



Evaluation of the clinical and epidemiological profile of patients with paracoccidioidomycosis in a public hospital

*Avaliação do perfil clínico e epidemiológico de pacientes com paracoccidioidomicose em um hospital público
Evaluación del perfil clínico y epidemiológico de los pacientes con paracoccidioidomicosis en un hospital público*

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ABSTRACT

Background and Objectives: The incidence of Paracoccidioidomycosis (PCM) may be underestimated due to the lack of mandatory notification of cases, as systemic mycoses in Brazil are not included in the national list of notifiable diseases. The aim of this study was to evaluate the clinical and epidemiological profile of patients with PCM at a reference center for infectious diseases in Piauí. **Methods:** This is a retrospective, quantitative-descriptive study. It was carried out in a hospital specializing in tropical diseases. A data collection form was used. We included medical records in which the patients had a final diagnosis of PCM, with a hospitalization date between October 2018 and September 2023. Medical records whose final diagnosis was not PCM and that the information was not complete in the medical record were excluded. **Results:** Of the inpatient records checked, 20 were confirmed. Of the patients affected, 100% were male, with the predominant age range between 30 and 60 years (60%), from rural areas, working as farmers (60%). The disease manifested itself in its chronic form (55%), with focal and multifocal lesions being equally prevalent (50%), with an onset time of less than one year (60%), and the presence of secretion (60%). **Conclusion:** The data obtained contributes to a better understanding and perception of the epidemiology of PCM, demonstrating the need to formulate public health policies capable of giving visibility to this neglected disease, which requires strategies for its prevention, diagnosis and treatment.

Keywords: *Paracoccidioidomycosis. Epidemiology. Clinical aspects. Public Hospitals. Retrospective Studies.*

RESUMO

Justificativa e Objetivos: A incidência da Paracoccidioidomicose (PCM) pode estar subestimada em decorrência da ausência de notificação obrigatória dos casos, pois no Brasil micoses sistêmicas não estão inclusas na lista nacional de agravos de notificação compulsória. O objetivo do estudo é avaliar o perfil clínico e epidemiológico de pacientes com PCM em um centro de referência para doenças infecciosas no Piauí. **Métodos:** Trata-se de um estudo retrospectivo e quantitativo-descriptivo. Realizado em hospital especializado em doenças tropicais. Foi utilizado como instrumento de coleta de dados um formulário. Foram incluídos os prontuários nos quais os pacientes tiveram diagnóstico final de PCM, com data de internação entre outubro de 2018 e setembro de 2023. Foram excluídos prontuários cujo diagnóstico final não tenham sido de PCM e que as informações não estiveram completas no prontuário. **Resultados:** Dos prontuários verificados de pacientes internados, 20 foram confirmados. Entre os pacientes acometidos 100% eram do sexo masculino, com a faixa etária predominante entre 30 e 60 anos (60%), originário da zona rural, exercendo a atividade laboral de lavradores (60%). A doença se manifestou na sua forma crônica (55%), tendo a extensão da lesão focal e multifocal igualmente prevalente (50%), com o tempo de surgimento menor que um ano (60%), com presença de secreção (60%). **Conclusão:** Os dados obtidos colaboram para uma melhor compreensão e percepção da epidemiologia da PCM demonstrando a necessidade de formulação de políticas de saúde pública capazes de dar visibilidade à doença negligenciada e que requer estratégias de prevenção, diagnóstico e tratamento da PCM.

Descriptores: *Paracoccidioidomycose. Epidemiologia. Aspectos clínicos. Hospitais públicos. Estudos Retrospectivos.*

RESUMEN

Justificación y Objetivos: La incidencia de Paracoccidioidomicosis (PCM) puede estar subestimada debido a la falta de notificación obligatoria de los casos, ya que las micosis sistémicas en Brasil no están incluidas en la lista nacional de enfermedades de declaración obligatoria. El objetivo de este estudio fue evaluar el perfil clínico y epidemiológico de los pacientes con PCM en un centro de referencia para enfermedades infecciosas en Piauí. **Métodos:** Se trata de un estudio retrospectivo, cuantitativo-descriptivo. Fue realizado en un hospital especializado en enfermedades tropicales. Se utilizó un formulario de recolección de datos. Se incluyeron historias clínicas en las que los pacientes tenían diagnóstico final de PCM, con fecha de hospitalización entre octubre de 2018 y septiembre de 2023. Se excluyeron las historias clínicas cuyo diagnóstico final no fuera PCM y que la información no estuviera completa en la historia clínica. **Resultados:** De las historias clínicas revisadas de pacientes hospitalizados, se confirmaron 20. De los pacientes afectados, el 100% eran varones, con el rango de edad predominante entre 30 y 60 años (60%), procedentes de zonas rurales, que trabajaban como agricultores (60%). La enfermedad se manifestó en su forma crónica (55%), con igual prevalencia de lesiones focales y multifocales (50%), con un tiempo de aparición inferior a un año (60%) y presencia de secreción (60%). **Conclusión:** Los datos obtenidos contribuyen para una mejor comprensión y percepción de la epidemiología de la PCM, demostrando la necesidad de formulación de políticas de salud pública capaces de dar visibilidad a esta enfermedad desatendida, que requiere estrategias para su prevención, diagnóstico y tratamiento.

Palabras Clave: *Paracoccidioidomicosis. Epidemiología. Aspectos clínicos. Hospitales Públicos. Estudios Retrospectivos.*

INTRODUCTION

Paracoccidioidomycosis (PCM) is a systemic disease resulting from infection caused by a dimorphic fungus that is endemic in the Americas, found from Mexico to Argentina, with the highest incidence in Brazil, Venezuela, and Colombia. *Paracoccidioides brasiliensis* prefers moist soil and regions with medium to high rainfall, mild temperatures, and the presence of forests and rivers. Infection by *Paracoccidioides* sp. is observed in areas of soil management work activities. Humans and nine-banded armadillos (*Dasypus novemcinctus*) are the main accidental hosts. However, human-to-human transmission has not yet been reported.¹

Thus, contamination occurs through inhalation of propagules from the mycelial (saprophytic) phase of the pathogen. In the body, the propagules transform into yeast and infection sets in. It is estimated that approximately 10 million people are infected in South America, and up to 2% have developed symptoms of PCM. Most develop the disease years after infection, mainly presenting with pulmonary disease.^{2,3}

Given this, PCM manifests as a pneumopathology linked to mucosal and skin lesions, which, when established in the lungs, transforms into a yeast-like form. From the lung parenchyma, it can spread via the bloodstream and lymphatic system to other organs, such as the spleen, liver, bones, and central nervous system. The primary phase of infection usually involves young individuals, as a limited pulmonary disease, which rarely progresses to the acute/subacute stage of the disease, unlike chronic cases, in which individuals have long periods of latency and, during reactivation, pulmonary and/or other organ involvement is observed.⁴

Depending on the incubation period and the characteristics of the infected individuals, PCM usually causes a transient pulmonary infection that can evolve from a subacute to an acute form or, more frequently, can reactivate later as a chronic and insidious disease. In addition, symptoms may manifest later, years or decades later, when the patient may be residing in the city or even in another country outside the endemic region.^{6,7}

In the state of Piauí, many families, especially in rural areas, depend on family farming for their livelihood and are therefore constantly exposed to soil contaminated by *Paracoccidioides brasiliensis* in its mycelial form and other pathogens. In addition, armadillo hunting is a very common practice in these regions, which makes them susceptible to contracting mycosis and developing the disease. Due to the lack of mandatory reporting of cases, there are no accurate references on the disease, and data collection for epidemiological understanding is carried out in case studies, hospital information, and the Unified Health System (SUS).^{6,8}

This study seeks to understand the clinical and epidemiological profile of Paracoccidioidomycosis (PCM) in an endemic region of Piauí, where the disease is underreported and little investigated. The absence of mandatory reporting makes it difficult to obtain accurate data, hindering prevention and treatment strategies. The analysis of cases in a reference center contributes to improve epidemiological surveillance and guide control measures.

METHODS

This is a retrospective, quantitative-descriptive study that aims to examine the characteristics of a group: its distribution by age, gender, origin, educational level, income level, physical health status, and other variables. One of its most significant characteristics is that it allows for a standardized data collection technique.⁹

This study was conducted between September and November 2023 at a hospital specializing in tropical diseases, located in the municipality of Teresina, in the state of Piauí, which provides care to the population through an agreement with the Unified Health System (SUS), where a wide range of infectious and parasitic diseases are treated, including PCM.

Thus, all patients affected by PCM who had been hospitalized in the last 5 years at a referral hospital in the city of Teresina, Piauí, participated in the study. According to information collected at the hospital where the study was conducted, an average of 10 patients are hospitalized annually. Therefore, for this research, all medical records of patients hospitalized with a diagnosis of PCM were used, totaling 20 medical records for data collection. It is worth noting that, since the intention was to work with the total sample, it was unnecessary to perform a sample calculation.

The study included medical records in which patients had a final diagnosis of PCM, without restriction of gender, including young people, adults, and the elderly, with a date of admission from October 2018 onwards, with complete hospitalization information. Medical records in which the information was incomplete were excluded.

A form created by the researchers was used as a data collection tool, which underwent pretesting with three medical records, where it was evaluated and improved. The data obtained were organized in an Excel® spreadsheet and subsequently transferred to a statistical program, which resulted in the construction of graphs and tables. We opted to use the Statistical Package for the Social Sciences (SPSS) version 28, which is available for purchase.

For the descriptive statistical analysis of the data, we used SPSS® version 28 to calculate the absolute and relative frequencies (%) of the categorical variables. Due to the small sample size, no inferential tests were

applied. In parallel, descriptive statistics made it possible to identify relevant clinical and epidemiological patterns of PCM.

To analyze the association between categorical variables, Fisher's exact test was used, considering the small sample size of the study. This test proved to be adequate because it does not require large samples and offers greater statistical precision in the analysis of contingency tables with small frequencies.

The study was submitted to the Research Ethics Committee of the State University of Piauí (REC) and began after approval, under opinion No. 6,190,978 and the Certificate of Ethical Presentation and Appraisal (CAAE): 71167423.4.0000. 5209, approved on July 19, 2023, in accordance with Resolution No. 466, of December 12, 2012, of the National Health Council (CNS).

For data collection, all patients involved in the study were guaranteed anonymity, and for this purpose, their names were not disclosed on the collection forms. We emphasize that, in accordance with CNS Resolution No. 466/2012, the Research Ethics Committee (REC) waived the application of the IC, considering the low risk and the use of anonymized retrospective data. A formal justification was prepared and approved by the REC, guaranteeing the confidentiality and privacy of patients.

RESULTS

A total of 2,488 medical records of patients admitted to the hospital with various diseases were reviewed between October 2018 and September 2023. Among the medical records analyzed, 26 diagnostic hypotheses of PCM were identified. Of these, 20 were confirmed as positive through histopathological examination of sputum. The number of medical records analyzed per year, with suspected and confirmed cases of PCM, is shown below (Figure 1).

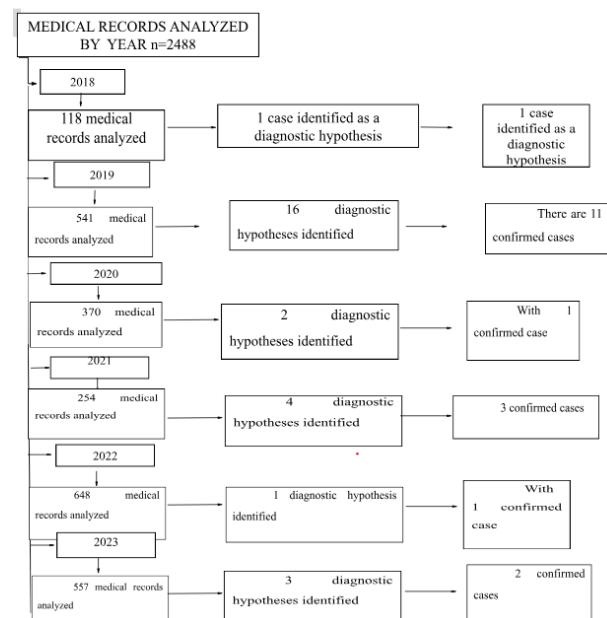


Figure 1. Flowchart showing the distribution of the number of medical records analyzed from 2018 to 2023.

Given the clinical and epidemiological characteristics presented in the study sample, it was evident that males were the only ones affected (100%). The dominant age group was between 30 and 60 years old (60%), and in the sample studied, all cases were male (100%). Regarding the sociodemographic profile, most patients (60%) were between 30 and 60 years old, came from rural areas of the state of Piauí, had incomplete elementary school education, a monthly income of 1 to 2 minimum wages, and worked in agriculture (60%) (Table 1).

Table 1. Sociodemographic characteristics of patients diagnosed with PCM at a public referral hospital in Teresina, Piauí, 2023 (N=20).

Variable	N (%)
Gender	
Male	20 (100)
Female	0
Age at Diagnosis	
Up to 30 years	7 (35)
30 to 60 years old	12 (60)
Over 60 years old	1 (5)
State of Origin	
Maranhão	2 (10)
Pará	1 (5)
Piauí	17 (85)
Residential Area	
Rural	19 (95)
Urban	1 (5)
Education	
No schooling	2 (10)
Incomplete elementary school education	10 (50)
Complete elementary school education	4 (20)
Incomplete high school education	2 (10)
Complete high school education	2 (10)
Month income	
Less than 1 minimum wage	1 (5)
Between 1 and 2 minimum wages	19 (95)
Profession	
Retired	1 (5)
Self-employed	2 (10)
Student	1 (5)
Farmer	12 (60)
Driver	1 (5)
Bricklayer	1 (5)
Fisherman	1 (5)
Rural producer	1 (5)

Analysis of the disease history revealed that paracoccidioidomycosis (PCM) manifested predominantly in the chronic form (55%), with an equal distribution between focal and multifocal lesions (50% each). It was found that the time of onset of symptoms ranged from 3 to 6 months in 60% of cases, accompanied by the presence of secretion in the lesions (60%) and weight loss of up to 15 kg (Table 2).

Table 2. Clinical characteristics of patients diagnosed with PCM at a public referral hospital in Teresina, Piauí, 2023 (N=20).

Variable	N (%)
Clinical Form of PCM	
Acute/Subacute	7 (35.0)
Chronic	11 (55.0)
Not reported	2 (10.0)
Extent of Injury	
Focal	10 (50.0)
Multifocal	10 (50.0)
Time of Lesion Appearance	
Up to 3 months	4 (20.0)
From 3 to 6 months	6 (30.0)
From 6 months to 1 year	2 (10.0)
More than 1 year	1 (5.0)
Not reported	7 (35.0)
Presence of Secretion	
No	8 (40.0)
Yes	12 (60.0)
Weight Loss	
No	2 (10.0)
Yes	18 (90.0)
Weight Reduction	
Up to 15 kilograms	6 (33.4)
From 15 to 30 kilograms	0
Over 30 kilograms	1 (5.5)
Not specified	11 (61.1)

The main regions of the body affected by PCM lesions were identified as the respiratory tract (pharynx, lungs, larynx) as the most affected, followed by the oral cavity (hard palate, soft palate, lips), cervical region, axillary region, testicles, inguinal region, skin, and upper and lower limbs (Figure 2).

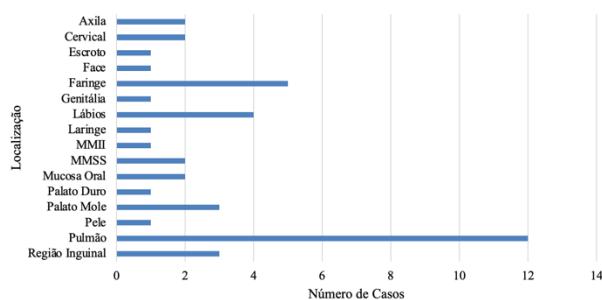


Figure 2. Location of the lesion in patients diagnosed with PCM at a public referral hospital in Teresina, PI, 2023 (N=20).

Regarding the pharmacological treatment of PCM, the antifungal drugs itraconazole and amphotericin B were the main drugs used. Other drugs such as ambroxol, ceftriaxone, sulfamethoxazole+trimethoprim (SMZ+TMP), and azidothymidine (AZT) were used to manage secondary conditions or associated complications (Figure 3).

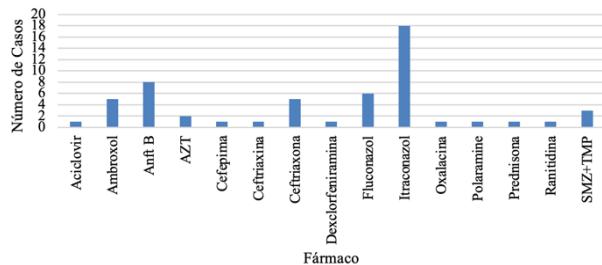


Figure 3. Drugs used in the treatment of patients diagnosed with PCM in a public referral hospital in Teresina, PI, 2023 (N=20).

DISCUSSION

Among the 2,488 medical records analyzed, only 20 cases were confirmed between October 2018 and September 2023. It can be seen that in 2019 there was a significant increase in the number of cases, with a significant decrease the following year, precisely the year the Covid-19 pandemic broke out. It can be assumed that there was underreporting, since PCM, in addition to not being mandatory for reporting, has symptoms similar to other diseases, including the coronavirus.

Furthermore, the study demonstrated that 100% of patients affected by PCM are male. Studies indicate that in the adult population there is a ratio of 5.4 to 10 infected men for every woman. This occurs due to the action of the female hormone estradiol 17-β (hormone that regulates menstruation), which inhibits the transformation of mycelium or conidia into yeast (pathogenic form), preventing the development and progression of the disease, making the disease predominantly male.^{4,10}

Concurrently, the age group most affected among the cases investigated is between 30 and 60 years old, since individuals frequently affected by the pathogen are in the most productive phase of their lives because they are exposed to the pathogen in the daily exercise of their work activities.⁴

Furthermore, the results of the study showed that 95% of affected patients are residents of rural areas, while 5% reside in urban areas, and more than half of those residing in rural areas are farmers, since one of the main risk factors for contracting the disease is exposure to soil contaminated by armadillo excrement containing PCM conidia in rural areas, making it an occupational disease for farmers in endemic regions.⁷

In addition, research has shown that the clinical manifestations of the disease present in acute/subacute (juvenile) and chronic forms, with the latter being more prevalent (more than 50% of confirmed cases). Studies show that the juvenile clinical form is prevalent in children and young adults, who have an inadequate Th2 cell response to control fungal infection. The chronic form manifests in 80 to 95% of cases, affecting

individuals of productive age (after the third decade of life).¹¹

Approximately 60% of patients suffering from the chronic form of the disease develop lung lesions. Apparently, this sequela is due to continuous stimulation of fungal antigens and subsequent activation of the immune system and changes in its repair mechanisms. Although long-term antifungal therapy is effective in treating active PCM, it does not seem to affect the development of pulmonary fibrosis.¹²

From a clinical perspective, the research showed that the drugs most commonly used to treat PCM were Itraconazole, Fluconazole, Amphotericin B, and Sulfamethoxazole/Trimethoprim, also known as Cotrimoxazole. According to studies, until the 1940s, there were not enough therapeutic drugs to treat the disease, which is why it was considered fatal. Since then, several therapeutic drugs have been used and have shown promising results. According to clinical research, the drugs currently available are sulfonamides (including cotrimoxazole), amphotericin B deoxycholate, ketoconazole, and triazole derivatives (itraconazole, fluconazole, voriconazole).¹³

Studies have shown that itraconazole is 100 times more active than ketoconazole against PCM, as it is more effective and tolerable, and is considered the drug of choice for controlling patients with lower risk of death and lower recurrence rates. Voriconazole is also a second-generation triazole derivative that has been shown to be as effective as itraconazole, but has been reported to be less safe. Another option is fluconazole, used in cases of elevated liver enzymes, hypersensitivity to sulfonamides or amphotericin B, and neurococcidioidomycosis. Intravenous fluconazole, voriconazole, and itraconazole are available in some countries. In Brazil, itraconazole is used as a long-term therapeutic measure.^{13,14}

However, these antifungals have several disadvantages, such as: (i) Azoles have fungistatic, but not fungicidal, effects against *P. brasiliensis* in vivo; (ii) Although azoles are considered safe and effective, treatment is prolonged and its efficacy is variable, ranging from a few months to a year, depending on the patient's condition; (iii) Amphotericin B is highly nephrotoxic.¹²

PCM is a disease that remains neglected by public health, despite being associated with high morbidity and mortality rates. There is still a need for epidemiological studies in areas where the disease is endemic. The above data identified the epidemiological profiles and clinical aspects of populations affected by PCM, which allows health surveillance to create preventive measures aimed primarily at the most vulnerable groups affected by this disease.⁸

Systemic mycoses represent a public health problem in Brazil due to the difficulties in differentiating the

symptoms of PCM, as they resemble other pathologies, in addition to the diagnosis and treatment of the disease, which corroborates the high morbidity and mortality rates. The data obtained in this study contribute to a better understanding and perception of the epidemiology of PCM in endemic areas, thus demonstrating the need for public health policies that seek better strategies for the diagnosis and treatment of PCM.

The main limiting factors were the small sample size, which restricts the generalization of the findings. The retrospective nature and dependence on medical records may have led to data loss and underreporting. In addition, the absence of mandatory reporting of PCM in Brazil makes it difficult to estimate the disease more accurately. Despite this, the study contributes to the knowledge of PCM in a little-explored endemic region.

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AUTHORS' CONTRIBUTIONS

Mauro Roberto Biá da Silva research supervisor, contributed to the structuring of the research, made corrections at all stages, structured the methodology, guided the construction of the research form and data collection. **Francisca Aline Amaral da Silva** co-supervisor of the research, supported the supervisor, proofread the text, made corrections at all stages, and corrected the references. **Joice Pereira Carvalho** research assistant, contributed to the writing of the research, construction of the research form, data collection, and interpretation of the collected data.

All authors approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.

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