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Risk Factors and Prognostic Predictors of Ventilator-Associated Pneumonia in a Tertiary Care Hospital

Üçüncü Basamak Bir Hastanede Ventilatörle İlişkili Pnömoninin Prognostik Belirteçleri ve Risk Faktörleri

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ABSTRACT

Introduction: *It was aimed to evaluate the risk factors for the development of ventilator-associated pneumonia (VAP) and clinical outcomes and prognostic predictors of VAP.*

Materials and Methods: *This retrospective and single-center study included patients aged ≥18 years who were diagnosed with VAP in the ICU. Patients were divided into two groups with VAP or without VAP. Univariable and multivariable analyses were used to assess risk factors and prognostic predictors of VAP.*

Results: *A total of 177 patients were evaluated. Mean length of intensive care unit (ICU) stay and the duration of mechanical ventilation was longer in patients with VAP than in patients without VAP [29 (3-107) vs. 12 (3-70) days, 22 (3-90) vs. 10 (3-45) days; p< 0.001]. Rectal colonization with carbapenem-resistant Klebsiella pneumoniae (CRKp) was found to be higher in the VAP group compared to the non-VAP group (n= 41, 58% vs. n= 25, 24%, p< 0.001). Ventilation period (OR= 1.07; 95% CI 1.02-1.12, p= 0.003), smoking (OR= 3.89; 95% CI 1.68-8.9, p= 0.001), and rectal colonization with CRKp (OR= 4.93; 95% CI 2.09-11.64, p< 0.001) were detected as independent risk factors for the development of VAP. Age (OR= 1.15; 95% CI 1.03-1.28, p= 0.01), SOFA score (OR= 1.60; 95% CI 1.05-2.43, p= 0.02) and rectal colonization with CRKp (OR= 15.2; 95% CI 2.33-99.01, p= 0.004) were detected as independent risk factors for mortality in patients with VAP.*

Conclusion: *In conclusion, decreasing the patient-related and hospital environment related risk factors, routine screening of rectal colonizations with CRKp, and continuous practicing of the universal infection control measures may significantly decrease the prevalence of ventilator-associated pneumonia.*

Key Words: *Ventilator-associated pneumonia; Carbapenem resistant Klebsiella pneumoniae; Rectal colonization; Mortality*

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ÖZ

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Giriş: *Bu çalışmada ventilatörle ilişkili pnömoni (VİP) gelişimi için risk faktörlerini, VİP' in klinik sonuçlarını ve prognostik belirleyicilerini araştırmayı amaçladık.*

Materyal ve Metod: *Retrospektif ve tek merkezli yürütülen çalışmaya yoğun bakım ünitesinde (YBÜ) VİP tanısı almış 18 yaş ve üzeri hastalar dahil edildi. Hastalar VİP gelişen ve gelişmeyen olarak iki gruba ayrıldı. VİP' in risk faktörlerini ve prognostik belirleyicilerini değerlendirmek için tek değişkenli ve çok değişkenli analizler kullanıldı.*

Bulgular: *Toplam 177 hasta değerlendirildi. Ortalama YBÜ'de yatış ve mekanik ventilasyon süresi, VİP gelişen hastalarda gelişmeyen hastalara göre daha uzundu [29 (3-107) vs. 12 (3-70) gün, 22 (3-90) ve 10 (3-45) gün; p< 0.001]. Rektal karbapeneme dirençli Klebsiella pneumoniae (KDKp) kolonizasyonu VİP gelişmeyen gruba göre VİP grubunda daha yüksek bulundu (n= 41, %58 ve n= 25, %24, p< 0.001). Ventilasyon süresi (OR= 1.07; %95 CI 1.02-1.12, p= 0.003), sigara kullanımı (OR= 3.89; %95 CI 1.68-8.9, p= 0.001) ve rektal KDKp kolonizasyonu (OR= 4.93; %95 CI) 2.09-11.64, p< 0.001) VİP gelişimi için bağımsız risk faktörleri olarak saptandı. Yaş (OR= 1.15; %95 CI 1.03-1.28, p= 0.01), SOFA skoru (OR= 1.60; %95 CI 1.05-2.43, p= 0.02) ve rektal KDKp kolonizasyonu (OR= 15.2; %95 CI 2.33-99.01, p= 0.004) VİP grubunda mortalite için bağımsız risk faktörleri olarak saptandı.*

Sonuç: *Hasta ve hastane ortamı ile ilişkili risk faktörlerinin azaltılması, rektal KDKp kolonizasyonun rutin olarak taranması ve evrensel enfeksiyon kontrol önlemlerinin sürekli uygulanması ventilatörle ilişkili pnömoni prevalansını önemli ölçüde azaltabilir.*

Anahtar Kelimeler: *Ventilatörle ilişkili pnömoni; Karbapeneme dirençli Klebsiella pneumoniae; Rektal kolonizasyon; Mortalite*

INTRODUCTION

Hospital-acquired pneumonia and ventilator-associated pneumonia (VAP) are among the leading causes of these infections and important causes mortality[1,2]. One-third of nosocomial pneumonias develop in intensive care patients, and majority of them are VAP patients[3]. According to the studies from different countries, VAP rates are between 0.9-19 per 1000 ventilator days[4-6]. VAP causes elongation in length of stay in the hospital and the length of ventilation days, resulting in an increase in costs[7,8]. The estimated mortality rate in patients with VAP due to all causes vary between 20-50%[1,9]. In this study, it was aimed to investigate the risk factors for the development of VAP and evaluate the clinical outcomes, and prognostic predictors in patients diagnosed with VAP in a tertiary hospital.

MATERIALS and METHODS

Study Setting

A retrospective study was conducted between 01 April 2016-31 March 2017 with patients aged >18 years, intubated more than 48 hours and hospitalized in the ICUs. Patients were divided into two categories with VAP or without VAP. The diagnosis of VAP was made in accordance with the diagnostic criteria of the Centers for Disease Control and Prevention (CDC)[10]. Accordingly, diagnosis of VAP was made with the detection of two criteria below in addition to fever (>38°C), leukopenia (≤4000/mm^3), or leukocytosis (>12.000/mm^3) accompanying with radiological changes in patients receiving mechanical ventilation (MV) support at least for 48 hours, and detection of mental change of unknown origin in patients aged above 70 years:

- Development of purulent expectoration or change in the character of expectoration or increase in respiratory secretions or the increased need of aspiration
- Newly emerging or deteriorated cough, dyspnea, or tachypnea
- Presence of crackles or bronchial respiratory sounds
- Deterioration of oxygenation (desaturation, PaO_2/FiO_2<240), increased need of oxygen or ventilator support.

Patients with community-acquired pneumoniae were not included to the study. Patients were evaluated at daily visits by infectious diseases and clinical microbiology specialists in intensive care. The data were obtained from the patient files, and from the electronic database. The demographic, clinical, and laboratory results of the patients were separately recorded in the follow-up forms. The first VAP attack was included in the analyses. The results of the rectal carbapenem-resistant *K. pneumonia* (CRKp) colonization screening that were routinely performed for surveillance were also recorded.

Identification of the Bacterial Strains

Bacterial strains growing in the endotracheal aspirate (ETA) as $\geq 10^5$ cfu/mL or broncho alveolar lavage fluid (BAL) as $\geq 10^4$ cfu/mL, of patients with VAP aged >18 years, intubated more than 48 hours and hospitalized in the Intensive Care Unit (ICU) were identified using the classical biochemical method. Accordingly, the fermentative, urease and citrate positive, motionless, and indole-negative bacteria were named as *K. pneumoniae*, non-fermentative, oxidase-negative, and motionless bacteria were identified as *Acinetobacter* spp., and non-fermentative, oxidase-positive bacteria were identified as *Pseudomonas* spp. *Enteric bacteria*, that were difficult to describe, were identified using API® 20E and 20NE (bioMérieux, Marcy l'Etoile, France). According to the European Committee on Antimicrobial Susceptibility Testing (EUCAST)[11] criteria by Kirby-Bauer disk diffusion method, imipenem and meropenem <16 mm, ertapenem <22 mm for *K. pneumoniae*; *Acinetobacter* spp. for imipenem <17 mm, meropenem <15 mm; *Pseudomonas* spp. Carbapenem resistance was considered in strains with imipenem <17 mm and meropenem <18 mm zone diameters. Confirmation of carbapenem resistance by Etest® or liquid microdilution method for *K. pneumoniae*, *Acinetobacter* spp. and *Pseudomonas* spp. It was performed by measuring the minimum inhibitory concentration (MIC) value of imipenem and meropenem as >8 mg/lt.

Statistical Analysis

IBM Statistical Package for Social Sciences (SPSS) for Windows, Version 21.0 (SPSS, IBM Corp., Armonk, NY, USA) program was used in the statistical analysis. In the analysis of the continuous variables, Student's t test was used in normal distribution, and Mann-Whitney U test was used in non-normal distribution; and $\chi 2$ test or Fisher's exact test were used in the analysis of the categorical variables. Logistic regression analysis was performed for detection of the independent parameters. Risk and the ratio of the relative possibilities were demonstrated as "odds ratio (OR)". P< 0.05 was regarded statistically significant.

RESULTS

One hundred and seventy-seven patients who were suitable for the inclusion criteria were evaluated. There were 85 VAP attacks in 71 patients, and VAP rate was 8.6. Only first VAP attacks were included in the study. Mean age was 62 (range, 19-89) years, and 46 (65%) were males in the patients who developed ventilator-associated pneumonia. No difference was detected regarding age and sex between the patients with and without VAP (p= 0.17, and 0.11, respectively). In patients with VAP, mean ICU length of stay and duration of mechanical ventilation was longer compared to patients without VAP [29 (3-107) vs. 12 (3-70) days; 22 (3-90) vs. 10 (3-45) days respectively; p< 0.001]. Rectal colonization with CRKp patients was found to be higher in the VAP group compared to the non-VAP group [41 (58%) vs. 25 (24%), p< 0.001] (Table 1). Duration of mechanical ventilation (OR= 1.07; 95% CI 1.02-1.12, p= 0.003), rectal colonization with CRKp (OR= 4.93; 95% CI 2.09-11.64, p< 0.001), and smoking (OR= 3.89; 95% CI 1.68-8.9,

Table 1. The comparison of the demographics and clinical features of patients with VAP and without VAP

	Patients with VAP (n= 71)Number (%)	Patients with no VAP (n= 106) Number (%)	p
Age (Years)	62 (19-89)	61 (27-88)	0.172
Sex			
Female	25 (35)	50 (47)	0.115
Male	46 (65)	56 (53)	
ICU length of stay (days)	29 (3-107)	12 (3-70)	< **0.001**
Duration of mechanical ventilation (days)	22 (3-90)	10 (3-45)	<**0.001**
BMI (±SD)	28.3 ± 10.1	25.6 ± 4.8	0.101
SOFA Score (±SD)	5.8 ± 2.9	5.6 ± 2.9	0.499
Charlson comorbidity index (±SD)	4.03 ± 3.1	4.1 ± 2.9	0.711
CRKp colonisation	41 (58)	25 (24)	< **0.001**
Hospitalisation within the last 6 months	44 (62)	81 (76)	**0.039**
Antibiotic use within the last 3 months	46 (64)	82 (77)	0.067
Smoking	35 (49)	29 (27)	**0.003**
Blood product use	50 (70)	58 (55)	**0.036**
Decubitus ulcer	26 (37)	23 (22)	**0.03**
Steroid use	25 (35)	42 (40)	0.553
Tracheostomy	16 (23)	17 (16)	0.277
Reintubation	13 (18)	5 (5)	**0.003**
Parenteral nutrition	7 (10)	13 (12)	0.620
Trauma history	10 (14)	11 (10)	0.455

VAP: Ventilator-associated pneumonia, ICU: Intensive care unit, BMI: Body mass index, SOFA: Sequential organ failure assessment, CRKp: Carbapenem-resistant *K. pneumonia*, SD: Standard deviation.

Table 2. Multivariate analysis of the risk factors contributing to the development of VAP

			95% CI	
	P	OR	Minimum	Maximum
ICU length of stay (days)	0.81	1	0.97	1.03
Duration of mechanical ventilation (days)	**0.003**	1.07	1.02	1.12
Rectal CRKp colonisation	**<0.001**	4.93	2.09	11.64
Hospitalisation in the last 6 months	**0.05**	0.22	0.05	0.88
Antibiotic use in the last 3 months	0.79	1.19	0.31	4.53
Smoking	**0.001**	3.89	1.68	8.9
Blood product use	0.17	1.76	0.78	4.00
Decubitus ulcer	0.40	1.47	0.59	3.67
Reintubation	0.94	1.05	0.24	4.46

VAP: Ventilator-associated pneumonia, ICU: Intensive care unit, CRKp: Carbapenem-resistant *K. pneumonia*, OR: Odds ratio, CI: Confidence interval.

p= 0.001) were detected as the independent risk factors contributing to the development of VAP (Table 2). Patients were mostly admitted to the ICUs due to sepsis and respiratory insufficiency.

Table 3. The causes for ICU transfer of patients with VAP

Diagnosis at admission	Patients with VAP (n= 71) Number (%)	Patients with no VAP (n= 106) Number (%)	p
Sepsis	16 (23)	32 (30)	0.26
Respiratory insufficiency	17 (24)	26 (25)	0.92
Postoperative care	7 (10)	9 (9)	0.75
Myocardial infarction	6 (9)	1 (1)	**0.01**
Neuroleptic malignant syndrome	1 (1)	2 (2)	0.80
CNS infection	1 (1)	4 (4)	0.64
Stroke	7 (10)	5 (3)	0.19
Crush syndrome	9 (13)	6 (5)	0.10
Anaphylaxis	1 (1)	3 (3)	0.53
AKF	1 (1)	4 (4)	0.35
Confusion	1(1)	3 (3)	0.53
Intox	4 (6)	11(10)	2.66

VAP: Ventilator-associated pneumonia, ICU: Intensive care unit, CNS: Central nervous system, AKF: Acute kidney failure.

Table 4. Distribution of causative microorganisms for VAP

Bacteria	n (%) n= 81
K. pneumoniae	35 (43)
Pseudomonas spp.	22 (27)
P. aeruginosa	20 (24)
P. stutzeri	2 (3)
Acinetobacter baumannii	15 (19)
Other gram-negative enteric bacilli	5 (6)
Escherichia coli	3 (4)
Enterobacter aerogenes	2(3)
Corynebacterium spp.	3 (4)
Methicillin resistant *S. aureus*	1 (1)

VAP: Ventilator-associated pneumonia.

No significant difference was detected regarding ICU admittance diagnosis except myocardial infarction (p= 0.01) in comparison of the groups with VAP and without VAP (Table 3). Eighty-one pathogens were isolated from the samples of 71 VAP episodes. The distribution of VAP agents is shown in Table 4. Among the VAP agents, 14 (40%) *K. pneumonia*, *Pseudomonas* spp. (20 *P. aeruginosa*, 2 P. stutzeri) 13 (59%) and 14 (93%) *Acinetobacter baumanii* strains were carbapenem resistant. Forty-three (48.9%) of the patients in the VAP group and 45 (42.5%) of the patients without VAP died (p=.01). Univariate analysis revealed that age, body mass index, rectal colonization with CRKp, Charlson comorbidity index, SOFA score, hospital stay in the last 6 months, and antibiotic use in the last three months were associated with mortality in patients with VAP (p< 0.001, 0.03, <0.001, <0.001, 0.01, 0.001, 0.01, respectively) (Table 5). Multivariate analysis revealed that age, SOFA score, and rectal colonization with CRKp were independent risk factors for mortality in patients with VAP (OR= 1.15, 1.60, 15.21; 95% CI= 1.03-1.28, 1.05-2.43, 2.33-99.01, respectively) (Table 6).

DISCUSSION

In this study, etiological factors, clinical characteristics and outcomes of patients with VAP in tertiary ICU were investigated. It was detected that the duration of mechanical ventilation, rectal colonization with CRKp, and smoking were independent risk factors contributing to the development of VAP. Additionally, we found high mortality rates in the VAP group and revealed that age, SOFA score, and rectal colonization with CRKp were independent risk factors for mortality in patients with VAP.

Table 5. Comparison of the demographic and clinical features of the deceased and survivor patients with VAP

Demographic and clinical features	Dead (n= 43) Number (%)	Survived (n= 28) Number (%)	p
Age (Years)	69.49 ± 12.24	50.21 ± 14.46	**<0.001**
Sex			
Female	17 (40)	8 (29)	0.34
Male	26 (60)	20 (71)	
Period in ICU (days ± SD)	33.98 ± 19.57	36.16 ± 27.25	0.88
Ventilation Period (days ± SD)	29.7 ± 19	28.2 ± 20	0.60
SOFA Score	5 (1-12)	4 (1-14)	**0.01**
Charlson comorbidity index	5 (0-13)	2 (0-9)	**<0.001**
BMI (± SD)	29.7 ± 12.4	26.2 ± 3.8	**0.03**
Rectal CRKp colonisation (n= 42)	34 (79)	8 (29)	**<0.001**
Hospitalisation (last 6 months) (n= 44)	33 (77)	11 (39)	**0.001**
Antibiotic use (last 3 months) (n= 46)	33 (77)	13 (46)	**0.01**
Receiving health care * (n= 27)	17 (40)	10 (36)	0.74
Smoking (n= 35)	20 (47)	15 (54)	0.56
Detection of multiple VAP factors (n=10)	7 (16)	3 (11)	0.73
VAP factor with MDR (n= 50)	33 (77)	17 (61)	0.14
Bacteremia (n= 18)	9 (21)	9 (32)	0.28
Procalcitonin (µg/lt ± SD)	2.6 ± 5.8	1.3 ± 1.2	0.14
CRP (mg/lt ± SD)	150 ± 98.5	158 ± 86.2	0.52

VAP: Ventilator-associated pneumoni, ICU: Intensive care unit, SOFA: Sequential organ failure assessment, BMI: Body mass index. CRKp: Carbapenem-resistant *K. pneumonia*, MDR: Multi-drug resistant, CRP: C-reaktif protein, SD: Standard deviation.
* Oncet a medical facility.

Table 6. Multivariate analysis of independent risk factors contrubuting to mortality in patients with VAP

			95% CI	
	p	OR	Minimum	Maximum
Age	**0.01**	1.15	1.03	1.28
SOFA score	**0.02**	1.60	1.05	2.43
Charlson comorbidity index	0.95	1.01	0.64	1.58
Rectal CRKp colonisation	**0.004**	15.21	2.33	99.01
Hospitalisation (last 6 months)	0.51	2.72	0.13	54.80
Antibiotic use (last 3 months)	0.98	0.97	0.05	18.23
BMI	0.40	1.04	0.94	1.15

Ventilator-associated pneumonia. SOFA: Sequential organ failure assessment, CRKp: Carbapenem-resistant *K. pneumonia*, BMI: Body Mass Index. OR: Odds ratio, CI: Confidence interval.

Infections that develop in the ICUs are one of the significant problems increasing treatment costs in addition to morbidity and mortality. Ventilator- associated pneumonia are infections which have the most contribution to mortality in intensive care units[7,8,12]. Although varying

by intensive care units, the average VAP rate in the general ICU in the United States (USA) is 0.7 per 1000 ventilator days according to the National Health Safety Network (NHSN) data[13]. In a multicenter study conducted in 25 different European countries, the incidence of VAP in hospitals performing major cardiac surgery has been reported to be 19.3[14]. Data of the International Nosocomial Infection control consortium (INICC) reported the rate 12.2 per 1000 ventilator days in developing countries for 2010-2015, and the surveillance data of the Turkish National Hospital Infections Surveillance system of 2020 reported the VAP rate as 10.7 per 1000 ventilator days for general ICU in tertiary care hospitals[5,15]. During our study, we found the VAP rate to be 8.6. The comparison of our results with INICC report showed the VAP detection rate lower, however, the rate was found higher compared with the data of the USA[13]. The difference was anticipated to be due to the comorbidity factors of the patients, hospital conditions, distribution of the pathogens, and the change of the antibiotic sensitivity patterns of these agents.

Although the change of local epidemiological features affected the incidence of VAP, patients who developed VAP with any agent are exposed to risks resulting from the ICU conditions. These risks are more intervention and longer ventilation period, more antibiotic use, and longer period hospital stay. CDC data has demonstrated that mean duration of ventilation and ICU length of stay is longer in patients with VAP compared to patients without VAP. Similar results have been reported from Europe, China, and Turkey[16-21]. Mean ventilation period has been found as 23.5 ± 10.3 days and ICU length of stay as 26.7 ± 16.3 days in a study of Karataş et al.[16]; however, we found the values as 22 and 29 days, respectively, in our study. This is consistent with our study results and studies showing that the risk of developing VIP increases with prolonged ventilation. In addition, the factors such as smoking, prior antibiotic use and rectal colonization with CRKp were found more frequently in patients with VAP in our study. In the literature, rectal CRKp colonization has not been shown as a risk factor for the development of VAP. However, it is known that colonization of the upper respiratory tract and gastrointestinal tract with bacteria and receiving treatment in centers with a high prevalence of antibiotic-resistant microorganisms are risk factors for the development of VAP[1,2]. In our study, we screened only rectal CRKp colonization, and this was found to be a risk factor for the development of VAP (p= 0.001).

The reason of admittance of patients to ICU may be directly effective in the development of VAP. Similar studies have reported that the rate of admittance of patients with VAP to ICU due to respiratory insufficiency higher[21,22]. This may be interpreted as that patients required more respiratory support and needed to use ventilator. However, no difference was detected in the other reasons of admission compared with the patients with no VAP in the study.

Mucosal damage and barotraumas due to prolonged use of ventilators in patients with VAP increased local colonization, microaspiration and infection development[23,24]. Similar studies have demonstrated that colonization with antibiotic resistant bacteria increased in ICU patients with ventilator support[25]. Carbapenem resistant *Enteric bacteria* (CREB) colonization more negatively affects treatment response and limits treatment options significantly in patients with VAP[25-27]. This condition contributes to the increase of mortality in patients who developed VAP[24-29]. Ling et al.[30] have reported that patients who had CREB colonization were 3.5 folds more mortal compared with the control group. In our study, it was found that patients with VAP has re-rectal colonization with CRKp more frequently (p= 0.001), and rectal colonization with CRKp was associated with an independent risk factor for the development of VAP (p= 0.001) and higher mortality in patients with VAP. The current status of carbapenem-resistant (CR) Enterobacteriaceae in Turkish hospitals is classified as class 5 (highest level) among 37 European countries, along with Greece, Malta and Italy[31]. In a study conducted in the ICU of our hospital in 2004, rectal colonization of resistant bacteria (Vancomycin-resistant enterococci, methicillin-resistant Staphylococcus aureus, extended-spectrum beta-lactamases and carbapenem-resistant Enterobacteriaceae) was

shown to be associated with hospital-acquired infections, and rectal carbapenem colonization was found to be 18% in the same study[32]. In our study, the rate of rectal carbapenem resistance was found to be 46% and increased. Vap rate was also higher in rectal CRKp carriers (58% vs 24%, p< 0.001).

In addition, 95% of VAP agents were gram-negative bacteria. Although the ranking varied within themselves, similarly, gram-negative bacteria constituted the majority in the studies that evaluated the bacteria which might be the VAP agents in the intensive care unit of our hospital[33-36]. This distribution, of which local epidemiological factors affected the politics of antibiotic use, brings the antibiotic resistant problem forward between the gram-negative bacteria. This significantly restricts the treatment of VAP due to CREB that has recently caused more serious problems particularly in ICUs.

The prevalence of mortality was higher in patients with VAP who were treated in ICU compared with patients without VAP. The mortality prevalence of other infections which developed in the ICU has been reported as 35% in urinary system infections, 37% in bacteremia-sepsis, and 45% in VAP[6]. Similarly, researchers reported VAP associated mortality higher in other studies[9,37,38]. The possible causes of this may be counted as the comorbidity factors of the patients, mucosal damage due to ventilation associated barotraumas, the deterioration of the protective epithelium in the respiratory tract, and mucociliary activity loss, the VAP causing bacterial flora, and antibiotic resistance pattern[39-42].

This study has several strengths. First, the SOFA score, which is used to determine the severity of the disease, and the Charlson comorbidity index, which is used to determine the comorbidities of the patients were included in the multivariate regression analysis. Second, patients were evaluated at daily visits by infectious diseases and clinical microbiology specialists in intensive care. Our study also has several limitations. First, it was retrospectively conducted in a single-center. Second, this study had a small sample size and in a limited period of time. The generalizability of our results may be limited.

CONCLUSION

Since ICU length of stay and the duration of ventilation days are longer in patients with VAP, patients in the ICU should be discharged as soon as possible. The prevention of CRKp is significantly important with continuous practices of the universal infection control measures because CRKp is most frequently transmitted from infected or colonized other patients to ICU patients. The significance of VAP prevention strategies is revealed once more because VAP has high mortality rates. In conclusion, decreasing patient-related and hospital environment related risk factors, routine screening of rectal colonizations with CRKp, and continuous practicing of the universal infection control measures may significantly decrease the prevalence of the ventilator-associated pneumonia.

ETHICS COMMITTEE APPROVAL

This study was approved by İstanbul University Clinical Research Ethics Committee (Decision no: 02, Date: 22.01.2016).

CONFLICT of INTEREST

None of the authors had conflict of interest.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: BÇ, GO, OÖ

Data Collection or Processing: BÇ, SB, GO

Analysis/Interpretation: BÇ, SSY, OÖ, HE

Literature Search: BÇ, SB

Writing: BÇ, OÖ, HE

Final Approval: All of authors

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