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Paralytic ileus in the United States: A cross-sectional study from the national inpatient sample

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Abstract

Introduction: Paralytic ileus is a common clinical condition leading to significant morbidity and mortality. Most studies to date have focused on postoperative ileus, a common but not exclusive cause of the condition. There are limited epidemiological data regarding the incidence and impact of paralytic ileus and its relationship to other clinical conditions. In this cross-sectional study, we analyzed national inpatient hospitalization trends, demographic variation, cost of care, length of stay, and mortality for paralytic ileus hospitalizations as a whole.

Methods: The National Inpatient Sample database was used to identify all hospitalizations with the diagnosis of paralytic ileus (International Classification of Diseases, 9th Revision code 560.1) as primary or secondary diagnosis during the period from 2001 to 2011. Statistical analysis was performed using Cochran–Armitage trend test, Wilcoxon rank sum test, and Poisson regression.

Results: In 2001, there were 362,561 hospitalizations with the diagnosis of paralytic ileus as compared to 470,110 in 2011 ($p < 0.0001$). The age group 65–79 years was most commonly affected by paralytic ileus throughout the study period. In-hospital all-cause mortality decreased from 6.03% in 2001 to 5.10% in 2011 ($p < 0.0001$). However, the average cost of care per hospitalization increased from US$19,739 in 2001 to US$26,198 in 2011 (adjusted for inflation, $p < 0.0001$).

Conclusion: There was a significant rise in the number of hospitalizations of paralytic ileus with increased cost of care and reduced all-cause mortality.

Keywords

Paralytic ileus, mortality, cost of disease

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Introduction

Ileus is a common clinical condition characterized by cessation of normal propulsive movements of the gastrointestinal (GI) tract that occurs in the absence of mechanical obstruction and does not typically require operative treatment.[1] It is most common following surgery and is a recognized and anticipated physiologic response to abdominal surgery.[2–4] If self-limited and of relatively short duration (typically 3–5 days), ileus is considered to be a normal physiologic response in this setting.[5] More protracted symptoms and signs of bowel dysfunction are referred to as paralytic or prolonged ileus. Paralytic ileus can also be caused by intra-abdominal infections, peritonitis, and medications such as psychotropic agents, opiates, and anticholinergics or other conditions.[4,6–8] Animal studies have linked bacterial endotoxins to postoperative ileus.[9] Other factors believed to be important in its pathogenesis include endogenously produced opioids as well as hormonal, neurologic, and metabolic factors.[10,11] At present, there are limited epidemiological data regarding the national incidence and impact of paralytic ileus and its relationship to other clinical conditions. Thus, we undertook this study to determine inpatient hospitalization trends, demographic variation, cost of care, length of stay (LOS), comorbidities, and mortality associated with paralytic ileus.

Methods

Source of data

The National Inpatient Sample (NIS) contains a 20% stratified sample of community hospitals in the United States and provides sampling weights to calculate national estimates.[12] This sample size is determined by the Agency for Healthcare Research and Quality (AHRQ) based on their experience with other similar databases.[13] This sample is weighted to obtain national estimates with high accuracy using weights published by Healthcare Cost and Utilization Project (HCUP).[12] Individuals' hospitalizations are de-identified. Each de-identified hospitalization information that includes demographics, comorbidities, LOS, cost of care and outcomes.

Study design

In this cross-sectional study, we identified all the hospitalizations from year 2001 to 2011 with a primary or secondary diagnosis of paralytic ileus using the International Classification of Diseases (ICD), 9th Revision, Clinical Modification, ICD-9 code 560.1. We excluded all hospitalizations with any missing information. There were 37,187,646 total hospitalizations in 2001 out of which 362,561 adult hospitalizations included a diagnosis of paralytic ileus. In 2011, there were 38,590,733 hospitalizations out of which 470,110 hospitalizations carried a diagnosis of paralytic ileus.

Variables and statistical analysis

The frequency of paralytic ileus-related hospitalizations was calculated for each year. We used Cochran–Armitage trend test and Wilcoxon rank sum test to analyze categorical variables and continuous variables, respectively.[14,15] Hospitalizations were stratified by age (18–34, 35–49, 50–64, 65–79, and $\geqslant$80 years), race (Black, White, Hispanic, and Others), sex, bed size (small, medium, and large), hospital region (Northeast, Midwest, South, and West), insurance (Medicare, Medicaid, private insurance, and others), and teaching status of the hospital (urban teaching, urban non-teaching, and rural). NIS publishes the description of these variables and they can be found in Supplemental Material 1.[16] The frequency of paralytic ileus per 100,000 hospitalizations for each categorical variable was calculated by dividing the number of hospitalizations with paralytic ileus by the total hospitalizations for each variable and multiplying the resultant number by 100,000. Assuming that the probability of events, that is, hospitalizations with paralytic ileus, follows a Poisson distribution; we used Poisson regression to calculate relative risk (RR).[17] This methodology has been used in previous NIS-based studies.[18,19] The RRs for each categorical variable depict the ratio of rate of paralytic ileus per 100,000 hospitalizations in 2011 in comparison with rate of paralytic ileus per 100,000 hospitalizations in 2001. We used SAS 9.4 (SAS Institute Inc., Cary, NC, USA) for statistical analyses.

Results

Demographics

The total number of hospitalizations with paralytic ileus increased from 362,561 in 2001 to 470,110 in 2011 (29.7% increase; $p < 0.0001$) (Figures 1(a) and 2). During the same time period, the total number of hospitalizations increased from 37,187,646 in 2001 to 38,590,733 in 2011 (3.77% increase; $p < 0.0001$) (Table 1). The incidence increased from 975 per 100,000 hospitalizations in 2001 to 1218 per 100,000 hospitalizations in 2011 (RR: 1.25; confidence interval (CI): 1.15–1.36; $p < 0.0001$). Between 2001 and 2011, the rate of hospitalization for ileus was highest for the age group 65–79; the overall rate of hospitalization increased from 1445/100,000 hospitalizations in 2001 to 1804/100,000 hospitalizations in 2011 (RR: 1.25; CI: 1.17–1.34; $p < 0.0001$) (Figure 3(a)). The largest increase was in age group 50–64 years (RR: 1.27; CI: 1.18–1.36; $p < 0.0001$) (Table 1). The rate also rose in those over age 80 but did not reach statistical significance (RR: 1.05; CI: 0.98–1.13; $p = 0.2$). Among men, the rate of hospitalization increased from 1118/100,000 hospitalizations in 2001 to 1486/100,000 hospitalizations in 2011 (RR: 1.33; CI: 1.23–1.44; $p < 0.0001$). In women, it increased from 876/100,000 hospitalizations to 1028/100,000 hospitalizations (RR: 1.18; CI: 1.07–1.29; $p = 0.0004$). During the study period, Whites consistently showed the highest rates of ileus of any racial group (2001 and 2011, respectively, 1074/100,000

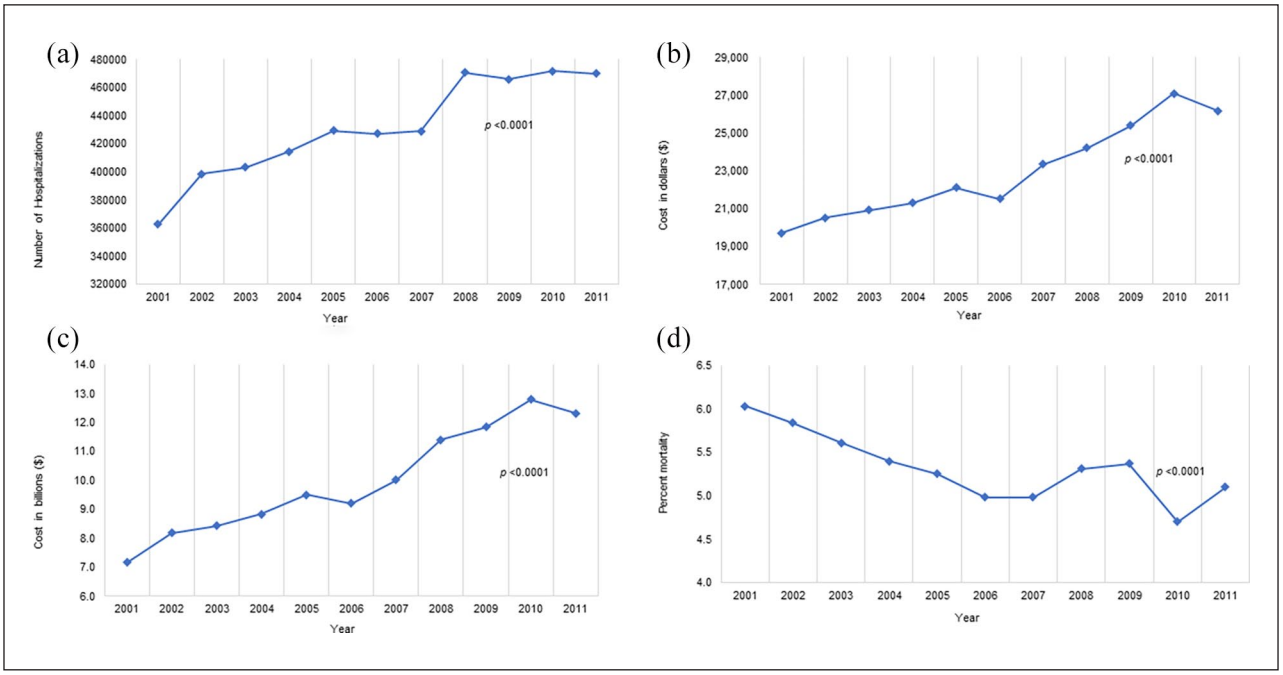

Figure 1. (a) Number of hospitalizations with paralytic ileus, (b) average cost of care for paralytic ileus–related hospitalizations, (c) total annual cost of care for paralytic ileus–related hospitalizations, and (d) all-cause inpatient mortality rate in paralytic ileus hospitalizations.

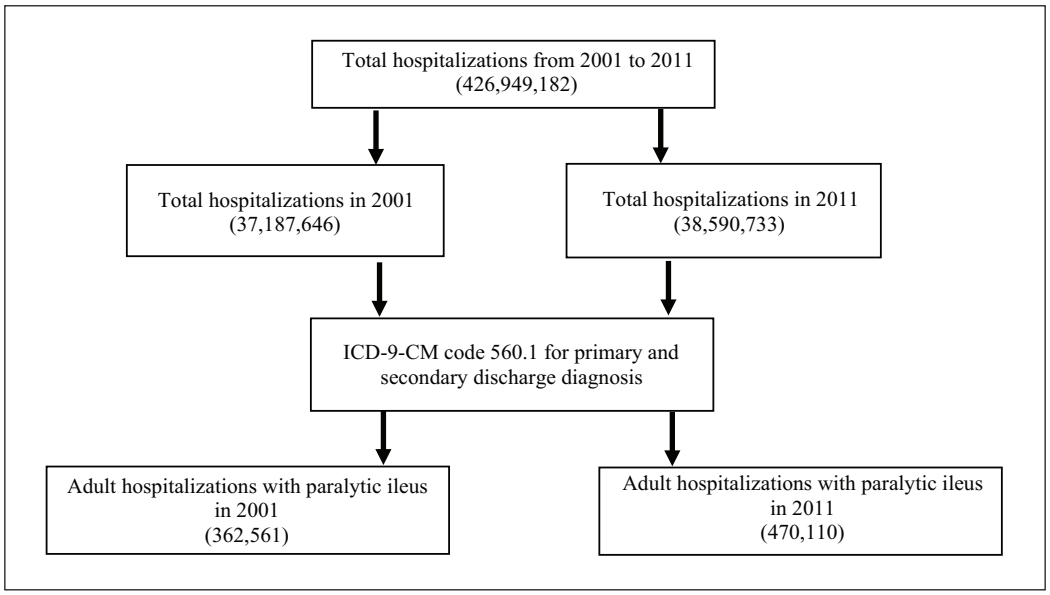

Figure 2. Sequential derivation of study population.

and 1364/100,000 (RR: 1.17; CI: 1.07–1.38; $p < 0.0001$) (Figure 3(b)). Between 2001 and 2011, the percent increase was highest in Hispanics (RR: 1.58; CI: 1.41–1.76; $p < 0.0001$). The percent increase was highest in low-income group (Quartile 1; RR: 1.42; CI: 1.3–1.55; $p < 0.0001$). Among the payment modes, Medicare paid for the highest number of hospitalizations in 2001 (1393/100,000 hospitalizations) and 2011 (1616/100,000 hospitalizations) (RR: 1.16; CI: 1.08–1.25; $p < 0.0001$). Medicaid paid for the least number of hospitalizations but the percent increase from 2001 to 2011 was significant (RR: 1.34; CI: 1.19–1.51; $p < 0.0001$).

Table 1. Frequency, percentage, and incidence of paralytic ileus hospitalizations: 2001 and 2011.

	Paralytic ileus hospitalizations in 2001		Paralytic ileus hospitalizations in 2011		Total hospitalizations in 2001		Total hospitalizations in 2011		Incidence per 100,000 hospitalizations in 2001	Incidence per 100,000 hospitalizations in 2011	Relative risk	Confidence interval		p value
	N	%	N	%	N	%	N	%	N	N				
	362,561	100	470,110	100	37,187,646	100	38,590,733	100	975	1218	1.25	1.15	1.36	<0.0001
Age in years														
18–34	26,197	7.2	33,183	7.1	6,181,760	16.6	6,253,698	16.2	424	531	1.25	1.1	1.42	0.0005
35–49	58,588	16.2	66,954	14.2	5,495,182	14.8	5,091,361	13.2	1066	1315	1.23	1.14	1.34	<0.0001
50–64	75,383	20.8	126,669	26.9	5,837,483	15.7	7,734,701	20	1291	1638	1.27	1.18	1.36	<0.0001
65–79	116,106	32	143,957	30.6	8,032,820	21.6	7,981,389	20.7	1445	1804	1.25	1.17	1.34	<0.0001
⩾80	74,628	20.6	86,364	18.4	5,283,848	14.2	5,835,197	15.1	1412	1480	1.05	0.98	1.13	0.2028
Sex														
Male	169,930	46.9	240,451	51.2	15,200,000	40.9	16,180,000	41.9	1118	1486	1.33	1.23	1.44	<0.0001
Female	192,615	53.1	229,500	48.8	21,980,000	59.1	22,330,000	57.9	876	1028	1.18	1.07	1.29	0.0004
Race														
White	204,057	56.3	313,081	66.6	19,000,000	51.1	22,960,000	59.5	1074	1364	1.27	1.17	1.38	<0.0001
Black	32,262	8.9	57,801	12.3	3,553,290	9.6	5,295,653	13.7	908	1091	1.2	1.1	1.31	<0.0001
Hispanic	17,564	4.8	35,771	7.6	3,322,886	8.9	4,282,784	11.1	529	835	1.58	1.41	1.76	<0.0001
Others	11,075	3.1	20,164	4.3	1,500,957	4	2,225,125	5.8	738	906	1.23	1.11	1.35	<0.0001
Region														
Northeast	53,970	14.9	69,468	14.8	7,408,742	19.9	7,528,258	19.5	728	923	1.27	1.15	1.4	<0.0001
Midwest	85,139	23.5	111,689	23.8	8,658,546	23.3	8,768,800	22.7	983	1274	1.3	1.19	1.41	<0.0001
South	153,028	42.2	199,640	42.5	14,130,000	38	14,800,000	38.4	1083	1349	1.25	1.15	1.35	<0.0001
West	70,424	19.4	89,313	19	6,990,950	18.8	7,490,746	19.4	1007	1192	1.18	1.09	1.29	<0.0001
Location														
Rural	64,450	17.8	55,286	11.8	5,800,650	15.6	4,583,458	11.9	1111	1206	1.09	1	1.18	0.0472
Urban non-teaching	164,672	45.4	195,483	41.6	15,270,000	41.1	15,470,000	40.1	1078	1264	1.17	1.08	1.27	0.0001
Urban teaching	133,438	36.8	212,979	45.3	16,120,000	43.3	18,010,000	46.7	828	1183	1.31	1.19	1.56	0.0001
Median household income														
Quartile 1	20,334	5.6	129,697	27.6	2,462,347	6.6	11,050,000	28.6	826	1174	1.42	1.3	1.55	<0.0001
Quartile 2	86,787	23.9	114,682	24.4	8,687,821	23.4	9,358,627	24.3	999	1225	1.23	1.13	1.33	<0.0001
Quartile 3	95,625	26.4	118,184	25.1	9,632,451	25.9	9,591,091	24.9	993	1232	1.24	1.14	1.35	<0.0001
Quartile 4	155,382	42.9	98,579	21	15,950,000	42.9	7,809,761	20.2	974	1262	1.3	1.19	1.41	<0.0001
Payment														
Medicare	191,214	52.7	247,848	52.7	13,730,000	36.9	15,340,000	39.7	1393	1616	1.16	1.08	1.25	<0.0001
Medicaid	28,758	7.9	45,764	9.7	6,378,286	17.2	7,577,744	19.6	451	604	1.34	1.19	1.51	<0.0001
Private insurance	120,635	33.3	140,791	30	14,120,000	38	12,230,000	31.7	854	1151	1.35	1.23	1.47	<0.0001
Others (includes self-pay)	21,100	5.8	34,179	7.3	2,862,092	7.7	3,334,975	8.6	737	1025	1.39	1.27	1.53	<0.0001
Bed size														
Small	42,637	11.8	61,543	13.1	4,150,678	11.2	4,687,738	12.2	1027	1313	1.28	1.18	1.39	<0.0001
Medium	90,447	25	111,282	23.7	9,884,631	26.6	9,345,705	24.2	915	1191	1.3	1.19	1.42	<0.0001
Large	229,477	63.3	290,922	61.9	23,150,000	62.3	24,030,000	62.3	991	1211	1.22	1.12	1.33	<0.0001
In-hospital Mortality	21,852	6	23,974	5.1	736,018	*	1,596,952	*	2969	1501	0.51	0.48	0.54	<0.0001
Average cost of care (US$)	19,739	#	26,198	#	*	#	*	#	#	#	#	#	#	#
Median LOS (IQ range)	8 (4–12)	#	9 (4–13)	#	*	#	*	#	#	#	#	#	#	#

*Non-contributory data.
#Incalculable data.
LOS: length of stay.

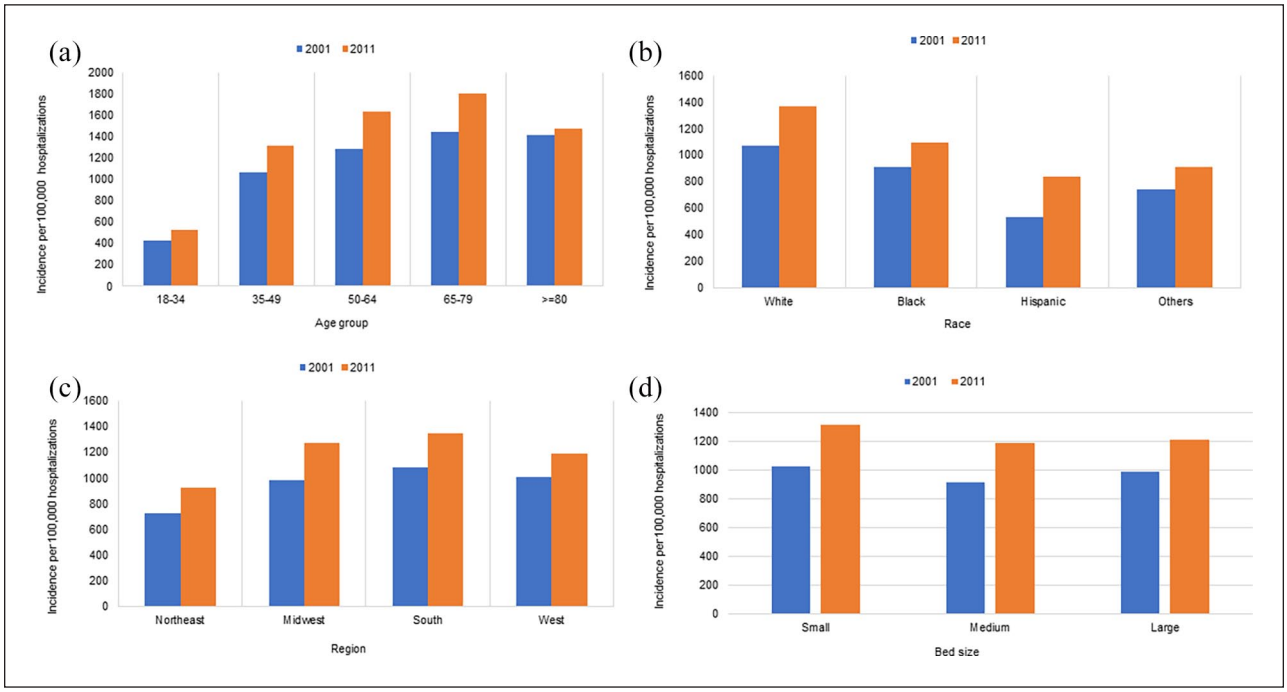

Figure 3. (a) Age-wise differences in incidence of paralytic ileus per 100,000 hospitalizations, (b) racial differences in incidence of paralytic ileus per 100,000 hospitalizations, (c) regional distribution of paralytic ileus per 100,000 hospitalizations, and (d) distribution of paralytic ileus per 100,000 hospitalizations according to bed size.

Hospital characteristics

The rise in incidence was higher in urban teaching hospitals (RR: 1.31; CI: 1.19–1.56; $p < 0.0001$) than urban non-teaching (RR: 1.17; CI: 1.08–1.27; $p < 0.0001$) and rural hospitals (RR: 1.09; CI: 1.001–1.18; $p < 0.0001$). The incidence was lowest in the Northeast (728/100,000 in 2001 and 923/100,000 in 2011) and highest in South (1083/100,000 in 2001 and 1349/100,000 in 2011). The incidence increased significantly in all the regions: Northeast (RR: 1.27; CI: 1.15–1.40; $p < 0.0001$), Midwest (RR: 1.3; CI: 1.19–1.41; $p < 0.0001$), South (RR: 1.25; CI: 1.15–1.35; $p < 0.0001$), and West (RR: 1.18; CI: 1.09–1.29; $p = 0.0001$) (Figure 3(c)). Hospitals with small bed size had the highest number of hospitalizations with paralytic ileus per 100,000 hospitalizations in 2001 and 2011 when compared to hospitals with medium and large bed size (Figure 3(d)). The incidence increased from 1027/100,000 hospitalizations in 2001 to 1313/100,000 hospitalizations in 2011 (RR: 1.28; CI: 1.18–1.39; $p < 0.0001$).

Length of stay, cost of care, and all-cause mortality

Median LOS increased from 8 days (interquartile range: 4–12 days) in 2001 to 9 days (interquartile range: 4–13 days) in 2011 ($p < 0.0001$). The mean cost of care per hospitalization increased from US$19,739 in 2001 to US$26,198 in 2011 (32.7% increase; $p < 0.0001$) (Figure 1(b)). The annual total cost of care for all paralytic ileus hospitalizations increased from US$7.1 billion in 2001 to US$12.3 billion in 2011 (73.2% increase; $p < 0.0001$) (Figure 1(c)). The percent mortality decreased from 6% in 2001 to 5.1% in 2011 (Figure 1(d)). Also, the number of deaths per 100,000 hospitalizations decreased from 2969 in 2001 to 1501 in 2011 (RR: 0.51; CI: 0.48–0.54; $p < 0.0001$).

Discussion

We found that the total number of hospitalizations with paralytic ileus increased by 29.7% between 2001 and 2011. The current body of literature focuses most intensively on paralytic ileus following surgery and offers strategies to mitigate against prolonged ileus.[20–23] However, it is currently not clear what factors are responsible for the increased rate of the condition. It is possible that increased use of medications like psychotropic agents and opiates, which reduce GI motility, may be contributory.[7,24] Higher rates of reporting may also result from the use of more sensitive diagnostic techniques.

The number of opioid prescriptions dispensed by the US pharmacies nearly tripled from 1991 to 2011.[25] From 1999 to 2010, sales of opioid analgesic quadrupled in the United States.[26] The rise in prescription opioids likely contributed to the increased incidence of paralytic ileus from 2001 to 2011. Older adults are frequently prescribed opioid treatment for chronic painful conditions like osteoarthritis, cancer, and back pain. They are more vulnerable to the side effects of opioid medications compared to young adults because of change in drug metabolism and reduced renal excretion associated with aging.[27] Also, cognitive decline in older adults can accidentally cause opioid overdose even from an appropriate

prescribed opioid regimen.[28] Moreover, psychotropic medications—antidepressants, anxiolytics, and antipsychotics—are commonly prescribed for older adults.[29] Our findings show that the rate of hospitalization for paralytic ileus was highest for the age group 65–79 compared with all other age groups between 2001 and 2011. Other conditions implicated in development of paralytic ileus are positive fluid balance after surgery, electrolyte abnormalities, and hypo-albuminemia.[2,30] We could not assess the relationship of these conditions with ileus as NIS database does not provide data on laboratory findings and fluid balance. In conclusion, prescribers must be wary of the risk factors associated with paralytic ileus other than the traditional "postoperative ileus."

The highest incidence per 100,000 hospitalizations for paralytic ileus was seen in the age group 65–79 years. Such results have been reported previously for patients with postoperative ileus (POI).[31] This is not unexpected, as age-related changes in rate of colonic transit autonomic and innervation have been well described.[32–35] The incidence per 100,000 hospitalizations was higher in males than females in both, 2001 and 2011, findings that are consistent with prior reports.[36,37] Further studies are required to determine whether these differences arise from anatomical and/or physiological variables or perhaps differences in management.

A 2017 study analyzed NIS database to ascertain demographic distributions of prescription opioid overdose–related (POD) hospitalizations from 2000 through 2014.[38] They found that POD hospitalization rates were highest in the South when compared to other regions during the study period. The hospitalization rate for paralytic ileus was highest in the South in our study. Thus, it is plausible that opioid overdose–related hospitalization contributed to the observed high hospitalization rate of paralytic ileus in the South. Further studies are needed to confirm this finding. We found that the percent increase in paralytic ileus hospitalization rate was highest in the lowest income group (0–25th percentile of median household income in the patient's ZIP code) from 2001 to 2011. It is well known that nutrient-poor energy-dense diets are preferentially consumed by persons of low-income groups.[39] Patients in a poor nutritional state are prone to developing paralytic ileus due to hypoproteinemia and vitamin deficiencies.[40]

The consequences of paralytic ileus are significant, as patients are often immobile, uncomfortable, and are at risk of other complications and prolonged hospital stay.[5] Our findings show that the cost of care per hospitalization increased by 32.7% from 2001 to 2011. Earlier reports estimated the cost of managing POI to be between US$750 million and 1.6 billion annually.[41,42] The percent increase in annual total cost of all paralytic ileus hospitalizations was 73.2% in our study, reaching 12.3 billion in 2011. Given the burden to patients and the health care system related to ileus, studies identifying more effective strategies are warranted.[43]

The Postoperative Ileus Management Council (PIMC) National Experts' Clinical Consensus Panel reported mortality in POI patients as 6.5%.[44] We found a mortality rate between 5% and 6% throughout the study period. The mortality rates are comparable irrespective of the cause of paralytic ileus.

Conservative management by keeping patient nil per os (NPO), encouraging mobilization, and placing a nasogastric tube is recommended in paralytic ileus. There is some evidence that chewing gum after abdominal surgery reduced the incidence of POI.[45,46] Mastication causes stimulation of cephalic-vagal circuits, which in turn increases GI motility and reduces POI rates.[47] Since paralytic ileus is a GI motility problem, future studies focusing on whether chewing gum is beneficial in paralytic ileus due to causes other than surgery are warranted. Enhanced recovery protocol (ERP) and enhanced recovery after surgery (ERAS) protocols are designed as a means to improve patient outcomes, which include early return of bowel function and early hospital discharge.[48] In a retrospective study on 513 consecutive colorectal ERAS patients, Grass et al.[49] noted that compliance with the ERAS protocol helped to prevent POI. In 2018, ERAS Society guidelines recommended that there is a high-quality evidence for ERAS protocol in preventing POI.[50] However, in 2020, a meta-analysis comprising 1830 patients showed that ERAS may increase the risk of POI.[51] Our study shows that paralytic ileus hospitalizations increased from 2001 to 2011. Even if these protocols were applied during the study period, NIS database does not have separate ICD-9 codes to identify such them. Hence, we could not determine the impact of such protocols on the observed trends in this study.

The NIS database permitted us to analyze a large sample consisting of hospitalizations across the entire country. This reduces bias seen in studies which are confined to one hospital or region.[52] However, our analysis has some limitations. We could not differentiate the hospitalizations with a new diagnosis of paralytic ileus from the old hospitalizations. Also, it is known that administrative databases are susceptible to errors arising from coding inaccuracies. Most studies evaluating the incidence of POI are done using ICD-9 codes. However, POI is often considered an unavoidable event and these codes are not consistently used leading to underestimation of POI.[21] Also, we could not separate the number of paralytic ileus hospitalizations from POI and hospitalizations from other causes because NIS does not carry a separate code for POI. Thus, we could not identify the type and duration of the procedures the patients might have undergone prior to developing POI. Subsequently, the confounding effect of type of procedure on the outcomes could not be assessed. Each individual hospitalization is included as a separate entry in the NIS. It is not possible to separate index cases from readmissions. NIS considers each hospitalization as separate entry. Thus, it is possible that our analysis could have overestimated the number of hospitalizations with

paralytic ileus. Also, we could not determine the temporal association between the type of procedure that the patients underwent and the risk of development of POI due to limitations with coding of the NIS database.

Conclusion

There was a significant increase in the number of paralytic ileus–related hospitalizations along with increase in the cost of care, but with a substantial reduction in mortality rates over that time period. Further studies are needed to identify factors which may be contributing to the overall increase in the rates of paralytic ileus and to permit development of more effective preventive and treatment strategies for this condition.

Author contributions

Planning and conducting the study: S.S., K.F.H., C.N., and W.S.A. Collecting, analyzing, and interpreting data: A.P., S.S., R.C.C., H.S., and U.M. Drafting the manuscript: All authors.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Ethical approval was not sought for the present study because

- HCUP Databases are Limited Data Sets.
- HCUP databases conform to the definition of a limited data set. A limited data set is healthcare data in which 16 direct identifiers, specified in the Privacy Rule, have been removed.
- Under HIPAA, review by an institutional review board (IRB) is not required for use of limited data sets.

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Supplemental material

Supplemental material for this article is available online.

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