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Association of Number of Oral bacteria with Ventilator-Associated Pneumonia and Delirium in Patients in the Intensive Care Unit

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Abstract

Objectives: Ventilator-associated pneumonia (VAP) and delirium are major complications among patients in the intensive care unit (ICU). The impact of oral bacterial count on these conditions is not well understood. This study aimed to explore the association between oral bacterial load and the incidence of VAP and delirium in ICU patients.

Methods: In this single-center longitudinal study, 130 patients admitted to the ICU from September 2022 to May 2023 were included. Oral bacteria counts on the tongue were quantified, and assessments of oral health using the Oral Health Assessment Tool (OHAT) and oral moisture levels were also conducted. We examined the associations between oral bacterial count, OHAT scores, and oral moisture with the incidence of VAP and delirium.

Results: The incidence rates of VAP and delirium were 31.4% and 35.4%, respectively. Patients with a high oral bacterial load ($\geq 5.0 \times 10^7$ CFU/mL) at ICU admission had a higher likelihood of developing VAP (odds ratio [OR] 7.43, 95% confidence interval [CI] 1.68-32.87) and delirium (OR 3.30, 95% CI 1.04-10.44) compared with those with lower bacterial counts ($< 1.0 \times 10^7$ CFU/mL). No significant associations were found between OHAT scores and oral moisture and the occurrence of VAP or delirium.

Conclusion: A higher oral bacterial count at ICU admission was associated with increased incidences of VAP and delirium.

Keywords

oral bacterial count, ventilator-associated pneumonia, delirium, intensive care unit, oral care

Introduction

Ventilator-associated pneumonia (VAP) and delirium frequently occur in the intensive care unit (ICU) and are associated with increased mortality rates.^{1,2} VAP, a hospital-acquired pneumonia, develops in patients more than 48 h after initiating invasive mechanical ventilation and represents one of the most common ICU-acquired infections. The incidence of VAP varies widely, ranging from 5% to 40%, depending on the setting and diagnostic criteria.¹ Aspiration of colonized oral microorganisms, often due to inadequate oral care, is a major cause of VAP.³⁻⁵ In response, several oral care protocols have been implemented,^{4,6} collectively referred to as “VAP bundles”, to reduce the incidence of this infection.⁷ Despite these efforts, comprehensive data on the exact number of oral bacteria present in ICU patients are lacking.

Delirium, characterized by the acute onset of cerebral dysfunction, changes in baseline mental status, inattention, and either disorganized thinking or an altered level of consciousness, also poses a significant challenge in the ICU, affecting 45% to 87% of patients during their stay.⁸ Notably, intubated patients are particularly susceptible, with delirium rates approaching 80%.^{9,10} Risk factors for delirium include

advanced age, sedative medications, and prolonged ICU stays.^{9,11} Concurrently, VAP is known to prolong the need for sedation and ICU admission, thereby indirectly contributing to the risk of delirium.

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Therefore, this study aims to investigate the impact of oral hygiene—specifically, the quantification of oral bacteria—on the incidence of VAP and delirium in ICU patients.

Materials and Methods

Study Design and Setting

This retrospective cohort study involved reviewing the medical records of patients treated in the ICU at a single tertiary hospital in Japan for more than 48 h. Of the 213 patients admitted to the ICU from September 2022 to May 2023, 213 underwent oral examinations and tongue bacterial count measurements. Of these, people who met the exclusion criteria ($n=83$) were excluded. After excluding missing values, 130 people were included in the analysis. Data collection including bacterial count was conducted within 24 h after admission to the ICU. No oral care was provided by nurses before data collection. Exclusion criteria included patients younger than 20 years, those with an ICU stay shorter than 48 h, individuals with dementia, patients in a comatose state for the duration of their ICU stay, those testing positive for COVID-19, and patients who died during their ICU stay. The final sample included 130 patients (Figure 1).

Data Collection Tools and Methods

We systematically collected data from the time of ICU admission to discharge, utilizing an electronic patient data management system during routine clinical practice. Assessments of oral condition and bacterial counts were conducted at ICU admission, three days post-admission, and at ICU discharge.

Baseline Clinical Characteristics

We evaluated baseline characteristics including age, sex, Sequential Organ Failure Assessment (SOFA) score to determine severity of illness, diagnosis at admission, surgical status, ventilator use and duration, sedative and analgesic use, lengths of hospital and ICU stays, and post-ICU mortality (Table 1).

Oral Conditions

Oral assessments were performed by dentists and dental hygienists. These assessments included evaluating the number of teeth, presence of caries, presence of teeth with ≥ 4 -mm periodontal pocket depth, presence of dry mouth, and tongue bacterial count during the patients' stay in the ICU. We utilized the Oral Health Assessment Tool (OHAT) to assess oral health status.¹² The OHAT enables visual evaluation across eight dimensions: lips, tongue, gums/tissues, saliva, natural teeth, dentures, oral cleanliness, and dental pain. Each dimension is scored on a scale ranging from healthy (0 points), oral changes (1 point), to unhealthy (2 points), with a higher score indicating poorer oral health. The presence or absence of thirst was assessed using an oral moisture meter (Mucus; Yoshida Ltd, Tokyo, Japan). According to the manufacturer's guidelines, a moisture level ≥ 29.6 was defined as normal, ≤ 27.9 as dry mouth, and 28.0–29.5 as borderline dry mouth.¹³

Oral Bacterial Counts

We focused on counting bacteria on the tongue rather than in saliva, given the instability of salivary fluid collection from intubated patients. To collect samples for oral bacterial counts, the center of the tongue was sampled using a sterile cotton swab attached to a constant-pressure specimen collection device (bacterial counter; Yoshida Ltd). The procedure followed the manufacturer's instructions.¹⁴ For analysis, we employed a bacterial count-measuring instrument (bacterial counter; Yoshida Ltd),¹⁵ which isolates bacteria in a liquid medium on an electrode. This instrument measures the change in impedance and calculates bacterial concentration (CFU/mL) in a 1-mL sample.

Daily Oral Care During ICU Stay

Oral care for patients in the ICU was administered by nurses using both toothbrushes and sponge brushes every eight hours for patients unable to consume food orally. For patients capable of oral intake, oral care was provided following each meal. The methods of oral care were not standardized, allowing

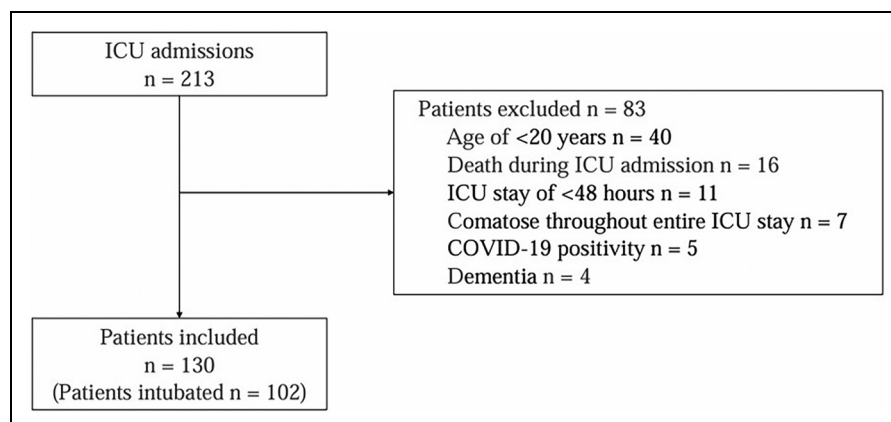


Figure 1. Flow diagram of the patients in the study. ICU, intensive care unit.

Table 1. Patient Characteristics.

	Study population (n = 130)
Age, years	65 (50, 74)
Male	79 (60.8)
SOFA score at ICU admission	6 (3, 9)
Diagnosis at ICU admission	
Cardiovascular disease	47 (36.2)
Cerebrovascular disease	20 (15.4)
Trauma	22 (16.9)
Sepsis	15 (11.5)
Others	26 (20.0)
Surgical treatment	75 (57.7)
Intubation	102 (78.5)
Duration of intubation, days (n = 102)	3 (1, 7)
Analgesics	93 (71.5)
Sedatives	106 (81.5)
Hospital length of stay, days	24 (17, 40)
ICU length of stay, days	6 (3, 12)
No oral feeding in ICU	78 (60.0)
Death after leaving ICU	18 (13.8)
Number of teeth	26 (17, 28)
Dental caries	27 (20.8)
Presence of teeth with ≥ 4 -mm periodontal pocket depth	56 (43.1)
OHAT total score	
ICU admission	7 (5, 10)
3 days after ICU admission	6 (4, 8)
Leaving ICU (3-28 days)	4 (2, 7)
Dry mouth score	
ICU admission	26.3 (24.0, 28.3)
3 days after ICU admission	27.3 (23.5, 29.0)
Leaving ICU (3-28 days)	27.6 (25.0, 29.0)
Tongue bacterial count (CFU/mL)	
ICU admission	
$< 1.0 \times 10^7$	54 (41.5)
$1.0-5.0 \times 10^7$	56 (43.1)
$\geq 5.0 \times 10^7$	20 (15.4)
3 days after ICU admission	
$< 1.0 \times 10^7$	70 (53.8)
$1.0-5.0 \times 10^7$	45 (34.6)
$\geq 5.0 \times 10^7$	15 (11.5)
Leaving ICU (3-28 days)	
$< 1.0 \times 10^7$	95 (73.1)
$1.0-5.0 \times 10^7$	27 (20.8)
$\geq 5.0 \times 10^7$	8 (6.2)

Data are presented as median (first quartile, third quartile) or n (%).
 SOFA, Sequential Organ Failure Assessment; ICU, intensive care unit;
 OHAT, Oral Health Assessment Tool; CFU, colony-forming units.

nurses to select techniques based on the specific oral conditions of the patients. Antibacterial solutions such as chlorhexidine and povidone-iodine were not used. When performing oral care, we used toothbrushes and sponge brushes with water. Upon the request of physicians or nurses, dentists or dental hygienists provided expert oral care support and guidance.

Ventilator-Associated Pneumonia

VAP is defined as pneumonia that develops 48 h or more following endotracheal intubation, characterized by new or

progressive infiltrate, along with systemic infection indicators such as fever, an increased C-reactive protein level, and/or elevated white blood cell count. Diagnosis of VAP was made by an ICU physician.¹⁶

Delirium

Delirium assessment in the ICU was conducted using the Intensive Care Delirium Screening Checklist, with a score greater than four indicating delirium.² Trained ICU nurses and intensivists independently evaluated patients. All ICU nurses received training on the proper use of delirium assessment techniques. A psychiatrist reassessed delirium to provide a reference for subsequent evaluations.

Data Analysis

Descriptive statistics were used to delineate the baseline characteristics of the patients. Continuous variables are expressed as mean $\pm$ standard deviation (SD), while categorical variables are presented as the number (%) of patients. Tongue bacterial counts were categorized into three categories: low ($< 1.0 \times 10^7$ CFU/mL), moderate ($1.0-5.0 \times 10^7$ CFU/mL), and high ($\geq 5.0 \times 10^7$ CFU/mL) based on the distribution (Table S1). The Shapiro–Wilk test was used to assess the normality of the continuous data. For the analysis of associations between VAP or delirium and their related factors, the *t*-test was applied to normally distributed data, the Mann–Whitney U test to non-parametric data, and the chi-square or Fisher's exact test to categorical variables. Multivariate logistic regression models were constructed with VAP and delirium as the dependent variables. Factors that showed a significant relationship with VAP or delirium in the bivariate analysis ($p < 0.05$) were included as covariates in the adjusted models. The odds ratio (OR) and 95% confidence interval (CI) were computed for each model. A *p*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS software for Windows, version 25.0 (IBM Japan, Tokyo, Japan).

Ethical Considerations

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Committee of Kyushu University, Approval No. 22115-00. The institutional ethics committee at Kyushu University approved this study and waived the requirement for informed consent.

Results

Patient Characteristics

The patients' baseline characteristics are shown in Table 1. The median age was 65 (range 50-74) years, with 79 (60.8%) of the patients being male. At ICU admission, the median SOFA score was 6 (3-9). Prior to ICU admission, 75

Table 2. The Association Between VAP and Related Factors in Patients with Intubation. (n = 102).

	VAP [*] , †		
	(n = 102)		
	No (n = 70)	Yes (n = 32)	p value
Age	60.2 ± 2.0	67.2 ± 2.8	0.041
Male (ref. female)	43 (61.4)	23 (71.9)	0.306
SOFA score at ICU admission	6.9 ± 0.5	6.6 ± 0.6	0.948
Diagnosis at admission			
Cardiovascular disease	33 (47.1)	11 (34.4)	0.227
Cerebrovascular disease	11 (15.7)	6 (18.8)	0.703
Trauma	15 (21.4)	2 (6.3)	0.080
Sepsis	4 (5.7)	5 (15.6)	0.135
Others	7 (10.0)	8 (25.0)	0.047
Surgical treatment (ref. no)	56 (80.0)	12 (37.5)	<0.001
Intubation (ref. no)			
Duration of intubation (n = 102)	4.3 ± 0.7	5.4 ± 0.6	0.009
Analgesic (ref. no)	57 (81.4)	27 (84.4)	0.717
Sedative (ref. no)	68 (97.1)	31 (96.9)	0.941
Hospital length of stay, days	43.9 ± 7.6	48.0 ± 9.2	0.642
ICU length of stay, days	10.6 ± 1.2	10.4 ± 1.0	0.158
Not oral feeding in ICU (ref. yes)	47 (67.1)	23 (71.9)	0.633
Number of teeth	20.8 ± 1.2	19.3 ± 1.8	0.497
Dental caries (ref. no)	12 (17.1)	7 (21.9)	0.569
Presence of teeth with periodontal pocket depth ≥4 mm (ref. no)	31 (44.3)	12 (37.5)	0.520
OHAT total score			
ICU admission	7.5 ± 0.4	7.9 ± 0.6	0.581
3 days after ICU admission	6.4 ± 0.4	6.6 ± 0.6	0.799
Leaving ICU	4.7 ± 0.4	5.2 ± 0.7	0.538
Dry mouth score			
ICU admission	25.3 ± 0.5	25.2 ± 0.9	0.624
3 days after ICU admission	25.4 ± 0.6	25.7 ± 0.8	0.922
Leaving ICU	25.9 ± 0.5	26.4 ± 0.7	0.902
Tongue bacteria count (CFU/mL)			
ICU admission (log ₁₀ CFU/mL)	6.70 ± 0.74	7.19 ± 0.81	0.238
< 1.0 × 10 ⁷	28 (40.0)	10 (31.3)	0.005
1.0 × 10 ⁷ -5.0 × 10 ⁷	36 (51.4)	11 (34.4)	
≥ 5.0 × 10 ⁷	6 (8.6)	11 (34.4)	
3 days after ICU admission (log ₁₀ CFU/mL)	6.66 ± 0.89	7.07 ± 0.71	0.023
< 1.0 × 10 ⁷	41 (58.6)	11 (34.4)	0.071
1.0 × 10 ⁷ -5.0 × 10 ⁷	22 (31.4)	15 (46.9)	
≥ 5.0 × 10 ⁷	7 (10.0)	6 (18.8)	
Leaving ICU (log ₁₀ CFU/mL)	6.49 ± 0.77	6.50 ± 0.83	0.964
< 1.0 × 10 ⁷	53 (75.7)	23 (71.9)	0.916
1.0 × 10 ⁷ -5.0 × 10 ⁷	13 (18.6)	7 (21.9)	
≥ 5.0 × 10 ⁷	4 (5.7)	2 (6.3)	

T test or Mann-Whitney U test for continuous variables and chi-square test or Fisher's exact test for categorical variables.

*Data are mean ± SD for continuous variables and n (%) for categorical variables.

†Patients with intubation (n = 102).

OR, odds ratio; CI, confidence interval; VAP, ventilator-associated pneumonia; SOFA, sequential organ failure assessment; ICU, intensive care unit; OHAT, oral health assessment tool; CFU, colony-forming units.

(57.7%) patients underwent surgical procedures, and 102 (78.5%) were intubated with a median intubation duration of 3 (1-7) days. Ninety-three (71.5%) patients received analgesics, and 106 (81.5%) received sedatives. The median hospital stay was 24 (17-40) days and the median ICU stay was 6

(3-12) days. Seventy-eight (60.0%) patients did not undergo oral feeding during their ICU stay. Regarding the patients' oral conditions, the mean number of teeth was 26 (17-28), 27 (20.8%) patients had caries, and 56 (43.1%) patients had periodontal pocket depths of ≥4 mm.

Table 3. The Association Between Delirium and Related Factors. (n = 130).

	Delirium*		
	(n = 130)		
	No (n = 84)	Yes (n = 46)	p value
Age	61.0 ± 1.7	63.2 ± 2.5	0.353
Male (ref. female)	53 (63.1)	26 (56.5)	0.463
SOFA score at ICU admission	6.4 ± 0.4	6.5 ± 0.5	0.853
Diagnosis at admission			
Cardiovascular disease	28 (33.3)	19 (41.3)	0.366
Cerebrovascular disease	13 (15.5)	7 (15.2)	0.969
Trauma	18 (21.4)	4 (8.7)	0.087
Sepsis	11 (13.1)	4 (8.7)	0.572
Others	14 (16.7)	12 (26.1)	0.199
Surgical treatment (ref. no)	47 (56.0)	28 (60.9)	0.587
Intubation (ref. no)	62 (73.8)	40 (87.0)	0.081
Duration of intubation (n = 102)	4.4 ± 0.7	5.1 ± 0.7	0.009
Analgesic (ref. no)	58 (69.0)	35 (76.1)	0.395
Sedative (ref. no)	63 (75.0)	43 (93.5)	0.009
Hospital length of stay, days	29.8 ± 3.1	59.8 ± 11.8	0.001
ICU length of stay, days	7.0 ± 0.7	12.8 ± 1.6	<0.001
Not oral feeding in ICU (ref. yes)	48 (57.1)	30 (65.2)	0.369
VAP (n = 102)	18 (29.0)	14 (35.0)	0.526
Number of teeth	22.2 ± 1.0	20.2 ± 1.5	0.821
Dental caries (ref. no)	17 (20.2)	10 (21.7)	0.840
Presence of teeth with periodontal pocket depth ≥4 mm (ref. no)	37 (44.0)	19 (41.3)	0.763
OHAT total score			
ICU admission	7.3 ± 0.3	7.6 ± 0.5	0.490
3 days after ICU admission	6.2 ± 0.4	6.2 ± 0.5	0.860
Leaving ICU	4.9 ± 0.4	4.7 ± 0.5	0.755
Dry mouth score			
ICU admission	25.6 ± 0.4	25.2 ± 0.8	0.998
3 days after ICU admission	25.7 ± 0.5	26.1 ± 0.7	0.447
Leaving ICU	26.5 ± 0.4	25.8 ± 0.7	0.659
Tongue bacteria count (CFU/mL)			
ICU admission (log10 CFU/mL)	6.83 ± 0.82	7.24 ± 0.71	0.005
< 1.0 × 10 ⁷	42 (50.0)	12 (26.1)	0.026
1.0 × 10 ⁷ -5.0 × 10 ⁷	32 (38.1)	24 (52.2)	
≥ 5.0 × 10 ⁷	10 (11.9)	10 (21.7)	
3 days after ICU admission (log10 CFU/mL)	6.67 ± 0.81	6.91 ± 0.88	0.118
< 1.0 × 10 ⁷	50 (59.5)	20 (43.5)	0.138
1.0 × 10 ⁷ -5.0 × 10 ⁷	27 (32.1)	18 (39.1)	
≥ 5.0 × 10 ⁷	7 (8.3)	8 (17.4)	
Leaving ICU (log10 CFU/mL)	6.44 ± 0.82	6.64 ± 0.71	0.168
< 1.0 × 10 ⁷	62 (73.8)	33 (71.7)	0.665
1.0 × 10 ⁷ -5.0 × 10 ⁷	18 (21.4)	9 (19.6)	
≥ 5.0 × 10 ⁷	4 (4.8)	4 (8.7)	

T test or Mann-Whitney U test for continuous variables and chi-square test or Fisher's exact test for categorical variables.

*Data are mean ± SD for continuous variables and n (%) for categorical variables.

OR, odds ratio; CI, confidence interval; VAP, ventilator-associated pneumonia; SOFA, sequential organ failure assessment; ICU, intensive care unit; OHAT, oral health assessment tool; CFU, colony-forming units.

Univariate Analysis for the Occurrence of VAP and Delirium

As shown in Table 2 and Table 3, the overall incidence of VAP and delirium in the ICU was 31.4% (32 of 102 patients) and 35.4% (46 of 130 patients), respectively. Patients with VAP were generally older and less likely to have received surgical

treatment compared with those without VAP. Regarding delirium, factors such as sedative use and longer stays in both the ICU and the hospital were associated with its occurrence. There was no association between changes in OHAT scores and the occurrence of VAP or delirium at any point in time. Similarly, the dry mouth score, measured by an oral moisture meter, was not associated with either VAP or delirium. Although the dry mouth score

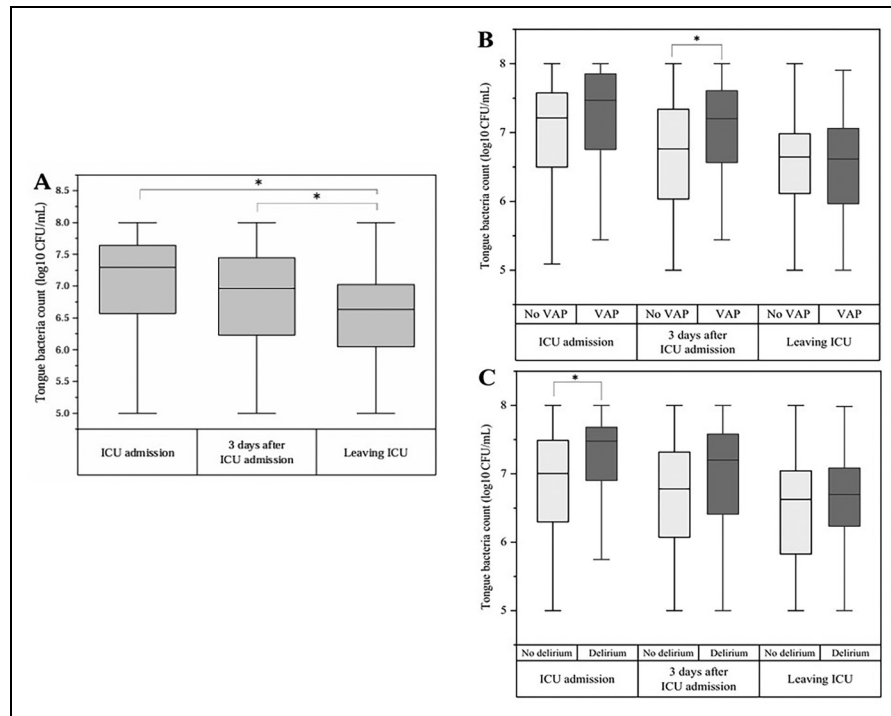


Figure 2. Number of tongue bacteria at ICU admission, 3 days after ICU admission, and upon leaving the ICU in 102 intubated patients (A). Comparisons of the number of tongue bacteria (B) between patients with and without VAP and (C) between patients with and without delirium at ICU admission, 3 days after ICU admission, and upon leaving the ICU. * $p < 0.05$. VAP, ventilator-associated pneumonia; ICU, intensive care unit.

generally improved during the ICU stay, the condition of dry mouth (scores ≤ 27.9) persisted until discharge from the ICU.

Tongue Bacterial Count

After admission to the ICU in 102 intubated patients, there was a tendency for the number of bacteria on the tongue to decrease. (Figure 2A). On the third day of ICU admission, patients with VAP exhibited significantly higher bacterial counts on the tongue compared with those without VAP (Figure 2B). Similarly, upon ICU admission, patients with delirium had significantly higher bacterial counts on their tongues than those without delirium (Figure 2C). We classified tongue bacterial counts based on the distribution (Table S1) as follows: low ($< 1.0 \times 10^7$ CFU/mL), moderate (1.0 – 5.0×10^7 CFU/mL), and high ($\geq 5.0 \times 10^7$ CFU/mL). Categorical variables are presented as the number (%) of patients. Figure 3A and 3B demonstrate that the rates of moderate and high bacterial counts at admission and on the third day after ICU admission were elevated in both the VAP and delirium groups. There were no significant differences in OHAT scores between patients with and without VAP or delirium. However, one OHAT category, cleanliness, was correlated with bacterial counts (Table S2).

Multivariate Analysis of the Association of Oral bacteria with VAP and Delirium

In the context of VAP and delirium, logistic regression analysis was performed using covariates that were significant in

univariate analysis. Hospital length of stay was excluded as a covariate in the multivariate analysis for VAP and delirium, as a longer hospital stay may result from complications associated with VAP and delirium. The disease category “others” was also excluded because of its heterogeneous nature. Results indicated that a high category of tongue bacteria ($\geq 5.0 \times 10^7$ CFU/mL) at ICU admission was significantly associated with the incidence of VAP (OR 7.43, 95% CI 1.68–32.87, $p = 0.008$) and delirium (OR 3.30, 95% CI 1.04–10.44, $p = 0.043$), after adjusting for covariates (Table 4 and Table 5). A high level of tongue bacteria category ($\geq 5.0 \times 10^7$ CFU/mL) at 3 days post-ICU admission was also associated with the incidence of VAP (OR 4.53, 95% CI 1.05–19.56, $p = 0.043$). Additionally, age and non-surgical treatments were independently associated with the occurrence of VAP. For delirium, the length of ICU stay was an independent factor, whereas sedative use was not.

Discussion

Numerous studies have established a robust association between pneumonia and poor oral hygiene, including conditions such as oral biofilms, inflammatory gingivitis, and periodontitis.^{5,6,17} However, the direct correlation between actual oral bacterial counts and VAP remains unclear. While this study found no significant correlation between the OHAT scores and VAP, an elevated bacterial load on the tongue was associated with a higher incidence of VAP.

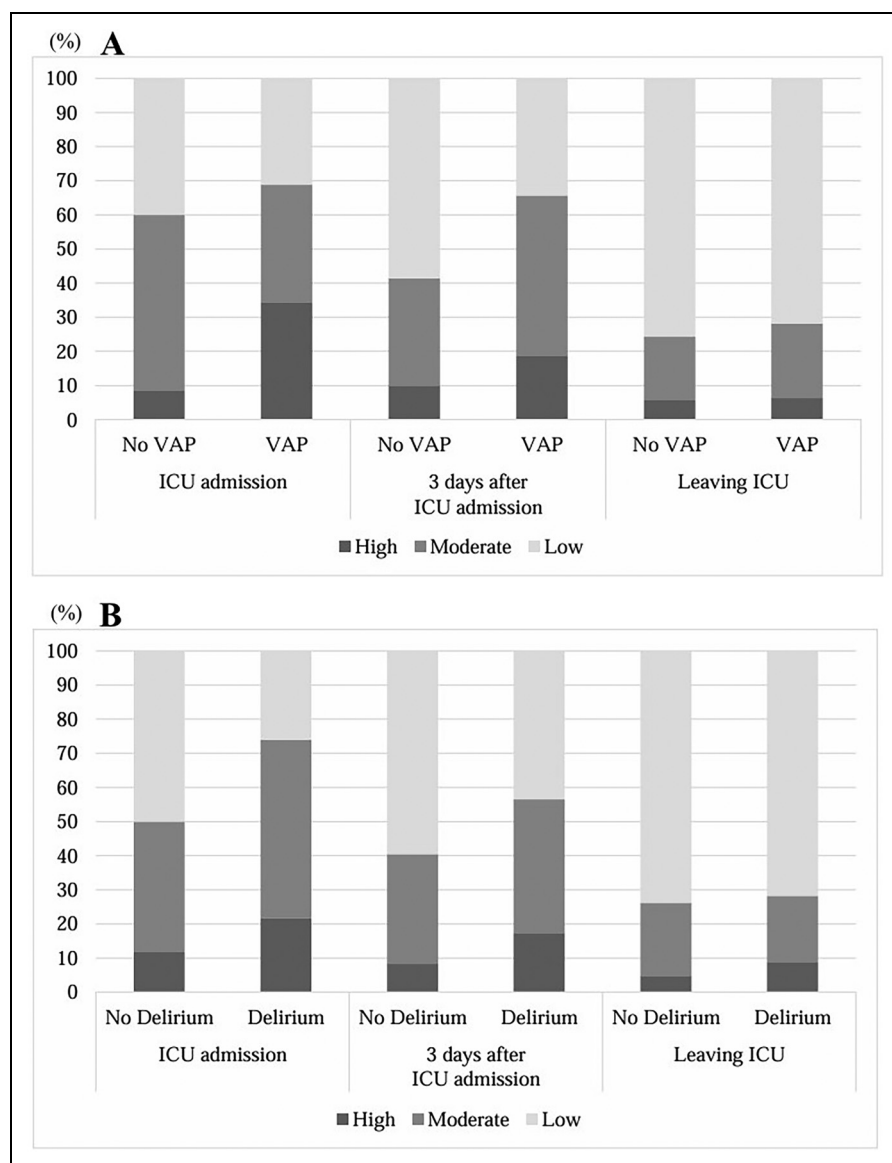


Figure 3. Temporal changes in the number of tongue bacteria between patients with and without VAP and between patients with and without delirium at ICU admission, 3 days after ICU admission, and upon leaving the ICU. The percentages of patients with a high level ($\geq 5.0 \times 10^7$ CFU/mL) and moderate level ($1.0\text{--}5.0 \times 10^7$ CFU/mL) of tongue bacteria are shown among patients with (A) VAP (the 102 patients who were intubated) and (B) delirium (all 130 patients in the study). VAP, ventilator-associated pneumonia; ICU, intensive care unit.

In our analysis, both OHAT scores and tongue bacterial counts showed a decreasing trend over time in patients in the ICU. This trend likely reflects effective oral assessments and care provided by nursing staff from the time of ICU admission. Our hospital emphasizes an integrated approach to medical and dental care, promoting multidisciplinary collaboration. Regular multidisciplinary conferences are conducted by ICU staff to disseminate knowledge about oral health management, and dentists along with dental hygienists routinely offer oral care guidance to nurses. As shown in Figure 2B, a higher bacterial count on the tongue at the time of ICU admission and three days post-admission correlated with a greater likelihood of VAP development. Notably, bacterial counts on day three, but not at admission, were significantly associated with VAP, as indicated by

both univariate and multivariate analyses (Table 2 and Table S3). Inadequate oral care is thought to be the reason for the high bacterial count on the tongue in VAP, but poor oral condition before admission to the ICU affects VAP more than oral care in the ICU. In emergency patients, saving their lives is the top priority, so tracheal intubation is often performed before oral care is performed, and contaminated matter in the mouth flows into the trachea through the intubation tube, increasing the possibility of causing VAP. All of the cases admitted to the ICU this time were emergency cases, which differed from the elective surgery cases in which the oral cavity condition was good beforehand. It has been reported that the onset of postoperative pneumonia in elective surgery cases is often due to the patient's own oral condition before operation,¹⁸

Table 4. Odds Ratios for VAP in Multivariate Logistic Regression Model in Patients with Intubation. (n = 102).

	VAP (n = 102)			
	Model 1 Adjusted OR (95% CI)	p value	Model 2 Adjusted OR (95% CI)	p value
Tongue bacteria count (CFU/mL) at ICU admission				
Low ($<1.0 \times 10^7$)	1		1	
Moderate ($1.0 \times 10^7 - 5.0 \times 10^7$)	0.82 (0.25–2.67)	0.816		
High ($\geq 5.0 \times 10^7$)	7.43 (1.68–32.87)	0.008		
Tongue bacteria count (CFU/mL) at 3 days after ICU admission				
Low ($<1.0 \times 10^7$)			1	
Moderate ($1.0 \times 10^7 - 5.0 \times 10^7$)			2.04 (0.67–6.24)	0.211
High ($\geq 5.0 \times 10^7$)			4.53 (1.05–19.56)	0.043
Age	1.04 (1.00–1.08)	0.040	1.04 (1.00–1.07)	0.039
Other diseases				
No	1			
Yes	2.34 (0.60–9.15)	0.223	2.30 (0.59–8.95)	0.228
Duration of intubation	1.06 (0.95–1.18)	0.318	1.05 (0.94–1.17)	0.386
Surgical treatment				
No	1		1	
Yes	0.10 (0.03–0.32)	<0.001	0.13 (0.05–0.39)	<0.001

Logistic regression models: VAP was the dependent variable and associated factors were the independent variable.

Model included all covariates associated with the outcome in the crude model ($p < 0.05$).

OR, odds ratio; CI, confidence interval; VAP, ventilator-associated pneumonia; ICU, intensive care unit; CFU, colony-forming units.

but since the cases in this study were emergency cases, it is presumed that many of them had insufficient oral care beforehand. As a result, we believe that some cases were not covered by daily oral care by nurses alone, leading to the onset of the disease. These findings suggest that the actual measurement of oral bacteria could serve as a valuable predictive tool for VAP in the ICU setting. Therefore, regular oral cleaning to reduce bacterial load represents a crucial preventative strategy against VAP.

In our study, we evaluated OHAT scores, moisture levels, and oral bacterial counts in relation to delirium. To our knowledge, this is the first investigation to explore the relationship between oral health—including bacterial counts—and delirium. While previous research has examined the link between VAP and oral health, none have specifically examined its association with delirium. It has been reported that prolonged intubation extended ICU stays due to VAP are potential risk factors for delirium.^{19–22} Therefore, we hypothesized a correlation between bacterial counts, VAP, and delirium. However, our findings did not reveal a statistically significant association between VAP and delirium. We also investigated whether prolonged intubation time due to VAP causes delirium, but no association was shown. Contrary to expectations, higher bacterial counts on the tongue at ICU admission were linked with the occurrence of delirium, suggesting that a large bacterial presence might itself contribute to the development of delirium.

The underlying mechanisms connecting higher bacterial counts to delirium remain speculative. The etiology of delirium is not fully understood, but recent studies suggest that factors such as drug toxicity, inflammation, and acute stress responses

can disrupt neurotransmission and contribute to delirium.^{23,24} Additionally, longer durations of mechanical ventilation and ICU stays have been associated with the development of delirium.^{19–22} Consequently, we considered VAP as a potential risk factor for delirium. Other research has shown that persistent intense thirst over 24 h increases delirium risk.²⁵ We evaluated the association between delirium and dry mouth scores, which were determined using oral moisture measurements. Our findings revealed no significant differences in oral moisture levels between patients with and without delirium. This lack of difference could be attributed to the generally high dry mouth scores observed in intubated patients, whose mouths remain open, potentially leading to an increased incidence of delirium among this group. It is also hypothesized that oral bacteria may pose a risk for various systemic diseases through translocation into the bloodstream and subsequent impacts on intestinal flora. In the present study, the only independent risk factor identified for delirium was the bacterial load on the tongue, reflecting typical oral bacterial counts. Future research should explore not only the quantity but also the species of oral bacteria that contribute to the development of delirium. Understanding the mechanisms through which these bacteria influence the onset of delirium is crucial for developing preventive strategies.

In conclusion, our study found that the quantity of bacteria on the tongue was associated with the incidence of VAP and delirium in ICU patients. These results suggest that improving oral assessment and care techniques in the ICU could lead to more effective strategies for managing and preventing these conditions.

Table 5. Odds Ratios for Delirium in Multivariate Logistic Regression Model. (n = 130).

	Delirium (n = 130)			
	Model 1 Adjusted OR (95% CI)	p value	Model 2 Adjusted OR (95% CI)	p value
Tongue bacteria count (CFU/mL) at ICU admission				
Low ($<1.0 \times 10^7$)	I			
Moderate ($1.0 \times 10^7 - 5.0 \times 10^7$)	2.46 (0.99–6.09)	0.052		
High ($\geq 5.0 \times 10^7$)	3.30 (1.04–10.44)	0.043		
Tongue bacteria count (CFU/mL) at 3 days after ICU admission				
Low ($<1.0 \times 10^7$)			I	
Moderate ($1.0 \times 10^7 - 5.0 \times 10^7$)			1.31 (0.56–3.07)	0.527
High ($\geq 5.0 \times 10^7$)			2.64 (0.80–8.74)	0.112
ICU length of stay	1.09 (1.02–1.14)	0.006	1.08 (1.02–1.14)	0.008
Sedative use				
No	I		I	
Yes	2.08 (0.53–8.20)	0.297	2.55 (0.66–9.86)	0.174

Logistic regression models: delirium was the dependent variable and associated factors were the independent variable.

Model included all covariates associated with the outcome in the crude model ($p < 0.05$).

OR, odds ratio; CI, confidence interval; ICU, intensive care unit; CFU, colony-forming units.

Conclusion

This study found a correlation between the presence of tongue bacteria and the incidence of VAP and delirium in ICU patients. These findings could inform the development of targeted oral assessment protocols and care strategies to effectively manage oral hygiene in ICU settings.

Limitations

This study had two main limitations. First, it was performed solely in a single ICU with a limited sample size. Second, based on best practice guidelines for the management of delirium, the selection and dosage of sedative and analgesic medications—particularly benzodiazepines, a recognized modifiable risk factor—might have significantly influenced the robustness of the data analysis. Although the bacterial species was not analyzed in this study, we believe that this will be necessary in the future. Our participants were a consecutive, term-limited sample in a single ICU, which may limit the generalizability of our results.

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Author Contributions

Conception and design: CA, TA, TJ, and AO; data analysis and interpretation: CA, TA, and MF; drafting the manuscript for intellectual content: CA, TA, TJ, and MF; revision of the manuscript: AO, and NW. All authors read and approved the final manuscript.

Availability of Date and Materials

All data generated or analysed during this study are included in this published article.

Consent for Publication

Not applicable.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethics Approval and Consent to Participate

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Committee of Kyushu University, Approval No. 22115-00. The institutional ethics committee at Kyushu University approved this study and waived the requirement for informed consent.

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Statement

Study participants or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Supplemental Material

Supplemental material for this article is available online.

References

- Papazian L, Klompas M, Luyt CE. Ventilator-associated pneumonia in adults: A narrative review. *Intensive Care Med.* 2020;46(5):888-906.
- Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med.* 2018;46(9):e825-e873.
- Modi AR, Kovacs CS. Hospital-acquired and ventilator-associated pneumonia: Diagnosis, management, and prevention. *Cleve Clin J Med.* 2020;87(10):633-639.
- Alecricum RX, Taminato M, Belasco A, et al. Strategies for preventing ventilator-associated pneumonia: An integrative review. *Rev Bras Enferm.* 2019;72(2):521-530.
- Paju S, Scannapieco FA. Oral biofilms, periodontitis, and pulmonary infections. *Oral Dis.* 2007;13(6):508-512.
- Raghavendran K, Mylotte JM, Scannapieco FA. Nursing home-associated pneumonia, hospital-acquired pneumonia and ventilator-associated pneumonia: The contribution of dental biofilms and periodontal inflammation. *Periodontol.* 2000;2007(44):164-177.
- Hellyer TP, Ewan V, Wilson P, et al. The Intensive Care Society recommended bundle of interventions for the prevention of ventilator-associated pneumonia. *J Intensive Care Soc.* 2016;17(3):238-243.
- Ansaloni L, Catena F, Chattat R, et al. Risk factors and incidence of postoperative delirium in elderly patients after elective and emergency surgery. *Br J Surg.* 2010;97(2):273-280.
- Roberts B, Rickard CM, Rajbhandari D, et al. Multicenter study of delirium in ICU patients using a simple screening tool. *Aust Crit Care.* 2005;18(1):6,8-9,11-4. doi:10.1016/S1036-7314(05)80019-0
- Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med.* 2013;41(1):263-306.
- Inouye SK. The dilemma of delirium: Clinical and research controversies regarding diagnosis and evaluation of delirium in hospitalized elderly medical patients. *Am J Med.* 1994;97(3):278-288.
- Chalmers JM, King PL, Spencer AJ, et al. The oral health assessment tool—validity and reliability. *Aust Dent J.* 2005;50(3):191-199.
- Fukushima Y, Yoda T, Araki R, et al. Evaluation of oral wetness using an improved moisture-checking device for the diagnosis of dry mouth. *Oral Sci Int.* 2017;14(2):33-36. https://doi.org/10.1016/S1348-8643(17)30017-4
- Hamada R, Suehiro J, Nakano M, et al. Development of rapid oral bacteria detection apparatus based on dielectrophoretic impedance measurement method. *IET Nanobiotechnol.* 2011;5(2):25-31.
- Kikutani T, Tamura F, Takahashi Y, et al. A novel rapid oral bacteria detection apparatus for effective oral care to prevent pneumonia. *Gerodontology.* 2012;29(2):e560-e565. doi:10.1111/j.1741-2358.2011.00517.x
- 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(5):309-332.
- Shi Q, Zhang B, Xing H, et al. Patients with chronic obstructive pulmonary disease suffer from worse periodontal health-evidence from a meta-analysis. *Front Physiol.* 2018;25(9):33. doi:10.3389/fphys.2018.00033
- Yuko I, Nomura Y, Takarada T, et al. Risk factors for postoperative pneumonia according to examination findings before surgery under general anesthesia. *Clin Ora Investing.* 2020;24(10):3577-3585. doi:10.1007/s00784-020-03230-7
- Lat I, McMillian W, Taylor S, et al. The impact of delirium on clinical outcomes in mechanically ventilated surgical and trauma patients. *Crit Care Med.* 2009;37(6):1898-1905.
- Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med.* 2004;32(4):955-962.
- Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: Systematic review and meta-analysis. *Br Med J.* 2015;350:h2538.
- Shamsizadeh M, Fathi Jouzdain A, Rahimi-Bashar F. Incidence and risk factors of ventilator-associated pneumonia among patients with delirium in the intensive care unit: A prospective observational study. *Crit Care Res Pract.* 2022;2022:4826933.
- Mayer EA, Padua D, Tillisch K. Altered brain-gut axis in autism: Comorbidity or causative mechanisms? *Bioassays.* 2014;36(10):933-939.
- Lee SP, Sung IK, Kim JH, et al. The effect of emotional stress and depression on the prevalence of digestive diseases. *J Neurogastroenterol Motil.* 2015;21(2):273-282.
- Sato K, Okajima M, Taniguchi T. Association of persistent intense thirst with delirium among critically ill patients: A cross-sectional study. *J Pain Symptom Manage.* 2019;57(6):1114-1120.