ORIGINAL ARTICLE

The efficiency of routine endotracheal aspirate cultures compared to bronchoalveolar lavage cultures in ventilator-associated pneumonia diagnosis

H Yagmurdur, AH Tezcan, O Karakurt[1], F Leblebici

Departments of Intensive Care and [1]Thoracic Surgery, Ankara Numune Training and Research Hospital, Ankara, Turkey

Abstract

Objective: Ventilator-associated pneumonia (VAP) is the most common nosocomial infection in İntensive Care Units (ICUs) and its mortality rate varies from 24% to 50%. The most important factor in decreasing the mortality is administering adequate antibiotics as early as possible. In this study, we investigate the efficiency of routine endotracheal aspirate (EA) cultures to identify the etiology of VAP earlier.

Materials and Methods: Fifty-nine patients who were accepted to our ICU with acute cerebrovascular disease with mechanical ventilation (MV) requirement were chosen for this study over a 12-month period. The patients intubated in our ICU were included in the study to exclude prior colonization. Upon ICU admission, the patient's; age, sex, comorbidities, diagnosis, acute physiology and chronic health evaluation II score, and sequential organ failure assessment (SOFA) score were recorded. When bronchoalveolar lavage (BAL) was performed, the SOFA score, temperature, leukocyte count, C-reactive protein levels, PaO_2/FiO_2 ratio, PCO_2, clinical pulmonary infection score value, length of MV, and presence of antimicrobiological treatments were recorded. Routine microbiological analysis was performed by EA (pre-VAP EA) twice weekly in all patients until the endotracheal tube was removed. When VAP was suspected, fiberoptic bronchoscopy examination with BAL was performed. A diagnosis of VAP was established when the BAL quantitative culture grew at least one microorganism at a concentration ≥10^4 cfu/mL.

Results: VAP was diagnosed in 41 (69%) of the 59 patients based on BAL culture results. Among 41 positive BAL cultures, pre-VAP EA identified the same microorganism with the same antibiotics resistance pattern in 23 (56%) patients. Regarding only late-onset VAP, pre-VAP EA identified the same microorganisms found by BAL culture in 17 (63%) of the 27 cases. Among 18 BAL culture negative patients, 7 (39%) patients had negative prior pre-VAP EA culture results. *Acinetobacter baumannii* was the most frequently isolated microorganism from BAL cultures (*n* = 21, 51%). The diagnostic value of pre-VAP EA results in predicting *A. baumannii* VAP documented with the following values (sensitivity: 62%; specificity: 95%, positive predictive value: 87%, negative predictive value: 82%).

Conclusion: VAP patients should be treated with international guidelines, but if pre-VAP EA cultures identify multidrug resistant pathogens, the initial antibiotic therapy should cover these microorganisms. Thus, quantitative EA cultures are a useful noninvasive diagnostic tool in critically ill patients suspected of having pneumonia especially in the case of VAP.

Key words: Appropriate antibiotics, bronchoalveolar lavage, routine endotracheal aspirate cultures, ventilator-associated pneumonia

Date of Acceptance: 26-May-2015

Address for correspondence:
Dr. AH Tezcan,
Ulku District, Talatpasa Street, N:5, Altindag, Ankara, Turkey.
E-mail: aysndr@gmail.com

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/1119-3077.164327

PMID: 26755218

How to cite this article: Yagmurdur H, Tezcan AH, Karakurt O, Leblebici F. The efficiency of routine endotracheal aspirate cultures compared to bronchoalveolar lavage cultures in ventilator-associated pneumonia diagnosis. Niger J Clin Pract 2016;19:46-51.

Introduction

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection in Intensive Care Unit (ICU) settings. It has variable prevalence rates, ranging from 6 to 50 cases per 100 admissions to the ICU.[1] VAP, has significant morbidity, prolonging the duration of mechanical ventilation (MV) as well as the length of stay in the ICU with all of the costs associated with that extended stay.[2] The mortality rate of VAP varies from 24% to 50%.[3] The mortality rate depends on age, present comorbidities, severity of the disease, and the characteristics of the etiologic agents. The mortality rate of VAP with highly resistant microorganisms can increase to 76%.[3] However, adequate antimicrobial therapy can improve patient survival if administered during the early stage of the illness.[4] Bronchoscopic sampling provides accurate but late microbiological data because of the time required to identify the microorganisms microbiologically. Administering inadequate empirical treatment earlier or changing antibiotic treatment after bronchoalveolar lavage (BAL) results is not sufficient to decrease mortality.[4] The BAL-based treatment strategy requires empirical broad spectrum antibiotic usage before microbiological results can be obtained. The American Thoracic Society (ATS) guidelines can help to select the initial treatment, but broad spectrum antibiotic usage is associated with the rise of resistant microorganisms and side effects on the patients.[1]

The appropriateness of routine endotracheal aspirate (EA) cultures for determining true initial antibiotic treatment is still controversial, but certain studies have reported positive results for this technique.[5-7]

The primary aim of this study was to determinate the efficiency of pre-VAP EA cultures for administering correct antibiotic treatment, as confirmed by BAL culture results. The secondary objective of the study was to identify the most common colonizers and their role in the causation of VAP.

Materials and Methods

This prospective study was conducted in the medical ICU in Ankara Numune Education and Research Hospital, which have 25 beds for adult patients. The study was approved by the Institutional Review Board of the hospital. Written informed consent was obtained from the patients' next of kin before beginning the study. Fifty-nine patients were included in this study over a 12-month period. All patients were chosen from individuals admitted first to our emergency service with the acute cerebrovascular disease (e.g. ischemia, hemorrhage) and then admitted to our ICU secondly because of respiratory support requirements. Patients from emergency service without intubation initially were included in the study, if their emergency service stay was longer than 6 h they were not included in the study. Upon ICU admission, the patient's age, gender, comorbidities, diagnosis, Glasgow Coma scale, acute physiology and chronic health evaluation II score,[8] and sequential organ failure assessment (SOFA) score[9] were recorded. When BAL was performed, the SOFA score, temperature, leukocyte count, C-reactive protein (CRP) levels (mg/L), PaO_2/FiO_2 ratio, PCO_2, clinical pulmonary infection score (CPIS),[10] length of MV and presence of antimicrobiological treatments were recorded. Further information including the BAL culture results, modification of antimicrobiological treatment, length of ICU stay and outcome was also recorded.

Sample collection

Routine microbiological analysis was performed by EAs twice weekly in all patients until the endotracheal tube was removed. EA was performed using a sterile catheter with a specimen trap kit (Medbar Aspiration Kit; Izmir, Turkey). Before aspiration, a suction catheter was introduced below the intubation tube in the tracheobronchial tree. Standard methods were used for bacterial identification and antibiotics susceptibility tests and performed for bacteria present at a concentration $\geq 10^4$ cfu/mL. Only the pre-VAP EA, performed immediately before VAP was suspected, was considered for the study.

Ventilator-associated pneumonia diagnosis

One investigator performed daily rounds in the ICU to determine VAP based on each patient's physical examination, medical records, chest radiograph, and microbiological analysis results. Criteria for suspected VAP were as follows:[5]

- Patient who was mechanically ventilated more than 48 h
- New infiltrate or progression of the prior infiltrate on chest radiograph
- Occurrence of two of the following four criteria: Fever (>38°C), leukocyte count changes (>10 × 10^9 cells/L or <5 × 10^9 cells/L), purulent secretions, gas exchange degradation.

The development of VAP during the first 5 days of MV was termed early-onset VAP, and after the 5th day of mechanic ventilation, it was termed late-onset VAP.[5]

When VAP was suspected, fiberoptic bronchoscopy examination with BAL was performed. BAL was particularly performed in the suspected lobe. To deliver the BAL specimen, three sequential aliquots of 50 ml each were used. Hand suction was applied, and the first aliquot was withheld from microbiological analysis. Subsequent aliquots were pooled and fluid transported to the laboratory on ice within 1 h to perform standard methods of bacteriological identification and antibiotic susceptibility tests. A diagnosis of VAP was established when the BAL

quantitative culture grew at least one microorganism at a concentration $\geq 10^4$ cfu/mL.

In this study, we tried to compare pre-VAP EA and BAL results and to identify the pneumonia determination ability of pre-VAP EA. The two culture results were considered the same if the microorganism concentration was higher than 10^4 cfu/mL and displayed the same antibiotic susceptibility patterns. Microorganisms were classified into two groups; organisms with a high-risk of multidrug resistance (MDR) (*Pseudomonas* species, *Acinetobacter* species, *Stenotrophomonas* species, methicillin-resistant *Staphylococcus aureus*) and organisms with a low risk of MDR (all other bacteria). In our ICU, an infectious disease specialist who was blind to the study managed the antimicrobiological therapy with pre-VAP EA and BAL culture results.

Statistical analysis

The data are expressed as the mean ± standard deviation for normally distributed data and median with interquartile range for nonnormally distributed data. Variables were compared using Student's *t*-test and the Wilcoxon rank-sum test. The Chi-square test or the Fisher exact test was used to compare categorical variables.

Results

Based on criteria defined above, 59 BAL procedures were performed under suspicion of VAP. The characteristics of the 59 patients with suspected VAP are shown in Table 1. VAP was diagnosed in 41 (69%) of the 59 patients based on the BAL culture results. The ICU mortality rate of patients with VAP was 37% (15/41) and hospital mortality rate of these patients was 41% (17/41). VAP was diagnosed in 14 (34%) of the 41 patients in the first 5 days of MV (early-onset VAP) and 27 (66%) of the 41 patients after the 5th day of MV (late onset VAP).

Among 41 positive BAL cultures, pre-VAP EA identified the same microorganism with the same antibiotic resistance pattern in 23 (56%) patients. Thus, these patients continued to receive the same correct antibiotics. Regarding only late-onset VAP, pre-VAP EA had identified the same microorganisms found by the BAL culture in 17 (63%) of the 27 cases [Table 2].

Eleven patients (19%) with suspected VAP had positive pre-VAP EA cultures and received antibiotics according to these results while waiting for BAL cultures, but the BAL culture results were sterile.

Among 41 patients, 7 (17%) had negative pre-VAP EA results but received antibiotics according to ATS guidelines because of the clinical VAP suspicion. These patients' BAL cultures identified microorganisms, and six of them continued the same antibiotic regimen, while one underwent a change from the therapy applied prior to the BAL results. Among 18 BAL culture negative patients, 7 (39%) patients' prior pre-VAP EA culture results were

Table 1: Characteristics of the 59 patients with suspected VAP

Characteristics upon ICU admission	Value
Age (years)	71±16
Sex	
Female	34
Male	25
Comorbidity	
Chronic respiratory disease	9 (15)
Diabetes mellitus	15 (25.4)
NHYA class 4	5 (8.5)
Dialysis-dependent end stage renal disease	6 (10)
Cancer	4 (7)
Cirrhosis	1 (2)
APACHE II	19±7
SOFA	6±3
GCS	5.6±1

Values are given as the mean±SD or number (%). SD=Standard deviation; ICU=Intensive Care Unit; VAP=Ventilator-associated pneumonia; SOFA=Sequential organ failure assessment; APACHE=Acute physiology and chronic health evaluation; GCS=Glasgow coma scale

Table 2: Correspondence between results of BAL and pre-VAP culture

	BAL culture results	
	Early-onset VAP (*n*=14)	Late-onset VAP (*n*=27)
Pre-VAP EA		
Same	6 (43)	17 (63)
Different	5 (36)	6 (22)
No growth	3 (21)	4 (15)

Values given as number (%). Same pre-VAP EA=Same bacteria and antibiotic sensitivity pattern; Different pre-VAP EA=Different bacteria or different susceptibility to antibiotics; No growth=Nothing isolated from pre-VAP culture, but bacteria were identified with BAL and diagnosed as VAP. VAP=Ventilator-associated pneumonia; BAL=Bronchoalveolar lavage; EA=Endotracheal aspirate

Table 3: Relationship between bacteria with high-risk of MDR and VAP onset time

	Early-onset VAP	Late-onset VAP	Total
High-risk of MDR bacteria			
Acinetobacter baumannii	6	15	21
Pseudomonas aeruginosa	2	5	7
Methicillin-resistant Staphylococcus aureus	0	1	1
Stenotrophomonas maltophilia	1	0	1
Total	9	21	30
Others	5	6	11
Total	14	27	41

Values given as number. VAP=Ventilator-associated pneumonia; MDR=Multidrug resistant

also negative. Among our 59 patients, the pre-VAP EA culture results and BAL culture results were identical in 30 (51%) patients.

Acinetobacter baumannii was the microorganism most frequently isolated from BAL cultures (n = 21, 51%). Fifteen of these 21 patients had late-onset VAP [Table 3]. Thirteen of these 21 patients (sensitivity was 62%) was identified by pre-VAP EA cultures but eight of them did not. Pre-VAP EA culture results identified *A. baumannii* in 15 patients but 13 of them corrected by BAL culture results (positive predictive value [PPV] was 87%). Through 38 *A. baumannii* negative BAL culture results, 2 of them had false positive pre-VAP EA culture results (specifity was 95%). The second most frequently isolated microorganism was *Pseudomonas aeruginosa* (n = 7, 17%). Three of these 7 patients (sensitivity was 43%) were identified by pre-VAP EA cultures but four of them did not. Pre-VAP EA culture results identified *P. aeruginosa* in 9 patients but three of them corrected by BAL culture results (PPV was 33%). Through 52 *P. aeruginosa* negative BAL culture results, 6 of them had false positive pre-VAP EA culture results (specificity was 88%).

The mean VAP onset time was 7.7 ± 4.8 days. After BAL culture results, 27 patients were diagnosed with late-onset VAP, 21 (78%) of them with a high-risk of MDR bacteria. High-risk bacteria were isolated from nine (64%) of the 14 early-onset VAP patients. There was no statistical relationship between VAP onset time and microorganisms with a high-risk of MDR bacteria (P > 0.05) [Table 3]. The diagnostic value of pre-VAP EA results in predicting subsequent VAP pathogens documented by sensitivity, specificity and predictive values as shown in Table 4. There were no clinical criteria associated with BAL results except for CPIS. The most commonly used laboratory findings, such as WBC count and CRP levels were not significantly different between the two groups. The mean length of MV at the time of BAL was not different between two groups [Table 5].

Table 4: Diagnostic value of pre-VAP EA results in predicting VAP pathogens

VAP pathogen	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
All pathogens	60	39	69	30
Acinetobacter baumannii	62	95	87	82
Pseudomonas aeruginosa	43	88	33	92

VAP=Ventilator-associated pneumonia; PPV=Positive predictive value; NPV=Negative predictive value; EA=Endotracheal aspirate

Table 5: Clinical findings at the time of BAL

	≥10^4 cfu/mL	<10^4 cfu/mL	*P*
Temperature°C	37.3±0.7	37.2±0.8	0.541
WBC count (cells/mL)	12090±5274	13144±5543	0.512
CRP (mg/L)	114±68	118±79	0.873
SOFA	7 (3-14)	7 (3-17)	0.540
CPIS	6 (0-9)	4 (2-7)	0.001
Duration of MV at the time of BAL	8±5	7±4	0.604

Values are given as the mean±SD, median (minimum-maximum). MV=Mechanical ventilation; BAL=Bronchoalveolar lavage; SOFA=Sequential organ failure assessment; CPIS=Clinical pulmonary infection score; CRP=C-reactive protein; SD=Standard deviation

The patients who stayed in the ICU longer had higher mortality rates, but there was no statistically significant difference (P > 0.05). There was also no relationship between mortality rate and whether microorganism was high-risk for MDR (P > 0.05).

Discussion

This study has shown that quantitative EA culture is a useful noninvasive tool for the diagnosis of pneumonia pathogens in critically ill patients. Additionally, the results of quantitative EA cultures were comparable to the results of using invasive methods and were helpful in limiting the prescription of broad-spectrum antibiotics. Among our 41 VAP patients, most of them had (66%) late onset VAP, in contrast to an earlier large US study[2] but similar to the study by Michel *et al*.[5] Because we chose patients who did not stay for days or any other services before our critical care, there was no interaction potential for early colonization. *A. baumannii* (51%) and *P. aeruginosa* (17%) were the most commonly identified microorganisms based on the BAL results. *Stenotrophomonas* species was identified only in one patient, and methicillin-resistant *S. aureus* was identified only in one patient. These microorganisms are referred to as MDR pathogens, which have been identified as having high levels of drug resistance and which make VAP treatment difficult.[1,11] Previous studies have shown that inadequate antibiotic therapy with VAP patients decreases the survival rate.[12-15] Rello *et al*.[15] demonstrated that the mortality rates of VAP patients with adequate and inadequate antibiotic therapy were 15.4% and 37%, respectively. In this study, we found that pre-VAP EA was successful in 23 (56%) of the 41 VAP patients where the diagnosis was confirmed by BAL. These results differ between studies; Hayon *et al*.[16] identified 35%, Joseph *et al*.[17] identified 60.9%, and Michel *et al*.[5] identified 95% of BAL culture results as consistent with pre-VAP EA cultures. The specificity of pre-VAP EA cultures was 39%; thus, EA surveillance cultures may protect patients from extra broad-spectrum antibiotics. Joseph *et al*. found the sensitivity of pre-VAP EA culture was 45% in predicting *A. baumannii* and 70% in predicting *P. aeruginosa*.[17] Depuydt *et al*. found the sensitivity of tracheal surveillance culture in predicting MDR pathogens was 69%.[18] In our study, we found the sensitivity of EA cultures was 62% for *A. baumannii* and 43% for *P. aeruginosa,* which was comparable to the studies above. In one study with 36 VAP patients, the pre-VAP EA specificity was 96% for *A. baumannii* and 96% for *P. aeruginosa*.[17] In our study,

the specificity of pre-VAP EA for the same microorganisms was 95% and 88%, respectively. These compatible values show that endotracheal surveillance cultures can exclude most patients without these highly resistant pathogen infections. For MDR pathogens, an EA culture based treatment strategy may be more useful than ATS strategies, which recommend broad-spectrum empiric antibiotics. The performance of routine quantitative culture of surveillance EA samples allowed us to prospectively and accurately determine the incidence and sequence of lower respiratory tract colonization with MDR pathogens in patients on MV.

Colonization with non-MDR pathogens had low sensitivity, specificity, PPV and NPV; thus, subsequent estimation of VAP microorganisms based on EA culture results may not be useful for determining the correct antibiotic regimen. Joseph *et al*.[2] found a high PPV (83%) for *A. baumannii* comparable with our study (87%). We may decide that pre-VAP EA culture results were useful enough to extend the initial antibiotic therapy for *A. baumannii*.

When VAP is suspected, and after having sampled the distal airways, clinicians have the following two options: Start antibiotic therapy or not. If they treat the patient, they can choose antibiotics according to guidelines or to published recommendations. In our practice, if there is an EA culture result, we base our antibiotic therapy on it; if there is not a EA culture, we use ATS guidelines.

We suggest that critical caregivers may use international guidelines to treat VAP, such as ATS guidelines, but if the pathogens identified from pre-VAP EA cultures are high-risk for MDR, such as *Acinetobacter* species, the antibiotic regimen must cover them. Pirracchio *et al*.[19] and Joseph *et al*.[17] suggested as we do that EA culture results provide supplementary information to international guidelines for each case. Rello *et al*.[20] demonstrated that the aetiology of infections may be different in each ICU. Therefore, ATS classifications may be insufficient to guide the initial antibiotic therapy in certain low risk grouped patients with highly resistant pathogens.

As Joseph *et al*.[17] and Depuydt *et al*.[18] showed and we suggested in our study, in ICUs with a high prevalence of microorganisms with a high-risk of MDR, pre-VAP EA-based strategies provide early appropriate antibiotic therapy and prevent unnecessary broad-spectrum antibiotic usage. Similarly, Depuydt *et al*. found that surveillance cultures performed in an ICU with a high prevalence of MDR pathogens contributed to high rates of early appropriate antibiotic therapy with limited use of broad spectrum antibiotics.[18]

In this study, we did not choose all ICU patients randomly to enlarge the sample size, we selected only VAP suspected patients accepted in ICU especially with respiratory malfunction secondary to acute cerebrovascular disease not secondary to pulmonary diseases. However, the only main limitation of our study is a small number of patients with VAP were studied in a single center. The small number of pathogens led to large 95% confidence interval for predictive values, limiting the certainty of the results. Therefore, our results need confirmation by larger multicenter clinical trials.

Conclusion

Pathogens with a high-risk of MDR were the most frequent microorganisms in VAP. VAP patients should be treated with ATS guidelines, but if pre-VAP EA cultures identify a high-risk of MDR pathogens, initial antibiotic therapy should cover these microorganisms. Thus, quantitative EA cultures are a useful noninvasive diagnostic tool in critically ill patients suspected of having pneumonia especially in the case of VAP.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Niederman MS, Craven DE. Guidelines for the management of adults with hospital-acquired, ventilatorassociated and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388-416.
2. Rello J, Ollendorf DA, Oster G, Vera-Llonch M, Bellm L, Redman R, *et al.* Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. Chest 2002;122:2115-21.
3. Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:867-903.
4. Vincent JL, Bihari DJ, Suter PM, Bruining HA, White J, Nicolas-Chanoin MH, *et al.* The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International Advisory Committee. JAMA 1995;274:639-44.
5. Michel F, Franceschini B, Berger P, Arnal JM, Gainnier M, Sainty JM, *et al.* Early antibiotic treatment for BAL-confirmed ventilator-associated pneumonia: A role for routine endotracheal aspirate cultures. Chest 2005;127:589-97.
6. Jung B, Sebbane M, Chanques G, Courouble P, Verzilli D, Perrigault PF, *et al.* Previous endotracheal aspirate allows guiding the initial treatment of ventilator-associated pneumonia. Intensive Care Med 2009;35:101-7.
7. Depuydt P, Benoit D, Vogelaers D, Claeys G, Verschraegen G, Vandewoude K, *et al.* Outcome in bacteremia associated with nosocomial pneumonia and the impact of pathogen prediction by tracheal surveillance cultures. Intensive Care Med 2006;32:1773-81.
8. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. Crit Care Med 1985;13:818-29.
9. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, *et al.* The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22:707-10.
10. Niederman MS, Craven DE, Bonten MJ, Chastre J, Craig WA, Fagon JY. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388-416.
11. Trouillet JL, Chastre J, Vuagnat A, Joly-Guillou ML, Combaux D, Dombret MC, *et al.* Ventilator-associated pneumonia caused by potentially drug-resistant bacteria. Am J Respir Crit Care Med 1998;157:531-9.

12. Luna CM, Vujacich P, Niederman MS, Vay C, Gherardi C, Matera J, *et al.* Impact of BAL data on the therapy and outcome of ventilator-associated pneumonia. Chest 1997;111:676-85.
13. Kollef MH, Ward S. The influence of mini-BAL cultures on patient outcomes: Implications for the antibiotic management of ventilator-associated pneumonia. Chest 1998;113:412-20.
14. Alvarez-Lerma F. Modification of empiric antibiotic treatment in patients with pneumonia acquired in the intensive care unit. ICU-Acquired Pneumonia Study Group. Intensive Care Med 1996;22:387-94.
15. Rello J, Gallego M, Mariscal D, Soñora R, Valles J. The value of routine microbial investigation in ventilator-associated pneumonia. Am J Respir Crit Care Med 1997;156:196-200.
16. Hayon J, Figliolini C, Combes A, Trouillet JL, Kassis N, Dombret MC, *et al.* Role of serial routine microbiologic culture results in the initial management of ventilator-associated pneumonia. Am J Respir Crit Care Med 2002;165:41-6.
17. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia: Role of colonizers and value of routine endotracheal aspirate cultures. Int J Infect Dis 2010;14:e723-9.
18. Depuydt P, Benoit D, Vogelaers D, Decruyenaere J, Vandijck D, Claeys G, *et al.* Systematic surveillance cultures as a tool to predict involvement of multidrug antibiotic resistant bacteria in ventilator-associated pneumonia. Intensive Care Med 2008;34:675-82.
19. Pirracchio R, Mateo J, Raskine L, Rigon MR, Lukaszewicz AC, Mebazaa A, *et al.* Can bacteriological upper airway samples obtained at intensive care unit admission guide empiric antibiotherapy for ventilator-associated pneumonia? Crit Care Med 2009;37:2559-63.
20. Rello J, Sa-Borges M, Correa H, Leal SR, Baraibar J. Variations in etiology of ventilator-associated pneumonia across four treatment sites: Implications for antimicrobial prescribing practices. Am J Respir Crit Care Med 1999;160:608-13.