Healthcare-associated Infection in Intensive Care Units: Overall Analysis of Patient Criticality by Acute Physiology and Chronic Health Evaluation IV Scoring and Pathogenic Characteristics

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ABSTRACT

Objectives: To compare the predicted vs observed mortality rate, criticality, and length of stay of the patients with healthcare-associated infections (HAIs) in intensive care units (ICUs) of a tertiary health center through acute physiology and chronic health evaluation (APACHE) IV scoring. To analyze the drug sensitivity pattern of the isolated pathogen.

Design: This is a prospective observational study involving the patients admitted to various ICUs of a tertiary care teaching hospital. Among 1,229 patients who were admitted in the ICUs for a period of 2.5 months (74 days), 767 patients stayed beyond 48 hours. They were monitored and 87 of them who developed HAIs were included in the study. The organisms isolated from the infection site were identified, and the drug resistance pattern was reported as per standard guidelines. The patients were followed up till their discharge, and adequate details pertaining to the study were collected including demographic details and physiological and biochemical parameters to calculate APACHE IV score, length of stay, and prognosis.

Setting: Intensive care units of JSS Hospital, Mysuru, Karnataka, India.

Subjects/patients: All patients who developed HAI in ICUs.

Interventions: Nil.

Measurements and main results: The HAI rate observed in this study was 15.7%. Ventilator-associated pneumonia (VAP) was the most common type of infection. *Klebsiella* and *Acinetobacter* were the frequently isolated organisms. There was a high prevalence of drug resistance among these pathogens. The ICU mortality in infected patients was 21.83%, roughly twice as that of uninfected patients. The observed length of stay was 11.66 ($\pm$8.53) days.

Conclusion: Healthcare-associated infection was associated with long duration of ICU stay. There was a high prevalence of drug resistance to various antibiotics. Acute physiology and chronic health evaluation IV score was not found to be good scoring system to predict the mortality and length of stay in the patients who had HAI.

Keywords: Acute physiology and chronic health evaluation IV score, Criticality, Drug resistance, Healthcare-associated infection, Intensive care unit, Nosocomial.

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INTRODUCTION

Healthcare-associated infection (HAI) can be defined as "an infection acquired in an acute care setting which was not present or incubating at the time of admission."[1] It was also considered as infection that was not incubating at the time of admission and arising after 48 hours of admission.[2,3] According to the World Health Organization data, published on "The Burden of Health-Care Associated Infection Worldwide" from 1995 to 2008, the prevalence of HAI in developed countries varied between 5.1% and 11.6%. The burden of HAI is much higher in developing countries and among high-risk populations, such as patients admitted in critical care units.[4] The incidence of these infections in critical care units is quite high in India ranging from 9.6% to 17.7%.[5,6] Several risk factors contributing to these infections include poor health status, catheterization, endotracheal intubation, re-intubation, tracheostomy, placement of nasogastric tube, mechanical ventilation, higher APACHE II score, and length of ICU stay among others.[7]

Among all ICU-related infections, respiratory tract infections and urinary tract infections (UTIs) were more frequent.[5,8]

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The common organisms contributing to these HAIs include *Klebsiella*, *Acinetobacter*, *Escherichia coli*, *Pseudomonas*, and *Candida*.[7,9] In addition, high prevalence of drug resistance in these organisms is a major problem. They contribute to higher morbidity and mortality of patients.[10–13] It is evident that HAIs in ICUs are

an important cause of increased duration of hospital stay, cost of treatment, morbidity, and mortality. Hence, an additional study on this topic assumes greater importance.

MATERIALS AND METHODS

This is a prospective observational study involving the patients admitted to the ICUs of a tertiary care teaching hospital. Six ICUs with a total of 72 beds were included in the study. They include ICU, medical intensive care unit (MICU), respiratory intensive care unit (RICU), neurosurgical intensive care unit (NSICU), surgical intensive care unit (SICU), step-down surgical intensive care unit (SDSICU).

Approval from the Institutional Ethics Committee was obtained prior to the study. Among 1,229 patients who were admitted in the ICUs for a period of 2.5 months (74 days), 767 patients stayed beyond 48 hours. They were monitored, and 87 of them who developed HAIs were included in the study. Those who had infection before 48 hours of admission were included in the uninfected group unless they showed a different infection or infection at a different site. Patients who were readmitted in the ICUs were considered as new admissions. Informed consent was obtained from eligible patients; however, in certain cases, due to the inability of the patient, consent was obtained from the guardian/relative.

The sample size was 87 patients who were followed up till their discharge, and adequate details pertaining to the study were collected. Details about the age of the patient, cause for admission, site from where the patient was brought to the ICU, prior hospitalization, comorbid conditions, alcohol intake, and smoking habits were obtained. Several physiological parameters were assessed on the first day, to determine the criticality and the prognosis of the patient. This was done using APACHE IV score and acute physiology score (APS), which also predict the mortality and length of stay in the ICU. The patients were followed up to know the duration of stay and mortality. The actual morality and the length of stay were compared with the predicted data, except for patients who opted for voluntary discharge. Acute Physiology and Chronic Health Evaluation IV and APS scoring was calculated by using the following online website: https://intensivecarenetwork.com/Calculators/Files/Apache4.html. The data [e.g., bilirublin levels, FiO_2, blood pressure (BP), sodium levels, and Glasgow Coma Scale (GCS)] were collected from all patients admitted to ICUs during the study period. The worst values of vitals and laboratory parameters of the first 24 hours were considered for calculation. However, the above scores were calculated only from study subjects who developed HAI 48 hours later. Additional information including admission information, operative status, and chronic health condition (as applicable to the above score calculator) was collected from these subjects.

The HAI was identified according to the latest Centers for Disease Control (CDC) definitions.[1] The HAI rates were expressed in terms of 1,000 patient days. Specific infections [e.g., VAP and surgical site infection (SSI)] were expressed in terms of the number of infections per 1,000 device days.

The organisms isolated from the infection site were identified according to standard operating procedures of the department of microbiology. Bacterial isolates were identified using gram staining, culture on routine media (e.g., blood agar and MacConkey agar), while selective media and biochemical tests were used wherever necessary. Fungal isolates were identified by cultures on Sabouraud dextrose agar, Sabouraud dextrose chloramphenicol agar along with gram staining, lactophenol cotton blue mount, and germ tube testing.[14,15] The antimicrobial sensitivity pattern was tested by Kirby–Bauer disk diffusion method. The results of these tests were reported as per the Clinical Laboratory Standards Institute Guidelines.[16]

The data that were collected in the study were analyzed using standard statistical methods. Qualitative data were expressed as number and percentage while quantitative data were expressed as mean with standard deviation (SD). In addition, the data analysis was performed by Mann–Whitney U and Spearman's correlation test wherever necessary. A p value of <0.05 was considered statistically significant. The accuracy of APACHE IV in predicting the mortality was assessed by using receiver operating characteristic (ROC) curve. SPSS version 19 (SPSS, Inc., Chicago, IL, USA) was used for the analysis.

RESULTS

Part 1: Demographic Details

The data were collected from 87 patients with a mean age of 52.06 years (±17.4). Among these patients, 80% were male and 20% were female. A maximum number of patients were admitted for trauma (47.1%), followed by infection (17.2%) and cerebrovascular accident (12.6%). Majority of the patients were admitted to NICU and MICU which together constituted more than 50% of all subjects. Step-down surgical ICU and RICU have the least number of subjects of 7 and 8%, respectively. Roughly 20% of the patients were shifted to the ICU postoperatively, while the rest were nonoperative cases. Upon assessment of comorbidities of the patient, 30 (34%) were diabetic and 33 (38%) had hypertension. Moreover, one third of the patients were chronic alcoholics, while one fourth had a history of chronic smoking.

Part 2: Mortality and Criticality Assessment

Outcome of the patients: 59 (67.8%) were discharged, 19 (21.8%) patients expired, and 9 (10.3%) were discharged against medical advice (DAMA).

Mortality of Patients

- Overall ICU mortality n/N (%): 144/1,229 (11.7%)
- Mortality of those admitted >48 hours n/N (%): 82/767 (10.69%)
- Mortality of those with HAI n (%): 19/87 (21.83%)

Those who developed hospital-acquired infection had twice the mortality rate when compared with those who were admitted for more than 48 hours. The overall ICU mortality remained almost equal to the mortality rate post 48 hours.

Criticality of patients assessed by APACHE IV score, APS, predicted length of stay, and mortality is described in Table 1. For statistical analysis and inference, those who were DAMA were excluded as true mortality, and the length of stay would remain unknown for such patients. Therefore, the results are summarized for two sets of patients (overall and excluding DAMA patients), while statistical analysis was performed for the latter.

The statistical analysis compared the effectiveness of APACHE IV scoring to predict the mortality and length of stay of patients ($n = 78$).

Mortality

The ROC curve plotted for APACHE IV score and observed mortality showed an area under the curve (AOC) of 0.736, 95% confidence interval (CI) (0.638–0.833).

Table 1: Criticality assessment

Characteristics	Total (n = 87)	Excluding DAMA (n = 78)
Age, mean ± SD	52.06 (±17.45)	52.06 (±17.39)
APACHE IV score, mean ± SD	41.34 (±25.10)	39.31 (±22.25)
APS score, mean ± SD	34.37 (±21.54)	32.50 (±18.79)
Predicted mortality, mean (as %)	13.35%	12.27%
Observed mortality, n (%)	19 (21.80%)	24.40%
Predicted length of stay, mean ± SD	6.57 (±1.80)	6.61 (±1.79)
Observed length of stay, mean ± SD	11.66 (±8.53)	11.95 (±8.73)

Fig. 1: The receiver operating characteristic curve plotted for predicted mortality and observed mortality showed an area under the curve of 0.708, 95% confidence interval (0.607–0.808)

The ROC curve plotted for predicted mortality and observed mortality showed an AOC of 0.708, 95% CI (0.607–0.808), as shown in Figure 1.

Length of Stay

On performing Spearman's correlation test between APACHE IV score 39.31 (±22.25) and length of ICU stay 11.96 (±8.73) days, the following result was obtained: correlation coefficient = 0.155, p value = 0.176. There is a weak positive correlation between APACHE IV score and length of stay ($r = 0.15$) of patients which was not found to be statistically significant.

The predicted and observed lengths of stay were compared by Mann–Whitney U test. The p value obtained was <0.001. There is a statistically significant difference between the predicted and observed lengths of stay, indicating that APACHE IV scoring system was not a reliable method for length of stay prediction in those who developed hospital-acquired infection.

Part 3: HAIs and Drug Resistance of the Pathogen

Total no. of HAIs: 121

Hospital-acquired infection rate: 121/767 = 15.7%

The mean duration of stay until the infection developed is 4.84 ± 3.29 days.

Infection rates expressed in terms of x per 1,000 patient days/device days are:

- Overall HAI rate: 30.54/1,000 patient days
- Ventilator-associated pneumonia rate: 39.3/1,000 ventilator days
- Urinary tract infection rate: 4.78/1,000 catheter days
- Central line–associated bloodstream infection (CLABSI) rate: 3.98/1,000 central line days

The common infections are VAP (49%), catheter-associated UTI (13%), surgical site infection (12%), bloodstream infection (12%), and others (Table 2). The most common organism was *Klebsiella* (29%), followed by *Acinetobacter* (24%), *Pseudomonas* (9%), *Candida* (9%), *Staphylococcus* (9%), and others. Table 3 describes the distribution of various organisms. Table 4 describes the drug resistance pattern of gram-negative organisms.

For comparing the number of infections with the length of stay, patients ($n = 78$) were divided into two groups. A comparison between those who had one infection and those who had two or more infections showed a significant difference in length of stay when analyzed by Mann–Whitney U test ($p < 0.001$).
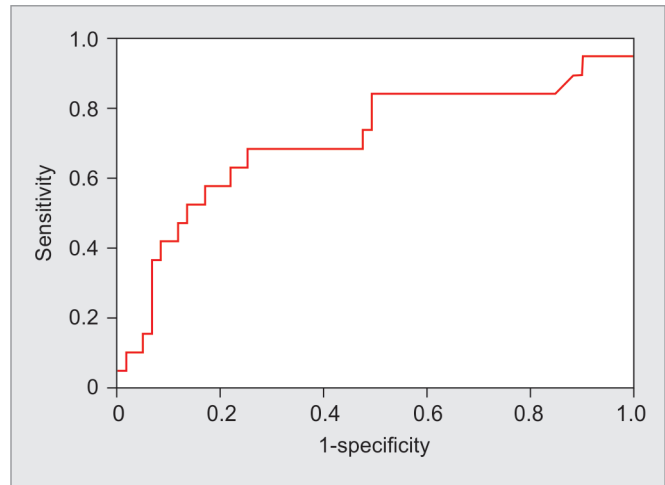
Length of stay of patients with <2 infections: 10.41 ± 5.89 days
Length of stay of patients with >2 infections: 27.65 ± 15.98 days
p value: <0.001

Similar results were obtained when the subjects were divided into groups with <3 infections and ≥3 infections ($p = 0.018$). However, the mean difference in the length of stay was lesser than the previous grouping. This could be explained by higher mortality in those who had more infections.

Length of stay of patients with <3 infections: 11.45 ± 8.32 days
Length of stay of patients with >3 infections: 24.66 ± 10.78 days
p value: 0.018

Therefore, from the insignificant weak correlation between APACHE IV scoring and length of stay and the above comparison, it is evident that higher number of hospital-acquired infections is associated with longer duration of ICU stay.

DISCUSSION

Healthcare-associated infections are invariably associated with increased length of ICU stay and hospital stay.[17] In addition, they contribute to a higher cost of medical treatment reaching around 3.5 billion dollars annually.[18] Some studies have shown that there has not been increased mortality of patients with ICU-related infections,[7,8,19] while other studies have reported the contrary.[20–22] This study has shown that the mortality rate in infected patients to be almost twice as that of uninfected ICU patients. This can be attributed to the underlying conditions, comorbidities, cause for admission, age, criticality, and other factors apart from infection. Moreover, for a lot of patients, the cause for admission was trauma. According to a Swedish study, trauma with open fractures increased the risk of infection more than twice, mainly due to wound infections while infection prolonged length of stay 8–9 days and doubled the risk of death.[23] Our study also showed a high number of patients with diabetes mellitus, hypertension, and associated habits like chronic smoking and alcoholism. However, comparative prospective studies with a larger sample size of infected and uninfected patients are required for understanding the impact of these factors.

Acute physiology and chronic health evaluation IV scoring[24,25] to predict the length of stay and mortality of ICU patients was

Table 2: Infections in intensive care units

Type of infection	Sample collected	ICU	MICU	NSICU	RICU	SICU	SDSICU	Total
VAP	Endotracheal aspirate	9	9	22	5	11	3	59 (48.7%)
CAUTI	Urine	0	6	6	1	2	1	16 (13.2%)
SSI	Pus	2	4	3	1	3	2	15 (12.3%)
Bloodstream infection	Blood	3	4	3	2	3	0	15 (12.3%)
Pneumonia (non-VAP)	Sputum	2	3	0	1	0	1	7 (5.7%)
CLABSI	Catheter tips	0	0	2	1	0	0	3 (2.4%)
Meningitis	CSF	0	0	2	0	0	0	2 (1.6%)
Pleuritis	Pleural fluid	0	0	1	0	1	0	2 (1.6%)
Conjunctivitis	Eye swab	0	0	1	0	0	0	1 (<1%)
URTI	Throat swab	0	0	0	1	0	0	1 (<1%)
Total		16 (13.2%)	26 (21.4%)	40 (33%)	12 (9.9%)	20 (16.5%)	7 (5.7%)	121

CAUTI, catheter-associated urinary tract infection; CSF, cerebrospinal fluid; URTI, upper respiratory tract infection

Table 3: Organisms isolated from various infections

Type	Organism	CAUTI	SSI	VAP	Pneumonia (non-VAP)	Blood	Other	Total
Non-fermenters	Acinetobacter	0	1	26	2	1	1	31
	Pseudomonas	0	2	9	0	0	1	12
	Burkholderia	0	0	0	1	1	0	2
Enterobacteriaceae	Klebsiella	5	7	18	3	3	1	37
	E. coli	2	2	1	1	0	0	6
	Serratia	0	0	4	0	3	1	8
	Enterobacter	1	0	1	0	1	0	3
	Citrobacter	0	0	1	0	0	0	1
Gram-positive organisms	Staphylococcus aureus	0	0	0	0	1	0	1
	Staphylococcus (coagulase negative)	1	2	0	0	4	3	10
	Streptococcus	0	2	0	0	1	0	3
	Enterococci	1	2	0	0	0	0	3
Fungal	Candida	6	0	2	0	0	3	11
	Total	16	18	62	7	15	10	128

not found to be a good method in those who suffered HAI. In our study, there was a weak positive correlation between the score and observed length of stay. When comparing the predicted and actual length of stay of ICU stay, there was a statistically significant difference. Limitations of APACHE IV scoring, as explained by various studies, could be due to (a) estimations achieved based on American population function better when compared with other populations where the scores are not derived from[26] and the need for recalibration[26,27] and (b) other scoring methods are superior to APACHE IV in trauma patients.[28] The validity of these reasons can only be confirmed by comparative studies between infected vs uninfected groups, where the uninfected group would also show similar results. Another reason for the poor performance of the APACHE IV scoring could be the effect of infection itself. Increased mortality rate and longer duration of stay could explain the failure of scoring system in these selected subjects. Therefore, understanding the risk factors for infections and other limitations of APACHE IV scoring can aid in recalibrating the scoring system.

The study reports a high occurrence of HAIs in ICUs. Ventilator-associated pneumonia being the commonest infection was most commonly associated with *Acinetobacter*. It is in consistent with other studies.[5] However, *Klebsiella* was the most prevalent organism overall.

Among UTIs, *Candida* was the commonest isolate, similar to studies from the United States and China.[3,29] Gram-positive organisms were mostly associated with bloodstream infections. Drug resistance to various antimicrobials was seen to a large extent among the pathogens that were isolated. Non-fermenters and Enterobacteriaceae showed very high resistance to third-generation cephalosporins, carbapenems, and aminoglycosides. Irrational use of antibiotics would lead to a higher prevalence of these organisms which leaves us with few antibiotics like tigecycline and colistin.

Therefore, ICU-related infections in hospitals have become a common problem worldwide, and they contribute significantly to morbidity and mortality. Efforts to prevent colonization of pathogens in device-related areas, following strict aseptic precautions, and hand hygiene are some measures to reduce the disease burden.[30]

Conclusion

The HAI rate observed in this study was 15.7%. Ventilator-associated pneumonia was the most common type of infection. *Klebsiella* and *Acinetobacter* were the frequently isolated organisms. There was a high prevalence of drug resistance among these pathogens.

Table 4: Drug resistance mean gram-negative organisms

Antimicrobial	Acinetobacter (n = 31)	Pseudomonas (n = 12)	Total[a] (n = 45)	Klebsiella (n = 37)	Serratia (n = 8)	Total[b] (n = 55)	Total (n = 100)
Amikacin	30 (96.7%)	8 (66.6%)	40 (88.8%)	30 (81%)	2 (25%)	37 (67.2%)	77
Aztreonam	30 (96.7%)	3 (25%)	33 (73.3%)	37 (100%)	8 (100%)	55 (100%)	88
Cefepime	29 (93.5%)	8 (66.6%)	39 (86.6%)	36 (97.2%)	5 (62.5%)	47 (85.4%)	86
Cefoperazone/sulbactam	27 (87%)	8 (66.6%)	35 (77.7%)	36 (97.2%)	2 (25%)	44 (80%)	79
Ceftazidime	30 (96.7%)	8 (66.6%)	38 (84.4%)	37 (100%)	8 (100%)	55 (100%)	93
Ciprofloxacin	30 (96.7%)	8 (66.6%)	40 (88.8%)	36 (97.2%)	4 (50%)	47 (85.4%)	87
Doripenem	30 (96.7%)	8 (66.6%)	40 (88.8%)	37 (100%)	6 (75%)	53 (96.3%)	93
Gentamicin	27 (87%)	7 (58.3)	36 (80%)	24 (64.8%)	3 (37.5%)	32 (58.1%)	68
Imipenem	30 (96.7%)	8 (66.6%)	40 (88.8%)	33 (89%)	8 (100%)	46 (83.6%)	86
Levofloxacin	29 (93.5%)	7 (58.3)	38 (84.4%)	37 (100%)	6 (75%)	53 (96.3%)	91
Meropenem	29 (93.5%)	9 (75%)	39 (86.6)	36 (97.2%)	4 (50%)	43 (78.1%)	82
Piperacillin/tazobactam	29 (93.5%)	9 (75%)	39 (86.6)	36 (97.2%)	7 (87.5%)	4,8 (87.2%)	87
Minocycline	9 (29%)	–	–	36 (97.2%)	2 (25%)	48 (87.2%)	–
Tigecycline	0 (0%)	6 (50%)	6 (13.3%)	17 (45.9%)	1 (12.5%)	20 (36.3%)	26
Colistin	0 (0%)	0 (0%)	0 (%)	0 (0%)	0 (0%)	1 (1.8%)	1
Tlcarcillin	–	10 (83.3%)	–	37 (100%)	8 (100%)	–	–
Cotrimoxazole	–	–	–	33 (89%)	7 (87.5%)	–	–

[a]Including all non-fermenters
[b]Including all Enterobacteriaceae

The ICU mortality in infected patients was 21.83%, roughly twice as that of uninfected patients. Healthcare-associated infection was also associated with long duration of ICU stay. Acute Physiology and Chronic Health Evaluation IV score was not found to be a good scoring system to predict the mortality and length of stay in the patients who had HAI.

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