ORIGINAL ARTICLE e-ISSN: 2349-0659 p-ISSN; 2350-0964

A Study of Nosocomial Infections in Intensive Care Units of Local Tertiary Care Hospitals

Sanjay Agrawal[1], Rahul Kewal Kumar[2]*

Abstract

Introduction: It has been reported that the incidence of nosocomial infections in the intensive care unit (ICU) is about 2–5 times higher than in the general in-patient hospital population. The objectives of the present study were to determine the incidence of nosocomial infection, to identify possible risk factors for these infections, to clarify the distribution of the causative pathogens, and to evaluate the outcome of the infected patients in terms of length of ICU and hospital stay and mortality. **Methods:** This was a retrospective and analytical study. For classification of the different causative pathogens associated with nosocomial infections, all the microorganisms isolated on culture from each of the patients with confirmed infection according to the Centers for Disease Control and Prevention definitions were recorded and their relative frequency of isolation was determined as percentage. Bacterial isolates were identified by Gram stain, cultures on routine media and where necessary, selective media, and specific biochemical tests following standard protocols. **Results:** Nosocomial infections were in 28 patients. The most frequently diagnosed nosocomial infection was nosocomial pneumonia. A total of 39 pathogens were isolated on culture and accounted for the nosocomial infections in 28 patients. Some infections were polymicrobial. Gram-negative *Enterobacteriaceae* were the most frequently isolated pathogens. There was no statistically significant difference between the hospital mortality rates among the patients with and without nosocomial infection. **Conclusion:** Gram-negative *Enterobacteriaceae*, as a group, were the most frequently isolated pathogens, while *Pseudomonas aeruginosa* was the single most frequent causative organism. The acquisition of nosocomial infections in the ICU resulted in significantly increased length of ICU and hospital stay, but did not result in statistically significant increase in ICU or hospital mortality. These findings can now be utilized toward planning a surveillance program for nosocomial infection in our ICU setting as a first step toward a better infection control strategy.

Keywords: Gram-negative *Enterobacteriaceae*, Intensive care unit, Nosocomial infections, Ventilator-associated pneumonia

Asian Pac. J. Health Sci., (2021); DOI: 10.21276/apjhs.2021.8.2.01

Introduction

A nosocomial infection is defined as an infection that is not present or incubating when the patient is admitted to hospital or other health-care facility. National nosocomial infections surveillance system has defined nosocomial infection as a localized or systemic condition that results from an adverse reaction to the presence of an infectious agent(s) or its toxin(s) that was not present or incubating at the time of admission to the hospital. The important nosocomial infections in the intensive care unit (ICU) based on frequency and potential severity include urinary tract infection (UTI), pneumonia, bloodstream infections (BSIs), skin and soft-tissue infections, gastroenteritis, hepatitis, and meningitis.[1] It has been reported that the incidence of nosocomial infections in the ICU is about 2–5 times higher than in the general in-patient hospital population.[2] The increased morbidity and mortality associated with nosocomial infections in the ICU are a matter of serious concern today. Serious medicolegal issues also arise in this context, since the patient or their families sometimes blame the hospital staff for the infection and demand compensation.[3] It has been reported that in hospitals with an effective program for nosocomial infection surveillance, infection rates can be reduced by approximately one-third.[4] In our setting that of a busy ICU in a tertiary care teaching hospital in the public sector, survey of nosocomial infection has not been carried out in the recent past. The objectives of the present study were to determine the incidence of nosocomial infection, to identify possible risk factors for these infections, to clarify the distribution of the causative pathogens, and to evaluate the outcome of the infected patients in terms of length of ICU and hospital stay and mortality.

[1]Associate Professor, Department of General Medicine, Raipur Institute of Medical Sciences, Raipur, Chhattisgarh, India

[2]Associate Professor, Department of Community Medicine, Raipur Institute of Medical Sciences, Raipur, Chhattisgarh, India

Corresponding Author: Rahul Kewal Kumar, Department of Community Medicine, Raipur Institute of Medical Sciences, Raipur, Chhattisgarh, India. E-mail: doctormanoj34@gmail.com

How to cite this article: Agarwal S, Kumar RK. A Study of Nosocomial Infections in Intensive Care Units of Local Tertiary Care Hospitals. Asian Pac. J. Health Sci., 2021; 8(2):1-4.

Source of support: Nil

Conflicts of interest: None.

Received: 10/13/2020 **Revised:** 11/01/2021 **Accepted:** 08/02/2021

Methods

This retrospective and analytical study involved prior consent from hospital authorities/medical superintendents of the randomly selected local private tertiary care hospitals to see the records of the patients from medical records department with the disclosure that the data will be used only for study purpose. Identity (names) was hidden and medical record numbers were used to generate the data for analysis.

The study was conducted within ethical standards and does not involve any direct intervention to any mentioned subjects nor any physical examination was performed. Randomization was done using computer tables in selecting data. All patients data had details of standard clinical examinations, routine biochemical and hematological investigations. For the purpose of the present study,

data of 200 of the randomly selected patients (candidates/study subjects) were retrospectively identified. The medical records for these patients were reviewed for the collection and classification.

A retrospective analysis of medical records of all adult (age more than 18 years) patients admitted to ICU of local tertiary care hospitals over 6 months was done. Only those patients admitted to ICU for more than 48 h were analyzed. Those with evidence of new infection after 48 h of ICU admission (nosocomial infection) were included in the study (study group). Demographic characteristics (age, gender, and admission diagnosis), site of infection (skin and soft tissue including surgical site infections, respiratory tract, genitourinary system, abdominal infections, BSI, and central nervous system infections), microorganisms isolated from the site or blood (more details *Escherichia coli*, *Acinetobacter*, *Pseudomonas*, *Klebsiella*, *Methicillin-resistant Staphylococcus aureus*, *Citrobacter*, *Candida* spp., and others), antibiotic sensitivity profile, and resistance pattern were noted. The study group was matched (age, gender, and admission diagnosis) with ICU patients during the study that did not have nosocomial infections. The primary outcome was ICU mortality. The secondary outcome was number of days spent in ICU. The duration of ICU stay and mortality in both groups was statistically analyzed using Chi-square test.

Nosocomial infections were diagnosed according to the standard definition of the (United States Centers for Disease Control and Prevention [CDC]).[6,7] It was ensured in the records that antimicrobial therapy was administered to the patients as necessary and cultures were requisitioned when infection was suspected. Patients were always sampled for microbial culture before starting a new antimicrobial. Appropriate essential investigations were regularly performed as needed.

The following factors were recorded as present (at any time during the ICU stay) or absent in a particular patient before the development of ICU-acquired infection: Underlying disease, comorbidity, central venous catheterization, pulmonary arterial catheterization, invasive arterial catheterization, peripheral venous catheterization, urinary catheterization, endotracheal intubation, re-intubation, tracheostomy, nasogastric tube insertion, mechanical ventilation, surgical procedure, prior antimicrobial therapy, antacid and stress ulcer prophylaxis therapy, sedative-analgesic therapy, vasopressor therapy, parenteral nutrition, enteral nutrition, horizontal body position with head at <30°, blood transfusion, hypoalbuminemia, diabetes mellitus, chronic renal failure, chronic alcoholism, malnutrition, and immunocompromise.

For classification of the different causative pathogens associated with nosocomial infections, all the microorganisms isolated on culture from each of the patients with confirmed infection according to the CDC definitions were recorded and their relative frequency of isolation was determined as percentage.[6,7] Bacterial isolates were identified by Gram stain, cultures on routine media (e.g., blood agar and MacConkey agar), and, where necessary, selective media and specific biochemical tests following standard protocols.[8,9] Fungal isolates were identified by cultures on Sabouraud dextrose agar, and Sabouraud dextrose chloramphenicol agar media, followed by Gram stain, lactophenol cotton blue mount, and germ tube testing following standard protocols.[10] For assessing outcome, each patient was followed up till ICU and hospital discharge or death. Length of ICU stay and hospital stay was recorded as the number of days from admission to discharge from the ICU and hospital, respectively. The length of ICU and hospital stay in patients with and without nosocomial infections and also the ICU and hospital mortality rates in patients were statistically compared.

Continuous data were expressed as mean ± standard deviation. The data were analyzed by IBM SPSS Statistics 23. All quantitative data were coded and transformed into an Excel master sheet for computer programming. A Chi-square test was used to evaluate categorical variables for analysis. Overall, $P < 0.05$ was proposed to represent statistical significance after correction.

Results

We observed that the ICU-acquired nosocomial infections were in 28 patients (14%; 95% CI: 7.89–16.07%). These 28 patients developed one type of nosocomial infection each. The most frequently diagnosed nosocomial infection was nosocomial pneumonia. Combining both ventilator-associated pneumonia (VAP) and non-VAP, nosocomial pneumonia was found in 16 (57.14%; 95% CI: 44.41–79.73%) of the 28 infected patients. Taken separately, VAP was diagnosed in 9 (32.14%) and non-ventilator-associated nosocomial pneumonia was diagnosed in 7 (25%) of the infected patients. UTI was diagnosed in 8 (28.57%) out of the 28 infections and central venous catheter-related BSI was detected in 3 (10.7%) patients. Hence, when judged separately, VAP was the most common ICU-acquired infection detected. On the calculation of the infection rate per 1000 patient's days or per 1000 device days, the following values were obtained:

- Overall nosocomial infection rate = 17.21/1000 patient days
- Nosocomial pneumonia rate (both VAP and non-VAP) = 10.62/1000 patient days
- VAP rate = 27.2/1000 ventilator days
- Non-VAP rate = 4.21/1000 patient days
- UTI= 7.94/1000 catheter days
- Central venous catheter-associated BSI rate = 2.85/1000 central venous catheter days.

On comparison of putative risk factors of nosocomial infection by univariate analysis, prior antimicrobial therapy, antacid use, hypoalbuminemia, malnutrition, urinary catheterization, endotracheal intubation, reintubation, tracheostomy, placement of nasogastric tube, mechanical ventilation, acute physiology and chronic health evaluation II (APACHE II) score >13, and length of ICU stay were found to be statistically significant. Out of these, prior antimicrobial therapy, urinary catheterization, and length of ICU stay were found to be statistically significant risk factors for nosocomial infection by multivariate analysis.

A total of 39 pathogens were isolated on culture and accounted for the nosocomial infections in 28 patients. Some infections were polymicrobial. Gram-negative *Enterobacteriaceae* were the most frequently isolated pathogens (n = 14; 35.89%) closely followed by *Pseudomonas* species (n = 13; 33.3%, *Pseudomonas aeruginosa* = 12 and *Burkholderia cepacia* = 1).

There was no statistically significant difference between the hospital mortality rates among the patients with and without nosocomial infection (P = 0.267). There was a trend toward greater mortality in the ICU in patients with nosocomial infection than in patients without, but this did not reach statistical significance (P = 0.09).

Discussion

The prevention of ICU-acquired infections demands knowledge of the infection rates and of the sources, the pathogens involved as well as the common risk factors for infection. The incidence of nosocomial infections varies according to the setting, that

is, the type of hospital or ICU, the patient population, and the precise definition and surveillance techniques used to identify a nosocomial infection.[11] A large cohort multicentric international study has reported at least one ICU-acquired infection in 18.9% of patients, with an incidence ranging from 2.3% to 49.2% across the centers.[12] In a 1-day point prevalence study involving 1265 ICUs from 76 countries (extended prevalence of infection in intensive care [EPIC II] study), 51% of patients were found to have nosocomial infection. However, the rates of infections varied considerably according to the country, with Greece and Portugal having the highest and Switzerland and Germany and the Netherlands having the lowest infection rates.[13] Other studies[14,15] have reported incidence rates between 9% and 37%, depending largely on the populations studied. Crude infection rates might not be representative of the overall problem since they do not take into account the patients' intrinsic risk of infection or extrinsic risks associated with exposure to medical interventions.[16] The findings in our study were found to be closer to the lower range of incidence rates reported in the other studies referred above. This difference in findings is not necessarily related to better quality of care, since many other factors may be responsible including difference in the criteria for patient selection, the case mix, ICU type, length of stay, rate of device utilization, and discharge criteria.[17,18] The patients from a single institution can present with different risk of infection in the context of differing case mix, severity of illness, and utilization rates of invasive devices.[19] In the EPIC II study,[13] the most frequently reported sites for ICU-acquired infections were the lungs (64%), abdominal (19%), and bloodstream (15%). Data from the United States National Nosocomial infections surveillance system showed that the nosocomial pneumonia accounted for 31% of all nosocomial infections followed by UTIs and BSIs.[19] The site distribution of nosocomial infections in this study broadly conforms to the findings of earlier and larger studies mentioned above. The precise pattern of causative organisms, whether bacterial or fungal, varies across countries and between ICUs according to patient case mix, site of infection, antibiotic protocols, infection control practice and local ecology, and resistance patterns.[20] Although recent years have seen swings in the pathogen pattern toward Gram-positive bacterial infections,[21,22] still, most studies report that more than half of the nosocomial infections occurring in the ICU are due to Gram-negative bacteria.[13,19] In our study too, the most commonly isolated organisms were Gram-negative *Enterobacteriaceae* followed closely by *Pseudomonas* species. The detection of *Candida* species in 15% of the isolates in the present study is also consistent to some extent with the studies of Pittet and Wenzel[23] and Edgeworth *et al*.[24] who have reported that fungal pathogens are also becoming increasingly common among patients with nosocomial BSIs. ICU-acquired infections have been reported to be associated with increased length of ICU and hospital stays.[24] Correa and Pittet[26] reported an additional cost of about $3.5 billion/year due to ICU-acquired infections. The findings in the present study are corroborative. Crude mortality rates associated with nosocomial infection vary from 12% to 80%, dependent on the population studied and the definitions used.[20] Whereas some studies do report increased mortality associated with nosocomial infections,[27,28] other studies, like those of Rello *et al*.,[29] have not shown higher mortality, emphasizing the problems in defining cause-effect relationship in these individuals. In the study by Rosenthal *et al*.,[30] crude mortality rate for patients with device associated infections ranged from 35.2% (for central venous catheter associated BSI) to 44.9% (for VAP). In the present study, there was a trend, but no statistically significant difference in ICU mortality rate in the patients with compared to those without nosocomial infection despite a significantly greater proportion of infection patients falling in the higher APACHE II category. A probable explanation for the lack of difference could be a variation in the baseline severity of illness mentioned before and described by Vincent.[20] Another factor that may have prevented the trend from becoming statistically significant is the relatively small number of deaths in both arms observed over the 6-month study period. A longer study may have produced more deaths leading to the observed difference becoming statistically significant. Although there is a plethora of studies detailing the risk factors for various types of nosocomial infections in various groups of patients, more commonly identified risk factors can be divided into four groups: (a) Those related to underlying health impairment; (b) those related to the acute disease process; (c) those related to use of invasive procedures; and (d) those related to other treatment modalities. Diverse studies have described various features of underlying health impairment, such as chronic lung disease,[31] immunocompromise, increased age,[14] and malnutrition[32], as independent risk factors for nosocomial infections. It has been reported in some studies[17,33] that the risk of developing nosocomial infections increased with high APACHE II score. Invasive device utilization such as central venous or urinary catheterization, intubation, tracheostomy, and mechanical ventilation has been reported as significant risk factors for infection in many studies.[13,17,18,33] The EPIC II study[13] reported that medical admission, admission after emergency surgery or trauma, referral from the hospital floor, emergency room, or other hospital, the presence of chronic obstructive pulmonary disease, cancer, HIV, older age, mechanical ventilation, renal replacement therapy, and greater simplified acute physiology score II were found to be independently associated with a higher risk of infection. The findings in this study are partly in agreement with earlier studies.[27,33]

Conclusion

In this study, nosocomial infections were diagnosed in 14% of the patients. Nosocomial pneumonia (both ventilator and non-ventilator associated) was the most frequently detected infection followed by urinary tract and central venous catheter-associated BSIs. Length of ICU stay, prior antimicrobial therapy, and urinary catheterization were found to be significant risk factors associated with the acquisition of nosocomial infections. Gram-negative *Enterobacteriaceae*, as a group, were the most frequently isolated pathogens, while *P. aeruginosa* was the single most frequent causative organism. The acquisition of nosocomial infections in the ICU resulted in significantly increased length of ICU and hospital stay, but did not result in statistically significant increase in ICU or hospital mortality. These findings can now be utilized toward planning a surveillance program for nosocomial infection in our ICU setting as a first step toward a better infection control strategy.

Study Limitations

The main limitations of this study include its retrospective design (data of past admitted patients) with a limited number of participants (n = 200). We have not studied the long-term outcomes, and it may be that although we are not seeing any

difference in short-term outcomes, they may become apparent in the long term.

Acknowledgments

We would like to thank all the hospital authorities of the participating tertiary care hospitals. Our seniors and head of department for his always available guidance to us.

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