

# Paracoccidioidomycosis prevalence in a public laboratory of the Brazilian unified health system

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## ABSTRACT:

Paracoccidioidomycosis (PCM) is a systemic fungal disease with oral manifestations that is the most prevalent in Latin America. The purpose of this cross-sectional epidemiological study was to examine the prevalence of PCM in the Public Laboratory (MT Laboratory) of the Brazilian Unified Health System in Mato Grosso. The following data from 3670 cytological and histopathological reports of oral lesions issued by the MT Laboratory over a 4-year (2004–2008) period were analyzed: diagnostic method (oral exfoliative cytology or biopsy), diagnosis by year, origin of cases (urban or rural), and patient gender and age. In the assessment period, 96 cases (2.6%) of PCM were diagnosed. Most cases originated from rural areas (94%), and PCM was the most prevalent in men (97.9%) and in the fifth decade of life (35.4%). These results show that Mato Grosso had a considerable number of PCM cases over a small period, suggesting that this state is an endemic region for PCM in Brazil.

**Keywords:** epidemiology, laboratories, oral diseases, paracoccidioidomycosis, public health.

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## INTRODUCTION

The impact of human pathogens has been assessed for a long time in biomedical sciences. However, these microorganisms are still affecting populations with poor socioeconomic conditions<sup>1</sup>. An infectious disease with high morbidity and commonly found in poor areas is paracoccidioidomycosis (PCM), also known as South American blastomycosis. This systemic fungal disease is considered an endemic mycosis in Central and South America<sup>2,3,4,5,6</sup>. It is quite prevalent in Brazil, Colombia, Venezuela, and Argentina but extremely unusual in others continents<sup>7</sup>.

The etiological agent of PCM is a dimorphic fungus called *Paracoccidioides brasiliensis*. Adolf Lutz first described it in 1908<sup>8</sup>. This fungus is found in humid geographic areas, enclosed by rivers, lakes, and swamps, with minimum temperature variations<sup>9</sup>. Rural workers are more susceptible to PCM, especially those who come in direct contact with soil, such as farmers<sup>3,4,5</sup>. Besides the environmental influence, tobacco use, alcohol use, and poverty are associated with this pathology<sup>3,4,6,9,10</sup>.

The infection by *Paracoccidioides brasiliensis* often begins via fungal inhalation and then spreads to the other parts of the body by blood and lymphatic vessels<sup>11</sup>. PCM has several clinical forms, such as acute or subacute and chronic<sup>4,11</sup>. The acute and subacute forms present cervical and intra-abdominal lymphadenomegaly, facial cutaneous lesions, osteoarticular lesions, hepatomegaly<sup>12</sup>, genital manifestations<sup>13</sup>, and complications related to pulmonary, adrenal, and central nervous system lesions<sup>4</sup>. In the oral cavity, the disease is expressed as multiple, papuloerosive, ulcerated, and hypertrophic lesions, with slow evolution, appearing granulous and reddish, and involving the gingiva, oral mucosa, palate, tongue, and floor of the mouth<sup>14,15</sup>. Treatment consists of specific antifungal therapy as well as supportive therapy for the complications associated with the involvement of different organs<sup>4</sup>.

Brazil has the highest prevalence of PCM cases in Latin America<sup>3</sup>, thus becoming the most endemic country for PCM in the world<sup>16</sup>. In a 15-year (1980–1995) analysis of deaths caused by this disease in Brazil, Coutinho et al.<sup>16</sup> evidenced 3181 deaths, averaging 1.85 deaths per 100,000 inhabitants. The Brazilian state with the highest mortality is South Mato Grosso (4.39 deaths per 100,000 inhabitants), followed by Rondônia (3.65 deaths per 100,000 inhabitants), Paraná (3.48–3.52 deaths per 100,000 inhabitants), and Mato Grosso (3.22 deaths per 100,000 inhabitants)<sup>17</sup>.

Mato Grosso, located in the central-western region of Brazil, is considered an endemic area for PCM<sup>3</sup>. It spans 903,357,908 km<sup>2</sup> and had an estimated population of 2,854,642 people in 2007<sup>18</sup>. Its economy is based on agronomic and cattle-

-breeding activities, with 114,148 agronomic and breeding farms, totaling 48,355,569 hectares. Mato Grosso is an Amazonian state, with 17,758,922 hectares of wooded and forested areas, and has a humid tropical climate<sup>19</sup>. The predominant vegetation is Cerrado, which resembles a savanna, and the state owns part of the world's largest seasonal wetland, known as the Pantanal<sup>20</sup>.

Given its different environment (Amazon, Cerrado, and Pantanal) with large forests and economy based on agriculture, we hypothesized that Mato Grosso would show a higher prevalence of PCM. However, the healthcare authorities has instituted a diagnosis system to be employed by the primary care network of the Brazilian Unified Health System; thus, an oral diagnostic network including an oral pathology public service provided by the public laboratory of the state (MT Laboratory) was established. This policy, set by the state law 8.342/2005, has facilitated the delivery of free-of-charge diagnostic procedures to Brazilians living in Mato Grosso<sup>21</sup>. Therefore, the prevalence of PCM should increase after this network is set up in primary care as well. The aim of this study was to examine the prevalence of PCM in the Public Laboratory of the Brazilian Unified Health System in Mato Grosso after 4 years of the primary care network of oral-diseases-diagnostic policy by law 8342/2005<sup>21</sup>.

## MATERIALS AND METHODS

### DESIGN

This cross-sectional epidemiological study was approved by the Ethical Research Committee of the Mato Grosso State Public Health School (439/2009). Informed consent was not required because the research did not directly involve patients. Both cytological and histopathological reports issued by the oral pathology service of the MT Laboratory were used as the research source. Histopathological reports, which are considered the gold standard to confirm oral cancer<sup>22</sup>, were used in a similar study by Blotta et al.<sup>23</sup>.

### SAMPLE

The cytological and histopathologic reports in the oral pathology lesions database of MT Laboratory of the Brazilian Unified Health System (SUS) were used as the research source. This sample seems to be representative, considering that the MT Laboratory is the referral center for 1255 health institutions in Mato Grosso<sup>24</sup>. The study included 3670 reports issued between November 2004 (date of the beginning of the oral pathology service) and December 2008. All reports of oral exfoliative cytology and biopsy were considered relevant to oral lesions. The MT Laboratory does not register other diagnostic methods for PCM, such as direct mycological examination, culture, serological examination, and intradermatological reaction.

## DATA ANALYSIS

Only reports related to PCM were analyzed. The following variables were examined: diagnostic method (oral exfoliative cytology or biopsy), diagnosis by year, origin of cases (urban or rural), and patient gender and age. Incomplete data such as skin color, occupation, and anatomical site were not included, because the purpose of this research was to evidence only the prevalence of PCM in Mato Grosso. After data collection, analysis, and tabulation, a descriptive analysis was performed.

## RESULTS

The 3670 selected records included 508 (13.8%) exfoliative cytology and 3162 (86.2%) biopsy reports. Among these, 96 (2.6%) cases of PCM were diagnosed (33 [34.4%] by exfoliative cytology and 63 [65.6%] by biopsy; Table 1). PCM was the most prevalent in 2006 (38 [3.7%] cases; Table 1).

The age of the patients diagnosed with PCM ranged from 21 to 74 years, with a mean age of 48.5 years. The highest prevalence of this disease was noted in the fifth decade of life (34 [35.4%] cases), followed by the sixth decade of life (23 [23.9%] cases; Table 2). Concerning gender, between 2004 and 2008, 2 (2.1%) female patients and 94 (97.9%) male patients were diagnosed with PCM (1:47 ratio). In terms of origin, nearly all the affected patients lived in Mato Grosso: 90 (94.0%) and 6 (6.0%) were rural and urban inhabitants, respectively.

**Table 1.** Number of paracoccidioidomycosis (PCM) cases and other oral lesions diagnosed by oral exfoliative cytology and biopsy (N = 3670) at the MT Laboratory, Mato Grosso, Brazil, in 2004–2008.

Year	Other lesions			PCM			Annual total
	Cytology	Biopsy	Total	Cytology	Biopsy	Total	
2004	45	23	68	1	2	3	71
2005	93	278	371	6	11	17	388
2006	82	888	970	12	26	38	1008
2007	167	997	1164	10	16	26	1190
2008	88	913	1001	4	8	12	1013
Total	475	3099	3574	33	63	96	3670

## DISCUSSION

The scientific literature shows that the occurrence of PCM outside Latin America is rare<sup>7</sup>. Although some cases have been reported in Germany<sup>25</sup>, Austria<sup>26</sup>, the Netherlands<sup>7</sup>, and the United Kingdom<sup>27</sup>, all the patients had traveled or lived in Central or South America or were immigrants from the continent. Despite these cases, the existence of *Paracoccidioides brasiliensis* has been reported only in Latin America<sup>28</sup>.

**Table 2.** Age-related distribution of paracoccidioidomycosis cases diagnosed at the MT Laboratory, Mato Grosso, Brazil, in 2004–2008.

Age group	Number of cases	%
21–30	04	4.16
31–40	18	18.75
41–50	34	35.41
51–60	23	23.95
61–70	13	13.54
71–80	02	2.08
Not informed	02	2.08
Total	96	100.0

The great majority of PCM cases have been reported in South America, such as in Bolívar, Venezuela (193 cases)<sup>29</sup>, Formosa, Argentina (24 cases)<sup>10</sup>, and Corrientes, Argentina (21 cases)<sup>2</sup>. Although Brazil is considered an endemic country for PCM<sup>4</sup>, disease notification is not compulsory and information on its incidence is scarce, hampering the characterization of this disease<sup>9</sup>. The estimates of prevalence, incidence, and morbidity of this mycosis are based on epidemiological reports, records, and some case investigations<sup>4</sup>. However, the data on the epidemiological profile of PCM is primarily restricted to studies in Brazil (Table 3).

**Table 3.** Epidemiological studies of paracoccidioidomycosis in Brazil.

Author (year)	State	Period	Number of cases
Blotta et al. <sup>23</sup>	São Paulo	1988–1996	584
Paniago et al. <sup>31</sup>	South Mato Grosso	1980–1999	422
Campos et al. <sup>12</sup>	Federal District	1984–2005	76
Verli et al. <sup>30</sup>	South Rio Grande	1976–2004	61
Bicalho et al. <sup>36</sup>	Minas Gerais	1955–1998	62

According to the oral pathology database of the MT Laboratory, 96 PCM cases were recorded between 2004 and 2008. The largest cases series of PCM in Brazil was obtained in the southeastern state of São Paulo, where 584 cases were diagnosed at the University Hospital of Campinas<sup>22</sup>. In absolute values, the MT Laboratory registered the fourth highest number of cases over only 4 years, where PCM was diagnosed by oral exfoliative cytology and biopsy. This fact indicates a high prevalence of PCM in Mato Grosso.

PCM can be diagnosed by biopsy, oral exfoliative cytology, direct mycological examination, culture, serological examination, and intradermatological reaction<sup>12</sup>. In the present study, the vast majority of cases were diagnosed through biopsy (86.2%), which is a more complex method than oral exfoliative cytology. Data related to the diagnostic method at the MT Labo-

ratory can indicate whether the diagnosis was accomplished in an advanced stage of PCM, and includes oral cancer as a differential diagnosis. Biopsies of oral lesions, which are extensive, ulcerative, and painful, are uncommon in routine dentistry, which can lead to late diagnosis in many cases, causing serious problems for the patients<sup>9</sup>. Talhari et al.<sup>6</sup> indicated that oral exfoliative cytology is a useful and valid procedure for diagnosing PCM, because it is easy to perform, has lower operational cost, does not present side effects, and can be used as an ambulatory routine examination to diagnose suspected oral lesions.

In this study, PCM was the most prevalent in the fifth decade of life, similar to findings of Silva Campos et al.<sup>12</sup>, who analyzed 76 PCM cases at the University Hospital of Brasília between 1984 and 2005. In the study by Verli et al.<sup>31</sup>, among 61 PCM cases in the state of South Rio Grande, 70.5% of the patients were aged between 40 and 59 years, which is a slightly older age group than that found in Mato Grosso, but 63.7% were in the same age range. Therefore, the greatest majority of patients with PCM are in their productive stage of life, as indicated by Shikanai-Yasuda et al.<sup>4</sup>. Men are more susceptible to the disease, whereas women are infected during conditions of immunosuppression<sup>4,9</sup>. The male-to-female ratio in the present study was 47:1, which is higher than that reported by Blotta et al.<sup>23</sup> and Campos et al.<sup>12</sup> but near the finding observed by Verli et al.<sup>31</sup>, which of 95% patients were men.

Regarding the origin, those living in the countryside are more likely to be infected due to the association between *Paracoccidioides brasiliensis* and agricultural and cattle-breeding activities<sup>4,9</sup>. In Mato Grosso, 94% of the analyzed sample lived in the countryside, with agriculture and cattle breeding as the main economic activities and near larger wooded and forested areas (17,758,922 hectares). Paniago et al.<sup>30</sup> found that of 422 patients in South Mato Grosso, 90.5% lived in the countryside and 45.5% worked in rural areas. Verli et al.<sup>31</sup> noted similar findings in South Rio Grande, where 73.7% of the patients were from agricultural regions. In rural South India, Ray et al.<sup>32</sup> reported that pulmonary eosinophilia, a tropical disease, represented the greatest cause of morbidity. In the same study, the authors associated the occurrence of tropical diseases with poor areas<sup>33</sup>.

Associated with larger areas of forests and intensive activity of agriculture and cattle breeding, until 2003, over 33.37% of the population in Mato Grosso lived below the poverty line<sup>34</sup>. The state had the fourth highest mortality between 1980 and 1995, even without a system of PCM case notification<sup>16</sup>. Hurt et al.<sup>35</sup> analyzed the impact of socioeconomic factors in a rural population in Bangladesh and verified that these factors, mainly education, influenced the mortality caused by infectious diseases in a rural population in this country. In a systematic

review of infectious diseases and social determinants of health, Cohen et al.<sup>1</sup> stated the paucity of social research concerning infectious diseases, suggesting the necessity of increasing the dialogue between researchers of infectious diseases and social epidemiologists.

Shikanai-Yasuda et al.<sup>4</sup> asserted that PCM represents an important public health problem, considering its high associated morbidity and mortality, mainly in low-income segments, such as rural workers. The same authors observed that social and economic costs of the complications caused by PCM have not been adequately measured by the scientific community and health authorities<sup>4</sup>. Another determinant of the growth of cases and deaths caused by this disease is the deficiency of access and support on the health service network, favoring later diagnosis. According to Brazilian Institute of Geography and Statistics, Mato Grosso has 1255 public health institutions, but an oral pathology service in a public laboratory was not established until 2004<sup>36</sup>. Borges et al.<sup>36</sup> reported that Mato Grosso has established a specific law creating a broad system for oral lesion diagnoses, beginning at primary health care facilities with referral to the MT Laboratory mainly for oral exfoliative cytology and biopsy.

In conclusion, we examined the prevalence of PCM in the MT Laboratory, Mato Grosso, Brazil. The results show that Mato Grosso had a considerable number of PCM cases over a small period, suggesting that it is an endemic region for the disease in Brazil. The disease was the most prevalent in men of productive age, causing serious health conditions in these patients and evidencing a public health problem for the Brazilian Unified Health System.

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