Kidney Medicine

Acute Kidney Injury in Inflammatory Bowel Disease Patients: A Nationwide Comparative Analysis

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Rationale & Objective: About 25%-40% of patients with inflammatory bowel disease (IBD) may have extraintestinal manifestations, mainly involving the liver, skin, and joints. Kidney involvement in patients with IBD has been reported, but there are no estimates of its prevalence in population-based studies in the United States. We compared the frequency of acute kidney injury (AKI) among hospitalizations with IBD with that among hospitalizations with collagen vascular diseases and hospitalizations with neither condition.

Study Design: Retrospective, population-based cohort study.

Setting & Participants: Healthcare Cost and Utilization Project-Nationwide Inpatient Sample database.

Outcomes: AKI and AKI requiring dialysis.

Analytical Approach: Regression models were used to compare the occurrence of AKI among groups. Inverse probability of treatment weighting was applied to balance groups on covariates.

Results: The final sample comprised 5,735,804 hospitalizations, including 57,121 with IBD, 159,930 with collagen vascular diseases, and 5,518,753 with neither IBD nor collagen vascular diseases. AKI was observed in 13%, 15%, and 12.2% of hospitalizations with IBD, collagen vascular diseases, and the general population, respectively. When adjusting for demographic, hospital, and clinical characteristics using inverse probability of treatment weighting, hospitalizations with IBD had higher odds of being diagnosed with AKI than both those with collagen vascular diseases (odds ratio [OR], 1.32; 95% confidence interval [CI], 1.27-1.38) and the general population (OR, 1.27; 95% CI, 1.23-1.31) and also had higher odds of being diagnosed with AKI requiring dialysis than those with collagen vascular diseases (OR, 1.59; 95% CI, 1.31-1.94) or than the general population (OR, 1.45; 95% CI, 1.25-1.68).

Limitations: Cross-sectional analysis, underreporting of International Classification of Diseases codes, and analyses relevant to in-hospital stays only.

Conclusions: The prevalence and risk of AKI among hospitalizations with IBD is greater than that of hospitalizations with collagen vascular diseases and the general population. Coexisting kidney disease should be considered among patients with a known diagnosis of IBD.

Complete author and article information provided before references.

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Extraintestinal manifestations occur in 25%-40% of patients with inflammatory bowel disease (IBD), commonly affecting the skin, liver, and joints.[1] Case reports and studies with small sample sizes have suggested that patients with IBD have various forms of kidney disease and have speculated a shared pathogenic mechanism related to dysregulated immune response.[2-4] Estimates of the prevalence of kidney diseases in large population-based cohort of patients with IBD are lacking in the United States.

We examined the frequency of acute kidney injury (AKI) in patients with IBD (both Crohn's disease [CD] and ulcerative colitis [UC]) compared with that of patients without IBD in a national cohort of hospitalized patients, the National Inpatient Sample (NIS), which is the largest publicly available all-payer inpatient database, developed for Healthcare Cost and Utilization Project (HCUP).[5] We focused on AKI given the high specificity and positive predictive value of the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnostic and procedural codes for AKI and AKI requiring dialysis previously demonstrated in administrative and claims databases.[6] We compared the frequency of AKI among hospitalizations with IBD to hospitalizations with collagen vascular diseases and those with neither disease, before and after adjusting for demographic, hospital, and clinical characteristics. Patients with collagen vascular diseases (systemic lupus erythematosus, rheumatoid arthritis, others) are well known to have kidney involvement. The primary hypothesis was that the prevalence of AKI among hospitalizations with IBD is comparable to that in hospitalizations with collagen vascular diseases and higher than that for hospitalizations with neither IBD nor collagen vascular diseases.

METHODS

Data Source

The HCUP-NIS database was analyzed for the year 2014. The NIS is the largest publicly available all-payer inpatient health care database in the United States.[5,7] It captures an ~20% stratified sample of all discharges from US community hospitals across 44 states and the District of Columbia and contains deidentified, unweighted data from 7 million hospital stays each year. The NIS covers >96% of the US population and includes >94% of discharges from US community hospitals. The NIS contains deidentified

PLAIN LANGUAGE SUMMARY

As a nephrologist, we have evaluated many patients with inflammatory bowel disease with various forms of kidney disease, both inflammatory and noninflammatory. Based on a multitude of factors, we have always wondered if there are shared immune mechanisms between the gut and kidney that could explain the underlying inflammation in both organs. In addition, based on recent studies of other autoimmune/inflammatory diseases, there is growing interest in the role of the gut microbiome (microorganisms that reside in our gut) and its influence on the immune system as well as how both the altered microbiome and immune system affect the kidneys. As a first step, we wanted to understand if some forms of kidney disease are more prevalent in patients with inflammatory bowel disease than in the general population, which possibly suggests a shared pathogenesis.

clinical and nonclinical data elements for each hospital stay—patient demographics, hospital characteristics (bed size, ownership, urban/rural, and region of the country), expected payment source, total charges, length of stay, severity and comorbidity measures, and *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis and procedure codes. The unit of analysis in the NIS data set is hospital discharges and not individual patients.[5] We analyzed the 2014 data set because this was the latest available data set that used ICD-9-CM codes before switching to ICD-10-CM codes in the year 2015. The study was determined exempt for review by the UNC Institutional Review Board because the data set is deidentified and publicly available.

Study Sample

We examined the discharge records of patients aged ≥18 years (N = 5,950,391; Fig 1). We excluded hospitalizations that had discharge codes for end-stage kidney disease and kidney transplantation. Because our main aim was to estimate the prevalence of AKI in the IBD population and compare it with hospitalizations with collagen vascular diseases and the general population, we excluded hospital stays with dual diagnosis codes of IBD and collagen vascular diseases. ICD-9 CM codes were used to identify patients having IBD if the discharge record carried any diagnosis code of UC or CD.[8] For the collagen vascular disease comparison group, ICD-9-CM codes were used to identify those with collagen vascular diseases—systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, sarcoidosis, ankylosing spondylitis, and scleroderma.[9,10] Discharges with no diagnosis codes for IBD or collagen vascular diseases were included in the general population group (Table 1).

Dependent Variable

Our primary outcome of interest was a binary indicator for the presence/absence of AKI. We also constructed a 3-category variable further differentiating hospitalizations

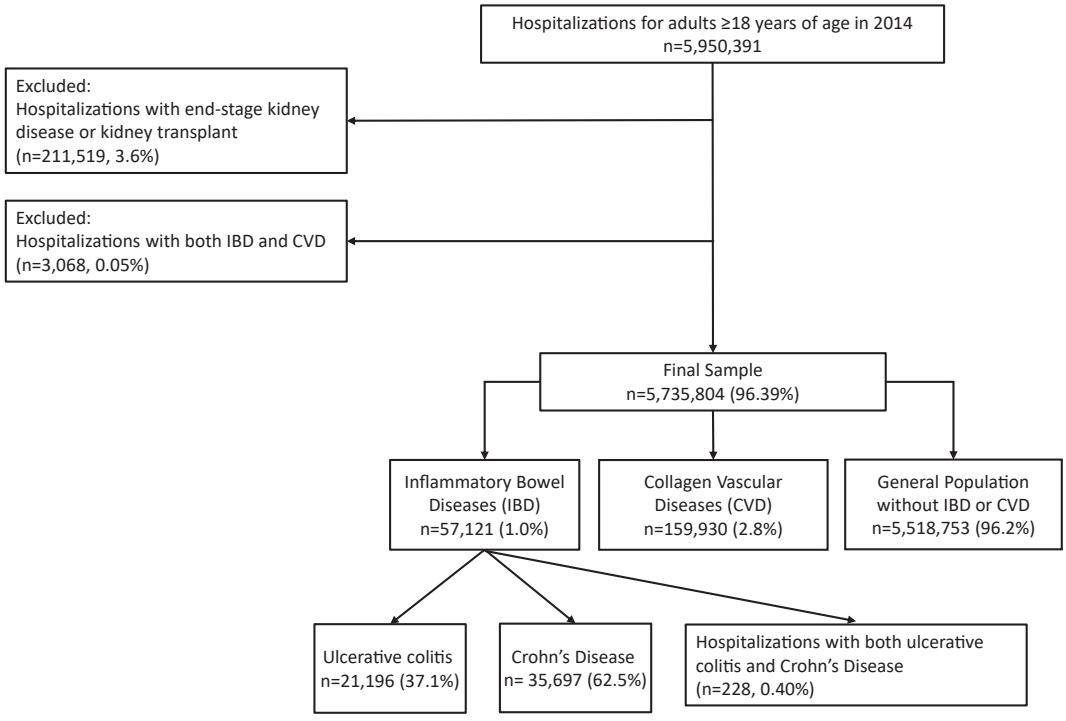

Figure 1. Flow chart showing included and excluded hospitalizations of the 3 different cohorts.

Table 1. Claims-Based Algorithms Used to Define Inclusion/Exclusion Criteria and Study Variables

	ICD-9-CM-Based Algorithms
Inclusion/exclusion criteria	
End-stage kidney disease (ESKD)	Diagnosis code 585.6 Procedure code: 39.27, 39.42, 39.43, 39.93, 54.98 **OR** One of the following codes without a diagnosis code of acute kidney injury (ICD-9-CM of 584.x): Diagnosis Code: V45.1(renal dialysis status), V56.0 (extracorporeal dialysis), V56.1 (fitting and adjustment of extracorporeal dialysis catheter), V56.2 (fitting and adjustment of peritoneal dialysis catheter), V56.31 (encounter for adequacy testing for hemodialysis), V56.32 (encounter for adequacy testing for peritoneal dialysis), V56.8 (other dialysis) Procedure code: 39.95 (hemodialysis); 54.98: peritoneal dialysis
Kidney transplant	Diagnosis codes: 996.81, V42.0
Inflammatory bowel disease	
Crohn's disease	Diagnosis codes: 555.0, 555.1, 555.2, 555.9
Ulcerative colitis	Diagnosis codes: 556.0, 556.1, 556.2, 556.3, 556.4, 556.5, 556.6, 556.8, 556.9
Connective tissue disorder (CVD)	Diagnosis codes:
Rheumatoid arthritis	714.0, 714.1, 714.2, 714.3, 714.4, 714.9
SLE	710
Sjögren's syndrome	710.2
Sarcoidosis	135
Scleroderma	710.1
Ankylosing spondylitis	720
Dermatomyositis	710.3
Polymyositis	710.4
Others (other specified and unspecified diffuse diseases of connective tissue, eosinophilia myalgia syndrome)	710.5, 710.8, 710.9
Dependent variable	
Acute kidney injury (AKI)	Diagnosis code: 584.5, 584.6, 584.7, 584.8, 584.9
AKI requiring dialysis	An AKI diagnosis code PLUS one of the following: Diagnosis code: V45.1, V56.0, V56.1 Procedure code: 39.95
Other comorbid conditions	
HTN	401.0, 401.1, 401.9, 405.0, 405.1, 405.9
DM	
Obesity (obesity, morbid obesity, and obesity hypoventilation syndrome, respectively)	278.00, 278.01, 278.03
Contrast administration	88.4, 88.40, 88.41, 88.42, 88.43, 88.44, 88.45, 88.46, 88.47, 88.48, 88.49 88.5, 88.50, 88.51, 88.52, 88.53, 88.54, 88.55, 88.56, 88.57, 88.58, 88.59 88.6, 88.60, 88.61, 88.62, 88.63, 88.64, 88.65, 88.66, 88.67, 88.68

Abbreviations: CVD, collagen vascular disease; DM, diabetes mellitus; ESKD, end-stage kidney disease; HTN, hypertension; ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; SLE, systemic lupus erythematosus.

with AKI requiring dialysis, AKI not requiring dialysis, and no AKI. AKI was identified with ICD-9-CM diagnosis codes of 584.5 (AKI, with lesion of tubular necrosis), 584.6 (AKI, with lesion of renal cortical necrosis), 584.7 (AKI, with lesion of renal medullary/papillary necrosis), 584.8 (AKI, with other specified pathologic lesion in kidney), or 584.9 (AKI, unspecified).[6] AKI requiring dialysis was identified based on the presence of both an AKI diagnosis code and dialysis codes (V39.95: hemodialysis; V45.1: renal dialysis status; V56.0: extracorporeal dialysis; V56.1: fitting and adjustment of extracorporeal dialysis catheter) on the same discharge record.[6,11] Based on previous studies, the ICD-9-CM codes for AKI have low sensitivity (35.4%) but high specificity (97.7%) and a negative predictive value of 96.1%, suggesting few false positives. ICD-9-CM codes for AKI requiring dialysis have high positive predictive value (94.0%) and negative predictive value (90.0%).[6,12]

Covariates

We included covariates that are potentially associated with both IBD and the outcome of interest, and excluded those factors (eg, sepsis, surgeries) that could be on the causal

pathway of the association of IBD and AKI. The covariates included patient demographics, hospital characteristics, and clinical variables that are potential confounders of the relationship between IBD and kidney diseases: age group (18-39 years, 40-59 years, >60 years), sex, race/ethnicity, hospital type (government, nonfederal; private, nonprofit; private-investor-owned), hospital region (northeast, midwest, south, west), rurality and teaching status of the hospital (categorized as rural, urban nonteaching, and urban teaching), hospital size (small, medium, large), hypertension, obesity, tobacco use, contrast administration, and Charlson Comorbidity Index. Race/ethnicity was coded as White, Black, Hispanic, Asian, or Pacific Islander, and others (including Native American).[5] The Charlson Comorbidity Index is a prognostic index of comorbid conditions, with each individual condition weighted depending on mortality risk.[13,14] We modified the Charlson Comorbidity Index to remove kidney diseases and connective tissue disorders for this study to ensure non-overlap with the exposure group variable and categorized scores as ≤1, 2, and ≥3 for this analysis. Details on the ICD-9-CM codes used to identify the other clinical variables are shown in Table 1.

Statistical Analysis

Descriptive statistics (frequency and percentage) were generated for all variables. The demographic, hospital, and clinical characteristics were compared between IBD and collagen vascular diseases and between IBD and general population using χ^2 tests for categorical variables. Missing values on the age, sex, and insurance payer variables were imputed using hot-deck imputation, which replaces the missing values with a randomly selected observed value for another participant and should minimize the potential deflation of the variance estimates in the analysis step.[5] Survey data analyses were done with SAS (version 9.4, SAS Institute) survey procedures, specifying the NIS hospital stratum as the stratum identifier and the NIS hospital number as the cluster identifier. Frequencies and percentages of hospitalizations with AKI vs no AKI, as well as AKI requiring dialysis, AKI not requiring dialysis, and no AKI, were reported, both before and after applying the HCUP discharge weight. The discharge weight allows for estimation of the total number of hospital discharges of interest at non-rehabilitation, non-long term acute care community hospitals located in the United States.

To determine whether the occurrence of AKI differed in hospitalizations with IBD vs collagen vascular diseases, as well as IBD vs the general population, we estimated a series of logistic regression models. To control for the measured covariates as potential confounders, inverse probability of treatment weighting (IPTW) was used to balance the IBD and collagen vascular diseases groups (or IBD and general population groups) on these factors. This method estimated IPTWs representing the propensity for having IBD vs collagen vascular diseases (or having IBD vs being in the general population) based on the covariates. Hospitalizations in each group were subsequently weighted so that the 2 groups being compared are optimally balanced on the covariates. To assess balance after application of IPTW, we calculated standardized mean differences between the IBD and general population groups and the IBD and collagen vascular disease groups. The last step was to create a final weight for the discharge that is equal to the product of the IPTW multiplied by the original HCUP discharge weight and apply this final weight in the logistic regression models. Weighted binomial logistic regression was used for the outcome of AKI vs no AKI, whereas weighted multinomial logistic regression was used for the 3-category outcome of no AKI, AKI requiring dialysis, and AKI not requiring dialysis. All analyses were conducted with SAS.

RESULTS

Our final sample consisted of 5,735,804 hospitalizations, including 3 subgroups: (1) IBD (n = 57,121; 1.0%), (2) collagen vascular diseases (n =159,930; 2.8%), and (3) a general hospitalized population without IBD or collagen vascular diseases (n = 5,518,753; 96.2%) (Fig 1). Among 57,121 hospital stays with IBD, 62.5% had a diagnosis code for CD (n = 35,697), 37.1% had a diagnosis code for UC (n = 21,196), and 0.40% had diagnosis codes for both CD and UC. After applying HCUP discharge weights, the analytic sample represented an estimated 285,605 hospitalizations among patients with IBD, 799,650 among patients with collagen vascular diseases, and 27,593,773 general population hospitalizations.

Baseline characteristics are shown in Tables 2 and 3. Before application of IPTW, patients in the IBD group were younger than those in the general population and collagen vascular disease group and were more likely to be White. They were less likely to have comorbid conditions of hypertension and obesity but more likely to have tobacco use. Patients in the IBD group had lower Charlson Comorbidity Index scores and were less likely to have contrast administration. After application of IPTW, standardized mean differences were all <10% between groups, indicating good balance.

Risk of AKI

After applying discharge weights, AKI was observed in 13%, 15%, and 12.2% of hospitalizations with IBD, collagen vascular diseases, and the general population, respectively. Most hospitalizations with AKI did not require dialysis; the proportions of IBD, collagen vascular diseases, and general population hospitalizations that had AKI requiring dialysis were 0.40%, 0.44%, and 0.34%, respectively (Table 4).

In an unadjusted analysis, applying only the discharge weights without IPTW and clinical predictors, hospitalizations with IBD demonstrated reduced odds of being diagnosed with AKI than hospitalizations with collagen vascular diseases (odds ratio [OR], 0.85; 95% confidence interval [CI], 0.82-0.87), whereas compared with the

Table 2. Comparison of Demographic, Hospital, and Clinical Characteristics Between IBD and General Populations (Without IBD/CVD) in 2014 HCUP-NIS Data

	Unweighted Frequency/Proportions		IPTW Frequency/Proportions[a]		Standardized Mean Difference[a]
	IBD	General Population Without IBD/CVD	IBD	General Population Without IBD/CVD	IBD – General Population Without IBD/CVD
	N = 57,121	N = 5,518,753	N = 5,652,425	N = 5,575,867	(Weighted)
Patient demographics					
Age, y					
18-39	17,691 (30.9%)	1,422,007 (25.8%)	1,370,914 (24.3%)	1,439,685 (25.8%)	0.03
40-59	18,025 (31.6%)	1,371,167 (24.8%)	1,384,276 (24.5%)	1,389,191 (24.9%)	0.01
>60	21,405 (37.5%)	2,725,579 (49.4%)	2,897,235 (51.3%)	2,746,991 (49.3%)	−0.04
Sex					
Male	25,114 (43.9%)	2,268,585 (41.1%)	2,229,206 (39.4%)	2,293,685 (41.1%)	−0.03
Race/ethnicity					
White	45,266 (79.2%)	3,814,967 (69.1%)	3,909,274 (69.2%)	3,860,227 (69.2%)	0.00
Black	6,138 (10.8%)	777,706 (14.1%)	775,456 (13.7%)	783,843 (14.1%)	0.01
Hispanic	3,438 (6.0%)	584,890 (10.6%)	611,569 (10.8%)	588,328 (10.6%)	−0.01
Asian or Pacific Islander	643 (1.1%)	140,796 (2.6%)	147,128 (2.6%)	141,439 (2.5%)	−0.00
Others	1,636 (2.9%)	200,394 (3.6%)	208,998 (3.7%)	202,030 (3.6%)	−0.00
Hospital characteristics					
Hospital type					
Government, nonfederal	6,065 (10.6%)	678,178 (12.3%)	677,822 (12.0%)	684,242 (12.3%)	0.01
Private, nonprofit	44,612 (78.1%)	4,009,840 (72.7%)	4,129,904 (73.1%)	4,054,447 (72.7%)	−0.01
Private, investor-owned	6,444 (11.3%)	830,735 (15.0%)	844,699 (14.9%)	837,178 (15.0%)	0.00
Region					
Northeast	12,401 (21.7%)	1,058,591 (19.2%)	1,072,356 (19.0%)	1,070,989 (19.2%)	0.01
Midwest	14,418 (25.2%)	1,248,217 (22.6%)	1,301,356 (23.0%)	1,262,634 (22.6%)	−0.01
South	20,524 (35.9%)	2,151,956 (39.0%)	2,177,577 (38.5%)	2,172,476 (39.0%)	0.01
West	9,778 (17.1%)	1,059,989 (19.2%)	1,101,135 (19.5%)	1,069,768 (19.2%)	−0.01
Rural/urban					
Rural	4,652 (8.1%)	552,703 (10.0%)	576,676 (10.2%)	557,355 (10.0%)	−0.01
Urban, nonteaching	14,073 (24.6%)	1,497,394 (27.1%)	1,543,135 (27.3%)	1,511,468 (27.1%)	−0.00
Urban, teaching	38,396 (67.2%)	3,468,656 (62.8%)	3,532,614 (62.5%)	3,507,044 (62.9%)	0.01
Bed size					
Small	10,126 (17.7%)	1,049,957 (19.0%)	1,094,222 (19.4%)	1,060,085 (19.0%)	−0.01
Medium	16,257 (28.5%)	1,619,773 (29.3%)	1,661,787 (29.4%)	1,636,029 (29.3%)	−0.00
Large	30,738 (53.8%)	2,849,023 (51.6%)	2,896,417 (51.2%)	2,879,754 (51.6%)	0.01
Clinical characteristics					
HTN	17,996 (31.5%)	2,197,587 (39.8%)	2,338,966 (41.4%)	2,215,591 (39.7%)	−0.03
Obesity	5,251 (9.2%)	724,773 (13.1%)	783,074 (13.9%)	730,026 (13.1%)	−0.02

(Continued)

Table 2 (Cont'd). Comparison of Demographic, Hospital, and Clinical Characteristics Between IBD and General Populations (Without IBD/CVD) in 2014 HCUP-NIS Data

	Unweighted Frequency/Proportions		IPTW Frequency/Proportions[a]		Standardized Mean Difference[a]
	IBD	General Population Without IBD/CVD	IBD	General Population Without IBD/CVD	IBD – General Population Without IBD/CVD
	N = 57,121	N = 5,518,753	N = 5,652,425	N = 5,575,867	(Weighted)
Tobacco use	9,660 (17.0%)	843,774 (15.3%)	878,495 (15.5%)	853,438 (15.3%)	−0.01
Charlson Comorbidity Index					
Score ≤1	45,768 (80.1%)	3,845,676 (69.7%)	3,863,485 (68.4%)	3,891,432 (69.8%)	−0.01
Score 2	5,731 (10.0%)	825,073 (14.9%)	873,730 (15.5%)	830,806 (14.9%)	0.03
Score ≥3	5,622 (9.8%)	848,004 (15.4%)	915,210 (16.2%)	853,628 (15.3%)	−0.02
Contrast administration	1,381 (2.4%)	260,031 (4.7%)	297,954 (5.3%)	261,413 (4.7%)	−0.03

Abbreviations: CVD, collagen vascular disease; HCUP-NIS, Healthcare Cost and Utilization Project-Nationwide Inpatient Sample; HTN, hypertension; IBD, inflammatory bowel disease; IPTW, inverse probability of treatment weighting.
[a]The weighted frequency/proportions and standardized mean differences were calculated using IPTW. All *P* values < 0.0001.

general population, hospitalizations with IBD demonstrated higher odds of being diagnosed with AKI (OR, 1.07; 95% CI, 1.04-1.10). However, when adjusting for demographic, hospital, and clinical characteristics using IPTW, hospitalizations with IBD had higher odds of being diagnosed with AKI than both the collagen vascular disease group (OR, 1.32; 95% CI, 1.27-1.38) and the general population (OR, 1.27, 95% CI, 1.23-1.31) (Table 5).

AKI With and Without Requiring Dialysis

When applying only discharge weights, hospitalizations with IBD had reduced odds of being diagnosed with AKI requiring dialysis than those with collagen vascular diseases (OR, 0.91; 95% CI, 0.78-1.07) and higher odds of being diagnosed with AKI requiring dialysis than the general population (OR, 1.20, 95% CI, 1.05-1.37). On adjustment for demographic, hospital, and clinical characteristics using IPTW, hospitalizations with IBD had higher odds of being diagnosed with AKI requiring dialysis than hospitalizations with collagen vascular diseases (OR, 1.59; 95% CI, 1.31-1.94) and the general population (OR, 1.45; 95% CI, 1.25-1.68). After applying IPTW, the odds of AKI without dialysis remained higher among hospitalizations with IBD than those with collagen vascular diseases and those without IBD and collagen vascular diseases (Table 5).

DISCUSSION

In this study using the NIS data set and after adjusting for potential confounders, we observed a higher frequency of AKI (with or without dialysis) among hospitalizations with IBD than hospitalizations with either collagen vascular diseases or those with neither IBD nor collagen vascular diseases. These relationships persisted when looking at AKI as a whole, as well as when examining AKI with and without dialysis in separate analyses.

The findings presented here are consistent with previously published studies. To our knowledge, this is the first large, population-based study in the United States. Strengths of our approach include a nationally representative, large cohort of almost 6 million hospital stays; the use of previously validated ICD-9-CM codes; and the use of 2 comparison groups—hospitalizations for collagen vascular diseases (a group with known higher prevalence of kidney disease) and hospitalizations involving neither collagen vascular diseases nor IBD.

The prevalence of AKI of 13% in our study is higher than previously reported. In a retrospective study of 775 IBD patients, the prevalence of reduced kidney function (defined by serum creatinine >1.5 mg/dL) was 2% among patients with CD and 0% among those with UC.[15] In another study of 250 participants, the frequency of renal insufficiency (defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2) was estimated at 15.9%, with AKI accounting for 5.5% and chronic kidney disease for 10.4% of cases.[16] Both of these studies were limited by

Table 3. Comparison of Demographics, Hospital, and Clinical Characteristics Between IBD and CVD in 2014 HCUP-NIS Data

	Unweighted Frequency/Proportions		IPTW Frequency/Proportions[a]		Standardized Mean Difference[a]
	IBD	CVD	IBD	CVD	IBD – CVD
	N = 57,121	N = 159,930	N = 224,333	N = 215,392	(Weighted)
Patient demographics					
Age, y					
18-39	17,691 (30.9%)	14,782 (9.2%)	30,208 (13.5%)	30,242 (14.0%)	0.01
40-59	18,025 (31.6%)	45,435 (28.4%)	61,348 (27.3%)	63,318 (29.4%)	0.04
>60	21,405 (37.5%)	99,713 (62.4%)	132,777 (59.2%)	121,832 (56.6%)	−0.05
Sex					
Male	25,114 (43.9%)	38,486 (24.1%)	63,452(28.3%)	62,043(28.8%)	−0.01
Race/Ethnicity					
White	45,266 (79.2%)	111,809 (69.9%)	162,073 (72.2%)	155,698 (72.3%)	0.00
Black	6,138 (10.8%)	27,590 (17.2%)	34,599 (15.4%)	33,591 (15.6%)	0.00
Hispanic	3,438 (6.0%)	13,181 (8.2%)	17,519 (7.8%)	16,534 (7.7%)	−0.01
Asian or Pacific Islander	643 (1.1%)	2,566 (1.6%)	3,559 (1.6%)	3,202 (1.5%)	−0.01
Others	1,636 (2.9%)	4,784 (3.0%)	6,584 (2.9%)	6,367 (3.0%)	0.00
Hospital characteristics					
Hospital type					
Government, nonfederal	6,065 (10.6%)	17,705 (11.1%)	23,920 (10.7%)	23,561 (10.9%)	0.01
Private, nonprofit	44,612 (78.1%)	119,848 (74.9%)	171,012 (76.2%)	163,193 (75.8%)	−0.01
Private, investor-owned	6,444 (11.3%)	22,377 (14.0%)	29,401 (13.1%)	28,638 (13.3%)	0.01
Region					
Northeast	12,401 (21.7%)	29,215 (18.3%)	43,164(19.2%)	41,220(19.1%)	−0.00
Midwest	14,418 (25.2%)	37,908 (23.7%)	54,736 (24.4%)	51,942 (24.1%)	−0.01
South	20,524 (35.9%)	64,149 (40.1%)	85,395 (38.1%)	83,915 (39.0%)	0.01
West	9,778 (17.1%)	28,658 (17.9%)	41,038 (18.3%)	38,315 (17.8%)	−0.01
Rural/urban					
Rural	4,652 (8.1%)	14,959 (9.3%)	20,303 (9.1%)	19,529 (9.1%)	0.00
Urban, nonteaching	14,073 (24.6%)	42,977 (26.8%)	58,262 (26.0%)	56,654 (26.3%)	0.01
Urban, teaching	38,396 (67.2%)	101,994 (63.8%)	145,769 (65.0%)	139,210 (64.6%)	−0.01
Bed size					
Small	10,126 (17.7%)	30,105 (18.8%)	40,749 (18.2%)	40,031 (18.6%)	0.01
Medium	16,257 (28.5%)	46,493 (29.1%)	64,178 (28.6%)	62,119 (28.8%)	0.01
Large	30,738 (53.8%)	83,332 (52.1%)	119,407 (53.2%)	113,241 (52.6%)	−0.01
Clinical characteristics					
HTN	17,996 (31.5%)	79,326 (49.6%)	104,240 (46.5%)	97,841 (45.4%)	−0.02
Obesity	5,251 (9.2%)	25,455 (15.9%)	33,436 (14.9%)	30,892 (14.3%)	−0.02
Tobacco use	9,660 (17.0%)	21,317 (13.3%)	31,714 (14.1%)	31,054 (14.4%)	0.01
Charlson Comorbidity Index					
Score ≤1	45,768 (80.1%)	57,483 (35.9%)	103,124 (46.0%)	101,466 (47.1%)	0.03
Score 2	5,731 (10.0%)	47,477 (29.7%)	57,999 (25.9%)	53,317 (24.8%)	−0.03
Score ≥3	5,622 (9.8%)	54,970 (34.4%)	63,210 (28.2%)	60,609 (28.1%)	−0.00
Contrast administration	1,381 (2.4%)	7,449 (4.7%)	10,051(4.5%)	8,911(4.1%)	−0.02

Abbreviations: CVD, collagen vascular disease; HCUP-NIS, Healthcare Cost and Utilization Project-Nationwide Inpatient Sample; HTN, hypertension; IBD, inflammatory bowel disease; IPTW, inverse probability of treatment weighting.
[a]The weighted frequency/proportions and standardized mean differences were calculated using IPTW. All *P* values < 0.0001.

small sample size, evaluation of single-center data, and unconventional definitions of AKI.

In a large population-based study using the UK Biobank cohort, participants with IBD had a higher risk of developing AKI than those without IBD (hazard ratio, 1.70; 95% CI, 1.37-1.79) after adjusting for participants demographics, biological, socioeconomic, and self-rated health variables.[17] In another population-based study from Sweden, using data from a single health care utilization cohort covering 20%-25% of the population of Sweden, participants with IBD also had higher risks of developing AKI than those without IBD (hazard ratio, 1.97; 95% CI, 1.70-2.29).[18]

The findings of our study are in line with the aforementioned large population-based studies, but the reported risks of developing AKI vary among different cohorts, which

Table 4. Prevalence of Acute Kidney Injury (AKI) in Hospitalized Patients With IBD, CVD, and the General Population Without IBD/CVD

	IBD N = 57,121	CVD N = 159,930	General Population Without IBD/CVD N = 5,518,753
No AKI			
Unweighted frequency	49,718	135,980	4,846,362
Weighted frequency	248,590	679,900	24,231,817
Percent	87%	85%	87.8%
All AKI			
Unweighted frequency	7,403	23,950	672,391
Weighted frequency	37,015	119,750	3,361,956
Percent	13%	15%	12.2%
AKI not requiring dialysis			
Unweighted frequency	7,170	23,253	653,439
Weighted frequency	35,850	116,265	3,267,196
Percent	12.6%	14.5%	11.8%
AKI requiring dialysis			
Unweighted frequency	233	697	18,952
Weighted frequency	1,165	3,485	94,760
Percent	0.40%	0.44%	0.34%

Abbreviations: AKI, acute kidney injury; CVD, collagen vascular disease; IBD, inflammatory bowel disease.

could be secondary to different study designs, comparative groups, confounding factors, and ancestral backgrounds.

We found an unexpected higher prevalence of AKI among IBD hospitalizations than collagen vascular disease hospitalizations after adjusting for multiple confounders, possibly because of multitude of risk factors for AKI among IBD hospitalizations, particularly hypovolemia-associated tubular injury, sepsis, and surgeries.

AKI is likely to be the most prevalent form of kidney involvement among patients with IBD secondary to tubular injury related to hypovolemia during IBD disease exacerbation, glomerular-tubular diseases, and drug toxicity. Our study did not evaluate the underlying cause of AKI because of lack of disease-specific, validated ICD-9-CM codes.

Primarily, immunoglobulin Anephropathy, tubulointerstitial nephritis, and arterionephrosclerosis are the predominant histologic variants described in patients with IBD who present with hematuria and/or proteinuria, with or without kidney injury.[19] Interstitial nephritis may occur secondary to a hypersentivity reaction to many different medications including 5-amino salicylic acid derivatives, but also may be evident in treatment-naïve patients with IBD, suggestive of a possible shared immunopathogenesis.[2,20-23] Genetic predisposition, translocation of proinflammatory and GdA1-secreting plasma cells from gut to circulation, and gut inflammatory state are some of the mechanisms that have been cited for the possible association between immunoglobulin A nephropathy and IBD.[24,25]

Table 5. Odds Ratios and 95% Confidence Intervals of Developing AKI in Hospitalized Patients With IBD Compared to Hospitalized General Population Without IBD/CVD and Those With CVD

	IBD vs CVD OR (95% CI)	IBD vs General Population OR (95% CI)
Binomial logistic regression: unadjusted (discharge weights only)		
AKI vs no AKI	0.85 (0.82, 0.87)	1.07 (1.04, 1.10)
Binomial logistic regression: adjusted (IPTWs and discharge weights)[a]		
AKI vs no AKI	1.32 (1.27, 1.38)	1.27 (1.23, 1.31)
Multinomial logistic regression: unadjusted (discharge weights only)		
AKI requiring dialysis vs no AKI	0.91 (0.78, 1.07)	1.20 (1.05, 1.37)
AKI not requiring dialysis vs no AKI	0.84 (0.82, 0.87)	1.07 (1.04, 1.10)
Multinomial logistic regression: adjusted (IPTWs and discharge weights)[a]		
AKI requiring dialysis vs no AKI	1.59 (1.31, 1.94)	1.45 (1.25, 1.68)
AKI not requiring dialysis vs no AKI	1.31 (1.26, 1.37)	1.27 (1.27, 1.31)

Abbreviations: AKI, acute kidney injury; CI, confidence interval; CVD, collagen vascular disease; IBD, inflammatory bowel disease; IPTW, inverse probability of treatment weighting; OR, odds ratio.
[a]Adjusted for demographics, hospital characteristics, hypertension, Charlson Comorbidity Index, contrast, obesity, and tobacco use, and weighted by the product of IPTWs and discharge weights.

Moreover, Rehnberg et al[26] reported a cumulative end-stage kidney disease incidence of 50% in patients with immunoglobulin A nephropathy and IBD compared with 1.5% in patients with IBD without immunoglobulin A nephropathy. Secondary amyloidosis because of deposition of amyloid fibrils is a rare manifestation in patients with IBD, while the prevalence of nephrolithiasis, particularly oxalate and uric acid stones, is much higher in patients with IBD than in the general population.[20]

There are some limitations of our study. Although the ICD-9-CM codes for AKI and AKI requiring dialysis have been previously validated, patients with AKI as a primary diagnosis may not be coded for IBD or collagen vascular diseases as their secondary diagnosis, thus resulting in underreporting. Additionally, the cross-sectional analysis, where both the exposure and outcome were assessed simultaneously, limits causal inference. Furthermore, misclassification of both the exposure and outcome may have occurred; as long as it is nondifferential, it would bias the results toward the null. The NIS data capture only in-hospital stays, and therefore, milder forms of AKI managed in outpatient settings were not included. Finally, the NIS data set lacked reporting of medications.

In conclusion, we show that the prevalence and risk of AKI among hospitalizations with IBD is higher than hospitalizations in the collagen vascular disease and general population groups. Future multicenter longitudinal studies are required to confirm our findings and evaluate the renal outcome.

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