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Original Article

Impact of Covid-19 on the profile of mycoses reported in a public hospital in Paraíba, Brazil

Impacto da Covid-19 no perfil das micoses reportadas em um hospital público da Paraíba, Brasil
Impacto de la Covid-19 en el perfil de las micosis notificadas en un hospital público de Paraíba, Brasil

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ABSTRACT

Background and Objectives: Covid-19 can lead to critical immunological conditions, requiring hospitalization in intensive care units. The risk of fungal co-infections increases in these patients, especially if they are on mechanical ventilation, using invasive devices and/or broad-spectrum antibiotics. Secondary fungal infections can worsen the symptoms of the disease, make prognosis and treatment more difficult, and increase mortality and hospital stay rates. Thus, the objective of the present study was to evaluate the influence of the Covid-19 pandemic on the distribution of fungal infections in patients admitted to a university hospital in Paraíba during the period from 2020 to 2022. **Methods:** A total of 456 medical records from the period between March 2020 and July 2022 sent to the Mycology department with suspected fungal infection were analyzed. **Results:** Of the medical records evaluated, 120 presented infection by some fungus. Only 17 medical records came from the Covid ICU and 14 of them were positive for some mycosis. The *Candida* genus stood out as the most prevalent. It was identified in more than 90% of patients evaluated in the general group and in 85.7% of patients admitted to the Covid ICU. *Aspergillus* spp., *Rhizopus* spp. and *Mucor* spp. were also reported to a lesser extent. **Conclusion:** The profile of hospital fungal infections was impacted by the pandemic, since a high percentage of Covid ICU patients affected by mycoses was observed in comparison to patients in other departments.

Keywords: *Fungal Infections. Co-infection. Intensive Care Unit. Healthcare-Associated Infection.*

RESUMO

Justificativa e Objetivos: A Covid-19 pode levar a uma condição imunológica crítica, com necessidade de internação em unidades de terapia intensiva. O risco de coinfecções fúngicas aumenta nesses pacientes, sobretudo se estiverem sob ventilação mecânica, fazendo uso de dispositivos invasivos e/ou antibióticos de largo espectro. Infecções fúngicas secundárias podem agravar os sintomas da doença, dificultar o prognóstico e o tratamento e elevar as taxas de mortalidade e permanência hospitalar. Dessa forma, o objetivo do presente trabalho foi avaliar a influência da pandemia de Covid-19 na distribuição de infecções fúngicas em pacientes internados em um hospital universitário na Paraíba no período de 2020 a 2022. **Métodos:** Foram analisados 456 prontuários do período entre março de 2020 e julho de 2022 encaminhados ao setor de Micologia com suspeita de infecção fúngica. **Resultados:** Dos prontuários avaliados, 120 apresentavam infecção por algum fungo. Apenas 17 prontuários advinham da UTI Covid e 14 deles foram positivos para alguma micose. O gênero *Candida* destacou-se como o mais prevalente, sendo identificado em mais de 90% dos pacientes avaliados no conjunto geral, e em 85,7% dos pacientes internados na UTI Covid. Também foram reportados, em menor frequência, *Aspergillus* spp., *Rhizopus* spp. e *Mucor* spp. **Conclusão:** O perfil das infecções fúngicas hospitalares foi impactado pela pandemia, visto que foi observada uma alta porcentagem de pacientes da UTI Covid acometidos por micoses, em comparação com os pacientes dos demais setores.

Descritores: *Infecções Fúngicas. Coinfecção. Unidade de Terapia Intensiva. Infecção Relacionada à Assistência à Saúde.*

RESUMEN

Justificación y Objetivos: La Covid-19 puede provocar estados inmunológicos críticos que requieren hospitalización en unidades de cuidados intensivos. El riesgo de coinfecciones fúngicas aumenta en estos pacientes, especialmente si reciben ventilación mecánica, utilizan dispositivos invasivos y/o antibióticos de amplio espectro. Las infecciones fúngicas secundarias pueden agravar los síntomas de la enfermedad, dificultar el pronóstico y el tratamiento y aumentar las tasas de mortalidad y la estancia hospitalaria. Así, el objetivo del presente estudio fue evaluar la influencia de la pandemia de Covid-19 en la distribución de las infecciones fúngicas en pacientes ingresados en un hospital universitario de Paraíba durante el período de 2020 a 2022. **Métodos:** Se analizaron 456 historiales médicos del período comprendido entre marzo de 2020 y julio de 2022 enviados al departamento de Micología con sospecha de infección fúngica. **Resultados:** De los historiales evaluados, 120 presentaron infección por algún hongo. Sólo 17 historias clínicas procedían de la UCI Covid y 14 de ellas fueron positivos para alguna micosis. El género *Candida* se destacó como el más prevalente, identificándose en más del 90% de los pacientes evaluados en el grupo general, y en el 85,7% de los pacientes ingresados en la UCI Covid. También se reportaron, en menor medida, *Aspergillus* spp. y *Rhizopus* spp. y *Mucor* spp. **Conclusión:** El perfil de las infecciones fúngicas hospitalarias fue impactado por la pandemia, ya que se observó un alto porcentaje de pacientes de la UCI Covid afectados por micosis en comparación con los pacientes de otros sectores.

Palabras Clave: *Infecciones fúngicas. Coinfección. Unidad de Cuidados Intensivos. Infección Asociada a la Atención Sanitaria.*

INTRODUCTION

In December 2019, a viral outbreak began in China, causing a respiratory illness similar to pneumonia. After genomic analysis, the causative agent was identified as a novel coronavirus called SARS-CoV-2. Initially, it caused mild symptoms in healthy people but could become severe in immunocompromised individuals.[1-2] On March 11, 2020, due to the rapid global spread of the respiratory syndrome caused by SARS-CoV-2, the World Health Organization (WHO) declared the Covid-19 pandemic.[3]

During the virus's incubation period, which lasts between two and 14 days, more viral particles are produced, ready to infect other hosts.[4] Although the most common symptoms are similar to those of other viral illnesses (dry cough and fever), they can worsen to the point of requiring hospitalization. This critical manifestation of Covid-19 can be explained by the aggressive inflammatory response caused by the release of pro-inflammatory mediators and the immunosuppression caused by the reduction in CD4+ T and CD8+ T lymphocytes in patients.[5-6] This critical immunological condition, combined with intensive care unit (ICU) admission, increases the risk of fungal coinfections in these patients, especially if they are on mechanical ventilation, using catheters and broad-spectrum antibiotics.[7]

Therefore, fungal coinfections in the context of Covid-19 deserve further study, as these microorganisms generally have the potential to aggravate disease symptoms, complicate prognosis and treatment, and increase mortality rates and length of hospital stay.[5] Candidemia, mucormycosis, and aspergillosis deserve special mention as they are the three most frequently reported secondary infections in Covid-19 patients.[6,8-9] Therefore, studies on this topic are necessary to understand the profile of the most present microorganisms in hospital environments, and to develop strategies and solutions from a public health perspective.

The objective of this study was to evaluate the influence of the Covid-19 pandemic on the distribution of fungal infections in patients admitted to a university hospital in the state of Paraíba from 2020 to 2022.

METHODS

Study location

The study was conducted at a public university hospital in the city of João Pessoa, Paraíba, Brazil.

Study design and period

This is a descriptive, cross-sectional, retrospective study. Data were collected from March 2020 (the beginning of the Covid-19 pandemic) to July 2022 (when the Covid ICU was closed at the hospital).

Data source

Data were collected from all medical records with suspected fungal infections of patients admitted to the ICU (general, neonatal, pediatric, and Covid) and other hospital departments and referred to the Mycology Department of the Clinical Analysis Laboratory Unit. Data collection included the date of sample collection, department of origin, patient sex and age, type of sample collected, result, and microorganism isolated. Medical records without suspected fungal infection were excluded from the study analysis.

Statistical Analysis

Data were tabulated using the *Microsoft Excel 2007*® software to enable descriptive analysis of the fungal infection profile.

Ethical aspects

The study was submitted to the Research Ethics Committee of the Center of Medical Sciences at the Universidade Federal da Paraíba (CAAE 47435121.0.0000.8069), and approved on July 1, 2021, under opinion number 4.820.953, in accordance with recommendations of Resolution 466/2012 of the National Health Council.

RESULTS

In total, data were collected from 456 medical records of patients with suspected fungal infections sent to the Mycology department of the Clinical Analysis Laboratory Unit. Of these, 222 were from female patients and 234 from male patients male, mean age of 41.3 years. Of the 456 medical records, 120 tested positive for some form of mycosis, with some fungus identified (Table 1).

Table 1. Distribution of fungi causing mycoses in patients admitted to a public university hospital in João Pessoa, Paraíba (2020-2022).

Fungus	N (%)	Priority level according to the World Health Organization[9]
Aspergillus flavus	2 (1.7)	-
Aspergillus niger	1 (0.8)	-
Candida albicans (or suggestive of *Candida albicans)*	60 (50)	Critical
Candida parapsilosis	26 (21.7)	High
Candida spp. (or suggestive of *Candida* spp.)	8 (6.7)	-
Candida tropicalis	15 (12.5)	High
Cryptococcus neoformans	1 (0.8)	Critical
Unidentified yeast	2 (1.7)	-
Mucor spp.	2 (1.7)	High
Rhizopus spp.	1 (0.8)	High
Trichosporon spp.	1 (0.8)	-
Unspecified zygomycete	1 (0.8)	High

The isolated fungi came from various types of biological samples; the most common was urine, followed by blood samples (Table 2).

Table 2. Origin of samples positive for mycoses in patients admitted to a public university hospital in João Pessoa, Paraíba (2020-2022).

Biological sample	Fungus	N (%)
Liver abscess	*Candida parapsilosis*	1 (0.8)
Unidentified sample	*Candida albicans*	1 (0.8)
Tracheal aspirate	*Aspergillus flavus*	1 (0.8)
	Candida albicans	1 (0.8)
Peripancreatic collection	*Candida* spp.	1 (0.8)
Maxillary sinus crust	Zygomycete	1 (0.8)
Sputum	*Candida albicans*	2 (1.6)
	Candida parapsilosis	1 (0.8)
	Trichosporon spp.	1 (0.8)
Fragment of a facial lesion	*Mucor* spp.	2 (1.6)
Fragment of the maxillary sinus	*Candida parapsilosis*	1 (0.8)
Bronchoalveolar fluid	*Candida albicans*	3 (2.4)
	Candida parapsilosis	3 (2.4)
Tracheal lavage	*Candida albicans*	1 (0.8)
Cerebrospinal fluid	*Cryptococcus neoformans*	1 (0.8)
Ascitic fluid	Suggestive of *Candida* spp.	1 (0.8)
Pleural fluid	*Candida albicans*	1 (0.8)
Nasal mucosa and ethmoid and maxillary secretion	*Aspergillus flavus*	1 (0.8)
Blood	*Candida albicans*	8 (6.6)
	Candida parapsilosis	5 (4.0)
	Candida tropicalis	4 (3.2)
	Unidentified yeast	1 (0.8)
Tracheal secretion	*Aspergillus niger*	1 (0.8)
	Candida albicans	5 (4.0)
	Candida tropicalis	2 (1.6)
Vaginal secretion	*Candida tropicalis*	1 (0.8)
Skin lesion swab	*Candida tropicalis*	1 (0.8)
Necrotic tissue from the nasal cavity	*Rhizopus* spp.	1 (0.8)
Urine	*Candida albicans* (or suggestive of *Candida albicans*)	38 (31.7)
	Candida parapsilosis	17 (14.1)
	Candida spp.	6 (5.0)
	Candida tropicalis	7 (5.8)
	Unidentified yeast	1 (0.8)

Of the 456 medical records analyzed, 229 belonged to patients admitted to the ICU: 17 from the Covid ICU and 212 from the non- Covid ICU (general, neonatal, and pediatric). Among the 212 in the non- Covid ICU, 65 (30.7%) tested positive for some form of mycosis: 57 in the general ICU, five in the neonatal ICU, and three in the pediatric ICU. In the Covid ICU, 14 (82%) of the 17 medical records tested positive for fungal infection (Table 3).

Table 3. Distribution of fungi causing mycoses in intensive care units of patients admitted to a public university hospital in João Pessoa, Paraíba (2020-2022).

Sector of origin	Fungus	N (%)
General ICU	*Aspergillus niger*	1 (1.26)
	Candida albicans (or suggestive of *Candida albicans*)	27 (34.18)
	Candida parapsilosis	17 (21.5)
	Candida spp. (or suggestive of *Candida* spp.)	4 (5.1)
	Candida tropicalis	6 (7.6)
	Mucor spp.	2 (2.5)
Covid ICU	*Aspergillus flavus*	1 (1.26)
	Candida albicans	7 (8.9)
	Candida parapsilosis	1 (1.26)
	Candida tropicalis	4 (5.1)
	Unidentified yeast	1 (1.26)
Neonatal ICU	*Candida albicans*	3 (3.8)
	Candida parapsilosis	2 (2.5)
Pediatric ICU	*Candida albicans*	1 (1.26)
	Candida parapsilosis	1 (1.26)
	Candida tropicalis	1 (1.26)

DISCUSSION

Fungal infections are a major public health problem that demands greater attention and resources from health authorities. Although medical advances are being made to treat other diseases, cases of invasive fungal infections are steadily increasing, while access to quality diagnostics and treatment remains severely limited. Individuals with weakened immunity due to pre-existing health problems (autoimmune diseases, cancer, diabetes, among others) and those taking broad-spectrum antibiotics and/or corticosteroids are more prone to infections by pathogenic fungi.[9]

Furthermore, although hospitals are environments dedicated to the treatment and well-being of patients, they tend to be places prone to secondary infections.[10] Nevertheless, the sudden emergence of Covid-19 and its frenetic spread have forced hospitals around the world to adapt to accommodate those affected by the disease. The invasive methods used in the treatment of ICU patients, especially in Covid ICUs, such as intubation,

catheterization, mechanical ventilation, and the use of multiple antibiotics, combined with prior immunosuppression, make this ward a primary source for approximately 25% of all hospital infections.[11] Therefore, the creation of Covid wards favored the incidence of fungi compared to other wards and increased the morbidity and mortality of hospitalized patients.12 These findings are corroborated by the data found in this study. A positive result for some mycosis was found in 14 (82%) out of the 17 medical records from the Covid ICU, while only 41 (18%) of the 227 medical records from non-ICU wards and 65 (30.7%) of the 212 medical records from non- Covid ICUs obtained this same result.

The *Candida* genus is certainly the most documented in hospital-acquired infections, accounting for approximately 80% of all mycoses in this setting, and its incidence is 10 to 20 times higher in ICUs than in other areas.[13-14] In this study, almost 91% of reported fungal infections were caused by *Candida* spp. (50% by *C. albicans*, 21.7% by *C. parapsilosis*, 12.5% by *C. tropicalis*, and 6.7% by unidentified species). In the Covid ICU, in particular, this study found that infections caused by *Candida* spp. accounted for 85.7% of mycosis diagnoses. This reinforces the idea that this hospital area, like others, has great potential for the emergence and transmission of fungal coinfections.[12]

As observed in this study, *Candida albicans* is the prominent species among mycoses seen in hospital records during the pandemic period evaluated. It appeared in 50% of diagnoses (n=60), the majority (n=38) of which were from urine samples. This species is in the WHO's critical priority group. Due to its virulence factors, it can cause infections of mucous membranes such as the oropharynx, esophagus and vagina, or invade internal organs and the bloodstream, causing invasive candidiasis, which has a high mortality risk (20% to 50%) and particularly affects immunocompromised individuals.[8-9,15]

Although *Candida albicans* is the most commonly isolated species, non-albicans species have recently emerged, among which *C. parapsilosis* and *C. tropicalis* are the most frequently reported.[16] According to the WHO, both species are in the high-priority group and, like the others, can cause invasive infections with a significant mortality risk.[9] A study in Portugal evaluated the incidence of *Candida* in a cancer hospital over six years, and among 119 isolates, *C. parapsilosis* represented approximately 20% of infections caused by *non-albicans Candida*, followed by *C. tropicalis* with 8.4%.[17] Consistent with this information, in that study, 21.7% of all mycoses were caused by *C. parapsilosis* and 12.5% by *C. tropicalis*.

Furthermore, it is important to highlight that in 6.7% of *Candida* spp. diagnoses in the hospital under study, the species was not identified. This suggests underreporting of other potential species of concern, such as *Candida auris*. This pathogen has caused outbreaks in many countries in recent years and its incidence has increased during the pandemic. In Brazil, there have been three outbreaks of infection by this agent. The first isolated case in an ICU patient occurred in a hospital in Salvador, Bahia, Brazil, and was reported in December 2020.[18] This species is in the WHO's critical priority group because it causes invasive candidiasis with a high mortality rate and is resistant to many antifungals.[9]

Aspergillosis have also been identified in immunocompromised patients and in association with Covid-19.[12,19] *Aspergillus* spp. causes an opportunistic infectious disease that commonly affects hospitalized individuals. Conidia of this fungus can be found on clothing, ventilation systems, and other objects, where they are prone to inhalation by a host. Therefore, patients on mechanical ventilation, especially those already infected with Covid-19, become vulnerable to this microorganism and increase their chances of death.[19] In a study conducted from February to December 2020 in a Brazilian referral hospital, the authors observed eight cases of fungal coinfection in Covid-19 patients, three of which (37.5%) were cases of aspergillosis.[20] In our study, only one patient (7%) in the Covid ICU was diagnosed with pulmonary aspergillosis.

Not unlike this, mucormycosis (or zygomycosis), which can be caused by zygomycetes such as *Mucor* spp. and *Rhizopus* spp., although less frequent, also threatens patients with underlying diseases, those undergoing glucocorticoid treatment and/or invasive medical interventions when associated with Covid-19.[19] In June 2021, India recorded more than 28,000 cases of mucormycosis in the midst of the pandemic, in addition to having confirmed almost half of the total Covid-19 cases.[21] The country also has the largest number of diabetic adults in the world, which is associated with the high incidence of mucormycosis, as this comorbidity is one of the main risk factors.[12,19] According to the Ministry of Health, Brazil recorded 99 cases of mucormycosis in 2021 and 14 cases in 2022, corroborating the idea that based on the latest data available (2021-2022), the incidence of this disease is not high.[22] This information can elucidate the fact that in our study only 0.83% (n=1) of the general diagnoses of fungal infections were caused by *Rhizopus* spp. and an unspecified zygomycete, and approximately 1.7% (n=2) were caused by *Mucor* spp. (from the general ICU), although fungi of the order Mucorales are listed in the WHO high-priority group.[9]

The other fungi found in this study had a very low incidence in the hospital as a whole (0.83% *Trichosporon* spp., 0.83% *Cryptococcus neoformans*; n=1 for both) and no incidence in the ICUs. *Trichosporon* spp. is an opportunistic yeast that can be

found as a cause of sepsis in neutropenic individuals subject to invasive devices and drug treatments. Therefore, it may contribute to a worse prognosis for patients already suffering from Covid-19.[23] In a study conducted between July and September 2020, the incidence of fungemia caused by a species of *Trichosporon* was reported in a hospital in Salvador, Bahia. Of the 183 patients admitted to the Covid ICU, seven (3.8%) had fungemia caused by *Trichosporon* spp., and 18 (9.8%) by *Candida* spp.[23] In agreement with this study, only one case of *Trichosporon* spp. was found in our study, and the patient did not come from the ICU.

Cryptococcus neoformans is an opportunistic yeast that can cause invasive cryptococcosis when inhaled and disseminated through the bloodstream to internal organs. The high mortality rate of this species, especially in patients with HIV, immunocompromised individuals, with autoimmune diseases and decompensated liver cirrhosis, also places it in the WHO's critical priority group.[9] Co-infection with Covid-19 is scarcely documented in the literature, perhaps due to low incidence or possible underreporting. However, among 716 Covid-19-positive individuals followed in a study, one case was reported in Brazil.[24] Only one case of *C. neoformans* was reported in the present study, but the patient was not in the Covid ICU, indicating a low incidence of this fungus during the Covid-19 pandemic at the hospital under study.

A limitation of this study was the lack of information recorded in some patients' medical records. In addition, because the researchers chose to conduct the study exclusively in critical care settings (ICUs), the sample size was smaller than expected, which constituted another limitation of the study.

Given our findings, the importance of studying fungal infections in hospital settings is clear. Furthermore, our research data, consistent with the literature, also showed that during the pandemic, these fungal infections plagued hospitalized individuals, particularly those with Covid-19, as they were immunosuppressed and/or using invasive devices during ICU treatment. Therefore, we conclude that the profile of hospital-acquired fungal infections was impacted by the pandemic in the public hospital under study, as it resulted in a higher incidence of Covid ICU patients with fungal infections compared to patients in other wards.

TEXTO.

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AUTHORS' CONTRIBUTIONS

Mariana de Assis Valverde contributed to the literature search, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Natan Gomes Emmanuel** contributed to the literature search, writing the abstract, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review, and statistics. **Ana Paloma Tavares** contributed to writing the abstract, interpretation and description of results, review, and statistics. **Wallace Felipe Blohem Pessoa** contributed to project administration, bibliographic research, writing the abstract, introduction, methodology, discussion, interpretation and description of results, conclusions, review and statistics.

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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