Tepecik Eğit. ve Araşt. Hast. Dergisi 2017; 27(1):25-30
doi:10.5222/terh.2017.025

Araştırma

Investigation of mortality predictors in general intensive care unit patients with nosocomial sepsis: A retrospective cohort study

Genel yoğun bakım ünitesindeki nozokomiyal sepsisli hastalarda mortalite belirteçlerinin araştırılması: Geriye yönelik bir kohort çalışması

Şebnem ÇALIK[1], Alpay ARI[1], Meltem AVCI[1], Fulya YILMAZ DURAN[2], Buket TOPÇU[3], Murat Yaşar ÖZKALKANLI[4], Selma TOSUN[1], Hatice ULUER[5]

[1]İzmir Bozyaka Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Bölümü, İzmir
[2]İzmir Bozyaka Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Bölümü, İzmir
[3]Urla Devlet Hastanesi, Anesteziyoloji ve Reanimasyon Bölümü, İzmir
[4]Katip Çelebi Üniversitesi Tıp Fakültesi İzmir Atatürk Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Bölümü, İzmir
[5]Ege Üniversitesi Tıp Fakültesi, Biyoistatistik Bölümü, İzmir

ABSTRACT

Objective: Nosocomial sepsis is among the major factors contributing to mortality in intensive care units (ICUs). Mortality predictors in general ICU patients with nosocomial sepsis were investigated.
Methods: This retrospective cohort study was conducted between January 1, 2013 and May 1, 2014 in two general ICUs of a training and research hospital. In total, 95 sepsis attacks developing in 83 patients were included in the study. Data from patients' medical records were recorded on standardised forms.
Results: Sepsis was detected in 21.2 cases per 100 ICU admissions. The median length of ICU stay was 37.56±39.595 (range, 1-173) days. Study population consisted of 43 (51.8%) male and 40 (48.2%) female patients. Their ages ranged from 18 to 90 (mean, 69±15.753) years. The median APACHE II score was 26.9±6.4 (range, 15-45). The primary reasons for admission were medical problems in 62 (74.7%), elective surgeries in 13 (15.7%), and emergency surgeries in 10 (12.8%) patients. Pneumonia (80%) accounted for the majority of nosocomial cases of sepsis detected in the ICUs. *Pseudomonas aeruginosa* (24.6%), *Acinetobacter baumannii* (24.6%), and *Klebsiella pneumoniae* (18.5%) were the most frequently isolated microorganisms. Rate of mortality secondary to nosocomial sepsis was 41 percent. In conclusion, multivariate logistic regression showed that emergency surgery (p=0.004), an increase in the SOFA score (p=0.001), and haemodialysis required for acute renal failure (p=0.004) were statistically significant risk factors for mortality due to nosocomial sepsis.
Conclusions: Monitoring SOFA scores may be useful for the monitorization of the patients with nosocomial sepsis.

Key words: Nosocomial sepsis, intensive care unit, mortality predictor

ÖZ

Amaç: Nozokomiyal sepsis yoğun bakım ünitelerinde (YBÜ) mortaliteye katkıda bulunan ana faktörlerden biridir. Genel YBÜ'ndeki nozokomiyal sepsisli hastalarda mortalite belirteçleri araştırıldı.
Yöntemler: Bu geriye yönelik çalışma 1 Ocak 2013 ve 1 Mayıs 2014 tarihleri arasında bir eğitim ve araştırma hastanesinin iki genel YBÜ'nde gerçekleştirildi. Hastaların tıbbi kayıtları standart formlara kaydedildi. Toplamda, 83 hastada gelişen 95 sepsis atağı dahil edildi. Hasta tıbbi kayıtlarından elde edilen veriler standart formlara kaydedildi.
Bulgular: Sepsis insidansı 100 YBÜ kabul başına 21,2 olguydu. Ortalama YBÜ'de kalış süresi 37,56±39,595 (aralık, 1-173) gündü. Hastaların, 43'ü (%51,8) erkek ve 40'ı (%48,2) kadındı. Yaşları 18 ile 90 (ortanca, 69±15,753) yıl arasında değişmekteydi. Medyan APACHE II skoru 26,9±6,4 (aralık, 15-45) idi. Kabul için temel nedenleri 62'sinde (%74,7) tıbbi sorunlar, 13'ünde (%15,7) seçmeli ameliyatlar ve 10'unda (%12,8) acil ameliyatlardı. Pnömoni (%80) YBÜ'de nozokomiyal sepsisli olguların çoğunluğunu oluşturuyordu. *Pseudomonas aeruginosa* (%24,6), *Acinetobacter baumannii* (%24,6) ve *Klebsiella pneumoniae* (%18,5) en sık izole edilmiş mikroorganizmalardı. Nozokomiyal sepsis nedeniyle ölüm oranı %41'di. Sonuç olarak, çok değişkenli lojistik regresyon acil cerrahi (p=0,004), SOFA skorundaki artış (p=0,001) ve hemodiyaliz gerektirmiş akut böbrek yetmezliğinin (p=0,004) nozokomiyal sepsis nedeniyle ölüm için istatistiksel olarak anlamlı risk faktörleri olduğunu gösterdi.
Sonuç: SOFA skorunu izleme nozokomiyal sepsisli hastaların izleminde yararlı olabilir.

Anahtar kelimeler: Nozokomiyal sepsis, yoğun bakım ünitesi, mortalite belirteci

Alındığı tarih: 02.02.2016
Kabul tarihi: 09.06.2016

Yazışma adresi: Uzm. Dr. Şebnem Çalık, İzmir Bozyaka Eğitim ve Araştırma Hastanesi, Bozyaka-İzmir
e-mail: sebnemozkoren@yahoo.com

INTRODUCTION

Nosocomial sepsis is among the major factors contributing to mortality in intensive care units (ICUs) and causes a significant disease burden and negative economic impact. The incidence of sepsis varies among different racial and ethnic groups. Between 6 and 54% of the patients admitted to ICUs have severe sepsis, and the mortality rate for these patients varies from 20 to 60%, which increases stepwise with increasing disease severity. Several studies have described the epidemiology, risk factors, and outcomes of sepsis, severe sepsis, and septic shock [1-4]. However, why some patients recover from sepsis while others do not, remains unclear. Mortality predictors in patients with nosocomial sepsis in two general ICUs were investigated in this study.

MATERIAL and METHODS

Study design

This retrospective cohort study was conducted between January 1, 2013 and May 1, 2014 in two ICUs with a total number of 34 beds of a training and research hospital. The infection control team consists of one clinical director of the department of Infectious Diseases and Clinical Microbiology (IDCM), three IDCM specialists, and two infection control nurses. IDCM specialists and infection control nurses evaluated patients' clinical and laboratory data in the ICUs each day. The same infection team visited ICU patients regularly during the study period.

Study group

In total, 390 adult patients who were admitted to and stayed longer than 48 h in the ICUs were evaluated. Patients diagnosed with sepsis by an IDCM specialist were included. This study was conducted using the CDC definitions and the American College of Chest Physicians/Society of Critical Care Medicine criteria for sepsis [5,6]. In total, 95 nosocomial attacks of sepsis were identified in 83 patients. Patients diagnosed with burns and acute pancreatitis potentially leading to systemic inflammatory response syndrome were excluded. Data from patients' medical records and the electronic patient data monitoring system were recorded on standardised forms, and predictors of mortality among hospital-acquired sepsis in ICU patients were evaluated. All patients were evaluated for 14 days after developing sepsis in the study.

Medical records included demographic characteristics, primary reason(s) for ICU admission (medical, elective surgery, emergency surgery), referrals of the patients (home or another hospital), pre-existing chronic comorbidities, length of stay in ICUs prior to onset of sepsis, extrinsic factors (presence of community- and hospital-acquired infection on admission, more than one nosocomial sepsis attack, inadequate empirical treatment, total parenteral nutrition, steroid therapy), routine laboratory findings, severity of sepsis (Acute Physiology and Chronic Health Condition and Sequential Organ Failure Assessment scores), and several other factors (use of vasopressor drugs [dopamine, dobutamine, adrenaline, noradrenaline], blood, and blood products, haemodialysis due to acute renal failure,).

Acute Physiology and Chronic Health Condition (APACHE) II scores at admission were obtained from patient files. APACHE II scores were determined using the 'worst' values within the initial 24 h of ICU admission for disease severity assessment. APACHE was introduced in 1981. APACHE II was formulated in 1985 to estimate risk based on data available within the first 24 h of admission. APACHE II is a widely used scoring system to quantify the severity of illness in ICUs and has been validated in many clinical trials [7]. The Sequential Organ Failure Assessment (SOFA) score is not used routinely but we included it, because the SOFA score was developed as a tool to quantitatively describe the time course of organ dysfunction, and changes in SOFA scores (ΔSOFA) have been correlated with prognosis [8]. SOFA was calculated using the following parameters: PaO_2/FiO_2, platelet count, bilirubin, blood pressure, the use of vasopressor agents, the Glasgow coma scale score, and creatinine or urine output.

Additionally, routine laboratory findings recorded at initial presentation and at 96 h after sepsis diagnosis using a commercial analyser were assessed by an anaesthesiology and recovery specialist [9].

Types of infections were categorised as pneumonia, peritonitis, urinary tract infection, soft tissue infection, skin infection, catheter-related infection, or infections localized on multiple sites. Effectiveness of antibiotherapy was assessed based on microbial culture results, the known susceptibility of the organism to the antimicrobials used, and antimicrobial susceptibility testing [5]. Empirical treatment and the multidrug-resistant microorganisms discovered were included among the risk factors.

Because all patients received them, H2 receptor blockers, enteral nutrition, central intravenous catheterisation, endotracheal intubation, mechanical ventilation, sedative medication, and urinary catheterisation were excluded from the statistical analysis.

The study was approved by the local ethics committee.

Statistical analyses

Analyses were performed using the SPSS software (ver. 15). In univariate analyses, for comparing exited and surviving cases, categorical data were tested by $\chi 2$ tests and t-tests were used for the comparison of means of the two groups. A p-value of <0.05 was considered to indicate statistical significance. Parameters found to be statistically significant in the univariate analyses were evaluated in a multivariate logistic regression to predict the risk of mortality.

RESULTS

In total, 95 attacks of nosocomial sepsis were identified in 83 patients. Thus, the incidence of sepsis in the present study was 21.2 cases per 100 ICU admissions. The median length of stay in the ICU was 37.6±39.6 (range, 1 173) days. Of the 83 patients, 43 (51.8%) were males and 40 (48.2%) females. Their ages ranged from 18 to 90 (mean, 69±15.8) years. The mean APACHE II score was 26.9±6.4 (range, 15-45). The primary reasons for admission were medical problems in 62 (74.7%), elective surgeries in 13 (15.7%), and emergency surgeries in 10 (12.8%) patients. At ICU admission, infection was present in 21 (38%) cases, of whom 8 (38.1%) of these had nosocomial and 13 (61.9%) community-acquired infections. The ICU mortality rate due to nosocomial sepsis was 41 percent. Characteristics of the patients who survived, and exited are shown in Table 1. Laboratory findings and scores of the patients and exited are shown in Table 2.

Table 1. Characteristics of patients who survived versus did not survive.

	Survivors n (%)	Non-survivors n (%)	P value
Number of attacks	56 (58.9%)	39 (41.1%)	-
Age, years	66.9±2.2	73.6±2.1	0.027
Type of admission			
Medical	46 (82.1%)	24 (61.5%)	0.020
Elective surgery	8 (14.3%)	7 (18%)	
Emergency surgery	2 (3.6%)	8 (20.5%)	
Pre-existing chronic comorbidities			
Chronic renal disease	3 (5.4%)	6 (15.4%)	0.101
Trauma	8 (14.3%)	5 (8.9%)	0.545
Congestive heart failure	8 (14.3%)	3 (7.6%)	0.323
Cirrhosis / liver failure	3 (5.6%)	0 (0%)	0.142
Diabetes mellitus	22 (39.2%)	10 (14.5%)	0.166
Chronic obstructive pulmonary disease	12 (21.4%)	8 (20.5%)	0.914
Haematological malignancy	2 (3.6%)	3 (7.7%)	0.376
Acute cerebrovascular disease	10 (17.9%)	5 (12.9%)	0.508
Chronic neurological disease	7 (12.5%)	6 (15.4%)	0.687
Solid organ transplantation	13 (23.2%)	8 (20.5%)	0.755
Extrinsic factors			
Length of stay in ICU prior to sepsis onset (days)	42.6±5.7	30.3±5.4	0.198
Presence of community-acquired infection on admission	6 (10.7%)	7 (17.9%)	0.313
More than one nosocomial sepsis attack	12 (21.4%)	4 (10.3%)	0.152
Inadequate empirical treatment	10 (17.9%)	13 (33.3%)	0.444
Total parenteral nutrition	13 (23.2%)	14 (35.9%)	0.178
Steroid therapy	5 (8.9%)	7 (17.9%)	0.193
Requirements			
Erythrocyte transfusion	22 (39.2%)	27 (69.2%)	0.004
Platelet transfusion	2 (3.6%)	4 (10.3%)	0.188
Fresh frozen plasma transfusion	6 (10.7%)	14 (35.9%)	0.003
Vasopressor drugs	7 (12.5%)	16 (41%)	0.001
Haemodialysis required for acute renal failure	5 (8.9%)	15	0.001

Results of the univariate analyses showed that age (P=0.027), emergency surgery (before or after admission to the ICU) (P=0.020), erythrocyte transfusion (P=0.004), fresh frozen plasma transfusion (P=0.003), vasopressor use (P=0.001), haemodialysis required for acute renal failure (P=0.001), white blood cell

Table 2. Laboratory findings and scores of patients who survived versus did not survive (mean ± standard deviation).

	Survivors	Non-survivors	P value
White blood cells ($\times10^3$/mm^3)	12824.5±830	15998.7±1287	0.037
Neutrophils ($\times10^3$/mm^3)	10673.8±774.8	14025.4±1253.8	0.021
Platelets (K/μL)	249377±16045.8	227741±19706.6	0.454
Red blood cell distribution width (RDW)	16.5±0.4	17.4±0.5	0.105
Haemoglobin (g/dL)	9.9±0.2	10±0.5	0.680
Haematocrit (%)	31.2±0.8	30.5±1.1	0.570
Albumin (mg/dL)	2.6±0.7	2.3±0.8	0.020
Globulins (mg/dL)	2.9±0.08	3.5±0.7	0.184
Glucose (mg/dL)	148±6.9	144.9±9.4	0.610
Creatinine (mg/dL)	1.1±0.1	2.1±0.3	0.000
Total cholesterol (mg/dL)	130.5±6.3	105.8±6.4	0.010
Triglycerides (mg/dL)	122.2±10.5	127.6±12	0.690
HDL (mg/dL)	29.6± 2	23.9±2	0.060
LDL (mg/dL)	80.9±5.3	78.4±25	0.005
Lactate (mmol/L)	1.7±0.1	2.1±0.1	0.048
Alanine transaminase (U/L)	46.3±7.5	41.6±11.1	0.376
Aspartate transaminase (U/L)	52.1±9.6	57.8±14.1	0.847
Amylase (U/L)	60.4±7	89.2±17.4	0.254
Prothrombin time (s)	15.9±0.6	16.3±0.8	0.547
APTT (s)	32.9±1.7	38.5±4.3	0.683
INR	1.2±0.0623	1.2±0.1	0.653
Scores			
APACHE II score	25.8±0.7	28.6±1.2	0.035
SOFA score-1	7.4±3.7	8.3±3.3	0.207
Increase in SOFA score	1.8±0.1	1.5±0.1	0.002

count (P=0.037), neutrophil count (P=0.021), levels of albumin (P=0.020), creatinine (P<0.001), total cholesterol (P=0.010), and lactate (P=0.048), APACHE II scores (P=0.035), and an increase in the SOFA score (P=0.002) were associated with mortality from nosocomial sepsis. The parameters found to be statistically significant in the univariate analyses were evaluated in a multivariate logistic regression to predict the risk of mortality.

Table 3. Multivariate logistic regression analysis to determine independent predictors of nosocomial sepsis-related mortality.

Variable	P	Adjusted odds ratio	95% confidence interval	
			Lower	Lower
Emergency surgery	0.004	13.713	2.555	2.555
Increase in the SOFA score	0.000	8.655	2.827	2.827
Haemodialysis required for acute renal failure	0.004	7.126	1.877	1.877

The final multivariate logistic regression results showed that emergency surgery (P=0.004), an increase in the SOFA score (P=0.001), and haemodialysis required for acute renal failure (P=0.004) were statistically significant risk factors for mortality due to nosocomial sepsis (Table 3).

The distribution of causative microorganisms according to the site of nosocomial sepsis is shown in Table 4. Pneumonia (80%) accounted for most of the nosocomial sepsis cases encountered in the ICU. *Pseudomonas aeruginosa* (24.6%), *Acinetobacter baumannii* (24.6%), and *Klebsiella pneumoniae* (18.5%) were the most commonly identified microorganisms. No microorganisms were isolated in 14 (14.7%) patients. Multiple drug-resistant microorganisms were isolated from cultures from 52 (54.7%) patients, of whom 26 (50%) survived and 26 (50%) did not. Attacks of nosocomial sepsis due to multiple drug-resistant microorganisms and inadequate empiri-

Table 4. Distribution of causative microorganisms by site of nosocomial sepsis.

	Pulmonary n (%)	Urinary tract n (%)	Skin-soft tissue n (%)	Intra-abdominal n (%)	Catheter n (%)	Total n (%)
Pseudomonas aeruginosa	23 (24.2%)	0 (0%)	1(1%)	0 (0%)	0 (0%)	24 (25.2%)
Acinetobacter baumannii	16 (16.8%)	0 (0%)	1 (1%)	1 (1%)	2 (2.1%)	20 (21%)
Klebsiella pneumoniae	11 (11.5%)	2 (2.1%)	1 (1%)	0 (0%)	1 (1%)	15 (15.7%)
Escherichia coli	2 (2.1%)	0 (0%)	2 (2.1%)	0 (0%)	1 (1%)	5 (5.2%)
Staphylococcus aureus	4 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (4.2%)
Serratia marcescens	2 (2.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2.1%)
Enterobacter cloacae	2 (2.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (2.1%)
Acinetobacter lwoffii	1 (1%)	1 (1%)	0 (0%)	0 (0%)	0 (0%)	2 (2.1%)
Proteus mirabilis	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Citrobacter freundii	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Streptococcus parcinus	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Candida albicans	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Candida tropicalis	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Enterobacter aerogenes	1 (1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Vancomycin-resistant *Enterococcus*	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	1 (1%)
Microorganism could not be isolated	9 (9.4%)	0 (0%)	1 (1%)	4 (4.2%)	0 (0%)	14 (14.7%)
Total	76 (%80)	3 (3.1%)	6 (6.3%)	5 (5.2%)	5 (5.2%)	95 (100%)

cal antibiotic therapy were apparently not associated with mortality (P=0.126 and P=0.444, respectively).

DISCUSSION

Nosocomial sepsis is among the major factors contributing to mortality in ICUs. Several studies have described the epidemiology, risk factors, and outcomes of sepsis [1-4]. However, why some patients recover from sepsis while others do not remains unclear. Our analysis showed that emergency surgery, an increase in the SOFA score, and haemodialysis required for acute renal failure were risk factors for mortality in nosocomial sepsis.

In our study, the mean age of the patients was 69±15.753 years. Because of the high mean age in both groups, age was not an indicator of sepsis-related mortality. Elderly patients (age ≥ 65 years) are a growing subset of the population in most countries. Elderly patients are more likely to be admitted to ICUs and to have more comorbid diseases (cardiovascular disease, chronic liver disease, chronic renal disease, hypertension, and diabetes mellitus) compared with younger patients [10]. Emergency surgery in elderly patients was associated with a 10-15-fold increase in morbidity and a 3-5-fold increase in mortality compared with elective surgery for this age group. Of particular concern is surgery occurring on an emergency basis in elderly patients [11]. We found emergency surgery to be statistically important for the prediction of nosocomial sepsis. Thus, emergency surgery should be avoided in patients, especially in elderly patients.

Clinical assessment of illness severity is an essential component of medical practice, including in the ICU, to predict mortality and morbidity of critically ill patients [7,8]. However, APACHE II scores were not significant for sepsis-related mortality. We thought that because the APACHE II score is applied within the first 24 h on critically ill patients and does not reflect subsequent physiological changes or complications, especially in the long-term hospitalised patients, it would be important. An increase in SOFA scores over 98 h was independently associated with mortality due to sepsis. Few studies have investigated the value of changes in SOFA scores during sepsis to assess outcome (kaynak). Ferreira et al. [12] demonstrated that an increase in the SOFA score during the first 48 h in the ICU predicted a mortality rate of 50%, independent of the initial SOFA score. Russell et al. [13] investigated changes in patients with severe sepsis over the first 72 h and reported that increases in the severity of neurological, coagulopathies, and renal dysfunction were associated with higher 30-day mortality rates. Degoricija et al. [14] evaluated 314 episodes of sepsis in a medical ICU and reported that poor outcome was associated with higher SOFA scores on day 1 in the ICU. Also, Ylipalosaari et al. [15] reported SOFA scores of > 8 on admission among patients who subsequently developed an ICU acquired infection. We thought that monitoring the SOFA scores might be useful in the follow-up of the patients with nosocomial sepsis.

Acute renal failure develops in up to two-thirds of ICU patients, and sepsis is the most common contributing factor. Moreover, acute renal failure that develops in septic patients is consistently linked to higher mortality rates and increased consumption of healthcare resources. The pathophysiology of septic acute renal failure is still not fully understood [16]. It has been reported that patients with acute renal failure had higher SOFA scores relative to those without acute renal failure. The incidence of sepsis is expected to increase further as the population ages, as will the incidence of septic acute renal failure [17]. Thus, haemodialysis required for acute renal failure should be considered as a strong, independent risk factor for mortality, as is seen in our results. In elderly populations, there is increased susceptibility to drug toxicity, partially owing to altered drug pharmacokinetics and pharmacodynamics [18]. Prevention of septic acute renal failure may be possible by early diagnosis of advanced cases with sepsis encountered in ICUs.

The results of different ICU studies have yielded different rates and types of infection. In a prevalence study involving ICUs in 17 European countries, pneumonia (46.9%), lower respiratory tract infection (17.8%), urinary tract infection (17.6%), and bloods-

tream infection (12%) were the most frequent types of ICU infections reported [19]. In our study, pneumonias (80%) accounted for most of the cases with nosocomial sepsis. *Pseudomonas aeruginosa, Acinetobacter baumannii*, and *Klebsiella pneumoniae* were the most frequently isolated microorganisms in cases with pneumoniae encountered in our ICUs. Attacks of nosocomial sepsis due to multiple drug-resistant microorganisms and inadequate empirical treatment were not statistically significant for mortality. This may be due to the regular visits of IDCM specialists to ICU patients regularly, and their providing appropriate empirical antimicrobial therapy against the most likely pathogens, based on each patient's presenting illness, previously documented data on local antibiotic resistance patterns in the wards, and rapid changes in antibiotics according to culture results.

In conclusion, sepsis is an important health problem associated with a high mortality rate in hospitals, especially in ICUs. Emergency surgery, an increase in the SOFA score, and the need for haemodialysis due to acute renal failure were risk factors contributing to fatal outcomes. We consider that monitoring SOFA scores may be useful in the monitorization of these patients with nosocomial sepsis.

There was no funding or conflict of interest to declare.

REFERENCES

1. Zhou J, Qian C, Zhao M, Yu X, Kang Y, Ma X, et al. Epidemiology and outcome of severe sepsis and septic shock in intensive care units in mainland China. *PLoS One* 2014;9:e107181. http://dx.doi.org/10.1371/journal.pone.0107181
2. Sinha N, Agarwal J, Srivastava S, Singh M. Analysis of carbapenem-resistant Acinetobacter from a tertiary care setting in North India. *Indian J Med Microbiol* 2013;31:60-63. http://dx.doi.org/10.4103/0255-0857.108724
3. Gignon M, Farcy S, Schmit JL, Ganry O. Prevention of healthcare-associated infections in general practice: current practice and drivers for change in a French study. *Indian J Med Microbiol* 2012;30:69-75. http://dx.doi.org/10.4103/0255-0857.93040
4. Rodríguez F, Barrera L, De La Rosa G, Dennis R, Due-as C, Granados M, et al. The epidemiology of sepsis in Colombia: a prospective multicenter cohort study in ten university hospitals. *Crit Care Med* 2011;39:1675-1682. http://dx.doi.org/10.1097/CCM.0b013e318218a35e
5. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:309-32. http://dx.doi.org/10.1016/j.ajic.2008.03.002
6. Surviving Sepsis Campaign. International Guidelines for Management of Severe Sepsis and Septic Shock: 2012. http://www.sccm.org/Documents/SSC-Guidelines.pdf (accessed 29 January 2016).
7. Parajuli BD, Shrestha GS, Pradhan B, Amatya R. Comparison of acute physiology and chronic health evaluation II and acute physiology and chronic health evaluation IV to predict intensive care unit mortality. *Indian J Crit Care Med* 2015;19:87-91. http://dx.doi.org/10.4103/0972-5229.151016
8. Moreno R, Vincent JL, Matos R, Mendonça A, Cantraine F, Thijs L, et al. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. *Intensive Care Med* 1999;25:686-696. http://dx.doi.org/10.1007/s001340050931
9. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med* 1998;26:1793-1800. http://dx.doi.org/10.1097/00003246-199811000-00016
10. Al-Dorzi HM, Tamim HM, Mundekkadan S, Sohail MR, Arabi YM .Characteristics, management and outcomes of critically ill patients who are 80 years and older: a retrospective comparative cohort study. *BMC Anesthesiol* 2014;14:126. http://dx.doi.org/10.1186/1471-2253-14-126
11. Davis P, Hayden J, Springer J, Bailey J, Molinari M, Johnson P. Prognostic factors for morbidity and mortality in elderly patients undegoing acute gastrintestinal surgery: a systematic review. *Can J Surg* 2014;57:E44-52.
12. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. *JAMA* 2001;286:1754-1758. http://dx.doi.org/10.1001/jama.286.14.1754
13. Russell JA, Singer J, Bernard GR, et al: Changing pattern of organ dysfunction in early human sepsis is related to mortality. *Crit Care Med* 2000;28:3405-3411. http://dx.doi.org/10.1097/00003246-200010000-00005
14. Degoricija V, Sharma M, Legac A, Gradiser M, Sefer S, Vucicević Z. Survival analysis of 314 episodes of sepsis in medical intensive care unit in university hospital:impact of intensive care unit performance and antimicrobial therapy. *Croat Med J* 2006;47:385-97.
15. Ylipalosaari P, Ala-Kokko TI, Laurila Ji Ohtonen P, Syrjala H. Intensive care acquired infection is an independent risk factor for hospital mortality: a prospective cohort study. *Crit Care* 2006;10:R66. http://dx.doi.org/10.1186/cc4902
16. Plataki M, Kashani K, Cabello-Garza J, Maldonado F, Kashyap R, Kor DJ, et al. Predictors of acute kidney injury in septic shock patients: an observational cohort study. *Clin J Am Soc Nephrol* 2011;6:1744-1751. http://dx.doi.org/10.2215/CJN.05480610
17. Wijewickrama ES, Ratnayake GM, Wikramaratne C, Sheriff R, Rajapakse S. Incidences and clinical outcomes of acute kidney injury in the ICU. *BMC Res Notes* 2014;7:305. http://dx.doi.org/10.1186/1756-0500-7-305
18. Medve L, Antek C, Paloczi B, Kocsi S, Gartner B, Marjanek Z, et al. Epidemiology of acute kidney injury in Hungarian intensive care units: a multicenter, prospective, observational study. *BMC Nephrol* 2011;12:43. http://dx.doi.org/10.1186/1471-2369-12-43
19. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, et al. The prevalence of in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. *J Am Med Assoc* 1995;274:639-644. http://dx.doi.org/10.1001/jama.1995.03530080055041