ORIGINAL ARTICLE

Epidemiology of Intensive Care Unit-acquired Infections in a Tertiary Care Hospital of North India

Amit Kumar[1], Dhruva Chaudhry[2], Nidhi Goel[3], Shweta Tanwar[4]

Abstract

Background: The majority of nosocomial infections in the hospital setting are found in intensive care units (ICUs). The present study was undertaken to determine the incidence, risk factors, causative microorganisms, and outcome of various ICU-acquired infections.

Materials and methods: The patients admitted to the ICU of a teaching hospital in North India were prospectively studied. Detailed history, clinical examination, acute physiology and chronic health evaluation score II, simplified acute physiology score II, sequential organ failure assessment score, and baseline investigations were recorded. Patients were assessed daily till 14th day for nosocomial infection as per Centers for Disease Control and Prevention (CDC) guidelines and were followed till death or discharge. Incidence, risk factors, and outcome parameters were calculated using Student *t*-test, Chi-square test, and stepwise multivariate logistic regression model.

Results: The overall incidence rate of ICU infections was 27.9%. The most common ICU-acquired infection was ventilator-associated pneumonia followed by catheter-related bloodstream infection and catheter-associated urinary tract infection. *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae* were implicated in most of the infections. ICU length of stay (LOS) >7 days, neurological dysfunction, endotracheal intubation, ischemic heart disease, and use of antacids/H_2 blockers were significantly associated with ICU-acquired infections. The mortality rate was 32.8 and 28.8% in patients with and without ICU infections, respectively ($p = 0.531$). The ICU LOS (19.23 $\pm$ 12.79 days) was significantly higher in the ICU infections group ($p < 0.001$).

Conclusion: Ventilator-associated pneumonia was the most common nosocomial infection in our study. Gram-negative microorganisms were the predominant causative agents for various ICU-acquired infections. Mortality was not found to be affected but ICU LOS was significantly prolonged as a consequence of the development of ICU-acquired infection.

Keywords: Catheter-associated urinary tract infection, Catheter-related bloodstream infection, ICU-acquired infections, ICU mortality, Incidence, Ventilator-associated pneumonia.

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Introduction

Nosocomial infection is defined as an infection acquired during the hospital stay without any evidence that the infection was present or incubating at the time of admission.[1] Intensive care units (ICUs) with severely ill patients surrounded by an environment of equipment, resistant microbes, and overworked health care workers have emerged as hubs of nosocomial infections. Advanced modalities of treatment and interventions, including organ replacement therapies have improved the survival rate of severely ill patients in the ICUs where the prevalence of nosocomial has been reported to be more than twofold compared to general ward.[2–4] Selection pressure caused by indiscriminate use of antibiotics has also led to emergence of highly resistant microorganisms. Particularly ventilator-associated pneumonia (VAP) and catheter-related bloodstream infection (CRBSI) are the cause for significant morbidity and mortality in the ICU.

Most of the studies related to nosocomial infections have been conducted in developed countries despite the fact that these infections constitute a huge global burden both in terms of morbidity, mortality, and economic costs. International data related to the prevalence, risk factors, associated causative pathogens, and outcomes of these infections are necessary to create awareness and development of international guidelines. In the context of the availability of limited data regarding the epidemiology of nosocomial infections in the Indian ICUs, this study was carried out. The objectives were to determine the incidence, causative microorganisms, risk factors, and outcome of ICU-acquired infections. The outcome was measured in terms of ICU length of stay (LOS) and the associated mortality.

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Conflict of interest: None

Materials and Methods

This prospective observational study was carried out in the multidisciplinary ICU of the Department of Pulmonary and Critical Care Medicine in a teaching hospital for a period of 18 months. The institutional ethics board had approved the study protocol.

Patients with more than 48 hours of ICU stay were included in the study. Informed consent was obtained. The presence of acquired ICU infection [VAP, CRBSI, and catheter-associated urinary tract infection (CAUTI)] was assessed daily till the 14th day of ICU admission. Patients with ICU stay ≤48 hours, age ≤18 years or ≥80 years, transferred in from other ICUs, readmission, patients with burns, known human immunodeficiency virus seropositivity, or with solid organ/bone marrow transplantation were excluded from the study. A detailed history of each patient was taken, and information regarding the following parameters was obtained: smoking, alcohol/drug abuse, ischemic heart disease (IHD), chronic obstructive pulmonary disease (COPD), diabetes mellitus, malignancy, chronic liver disease, chronic renal disease, and past or current use of steroids. The severity of underlying disease was assessed by acute physiology and chronic health evaluation score II (APACHE II) and simplified acute physiology score II (SAPS II) calculated at the time of admission. Organ/multiorgan dysfunction during the ICU stay was assessed by sequential organ failure assessment (SOFA) score. VAP was clinically diagnosed using modified clinical pulmonary infection score (CPIS) as a screening method. A modified CPIS >6 was considered suggestive of VAP. Definitive diagnosis of VAP was confirmed with culture of samples showing significant growth. Nosocomial infections were defined as per the standard definition of the Centers for Disease Control and Prevention (CDC). Whenever an infection was suspected, an appropriate specimen (trachea-bronchial secretions, blood, or urine) was collected using the standard protocol. Standard microbiological methods were used to identify the causative microorganism. The outcome of the patient was measured in terms of ICU LOS and the 28-day mortality/survival. The study diagram is depicted in Flowchart 1. SPSS software (version 20) was used for statistical analysis. Mean and standard deviation were used to denote continuous variables whereas categorical variables were expressed as number and percentage. Comparison analysis was done using the Student *t*-test and the Chi-square test for continuous and categorical variables, respectively. Assessment of risk factors for ICU-acquired infections was done with a multivariate logistic regression model through a stepwise forward procedure. Statistical significance was defined as $p < 0.05$.

Results

A total of 621 patients were admitted to the ICU during the study period out of which 290 patients were included in the study according to the inclusion and exclusion criteria. Table 1 shows the demographic and main clinical characteristics of the patients. Out of 290 patients, 64 patients (22.1%) developed 81 device-associated infections with an infection rate of 27.93%. Table 2 shows the distribution of various ICU-acquired infections. Ventilator-associated pneumonia was most common accounting for 65.43% of all infections. Catheter-related bloodstream infections accounted for 22.22% and CAUTIs constituted 12.35% of all ICU-acquired infections. The incidence density of VAP was 17.65/1,000 ventilator days while that of CRBSI and CAUTI were 10.5/1,000 central venous catheter days and 2.6/1,000 catheter days, respectively. Various etiological agents of VAP, CRBSI, and CAUTI are depicted in Figures 1, 2, and 3, respectively. The most common bacteria associated with VAP was *Pseudomonas aeruginosa* (27%) followed by *Acinetobacter baumannii* (22%), while for CRBSI, the most common organisms were *P. aeruginosa* and *Klebsiella pneumoniae* (22% each). Catheter-associated urinary tract infection was most commonly caused by *Enterococcus* spp (46%).

Univariate analysis (Table 3) showed that the risk factors associated significantly with ICU-acquired infections were smoking, COPD, IHD, nasogastric tube, use of antacids/H_2 blockers, neurological dysfunction, endotracheal intubation, and ICU LOS >7 days. The ICU LOS >7 days, neurological dysfunction, endotracheal intubation, IHD, and the use of antacids/H_2 blockers were found to be statistically significant in multivariate logistic

Flowchart 1: Study diagram

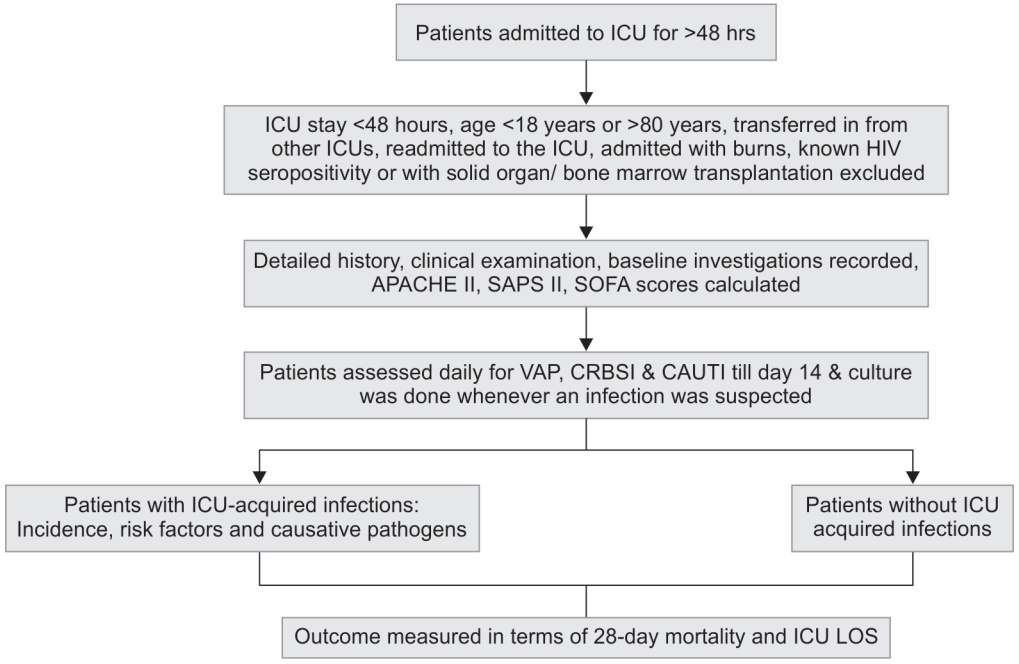

Table 1: Demographic data and clinical characteristics

Sl. No.	*Variable*	*Patients with ICU-acquired infections (64)*	*Patients without ICU-acquired infections (226)*	*Total (290)*
1	Age	37.4 ± 17.3 years	39.8 ± 16.3 years	39.3 ± 16.5 years
2	Male sex	37	138	175
3	Alcohol abuse	26	68	94
4	Smoking	34	63	97
5	Diabetes	10	72	82
6	COPD	17	35	52
7	Malignancy	02	05	07
8	Chronic liver disease	05	68	73
9	Chronic renal disease	03	19	22
10	Ischemic heart disease	10	13	23
11	Neurological dysfunction	36	49	85
12	Past or current use of systemic steroids	15	76	91
13	Endotracheal intubation	57	144	201
14	Tracheostomy	27		
15	Central venous catheter	48	155	203
16	Urinary catheter	64	223	286
17	ICU stay >7 days	53	87	140
18	Nasogastric tube	60	167	227
19	Antacids/H_2 blockers	61	174	235
20	Medical admission	52	179	231
21	Surgical admission	12	47	59

Table 2: Distribution of ICU-acquired infections

ICU-acquired infection	*No. of infections (%)*	*Incidence density/1,000 device days*
VAP	53 (65.43)	17.65/1,000 ventilator days
CRBSI	18 (22.22)	10.5/1,000 central venous catheter days
CAUTI	10 (12.35)	2.6/1,000 catheter days

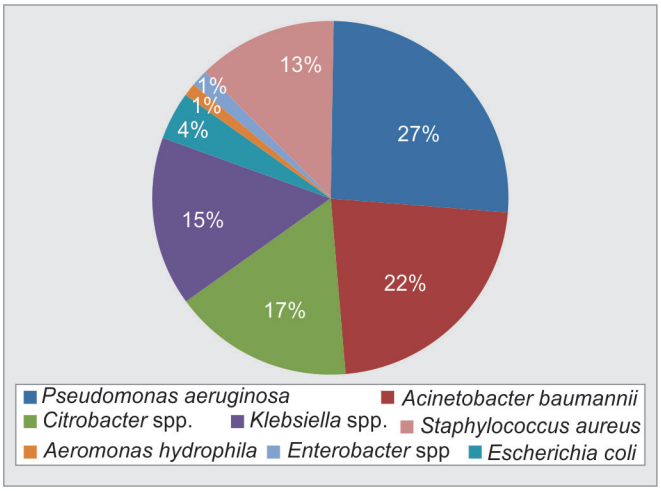

Fig. 1: Etiological agents of VAP

regression analysis and thus could be considered as independent risk factors for the development of ICU-acquired infections (Table 4).

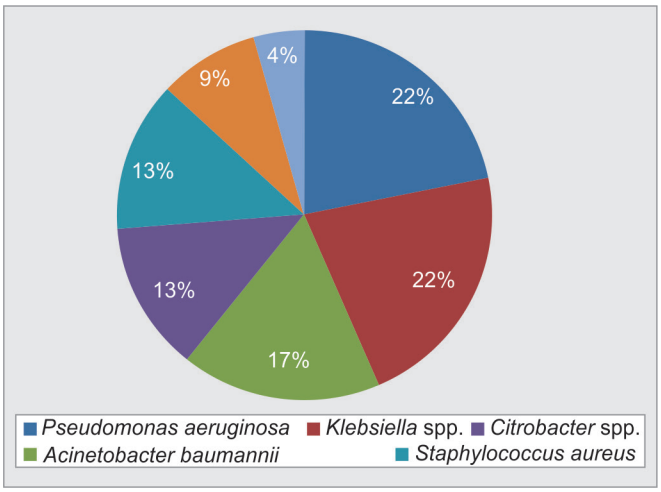

Fig. 2: Etiological agents of CRBSI

The 28-day mortality in the ICU infections group was observed to be 32.81% whereas it was 28.8% in patients without ICU-acquired infections and there was no significant difference ($p = 0.531$). The ICU LOS was found to be significantly longer in patients with ICU-acquired infections (19.23 ± 12.79 days) as compared to patients without ICU-acquired infections (7.57 ± 6.82 days) with $p < 0.001$.

Table 5 compares the severity scores between survivors and nonsurvivors among the patients with ICU-acquired infections. The severity of underlying disease as determined with APACHE II and SAPS II scores was observed to be significantly higher in the

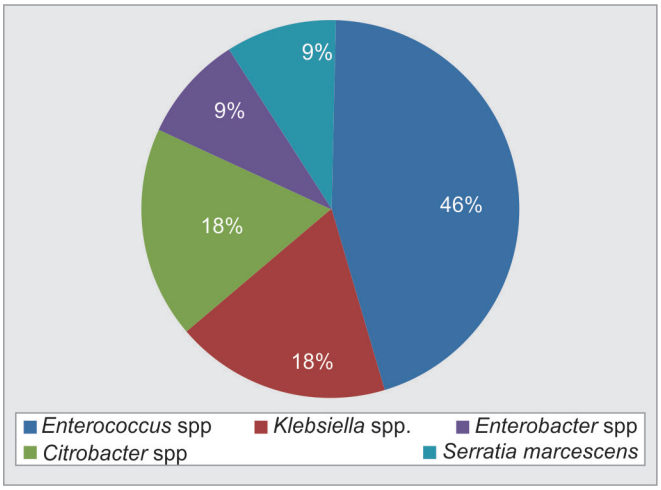

Fig. 3: Etiological agents of CAUTI

Table 3: Univariate analysis of risk factors for ICU-acquired infections

Sl. No.	*Variable*	*Odds ratio*	*95% confidence interval*	*p value*
1	Age >50 years	0.83	0.46–1.52	0.553
2	Male gender	0.87	0.49–1.54	0.639
3	Alcohol	1.59	0.89–2.82	0.113
4	Smoking	2.75	1.55–4.88	0.0005
5	COPD	1.97	1.55–4.87	0.044
6	Chronic liver disease	0.19	0.08–0.51	0.0009
7	Chronic renal disease	0.54	0.15–1.87	0.328
8	Malignancy	1.42	0.27–7.53	0.676
9	IHD	3.03	1.26–7.29	0.013
10	Past or current use of systemic steroids	0.60	0.31–1.14	0.123
11	Nasogastric tube	5.29	1.84–15.22	0.002
12	Antacids/H_2 blockers	6.07	1.83–20.17	0.003
13	Diabetes	0.39	0.19–0.82	0.013
14	Neurological dysfunction	4.64	2.58–8.35	<0.0001
15	Medical admission	1.14	0.56–2.30	0.719
16	Endotracheal intubation	4.64	2.02–10.63	0.0003
17	Central venous catheter	1.37	0.73–2.58	0.324
18	Urinary catheter	0.85	0.08–8.29	0.887
19	ICU stay >7 days	7.69	3.81–15.54	<0.0001

Table 4: Multivariate logistic regression analysis of risk factors for ICU-acquired infections

Sl. No.	*Variable*	*Odds ratio*	*95% CI*	*p value*
1	ICU stay >7 days	6.67	3.03–14.68	<0.0001
2	Neurological dysfunction	5.48	2.74–10.97	<0.0001
3	Endotracheal intubation	3.01	1.13–8.02	0.0274
4	IHD	5.14	1.73–15.29	0.0032
5	Antacids/H_2 blockers	4.48	1.19–16.88	0.0268

Table 5: Comparison of severity scores in survivors and nonsurvivors

Severity score	*All patients*	*Survivors*	*Nonsurvivors*	*p value*
APACHE II	19.73 ± 6.99	17.86 ± 6.44	23.57 ± 6.61	0.002
SAPS II	45.5 ± 15.12	42.86 ± 13.71	50.90 ± 16.75	0.045
SOFA	6.39 ± 3.53	5.38 ± 2.99	8.45 ± 3.80	0.000

nonsurvivor group with *p* values of 0.002 and 0.045, respectively. Similarly, SOFA score during the ICU stay was significantly higher in the nonsurvivors ($p = 0.000$). Duration of mechanical ventilation was found to be significantly shorter in the nonsurvivor group ($p = 0.003$). The LOS in the ICU ($p = 0.000$) as well as in the hospital ($p = 0.000$) was significantly shorter in the nonsurvivors as shown in Table 6.

Discussion

The prospective design and systematic identification of various nosocomial infections in the ICU contribute significant strength to this study. A detailed and thorough data was collected regarding the type of admission, comorbidities, use of steroids, various severity scores (APACHE II, SAPS II, and SOFA scores), and daily evaluation was done in search of any ICU-acquired infection.

The incidence of ICU infections in the present study (27.9%) is consistent with reports of the studies conducted in other Indian ICUs. Datta et al. reported an infection rate of 29.1% for ICU-acquired infections.[5] Similarly in another study by Ravi et al., the incidence of ICU-acquired infections in a tertiary care hospital of South India was 25%.[6] VAP was the commonest nosocomial infection in our study (65.43%) in concurrence with the study by Mukhopadhyay et al. wherein 53.9% of patients developed one or more episodes of nosocomial pneumonia.[7] Our VAP rate of 17.65/1,000 ventilator days is higher than that reported in various studies conducted in Indian ICUs and other developing countries. In a study conducted by International Infection Control Consortium in seven Indian ICUs, the infection rate for VAP was 10.46/1,000 ventilator days.[8] Similarly in a study by Dutta et al., the incidence of VAP was found to be 6.04/1,000 ventilator days.[5] A higher incidence rate for VAP in the present study can be attributed to the lack of adequate number of nursing staff in our ICU. *P. aeruginosa* and *A. baumannii* were found to be the most common organisms associated with VAP which is similar to the observations reported by Gupta et al.[11] Similar etiological profile of VAP was also reported by Joseph et al.[12]

In our study, CRBSI was the second most common nosocomial infection (22.2%) after VAP. This finding is in accordance with the earlier studies.[10,13,14] The incidence rate of CRBSI reported in the present study (10.5/1,000 central venous catheter days) is higher than that reported in previous studies. Habibi et al. found the incidence rate of CRBSI to be 3.4/1,000 central venous catheter days.[15] In a similar study by Mehta et al., the infection rate for CRBSI was 7.92/1,000 central venous catheter days.[8] Considering these values, the rate of CRBSI was significantly higher in our ICU but is comparable with that of 55 ICUs in developing countries (12.8/1,000 central venous catheter days).[16] A higher rate for CRBSI similar to that reported in our study was also observed by Datta et al. (13.86/1,000 central line days).[5] The incidence of CRBSI depends upon multiple factors such as the site of insertion, frequency of dressing changes, catheter manipulation, topical antimicrobial agent, and patient's primary illness.[17] *P. aeruginosa* and *K. pneumoniae* were the two

Table 6: Comparison of duration of mechanical ventilation, length of stay in ICU, and hospital in survivors and nonsurvivors

	All patients	*Survivors*	*Nonsurvivors*	*p value*
Duration of mechanical ventilation (days)	16.33 ± 11.45	19.35 ± 12.63	10.27 ± 5.39	0.003
ICU LOS (days)	19.23 ± 12.79	23.30 ± 13.43	10.90 ± 5.38	0.000
Hospital LOS (days)	23.91 ± 16.06	29.54 ± 16.25	12.38 ± 7.05	0.000

most common organisms accounting for 44% of catheter-related bloodstream infections in the present study in contrast with other studies where *Staphylococcus aureus* has been reported to be the most prevailing organism.[17,18] However, several factors, such as antibiotic protocols, local ecology, and the resistance patterns affect the precise pattern of causative microbes in an ICU.[19]

Catheter-associated urinary tract infection occupied the third rank of nosocomial infections in our study (12.35%) in concurrence with the studies done by Appelgren et al., Vosylius et al., and Alberti et al.[10,20,21] However, we found a much lower incidence rate in our ICU (2.6/1,000 catheter-days) as compared to other studies.[5,16] A rate comparable to that of our study was reported by Agarwal et al. (1.5/1,000 catheter-days) and it was suggested that failure to differentiate between colonization and infection might have led to over diagnosis of UTI in earlier studies.[22] *Enterococcus* spp caused the maximum number of CAUTIs in our study. Laupland et al. also reported *Enterococcus* spp as the commonest pathogen causing CAUTI in their study.[23] On the contrary, most studies on CAUTI have shown the predominance of gram-negative bacilli.[5,10,20]

In the sophisticated environment of ICU, several risk factors may contribute to the development of infections like the severity of the underlying condition, endotracheal intubation, various invasive devices, neuroparalytic agents, multiple antibiotics, immunosuppression, poor infection control practices, and neurological dysfunction. In the present study, the risk factors having significant association with ICU-acquired infections, as observed in multivariate logistic regression analysis, were neurological dysfunction, endotracheal intubation, ICU LOS >7 days, use of antacids/H_2 blockers, and IHD. More than half of the patients with ICU-acquired infections had underlying neurological dysfunction predominantly caused by traumatic head injury, organophosphate poisoning, and neuroparalytic snake envenoming. Decreased level of consciousness results in loss of the cough and gag reflexes contributing to pooling of secretions and aspiration and therefore increased risk of VAP. Also, these patients had difficulty in weaning, which further predisposed them to infection. Increased risk of infection in patients with neurological dysfunction has also been demonstrated by Fernandez et al. and Appelgren et al.[9,10] Use of invasive device, such as endotracheal intubation almost always, leads to increased risk of infection. The ICU LOS as an imperative risk factor for acquired infection has also been cited important by various authors.[15,22,24] As the devices remain inserted for a longer time with longer ICU stay, the chances of infection with multidrug-resistant microbes also increases. The use of H_2 blockers/proton pump inhibitor for stress ulcer prophylaxis inhibits the gastric acid secretion causing increased gastric colonization and retrograde colonization leading to development of VAP. This has been supported by the observation of Herzig et al. that the use of acid-suppressive medication increased the odds of hospital-acquired pneumonia by 30%.[29] In a study of 1,014 mechanically ventilated patients, cardiac disease was found to be significantly associated with VAP in concordance with the observation of this study.[30]

The 28-day mortality rate for ICU-acquired infections (32.8%) in the present study is comparable with that reported in various studies.[24,25] The nonsurvivors had significantly higher APACHE II, SAPS II, and SOFA scores. The severity scores have earlier been reported to modify the relationship between ICU-acquired infections and mortality.[14,20]

The ICU and hospital LOS and the duration of mechanical ventilation in the present study were considerably shorter in the nonsurvivors. This was due to the fact that the nonsurvivors had the more severe underlying condition as depicted by higher severity scores and they were too sick to survive. Cavanillas et al. had also reported that the mortality could be attributed to the severity of underlying disease rather than infection in patients with high APACHE II scores.[14]

The ICU-acquired infections did not affect mortality significantly in the present study. Although many studies have observed nosocomial infections in the ICU to be an independent risk factor for mortality but major consensus revealed no difference. In a study done by Cardoso et al., healthcare-associated infections did not cause a significant rise in mortality.[26] Bregeon et al. also reported that VAP was not an independent risk factor for mortality.[27] Likewise, Rello et al. demonstrated that the mortality was not altered significantly in patients with CRBSI.[28] Laupland et al. showed similar observations in the context of CAUTI and ICU mortality.[23] All these studies suggest that there are several risk factors that affect mortality in the ICU and thus a direct association between nosocomial infection and ICU mortality could not be established formally. In the present study also, the patients who later died were already critically ill as shown by higher APACHE II, SAPS II, and SOFA scores. Thus, assessment of mortality was not straightforward as nosocomial infections and mortality share several risk factors that confound the relationship. On the contrary, the ICU LOS was found to be significantly longer in the patients who acquired nosocomial infections (19.23 ± 12.79 days). Vosylius et al. also observed a longer ICU stay among the patients who developed an ICU infection.[20] This can be due to the fact that the time period for which the devices remain inserted increases with the duration of ICU stay which further predisposes to colonization with potential microorganisms and subsequent infection. But whether the prolonged stay occurred due to infection or the infection developed because of prolonged stay remained an unanswered question as in earlier studies.[24–27]

The study has various limitations. First, the generalization of findings may be limited owing to the fact that it was a single ICU study. Second, the long-term consequences of ICU infections could have been studied as it is important for the development of strategies to improve the quality of life of such patients.

Conclusion

The most commonly observed nosocomial infection was VAP followed by CRBSI and CAUTI. Majority of the ICU-acquired infections were caused by gram-negative organisms, predominantly *P. aeruginosa* and *A. baumannii*. Although the ICU-acquired infections did not affect the mortality, there was a significant increase in the LOS in the ICU which has serious repercussions on financial resources of both ICU and the patients.

Author Contributions

Amit Kumar, Dhruva Chaudhry, and Nidhi Goel created the conceptualization of the work. Amit Kumar, Dhruva Chaudhry, and Nidhi Goel verified the methodology. Investigation and visualization was done by Amit Kumar. Data interpretation was completed by Amit Kumar and Shweta Tanwar. Software, validation, and formal analysis was performed by Amit Kumar and Shweta Tanwar. Amit Kumar drafted the manuscript. Dhruva Chaudhry and Nidhi Goel supervised the project. All authors contributed to the writing, reviewing, editing, and final approval of the manuscript to be published.

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