Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

Original research article

Ventilator-associated pneumonia risk factors, clinical and biochemical characteristics and predictive variables

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Abstract

Background: Connected to the Ventilator Patients who develop pneumonia after 48 hours of intubation are considered to have developed pneumonia. It causes a lot of trouble and costs a lot of money because of things like hospital stays and deaths. It has been estimated that 3% of intubated patients develop VAP daily within the first five days.

Material and Methods: This prospective observational study was carried out in the several Intensive Care Units at the tertiary referral center for pulmonary medicine in Tamil Nadu, Sri Sathya Sai Medical College and Hospital. Between July 2021 and June 2022, this research was conducted.

Results: Since we wanted to learn the clinical and biological profile of VAP in our ICUs, we took these precautions to make sure none of the data we collected was tainted in any way. The patients in the study had a mean age of 45. The median time to develop ventilator-related pneumonia after intubation was 7 days. On average, they spent 14 days in the hospital and spent a total of 23 days there. Procalcitonin levels were only checked in 59 individuals. One patient was released from the intensive care unit (ICU) before treatment was finished at their request.

Conclusion: Later-onset VAP, or Late VAP, is more likely in ventilated patients who had normal chest x-rays at the time of intubation. Acinetobacter is the most prevalent microbe, followed by Pseudomonas and Klebsiella. The prevalence of resistant species over sensitive ones did not affect the results.

Keywords: Pneumonia, biological profiles, prognostic markers, and risk factors

Introduction

After 48 hours of intubation, pneumonia in a patient is considered to be Ventilator-Associated Pneumonia (VAP). It causes a lot of trouble and costs a lot of money because of things like hospital stays and deaths [1, 2]. It has been estimated that 3% of intubated patients develop VAP daily within the first five days. Mortality rates are higher and multi-drug resistance bacteria are more likely to be the cause of late-onset VAP, defined as VAP that develops after 5 days of intubation. A patient is said to have VAP if they acquire pneumonia within 48 hours of intubation but had no symptoms of a lung infection beforehand [3, 4]. The lung parenchyma and the lower respiratory tract are invaded by microorganisms, leading to VAP. When the oro-pharynx and airways are compromised by endo-tracheal intubation and mechanical breathing, the body's first line of defense against microbial invasion is weakened [4-6].

Patients on mechanical ventilation in intensive care units around the world frequently experience ventilator-associated pneumonia (VAP). During their time intubated, about 28% of patients develop VAP. The worldwide incidence of VAPs has been studied extensively, and various estimates place it between 3% and 30%. The longer a patient is intubated, the greater their risk of getting VAP. VAP has a daily incidence rate of 3% for the first 5 days. Later VAP has been shown to increase the time a patient requires artificial ventilation from 10 days to 32 days in another investigation [5-7].

Another study found that patients with VAP stayed in the intensive care unit for a median of 21 days, while the control group stayed for a median of 15 days. When surviving pairs of patients with VAP were compared, it was found that their ICU stays were prolonged by a mean of 20 days. Trauma patients with pneumonia had longer hospital stays (43 days on average), ICU stays (20.5 days), and mechanical ventilation times (12 days) compared to their matched controls [8]. It's common for patients to develop VAP after surgery. About a third of the pulmonary infiltrates in intensive care unit patients are due to this. The incidence of VAP in the recovery period was found to be 17% in a research conducted in 1981.

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

Serum indices of severity of the main condition, such as low serum albumin, were linked to the onset of pneumonia. Smoking history, prolonged hospitalization prior to surgery, a lengthy operating time, and procedures performed on the thorax or abdomen were also identified as significant risk factors for postoperative pneumonia. Here we have another adult comparative study [9].

The study's goals are to collect data on the prevalence and incidence of VAP as well as its clinical and microbiological characteristics. Patients with VAP in the Medical/Surgical ICU, Surgical HDU, and Respiratory Medicine HDU will have their demographic and clinical information gathered, as well as their CPIS score, APACHE-II score, MOD score, and culture results from an endotracheal aspirate, bronchoalveolar lavage, or bronchial wash monitored. Patients will be tracked from the time they are admitted to the hospital until they are released so that mortality and outcomes can be assessed. Results from different intensive care units will be compared [10].

The researchers set out to learn more about the characteristics of patients with Ventilator-Associated Pneumonia by analyzing their clinical and microbiological data. The purpose of this research was to examine the clinical presentation of VAP in Indian intensive care units and hospital wards. With the goal of characterizing the VAP microbiome. The goal of this study is to compare the microbiologic profiles of intensive care units and hospital wards within the same medical facility.

Material and Methods

The Department of Pulmonary Medicine Sri Sathya Sai Medical College and Hospital, a tertiary referral facility in Tamil Nadu, is where this prospective observational study was carried out in multiple Intensive Care Units. Between July 2021 and June 2022, this study was conducted.

Inclusion criteria

- Patients intubated and admitted to the Intensive Care Unit.
- Clinicoradiological evidence of pneumonia.

Exclusion criteria

- Pneumonia prior to intubation or within 48 hours after intubation.
- Intubated externally.
- Any anomalous opacity on chest x-ray at the time of intubation.

A chest x-ray will be performed on any patient who presents with new symptoms such as fever, purulent discharges, leukocytosis, and a decrease in oxygen saturation. Patients will be considered for inclusion if a medical professional has diagnosed them with HAP. Modified CDC Criteria for 2014 will be used to make the diagnosis. Procalcitonin levels, microbiologic results of any respiratory and blood sample cultures, CPIS score, MOD score, and APACHE-II score will all be determined. They'll be monitored in the ICU/HDU and throughout their hospital stay until they're ready to go home. A clinically meaningful difference was defined as a difference of at least 2 intensive care unit (ICU) days or 4 hospital days.

Statistical Methods

The relationship between the continuous variables Procalcitonin, Modified CPIS Score, MOD Score, and APACHE-II Score at the time of diagnosis and the end result in VAP was determined using logistic regression analysis. Patients with VAP had their median and mean survival times analyzed, along with their correlations to procalcitonin levels, CPIS scores, MOD scores, and APACHE II scores at the time of diagnosis. Median values were compared using the Ranksum Test between 2 groups, and using the Kruskal-Wallis Test across the 3 intensive care units. ANOVA is used to compare the means of many variables among ICUs, while the T-test is used to compare the means of a single variable across two groups.

Results

The Medical, Surgical, and A-block Intensive Care Units each handled 1,000 intubated patients. Clinical suspicion of ventilator-associated pneumonia led to the examination of 150 individuals. Sixty-eight patients were included in the study because they met the Modified CDC criteria and the inclusion criteria, and they were tracked from the time they were admitted to the hospital until they were either released or died. Despite meeting the Modified CDC criteria for the diagnosis of Ventilator-Associated Pneumonia, patients with preexisting lung opacities were not included in the study. Since we wanted to learn the clinical and biological profile of VAP in our ICUs, we took these precautions to make sure none of the data we collected was tainted in any way. The patients in the study had a mean age of 45. The median time to develop ventilator-related pneumonia after intubation was 7 days. On average, they spent 14 days in the hospital and spent a total of 23 days there. Procalcitonin levels were only checked in 59 individuals. One patient was released from the intensive care unit (ICU) before treatment was finished at their request. Since the primary goal was to identify "prognostic factors towards the outcome," his data was excluded.

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

The median age of the surgical intensive care unit's patients was 45. The median time for VAP to appear was 7 days. There was an average of 15 days spent in the intensive care unit and an average of 22 days spent in the hospital. Patients in the Medical Intensive Care Unit had a median age of 46, a median duration of VAP of 6 days, a median duration of ICU stay of 15 days, and a median duration of hospitalization of 25 days. On average, patients in the AICU were 12 days old when VAP was diagnosed, 9 days old when they left the ICU, and 15 days old overall.
The median age is shown together with the standard deviation in brackets below the mean age to show the spread of ages. The median was used for the rest of the variables due to the large spread seen throughout the scales: hospital days, intensive care unit days, day of developing VAP, APCHE-III, MODS, Modified CPIS, and procalcitonin levels. Below the median value, in parentheses, are the minimum and maximum figures.

Ratio of early and late VAPS

Table 1: Comparison of early and late VAP across the 3 ICUs

	Early VAP	Late VAP
AICU	1/5	6/7
MICU	16/40	25/42
SICU	10/30	21/30
Total	30/79	50/79

In all Intensive Care Units, the incidence of early VAP was significantly lower than that of late VAP. The values from each ICU were compared using an analysis of variance (ANOVA). There was no statistically significant difference in the rates of Early and Late VAP between the three ICU.

Distribution of Sex

Table 2: Cohort sex distribution throughout the various arms

Sex	AICU	MICU	SICU	Total
Female % (n)	16.00	35.00	52.00	40.00
Male % (n)	84.00	65.00	48.00	60.00

The three arms' sex distributions were compared using the ANOVA test, but no discernible differences were found. The cohort consisted of 47 men and 31 women.

Percentage of patients who are immunocompromised
The majority of the study participants had functioning immune systems. Immunocompromised individuals made up 11.54% of the study population. Immunosuppression was brought on by hematological cancers, disseminated cancers treated with chemotherapy, and failure of the liver and kidney cells.

Mortality

Table 3: Death rates in different ICUs

Mortality	AICU	MICU	SICU	Total
Death (n)	100	20	39.00	38.00
Alive (n)	0	30	61.00	62.00

The mortality of patients who had developed VAP in various ICUs was compared using the ANOVA test. In contrast to the mortality rates in the medical and surgical ICU, the mortality rate in the AICU was 100%, which was remarkable.

Bacteriological Profile
45 out of 78 patients had evidence of the growth of numerous organisms in substantial amounts in the ET aspirate culture.

Table 4: Common microorganisms in different ICUs

	Pseudomonas	Klebsiella	Acinetobacter
AICU	3/9	2/7	2/7
MICU	14/64	6/62	31/62
SICU	9/42	5/42	17/42
Total	20/122	16/122	50/122

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

Regardless of whether the patients in the ICU had undergone surgery or not, the bacterial profile was essentially the same. Most commonly found were Ainetobacter spp., followed by pseudomonas, and finally Klebsiella. The bacteriological profile of the early and late VAP was same. When comparing the prevalence of resistant organisms across intensive care units (ICUs), no statistically significant variation was found using an analysis of variance (ANOVA) test.

ICU, hospital stay, and mortality

The median age is shown together with the standard deviation in brackets below the mean age to show the spread of ages. The median was used for the other variables due to the large spread seen across the APCHE-III, MODS, Modified CPIS, and Procalcitonin levels. Below the median value, in parentheses, are the minimum and maximum figures. Median values of scores and procalcitonin levels were compared using the Ranksum Test, and the mean 'age' of those who died and those who recovered was compared using the T-test. The median APACHE-III score for those who did not make it was 96, whereas it was 66 for those who did. Those who passed away had a median MOD of 10, while those who made it had a score of 7. Both the APACHE-III and MOD scores varied significantly between the two groups. There was no statistically significant correlation between the modified CPIS score and procalcitonin concentrations.

Procalcitonin

Table 5: Mean procalcitonin levels in both the living and the dead

	Mean	95% CI
Mortality (n=24)	34.45	15.78-55.22
Alive (n=35)	18.27	7.12-26.14

Between those who succumbed to their illness and those who survived, the mean procalcitonin level was 18.27 and 34.45, respectively. However, no statistically significant results were found.

Table 6: Predictive value of procalcitonin at 4ng/dl

Procalcitonin (ng/dl)	Mortality	Alive	Total
<4	9	16	24
>4	15	19	35
Total	24	35	59

The researchers tested whether or not a procalcitonin level of 4 ng/dl might be used as a predictor of mortality. However, no noteworthy occurrences were recorded. The protein procalcitonin could not be separated from other risk factors for death.

Discussion

During the study period, patients with symptoms of Ventilator Associated Pneumonia who had been admitted and intubated at different ICUs were assessed. To achieve a diagnosis of VAP, we adapted the CDC's criteria. Only patients with confirmed cases of VAP were included in this analysis; those who had pulmonary opacities at the time of admission or intubation were ruled out. As a result, the true number of VAP cases may have been underestimated [11, 12]. At the time of VAP diagnosis, the patient's APACHE-III score, MODS score, Modified CPIS score, and procalcitonin level were recorded. The study participants were followed up with until the day they were either released or passed away. The clinical and bacterial characteristics of the study population were investigated and researched at length. The procalcitonin levels and several other scores have been analyzed to see if they may be used as predictors of clinical outcome, including mortality and, for those who do survive, ICU and hospital length of stay. Clinical significance was arbitrarily set as a difference of 2 intensive care unit (ICU) days and 4 total hospital days. The patients in the study had a mean age of 45. Ventilator-associated pneumonia (VAP) often manifests itself 7 days after intubation. On average, they spent 14 days in the hospital and spent a total of 23 days there. Procalcitonin levels were only checked in 59 individuals. The ICU staff went against their better judgment and sent one patient home before treatment was finished. Therefore, he was excluded from the study's main purpose, which was to identify prognostic factors for the outcome [13, 14].
Patients with VAP in different ICUs had their mortality rates compared using an analysis of variance (ANOVA). When compared to the mortality rates in the medical and surgical ICU, the 100% mortality rate in the AICU stands out as particularly high. All six patients transferred from the AICU were extremely ill and in need of intensive care, with many of them suffering from disseminated or hematological malignancies and undergoing chemotherapy. Patients in AICU have a higher death rate than patients in other ICUs because their APACHE III scores are higher. The overall mortality rate was 30.96%. This suggestion defines a drug-resistant organism as one that has developed resistance to three or more drug classes that are normally effective against that species. ET Aspirate from the cohort showed

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

a 91.03% growth rate of resistant microbes. When comparing the prevalence of resistant organisms across intensive care units (ICUs), no statistically significant variation was found using an analysis of variance (ANOVA) test [15-17].

The median age, mean age, APCHE-III score, Modified Combined Severity Index score, and procalcitonin levels were calculated, and they were analyzed to see if they could be used to predict the clinical outcome (death rate, length of intensive care unit stay, and overall hospital stay for those who survived). Since the range of scores and procalcitonin levels was large, the median was used. Median values of scores and procalcitonin levels were compared using the Ranksum Test, and the mean 'age' of those who died and those who recovered was compared using the T-test. The median APACHE-III score for those who did not make it was 96, whereas it was 66 for those who did. Those who passed away had a median MOD of 10, while those who made it had a score of 7. Both the APACHE-III and MOD scores varied significantly between the two groups. There was no statistically significant correlation between the modified CPIS score and procalcitonin concentrations [18-20].

Those who made it through the sickness had a mean procalcitonin level of 17.47, whereas those who died had a level of 35.36. But no significant statistical differences were found. The researchers tested whether or not a procalcitonin level of 4 ng/dl might be used as a predictor of mortality. However, no noteworthy occurrences were recorded. As a standalone indicator of mortality, procalcitonin came up short. Due to the inability to produce a definitive ROC curve, the median survival analysis, as well as the number of days spent in the intensive care unit and the hospital, were performed using an arbitrary threshold of 4ng/dl, which was significantly higher than the cutoff of 1.5ng/dl in the prior research. Patients with a Procalcitonin level of less than 4 ng/dl had a median ICU survival of 37 days, while those with a Procalcitonin level of 4 ng/dl or more only survived for 16 days on average. The contrast, though, was noticeable from a medical standpoint [21-23].

Those with a procalcitonin level at diagnosis of less than 4ng/dl spent a median of 13 days in the intensive care unit, whereas those with a level of 4ng/dl or higher spent a median of 9.5 days; this difference was not statistically significant. There was no statistically significant difference in hospital stays between patients whose procalcitonin levels were below 4ng/dl at diagnosis and those whose levels were 4ng/dl or higher; the median stays for both groups were 26 days. Our study was unable to establish Procalcitonin as a predictor of prognosis in VAP patients, save for the median survival in terms of ICU days. Perhaps if procalcitonin levels had been tracked in real time, along with any subsequent increases or decreases in trend, a more accurate prediction could have been made [24-26].

There was no statistically significant difference in hospital length of stay between patients with an APACHE III score of less than 80 and those with a score of 80 or higher; nevertheless, the difference was clinically significant. Hospital stays were shorter for patients with lower APACHE III scores at diagnosis (19 days vs. 28.5); this difference was not statistically significant but clinically meaningful. A high APACHE III score was found to be an excellent predictor of survival in patients with ventilator-associated pneumonia. Patients who lost their battle with illness had a mean mod CPIS score of 5.5, while those who pulled through had a score of 5.26. Neither group differed from the other in any meaningful way. The data were analyzed to see if a modified CPIS score of 6 or higher can be utilized as a mortality predictor. Antibiotic treatment can be discontinued in patients with ventilator-associated pneumonia if their CPIS score is less than 6. However, no statistically significant link was found [26-28].

Conclusion

Later-onset VAP, or Late VAP, is more likely in ventilated patients who had normal chest x-rays at the time of intubation. Acinetobacter is the most prevalent microbe, followed by Pseudomonas and Klebsiella. The prevalence of resistant species over sensitive ones did not affect the results. The APACHE III score at the time of VAP diagnosis is an excellent predictor of mortality, length of intensive care unit admission, and overall hospital length of stay. A patient's median survival time in intensive care unit days can be predicted by their modified CPIS score at the time of diagnosis of VAP. A high MODS score at the time of VAP diagnosis is associated with a shorter median survival time in the intensive care unit. Being above 45 increases the likelihood of dying. It made no difference in terms of mortality whether the ET aspirate culture grew a resistant organism or multiple organisms, but polymicrobial infection will increase the ICU and hospital stay. Those who get VAP later in life are more likely to die from it. Although most Acinetobacter infections were resistant to more than 3 classes of first-line antimicrobial agents, they had a better outcome in terms of overall ICU and hospital lengths of stay.

Funding: None.

Conflict of Interest: None.

References

1. Ventilator-Associated Pneumonia: Overview of Nosocomial Pneumonias, Epidemiology of VAP, Clinical Presentation of VAP. 2015 Jun. Available from:

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

http://emedicine.medscape.com/article/304836-overview
2. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia: A review. Eur J Intern Med. 2010 Oct;21(5):360-8.
3. Melsen WG, Rovers MM, Koeman M, Bonten MJM. Estimating the attributable mortality of ventilator-associated pneumonia from randomized prevention studies. Crit Care Med. 2011 Dec;39(12):2736-42.
4. Luyt CE, Guérin V, Combes A, Trouillet JL, Ayed SB, Bernard M, *et al*. Procalcitonin Kinetics as a Prognostic Marker of Ventilator-associated Pneumonia. Am J Respir Crit Care Med. 2005 Jan;171(1):48-53.
5. Joseph NM, Sistla S, Dutta TK, Badhe AS, Parija SC. Ventilator-associated pneumonia in a tertiary care hospital in India: incidence and risk factors. J Infect Dev Ctries. 2009;3(10):771-7.
6. Nasia Safdar CJC. The pathogenesis of ventilator-associated pneumonia: its relevance to developing effective strategies for prevention. Respir Care. 2005;50(6):725-39; Discussion 739-41.
7. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for hospital-acquired pneumonia. JAMA. 2009 May;301(20):2120-8.
8. Duszyńska W, Barteczko B, Kübler A. [Monitoring of nosocomial infections using the HELICS network]. Anestezjol Intensywna Ter. 2008 Mar;40(1):17-21.
9. Zilberberg MD, Shorr AF. Ventilator-Associated Pneumonia: The Clinical Pulmonary Infection Score as a Surrogate for Diagnostics and Outcome. Clin Infect Dis. 2010 Aug;51(1):S131-5.
10. Park DR. The Microbiology of Ventilator-Associated Pneumonia. Respir Care. 2005 Jun;50(6):742-65.
11. Koenig SM, Truwit JD. Ventilator-associated pneumonia: diagnosis, treatment, and prevention. Clin Microbiol Rev. 2006 Oct;19(4):637-57.
12. Craven DE. Epidemiology of ventilator-associated pneumonia. Chest. 2000 Apr;117(4(2)):186S-187S.
13. Goel V, Hogade SA, Karadesai S. Ventilator associated pneumonia in a medical intensive care unit: Microbial aetiology, susceptibility patterns of isolated microorganisms and outcome. Indian J Anaesth. 2012;56(6):558-62.
14. Iregui M, Ward S, Sherman G, Fraser VJ, Kollef MH. Clinical importance of delays in the initiation of appropriate antibiotic treatment for ventilator-associated pneumonia. Chest. 2002 Jul;122(1):262-8.
15. Niederman MS. The clinical diagnosis of ventilator-associated pneumonia. Respiratory Care. 2005;50:788-796.
16. Huang KT, Tseng CC, Fang WF, Lin MC. An early predictor of the outcome of patients with ventilator-associated pneumonia. Chang Gung Med J. 2010 May-Jun:33(3):274-82.
17. Marshall JC, *et al*. Crit Care Med 1995;23:1638-52. [Cited by: De Campos T, *et al*. JOP. J Pancreas (Online). 2008;9(6):690-697.
18. The Diagnostic and Prognostic Value of Serum Procalcitonin among Ventilator Associated Pneumonia Patients* [Internet]. [cited 2015 Jul 1]. Available from: http://www.scirp.org/journal/PaperInformation.aspx?PaperID=32033#.VZRIDUazkcc
19. Klompas M, Branson R, Eichenwald EC, Greene LR, Howell MD, Lee G, *et al*. Strategies to prevent ventilator-associated pneumonia in acute care hospitals: update. Infect Control Hosp. Epidemiol. 2014 Sep;35(2):S133-54.
20. Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. Crit Care Med. 2011 Aug;39(8):1985-91.
21. McClave SA, Lukan JK, Stefater JA, Lowen CC, Looney SW, Matheson PJ, *et al*. Poor validity of residual volumes as a marker for risk of aspiration in critically ill patients. Crit Care Med. 2005 Feb;33(2):324-30.
22. Chan EY, Ruest A, Meade MO, Cook DJ. Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. BMJ. 2007 Apr;334(7599):889.
23. Kollef MH, Morrow LE, Niederman MS, Leeper KV, Anzueto A, Benz-Scott L, *et al*. Clinical characteristics and treatment patterns among patients with ventilator-associated pneumonia. Chest. 2006 May;129(5):1210-8.
24. Kollef MH, Afessa B, Anzueto A, Veremakis C, Kerr KM, Margolis BD, *et al*. Silver-coated endotracheal tubes and incidence of ventilator-associated pneumonia: the NASCENT randomized trial. JAMA. 2008 Aug;300(7):805-13.
25. Roberts I, Yates D, Sandercock P, Farrell B, Wasserberg J, Lomas G, *et al*. Effect of intravenous corticosteroids on death within 14 days in 10008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial. Lancet Lond. Engl. 2004 Oct;364(9442):1321-8.
26. Steinberg KP, Hudson LD, Goodman RB, Hough CL, Lanken PN, Hyzy R, *et al*. Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome. N Engl. J Med. 2006

ISSN:0975 -3583,0976-2833 VOL13, ISSUE 07, 2022

Apr;354(16):1671-84.
27. Peter J, Chacko B, Moran J. Comparison of closed endotracheal suction versus open endotracheal suction in the development of ventilator-associated pneumonia in intensive care patients: An evaluation using meta-analytic techniques. Indian J Med Sci. 2007;61(4):201.
28. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, *et al*. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2012 Mar;18(3):268-81.