

## *Presence of Civatte Bodies in an oral lichen planus incisional biopsy sample*

## *Presença de corpos de Civatte em uma amostra de biópsia incisional de líquen plano oral*

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### ABSTRACT

**Objective:** Civatte bodies are colloid bodies of apoptotic keratinocytes located at the dermoepidermal junction and are common in several dermatoses, including lichen planus lesions. The present study aimed to determine the presence of Civatte bodies in a sample of incisional biopsies obtained from patients diagnosed with oral lichen planus. **Methods:** A retrospective cross-sectional study, carried out with 34 slides stained with hematoxylin-eosin from the archive of an Oral Pathology Laboratory of a Higher Education Institution. The sample obtained was classified into white and red lesions from the available clinical data. Histological analyses were performed under a light microscope, with 10x and 40x objectives, identifying the presence or absence of Civatte bodies. **Results:** Colloid bodies were present in 73.5% the total sample studied and in 74.2% white lesions. **Conclusion:** The Civatte bodies were frequent in all samples analysed and should thus be considered a criterion for histological diagnosis in lesions of Oral Lichen Planus.

**Indexing terms:** Apoptosis. Epithelium. Morphological and microscopic findings. Oral lichen planus.

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## RESUMO

**Objetivo:** *Corpos de Civatte são corpos coloidais de queratinócitos apoptóticos localizados na junção dermoepidérmica e que são frequentes em várias dermatoses, inclusive as lesões de líquen plano. O objetivo do presente trabalho foi determinar a presença de corpos de Civatte em uma amostra de biópsias incisoriais obtidas a partir de pacientes com diagnóstico de líquen plano oral (LPO). Métodos:* *Tratou-se de um estudo transversal retrospectivo, realizado com 34 casos cujas lâminas foram coradas pela hematoxilina-eosina, pertencentes ao arquivo de um Laboratório de Patologia Oral de Instituição de Ensino Superior. A amostra obtida foi classificada em lesões brancas e vermelhas a partir dos dados clínicos disponíveis. As análises histológicas foram realizadas em microscópio de luz, nas objetivas de 10x e 40x, com identificação dos corpos de Civatte como presentes ou ausentes. Resultados:* *Os corpos colóides estavam presentes em 73,5% da amostra total estudada e em 74,2% das lesões brancas. Conclusão:* *Os corpos de Civatte foram frequentes em todas as amostras analisadas e não devem ser negligenciados como critério de diagnóstico histopatológico em lesões de LPO.*

**Termos de indexação:** *Apoptose. Epitélio. Achados morfológicos e microscópicos. Líquen plano bucal.*

## INTRODUCTION

Lichen planus (LP) is a mucocutaneous inflammatory disease that can affect skin, nails, hair, and mucous surfaces, and the most affected regions are the oral, genital, and ocular regions. This condition prevails in between 0.1% and 5% the general population worldwide and it has a 2.2% incidence [1]. It usually occurs in women, in their forties and fifties [2] and rarely affects children [1].

LP is one of the dermatological diseases that most affect the oral mucosa and, in this case, may be the only clinical manifestation of the disease, characterised by of symmetrical and bilateral lesions, with an aspect of whitish tracery, characterising the stretch marks of Wickham. These consist of an essential diagnostic element of oral lichen planus (OLP), even if the lesion presents a pattern from another clinical subtype [3]. Such condition has varied clinical presentations that are classified as white lesions (reticular, papular, and plaque-like) and red lesions (erosive, atrophic, and bullous) [4].

Since 1978, the World Health Organization [5] (WHO) describes histopathological characteristics of the LP lesions, such as the presence of an ortho or parakeratinised layer, accompanied by a subepithelial band of inflammatory infiltration, consisting mainly of lymphocytes, with signs of degeneration of the basal layer and Civatte bodies [5].

Civatte bodies were first described by Raymond Sabouraud in 1912 and are colloid bodies of apoptotic keratinocytes [6]. These microscopic structures are usually found at the dermoepidermal junction and are characteristic of many dermatoses, such as lupus erythematosus, dermatomyositis, graft-versus-host-disease, erythema multiforme, pityriasis lichenoides, but they are more commonly found in lichen planus lesions [7].

The pathogenesis of the disease is not yet fully understood, and is considered an immunologically mediated condition, in which specific mechanisms occur, such as the presentation of antigens by the basal keratinocytes, activation of CD4+ T helper cells and the release of cytokines, which results in a cytotoxic reaction against the basal layer of epidermal cells. Also, non-specific mechanisms, such as mast cell degranulation and activation of metalloproteinases-1, result in an even higher accumulation of T cells, rupture of the basal layer, which consequently causes keratinocyte apoptosis, generating Civatte bodies [8].

Keratinocytes are able to synthesize and deposit the underlying extracellular matrix in a polarized fashion, including all the main components of the dermal-epidermal membrane [9]. Apoptotic keratinocytes, on the other hand, cannot perform this function, thus they are unable to repair the rupture that occurred in the basal layer, which may explain the chronicity of LP lesions and the difficulty in their therapeutic management [10].

This present work is relevant to identify the frequency of these keratinocytes (Civatte bodies), which have undergone apoptosis and contribute to the progressive degeneration of the basal layer, as depending on how often these bodies appear in LP lesions, the chronic nature of the disease could be at least partially justified.

This study aimed to determine the presence of Civatte bodies in a sample of incisional biopsies obtained from patients diagnosed with OLP.

## METHODS

This was a retrospective cross-sectional study, carried out using slides from the Laboratory of Oral Pathology archive.

The sample included histological slides obtained from incisional biopsies of patients from the Oral Injury Reference Centre: State University of Feira de Santana, Bahia who had a suggestive diagnosis of OLP confirmed by histopathological examination. Slides whose patients had a histopathological diagnosis of lichenoid reactions were excluded; patients without a final and/or suggestive diagnosis of epithelial dysplasia, cancer or other lesions that influence the OLP diagnosis, as well as those whose slides did not show conditions of reassessment, for example, because of the presence of fungi, were also excluded.

Out of the 43 cases in the file, from 2005 to 2019, 34 were suitable for morphological and descriptive analysis and were included in the study. Such analyses were performed after capturing the images under a light microscope. The 10x objective lenses were used to search for Civatte bodies and, after finding them, the 40x objective lenses were used, assessing the presence or absence of the bodies. This study carried out histological assessment of slides at the Oral Biochemistry Laboratory: Federal University of Bahia, Bahia.

Histological reports of the patients found at the Oral Injury Reference Centre provided data such as gender, age, and clinical subtypes of the lesions. The data were presented as descriptive statistics with means and percentages. Noteworthy, a single researcher previously calibrated to identify Civatte bodies carried out the assessment.

The research, in compliance with CNS Resolution 466/12, was approved by the Human Research Ethics Committee with number of opinions 2.659.387 and 3.189.846.

## RESULTS

From the 34 cases included in the sample, 79.42% were women, with more occurrences with women aged 51 or over (44.20%) (table 1).

Civatte bodies were present in 73.5% cases in the sample, and table 2 shows their distribution between white and red lesions.

**Table 1.** Frequency (n) and percentage (%) of socio-demographic characteristics of individuals with OLP, in the period 2005-2019.

Variables	n	%
<b>Age (n=34)</b>		
20 to 30 years old	2	5.90
31 to 40 years old	8	23.40
41 to 50 years old	9	26.50
51 years old or over	15	44.20
<b>Gender (n=34)</b>		
Male	7	20.58
Female	27	79.40
<b>Clinical type (n=34)</b>		
Reticular	28	82.36
Erosive	3	8.82
Plaque-like	3	8.82

Note: Oral Injury Reference Centre (2005-2019).

**Table 2.** Frequency (n) and percentage (%) of injuries as to the presence and absence of Civatte bodies in incisional biopsies of patients with OLP, in the period 2005-2019.

Clinical aspect of the lesions	Civatte bodies			
	Presence		Absence	
	n	%	n	%
White (n = 31)	23	74.20	8	25.80
Red (n=3)	2	66.70	1	33.30
Total (n=34)	25	73.5	09	26.5

Note: Oral Injury Reference Centre (2005-2019).

## DISCUSSION

Since 1978, WHO [5] has classified Civatte bodies as a histological feature of OLP injuries. van der Meij et al. [11] proposed to change the classification established by the WHO and stated that the presence of the subepithelial inflammatory band, composed of T lymphocytes, and the vacuolar alteration of the basal layer are still recognised as resources for the OLP diagnosis, while the presence of Civatte bodies was characterised as nonspecific for these lesions, since these histological structures are detected in many dermatoses, such as lupus erythematosus, dermatomyositis, graft-versus-host-disease, erythema multiforme, and lichenoid pityriasis. This study showed the high frequency of Civatte bodies regardless of the clinical subtypes of OLP, suggesting that the presence of these structures may be a relevant criterion for the histopathological diagnosis of such lesions, associated with the presence of other well-established criteria [11].

In 2014, Rad et al. [12] compared the correlation between the clinical and histopathological diagnoses of OLP with the Who criteria [5] and the WHO criteria modified by van Der Meij et al. [11]. In the latter, the presence of a zone in a well-defined inflammatory infiltrate band, formed by lymphocytes, and the absence of epithelial dysplasia were considered histological characteristics of LP lesions. The authors found greater disagreement among researchers when the WHO criteria were used, which was attributed to subjectivity in the histological interpretation of such findings [12]. Likewise, Cheng et al. [13] did not consider the presence of Civatte bodies nor the presence of an ortho or parakeratin layer as a histological diagnostic criterion for OLP in the studied slides. In such classification criteria and histopathological diagnosis for LP, Civatte bodies were not included or considered relevant. However, the high number of cases in this study in which such structures were found suggests the relevance of including this parameter in the assessments, as well as indicated by WHO in its diagnostic criteria, which shall be considered important and relevant for a final diagnosis [5].

Carvalho et al. [14] found that from the 10,292 cases in the period of 1988 and 2009, 82 (0.8%) cases corresponded to dermatological diseases immunologically mediated with manifestation in the oral cavity. Of these, 54 cases were OLP (65.8%), which were more frequent between the fifth and sixth decades of women's life. However, this study showed a higher frequency when adding the values found between the fourth and fifth decades of women's life [14]. These data are in accordance with the findings in the study by Navas-Alfaro et al. [15], who conducted a study with 59 biopsies of patients with LP or OLP and found a predominance in women in their forties and fifties. The authors observed the constant presence of Civatte bodies in 71% sample, but always discreetly. Similarly, this study could observe the high frequency of such a diagnostic criterion, as in 73.5% cases they were present in the analysed slides.

López-Jornet et al. [16] analysed histological and histomorphometric characteristics in OLP lesions, aiming at better qualifying and quantifying the results found, since histomorphometry provides better objectivity, reproducibility, and the possibility of comparing the results. These authors analysed 100 biopsied cases of OLP and concluded that Civatte bodies were present in 35% of these [16]. However, the value of such a finding may be because apoptotic cells occur and disappear in less than 24 hours [17], as well as because histological analysis is performed in two dimensions, which disfavours a careful observation of such histological findings. Furthermore, proportionally, the authors observed

a higher frequency of the presence of such histological structures in the group of red lesions (erosive, atrophic, and bullous). Although the percentage of presence of Civatte bodies is different between this study and the study by the aforementioned authors, the latter demonstrated a balanced proportion between clinical subtypes, which resulted in a more reliable correlation between the presence of such colloid bodies and the red lesions, which are symptomatic and have a greater potential for malignancy. This study could not perform a correlation between the frequency of Civatte bodies and the clinical subtypes of OLP lesions, as the sample assessed showed a high predominance of white lesions, mainly in the reticular form.

Bascones et al. [18] investigated the influence of apoptosis and cell cycle disruption mechanisms on the potential for malignancy in OLP and concluded that the number of epithelial cells that underwent apoptosis is relatively low in these lesions, and they are more commonly found in the basal layer than in other layers of the epithelial tissue. With the apoptosis of such cells, the mechanisms of the cell cycle change, which may favour a greater potential for malignancy. These authors found that Civatte bodies were present in 93.7% the cases studied and were discreet in 46.6% of the sample [18]. This study analysed the presence or absence of this diagnostic criterion and found that they were present in 74.2% the cases of white lesions, which confirms the importance of preserving the patient, due to the chronicity of such injuries. However, studies with more accurate methods, such as immunohistochemistry and histomorphometry, are necessary for more specific results when quantifying the presence of colloid bodies.

Thus, the presence of Civatte bodies should be considered a relevant criterion in the diagnosis of LP injuries, and more specifically of OLP, as it seems to be related to the chronic nature of these injuries. This is because the basal layer liquefaction progressively stimulates the death of keratinocytes [19], making tissue repair unfeasible, which seems to make the treatment not as effective in LP injuries.

This study had some limitations, such as the low-numbered sample, although it comprises the entire sample available from the last 14 years of the Oral Pathology Laboratory. Furthermore, the disparity in the clinical subtypes of the analysed sample, concerning white and red lesions, hinders a deeper analysis on the presence of these structures, interfering in the severity of the lesions. The subjectivity of an assessment made by a single observer, although trained for such an analysis, shall also be considered.

However, this study brings a high percentage of Civatte bodies in the analysed sample, confirming that the histological finding should be accounted as a diagnostic criterion, thus following what WHO [5] suggested in the first official classification of LP. Its presence should be related to the chronicity of these lesions and, therefore, it can provide a better management of affected patients.

## **CONCLUSION**

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Finally, Civatte bodies were frequent in the analysed sample and can be considered a relevant histological diagnosis criterion in OLP lesions.

## **Collaborators**

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ACB Sanches, GB Martins, VS Freitas, ALPV Pires contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. BA Frota and HRS Della Cella performed the research data collection. TCF Ramos and MC Oliveira performed the analysis and reviewed the manuscript. All authors discussed the results and approved the final version of the study.

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