

## Factors associated with oral biofilm in ICU patients with infectious diseases

*Fatores associados à presença de biofilme oral em pacientes internados na UTI*

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### Resumo

**Introdução:** A hospitalização pode provocar deterioração da saúde bucal, repercutindo em todo o corpo. A UTI pode ser um ambiente favorável ao acúmulo de biofilme oral em pacientes críticos. **Objetivo:** Identificar fatores associados à presença do biofilme em pacientes da UTI de um hospital de doenças infectocontagiosas. **Método:** Estudo retrospectivo, descritivo e inferencial, com abordagem quantitativa. Os dados foram obtidos em prontuários de pacientes da UTI, de janeiro de 2012 a julho de 2015. O biofilme foi avaliado de acordo com o índice de Greene e Vermillion. Os fatores influentes foram analisados por regressão logística. **Resultado:** Entre os pacientes da UTI, 69,1% eram homens, 60,7% pacientes com AIDS, 66,3% pacientes na enfermaria, 50,6% intubados e 50,0% sedados. Seus elementos orais eram na maioria normais. As seguintes características foram significativamente associadas a biofilmes orais: alterações orais nos lábios, gengivas, bochechas e palatos e sangramento. Pacientes da enfermaria apresentaram menor risco de apresentar biofilmes. **Conclusão:** o aumento do acúmulo de biofilme oral foi observado em pacientes com alterações na boca e a procedência do paciente foi associada à presença de biofilme.

**Descritores:** Hospital; paciente; saúde bucal; manifestações orais; biofilme.

### Abstract

**Introduction:** Hospitalization may cause a decline in oral health and affect the entire body. The intensive care unit (ICU) may be a favorable environment for oral biofilm to accumulate in critically ill patients. **Objective:** To identify factors associated with oral biofilm in ICU patients in a hospital for infectious diseases. **Method:** This was a retrospective, descriptive and inferential study with a quantitative approach. Data were collected from 178 medical records of patients from January 2012 to July 2015. Biofilm presence was assessed according to the Greene and Vermillion index. Potential influential factors were analyzed by logistic regression. **Result:** Among ICU patients, 69.1% were men, 60.7% had acquired immune deficiency (AIDS), 66.3% were ward patients, 50.6% were intubated, and 50.0% were sedated. The oral elements of the patients were mostly normal. The following characteristics were significantly associated with oral biofilm: changes in the lips, gums, cheeks, and palates and bleeding. Patients from the ward had a lower risk of biofilm. **Conclusion:** Increased oral biofilm accumulation was observed in patients with oral changes, and patient origin was associated with the presence of biofilm.

**Descriptors:** Hospital; patient; oral health; oral manifestations; biofilm.

## INTRODUCTION

The intensive care unit (ICU) is the department where critically ill patients, who require specific care, are hospitalized and treated<sup>1</sup>. The need for ICU admission stems from hemodynamic instabilities that require intensive care, including the monitoring and continuous administration of medications<sup>2</sup>. In this environment, patients have a weakened health status with a risk of death, and integrated care from the entire team is required because these patients are usually unconscious due to ventilatory support or their existing health condition.

Studies show that hospitalization causes deterioration in oral health<sup>3,4</sup>, and in the ICU environment, this situation is worsened due to the poor health status of these patients, which triggers local and systemic complications. These individuals often remain open-mouthed due to orotracheal intubation, which leads to oral mucosa dehydration. Thus, the possibility of tongue biofilm increases, favoring the production of volatile sulfur components, including mercaptans and sulfhydryls, which have an unpleasant

odor<sup>4,5</sup>. Furthermore, the poor oral health status of critical patients produces signs and symptoms such as periodontitis, gingivitis, otitis, chronic nasopharyngitis and xerostomia, which enhance infection outbreaks favorable to nosocomial pneumonia<sup>4-6</sup>.

The presence of biofilm is one of the primary factors in the development of dental caries. Biofilm is an assemblage of microorganisms, including *Streptococcus* and *Lactobacillus sp.* bacteria, which are etiological agents of dental caries<sup>7</sup>. However, other pathogens are often present in biofilm and may constitute vehicles for the development of other systemic diseases. Indeed, previous studies have reported the presence of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumonia* and *Escherichia coli*, bacteria that are responsible for hospital-acquired infections and outbreaks, in oral biofilm of intubated patients<sup>8,9</sup>.

Each cubic millimeter of dental biofilm contains approximately 100 million microorganisms (bacteria, fungi and viruses), and biofilm may serve as a pathogen reservoir. These microorganisms may diffuse into the bloodstream and/or be present in the saliva and aspirates, causing infections in other sites<sup>9</sup>.

Thus, oral health affects general health, and changes in the oral cavity of in-hospital patients, especially ICU patients, have strongly adverse effects on the entire organism. Accordingly, critical patient care must be conducted in an integral manner, effectively contributing to the control of oral biofilm and thereby minimizing systemic effects.

Knowledge of general and oral health statuses is key for developing effective therapeutic approaches, and such information is necessary for reducing the risk of a worsening clinical condition of critical patients and for promoting their general well-being.

In view of the above considerations, the aim of the present study was to identify factors related to the presence of biofilm in ICU patients in an infectious disease hospital.

## METHOD

This is a retrospective, quantitative study. Records for all patients admitted to the ICU of a public infectious diseases reference hospital in the state of Paraíba from January 2012 to July 2015 were evaluated. This study was approved by the Research Ethics Committee of the State Secretariat of Health (Secretaria Estadual de Saúde) under number 42727415.1.0000.5186.

Data collection was performed from May to July 2015 at the Clementino Fraga Infectious Diseases Hospital (Hospital de Doenças Infectocontagiosas Clementino Fraga), which is located in the city of João Pessoa. This center is the reference hospital for infectious diseases in the state of Paraíba; it has a six-bed ICU and a multidisciplinary team. Data of interest were collected from the ICU Dentistry Admission Form included in the patient charts. Thus, patients without oral health data were excluded from the study. Oral components were examined by dentists and hospital intensivists during routine procedures, without prior calibration.

The biofilm measurement scale used in this study was the Greene and Vermillion index. With this scale, dental surfaces are evaluated in parts and classified using scores from 0 to 3, as

follows: 0, surface without dental plaque; 1, dental plaque covering less than 1/3 of the tooth surface per plaque; 2, from 1/3 to 2/3 of the tooth surface is covered by plaque; and 3, more than 2/3 of the tooth surface is covered by plaque<sup>10</sup>.

A total of 525 patients were admitted to the ICU from January 2012 to July 2015. Thirteen collected charts lacked records of oral health items, and the attending healthcare professionals explained that those patients were unable to undergo evaluation upon admission. A total of 195 charts lacked ICU Dentistry Admission forms, and the forms were incomplete in 83 charts; 56 readmissions were disregarded. Ultimately, only 178 charts were used for descriptive analysis.

Initially, independent variables were defined according to the items shown in the ICU Dentistry Admission form, which included the evaluation of the general and oral health status of each critical patient.

Univariate logistic regression was performed using R software version 3.2.1 for statistical analysis. Independent variables were categorized according to Table 1. There was a decision to standardize the presence of biofilm, which was termed outcome (Y), into the following categories: responses with scores of 2 and 3 represented the presence of biofilm (Y=1); scores of 0 (zero) and 1 (one) indicated the absence of biofilm (Y=0). It is noteworthy that only patients with teeth were included in the inferential analysis (n=158).

The odds ratios (ORs) and their respective confidence intervals (CIs) were calculated to examine risk factors, with a p-value  $\leq 0.05$  being considered significant.

**Table 1.** Characterization according to gender, disease upon admission, origin, neurological function and ventilation mode of ICU patients with infectious diseases. João Pessoa-PB, 2015

Variables	N	%
<b>Gender</b>		
Male	123	69.1
Female	55	30.9
<b>Disease on admission*</b>		
AIDS	108	60.7
Respiratory complication	104	58.4
Tuberculosis	66	37.1
Other diseases	42	23.6
Genitourinary complications	20	11.2
Sepsis	19	10.7
Cardiocirculatory complications	19	10.7
Diabetes mellitus	11	6.2
Hepatic complications	09	5.1
Hematologic complications	08	4.5
Leprosy	07	3.9
Cancer	06	3.4

**Table 1.** Continued...

Variables	N	%
Gastrointestinal complications	05	2.8
Metabolic complications	03	1.7
<b>Origin</b>		
Ward	118	66.3
Walk-in clinic	26	14.6
Another hospital	21	11.8
Emergency department	06	3.4
Urgent care	04	2.2
Home	01	0.6
Surgical ward	01	0.6
Other origin	01	0.6
<b>Neurological Function</b>		
Sedated	89	50.0
Oriented	33	18.5
Conscious	22	12.4
Disoriented	20	11.2
Lethargic	06	3.4
Agitated	03	1.7
Drowsy	03	1.7
Comatose	02	1.2
<b>Ventilation</b>		
Orotracheal tube	90	50.6
Venturi mask	32	18.0
Spontaneous breathing	25	14.0
Nasal catheter	13	7.3
Invasive mechanical ventilation	12	6.7
Non-invasive ventilation	05	2.8
Tracheostomy	01	0.6

\*Some patients had more than one disease, which explains why the sum of the disease frequencies exceeds 100%.

## RESULT

Table 1 outlines the characterization of patients who were admitted to the ICU within the study period (n=178), showing that most patients were males (69.1%) and that most were admitted to the ICU with AIDS (60.7%). Most patients were from the ward (66.3%) and were sedated (50.0%) and intubated with an oro-tracheal tube as their mode of ventilation (50.6%).

Table 2 outlines the data for patient oral health status. The results showed that all patients had mouth floors that fell within the normal standards, and the lips, tongues and gums appeared normal in 56.2% (n=100), 52.8% (n=94) and 85.4% (n=152), respectively. Gingival

**Table 2.** Oral health status of 178 ICU patients in an infectious diseases hospital in João Pessoa-PB, 2015

Variables	N	%
<b>Floor of the mouth</b>		
Normal	178	100.0
Altered	0	0.0
<b>Lips</b>		
Normal	100	56.2
Chapped	55	30.9
Wounded	23	12.9
<b>Tongue</b>		
Normal	94	52.8
Biofilm*	78	43.8
Wounded	06	3.4
<b>Gums</b>		
Normal	152	85.4
Hyperplastic	18	10.1
Gingivorrhagia	07	3.9
Wounded	01	0.6
<b>Bleeding</b>		
Presence of bleeding	32	18.0
Absence of bleeding	146	82.0
<b>Cheek</b>		
Normal	173	97.2
Wounded	05	2.8
<b>Palate</b>		
Normal	175	98.3
Wounded	03	1.7
<b>Dental condition</b>		
Toothed	158	88.8
Toothless	20	11.2
<b>Oral Hygiene</b>		
0.12% Chlorhexidine	175	98.3
Sodium bicarbonate	03	1.7

\*The Greene and Vermillion index was used to assess the degree of biofilm.

bleeding was absent in 82% (n=146) of the patients, and 97.2% (n=173) had healthy cheeks; 98.3% (n=175) had palates without alterations. A total of 88.8% (n=157) of inpatients were toothed, and 56.2% (n=100) exhibited the presence of moderate or severe biofilm. Oral hygiene with chlorhexidine 0.12% was performed for 98.3% (n=175) of the patients.

Significant variables for biofilm outcome were subsequently determined, considering a p-value  $\leq 0.05$  for classifying their

presence (Y=1) or absence (Y=0) (Tables 3 and 4). A total of 158 patients who met the inclusion criteria of this study were included in this analysis.

Oral changes in the lips, gums, cheeks, and palates and bleeding were associated with the occurrence of biofilm, with patients exhibiting such changes having a higher risk of biofilm occurrence. Conversely, when the variable "origin of the ICU patient" was assessed, patients from the ward showed decreased biofilm accumulation.

## DISCUSSION

Hospital dentistry is regarded as a practice that is designed to care for oral changes, and it is used to assist with inpatient care. Dental surgeons support the diagnosis of oral changes and indicate coadjuvant treatments, conducting either trauma care activities or preventive, curative and restorative actions with the goal of maintaining the balance of the oral environment and increasing patient comfort<sup>11</sup>.

In the present study, most ICU patients were males with AIDS. Overall, the prevalence of human immunodeficiency virus (HIV) is higher among the male population. Data from the 2013 Epidemiological Bulletin (Boletim Epidemiológico) indicate that the male population remains the most affected, with 445,197 infected men in Brazil<sup>12</sup>, and therefore this disease continues to be a relevant public health problem. These patients are usually already hospitalized at the institution, which is the reference hospital for treating infectious diseases. When their symptoms worsen, they are referred to the ICU, which is why most cases are derived from the ward. Studies show that HIV patients are hospitalized due to co-morbidities<sup>13,14</sup>. In fact, co-infections with hepatitis C virus are related to increased hospitalization and mortality rates. In American and Western European countries, 5-12% of ICU patients are HIV positive<sup>14</sup>.

Half of the ICU patients in this study were sedated and intubated. ICU patients commonly progress with a compromised clinical status, experiencing a decline in all systems and often requiring ventilatory support, which involves patient sedation to stabilize their health condition. The combined use of analgesics and sedatives in patients who are subjected to mechanical ventilation (MV) provides an even better adaptation to ventilation than the isolated use of sedatives due to their respiratory and cough-reflex-depressant effects as well as their hypnotic effects<sup>15</sup>.

Sedative drugs, along with analgesics, are administered to critically ill patients who are subjected to routine invasive MV<sup>16</sup>. One study reports that 39% of ICU patients require mechanical ventilatory support and that 10% of them require lengthened intubation time, and these patients are predisposed to complications related to the prolonged use of intubation and hospital stays<sup>17</sup>.

The oral health evaluation of the study patients revealed a prevalence of normal oral structures, with predominantly normal lips, tongues, gums, cheeks, mouth floors and palates (56.2%, 52.8%, 85.4%, 97.2%, 100%, and 98.3%, respectively). Other studies have reported that ICU patients have impaired oral hygiene and that hospitalization itself may compromise oral health<sup>3,4,6,18</sup>, in contrast to the findings of the present study.

**Table 3.** Univariate analysis of non-significant (n=158) variables of interest for the "presence of biofilm" outcome in ICU patients in an infectious diseases hospital

Variables	N	%	P-value
<b>Gender</b>			
Male	123	70.9	0.168
Female	55	29.1	
<b>Age (in years)</b>			
Mean	43.9		0.054
<b>Diseases on admission</b>			
AIDS	102	60.7	0.289
Respiratory complications	93	58.9	0.927
Tuberculosis	56	35.4	0.975
Other diseases	42	26.6	0.799
Genitourinary complications	16	10.1	0.127
Sepsis	18	11.4	0.376
Cardiocirculatory complications	19	10.1	0.106
Diabetes mellitus	09	5.7	0.076
Hepatic complications	09	5.1	0.452
Hematologic complications	08	5.1	0.984
Leprosy	06	3.7	0.836
Cancer	04	2.5	0.610
Gastrointestinal complications	05	3.2	0.429
Metabolic complications	03	1.3	0.988
<b>Origin</b>			
Ward	102	64.5	0.022*
Walk-in clinic	26	14.6	
Another hospital	20	12.6	
Emergency department	06	3.8	
Urgent care	03	2.5	
Home	01	0.6	
Surgical ward	01	0.6	
Other origin	01	0.6	
<b>Neurological Function</b>			
Sedated	80	50.6	0.785
Oriented	28	17.7	
Conscious	18	11.4	
Disoriented	19	12.0	
Lethargic	04	3.2	
Agitated	03	1.9	
Drowsy	03	1.9	
Comatose	01	0.6	

**Table 3.** Continued...

Variables	N	%	P-value
<b>Ventilation</b>			
Orotracheal tube	81	51.3	0.086
Venturi Mask	25	15.8	
Spontaneous breathing	23	14.6	
Nasal catheter	11	7.0	
Invasive mechanical ventilation	12	7.6	
Non-invasive ventilation	05	3.2	
Tracheostomy	01	0.6	
<b>Floor of the mouth</b>			
Normal	158	100.0	NA**
Altered	0	0.0	
<b>Lips</b>			
Normal	85	53.8	0.001*
Chapped	52	32.9	
Wounded	21	13.3	
<b>Tongue</b>			
Normal	83	52.5	0.517
Biofilm	69	43.7	
Wounded	06	3.8	
<b>Gums</b>			
Normal	132	83.5	0.014*
Hyperplastic	18	11.4	
Gingivorrhagia	07	4.4	
Wounded	01	0.6	
<b>Bleeding</b>			
Presence of bleeding	32	20.3	0.007*
Absence of bleeding	126	79.7	
<b>Cheek</b>			
Normal	153	96.8	0.005*
Wounded	05	3.2	
<b>Palate</b>			
Normal	156	98.7	0.002*
Wounded	02	1.3	
<b>Oral Hygiene</b>			
0.12% Chlorhexidine	155	98.1	0.885
Bicarbonate	03	1.9	

\*Significant at  $\alpha=5\%$  (p-value  $\leq 0.05$ ). \*\*Not applicable.

The normal condition of the oral cavity in most of this study's patients may be explained by the fact that during the data collection period, the ICU team at the Clementino Fraga Hospital included a

dental surgeon who routinely performed inpatient oral hygiene using 0.12% chlorhexidine solution. The inclusion of such a healthcare professional within the hospital setting improves the oral health care of inpatients<sup>5</sup> and may promote increased oral health quality among these individuals. Furthermore, 0.12% chlorhexidine is a compound that is used for chemical biofilm control, and it reduces oral pathogen colonization<sup>5,19</sup>.

Patient origin was associated with biofilm accumulation, and patients from the ward had a lower odds of developing biofilm. Most patients who were admitted to the ICU were from the ward (66.3%), and the Clementino Fraga Hospital includes dentistry services to provide oral healthcare to in- and outpatients. This care may have contributed to the minimization of biofilm formation.

Oral changes in the lips, gums, cheeks, and palates as well as gingival bleeding were associated with biofilm formation. Some oral problems caused by hospitalization have been reported in other studies, including bleeding and changes in the gums and saliva<sup>20,21</sup>. Furthermore, the presence of soft tissue lesions in the oral region may favor bacterial adhesion and proliferation, causing infections<sup>22</sup> and damaging other structures. This type of condition creates an environment that is conducive to the development of biofilms.

Changes in the lips, including chapping and wounds, were found to be predisposing factors in biofilm onset. This problem may result from mouth dryness. Decreased salivary flow causes oral mucosa dehydration<sup>22</sup> and therefore mucosal wounds; moreover, it allows for increased biofilm (a stagnant organic matrix) formation on the back of the tongue. ICU patients usually progress with a compromised clinical status, that is, changes in the immune system, exposure to invasive procedures and therapeutic dehydration (a common practice to increase respiratory and cardiac functions), thereby causing xerostomia (reduced salivary flow)<sup>7</sup>. In addition, hyposalivation may be caused by the use of some antidepressant medications, antihistamines and antihypertensives, among others<sup>22</sup>.

The prolonged use of an oro-tracheal tube may also cause lip dryness because the tube causes the oral cavity to be open for long periods. This open-mouth status reduces the buffering and cleaning effects of the saliva<sup>22</sup> and may also cause mucosal lesions. A previous study showed that the presence of an oro-tracheal tube leads to damage in the labial mucosa, affects salivary viscosity and causes abnormalities on the back of the tongue<sup>21</sup>.

Saliva has a key role in oral balance and is involved in preventing periodontal diseases, protecting the soft and hard tissues of the mouth and regulating the pH of the oral biofilm, among other functions<sup>23</sup>. Decreased saliva production may affect soft and hard tissues by impairing their protective function and causing dental caries<sup>23</sup>, the presence of which increases the accumulation of microorganisms through mechanical retention of oral biofilm.

Oral changes, including bleeding, are caused by certain diseases, and they may lead to deficient wound healing in oral tissues and increased sensitivity to the development of oral tissue injuries<sup>5</sup>, thus affecting biofilm formation. Oral bleeding is a problem that affects ICU patients<sup>21</sup>; gingival bleeding was also found in this previous study, corroborating the results of the present research.

**Table 4.** Univariate analysis of factors associated with the presence of oral biofilm in patients who were admitted to the ICU of an infectious diseases hospital (n=158)

Variables	n	%	P-value	ODDS	95% CI
<b>Origin</b>					
Ward	102	64.5	0.022*	0.82	0.69; 0.97
Walk-in clinic	26	14.6			
Another hospital	20	12.6			
Emergency department	06	3.8			
Urgent care	03	2.5			
Home	01	0.6			
Surgical ward	01	0.6			
Other origin	01	0.6			
<b>Lips</b>					
Normal	85	53.8	0.001*	2.46	1.60; 3.77
Chapped	52	32.9			
Wounded	21	13.3			
<b>Gums</b>					
Normal	132	83.5	0.014*	3.43	1.28; 9.21
Hyperplastic	18	11.4			
Gingivorrhagia	07	4.4			
Wounded	01	0.6			
<b>Bleeding</b>					
Presence of bleeding	32	20.3	0.007*	5.40	2.08; 14.02
Absence of bleeding	126	79.7			
<b>Cheek</b>					
Normal	153	96.8	0.005*	1.59	1.15; 2.21
Wounded	05	3.2			
<b>Palate</b>					
Normal	156	98.7	0.002*	1.64	1.19; 2.27
Wounded	02	1.3			

\*Significant at  $\alpha=5\%$  (p-value  $\leq 0.05$ ).

Biofilm formation in the oral cavity of critically ill patients may worsen their health status because a biofilm is considered a microbial reservoir that is associated with infections<sup>5</sup>. One study showed that intense biofilm accumulation occurred after 72 hours of hospitalization<sup>24</sup>. Oral bacteria may be transferred to the lower airways in patients fitted with orotracheal tubes and cause pneumonia associated with MV. This finding was reported in a study that identified the presence of *S. aureus* and *P. aeruginosa*, which are potential respiratory pathogens, in oral biofilm<sup>25</sup>.

The findings of this study are based on data that were collected from a sample in a single hospital, and their generalization should be interpreted with due caution. A factor that may have contributed

to the present findings was the recording of patient evaluation data only upon ICU admission, without recording or incompletely recording patient progression. The presence of incomplete inpatient charts may have affected the study by considerably decreasing the sample size and omitting data that could be relevant to the outcome. The difficulty involved in performing clinical examinations due to patient severity may also have affected the oral health evaluation.

Further studies should be conducted to help identify factors that trigger biofilm formation because these matrices may harbor microorganisms that are able to cause systemic infections, thereby worsening a patient's condition. Knowledge about this subject has become relevant and has contributed to the development of more efficient procedures for biofilm removal. This knowledge may

even prevent biofilm accumulation, thereby reducing the risk of nosocomial infection.

## CONCLUSION

The overall condition and use of invasive devices in ICU patients may favor the emergence of biofilm, and biofilm accumulation was more pronounced in patients with changes in the lips, gums,

cheeks, and palate and bleeding; however, individuals from the ward presented a lower risk of biofilm.

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## CONFLICTS OF INTERESTS

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The authors declare no conflicts of interest.

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