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A multicentre study of oral paracoccidioidomycosis: Analysis of 320 cases and literature review

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Abstract

Objectives: To investigate the frequency of oral paracoccidioidomycosis from representative geographical regions of Brazil and to compare the data with a literature review.

Materials and methods: A retrospective study was conducted on 108,304 biopsies obtained from 1953 to 2016 at six Brazilian oral and maxillofacial pathology services. Demographic data and clinical and histopathological diagnosis of oral paracoccidioidomycosis were evaluated. A literature review of oral paracoccidioidomycosis studies published in three electronic databases was carried out. Data were analysed descriptively.

Results: A total of 320 cases of oral paracoccidioidomycosis were surveyed (0.3% of the oral lesions at the centres studied). The lesions were more frequent among male patients. The gingiva/alveolar ridge was the most affected site. Mean age of affected individuals was 51.3 years (±11.7). The literature review showed a higher incidence of oral paracoccidioidomycosis in the south-east and south regions of Brazil. Male individuals and individuals between 50 and 59 years were most affected.

Conclusions: Oral paracoccidioidomycosis is an uncommon lesion observed in oral biopsy samples. The differences in the relative frequency of oral paracoccidioidomycosis are related to geographical variations. Men between 50 and 59 years are more affected. This study provides helpful information for clinicians in the diagnosis of oral paracoccidioidomycosis.

KEYWORDS
diagnosis, epidemiology, fungal diseases, mycosis, paracoccidioides, paracoccidioidomycosis

1 | INTRODUCTION

More than 1.6 million people are estimated to die of fungal diseases worldwide each year, and about one billion people have cutaneous fungal infections (Cole, Govender, Chakrabarti, Sacarlal, & Denning, 2017). These lesions are on the list of neglected diseases in tropical and subtropical areas worldwide (Queiroz-Telles et al., 2017; WHO Department of Control of Neglected Tropical Diseases, 2013). Paracoccidioidomycosis (PCM) is a granulomatous infectious disease caused by the inhalation of the dimorphic fungus *Paracoccidioides brasiliensis* (Girardi & Scrofernecker, 2016; Meneses-García, Mosqueda-Taylor, Morales-de la Luz, & Rivera, 2002). Although a rare disorder from a global perspective, in Latin America PCM is the most prevalent endemic mycosis, followed by histoplasmosis (Queiroz-Telles et al., 2017). Currently, it is estimated that 10 million Latin Americans are infected with *P. brasiliensis*, and the incidence in Brazil is close 1 to 3.7 cases per 100,000 annually (Colombo, Tobón, Restrepo, Queiroz-Telles, & Nucci, 2011; Life International Fungal Education (LIFE), 2017; Queiroz-Telles et al., 2017). In an epidemiological study based on the Brazilian governmental database for a 10-year period, PCM was the major cause of death attributed to systemic mycoses (Prado, Silva, Laurenti, Travassos, & Taborda, 2009).

Soil is the main natural source of infectious conidia, and people living in rural areas represent a risk group for PCM (Queiroz-Telles et al., 2017). Recently, an outbreak of PCM has been reported in a Brazilian region, where deforestation and massive earth removal took place (Valle et al., 2017). According to the incubation period and the characteristics of the affected individuals, there are two clinical forms of PCM, that is acute/subacute and chronic (López-Martínez et al., 2014; Trindade et al., 2017). The chronic form (adult type) accounts for approximately 80% of PCM cases, mostly among rural male workers. The acute/subacute (juvenile type) form usually affects individuals up to 30 years of age of both genders (Coimbra Júnior et al., 1994; Meneses-García et al., 2002; Queiroz-Telles et al., 2017).

The diagnosis of PCM is based on the detection of fungal elements of *P. brasiliensis* by histopathological examination of specimens stained with haematoxylin–eosin (H&E; López-Martínez et al., 2014). Periodic acid–schiff (PAS) and Grocott–Gomori staining are also helpful staining techniques (Azenha, Caliento, Brentegani, & Lacerda, 2012; Girardi & Scrofernecker, 2016). The oropharynx may be the first anatomical site of manifestation, and lesions at this site are fairly common (Oliveira, Mariano, Santos Silva, Vargas, & Lopes, 2012). The classical clinical presentations are granular, erythematous or ulcerated lesions surrounded by jagged edges with a thin haemorrhagic dotted edge (Trindade et al., 2017). The oral cavity may be affected at one or multiple sites, with the gingiva and palate being the most prevalent sites (Oliveira et al., 2012; Webber, Martins, Oliveira, Munhoz, & Carrard, 2014).

The incidence of oral PCM lesions requires attention in terms of public health policies for diagnosis and treatment. Epidemiological studies based on oral and maxillofacial biopsies obtained at specialized services provide more accurate data for these goals (Bicalho, Santo, Aguiar, & Santos, 2001; Colombo et al., 2011; Sposto et al., 1993). Considering the importance of oral PCM for public health, the objective of the present multicentre study was to determine the frequency of oral PMC in a Brazilian population from four representative geographical areas. To the best of our knowledge, this is the first and the largest multicentre study reporting the frequency of oral PCM in Brazil. The article also provides discussion of the global condition of the demographic distribution and clinical characteristics of the disease in light of the literature.

2 | MATERIALS AND METHODS

2.1 | Multicentre study

2.1.1 | Study design and ethical approval

A total of 108,304 histopathological records of oral and maxillofacial biopsies were analysed in a retrospective study. The records were obtained from a consortium of six oral and maxillofacial pathology services from four regions of Brazil (Table 1). The study was approved by the Ethics Committee of the Federal University of Minas Gerais (Approval No. 016/2003). Patient anonymity was guaranteed according to the Declaration of Helsinki. Moreover, a literature review of cases of oral PCM published in three electronic databases was conducted.

2.1.2 | Sample

A total of 320 biopsy records of PCM were recovered. The oral PCM cases were analysed regarding patient gender, age and occupation (urban/rural), anatomical location, symptomatology (symptomatic/asymptomatic), and clinical and histopathological diagnosis of PCM lesions. The anatomical location of the lesions was also considered as follows: lips, gingiva/alveolar ridge, tongue, floor of the mouth, buccal mucosa, palate and oropharynx. The anatomical location was not analysed in terms of number of individuals, but rather in terms of number of lesions presented; that is, the same patient may have been affected at more than one anatomical site.

2.1.3 | Histopathological data

Histopathological data on PCM were reviewed retrospectively by six independent oral and maxillofacial pathologists with more than

TABLE 1 Sources of the cases reviewed

Institution	State	Geographical areas (km^2)[a]	Population (millions)	Years	Lesions biopsied during the period studied	Oral PCM (%)[b]	%[c]
UFPel[d]	Rio Grande do Sul	281,748	11,322,895	1959–2016	23,896	89 (27.8)	0.37
UFRGS[e]	Rio Grande do Sul	281,748	11,322,895	1953–2016	31,163	85 (26.6)	0.27
UFMG[f]	Minas Gerais	586,528	21,119,536	1953–2016	34,046	80 (25)	0.23
UFG[g]	Goiás	340,086	6,778,772	1996–2016	10,246	53 (16.6)	0.51
UFSC[h]	Santa Catarina	95,346	6,778,772	2006–2016	2,703	12 (3.7)	0.44
UPE[i]	Pernambuco	98,312	9,473,266	1990–2016	6,250	1 (0.3)	0.01
Total	–	–	–	–	108,304	320 (100)	1.83

Notes. PCM: paracoccidioidomycosis; Y: years of age.
[a]Data according to the Brazilian Institute of Geography and Statistics (IBGE, 2017)
[b]Percentage in relation to the number of cases of oral PCM
[c]Percentage of the sample of oral PCM at each centre
[d]Diagnostic Centre for Oral Diseases of the Federal University of Pelotas (south region)
[e]Department of Oral Pathology, School of Dentistry of the Federal University of Rio Grande do Sul (south region)
[f]Department of Oral Surgery and Pathology, School of Dentistry of the Federal University of Minas Gerais (south-east region)
[g]Department of Stomathology, School of Dentistry of the Federal University of Goiás (midwest region)
[h]Health Sciences Centre, School of Dentistry of the Federal University of Santa Catarina (south region)
[i]Department of Oral and Maxillofacial Pathology, School of Dentistry of the University of Pernambuco (north-east region).

20 years of experience. Histological evaluation of routine H&E and special staining such as PAS and Grocott–Gomori were performed to diagnose PCM, according to the study of Uribe, Zuluaga, León, and Restrepo (1987).

2.2 | Literature review

2.2.1 | Information sources, eligibility criteria and search

A review of the literature with no restriction of publication year was carried out to retrieve studies on oral PMC. The inclusion criteria were retrospective studies, case series and case reports. Exclusion criteria were studies in languages other than English, Spanish or Portuguese and studies with no available full texts. PubMed (National Library of Medicine), Web of Science (Thomson Reuters) and Scopus (Elsevier) electronic databases were examined to identify studies that could be included. The search was undertaken in July 2017 using entry terms and keywords as shown in Supporting Information Appendix S1. The retrieved references were exported to the EndNote software (Thompson Reuters, New York, NY, USA). After removal of duplicates, the selection of the studies was performed in two phases. In phase 1, titles/abstracts that met the eligibility criteria were included. If a title/abstract provided insufficient information for a decision about inclusion/exclusion, the full text was obtained and assessed in phase 2. Those who met the eligibility criteria were also included.

2.2.2 | Data extraction and items

The following data were extracted from the articles included in the literature review: author and year of publication, country, number of cases reported, participants' gender and age, and anatomical location of PCM.

2.2.3 | Data analysis

Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) software, version 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics was carried out to characterize the cases with respect to the following information: patient's gender, age and occupation, lesion's anatomical location and symptomatology.

3 | RESULTS

A total of 108,304 patients were diagnosed with oral and maxillofacial lesions at the centres studied; of these, 320 (0.3%) were oral PCM. The allocation of oral PCM cases by centre is presented in Table 1. No case of oral PCM according to the histopathological analysis was excluded from our survey. Age (decades) and gender distributions of individuals with oral PCM are shown in Figure 1. Age was

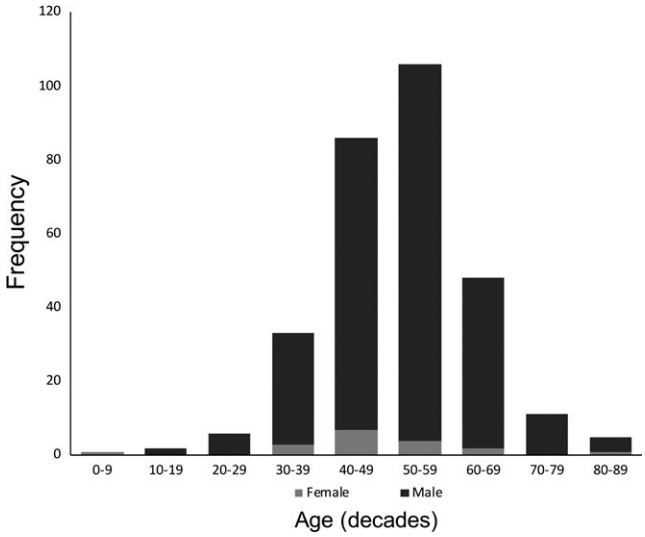

FIGURE 1 Distribution of cases of oral PCM according to the age and gender

not reported in 22 cases. The mean age at diagnosis was 51.3 years (±11.7). Individuals' age ranged between 7 and 89 years. The distribution according to the gender, occupation and symptomatology is provided in Table 2. A total 299 (93.4%) cases occurred in males and 21 (6.6%) in females (male-to-female ratio 14.2:1). Regarding occupation, 28.1% of the patients were rural workers and 24.4% were urban workers. In almost half the sample (*n* = 152), information regarding occupation was missing. Among the rural workers, farmers were more frequently affected (90%). Among urban individuals, most were construction workers (26.9%). Regarding symptomatology, most lesions proved to be symptomatic (44.7%; Table 2). Oral PCM affected different sites, the most common being gingiva/alveolar ridge (23.2%), lips (21.7%) and buccal mucosa (15.9%). Lesions in more than one region were observed in 144 patients; that is, 53% exhibited lesions at one anatomical location, 25.3% at two, 17.5% at three and 2.1% at four, and in 2.1%, the number of sites was not available.

Of 320 cases, 279 were diagnosed by means of incisional biopsies and no detail was provided in 34 cases. In 65% of cases, the histopathological diagnosis confirmed the clinical diagnosis of PCM. The other diagnostic hypotheses were squamous cell carcinoma (SCC; 26.5%), blastomycosis, tuberculosis and leishmaniasis (<5%). Microscopic evaluation of routine H&E-stained tissues of oral PCM revealed pseudoepitheliomatous hyperplasia besides ulceration of the overlying epithelium. A chronic inflammatory infiltrate with multinucleated giant cells was detected in the lamina propria (Figure 2a,b). Yeasts of *P. brasiliensis* were identified after special PAS and Grocott–Gomori staining (Figure 2c,d).

The literature review yielded 455 articles, and 46 articles were selected after applying inclusion and exclusion criteria, with 613 cases of oral PCM being detected (Table 3). The studies were conducted on three continents: Americas (608 cases), Europe (3 cases) and Asia (2 cases; Figure 3). Thirty-two articles were from Brazil (577 cases, with the three most affected states being Minas Gerais (*n* = 222), Paraná (*n* = 188) and São Paulo (*n* = 88), corresponding to 94.1% of the review sample. Forty-three articles reported the mean ages of the patients with oral PCM, demonstrating that individuals between 50 and 59 years were most affected. The review showed the involvement of 553 males (90.2%) and 60 females (9.8%). With respect to anatomical site, 265 cases occurred in the gingiva, 200 in the palate, 164 in the lips, 133 in the buccal mucosa, 97 in the tongue, 76 in the oropharynx and 36 in the floor of the mouth. Twenty-six articles contained information regarding occupation (527 cases), with 43.3% of the sample representing rural workers (228 cases).

TABLE 2 Socio-demographic and clinical characteristics of the sample

	Number (%)
Gender	
Male	299 (93.4)
Female	21 (6.6)
Occupation	
Urban	78 (24.4)
Rural	90 (28.1)
Unknown	152 (47.5)
Symptomatology	
Symptomatic	143 (44.7)
Asymptomatic	64 (20)
Unknown	113 (35.3)
Total	320 (100)
Anatomical location[a]	
Lips	116 (21.7)
Gingiva/alveolar ridge	124 (23.2)
Tongue	60 (11.2)
Floor of the mouth	33 (6.2)
Buccal mucosa	85 (15.9)
Palate	53 (9.9)
Oropharynx	56 (10.5)
Unknown	7 (1.3)
Total	534 (100)

[a]This variable was not analysed by the number of individuals, but by the number of lesions presented.

4 | DISCUSSION

Paracoccidioidomycosis, also known as Lutz disease or Lutz–Splendore–de Almeida mycosis, was first described by Dr. Adolpho Lutz approximately 110 years ago as a deep systemic condition (Colombo et al., 2011; Filho, 1950; Life International Fungal Education (LIFE), 2017). It is recognized as one of the main endemic mycoses in Latin America (Colombo et al., 2011; Life International Fungal Education (LIFE), 2017) and it is prevalent in Brazil,

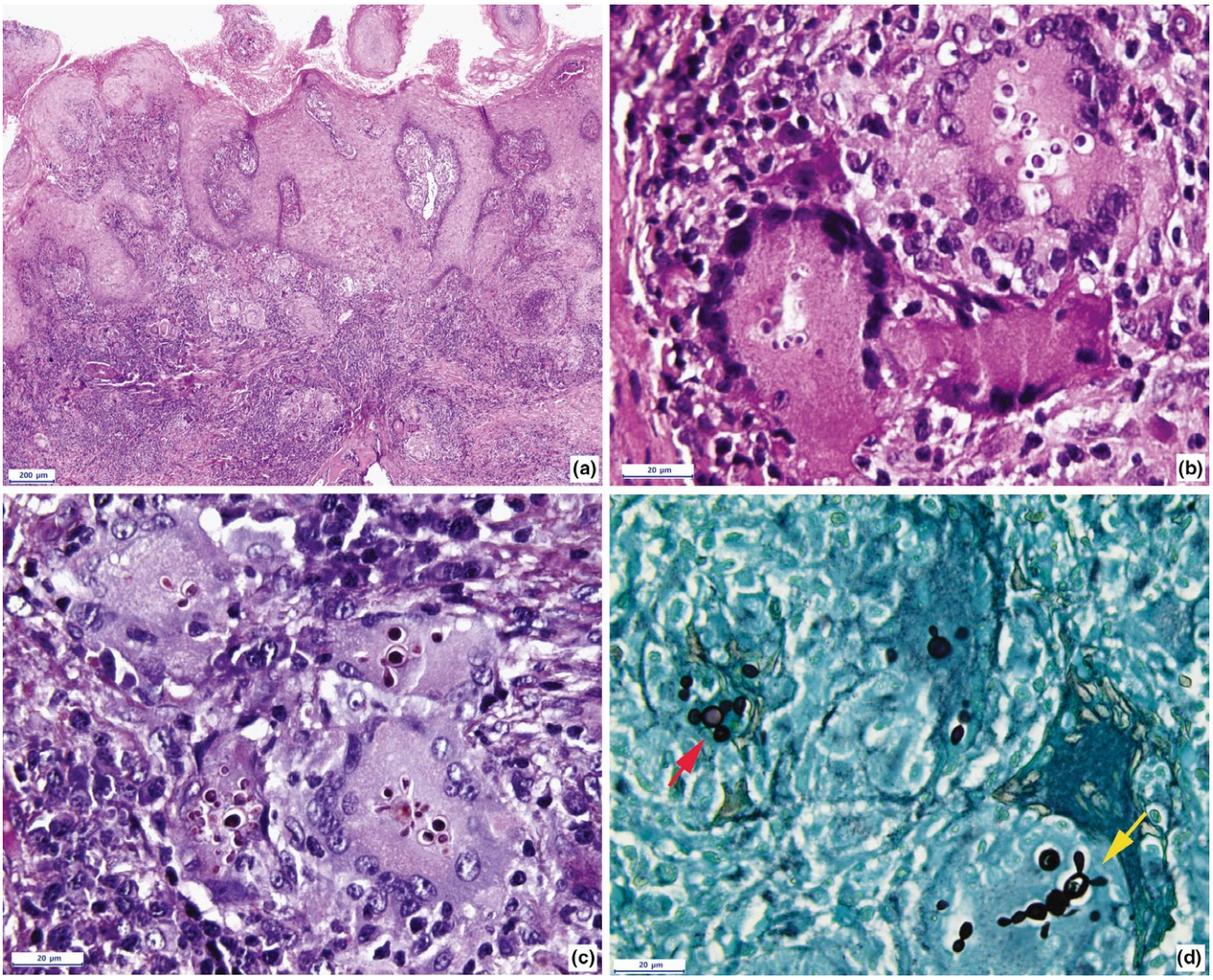

FIGURE 2 (a) Oral mucosa with pseudoepitheliomatous hyperplasia on overlying surface epithelium and a chronic inflammatory infiltrate in connective tissue (H&E staining, 4× magnification). (b) Multinucleated giant cells presented numerous rounded structures surrounded by a clear halo in the cytoplasm representing yeast cells of *Paracoccidioides brasiliensis*. This clear halo was birefringent when examined by light microscopy (H&E staining, 60× magnification). (c and d) Yeasts are readily identified in PAS-stained preparations (c—PAS staining, 60× magnification)—rounded structures surrounded by a clear halo and associated with red budding. Grocott–Gomori staining (d—Grocott–Gomori staining, 60× magnification) revealed black-pigmented round structures with budding and a "mariner's wheel" (red arrow) or "Mickey Mouse ears" (yellow arrow) aspect [Colour figure can be viewed at wileyonlinelibrary.com]

Venezuela, Colombia, Ecuador, Argentina and Mexico (Azenha et al., 2012; Bicalho et al., 2001; Colombo et al., 2011; Godoy & Reichart, 2003; López-Martínez et al., 2014; Sposto et al., 1993; Trindade et al., 2017). However, sporadic cases have been reported in other continents among individuals who visited endemic areas, as shown in Figure 3. In areas of larger endemicity, such as Brazil, mortality may reach over 20% (Brazão-Silva et al., 2011; Silva et al., 2007). *P. brasiliensis* has been isolated from soil, but its precise environmental niche remains undefined. Despite some uncertainties concerning its specific ecology, it is known that PCM develops in regions with mild temperatures, a humid climate with copious rainfalls and areas with abundant watercourses. These conditions are present in regions with tropical and subtropical forests, which are predominant in the regions studied herein (Colombo et al., 2011).

In this Brazilian survey, oral PCM represented 0.3% of cases among diagnosed oral and maxillofacial lesions. The availability of information about the oral manifestation of PCM is still scarce. Our study estimate concurs with the rate of 0.6% reported at single-centre studies in endemic areas (Brazão-Silva et al., 2011). Studies from Argentina and Mexico, however, did not provide the relative frequency of biopsied lesions (Godoy & Reichart, 2003; López-Martínez et al., 2014). The strength of our study is based on the report of the frequency of oral PMC at six reference centres in a multicentre collaboration. Moreover, results from a literature review are presented. According to this analysis, most cases were from developing countries in areas with increased soil humidity. Of the 613 oral PCM cases, only 10 were patients from developed countries; however, they had a history of travelling to some endemic area.

TABLE 3 Demographic data of oral paracoccidioidomycosis cases published in the literature

			Gender			Anatomical location						
Authors (year of publication)	Country	Cases (*n*)	Male	Female	Age	Lips	Gingiva	Tongue	Floor of the mouth	Palate	Buccal mucosa	Oropharynx
Salman and Sheppard (1962)	USA	1	1	0	55	0	1	0	0	0	0	0
Joseph et al. (1966)	USA	1	1	0	83	0	1	0	0	0	0	0
Murray et al. (1974)	USA	1	1	0	51	1	0	0	0	0	0	0
Lima et al. (1977)	Brazil	9	7	2	49.7	1	3	1	0	3	0	0
Pereira and Silva (1982)	Brazil	1	1	0	58	1	1	0	0	0	0	0
Lazow et al. (1990)	USA	1	1	0	59	0	1	0	0	0	0	0
de Almeida et al. (1991)	Brazil	3	2	1	46	0	1	1	0	1	2	0
Sposto et al. (1993)	Brazil	36	31	5	46.0	13	28	4	4	17	9	4
Sposto et al. (1994)	Brazil	14	13	1	46.6	6	9	0	0	6	3	3
Manns et al. (1996)	Canada	1	1	0	59	0	0	1	0	0	0	0
Weismann et al. (1995)	Brazil	1	0	1	12	0	0	0	0	1	0	0
Migliari et al. (1998)	Brazil	3	1	2	15.3	0	3	0	0	0	0	0
Giovani et al. (2000)	Brazil	1	0	1	29	0	1	0	0	0	0	0
Bicalho et al. (2001)	Brazil	62	60	2	40	14	32	0	1	18	10	1
Bisinelli et al. (2001)	Brazil	187	167	20	UN	68	35	31	7	40	25	42
Castro et al. (2001)	Brazil	1	1	0	36	0	0	0	0	1	0	0
Horré et al. (2002)	Germany	1	1	0	61	1	1	0	0	0	1	0
Meneses-García et al. (2002)	Mexico	2	2	0	59.5	0	1	0	0	1	1	0
Godoy and Reichart (2003)	Argentina	21	20	1	50	13	16	15	0	6	6	0
Verli et al. (2005)	Brazil	61	58	3	UN	0	39	22	16	38	10	15
Van Damme et al. (2006)	The Netherlands	1	1	0	60	0	0	0	0	0	1	0
Andrade et al. (2007)	Brazil	1	1	0	58	1	1	0	1	1	0	0
Silva et al. (2007)	Brazil	34	30	4	UN	12	18	6	0	13	14	6
Jahm et al. (2008)	Brazil	2	2	0	30.5	1	1	0	0	0	1	0
Sunada et al. (2008)	Japan	1	1	0	36	1	1	0	0	1	1	0
Talhari et al. (2008)	Brazil	1	1	0	47	1	0	0	0	0	0	0
Torres-Pereira et al. (2009)	Brazil	1	1	0	47	0	0	0	0	1	0	1
Brazão-Silva et al. (2011)	Brazil	66	62	4	45.2	6	44	6	0	31	34	0
León et al. (2010)	Peru	2	2	0	50	1	1	0	0	1	0	0
Azevedo et al. (2011)	Brazil	1	1	0	54	0	1	0	1	1	1	0

(Continues)

TABLE 3 (Continued)

Authors (year of publication)	Country	Cases (*n*)	Gender		Age	Anatomical location						
			Male	Female		Lips	Gingiva	Tongue	Floor of the mouth	Palate	Buccal mucosa	Oropharynx
de Oliveira Gondak et al. (2012)	Brazil	8	4	4	51.1	2	3	2	0	1	0	0
Onda et al. (2011)	Japan	1	1	0	39	1	0	0	0	0	1	0
Pontes et al. (2011)	Brazil	1	1	0	28	0	0	0	0	1	0	0
Zapata et al. (2011)	Colombia	1	1	0	56	1	1	0	0	0	0	0
Antunes Freitas et al. (2012)	Brazil	1	1	0	48	0	0	1	0	1	0	0
Azenha et al. (2012)	Brazil	18	16	2	50.2	5	3	5	2	4	9	0
Sargenti Neto et al. (2012)	Brazil	1	1	0	40	0	1	1	0	0	0	0
Pereira et al. (2012)	Brazil	1	0	1	38	1	1	0	0	0	0	0
Tubino et al. (2012)	Brazil	1	1	0	62	1	0	0	0	0	1	0
Soares et al. (2013)	Brazil	2	2	0	63.0	0	1	0	0	1	0	1
Pedreira et al. (2014)	Brazil	1	1	0	65	0	0	1	0	0	0	0
Webber et al. (2014)	Brazil	1	1	0	41	0	0	0	0	1	0	0
Girardi and Scrofernecker (2016)	Brazil	1	1	0	65	1	0	0	0	0	0	0
Trindade et al. (2017)	Brazil	55	50	5	46.7	11	11	2	4	9	3	3
Dang et al. (2017)	France	1	1	0	54	0	0	1	0	0	0	0
Dos Santos et al. (2017)	Brazil	1	0	1	48	0	1	0	0	1	0	0
Total	—	613	553	60	—	164	265	97	36	200	133	76

Note. *n*: number; UN: unknown; USA: United States.

FIGURE 3 World distribution of 613 cases of oral PCM reported in the literature [Colour figure can be viewed at wileyonlinelibrary.com]

According to the World Health Organization, a high prevalence of systemic PCM is associated with socio-economic factors (WHO Department of Control of Neglected Tropical Diseases, 2013). Those affected by fungal lesions are often individuals from poor countries living in isolated rural areas, urban slums or conflict zones (Queiroz-Telles et al., 2017). In the present study, most patients were rural workers. However, there was no information regarding occupation for almost half the sample investigated. Accordingly, it is important to consider that epidemiological approaches to PCM are challenging, as notification is noncompulsory and the disease is often underestimated (Queiroz-Telles et al., 2017; Trindade et al., 2017).

Epidemiological studies involving PCM lesions in other anatomical regions have been conducted in these different countries, and when compared with the oral region, the rate is much higher. According to Martinez (2015), over 15,000 cases of PCM were reported in Latin America between the mid-1930 s and 2012, and more than 12,000 cases were from Brazil. The sum of the incidence in Colombia, Venezuela and Ecuador is much smaller than the total for Brazil. Interestingly, in our study, only one patient was diagnosed in north-eastern Brazil. However, the patient had been living in the midwest (endemic region) at a young age. Therefore, this could be interpreted as additional evidence for endemic areas, which extend between latitudes 23°N and 34°S (Abreu e Silva, Salum, Figueiredo, & Cherubini, 2013). Another issue of concern is that an extremely long silent period between travel to an endemic area and manifestation of symptoms has been documented in such cases, with an average duration of 14 years and of as many as 60 years in some cases (Ajello & Polonelli, 1985). In this multicentre study, the mean age of individuals was 51.3 years, which is in accordance with previous reports (Bicalho et al., 2001; Brazão-Silva et al., 2011; Godoy & Reichart, 2003; Silva et al., 2007). The human infection occurs by inhalation, with the lungs being the first site affected. By haematogenous and lymphatic dissemination, other sites can be compromised, including the oral cavity. The mouth is involved in about half the cases (Bellissimo-Rodrigues, Bollela, Fonseca, & Martinez, 2013).

Oral PCM commonly shows an erythematous finely granular hyperplasia, speckled with multiple pinpoint haemorrhages and a mulberry-like surface. Areas of ulceration are also frequent (Almeida, Jorge Junior, & Scully, 2003; Sposto et al., 1993). In the present sample, the gingiva/alveolar ridge, lips and buccal mucosa were the most common anatomical sites. In agreement with the 613 cases analysed in the literature review, 27.3% were lesions diagnosed in gingiva, followed by the palate, the lips and the buccal mucosa. Some studies report that the findings in the gingiva region can range from 52% to 78% (Silva et al., 2007; Sposto et al., 1993). According to Brazão-Silva et al. (2011), inflammatory mediators produced in the context of pre-existing conventional periodontal disease could hypothetically contribute to the installation of the fungus. The hypothesis of whether gingival inflammation favours the development of the mycosis after local inoculation of the fungus or merely exacerbates the expression of the disease at the site is still being debated (Brazão-Silva et al., 2011; Silva et al., 2007).

It is important to consider other conditions in the differential clinical diagnosis of oral PCM (Girardi & Scrofernecker, 2016; Meneses-García et al., 2002). Some conditions that may show a similar clinical presentation include granulomatous lesions, that is

tuberculosis, sarcoidosis, Wegener's granulomatosis and other systemic fungal infections. Furthermore, oral PCM may also mimic SCC (Meneses-García et al., 2002). In our study, some of these conditions were included in the differential diagnosis. Oral PCM lesions usually exhibit histopathological findings of other granulomatous inflammations; however, special stains such as PAS and Grocott–Gomori reveal *P. brasiliensis*, thus being of help for a differential diagnosis (Meneses-García et al., 2002; Oliveira et al., 2012; Uribe et al., 1987).

This study analysing a large number of patients has shortcomings that should be recognized. Given the retrospective nature based on biopsy records, some data were missing on several occasions. The main reason for this limitation is the existence of the different protocols used for data collection and for reporting patient information across institutions. Thus, initiatives to use well-designed instruments for data collection should be encouraged. Additionally, the authors should also be encouraged to use reporting guidelines for case reports and case series (Riley et al., 2017). Another limitation was the unavailability of conventional chest radiographs for lung screening and serology for HIV at the six oral diagnostic centres. Concomitant HIV predisposes to opportunistic infections such as PCM (Prado et al., 2009). Following the diagnosis, patients were referred to several hospitals across the country, which precluded the retrieval of information about treatment and follow-up.

Fungal oral lesions are common in the Latin American population. Therefore, single- or multicentre prospective studies of some neglected tropical diseases are feasible and should be encouraged. There is a difficulty in determining the current frequency of the disease from biopsy records. The prevalence of oral lesions seems to depend on various additional factors. For instance, socio-economic and cultural factors may influence self-care measures and may affect healthcare seeking, leading to lesions' underdiagnosis. It is important to highlight that the notification of fungal oral lesions is important to implement preventive and early-diagnosis measures, which, in turn, will make treatment more effective and will improve prognosis.

In summary, oral PCM is an uncommon lesion detected in oral and maxillofacial biopsy samples. This fungal lesion affects predominantly men between 50 and 59 years. It is possible to infer that geographical variations help better explain the relative frequency of PCM. This study provides information that could be helpful to clinicians for the diagnosis of oral PCM.

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CONFLICT OF INTEREST

None to declare.

AUTHOR CONTRIBUTIONS

José Alcides Almeida de Arruda, João Luiz Gomes Carneiro Monteiro, Lauren Frenzel Schuch and Carla Mosconi conducted a literature review and organized the data of the clinical cases. Aline Carvalho Batista, Laura de Campos Hildebrand, Manoela Domingues Martins, Elena Riet Correa Rivero, Ana Paula Neutzling Gomes, Tarcília Aparecida Silva and Ana Carolina Uchoa Vasconcelos contributed with cases from their services and reviewed and classified all cases. Leni Verônica de Oliveira Silva contributed to the design of the work, while Lucas Guimarães Abreu was responsible for data interpretation. Ana Paula Veras Sobral and Ricardo Alves Mesquita contributed to the conception of the work. All authors drafted the article, approved the final version of the manuscript as submitted and agreed to be accountable for all aspects of the work.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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