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The primary aim of the *World Journal of Gastrointestinal Pathophysiology* (*WJGP*, *World J Gastrointest Pathophysiol*) is to provide scholars and readers from various fields of gastrointestinal pathophysiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGP mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal pathophysiology and covering a wide range of topics including disorders of the esophagus, stomach and duodenum, small intestines, pancreas, biliary system, and liver.

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ORIGINAL ARTICLE

Retrospective Study

Sepsis during short bowel syndrome hospitalizations: Identifying trends, disparities, and clinical outcomes in the United States

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Abstract

BACKGROUND

Short bowel syndrome (SBS) hospitalizations are often complicated with sepsis. There is a significant paucity of data on adult SBS hospitalizations in the United States and across the globe.

AIM

To assess trends and outcomes of SBS hospitalizations complicated by sepsis in the United States.

METHODS

The National Inpatient Sample was utilized to identify all adult SBS hospitalizations between 2005-2014. The study cohort was further divided based on the presence or absence of sepsis. Trends were identified, and hospitalization characteristics and clinical outcomes were compared. Predictors of mortality for SBS hospitalizations complicated with sepsis were assessed.

RESULTS

Of 247097 SBS hospitalizations, 21.7% were complicated by sepsis. Septic SBS hospitalizations had a rising trend of hospitalizations from 20.8% in 2005 to 23.5% in 2014 (P trend < 0.0001). Compared to non-septic SBS hospitalizations, septic SBS hospitalizations had a higher proportion of males (32.8% *vs* 29.3%, P < 0.0001), patients in the 35-49 (45.9% *vs* 42.5%, P < 0.0001) and 50-64 (32.1% *vs* 31.1%, P < 0.0001) age groups, and ethnic minorities, *i.e.*, Blacks (12.4% *vs* 11.3%, P < 0.0001) and Hispanics (6.7% *vs* 5.5%, P < 0.0001). Furthermore, septic SBS hospitalizations had a higher proportion of patients with intestinal transplantation (0.33% *vs* 0.22%, P < 0.0001), inpatient mortality (8.5% *vs* 1.4%, P < 0.0001), and mean length of stay (16.1 d *vs* 7.7 d, P < 0.0001) compared to the non-sepsis cohort. A younger age, female gender, White race, and presence of comorbidities such as anemia and depression were identified to be independent predictors of inpatient mortality for septic SBS hospitalizations.

CONCLUSION

Septic SBS hospitalizations had a rising trend between 2005-2014 and were associated with higher inpatient mortality compared to non-septic SBS hospitalizations.

Key Words: Short bowel syndrome; Sepsis; Outcomes; Mortality; Trends

Core Tip: Short bowel syndrome (SBS) is a well-known complication of small bowel surgical resection. Sepsis is a well-documented complication of SBS, particularly in infants and children. However, there is limited data on adult SBS hospitalizations complicated by sepsis in the United States. In this study, we noted that about one-fifth of SBS hospitalizations were complicated by sepsis. There was a higher proportion of men, individuals in the 35-64 age group, and ethnic minorities (Blacks and Hispanics) in the septic SBS cohort compared to the non-sepsis cohort. Septic SBS hospitalizations also had a higher length of stay and inpatient mortality compared to the non-sepsis cohort. Furthermore, younger age, female gender, White race, anemia, and depression were identified to be independent predictors of inpatient mortality for septic SBS hospitalizations.

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INTRODUCTION

Short bowel syndrome (SBS) is a well-known complication of surgical resection of the small bowel[1]. Nonsurgical causes include inflammatory bowel disease, cancer of the intestine, or ischemic and hemorrhagic vascular diseases of the gut[1,2]. Sepsis is a well-documented complication of SBS in infants and children, and these recurrent bloodstream infections (BSI) have been associated with higher rates of childhood morbidity and mortality[3,4]. The primary pathophysiologic mechanism implicated in the development of BSI is bacterial translocation from the gut to the bloodstream during enteral

feeding in children with SBS[5].

Most patients with SBS derive their nutrition *via* parenteral routes using indwelling venous catheters. Hence, these patients are at a greater-than-average risk of BSI from skin flora, especially if the indwelling catheter has been placed for a prolonged duration[4]. Moreover, parenteral nutrition leads to the impairment of immunological barriers (altered inflammatory responses) and physical barriers (secondary to villous atrophy) which may increase the risk of small bowel bacterial overgrowth (SBBO)[4,6].

SBS has established itself to be one of the strongest predictors of BSI in the pediatric population. However, there is a significant paucity of data on adult SBS hospitalizations complicated by sepsis, both in the United States and across the globe. Hence, this study was designed to investigate trends, hospitalization characteristics, predictors, racial disparities of Elixhauser co-morbidities, and gender disparities of Elixhauser co-morbidities for septic SBS hospitalizations in the United States. Furthermore, we also performed a comparative analysis for trends, hospitalization characteristics, and predictors between septic SBS and non-septic SBS hospitalizations.

MATERIALS AND METHODS

Data source

The National Inpatient Sample (NIS) is the largest, publicly available, multi-ethnic, all-payer inpatient database which is a part of the healthcare cost and utilization project (HCUP)[7,8]. HCUP is a family of healthcare databases and related software tools developed through a unique Federal-State-Industry partnership and sponsored by the Agency for Healthcare Research and Quality[9]. The NIS, when weighted, estimates more than 35 million hospitalizations nationally [7]. HCUP databases are limited data sets, which can be used to generate United States regional and national estimates[7].

Study population, design, and outcomes

We used the International Classification of Diseases, Clinical Modification (ICD-9-CM) codes to identify all adults (≥ 18 years of age) with SBS from the NIS database for the 2005-2014 period. The precedence of utilization of ICD-9-CM codes for SBS hospitalizations has already been established in previous studies[10,11]. Individuals < 18 years of age were excluded from the analysis. This study population was further divided based on the presence and absence of sepsis using the Clinical Classification Software diagnosis code "2", which has been used previously in multiple NIS-based studies[12, 13]. We then compared hospitalization characteristics (age, race, and gender), hospital-level characteristics (bed size, location, and admission type), and clinical outcomes [length of stay (LOS), all-cause inpatient mortality, and disposition status] between septic and non-septic SBS hospitalizations. Furthermore, the rates of comorbidities were calculated using Elixhauser Comorbidity Index codes provided by HCUP[14].

Statistical analysis

Statistical Analysis Software 9.3 (SAS Institute, Cary, NC, United States) was used for univariate and multivariate analyses. We used weighted values provided by HCUP to produce nationally representative estimates for all variables [15]. Categorical variables like gender, race, and comorbidities were compared using the Chi-squared (χ^2) test, and continuous variables like age and LOS were compared using the Wilcoxon rank-sum test. We also created a multivariate logistic regression model to determine predictors of inpatient mortality for SBS hospitalizations complicated by sepsis. P value ≤ 0.05 was considered statistically significant.

Ethical considerations

A review by our institutional review board was not required as the NIS database is Health Insurance Portability and Accountability Act protected and does not contain identifiable patient and hospital-level data[10].

RESULTS

Trends of septic SBS hospitalizations

Between 2005-2014, there were 247097 adult SBS hospitalizations in the United States. Of these, 53550 (21.7%) were complicated by sepsis. We noted a rising trend of SBS hospitalizations complicated by sepsis from 20.8% in 2005 to 23.5% in 2014 (P < 0.0001) (Table 1).

Hospitalization characteristics and clinical outcomes

Compared to non-septic SBS hospitalizations, septic SBS hospitalizations had a higher proportion of males (32.8% *vs* 29.3%, P < 0.0001), and patients in the 35-49 (45.9% *vs* 42.5%, P < 0.0001), and 50-64 (32.1% *vs* 31.1%, P < 0.0001) age groups. However, within the septic SBS cohort, a female predominance was noted (Table 2).

Racial disparities were also prevalent as we noted a higher proportion of ethnic minorities such as Blacks (12.4% *vs* 11.3%, P < 0.0001) and Hispanics (6.7% *vs* 5.5%, P < 0.0001) in the septic SBS cohort, while there was a higher proportion of Whites (80.0% *vs* 77.3%, P < 0.0001) in the non-septic cohort (Table 2).

From a hospital perspective, large (69.4% *vs* 64.6%, P < 0.0001), urban teaching (57.3% *vs* 51.8%, P < 0.0001) hospitals had a higher proportion of septic SBS hospitalizations compared to the non-septic cohort. Furthermore, there was a

Table 1 Trends for short bowel syndrome hospitalizations and septic short bowel syndrome hospitalizations in the United States from 2005-2014

Years	Short bowel syndrome hospitalizations	Septic short bowel syndrome hospitalizations	% of sepsis in short bowel syndrome hospitalizations
2005	4199	20198	20.8
2006	3908	20206	19.3
2007	4083	20206	20.2
2008	5762	26411	21.8
2009	5869	25810	22.7
2010	5640	25423	22.2
2011	5805	27647	21.0
2012	5780	27015	21.4
2013	6105	26900	22.7
2014	6400	27280	23.5
Total	53550	247097	21.7

higher proportion of emergent or urgent (19.3 *vs* 18.9%, $P < 0.0001$) septic SBS hospitalizations compared to the non-septic SBS cohort (Table 2).

The all-cause inpatient mortality was significantly higher for septic SBS hospitalizations (8.5% *vs* 1.4%, $P < 0.0001$) compared to the non-sepsis cohort. Additionally, we noted a longer mean LOS for septic SBS hospitalizations (16.1 d ± 0.4 d *vs* 7.7 d ± 0.1 d, $P < 0.0001$) compared to the non-septic cohort (Table 2).

Predictors of inpatient mortality for septic SBS hospitalizations

For septic SBS hospitalizations, the 18-44 age group had a 5.85 times higher risk of inpatient mortality compared to the ≥ 85 age group [odds ratio (OR): 5.85; 95% confidence interval (95%CI): 3.95-8.66, $P < 0.0001$; Table 3]. Hence, the risk of inpatient mortality decreased with increasing age. Additionally, women had a higher risk of inpatient mortality as compared to men (OR: 1.18; 95%CI: 1.02-1.38, $P = 0.03$). Race was also identified to be an independent predictor of all-cause inpatient mortality. Whites were noted to have a higher mortality risk (OR: 1.65; 95%CI: 1.17-2.33, $P = 0.005$) compared to other races. Furthermore, the presence of comorbidities such as deficiency anemias and depression were associated with a significantly higher risk of inpatient mortality for septic SBS hospitalizations (Table 3).

Intestinal transplantation and septic SBS hospitalizations

We noted a higher proportion of patients who had transplant of the intestine (TOI) for septic SBS hospitalizations (0.33% *vs* 0.22%, $P < 0.0001$) compared to the non-septic cohort (Table 1). However, due to limitations of the NIS database, we were unable to ascertain whether these hospitalizations took place within a year of undergoing TOI or later.

Racial disparities in exhauster comorbidities for septic SBS hospitalizations

A significantly higher proportion of septic SBS hospitalizations for Whites had comorbidities such as congestive heart failure, chronic pulmonary diseases, hypothyroidism, depression, and other psychiatric disorders (Table 4). Meanwhile, Blacks had significantly higher rates of comorbidities such as deficiency anemias, drug abuse, hypertension, obesity, and renal failure. Furthermore, Hispanics had the highest rates of comorbidities like coagulopathy, uncomplicated diabetes, and liver disease (Table 4).

Gender disparities in exhauster comorbidities for septic SBS hospitalizations

Septic SBS hospitalizations for women were noted to have higher rates of comorbidities such as deficiency anemias, depression, rheumatic disorders, chronic pulmonary disease, hypothyroidism, and obesity; however, men had higher rates of diabetes, drug abuse, liver disease, and renal failure (Table 5).

DISCUSSION

After surgical resection of the bowel in adults, there is a significant alteration of the nutritional, fluid, and electrolyte homeostasis, along with significant changes in the gut microbiome. These changes may lead to malabsorptive diarrhea, micronutrient deficiency, malnutrition, and SBBO[16]. Disruption of the intestinal microbiome seen in patients with SBBO impacts the production of antimicrobial peptides and immunomodulatory cells[17]. Furthermore, commensal bacteria dysbiosis may disrupt intestinal permeability leading to bacterial translocation in surrounding areas, thereby increasing

Table 2 Baseline hospitalization characteristics and clinical outcomes for septic and non-septic short bowel syndrome hospitalizations in the United States from 2005-2014

Variable	Non-septic short bowel syndrome hospitalizations	%	Septic short bowel syndrome hospitalizations	%	*P* value
Number of obs. (*n*)	193547	78.30	53550	21.70	
Age, yr (mean ± SE)	58.0 ± 0.3	-	57.9 ± 0.2	-	
Age, yr					< 0.0001
18-34	41979	21.70	10000	18.70	
35-49	82308	42.50	24561	45.90	
50-64	60113	31.10	17333	32.40	
≥ 65	9149	4.70	1655	3.10	
Gender					< 0.0001
Male	56601	29.30	17545	32.80	
Female	136916	70.80	36005	67.20	
Race					< 0.0001
White	130004	80.00	35660	77.30	
Black	18436	11.30	5730	12.40	
Hispanic	8866	5.50	3091	6.70	
Others	5274	3.20	1651	3.60	
Hospital location					< 0.0001
Rural	22155	11.50	4576	8.60	
Urban nonteaching	70692	36.70	18187	34.10	
Urban teaching	99780	51.80	30509	57.30	
Hospital bed size					< 0.0001
Small	22978	11.90	5107	9.60	
Medium	45289	23.50	11219	21.10	
Large	124360	64.60	36946	69.40	
Admission type					0.0100
Elective	157070	81.20	43201	80.70	
Emergent or Urgent	36477	18.90	10349	19.30	
Intestinal Transplant	430	0.22	178	0.33	< 0.0001
Disposition status					< 0.0001
Home	156802	81.10	34439	64.40	
Facility	33898	17.50	14497	27.10	
Inpatient mortality	2724	1.40	4537	8.50	< 0.0001
LOS, d (mean ± SE)	7.7 ± 0.1	-	16.1 ± 0.4	-	< 0.0001

LOS: Length of stay.

the risk of sepsis[17]. Despite known alteration of the intestine, current literature lacks data to support the routine use of antibiotics in SBS patients to prevent inflammatory gut changes[16]. Management for these patients is primarily focused on nutrition. However, patients with SBS who rely on parenteral nutrition are at increased risk of sepsis from catheter-associated infections, leading to increased hospitalizations[16]. This finding was highlighted in our study as we noted a rising trend of septic SBS hospitalizations from 20.8% in 2005 to 23.5% in 2014.

The utilization of prebiotics, probiotics, or antibiotics in SBS patients is controversial[16]. Intestinal transplantation is indicated in SBS patients with recurrent sepsis or those who are unable to receive total parenteral nutrition due to end-stage liver disease or end-stage loss of venous access[18]. Intestinal transplant significantly improves intestinal transit

Table 3 Predictors of mortality for septic short bowel syndrome hospitalizations in the United States from 2005-2014

Characteristics/co-morbidities	Odds ratio (95% confidence interval)	*P* value
Age (yr)		
18-44	5.85 (3.95-8.66)	< 0.0001
45-64	3.30 (2.37-4.59)	< 0.0001
65-84	1.75 (1.27-2.41)	0.001
≥ 85	Reference	
Gender		
Male	Reference	
Female	1.18 (1.02-1.38)	0.030
Race		
White	1.65 (1.17-2.33)	0.005
Black	1.28 (0.86-1.90)	0.220
Hispanic	1.22 (0.79-1.88)	0.360
Others	Reference	
Hospital bed size		
Small	1.16 (0.90-1.51)	0.250
Medium	1.10 (0.92-1.31)	0.320
Large	Reference	
Hospital type		
Rural	1.05 (0.79-1.38)	0.360
Urban non-teaching	0.94 (0.80-1.10)	0.420
Teaching	Reference	
Median household income		
Quartile 1	Reference	
Quartile 2	0.96 (0.78-1.18)	0.690
Quartile 3	1.03 (0.83-1.27)	0.800
Quartile 4	1.18 (0.94-1.47)	0.150
Co-morbidities		
Deficiency anemias	1.58 (1.35-1.85)	< 0.0001
Rheumatic disorders	1.20 (0.80-1.79)	0.380
Depression	1.66 (1.30-2.13)	< 0.0001
Drug abuse	1.51 (0.95-2.40)	0.090
Hypertension	1.16 (0.98-1.36)	0.080
Hypothyroidism	1.06 (0.83-1.34)	0.650
Lymphoma	2.48 (0.99-6.21)	0.050
Valvular disease	1.02 (0.73-1.41)	0.920

time, peristalsis, and the absorptive functions of the gut[19]. However, like any transplant, post-operative care for these patients requires lifelong immunosuppression, which imminently increases the risk for subsequent infections and sepsis. Expectedly, in our study, we noted a higher proportion of patients who had TOI in septic SBS hospitalizations compared to the non-sepsis cohort (Table 1).

Traditionally, sepsis tends to affect the elderly. However, a multicenter longitudinal cohort study in California from 2008-2015 noted that the highest overall increase in rates of sepsis and severe sepsis were for patients 18-44 years of age [20]. Although there were higher incidence rates of sepsis in the elderly, there was a notable increase in the relative risk of sepsis among young adults[20]. This was consistent with the findings in our study. In the septic SBS cohort, the 35-49 age

Table 4 Racial distribution of Elixhauser co-morbidities for septic short bowel syndrome hospitalizations in the United States from 2005-2014

Elixhauser co-morbidity	Whites	Blacks	Hispanics	Others	*P* value
Acquired immunodeficiency syndrome	0.0	1.0	0.3	0.0	< 0.0001
Alcohol abuse	1.6	2.4	0.8	1.4	< 0.0001
Deficiency anemias	38.8	49.0	45.4	37.6	< 0.0001
Rheumatic disorders	4.3	4.1	2.9	4.0	0.0040
Chronic blood loss anemia	2.1	2.1	2.3	3.2	0.0200
Congestive heart failure	11.2	10.8	8.6	9.8	< 0.0001
Chronic pulmonary disease	19.7	14.6	10.6	18.4	< 0.0001
Coagulopathy	15.4	16.9	19.1	16.9	< 0.0001
Depression	18.0	10.9	14.2	11.5	< 0.0001
Uncomplicated diabetes	11.4	14.4	17.7	17.0	< 0.0001
Diabetes with chronic complications	2.8	5.8	5.4	5.0	< 0.0001
Drug abuse	4.8	6.6	4.4	5.0	< 0.0001
Hypertension	32.4	42.5	34.5	34.6	< 0.0001
Hypothyroidism	13.5	10.4	8.8	8.6	< 0.0001
Liver disease	5.8	7.0	9.9	6.9	< 0.0001
Lymphoma	1.1	1.1	1.2	0.9	0.7500
Fluid and electrolyte disorders	57.5	62.5	61.2	58.2	< 0.0001
Metastatic cancer	4.5	4.4	5.2	8.6	< 0.0001
Neurological disorders	8.8	8.3	6.7	7.9	0.001
Obesity	5.6	6.3	5.7	6.9	0.0300
Paralysis	2.3	3.3	4.2	4.9	< 0.0001
Peripheral vascular disorders	6.8	7.4	7.0	6.5	0.4300
Psychiatric disorder	6.1	5.5	5.6	4.1	0.0030
Pulmonary circulation disorders	4.0	5.5	2.3	3.4	< 0.0001
Renal failure	21.2	30.7	16.7	18.8	< 0.0001
Solid tumor without metastasis	2.6	2.8	2.9	5.2	< 0.0001
Peptic ulcer disease excluding bleeding	0.1	0.1	0.1	0.0	0.3400
Valvular disease	5.2	4.8	3.8	5.3	0.0050
Weight loss	40.4	40.9	39.3	47.9	< 0.0001

group had the highest proportion of patients, while the ≥ 65 age group had the lowest proportion of patients (Table 2). On comparative analysis, septic SBS hospitalizations had a higher proportion of patients between the ages of 35-64 compared to the non-septic cohort. The exact reasons for the higher hospitalization rates of septic SBS younger patients are currently unknown, but may, in part, be due to a greater degree of awareness of sepsis in this subset population prompting them to seek immediate care or due to complications from comorbidities not previously common in this age group[20]. Nonetheless, additional prospective studies are needed to further investigate these findings.

A prospective observational cohort study of critically ill patients from 2011-2014 showed similar rates of sepsis and mortality between men and women[21]. However, there was a greater degree of endothelial cell activation in young women compared to men[21]. Increased gut permeability, often seen in patients with SBS, coupled with increased endothelial disruption of the vasculature may lead to the transportation of antigens and commensal gut microbiota from the intestine to the blood, making females even more prone to sepsis[22]. The findings of our study aligned with this current literature as females made up more than two-thirds of the total septic SBS hospitalizations in the United States.

The study by Siddiqui *et al*[2] reported that Whites made up 78% of all SBS hospitalizations in the United States. We report similar findings as septic SBS hospitalizations had a higher proportion of Whites (77.3%) compared to other ethnic minorities such as Blacks or Hispanics (Table 2). However, on comparative analysis, septic SBS hospitalizations had a higher proportion of Blacks (12.4% *vs* 11.3%, $P < 0.0001$) and Hispanics (6.7% *vs* 5.5%, $P < 0.0001$) compared to the non-

Table 5 Gender distribution of elixhauser co-morbidities for septic short bowel syndrome hospitalizations in the United States from 2005-2014

Elixhauser co-morbidity	Male	Female	*P* value
Acquired immunodeficiency syndrome	0.3	0.1	< 0.0001
Alcohol abuse	2.9	1.0	< 0.0001
Deficiency anemias	36.8	39.7	< 0.0001
Rheumatic disorders	2.0	5.1	< 0.0001
Chronic blood loss anemia	1.9	2.1	0.0800
Congestive heart failure	10.7	10.8	0.9000
Chronic pulmonary disease	16.7	19.0	< 0.0001
Coagulopathy	16.8	15.0	< 0.0001
Depression	12.4	18.1	< 0.0001
Uncomplicated diabetes	12.6	11.6	0.0010
Diabetes with chronic complications	3.9	2.7	< 0.0001
Drug abuse	5.1	4.5	0.0010
Hypertension	33.6	32.1	0.0010
Hypothyroidism	6.0	14.9	< 0.0001
Liver disease	7.4	5.3	< 0.0001
Lymphoma	1.4	0.9	< 0.0001
Fluid and electrolyte disorders	56.6	57.9	0.0030
Metastatic cancer	4.9	4.4	0.0020
Neurological disorders	7.0	8.8	< 0.0001
Obesity	3.8	6.4	< 0.0001
Paralysis	3.5	2.1	< 0.0001
Peripheral vascular disorders	8.1	5.9	< 0.0001
Psychiatric disorder	4.7	6.3	< 0.0001
Pulmonary circulation disorders	4.2	3.8	0.0400
Renal failure	26.3	18.8	< 0.0001
Solid tumor without metastasis	2.6	2.7	0.5900
Peptic ulcer disease excluding bleeding	0.0	0.1	< 0.0001
Valvular disease	5.2	4.7	0.0100
Weight loss	39.1	40.9	< 0.0001

septic cohort. This may, in part, be due to lack of healthcare facilities, and awareness about SBS among ethnic minorities leading to a progression of their disease and further complications by sepsis. Hence, we advocate for the need for urgent interventions to improve healthcare access, increase awareness about sepsis in SBS, and improve outpatient follow-up for these high-risk populations.

The all-cause inpatient mortality for SBS hospitalizations was found to be 1.4%. However, when these hospitalizations were complicated by sepsis, the all-cause inpatient mortality increased to 8.5%. This was in line with current literature which reports increased inpatient mortality for septic SBS hospitalizations[2]. Moreover, the presence of a greater number of comorbidities is also associated with higher rates of mortality in patients with sepsis[23]. A cohort study evaluating adult sepsis survivors identified age, sex, race, severe comorbidities, and site of initial infection to be long-term risk factors for mortality[24]. Similarly, in our study, independent risk factors that increased inpatient mortality for septic SBS hospitalizations are as follows.

Age

In our study, the risk of inpatient mortality was almost six times higher in the 18-44 age group compared to individuals ≥ 85 years of age. In 2013, a Quality and Cost of Primary Care study reported that younger patients were more likely to visit a healthcare provider for both mental and physical health conditions compared to the elderly population[25]. The

increased health awareness, highly accurate provider evaluation in younger adults without non-specific baseline symptoms, and presence of additional comorbidities which were previously not common in this age group may have led to increased diagnosis and associated inpatient mortality.

Gender

In 2011, a prospective clinical trial of intensive care unit patients reported that females with sepsis had higher mortality rates than males with sepsis[26]. Another study by Wilcox *et al*[27] noted similar gender outcomes. Similarly, in our study, septic SBS female patients had higher rates of all-cause inpatient mortality compared to males. Furthermore, we noted higher rates of deficiency anemias and depression in females compared to males, which was also independently associated with higher mortality rates in septic SBS hospitalizations.

Race

We noted that White septic SBS hospitalizations had a 1.65 times greater risk of inpatient mortality compared to other races. A study of Caucasians with acute respiratory distress syndrome (ARDS) secondary to pneumonia evaluated the FER rs4957796 TT genotype as a means of determining 90-d mortality risk[28]. Although this study specifically assessed ARDS patients and their survival in the setting of pneumonia, interestingly the FER gene is known to play a key role in the regulation of intestinal barrier function[29]. White septic SBS hospitalizations may have a higher mortality risk due to the absence of FER protein which may exacerbate intestinal dysfunction and increase bacterial translocation into the bloodstream leading to a greater severity of sepsis. However, additional prospective studies are needed to further validate our findings.

Comorbidities

In our study, deficiency anemias and depression were found to coincide with significantly greater mortality risk in septic SBS hospitalizations. Deficiency anemias are highly prevalent in SBS patients due to altered anatomy[30-33]. In septic SBS hospitalizations, deficiency anemia can negatively impact the host's defense and immunomodulatory response, increasing the severity of sepsis and overall mortality risk. Furthermore, severe depression has a known association with increased BSI, leading to sepsis and higher mortality rates[34,35]. Depression ultimately leads to decreased immune function and disruption of the brain-gut-microbiome axis, which may increase the host's risk for sepsis and adverse clinical outcomes.

Limitations

A key strength of this study is the study population which has been derived from one of the biggest, national, diverse, multi-ethnic databases in the United States. Through our analysis over 10 years, we are able to provide meaningful information on the trends of septic SBS hospitalizations. Furthermore, we also perform a unique comparative analysis between septic and non-septic SBS hospitalizations and identify predictors of inpatient mortality for septic SBS hospitalizations to give gastroenterologists real-world data on the patients at the highest risk of adverse clinical outcomes. However, we do acknowledge all the limitations associated with our study. We were unable to perform a detailed analysis after the 2014 study period as the NIS changed from ICD-9-CM to ICD-10-CM coding at the beginning of October 1, 2015. Converting ICD-9 to ICD-10 is an extremely challenging process as there are differences in the structure and granularity of codes. Hence, it would be impossible to find the exact matches for the codes with a high level of confidence Additionally, the NIS database lacks information on the time from hospitalization to diagnosis of sepsis, hospital course, treatment aspects, inpatient procedures, and pharmacological aspects of management. Lastly, the NIS is an administrative database. Therefore, the possibility of coding errors cannot be excluded. Despite these limitations, we believe that our study helps fill the current knowledge gaps for SBS hospitalizations complicated by sepsis in the US as this entity has not been studied extensively. We hope that the findings of our study can serve as a foundation for future prospective studies and randomized controlled trials.

CONCLUSION

In conclusion, SBS is a well-known complication of surgical resection of the intestine. Due to their dependence on parenteral nutrition using indwelling venous catheters, these patients are at increased risk of BSI and sepsis from bacterial translocation from the gut to the bloodstream during enteral feeding. In the United States from 2005-2014, we noted a rising trend of septic SBS hospitalizations with a significant female predominance. Compared to the non-septic cohort, septic SBS hospitalizations had a higher proportion of patients with TOI, higher all-cause inpatient mortality, and longer mean LOS. Independent predictors of mortality for septic SBS hospitalizations included White race, female gender, younger age, and those with associated comorbidities such as deficiency anemias and depression.

FOOTNOTES

Author contributions: Dahiya DS, Wachala J, Solanki S, and Jafri SM contributed to the conception and design; Dahiya DS, Solanki S, Kichloo A, and Jafri SM contributed to the administrative support; Dahiya DS, Wachala J, Solanki S, Solanki D, Kichloo A, Holcomb S, Mansuri U, Haq KS, Ali H, Gangwani MK, and Shah YR contributed to the provision, collection, and assembly of data; Dahiya DS,

Wachala J, Solanki S, Solanki D, Kichloo A, Holcomb S, Mansuri U, Haq KS, Ali H, Gangwani MK, Shah YR, Varghese T, Khan HMA, Horslen S, Schiano TD, and Jafri SM contributed to the review of literature and drafting the manuscript; Dahiya DS, Wachala J, Solanki S, Solanki D, Kichloo A, Holcomb S, Mansuri U, Haq KS, Ali H, Gangwani MK, Shah YR, Varghese T, Khan HMA, Horslen S, Schiano TD, and Jafri SM contributed to the revision of key components of the manuscript and final approval of manuscript; Dahiya DS, Wachala J, Solanki S, Solanki D, Kichloo A, Holcomb S, Mansuri U, Haq KS, Ali H, Gangwani MK, Shah YR, Varghese T, Khan HMA, Horslen S, Schiano TD, and Jafri SM are accountable for all aspects of the work.

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