

# INFECTIVE ENDOCARDITIS BY AGGREGATIBACTER ACTINOMYCETEMCOMITANS IN PREDISPOSED PATIENTS

## ENDOCARDITE INFECCIOSA POR AGGREGATIBACTER ACTINOMYCETEMCOMITANS EM PACIENTES PREDISPOSTOS

### ABSTRACT

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Received on 08/17/2018,  
Accepted on 03/12/2019.

**Objective:** Infective endocarditis (IE) corresponds to a microbial infection of the endocardium with the presence of platelet and fibrin clotting in its interior. When it is of periodontal origin, *Aggregatibacter actinomycetemcomitans* (Aa) is the bacterium most often related to the occurrence of this disease. The presence of Aa in the gingivitis and periodontitis of hospitalized patients and its association with predisposition to IE were evaluated. **Methods:** Periodontal probing was performed in 15 patients with gingivitis and periodontitis, aged 18 and 75 years, of both genders, and considered at risk for IE at a hospital in Itajaí – SC. One tooth of each patient was used for the sample, which was collected in cones of sterilized paper, transferred in containers, and processed in the laboratory. The samples were homogenized and aliquots of 0.1 ml were seeded in duplicate in blood agar plates, incubated for five days in microaerophilya at 37°C. Following visualization of characteristic bacterial colonies, biochemical and catalase reaction tests were conducted. The diagnosis of IE was performed following the modified Duke criteria. **Conclusion:** There was no incidence of patients at risk of IE related to the presence of Aa in the participants evaluated.

**Keywords:** Periodontal Disease; Endocarditis; Microbiology.

### RESUMO

**Objetivo:** A endocardite infecciosa (EI) corresponde a uma infecção microbiana do endocárdio com presença de coágulo de plaquetas e fibrina em seu interior. Quando é de origem periodontal, a *Aggregatibacter actinomycetemcomitans* (Aa) é a bactéria mais relacionada com a ocorrência dessa doença. Foi avaliada a presença de Aa em gengivites e periodontites de pacientes hospitalizados e sua associação na predisposição à EI. **Métodos:** Realizou-se a sondagem periodontal em 15 pacientes de um hospital de Itajaí, SC com gengivites e periodontites, entre 18 a 75 anos de idade, de ambos os sexos, considerados em risco de EI. Usou-se um dente de cada paciente como amostra, coletado em cones de papel esterilizado, transferência em recipientes e processamento no laboratório. As amostras foram homogeneizadas e alíquotas de 0,1 ml foram semeadas em duplicata em placas de ágar sangue, incubadas por cinco dias em microaerofilia a 37 °C. Depois da visualização das colônias bacterianas características, foram realizadas provas bioquímicas e reação de catalase. O diagnóstico de EI foi realizado seguindo os critérios de Duke modificado. **Conclusão:** Não houve incidência de pacientes com risco de EI relacionada com presença da Aa nos participantes avaliados.

**Descritores:** Doença Periodontal; Endocardite; Microbiologia.

### INTRODUCTION

Infectious endocarditis (IE) is an inflammation of the endocardium, the innermost layer of the heart, and may be infectious when the causative agents are fungi, viruses or bacteria.<sup>1</sup> This disease begins with the deposition of platelets and fibrin in the endocardium, colonized by bacteria or other types of microorganisms.<sup>2</sup>

The bacteria most related to IE are viridans group Streptococcus, which are present in large quantities in the oral cavity and are more able to adhere to platelet aggregates.<sup>2</sup> However, according to Cangussu et al.,<sup>3</sup> when we verify periodontal microorganisms involved in the occurrence of IE, the most related bacterium is *Aggregatibacter actinomycetemcomitans* (Aa). This bacterium is a gram-negative, capnophilic,

carbohydrate-fermenting, non-spore-forming, immobile, and facultative anaerobic rod.<sup>4</sup> It is directly related to the occurrence of localized aggressive periodontitis, having virulence factors that make it a periodontopathogenic agent, associated to the occurrence of IE after invasive dental treatment.<sup>5</sup>

Thus, it can be determined that transient bacteremia caused by periodontal diseases, such as periodontitis in predisposed individuals, may influence the occurrence of heart disease, in this case the IE. Therefore, with the verification of the presence of Aa in hospitalized patients predisposed to IE, the perspective of an aid in an early diagnosis is pointed out.

This way, the study aimed to verify the presence of Aa in cases of periodontitis and gingivitis in patients hospitalized in an intensive care unit at risk for IE.

## METHODS

This work was characterized as a qualitative experimental study. Approved by the Research Ethics Committee with opinion under number 1.868.885 and without any conflicts of interest. The patients were informed and signed the informed consent form (ICF) and, in the impossibility, this consent was given by someone responsible.

To perform such work, a periodontal survey of 15 patients admitted to the Intensive Care Unit of a hospital in the city of Itajaí (SC) was performed.

Inclusion criteria were those with gingivitis and periodontitis between 18 and 75 years of age of both genders, whether smokers or non-smokers, immunodeficient, diabetic, with disease in native valves, patients with prosthetic valve or with some cardiovascular impairment, considered as patients at risk for IE.

The diagnosis of IE was made by the attending physician using the criteria of Duke according to Salgado, Lamas and Bóia,<sup>6</sup> according to Chart 1.

The exclusion criterion was given by those under 18 years of age.

It was considered as the basis for the diagnosis for periodontitis probing depth (Pd)  $\geq$  4mm and positive gingival bleeding index (GBI); and PD  $\leq$  3mm and positive GBI for gingivitis. Probing was performed by the buccal surface at only three sites of the dental element, due to the difficult access, namely the buccal, mesial and distal gingival sulcus, through the buccal surface.

The collection period took place between March and June 2017.

For microbiological analysis, the methodology was modified according to Cortelli, Cortelli and Jorge.<sup>7</sup> As an analysis sample, one tooth from each patient with clinical signs of gingivitis or periodontitis was selected. The material was collected using sterile paper cones that were inserted in the most apical portion of the gingival sulcus and kept for 15 seconds with the aid of sterile forceps. They were subsequently transferred to sterile screw tubes containing 1mL of sterile saline. These were transported to the Microbiology laboratory of the Health Sciences Center (CCS-UNIVALI) and further processed.

Samples were homogenized on a mechanical shaker (vortex) for one minute and 0.1mL portions of samples were seeded in duplicate with Drigalsky handles on blood agar plates and incubated for five days in microaerophilia at 37°C.

The bacterium was initially identified using a magnifying glass, through the visualization of its characteristic colonies, followed by biochemical tests of sugar fermentation and catalase reaction for samples that were positive for characteristic colonies.

## RESULTS AND DISCUSSION

Regarding the gateway to IE, authors<sup>13</sup> reiterate the link between periodontal disease and IE, stating that the second most frequent gateway to IE was oral and dental, with a more frequent dental infectious focus than a dental procedure, i.e., regardless of the procedure, the predisposed patient is already classified as at risk for IE, when in itself presents some type of oral infection, for example, a periodontitis.

Chart 1. Diagnosis of infectious endocarditis, modified Duke's criteria.

<b>Major criteria</b>
• Positive blood cultures:
• Typical organisms grown in two different blood cultures: <i>Viridans</i> group <i>streptococcus</i> , <i>S. aureus</i> , <i>HACEK</i> ( <i>Haemophilus</i> , <i>Actinobacillus</i> , <i>Cardiobacterium</i> , <i>Eikenella</i> , or <i>Kingella</i> ), or Community-acquired <i>Streptococcus bovis</i> from a primary source of infection.;
• Persistently positive blood cultures with other organisms: two positive blood cultures more than 12 hours apart; or positivity in all three or most of four, with an interval between the first and last collection greater than one hour; or
• Culture, molecular biology test or IgG serology phase 1 > 1: 800 for <i>Coxiella burnetii</i> ;
Evidence of endocardial involvement:
Echocardiogram showing oscillating intracardiac mass without further explanation or abscess, or new partial dehiscence of a prosthetic valve, or new valve regurgitation
<b>Minor criteria</b>
IE predisposition:
• Prior IE, injecting drug use, prosthetic heart valve, or cardiac injury causing turbulent blood flow.
Fever above 38°C.
Vascular phenomenon:
• Arterial embolism, pulmonary infarction, mycotic aneurysm, intracranial or conjunctival hemorrhage, or Janeway lesions.
• Immune phenomenon:
• Glomerulonephritis, Osler's nodules, Roth's spots, positive rheumatoid factor.

Microbiological findings that do not meet the larger criteria. Note: The diagnosis of IE requires two major criteria, or one major and three minor. It likely requires one major criterion and one minor criterion or three minor criteria.

Based on the results obtained, it was initially observed a considerable prevalence of compromised oral hygiene conditions in the participants involved in the work performed, associated with the incidence of gingivitis and periodontitis associated with the presence of bacteria.

Evidencing the result presented in graph 1, where the majority of cases of periodontal disease occurred in individuals in an adult to elderly age group (31 years to over 70 years), it can be determined that the non-occurrence of the bacteria is due to the analysis more frequently occurred in adult individuals, and only one of the participants was within the juvenile age group. According to Cortelli, Cortelli and Jorge<sup>7</sup>, the presence of Aa bacteria is more frequent in young individuals with periodontal disease, localized aggressive periodontitis, and may vary from 40% to 100%.

Of the sample, 15 in all, associated with the predisposition of Infectious Endocarditis (IE), these were predisposed due to symptoms and causes associated with the pathologies, especially the cardiac ones present in intensive care unit (ICU) patients, because according to Rossini.<sup>10</sup> IE is not a disease that follows a pathognomonic pattern, and has different forms, varying according to the first clinical signs, the type of cardiac dysfunction, microorganism involved, presence or absence of complications, as well as patient characteristics. Because of this, access to reliable epidemiological data is difficult to find. The clinical picture of IE is very variable, ranging from severe sepsis and acute heart failure, to more severe cases of fever of obscure origin, as in the case of subacute endocarditis.

According to the 15 predisposed patients, 14 of them were diagnosed with periodontitis and one case of gingivitis (Table 1). The sample consisted of four women and 11 men, all of whom presented periodontitis, thus represented by 11 of 14 cases of periodontitis. (Figure 1) This result is consistent with numerous studies confirming that periodontal disease, such as periodontitis, is more frequent in men than in women.<sup>8</sup>

Regarding age, there is a prevalence of IE in elderly patients.<sup>9</sup> This statement is in agreement with Rossini,<sup>10</sup> who regarding the epidemiological profile, the incidence of IE increased considerably in the elderly. These observations are in line with the results presented in Figure 1, with 60% of the sample being patients over 51 years old. Thus, it is perceived the need to investigate lifestyle and medical history of patients by health professionals, in order to enable better forms of intervention and prevention for this population.<sup>9</sup>

According to Table 1, it was observed that of the 15 participants, most of them, around 93.33% presented periodontitis condition. According to Gomes and Esteves,<sup>11</sup> the presence of bacterial plaque in the mouth may generally influence medical therapies, which may be aggravated by the presence of periodontal disease. This result is in agreement with another study,<sup>12</sup> which comments on the link between periodontitis and cardiovascular disease.

Nicolosi<sup>14</sup> states in his study that the lack of studies on IE is very evident, due clearly to the difficulties in performing them, since the incidence of IE is low, as seen in this paper, thus, for a statistically more significant result it requires a sample with a large number of patients.

Aa, among the various IE-causing bacteria, is the periodontal microorganism, most frequently associated with the occurrence of this pathology.<sup>3</sup> Localized aggressive periodontitis is the form of periodontal disease most associated

Table 1. Dental elements examined, probing depth and gingival bleeding index for diagnosis.

Patient	Tooth	PD (mm)			GBI	Diagnosis
		V	D	M		
P1	43	3	5	4	+	Periodontitis
P2	14	4	4	5	+	Periodontitis
P3	12	4	5	7	+	Periodontitis
P4	41	6	3	3	+	Periodontitis
P5	44	3	5	4	+	Periodontitis
P6	35	2	6	2	+	Periodontitis
P7	12	7	4	3	+	Periodontitis
P8	43	5	6	3	+	Periodontitis
P9	33	6	2	3	+	Periodontitis
P10	43	5	6	3	+	Periodontitis
P11	33	2	4	3	+	Periodontitis
P12	34	2	5	3	+	Periodontitis
P13	44	2	4	7	+	Periodontitis
P14	44	2	4	3	+	Periodontitis
P15	41	2	2	2	+	Gingivitis

PS - probing depth; GSI - gingival bleeding index; V - vestibular face; D - distal face; M - mesial face. Source: Work data.

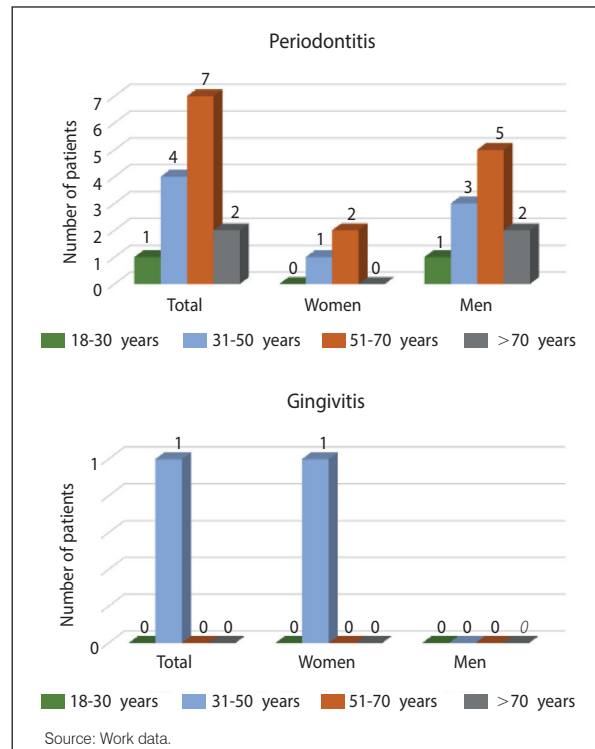


Figure 1. Gingivitis and Periodontitis diagnosis by average age and gender.

with the presence of this pathogen.<sup>7</sup> Still in relation to Aa, it was observed in the sample population that the presence of this pathogen was not conclusively evidenced by laboratory microbiological analysis. According to the results presented in Table 2, initially some samples submitted to the first stage of analysis to visualize characteristic bacterial colonies were positive, but following identification with the use of biochemical tests, these did not confirm positivity for the bacterium under analysis. The result is consistent with the negativity of the presence of the bacteria analyzed in the study by Costa et al.<sup>15</sup> that in the case of IE, the most commonly isolated microorganisms were *Streptococcus viridans* and *Staphylococcus*

*aureus*, also with Nicolossi<sup>13</sup>, who correlates IE with bacteremia caused by the *Streptococcus viridans* group. This result is also in agreement with Cortelli, Cortelli and Jorge,<sup>7</sup> showing the association between localized aggressive periodontitis and Aa, justifying the negativity of the sample, which did not present any patient with this diagnosis.

According to Figure 2, it is seen that of the participants evaluated, 15 in total, 10 had associated heart disease, and

Table 2. Plates with characteristic bacterial colony per patient, biochemical evidence and presence of *Aggregatibacter actinomycetemcomitans* (Aa).

Patient	Plates with characteristic bacterial colony	Biochemical Tests and Aa Identification
P1	No	
P2	No	
P3	Yes	Negative
P4	No	
P5	Yes	Negative
P6	No	
P7	No	
P8	Yes	Negative
P9	No	
P10	No	
P11	Yes	Negative
P12	No	
P13	No	
P14	Yes	Negative
P15	No	

Source: Work data.

of these, three patients had the diagnosis of IE, diagnosed by the attending physician using the modified Duke criteria<sup>6</sup> and identified with this diagnosis through the medical records, the other seven patients had other types of diseases that involved some cardiac involvement. The IE picture corresponded to 30% of the sample of patients in the cardiac ICU group. It is noteworthy that another study<sup>16</sup> pointed out that the incidence of IE is more prevalent in men, meeting the findings of this study, because of the three patients with IE, two were male, so men continue to be the most affected.

IE is initiated by the deposition of platelets and fibrins in the endocardium, colonized by bacteria or other types of microorganisms.<sup>2</sup> This is due to transient bacteremia,<sup>1</sup> reaching the heart and colonizing damaged or abnormal tissues, valves such as the endocardium, endothelium, pericardium, close to anatomical defects.<sup>17</sup> Studies<sup>9</sup> have confirmed this with regard to predisposition, showing that endocarditis is diagnosed in immunodeficient patients with degenerative changes of the left heart valves, hemodialysis patients, diabetics or drug users. Thus, it can be noted in Figure 2 that the individuals in the sample who underwent myocardial revascularization, pericardial drainage, carotid TCA, aortic dissection, acute myocardial infarction, the two diabetes patients and the two carriers of HIV +. as predisposed there is occurrence of IE.

Hospital dentistry can be defined as a practice aimed at the care of oral alterations that require procedures of high complexity multidisciplinary teams to the patient.<sup>11</sup> It is of great importance for the dental surgeon in the hospital environment,

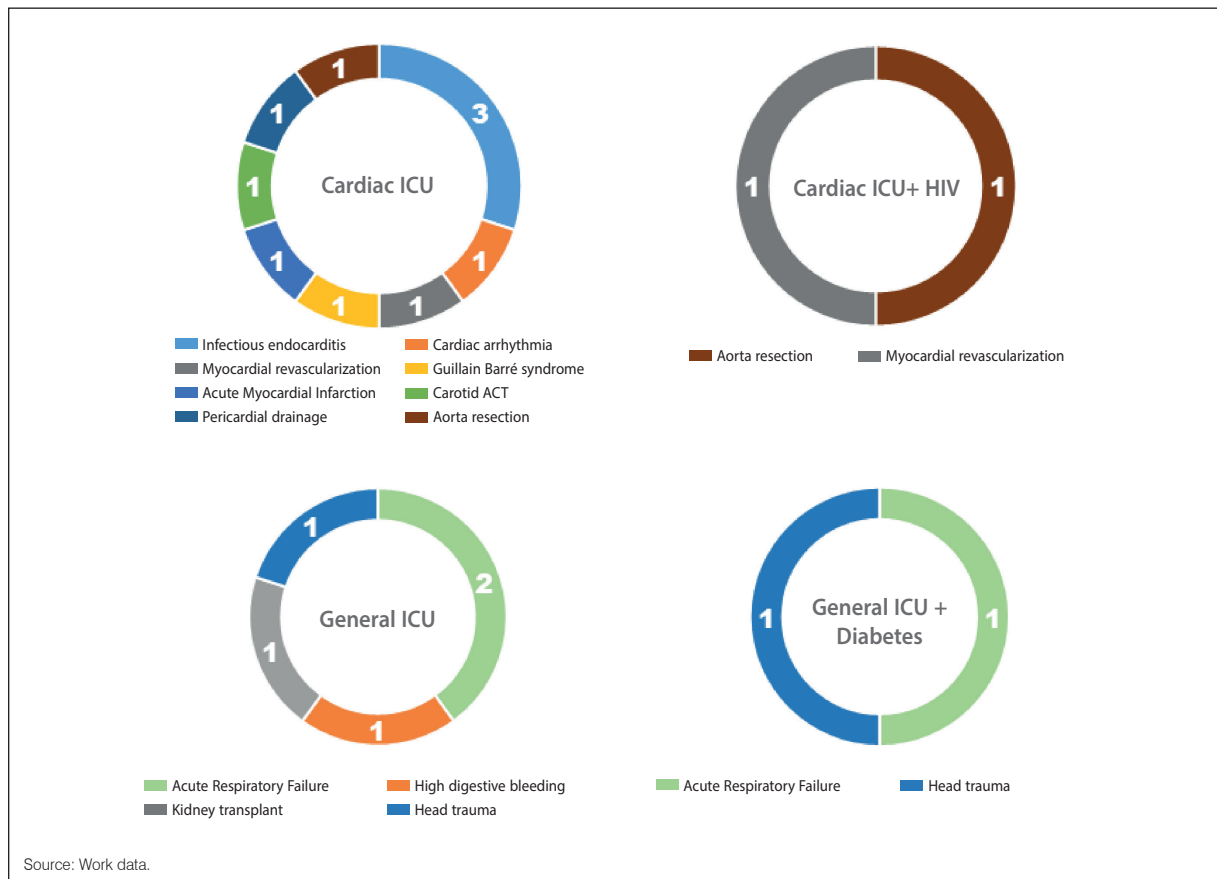


Figure 2. Pathologies found in the participants examined, divided into two groups by their respective Intensive Care Units (ICU) and associated cause.

to guide the patient with cardiac risk regarding oral hygiene habits and disease prevention, as the presence of some oral diseases, such as periodontal disease, may increase the risk of bacteremia associated with the patient's daily habits, such as brushing, flossing and chewing, reaffirming what has been commented on previously.<sup>2</sup>

Aiming at the sample population of this research, the role of the dentist in the hospital environment is extremely important, considering that the sample was 100% inserted in the Intensive Care Units (ICU) and that the clinical situation of oral hygiene was very compromised, with presence of periodontal disease in all. Authors<sup>11</sup> reported this importance due to the fact that, in the ICU, the patient is more exposed to the risk of infection, with a five to 10-fold increase in chances, further reinforcing the presence of this professional within the hospital. It is noteworthy that in the ICUs where the samples were collected, there was no dentist, thus reinforcing the real need for this professional in the hospital environment, reiterating the importance of hospital dentistry in Brazil.

## CONCLUSION

Infectious Endocarditis (IE) was evidenced against other cardiac pathologies in the sample population. There was no

incidence of IE related to the presence of *Aggregatibacter actinomycetemcomitans* in the participants evaluated in the sample, indicating that a more accurate estimate suggests that a larger number of participants and a longer evaluation period is needed.

## ACKNOWLEDGEMENTS

To Tatiana Bender Schmeling for her contribution to microbiological analysis.

To Ana Angélica Steil and Sônia Mezadri, for the authorization and help in their respective research laboratories in which they are responsible.

To the technical director of Hospital e Maternidade Marieta Konder Bornhausen, Dr. Lily Eing and the general director, Sister Mércia Lemes, for authorizing the collection in Intensive Care Units.

## CONFLICTS OF INTEREST

The author declares that he has no conflicts of interest in this work.

**AUTHORS' CONTRIBUTIONS:** Each author contributed individually and significantly to the development of the manuscript. JS, CYF, BHES and TBS were the main contributors in the writing of the manuscript. JS and TBS collected material from patients admitted to the Intensive Care Unit of the participating hospital. JS, CYF, TBS were the main performers of sample processing in the experimental part. JS, CYF, BHES and MMAGF contributed to the intellectual concept of the study. JS, CYF, BHES performed the analysis of the results. JS, CYF and BHES evaluated the data of the statistical analysis. JS, CYF, BHES and MMAGF performed the literature search, manuscript revision.

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