ORIGINAL RESEARCH

Incidence and Impact of Healthcare-associated Infections on Patients Primarily Admitted with Sepsis and Non-sepsis Diagnoses

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Abstract

Objectives: To compare the incidence of healthcare-associated infections (HAI) and their outcomes between patients admitted to the ICU with sepsis and those admitted with non-sepsis diagnoses.

Materials and methods: We performed a single-center, prospective, observational study of ICU patients at a tertiary level medical-surgical unit from April 2018 to October 2018. All patients admitted to the ICU with a length of stay (LOS) > 48 hours were included. Baseline data including demographics, co-morbidities, and severity of illness scores were collected. Index occurrence of HAI in all these patients was noted and data regarding organ support and patient outcomes were recorded. The incidence, complications, ICU LOS, and 30-day mortality of HAI were compared between the patients admitted to ICU originally with sepsis and non-sepsis diagnoses.

Results: A total of 271 patients were evaluated in our study ($N = 106$ for the sepsis group and $N = 165$ for the non-sepsis group). No significant difference between the groups was found in the incidence of HAI (29.2% in sepsis group vs 24.4% in non-sepsis group; $p = 0.07$). Complications (acute kidney injury (AKI): 71 vs 45%; $p = 0.01$, shock: 81 vs 55%; $p = 0.05$, need for mechanical ventilation (MV): 30 vs 15%; $p = 0.04$) were more common in sepsis group compared to the non-sepsis group. The ICU LOS (12.2 ± 5.2 days vs 8.8 ± 2.05 days; $p = 0.01$) was significantly longer in the sepsis group. There was no significant difference in 30-day mortality between the groups (45 vs 25%; $p = 0.07$).

Conclusions: The incidence of HAI seems to be similar between patients admitted with sepsis and non-sepsis diagnoses. However, patients admitted with sepsis develop higher rates of organ failure secondary to HAI and have a longer ICU LOS compared to patients admitted with non-sepsis diagnoses. The mortality rate of HAI did not differ between these two groups.

Keywords: Healthcare-associated infections, ICU-acquired infections, Organ dysfunction, Sepsis.

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-23760

Introduction

Sepsis causes a dysregulated host response to infection (SEPSIS-3) and is the leading cause of morbidity and mortality in hospitalized patients.[1,2] Patients with sepsis are known to enter an immunosuppressive phase that is characterized by apoptosis of immune cells, deficient immune cell responses, elevated levels of anti-inflammatory cytokines, and an increase in regulatory T and myeloid-derived suppressor cells.[3–5] As a consequence, many septic patients are at risk of developing healthcare-associated infections (HAI) in the ICU.[4–6] It is unclear whether patients admitted to the ICU with sepsis have a higher risk of secondary HAI[7] compared to those who are admitted to the ICU with other primary diagnoses (henceforth referred to as the "non-sepsis diagnoses"). The clinical characteristics and outcomes of HAI may also be distinctly different among ICU patients admitted with sepsis vs other non-sepsis diagnoses.

Hence, we prospectively sought to compare the incidence, clinical characteristics, and outcomes of HAI in patients who were admitted to the ICU with a primary diagnosis of sepsis to those admitted with non-sepsis diagnoses.

Materials and Methods

Study Design

A single-center, prospective, observational cohort study was conducted in a multidisciplinary critical care unit at Apollo Main Hospital, Chennai, between April 1, 2018, to October 30, 2018.

Definitions

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection (SEPSIS-3).[8] Organ dysfunction can be identified as an acute change in total sequential organ failure assessment (SOFA) score > 2 points consequent to an infection.[8]

Ventilator-associated pneumonia (VAP) was defined by clinical pulmonary infection score (CPIS) > 6.[9]

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How to cite this article: Chintamani A, Prakash B, Abraham BK, Kumar S, Ramakrishnan N, Venkataraman R. Incidence and Impact of Healthcare-associated Infections on Patients Primarily Admitted with Sepsis and Non-sepsis Diagnoses. Indian J Crit Care Med 2021;25(3): 292–295.

Source of support: Nil

Conflict of interest: None

Catheter-associated urinary tract infections (CAUTI), central line-associated bloodstream infections (CLABSI), and other infections were defined as per Centre for Disease Control and Prevention (CDC) guidelines.[10]

Acute kidney injury (AKI) was defined as an increase in the serum creatinine (SCr) level by >0.3 mg/dL within 48 hours or an increase in SCr to >1.5 times baseline, which is known or presumed to have occurred within the prior 7 days or urine volume < 0.5 mL/kg/h for 6 hours.[11]

Septic shock was defined as a subset of sepsis with persistent hypotension requiring vasopressors to maintain mean arterial pressure (MAP) ≥ 65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation.[8]

Respiratory failure was defined as any need for invasive mechanical ventilation (MV).

Septic encephalopathy was defined as diffuse cerebral dysfunction associated with the disturbing level of consciousness caused by an inflammatory response in sepsis in the absence of direct CNS pathology.

Inclusion Criteria

All patients admitted to the ICU with an ICU length of stay (LOS) > 48 hours were included.

Exclusion Criteria

Patients transferred from outside hospitals were excluded from the study.

Methods and Data Collection

Baseline data of patients including demographics, co-morbidities, SOFA scores, and details of organ support were collected.

Index occurrence of HAI in all these patients was noted and data regarding organ support and patient outcomes were recorded. Organ dysfunction was defined as new onset of AKI or requirement of organ support, such as vasopressors or mechanical ventilation. New worsening of any organ dysfunction after initial trend towards improvement temporally associated with the onset of new HAI was counted as new onset of organ dysfunction. The incidence, complications, ICU LOS, and 30-day mortality of HAI were compared between the patients admitted to ICU primarily with sepsis and non-sepsis diagnoses.

Our institutional ethics committee approved the study with a waiver of informed consent.

Statistical Analysis

The analysis was restricted to only the first episode of HAI. Demographic data were expressed as percentages or mean ± SD. Variables on admission like age, gender, comorbidities, SOFA score, and outcomes (complications, LOS, mortality) were analyzed and compared between sepsis and non-sepsis admission groups. For the comparison of sepsis and non-sepsis admission groups, a T-test was used to determine differences in continuous (quantitative) variables, and a chi-square test was used for assessing differences in categorical (qualitative) variables. The odds ratio (OR) was calculated to study the risk estimates between the groups. Statistical analysis was performed using SPSS software. A *p*-value < 0.05 was considered significant.

Results

During the study period, 395 patients with an ICU LOS of more than 48 hours were screened. Patients ($N = 124$) who were transferred from outside hospitals were excluded and 271 patients were finally included in the study. Among these, 106 patients were admitted to the ICU with sepsis while 165 patients had a non-sepsis diagnosis at the time of admission (Fig. 1).

Baseline data including demographics, co-morbidities, and SOFA scores were recorded (Table 1). There were no significant differences between the two groups in their baseline characteristics, except that the admission SOFA scores were higher for the patients with sepsis on admission (9.8 ± 2.4 vs 5.1 ± 1.8; $p = 0.001$).

The overall incidence of HAI was similar between both groups (29.2% in the sepsis admission group vs 24.4% in the non-sepsis admission group ($p = 0.3$; 95% CI: 0.7–2.2, OR: 1.2) (Table 2). However, there was a higher incidence of CLABSI in the sepsis admission group (26 vs 5%; $p = 0.01$) while the incidence of abdominal infections was higher in the non-sepsis admission group (8 vs 0%; $p = 0.02$). *Acinetobacter baumannii*, *Escherichia coli*, and *Klebsiella*

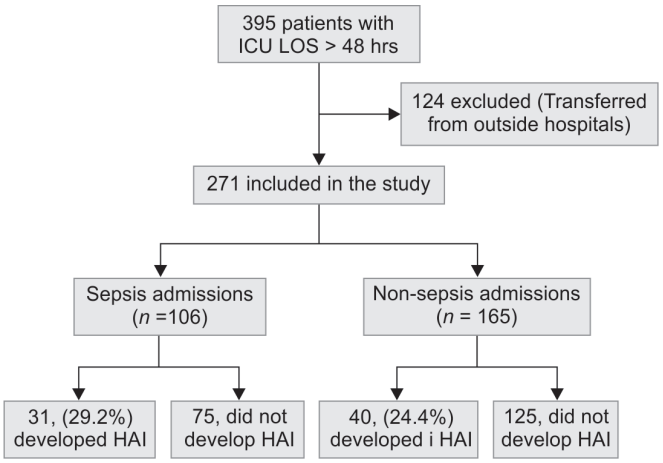

Fig. 1: Flow chart

Table 1: Baseline demographic characteristics, co-morbidities, and severity of illness

	Sepsis admissions	*Non-sepsis admissions*	*p-value*
Demographics			
Age	54.1 ± 15.7 years	55.2 ± 12.5 years	0.7
Sex			
Male	13 (42%)	21 (53%)	0.3
Female	18 (58%)	19 (48%)	0.3
Comorbidities			
Diabetes mellitus	18 (58%)	18 (45%)	0.2
Cardiovascular insufficiency	8 (26%)	7 (18%)	0.3
Renal insufficiency	4 (13%)	2 (5%)	0.2
Respiratory insufficiency	2 (7%)	1 (2%)	0.3
Immunocompromised state	1 (3%)	0	0.5
Malignancy	1 (3%)	1 (2%)	0.5
Liver insufficiency	0	6 (15%)	0.02
Severity of illness			
Shock	14 (45%)	11 (27%)	0.06
SOFA score	9.8 ± 2.4	5.1.75	0.001

Table 2: Incidence and relative proportions of healthcare-associated infections (HAI) in sepsis and non-sepsis admission groups

	Sepsis admissions (N = 106)	*Non-sepsis admissions (N = 165)*	*p-value*
No of HAI	31 (29.2%)	40 (24.4%)	0.3
Ventilator-associated pneumonia (VAP)	14 (45%)	13 (32%)	0.09
CLABSI	8 (26%)	2 (5%)	0.01
CAUTI	3 (10%)	8 (20%)	0.2
Hospital-acquired pneumonia	4 (14%)	9 (23%)	0.2
Abdominal infection	0	8 (20%)	0.02
Server-side template injection (SSTI)	2 (6%)	0	0.09

Note: The denominator for VAP, CLABSI, CAUTI, hospital-acquired pneumonia, abdominal infections, and SSTI is the total number of HAI in the respective groups

Table 3: Clinical characteristics and outcomes of secondary healthcare-associated (HAI) infections in sepsis and non-sepsis admission groups

Complications	*Sepsis admission*	*Non-sepsis admission*	*p-value*
Septic shock	25 (81%)	22 (55%)	0.02
AKI	22 (71%)	18 (45%)	0.03
Need for invasive MV (respiratory failure)	10 (30%)	5 (15%)	0.04
Disseminated intravascular coagulation (DIC)	2 (6%)	2 (5%)	0.8
Septic encephalopathy	1 (3%)	0	0.2
ICU LOS	12.7 ± 5.7 days	8.7 ± 2 days	0.001
Mortality	14 (45%)	11 (28%)	0.09

pneumoniae were the most common pathogens causing HAI in both groups.

Patients admitted with sepsis who developed secondary HAI had higher rates of shock (81 vs 55%; p=0.02), AKI (71 vs 45%; p=0.03), and need for invasive mechanical ventilation (30 vs 15%; $p = 0.04$) (Table 3). The ICU LOS (12.2 ± 5.2 days vs 8.8 ± 2.05 days; $p = 0.001$) was also significantly longer for the sepsis admission group (Table 3). There was no significant difference in 30-day mortality between the two groups (45 vs 28%; $p = 0.09$; 95% CI: 0.7–5.8, OR: 2) (Table 3).

Discussion

Amongst our study patients, 71 out of 271 developed HAI. The incidence of HAI was 29.2% in the sepsis admission group and 24.4% in the non-sepsis admission group. This rate is similar to that of other studies[12,14] with similar sample sizes, which have reported incidence of 23.8 and 23.6%, respectively. A total of 53% of patients in the sepsis group had pneumonia as ICU admission diagnosis. VAP in these patients was differentiated as a new-onset acute respiratory failure after 48 hours on mechanical ventilation with CPIS > 6 and microbiological evidence of nosocomial bacteria in the tracheal aspirate.

Our results are concordant with the study done by Van et al.,[15] which showed no significant difference in the incidence of HAI between sepsis admission and non-sepsis admission groups. *Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae* were the most common pathogens causing HAI as observed in several previous studies.[7,13–15] Our results could be due to several reasons: first, ours is a single-center study and likely underpowered to show a difference in the incidence of HAI. Second, several factors apart from the patient's immune response predispose one to HAI. Compliance with hand-hygiene, infection prevention bundles, antibiotic use practices, and nurse to patient ratio, all determine the occurrence of HAI, but these data were not collected as part of our study.

Complications like AKI, septic shock, and the need for invasive mechanical ventilation due to HAI were significantly higher in the sepsis group when compared to the non-sepsis group. Patients admitted with sepsis were sicker on admission and sepsis by causing a dysregulated immune response potentially predisposes an already sicker population to organ injury, exacerbates existing organ dysfunction, and delays any recovery.

The ICU LOS was longer in sepsis admissions compared to the non-sepsis admission group in our study. The higher ICU LOS in patients admitted with sepsis was probably due to the higher baseline severity of illness (SOFA) and the higher rates of organ dysfunction and shock among this group.

In concordance with our study, previous studies[7,12,15] have also shown mortality rate in the range of 40% in the sepsis admission group and 27% in the non-sepsis group.

The other study that compared sepsis and non-sepsis ICU admissions also described results similar to ours with longer ICU LOS in the sepsis admission group but no difference in mortality in comparison to non-sepsis admissions.[15] Our study is likely underpowered to show any differences in mortality.

The strengths of our study are that it is prospective and conducted with objective outcome assessments with pre-defined definitions for HAI. Ours is the largest study from a resource-limited setting. The limitation of our study is the data from only one center may not reflect general trends across all ICUs.

Conclusion

The incidence of HAI seems to be similar between patients admitted with sepsis and non-sepsis diagnoses. However, patients admitted with sepsis develop higher rates of organ failure secondary to HAI and have a longer ICU LOS compared to patients admitted with non-sepsis diagnoses. There is no difference in the mortality rates of patients admitted with sepsis and non-sepsis diagnoses.

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