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Authors

Sankaran, Satheeshkumar P
Villa, Alessandro
Sonis, Stephen

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Healthcare-associated infections among patients hospitalized for cancers of the lip, oral cavity and pharynx

Satheeshkumar P Sankaran [a,*], **Alessandro Villa** [b], **Stephen Sonis** [c,d,e]

[a] *Harvard Medical School, Boston MA, USA*
[b] *Department of Orofacial Sciences, University of California San Francisco, San Francisco, CA, USA*
[c] *Division of Oral Medicine, Brigham and Women's Hospital, Boston, MA, USA*
[d] *Dana-Farber Cancer Institute, Boston, MA, USA*
[e] *Department of Oral Medicine, Infection and Immunity, Harvard School of Dental Medicine, Boston, MA, USA*

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ABSTRACT

Introduction: The negative consequences of healthcare-associated infections (HAI) on the burden of illness (BOI) of cancer patients are well-established. However, there is a paucity of research on HAI among cancers of the lip, oral cavity and pharynx (CLOCP), and whether HAI-related BOI differed for other common solid tumors—malignant neoplasm of the colon (MNC) and malignant neoplasm of the lung (MNL).

Methods: We utilized the United States' National Inpatient Sample database 2017 to study longitudinal inpatient hospital stay of CLOCP, MNC and MNL. Patient demographics and hospital characteristics of patients were assessed, and the impact of HAI-related BOI compared based on differences in length of hospital stays (LOS), total charges during hospitalization and mortality were compared.

Findings: In 2017, of the 54,934 patients with CLOCP, 1.2% had HAI, compared to MNC (n=64,470) with 2% HAI and MNL (n=154,685) with 1.2% HAI. In adjusted multivariable regression analysis, we determined CLOCP patients with HAI had LOS of 5.6 days longer (95% CIs, 3.0—8.2 days, $P < 0.001$), and hospitalization charges of $40,341 higher (95%CIs 15,715—64,967, $P < 0.01$) than the non-HAI CLOCP patients. Mortality was not significantly different among HAI and non-HAI CLOCP patients (odds ratio: 0.80; 95%CIs 0.35—1.87, $P = 0.6$). In unadjusted analysis, LOS and total charges were higher for CLOCP-HAI patients vs. MNC-HAI or MNL-HAI patients.

Conclusion: HAI in patients with CLOCP patients were associated with an increased BOI, and this is considerably higher than observed in patients with MNC or MNL patients who had HAI.

* Corresponding author. Address: Department of Oral Oncology, Roswell park cancer center, Buffalo, NY, 14263, USA. Tel.: +1617 372-0427.
E-mail address: Satheesh.Sankaran@roswellpark.org (Satheeshkumar P. Sankaran).

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Introduction

According to a report from the Centers for the Disease Control and Prevention (CDC), the incidence of the cancers of the lip, oral cavity and pharynx (CLOCP) increased 0.6% per year on average from 2007-2016 [1]. Of the expected 53,260 of new cases of CLOCP diagnosed in the United States (US) this year [2], approximately 38% will be hospitalized for major surgical procedures [3]. While concomitant chemoradiation is a mainstay of treatment for patients with CLOCP, surgery is a significant component of the treatment regimen in approximately 50—80% of cases [3—7]. However, these treatment modalities lead to extended hospital stays, healthcare-associated infection (HAI), and increased financial constraints [8—12]. HAI initiates enormous burden leading to morbidity and mortality among CLOCP patients [10—12]. HAI is most frequently associated with acute care hospitals, ambulatory surgical centers, dialysis facilities, outpatient care, and long-term care facilities [13]. HAI risk is most significant among patients hospitalized for cancer treatment, cardiovascular diseases, pregnancy, and other diseases requiring complex treatment modalities [13—15]. While the HAI-burden of illness (BOI) has been studied broadly in hospitalized cancer patients and specifically for certain malignancies, it is poorly defined amongst patients admitted for the treatment of CLOCP.

The goal of this study was to define the impact of HAI-BOI for hospitalized CLOCP patients and to compare HAI-BOI for hospitalized CLOCP patients with two other solid tumors of the aerodigestive tract, malignant neoplasms of the colon (MNC) and malignant neoplasms of the lung (MNL).

Methods

Study design and data source

This study was a longitudinal hospital inpatient database analysis of CLOCP cases associated with HAI using discharge data from the 2017 National inpatient sample (NIS) database

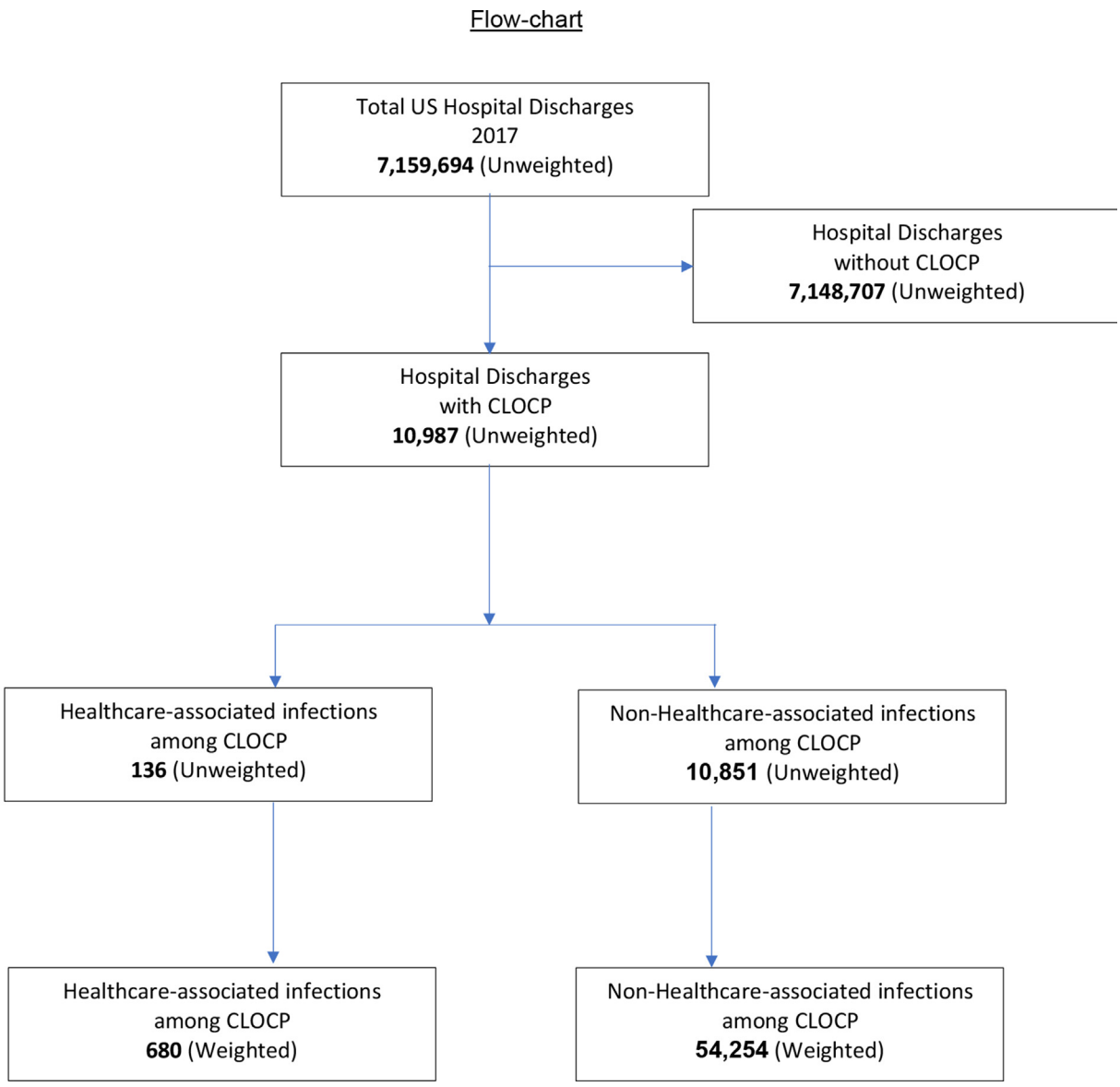

Figure 1. Flow chart of the cohort selection from the National In-patient Sample; sample size presented with weighted (original patient numbers) and unweighted numbers among CLOCP.

obtained from the Healthcare Cost and Utilization Project (HCUP) of the Agency for Healthcare Research and Quality (AHRQ) [16]. Briefly, 2017 NIS is structured as 20% stratified sample of discharges to represent 97% of all discharges of US inpatient hospital admissions with the exclusion of rehabilitation and long-term acute care hospitals. As this analysis was based on publicly available de-identified and anonymous data this study was exempted by the institutional IRB.

Study population

We included all patients hospitalized with a diagnosis of CLOCP in the year 2017. Specifically, we included the following ICD10-CM codes (C00 to C14): cancers of the lip, oral cavity and pharynx. We used ICD-10-CM billable codes to identify hospitalizations with HAI, mainly-ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), and Clostridium difficile infection (CDI). [supplementary file 1] We compared our findings with the MNC (ICD 10 CM C189) patients affected with HAI, and MNL (ICD 10 CM C3490) patients affected with HAI to see how the HAI-BOI varied across the three cohorts. The NIS records the length of stay (LOS) and total charges for hospitalization from every sampled inpatient record calculated in days and the United States Dollars separately.

Study measurements

We extracted data of the CLOCP, MNC, and MNL cohorts stratified by HAI and non-HAI groups. The three cancer cohorts' patient level and clinical level characteristics were extracted namely-age, sex, race, admission type (elective/non-elective; elective indicates whether patients were electively hospitalized), the payer type (Medicaid, Medicare, other/uninsured, etc.), patient location (using a six-category urban-rural classification scheme for US counties developed by the National Center for Health Statistics (NCHS)), admission origin (transferred-in, not-transferred), median household income based on patient's ZIP Code (this categorical variable provides a

Table I
Baseline characteristics of CLOCP patients with HAI and without HAI

Characteristics	Non HAI	HAI	*P value*
Age (mean (SD))	63.4 (13.5)	62.1 (15.4)	0.36
Female (%)	15730.0 (29.0)	190.0 (27.9)	0.79
Expected primary payer (%)			0.37
Medicare	26960.0 (49.8)	320.0 (47.1)	
Medicaid	8470.0 (15.6)	145.0 (21.3)	
Private insurance	15740.0 (29.1)	185.0 (27.2)	
self-pay	1210.0 (2.2)	5.0 (0.7)	
No charge	140.0 (0.3)	5.0 (0.7)	
Other	1640.0 (3.0)	20.0 (2.9)	
Elective (%)	19880.0 (36.7)	130.0 (19.1)	<0.001
Patient Location: NCHS Urban-Rural Code (%)			0.02
"Central" counties of metro areas of ≥1 million population	15665.0 (29.0)	135.0 (20.1)	
"Fringe" counties of metro areas of ≥1 million population	13950.0 (25.8)	145.0 (21.6)	
Counties in metro areas of 250,000—999,999 population.	11015.0 (20.4)	175.0 (26.1)	
Counties in metro areas of 50,000—249,999 population.	5155.0 (9.5)	65.0 (9.7)	
Micropolitan counties	4850.0 (9.0)	70.0 (10.4)	
Not metropolitan or micropolitan counties.	3400.0 (6.3)	80.0 (11.9)	
Race (%)			0.29
White	39035.0 (74.5)	500.0 (75.2)	
Black	5650.0 (10.8)	45.0 (6.8)	
Hispanic	3415.0 (6.5)	70.0 (10.5)	
Asian or Pacific Islander	1925.0 (3.7)	25.0 (3.8)	
Native American	240.0 (0.5)	5.0 (0.8)	
Other	2110.0 (4.0)	20.0 (3.0)	
Indicator of a transfer into the hospital (%)			0.006
Not transferred in or newborn admission	49410.0 (91.3)	575.0 (84.6)	
Transferred in from a different acute care hospital	2965.0 (5.5)	80.0 (11.8)	
Transferred in from another type of health facility	1715.0 (3.2)	25.0 (3.7)	
Median household income for patient's ZIP Code (based on current year)			0.001
0-25th percentile	15080.0 (28.3)	210.0 (31.6)	
26th to 50th percentile	13940.0 (26.2)	260.0 (39.1)	
51st to 75th percentile	12780.0 (24.0)	100.0 (15.0)	
76th to 100th percentile	11415.0 (21.5)	95.0 (14.3)	
Weighted Elixir score (mean (SD))	20.9 (12.2)	24.4 (11.8)	0.001

Abbreviations: SD=Standard deviation; NCHS=National Center for Health Statistics.
HAI=Healthcare associated infection; CLOCP= Cancers of the lip, oral cavity and pharynx.

quartile classification of the estimated median household income of residents in the patient's ZIP Code) and Elixhauser comorbidity index. The Elixhauser comorbidity index was used to categorize comorbidities (based on the ICD-10 code's definition of included comorbidities) as present or not in the HAI and non-HAI groups [17]. Our study exposure variable was HAI among patients hospitalized for treating CLOCP, MNC, and MNL. The outcome of interest included LOS in days (i.e., the total length of hospital stays of the first admission if it occurred), total charges for the hospitalization (in the United States Dollar ($)), and in-hospital mortality.

Statistical analysis

Descriptive statistics were used to describe the baseline patient and clinical characteristics. To analyze NIS survey data with complex sampling, we used the survey-weighted generalized linear model (svyglm) package [18]. Svyglm was used to fit the model (LOS, total charges, and mortality). We have fitted adjusted and unadjusted svyglm for LOS, total charges, and mortality. For the multivariable svyglm models of LOS, total charges, and mortality, we have adjusted for the age, sex, payer type, patient location, race, elective, an indicator of a transfer into the hospital, median household income, and comorbidity score. For the mortality model (binomial), we fitted a family referring quasibinomial to the svyglm. All analyses were two-tailed and statistical significance was determined using $P < 0.05$. All statistical analyses were performed using R 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

In 2017, the NIS documented a total of 54,934 CLOCP (weighted — original patient numbers) cancer discharges from the 7,159,694 (unweighted numbers — 20% of the total patients) patients admitted in the US hospitals; amongst these, there were 680 CLOCP (1.2%) having acquired HAI [Figure 1]. Overall, the most common HAI among CLOCP was CLABSI (39%), followed by CDI (33%), VAP (14%) and CAUTI (14%).

In the MNC cohort, there were 64,470 patients discharged with a primary diagnosis of MNC in the year 2017, and 1290 (2%) patients with MNC having acquired a minimum of one HAI during their in-hospital stay. In the MNL cohort of 2017, 154,685 patients were discharged with a primary diagnosis of the MNL; among these, 1805 (1.2%) patients acquired a minimum of one HAI during their in-hospital stay.

CLOCP

There were no statistically significant differences in the event of HAI and non-HAI when age, sex, payer type, and race were considered [Table I]. The mean [SD] age of CLOCP within HAI and non-HAI groups were 62.1 [15.4] and 63.4 [13.5] years, respectively, and most patients were males (HAI - 72% and non-HAI - 71%). Other details of the CLOCP stratified by the HAIs and non-HAIs are provided in the Table I. The Elixhauser comorbidity index was significantly different between the HAI and non-HAI group (mean [SD], non-HAI — 20.9 [12.2], HAI — 24.4 [11.8]; ($P = 0.001$)) [Supplementary file 2].

The unadjusted multivariable regression analysis showed the mean difference in the total charges between CLOCP patients with HAI compared to the CLOCP patients without HAI was $42,790 (95%CIs: 16,847—68,733, $P < 0.01$). The mean difference in the hospital LOS among CLOCP with HAI compared to the CLOCP patients without HAI was 6.5 days (95%CIs: 3.9—9.1, $P < 0.001$). In-hospital mortality was not significantly different in the CLOCP patients with HAI compared to the CLOCP without HAI (OR: 1.02, 95%CIs: 0.45—2.29, $P = 0.96$).

The adjusted multivariable regression analysis showed that the mean difference in the total charges between CLOCP patients with HAI compared to the CLOCP patients without HAI was $40,341 (95%CIs: $15,715 — $64,967; $P < 0.01$). The mean difference in the hospital LOS among CLOCP patients with HAI compared to the CLOCP patients without HAI was 5.6 days (95% CIs: 3.0—8.2 days; $P < 0.001$). In-hospital mortality was not significantly different in the CLOCP patients with HAI compared to the CLOCP patients without HAI (OR: 0.80; 95%CIs: 0.35—1.87; $P = 0.6$).

MNC cohort

The patient and clinical characteristics of the MNC HAI and MNC non-HAI are shown in Supplementary file 3. The unadjusted multivariable regression analysis showed the MNC patients with HAI had LOS of 3.1 days longer than the non-HAI MNC patients (95%CIs: 2.0—4.0 days; $P < 0.001$). MNC patients with HAI had hospitalization charges of $31,640 higher than those of non-HAI MNC patients (95%CIs: 17,308—45,972, $P < 0.001$). Mortality was not significantly different among HAI and non-HAI MNC patients (OR: 0.89, 95%CIs: 0.55—1.45; $P = 0.65$).

MNL cohort

The patient and clinical characteristics of the MNL HAI and MNL non-HAI are shown in Supplementary file 4. The unadjusted multivariable regression analysis showed that MNL patients with HAI had a LOS of 2.5 days longer than the non-HAI MNL patients (95%CIs: 1.8—3.3; $P < 0.001$). MNL patient with HAI had hospitalization charges of $22,707 higher than the non-HAI MNL patients, (95%CIs: 0,616—34,798; $P < 0.001$). Mortality was not significantly different among HAI and non-HAI MNL patients (OR = 1, 95%CIs: 0.72—1.41; $P = 0.96$).

Comparisons between CLOCP with MNC and MNL

Among the three cohorts (CLOCP and pharynx, MNC, and MNL), there were no statistically significant differences between HAI and non-HAI patient characteristics such as sex, age, race/ethnicity, and insurance type. However, the median household income and clinical level factors, such as admission type (elective/non-elective), and admission origin (transferred in vs not transferred), were significantly different in the CLOCP HAI vs non-HAI. Comorbidity scores were different between the HAI and non-HAI cohorts for each of the three tumor cohorts. The outcome (LOS, total charge, and mortality) of non-surgical treatments (Radiation therapy, chemotherapy, and immunotherapy) among CLOCP, MNC and MNL patients are provided in Table III.

Table II
Comparison of BOI (LOS, Total Charge and Mortality) among CLOCP, MNC and MNL stratified by HAI and nonHAI

Population	CLOCP		MNC		MNL	
	HAI (680)	Non-HAI (54254)	HAI (1290)	Non-HAI (63180)	HAI (1805)	Non-HAI (152880)
LOS in days (Mean (SD))	12.9 days (14.8)	6.7 days [7.2]	8.8 days (8.1)	5.7 days [6]	8.0 days (7.4)	5.46 days (5.47)
Total charges in USD (Mean (SD))	1,23,073 USD (1,53,129)	80,283 USD [103,706]	90, 997 USD (1,20,335)	59,357 USD [83,501]	79,396 USD (1,20,592)	56,688 [72,005]
Mortality (No & %)	30 (4.4%)	2340 [4.3]	85.0 (6.6%)	4615 [7.3]	195.0 (10.8%)	16405 [10.7]

Abbreviation: LOS – Length of Stay, USD -United States Dollar, CLOCP= Cancers of the lip, oral cavity and pharynx, MNC = Malignant neoplasm of Colon, MNL = Malignant neoplasm of Lungs, HAI = Healthcare-associated infections, SD = Standard deviation, BOI=Burden of illness.

Discussion

Not unexpectedly, our data indicate that the occurrence of HAI in hospitalized CLOCP patients was associated with increases in total charges and hospital LOS. There was no difference in mortality among HAI when compared to the non-HAI cohort. Our finding that CLOCP patients with HAI had longer LOS and higher total charges compared to the MNC and MNL patients suggests that the increase in BOI was not generalizable to all cancer diagnoses.

To the best of our knowledge, ICD 10 CM codes defining CLOCP and HAI (CLABSI, VAP, CAUTI, and CDI) have not previously been used synchronously. By comparing ICD 10 codes to the disease prevalence with other published studies and public data [2,3,11,12,19,20], ICD 10 CM codes seemed more reliable, and results were consistent in identifying hospital discharges with CLOCP and HAI diagnosis in the 2017 NIS cohort. This study leveraged strengths to the current literature, a novel perspective of the BOI due to HAI in CLOCP patients. When compared to other cancers of the aerodigestive tract, namely, MNC and MNL, HAI are very decisive among CLOCP patients.

The non-surgical and surgical treatment modalities and rate of hospitalization vary across the CLOCP, MNC, and MNL by site, stage, and cancer types, that said, hospitalization is typically required for all three cancers types when surgical intervention is included in the treatment plan [21–27]. Consequently, hospitalization is more common in patients with lung and colorectal cancers (3rd and 4th most common cancer hospitalization in the US) compared to HNC (8^{th} most frequent cancer hospitalization in the US) [28].

CLOCP with HAI generated an average total charge of $123,073, and an average LOS of 12.9 days. CLOCP associated HAI total charges and LOS are considerably larger than the MNC and MNL cohorts [Table II]. We estimated that total charges, LOS were lower when only non-surgical treatments were employed for all the three cancer cohorts [Table III]. For the CLOCP, multiple treatment strategies predispose to longer LOS and higher total charges than the single treatment alone. [29–31] The average cost of CLOCP cancer treatment during the first six months increased exponentially, and individuals who received surgery, radiation, and chemotherapy averaged $153,892 during the year after diagnosis [31]. Longitudinally, CLOCP patients have high variations in the total costs, influenced by multiple treatments, comorbidities, LOS and HAI [29–31], which limited the utility of the database used in this study. Concerning CLOCP, increases in LOS iare often associated with postoperative complications, including HAI [11,32,33]. However, acute treatment effects, functional impairment, short term disabilities add to the BOI on the CLOCP patients [31,32]. Looking at previous studies, old age is an independent risk factor for the LOS and hospital complications [33–39]. On the contrary, our study showed that CLOCP patients are younger than the MNC and MNL population. Accordingly, this study indicates that CLOCP patients are a high-risk group prone to increased BOI due to HAI during the primary hospitalization.

In our study, it is worth noting that the mortality was not significantly different across the HAI and non-HAI groups among CLOCP, MNC, and MNL cohorts. However, data from the National database (National Surgical Quality Improvement Program) where readmission information is available,

Table III
BOI (LOS, Total charge, and mortality) among cancers of the lip, oral cavity and pharynx, MNC and MNL when subjected to non-surgical therapies alone

Non-surgical treatment (radiation therapy, chemotherapy, and immunotherapy)	LOS (mean (SD))	Total charges (mean (SD))	Mortality (%)
CLOCP	5.6 days (6.9)	50862 USD (61434)	0.3%
MNC	3.3 days (3.4)	37467 USD (36634)	1.5 %
MNL	5.0 days (4.3)	50741 USD (52529)	6.3 %

Abbreviation: LOS — Length of Stay, USD -United States Dollar, CLOCP= Cancers of the lip, oral cavity and pharynx, MNC = Malignant neoplasm of Colon, MNL = Malignant neoplasm of Lungs, HAI = Healthcare-associated infections, SD = Standard deviation, BOI=Burden of illness.

demonstrated that postoperative complications and HAI were significantly correlated to 30-day mortality in the univariate and multivariate analysis during head and neck cancer readmission [40]. Noting this, we believe that the HAI and other factors during the primary hospital stays are an essential element predicting CLOCP 30-day mortality.

When noting covariates with significant differences in the HAI and non-HAI group of CLOCP cohort, we have adjusted these variables in the multivariable regression model along with other clinically significant confounders. While observing the differences in the BOI among CLOCP patients compared to the MNC and MNL, we concluded there might be additional factors that are very important for these differences. The presence of infectious microbes in the upper aerodigestive tract, smoking history, history of tobacco and alcohol abuse, and males are most commonly diagnosed with CLOCP; these factors might predispose to severe adverse HAI outcomes [41].

According to an estimate published in 2013, the total annual costs for the HAI were $9.8 billion (95% CI, 8.3—11.5 billion) [42]. Acquiring these infections is crucial in hospitalized patients; the risk increases with longer LOS and a lack of identifying high-risk populations [31,42,43]. When compared to the previous studies of CLOCP patients with in-hospital complications [11,44,45], our study was limited to HAI due to VAP, CLABSI, CDI, and CAUTI; these HAI, most commonly occur due to the increased microbial interference during the medical treatment. Although the CDC's effort to reduce HAI is still ongoing, our findings suggest CLOCP patients are at high risk for HAI, and our study is comparable to other studies in this regard [11,29].

Limitations

Lack of information regarding CLOCP stages, longitudinal follow-up, and exact treatment modalities employed for the CLOCP were some of the known limitations in our study. The claims data provide a snapshot of the disease processes and other health-related characteristics at an in-hospitalization timepoint. We have utilized the methodology which can be used to assess the in-hospital burden of HAI of the CLOCP population at a given time point.

Conclusion

Our study indicates that the US 2017 CLOCP patient cohort who acquired HAI, was associated with an increase in the LOS and total charges during their in-hospital stay. Besides, BOI in patients with CLOCP-HAI compared to the MNL-HAI and MNC-HAI patients was characterized by increased LOS and higher total charges. Amongst cancer patients, it is uncertain whether HAI serves as a risk factor for recurrence, secondary neoplasms, and survival. Mostly, these aspects of HAI are unknown and generally require actionable practices.

Authors contribution

Satheeshkumar PS: Concept and design, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and statistical analysis.

Sonis. S: Concept and design, critical revision of the manuscript for important intellectual content, and statistical analysis.

Villa A: Critical revision of the manuscript for important intellectual content.

Conflicts of interest

None.

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Appendix A. Supplementary data

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