Epidemiology and risk factors of intensive care unit-acquired infections: a prospective multicentre cohort study in a middle-income country

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INTRODUCTION This study aimed to determine the incidence and risk factors of infections among patients admitted to intensive care units (ICUs) in tertiary care hospitals in Turkey.

METHODS Adult patients who were admitted to the ICUs of five tertiary care hospitals for over 48 hours between June and December 2007 were monitored daily. Potential risk factors such as age, gender, comorbidities, diagnosis at admission, severity of disease (Acute Physiology and Chronic Health Evaluation II scores), exposure to antibiotics, history of invasive procedures and significant medical interventions were evaluated. A multivariate analysis of these risk factors was carried out using Cox regression.

RESULTS A total of 313 patients with a median ICU stay of 12 days were selected for the study. 236 infectious episodes (33.8/1,000 ICU-days) were diagnosed among 134 patients (42.8/100 patients) in this group. Multivariate analysis revealed that exposure to a cephalosporin antibiotic (hazard ratio [95% confidence interval] 1.55 [1.10–2.19]) was an independent risk factor, whereas having a tracheostomy cannula (0.53 [0.36–0.81]) or nasogastric tube (0.48 [0.33–0.70]) was protective. Patients admitted to the ICUs from surgical wards were significantly more exposed to cephalosporins.

CONCLUSION ICU-associated infections, which are quite high in Turkey, are largely due to inadequate infrastructure and facilities and understaffing. Abuse of antibiotics, particularly in patients who have undergone surgery, and prolonged ICU stays are significant risk factors for such infections.

Keywords: cephalosporins, intensive care units, multicentre study, nosocomial infections, risk factors
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INTRODUCTION

Nosocomial infections, which are the cause of substantial morbidity, mortality and financial burden, are frequently seen among patients admitted to intensive care units (ICUs), mostly due to the high incidence of predisposing factors such as high utilisation of antibiotics, prolonged use of invasive equipment and the existence of severe underlying diseases in these patients.[1-3] However, it is possible to contain infection rates through infection-control programmes that are based on surveillance studies of significant extrinsic and intrinsic risk factors.[4,5] A literature review revealed that studies from Turkish hospitals are scarce, and more importantly, inadequate in terms of risk analysis.[6-8] A multicentre prospective cohort study of patients admitted to the ICUs of tertiary-care hospitals from various regions of Turkey was thus undertaken to determine the incidence and significant risk factors associated with infections in this cohort.

METHODS

Eight tertiary-care hospitals located in different regions of Turkey participated in the study. However, data from three centres were excluded due to missing data in critical variables. Of the five hospitals included in the study, four were university hospitals and one was an education hospital. The mean bed capacity of these hospitals was 900 ± 237 beds, while that of the participating adult ICUs was 11.4 ± 1.9 beds (Table I). Although infection control teams were aiding to implement recommended infection control measures in these hospitals, the infrastructure, facilities and staffing levels in ICUs were mostly insufficient. While three ICUs had isolation rooms, none had a negatively pressurised isolation room (Table I). The median 24-hour nurse-to-patient ratio for these ICUs, calculated based on 90% working loads, was 1.1.[9] A database and a surveillance form were developed and distributed to the participating centres. Patients were monitored daily during their entire stay in ICUs by Infectious Diseases (ID) personnel. An ICU-associated infection was defined as an infection developed after 48 hours of ICU admission and diagnosed according to the Center for Disease Control and Prevention (CDC) definitions of nosocomial infections.[10] Patients re-admitted to the ICU within 72 hours of discharge were excluded.[6]

Variables such as demographics, underlying diseases, diagnosis at admission, disease severity at the time of ICU admission (Acute Physiology and Chronic Health Evaluation II [APACHE II] scores), exposure to antibiotics, and the types

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Table I. Findings on the participating hospitals.

Findings	Centre 1	Centre 2	Centre 3	Centre 4	Centre 5
Infrastructure (No.)					
ICU beds/total hospital bed capacity	13/1,100	10/1,200	14/800	10/750	10/650
Isolation rooms in ICUs	0	1	4	0	5
Hand sanitisers	13	4	14	11	10
Sinks	1	3	6	3	6
Staffing (No.)					
Doctors	3	3	2	3	3
Patients per nurse					
Morning shift	3	2	2	2	3
Night shift	4	4	3	4	4
Patients per nursing assistant					
Morning shift	4	4	4	4	4
Night shift	5	5	5	4	5
Professional upgrading opportunities (No. per yr)					
Educational sessions for ICU workers	1	1	12	4	1

ICU: intensive care unit

and duration of invasive procedures and medical interventions that were found to be frequently associated with studies on ICU-associated infections in the literature were monitored and recorded. For patients with ICU-acquired infections, time at risk (TAR) was defined as the time between ICU admission and diagnosis of the first infection episode; for non-infected patients, TAR was the entire duration of ICU stay. Only variables that existed or were established during the TAR period were included in the risk analysis.

Diagnosis at the time of admission to the ICU was recorded in four categories – trauma, sepsis, cardiovascular arrest and others. Underlying diseases were recorded according to the McCabe and Jackson classification.[11] Databases from the centres of study were checked for any missing information, and the omitted details sought and completed by personal communication, if so found. Statistical analyses were carried out on the aggregate data using STATA version 10.1 (StataCorp LP, College Station, TX, USA).

For univariate analysis, dichotomous variables were compared using Pearson's chi-square test and Fisher's exact test, where required, whereas continuous variables were compared using student's *t*-test. The Cox proportional hazards model using the Breslow method was used for multivariate analyses to handle tied failures. Cox regression models were constructed for variables that obtained a p-value < 0.1 in univariate tests in addition to variables that were mentioned as significant in the literature. Gender and severity scores were included in the initial model irrespective of their univariate p-values. Variables were eliminated in a stepwise backward selection process. The goodness of fit of the model was assessed based on the graphic representations of the residuals, log likelihood values and corresponding information criteria. The collinearity diagnostic test (collin) of STATA was applied to identify any instability in the model.

RESULTS

During the study period, 327 patients aged > 17 years stayed in the ICUs for more than 48 hours. 313 patients in the group (Centre 1: n = 53 [16.9%]; Centre 2: n = 42 [13.4%]; Centre 3: n = 61 [19.5%]; Centre 4: n = 90 [28.8%]; Centre 5: n = 67 [21.4%]), with a median ICU stay of 12 days and a total stay of 6,973 ICU-days, were found to be eligible for further analysis. The median ICU stay prior to infection was eight days. 178 (57%) patients were male and the mean age of the cohort was 53.8 years (95% confidence interval [CI] 51.5–56.0). Table II outlines the demographics and risk factors of patients with and without infections.

A total of 236 infectious episodes (33.8/1,000 ICU-days) were diagnosed in 134 patients (42.8/100 patients). Most patients with infections had only a single infectious episode (one episode: n = 71; two episodes: n = 34; three or more episodes: n = 29), although a majority of infectious episodes were caused by multiple microorganisms (one microorganism: n = 106 [45%]; multiple microorganisms: n = 130 [55%]). The most common diagnoses were bloodstream infections (26.8/100 patients; 12/1,000 ICU-days), ventilator-associated pneumonia (24.3/100 patients; 10.9/1,000 ICU days) and urinary tract infections (8.6/100 patients; 3.9/1,000 ICU days). *Pseudomonas* spp. (19.5%), *Acinetobacter* spp. (18.0%), *Staphylococcus aureus* (16.4%) and *Candida* spp. (12.5%) were the most frequently isolated microorganisms.

Univariate analysis revealed that having a non-fatal underlying disease (relative risk [95% CI] 0.72 [0.56–0.93]), the presence of a central vascular line (1.62 [1.08–2.42]), exposure to cephalosporin antibiotics (1.53 [1.20–1.96]), mechanical ventilation (2.00 [1.26–3.17]) and admission to the ICU with trauma (1.58 [1.19–2.09]) were significant factors. Exposure to a cephalosporin antibiotic and having a tracheostomy cannula or nasogastric tube were found to be significant factors based on incidence density analysis of extrinsic risk factors (Table III). Multivariate analyses showed that exposure to cephalosporins (hazard ratio [95% CI] 1.55 [1.10–2.19]) was an independent risk factor while having a tracheostomy cannula (0.53 [0.36–0.81]) or a nasogastric tube (0.48 [0.33–0.70]) was protective (Table IV).

Table II. Demographics and risk factors of patients with and without infections.

Variable*	No. (%)		p-value
	Patients with infections (n = 134)	Patients without infections (n = 179)	
Demographics			
Mean age ± SD (yrs)	52.9 ± 19.44	54.4 ± 20.22	0.503
Male gender	72 (53.73)	106 (59.22)	0.332
Comorbidity†			
Not fatal	63 (47.01)	110 (61.45)	0.011
Fatal	32 (23.88)	28 (15.64)	0.067
Ultimately fatal	1 (0.75)	5 (2.79)	0.243‡
Total	96 (71.64)	143 (79.89)	0.089
Invasive devices			
Central vascular line	115 (85.82)	132 (73.74)	0.010
Urinary catheter	132 (98.51)	175 (97.77)	0.636‡
Nasogastric tube	77 (57.46)	119 (66.48)	0.103
Pleural tube	7 (5.22)	7 (3.91)	0.592
Tracheostomy cannula	24 (17.91)	25 (13.97)	0.342
Exposure to antibiotics			
Carbapenem	28 (20.90)	41 (22.91)	0.671
Cephalosporin	57 (42.54)	45 (25.14)	0.001
Penicillin	27 (21.15)	30 (16.76)	0.442
Quinolone	7 (5.22)	6 (3.35)	0.569‡
Diagnose at ICU admission			
Cardiac arrest	11 (8.21)	15 (8.38)	0.957
Sepsis	12 (8.96)	27 (15.08)	0.104
Trauma	24 (17.91)	14 (7.82)	0.007
Others			
Parenteral nutrition	46 (34.33)	48 (26.82)	0.151
Mechanical ventilation	119 (88.81)	131 (73.18)	0.001
Mean APACHE II scores ± SD	20.3 ± 5.83	20.2 ± 7.68	0.945
Survivors	69 (51.49)	98 (54.75)	0.568

*Risk factors that occurred during the TAR period. † According to the McCabe and Jackson classification. ‡ Fisher's exact test.

Table III. Incidence density ratios of extrinsic risk factors.

Extrinsic risk factor	Incidence density ratio* (95% CI)
Invasive devices	
Central vascular line	0.82 (0.50–1.41)
Urinary catheter	1.31 (0.36–10.94)
Nasogastric tube	0.55 (0.38–0.78)
Pleural tube	1.28 (0.50–2.71)
Tracheostomy cannula	0.44 (0.28–0.67)
Exposure to antibiotics	
Carbapenem	1.13 (0.72–1.73)
Cephalosporin	2.04 (1.42–2.90)
Penicillin	1.30 (0.82–2.00)
Quinolone	1.31 (0.52–2.78)
Others	
Parenteral nutrition	1.34 (0.92–1.94)
Mechanical ventilation	1.19 (0.70–2.20)

CI: confidence interval

Table IV. Hazard ratios of variables used for Cox regression.

Variable	Hazard ratio (95% CI)	p-value
Exposure to cephalosporins	1.55 (1.10–2.19)	0.013
Tracheostomy cannula	0.53 (0.36–0.81)	0.003
Nasogastric tube	0.48 (0.33–0.70)	< 0.001
Fatal comorbidity	1.17 (0.78–1.75)	0.446
Male gender	0.71 (0.50–1.00)	0.053

CI: confidence interval

DISCUSSION

The study found remarkably higher ICU-associated infections in the participating centres (42.8%) when compared to similar reports in the literature from high-resource countries. For instance, the infection rates were 20.6% (range 9%–31%) in a large one-day point prevalence study of ICUs in 17 western European countries in 1992.[5] Similarly, lower infection rates were reported by the National Nosocomial Infections Surveillance (NNIS) System study,[12,13] which also had shorter median duration of ICU stays of 5.3 days.[12] By comparison, in our study, the median duration of ICU stay and the median ICU stay prior to the development of the first infectious episode (TAR or infection-free days) were longer at 12 days and eight days, respectively. Interestingly, TAR at eight days for our study was longer than even the median duration of ICUs stays for hospitals in the United States.

It was not entirely clear whether the high infection rates in our study were a cause of prolonged ICU stays or a result of it instead. However, the longer median duration of ICU stays and median TAR in our study may indicate that prolonged ICU stay, at least in some instances, was not a result but rather a reason for the higher ICU-associated infection rates seen in the participating Turkish hospitals. Overcrowding in the ICUs of our hospitals may also have a part to play, as the number of beds in the ICUs of participating

Turkish hospitals, relative to the total bed capacity of the hospital, were much lower than those reported in the NNIS study.

The study found that recommended infection control measures were being implemented by ID personnel in the participating hospitals and that hand hygiene was of top priority. Hands-free operating alcohol-based hand sanitisers were widely accessible, frequently used and preferred over hand washing in all participating ICUs. Although the superiority of this type of intervention to hand washing is not supported by firm evidence, such sanitisers are more convenient for ensuring hand hygiene and improve compliance, and therefore may help to decrease nosocomial infection rates.[14,15] It should be noted, however, that neither the availability of such conveniences nor the increased use of disposable equipment of any kind would compensate for the negative impacts of understaffing, as shown by a recent study which reported that understaffing jeopardises the quality of infection control independently in ICUs.[16]

Exposure to a cephalosporin antibiotic prior to the first infectious episode was found to be an independent risk factor for ICU-associated infections. To further clarify high cephalosporin exposure prior to infection in ICU patients, the frequency of cephalosporin usage was compared between surgical and medical patients admitted to the ICUs in this study. We found that surgical patients were significantly more exposed to a cephalosporin antibiotic than medical patients (79.5% vs. 20.5%; $p < 0.001$). It is likely that this is due to the practice of extended surgical prophylaxis by many surgeons in Turkey, who tend to extend prophylaxis beyond the recommended single-dose regimen to even a week's therapy without infection for the sake of convenience.

The presence of a nasogastric tube was found to be protective against infections. This might be due to two reasons: (1) the nasogastric tube enables the early institution of enteral feeding during the course of the disease, which restores gastrointestinal integrity and prevents infections;[17] (2) the tube decreases the incidence and burden of gastroesophageal reflux, which may protect against the occurrence of ventilator-associated pneumonia in some patients.[18] Similar arguments may also be valid for the tracheostomy cannula, the presence of which was found to be protective against ICU-associated infections as well. The early application of tracheostomy for ventilator-assisted respiration might be protective, as the cannula facilitates the aspiration of subglottic secretions and enables the early institution of enteral feeding too.[19,20]

The findings of this study indicate that the high infection rates seen in the ICUs of participating tertiary care Turkish hospitals may be associated with inadequate infrastructure and facilities, understaffing, abuse of antibiotics and the prolonged ICU stay of patients. The enforcement of infection control measures alone, without significant improvement in the above-mentioned variables, may not therefore sufficiently decrease infection rates to the desired levels.

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