

Prospective Study

Attributable cost of a nosocomial infection in the intensive care unit: A prospective cohort study

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Abstract

AIM

To study the impact of hospital-acquired infections (HAIs) on cost and outcome from intensive care units (ICU) in India.

METHODS

Adult patients (> 18 years) admitted over 1-year, to a 24-bed medical critical care unit in India, were enrolled prospectively. Treatment cost and outcome data were collected. This cost data was merged with HAI data collected prospectively by the Hospital Infection Control Committee. Only infections occurring during ICU stay were included. The impact of HAI on treatment cost and mortality was assessed.

RESULTS

The mean (\pm SD) age of the cohort ($n = 499$) was

42.3 ± 16.5 years. Acute physiology and chronic health evaluation- II score was 13.9 (95%CI: 13.3-14.5); 86% were ventilated. ICU and hospital length of stay were 7.8 ± 5.5 and 13.9 ± 10 d respectively. Hospital mortality was 27.9%. During ICU stay, 76 (15.3%) patients developed an infection (ventilator-associated pneumonia 50; bloodstream infection 35; urinary tract infections 3), translating to 19.7 infections/1000 ICU days. When compared with those who did not develop an infection, an infection occurring during ICU stay was associated with significantly higher treatment cost [median (inter-quartile range, IQR) INR 92893 (USD 1523) (IQR 57168-140286) *vs* INR 180469 (USD 2958) (IQR 140030-237525); $P < 0.001$ and longer duration of ICU (6.7 ± 4.5 d *vs* 13.4 ± 7.0 d; $P < 0.01$) and hospital stay (12.4 ± 8.2 d *vs* 21.8 ± 13.9 d; $P < 0.001$]. However ICU acquired infections did not impact hospital mortality (31.6% *vs* 27.2%; $P = 0.49$).

CONCLUSION

An infection acquired during ICU stay was associated with doubling of treatment cost and prolonged hospitalization but did not significantly increase mortality.

Key words: Attributable cost; Nosocomial infection; Length of stay; Mortality; Intensive care

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Core tip: There is paucity of data on the impact of hospital acquired infections (HAIs) on cost and outcome from intensive care units (ICU) in developing countries. In this prospective study of 499 patients admitted over 1-year to a medical ICU in India, there were 19.7 HAIs per 1000 ICU days. Occurrence of infection was associated with significantly higher treatment cost ($P < 0.001$); the median attributable cost of an infection was 87594 Rupees (USD 1436). Although ICU acquired infections increased ICU length of stay (6.7 ± 4.5 d *vs* 13.4 ± 7.0 d; $P < 0.01$), it did not impact mortality (31.6% *vs* 27.2%; $P = 0.49$).

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INTRODUCTION

Health care associated infection (HAI) is a major preventable complication in critically ill patients across the world^[1,2]. Whilst there is a significant body of information and evidence on the cost of these infections from developed countries, primary research from developing countries, in this area, is limited^[3,4]. Translation of results of studies from developed countries on the impact and cost of infections to situations in developing countries

may not be appropriate for several reasons: (1) different microbiological profile of HAIs^[5,6]; (2) perceived reluctance among physicians regarding treatment of HAIs that is probably based on the impression that these infections are associated with poor survival^[7,8]; and (3) limited resources and affordability which argues that resource allocation for the treatment of HAI would steal opportunities away from other potentially treatable patients, waiting for an intensive care unit (ICU) bed. The affordability issue is compounded by the fact that only about 10% of the estimated 70000 ICU beds in India are available in the public sector, where treatment is provided free of cost^[9]. This poses a major problem of demand-supply mismatch, not only in the public sector, but also in the private sector since the population that needs to be covered in India is over 1 billion. Minimal subscription to private health insurance and resource pooling being in its infancy results in significant out-of-pocket expenses that push several families below the poverty line^[10].

In the light of the above, a study was undertaken to evaluate the "cost" (in terms of money) and "impact" (in terms of clinical outcomes) of HAIs in developing countries. Such studies would facilitate investment on interventions that reduce infection as well as help plan appropriate allocation of the scarce resources of materials (ICU beds and equipment), manpower and money to address this problem in the ICU setting.

MATERIALS AND METHODS

In this study spanning 1-year, prospectively collected ICU cost data was merged with HAI data collected prospectively by the Hospital Infection Control Committee (HICC). ICU cost data was obtained from a study that looked at cost-utility as well as willingness-to-pay in patients admitted to the medical ICU^[11].

Patients and setting

The study was undertaken in a 24-bed medical critical care unit in a 2500-bed, university-affiliated, private teaching hospital in semi-urban India. In this hospital, other than the very few covered by private health insurance, the entire treatment cost is expected to be paid for by the patient.

During a 1-year period (January-December 2011), adult patients (> 18 years) admitted to the 24-bed medical critical care unit were enrolled if they stayed beyond 24-h in the ICU. Patients not consenting to participate, patients not admitted under internal medicine (e.g., hematological malignancies, chronic liver disease), or patients with surgical problems were excluded. A diagnosis of HAI was made only when a new infection occurred 48-h after hospital admission. The study was approved by the Institutional Review Board and Ethics committee (IRB No. 10011) and consent was obtained from patient or next-of-kin.

Costs

"Treatment cost", obtained from the hospital electronic

Table 1 Demographic data of the groups with and without hospital acquired infections

Features	HAI (<i>n</i> = 76)	No HAI (<i>n</i> = 420)	<i>P</i> value
Age, mean (SD), (yr)	39.4 (16.2)	42.9 (16.5)	0.04
Male:female	46:30	241:179	0.70
APACHE II score, mean (SD)	14.01 (4.7)	13.9 (6.0)	0.58
Diagnosis <i>n</i> (%)			
Sepsis (including scrub typhus)	27 (35.5)	195 (46.4)	
Deliberate self-harm	30 (39.4)	99 (23.6)	
Cardiac	4 (5.3)	34 (8.1)	0.11
Acute respiratory distress syndrome	5 (6.6)	28 (6.7)	
Neurological	6 (7.9)	43 (10.2)	
Others	4 (5.3)	21 (5.0)	

Data not available for 3 patients. HAI: Hospital acquired infection; APACHE: Acute physiology and chronic health evaluation; SD: Standard deviation.

system, was taken as the direct medical cost incurred from the time of admission to hospital until discharge from hospital (including ICU cost). This included bed and nursing charges, professional fees, equipment charges, investigations, oxygen charges, and medication costs^[12].

Infections

Infection data was obtained from the HICC that does daily active surveillance. Only infections occurring during ICU stay were included. Ventilator associated pneumonia (VAP), blood stream infections (BSI) and urinary tract infections (UTI) developing 48-h after hospital admission were the infections that were analysed. VAP and UTI were defined as per the CDC guidelines^[13]. BSI was defined as a positive blood culture with a recognized pathogen or the combination of clinical symptoms (fever > 38 °C, chills, hypotension) and two positive blood cultures for a common skin commensal from two separate blood samples drawn within 48 h^[14].

Outcome data

The impact of infections on outcomes was explored. This included its effect on length of stay (ICU and hospital) and hospital mortality. We also assessed the impact of individual infections (VAP, UTI and BSI) on mortality.

Statistical analysis

Frequencies and percentages were used to describe baseline data, overall hospital and ICU mortality. Continuous variables [Acute physiology and chronic health evaluation (APACHE) II score, cost and ICU and hospital length of stay] were expressed as mean [standard deviation (SD)] if data was normally distributed. Where data was not normally distributed (*e.g.*, treatment cost), it was expressed as median with interquartile range (IQR). Hospital mortality and length of stay (ICU and hospital) for the two groups, with HAI and without HAI, were calculated. χ^2 tests were used to compare proportions.

In order to study the impact of HAI on mortality, it was decided to adjust for disease severity and other potential confounders if mortality was significantly different between those who developed infection vs those who did not develop infection.

RESULTS

Baseline demographic data

During the study period, 1599 patients were admitted to medical critical care. A total of 499 patients were enrolled. Exclusion criteria were admission under other specialty units (*n* = 434), deaths or discharges within 24 h (*n* = 105), refusal of consent (*n* = 58) and those not recruited during public holidays or weekends (*n* = 503)^[11].

Demographic data are summarized in Table 1. The diagnosis included 122 different International Classification of Diseases (ICD) code entities and comprised predominantly of acute febrile illness including scrub typhus (44.4%), deliberate self-harm (26%), neurological illnesses (9.8%) and cardiac problems (7.6%).

The study cohort (*n* = 499) was relatively young with a mean (SD) age of 42.3 ± 16.5 years and mean APACHE-II of 13.9 (95%CI: 13.3-14.5); 86% of patients were invasively ventilated. The mean (SD) ICU length of stay was 7.8 ± 5.5 d.

Infection data

Infection data was available in 496 (99.4%) patients. During ICU stay, 76 patients (15.2%) developed an infection, translating to 19.7 infections/1000 ICU days. Patients who developed a HAI were significantly younger (*P* = 0.04) than those who did not develop a HAI (Table 1). However the gender distribution and APACHE-II score were not different between the groups. There were 50 episodes of VAP, 35 episodes of BSI and 3 episodes of UTI; 10 patients had more than one episode of infection. The median time to develop the infection followed an interesting pattern; VAP tended to occur in the first week of ICU stay (8 ± 5 d) while BSI occurred in the second week (11.4 ± 7 d) and UTI in the third week (18.7 ± 12.4 d).

Microbiological data

Overall, non-fermenting gram-negative carbapenem resistant organisms were isolated from 51 of the 88 episodes (36 VAP, 14 BSI and 1 UTI). There were 4 infections with colistin resistant organisms (3 VAP and 1 BSI). Twelve BSI isolates were susceptible gram-negative organisms. There was no Methicillin resistant staphylococcus aureus (MRSA) isolate in our cohort.

Outcome and cost data

Overall, infections were associated with doubling of length of stay (Table 2). However, mortality was similar in those who developed a HAI and those who did not develop it (Table 2). A logistic regression analysis was

Table 2 Impact of hospital-acquired infections on outcomes

Outcome	HAI (n = 76)	No HAI (n = 420)	P value
ICU length of stay, mean (SD), (d)	13.4 (7.0)	6.7 (4.5)	< 0.01
Hospital stay, mean (SD), (d)	21.8 (13.9)	12.4 (8.2)	< 0.001
In-hospital mortality	31.60%	27.20%	0.49
Mortality with VAP ¹	26%	27.2% ²	1.0
Mortality due to BSI ¹	37%	27.2% ²	0.24
CAUTI mortality ¹	33%	27.2% ²	1.0

¹Total number of patients with VAP was 50, BSI 35 and CAUTI 3; the total number of patients with individual infections exceed 76 since 10 patients had more than one infection source; ²Indicates patients who had no HAI during the entire course of intensive care stay; thus in the analysis for VAP, those with BSI or CAUTI were excluded from the no HAI group and for BSI those with VAP and CAUTI were excluded from the no HAI group. Data available only on 496 patients. VAP: Ventilator associated pneumonia; BSI: Blood stream infection; CAUTI: Catheter associated urinary tract infection; SD: Standard deviation; HAI: Hospital acquired infection.

Table 3 Comparison of overall cost between those with infection and those without infection

Type	HAI (n = 76)	No HAI ¹ (n = 420)	Cost difference	P value
Mean (SD) cost (INR)				
Any infection	226398 (226268)	115058 (93754)	111340	< 0.0001
VAP	235350 (253421)	115058 (93754)	120292	< 0.001
BSI	283887 (341916)	115058 (93754)	168829	< 0.001
CAUTI	190059 (34096)	115058 (93754)	155963	0.05
Median (IQR) cost (INR)				
Any infection	180469 (140030-237525)	92875 (57243-139104)	87594	< 0.0001
VAP	182991 (133038-238952)	92875 (57243-139104)	90116	< 0.0001
BSI	170753 (141788-238650)	92875 (57243-139104)	77878	< 0.0001
CAUTI	173085 (155818-190352)	92875 (57243-139104)	80210	0.06

¹The cost of no HAI is the same for all sub-categories of analysis based on source of infection since patients who developed any infection were not included in the "no HAI" group. At the time of the study, 1 USD = INR 61. Values in parenthesis indicate standard deviation. INR: Indian rupees; HAI: Hospital acquired infection; VAP: Ventilator associated pneumonia; BSI: Blood stream infection; CAUTI: Catheter associated urinary tract infection; SD: Standard deviation; IQR: Inter-quartile range.

not performed in view of the lack of effect of infection on mortality. Additionally, when individual infections were considered separately, there was no mortality difference between those who developed a specific infection [*i.e.*, VAP, BSI or catheter associated urinary tract infection (CAUTI)] vs those who did not develop any infection during ICU stay (Table 2).

An infection acquired in the ICU was associated with doubling of overall cost when compared with patients who did not develop an infection during hospitalization. When VAP, BSI and UTI were analysed independently, the overall cost (median IQR) of each infection was almost similar (Table 3). The median attributable cost of an infection worked out to INR 87594 (USD 1436).

DISCUSSION

This study provides insight and information on the burden (economic and otherwise) of common HAIs in the medical ICU of a developing country. While it could be argued that there is data from developed countries to this effect, our data with the different spectrum of infections (predominant VAP and few UTI) and microbiology (over 60% of the isolates carbapenem resistant) merit

reporting and discussion.

Nosocomial infections, individually and overall in our study, were associated with doubling of cost without any impact on mortality. The acquisition of infection was also associated with the need for an additional 7-10 d in the ICU, resulting in further constraining the already limited ICU resources in our setting. Although the increased length of ICU stay is consistent with the limited evidence available for VAP in other countries^[15], this has significant hospital infrastructure and public health implications in our setting.

These findings beg a response to the following questions. First, given the lack of impact of infections on mortality despite the antimicrobial resistance patterns, it is worth treating these infections. Second, should there be a focused approach to looking at measures to decrease infections and improving quality of patient care in ICU? On the face of it, the appropriate response to the above questions would be a resounding yes. However as alluded to, in view of the limited resources, treatment of patients with ICU acquired infections is likely to impact bed allocation to a patient with a more reversible problem. This, coupled with the inability to pay for the entire cost of treatment^[11], places an additional

economic burden on institutions that provide subsidy or charity. Denying on-going care for a potentially reversible problem (in this case a HAI) would violate ethical and moral principles of healthcare. Thus, the response to the second question assumes greater importance.

In India, ICU infrastructure and staffing are varied across hospitals^[16]. It is also known that nosocomial infection rates in developing countries are far higher than that in developed countries. Focusing on reducing the incidence of nosocomial infections would translate to better utilization of ICU beds and economic resources. In addition to rigid enforcement of hand hygiene measures, micromanaging central line handling and optimizing pneumonia prevention strategies may help reduce infection rates. In addition, hospital administrators need to consider optimizing staff-patient ratio and spacing between ICU beds, a problem that probably potentiates infection risk^[17,18]. The latter strategy would involve a cost shift from the patient (who bears the cost of an infection) to the hospital (in improving nursing ratio and bed spacing) that may be beyond the reach of many institutions.

This study, in the setting of a developing country, establishes the fact that an ICU acquired infection is associated with a significant increase in cost. The perception of poor survival is misplaced and patients who develop a HAI should be treated with cautious optimism. The utilitarian philosophy and steal phenomenon remains, since infections are associated with doubling of hospital stay and costs and are likely to prevent other patients from being treated in ICU. Efforts should be maximized on improving infection control practices since additional resource allocation in this setting may be challenging to the majority of health care settings.

COMMENTS

Background

Intensive care units (ICU) acquired infections are generally viewed with skepticism for several reasons. First, is a fact that treatment of ICU acquired infections would increase cost significantly and add pressure on the already stretched ICU resources second, is a perception that such infections would be associated with poor survival and third is an utilitarian philosophy that argues that such resource allocation would "steal" opportunities away from potentially treatable patients waiting for an ICU bed. This study aimed to explore the impact of ICU acquired infections on overall cost and mortality in a tertiary care hospital in a developing country. In this study spanning 1-year, prospectively collected ICU cost data incorporating direct and indirect cost was merged with nosocomial infection data collected by the hospital infection control committee.

Research frontiers

Health care associated infection (HAI) is a major preventable complication in critically ill patients across the world. Whilst there is a significant body of information and evidence on the cost of these infections from developed countries, primary research from developing countries, in this area, is limited. Additionally, translation of data from developed countries on the impact and cost of infections to situations in developing countries may not be appropriate given the different microbiological profile of HAIs.

Innovations and breakthroughs

This study has provided important information that suggests that paying attention to reducing nosocomial infections would not only translate to lower

costs, but also make more intensive care beds available for other patients needing them.

Applications

This study provides insight and information on the burden (economic and otherwise) of common HAIs in the medical ICU of a developing country. While we were not surprised with the finding that HAIs were associated with doubling of cost as compared to those without HAIs, it was reassuring to know that there was no evidence of association of increased mortality despite the antimicrobial resistance patterns. It is thus worth treating these infections and there should be an aggressive focused approach to decrease infections and improve quality of patient care in ICU.

Terminology

HAIs are defined as new infections that develop in the hospital after 48 h of admission. In this study, cost and impact on outcomes (death and length of stay) of common ICU acquired infections, ventilator associated pneumonia, blood stream infections and urinary tract infections were analysed.

Peer-review

The work is novel and good.

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