare outcomes of hospitalizations for IBD with and without a secondary diagnosis of Psoriasis. Outcomes of interest were inpatient mortality, length of stay, total hospital charges, need for blood transfusion, odds of having a secondary discharge diagnosis of deep venous thrombus (DVT)/pulmonary embolus (PE), sepsis, Acute kidney injury (AKI), and GI bleed.

Statistical analysis

Analyses were performed using statistical and data (STATA V.16).

Primary objective

A univariate logistic regression analysis using all variables and co-morbidities in table 1 was used to calculate unadjusted ORs for IBD being the principal diagnosis for hospitalizations with and without a secondary diagnosis of Psoriasis. Variables and co-morbidities were selected from literature review. Charleston index was used to adjust for comorbidity burden. All variables with p-values<0.1 were included in a multivariate logistic regression model which was used to calculate the adjusted OR (AOR) of IBD being the principal diagnosis for hospitalizations with and without a secondary diagnosis of Psoriasis. Values of $p<0.05$ were considered significant in the multivariate analysis.

Secondary objectives

Multivariate logistic and linear regression model with all variables and co-morbidities in table 1 were used accordingly to adjust for confounders for outcomes of hospitalizations for IBD with and without a secondary diagnosis

Table 1 Baseline characteristics of IBD hospitalizations with and without psoriasis

Variables	IBD (N=184 120) Without psoriasis (n=181 865)	With psoriasis (n=2255)	P value
Age (years)	44.79	45.03	0.767
Female	52.79	59.87	0.003
Race			<0.0001
White	72.99%	87.27%	Reference
Black	14.53%	3.01%	<0.0001
Hispanic	7.95%	6.94%	0.101
Asians	1.36%	1.39%	0.740
Native Americans	0.41%	0.23%	0.462
Others	2.76%	1.16%	0.021
Charleston Comorbidity Index			0.0768
0	68.17%	63.41%	
1	18.54%	23.28%	
2	6.83%	6.65%	
≥3	6.45%	6.65%	
Hospital bed size			0.7039
Small	18.44%	17.52%	
Medium	28.18%	27.05%	
Large	53.38%	55.43%	
Hospital teaching status			0.0821
Non-teaching	28.9%	25.06%	
Teaching	7.11%	74.94%	
Hospital location			0.0660
Rural	7.07%	4.88%	
Urban	92.93%	95.12%	
Expected primary payer			0.0060
Medicare	25.67%	23.57%	
Medicaid	20.08%	17.62%	
Private	48.49%	55.84%	
Self-pay	5.75%	2.97%	
Median household income (quartile)			0.0012
First (0–25th)	26.29%	21.75%	
Second (26th–50th)	25.27%	2.04%	
Third (51st–75th)	25.13%	2.87%	
Fourth (76th–100th)	23.31%	29.15%	
Hospital region			0.0765
Northeast	21.45%	25.72%	
Midwest	24.37%	23.73%	
South	3.82%	33.04%	
West	15.98%	17.52%	
Comorbidities			
Dyslipidemia	12.79%	16.19%	0.0341
Old MI	1.77%	1.33%	0.4856
Old PCI	0.17%	0%	0.3861
Old CABG	1.13%	0.89%	0.6243
Old pacemaker	0.60%	0.67%	0.8571
Atrial fibrillation/ flutter	3.14%	3.33%	0.8195
COPD	5.11%	3.99%	0.2791
Old stroke	2.28%	2.66%	0.5914
Hypertension	23.53%	27.49%	0.0571
Peripheral vessel disease	0.78%	1.33%	0.1932
Hypothyroidism	6.21%	10.86%	<0.0001
DM types 1 and 2	9.20%	11.75%	0.0601
Obesity	8.12%	11.75%	0.0051
CHF	2.54%	1.33%	0.1045
CKD	4.36%	3.99%	0.7144
Liver disease	3.78%	5.76%	0.0277
Electrolyte derangement	26.93%	26.16%	0.7227
Maintenance hemodialysis	0.32%	0%	0.2323
O_2 dependence	0.45%	0.44%	0.9951
Smoking	19.87%	25.28%	0.0061
Anemia	37.51%	35.03%	0.2812
CAD	5.01%	4.43%	0.5793
On anticoagulation	3.42%	3.1%	0.7298

CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, chronic congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; IBD, inflammatory bowel disease; median household income, median household income for patient's Zip code; MI, myocardial infarction; PCI, percutaneous coronary intervention.

of Psoriasis. All p-values were two sided, with 0.05 as the threshold for statistical significance.

RESULTS

There were over 71 million discharges included in the combined 2016 and 2017 NIS database. 184 120 hospitalizations were for adult patients with a principal diagnosis of IBD. 2255 (1.22%) of these hospitalizations have Psoriasis as a secondary diagnosis, while 181 865 (98.78%) hospitalizations did not have coexisting Psoriasis. Characteristics of hospitalizations for IBD with and without co-existing Psoriasis are displayed in table 1. Psoriasis group had more women (59.87% vs 52.79%, p=0.003).

Univariate association of baseline variables and comorbidities in table 1 with odds of IBD being the principal reason for hospitalization is shown in table 2. Hospitalizations with a secondary diagnosis of Psoriasis have an AOR: 2.66 (95% CI 2.40 to 2.96, p<0.0001) of IBD being the principal reason for hospitalization compared with hospitalizations without Psoriasis as a secondary diagnosis.

530 (0.29%) IBD hospitalizations resulted in inpatient mortality. All these deaths occurred in hospitalizations for IBD with psoriasis. IBD Hospitalizations with co-existing Psoriasis have similar LOS, total hospital charges, need for blood transfusion, likelihood of having a secondary discharge diagnosis of DVT/PE, gastro-intestinal bleed, sepsis, and acute kidney injury as compared with those without coexisting psoriasis (see table 3 for complete details of outcomes).

DISCUSSION

Patients with IBD and psoriasis have a common inflammatory pathway, and recent studies have demonstrated they can be treated concurrently.[16] A systematic review and meta-analysis showed an increased risk of development of IBD in patients with psoriasis.[1] A prospective study done by Li *et al* showed an increased risk of CD in patients with psoriatic arthritis.[17] IBD coexists in about 1%–2% of patients with psoriasis compared with 0.4% in the general population.[17] Other studies have reported increased incidence of psoriasis in patients with IBD and vice versa in patients with psoriasis.[12 13] A national Danish study carried out by

Table 2 Univariate association of baseline variables with the primary outcome*

Baseline variables	OR	P value
Age	0.99	<0.0001
Female	0.86	<0.0001
Race		
White	Reference	Reference
Black	0.84	<0.0001
Hispanic	0.57	<0.0001
Asians	0.39	<0.0001
Native Americans	0.55	<0.0001
Others	0.69	<0.0001
Charleston Comorbidity Index	0.58	<0.0001
Hospital bed size	1.05	0.001
Hospital teaching status	1.21	<0.0001
Hospital location	1.31	<0.0001
Expected primary payer	1.50	<0.0001
Median household income (quartile)	1.11	<0.0001
Hospital region	0.89	<0.0001
Dyslipidemia	0.39	<0.0001
Old MI	0.37	<0.0001
Old PCI	0.36	<0.0001
Old CABG	0.28	<0.0001
Old pacemaker	0.26	<0.0001
Atrial fibrillation/flutter	0.35	<0.0001
COPD	0.39	<0.0001
Old stroke	0.41	<0.0001
Hypertension	0.71	<0.0001
Peripheral vessel disease	0.28	<0.0001
Hypothyroidism	0.59	<0.0001
DM types 1 and 2	0.37	<0.0001
Obesity	0.64	<0.0001
CHF	0.18	<0.0001
CKD	0.29	<0.0001
Liver disease	0.94	0.018
Electrolyte derangement	1.59	<0.0001
Maintenance hemodialysis	0.14	<0.0001
O_2 dependence	0.15	<0.0001
Smoking	1.15	<0.0001
Anemia	2.18	<0.0001
CAD	0.31	<0.0001
On anticoagulation	0.53	<0.0001

*IBD as the principal diagnosis for hospitalizations.
CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, chronic congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; IBD, inflammatory bowel disease; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 3 Clinical outcomes of IBD hospitalizations with and without psoriasis

	IBD with psoriasis % (95% CI)	IBD without psoriasis % (95% CI)	Adjusted OR (95% CI)	P value
In-patient mortality	0	0.29	–	–
DVT/PE	1.77	1.58	1.35 (0.55 to 3.29)	0.514
Transfusion	3.55	5.84	0.60 (0.34 to 1.04)	0.070
GI bleed	2.88	3.62	0.86 (0.48 to 1.54)	0.617
Sepsis	0.44	1.08	0.25 (0.03 to 1.80)	0.167
AKI	6.65	7.32	0.98 (0.64 to 1.51)	0.925
			Adjusted mean difference	
LOS (days), mean	4.77	4.99	−0.23 (−0.67 to 0.21)	0.304
Total charges ($), mean	44 505	44 320	−1,013 (−8789 to 6762)	0.798

AKI, acute kidney injury; DVT, deep venous thrombus; GI, gastrointestinal; IBD, inflammatory bowel disease; LOS, length of stay; PE, pulmonary embolus.

Eggeberg *et al* found an increased incidence of both UC and CD in psoriatic patients.[14] This study also showed that use of biologics for treatment of psoriasis delayed the time to diagnosis of IBD since the medications used for the treatment of both conditions are similar.[14] These studies showed increased incidence or prevalence of IBD in patients with psoriasis, however, do not specifically look at risk of IBD hospitalizations in patients with psoriasis.[1 12–14 17 18]

The pathogenetic mechanisms for the association of psoriasis to IBD are as follows. Some studies have come to show that IBD and psoriasis share a common genetic loci on chromosome 6p 21.[1] Others have shown that IBD and psoriasis both show alterations in TH17 leading to increased levels of interleukins (ILs) like IL-15, IL-17, IL-22, IL-23 that play a significant role in the development of both conditions.[2] The skin and gut have similar characteristics like bountiful blood supply and similar microbiota colonization. IBD and psoriasis have both been shown to have decreased microbiome diversity contributing to similar immune responses.[1 2] Since recent technological advances have shown similar pathogenetic mechanisms for development of IBD and psoriasis, simultaneous treatment of both diseases with medications targeting tumor necrosis factor alpha (TNF-α) and IL-23 have been developed.[14]

In addition, recently, some studies have reported psoriatic eruptions in patients with IBD treated with anti-TNF-α treatments.[9 19 20] It has been suggested that the development of psoriatic lesions in these patients is due to the effect of interferon alpha (IFN-α) production from dendritic cells observed in psoriatic lesions. IFN-α is typically inhibited by TNF-α. Blocking TNF-α thus increases the production of IFN-α, thereby inducing new lesions or worsening already present lesions.[9 21] Although this association has been reported, other studies have reported a higher prevalence of psoriasis in patients with IBD independent of anti-TNF-α inhibitor therapy.[22]

Our study showed increased prevalence of obesity in IBD and coexisting psoriasis cohort compared with IBD only cohort (11.75% vs 8.12%, $p<0.05$). Psoriasis is a chronic inflammatory condition with constant production of cytokines which stimulates the hypothalamic–pituitary axis leading to central obesity. On the other hand, obesity could play a role in triggering psoriasis due to the chronic inflammatory state that is associated with obesity.[23]

The IBD and coexisting psoriasis cohort had higher prevalence of hypothyroidism compared with the IBD-only cohort in our study (10.86% vs 6.21%, $p<0.0001$). Bianchi *et al* and Antonelli *et al* all reported an increased incidence of autoimmune thyroiditis in patients with psoriasis.[24–26] These findings can be explained by Th1 cytokine release

since autoimmune thyroiditis and psoriasis are both Th1 immune-mediated inflammatory conditions.[26]

It is also worth noting that our data showed less prevalence of African–Americans in the IBD+psoriasis cohort compared with the IBD-only cohort. This is similar to a study carried out by Gelfand *et al*, which showed approximately 52% reduction of the prevalence of psoriasis in African–Americans.[27]

Our study also demonstrated that patients with coexisting psoriasis were three times more likely to be admitted for IBD hospitalization compared with those without psoriasis. However, psoriasis did not negatively impact hospital outcomes of IBD hospitalizations. Eppinga *et al* reported more extensive disease in patients with IBD and coexisting psoriasis, when compared with patients with only IBD.[12] They reported a 60% chance of extensive ileocolonic disease in patients with CD–psoriasis vs 40.1% in patients with CD only, and 33.3% chance of pancolitis in patients with Ulcerative Collitis (UC)–psoriasis vs 18.9% in patients with UC only.[12]

IL-17 inhibitors are medications that have recently been approved for the treatment of psoriasis and have shown tremendous strides in inducing remission of the disease.[28] Studies evaluating the use of IL-17 inhibitors (especially sekunimab and ixekizumab) for the treatment of psoriasis have reported increased incidence and even exacerbations of pre-existing IBD.[29] A small phase II study carried out by Hueber *et al* showed that IBD disease activity worsened in 15.4% of 59 patients assigned to treatment with sekunimab.[30] Recently, Gill *et al* performed a meta-analysis that showed that addition of an IL-17 inhibitor to the treatment for psoriasis increased the probability of the development of CD from 0.0010 to 0.0037 and increased the probability of the development of UC from 0.0010 to 0.0028.[31]

We postulate that our finding of increased odds of IBD hospitalizations in IBD–psoriasis cohort may be secondary to increased incidence and prevalence of IBD in patients with psoriasis, more extensive ileocolonic disease and pancolitis found in these cohort of patients and the detrimental effect of IL-17 inhibitors used sometimes for the treatment of psoriasis. Patients in both cohorts (IBD+psoriasis vs IBD alone) are managed similarly with immunosuppressive therapy and biological agents.[12 32] This may partly explain why there were no statistically significant differences in in-hospital outcomes between the IBD+psoriasis cohort and the IBD-only cohort. We recommend a multidisciplinary approach for these patients to optimize outcomes.

Our study has several strengths: (1) the NIS has a large sample size, which greatly increases the power of our study; (2) the NIS provides valuable insights on baseline demographic characteristics and in-hospital outcomes between IBD hospitalizations with and without concomitant psoriasis. Limitations of our study include the following: (1) NIS does not contain information on disease severity, disease duration and time of diagnosis; therefore, we cannot determine if underlying psoriasis or IBD severity may have affected our results, and if psoriasis diagnosis preceded or postceded the diagnosis of IBD in the IBD–psoriasis cohort. There is also no way of knowing the percentage of patients with IBD who had psoriasis de novo or after TNF-α inhibitor treatment; (2) studies on NIS are subject to associated biases of retrospective studies; (3) since the NIS is an administrative database, it uses ICD-10 codes to obtain relevant hospitalizations and clinical outcomes; there is therefore a possibility of coding errors; (4) we report data on IBD hospitalizations rather than patients; hence, patients admitted on multiple occasions would be included multiple times[33]; and (5) information on medication use such as immunosuppressant and medication compliance are not available in the NIS database.

Despite these limitations, our large sample database, scientific questions and analysis technique contributes to a largely understudied topic and aims to stimulate further studies.

CONCLUSIONS

Patients with psoriasis have almost three times the odds of being admitted for IBD compared with patients without psoriasis. Hospitalizations for IBD with coexisting psoriasis have similar hospital LOS, total hospital charges, rate of blood transfusion, odds of having a secondary discharge diagnosis of DVT/PE, GI bleed, sepsis, and AKI compared with those without psoriasis. The higher odds of extensive ileocolonic disease, pancolitis found in patients with IBD+psoriasis, as well as the possible use of some medications for the treatment of psoriasis may contribute to these findings. It is important for clinicians to consider concurrent psoriasis and IBD as a possible marker for more severe IBD. We therefore, encourage more large-scale prospective cohort studies to further evaluate this association.

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