

Pulmonary candidiasis in immunocompromised patients seen at Befelatanana University Hospital from 2018 to 2019

Zafindrasoa Domoina Rakotovao-Ravahatra^{*1}, Nambiniavo Marianne Ranoroahasimanana², Fenosoa Anita Tsatoromila³, Zakaso Mbololona Ravaoarisaina⁴, Fidiniaina Mamy Randriatsarafara⁵, Andriamiadana Luc Rakotovao⁶, Lala Rasoamialy-Soa Razanakolona⁷

¹Laboratory of Joseph Raseta Befelatanana University Hospital, Antananarivo, Madagascar

²Laboratory of Joseph Raseta Befelatanana University Hospital, Antananarivo, Madagascar

³National Center for Blood Transfusion in Antananarivo, Madagascar

⁴Laboratory of the University Hospital of Ambohimandra, Antananarivo, Madagascar

⁵National Institute of Public and Community Health in Antananarivo, Madagascar

⁶Biological Hematology, Laboratory of Joseph Raseta Befelatanana University Hospital, Antananarivo, Madagascar

⁷Parasitology-Myology, National HIV/AIDS Reference Laboratory Service at Analakely, Antananarivo, Madagascar

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Abstract

The Candidiasis occupies an increasingly important place in infectious pulmonary diseases in recent decades. The objectives of this study were to determine the incidence of yeast *Candida spp* in pulmonary samples, to describe the clinical and socio-demographic characteristics of these pulmonary infections and to propose suggestions to clinicians and biologists who analyze these pulmonary samples. This is a prospective and descriptive study from April 2018 to March 2019 in the laboratory of Joseph Raseta Befelatanana University Hospital. All *Candida spp* yeast positive pulmonary samples were identified by filamentation testing. The data was entered on the Epi-info 3.5.2 software. For a period of one year, 17 of the 107 pulmonary sampling (15.9%) were positive for yeasts of the genus *Candida spp*. Of these yeasts, 82.4% are represented by the species *Candida albicans*. The patients aged 40 and over (8.4%), the men (8.4%), the patients with pneumopathy (10.3%) and the patients hospitalized in the surgical resuscitation department (7.5%) were most affected by *Candida albican*. Simultaneous bacteriological examination showed a predominance of *Acinetobacter* bacteria. This study has highlighted the pertinence of mycological examination of any pulmonary sampling in the hospitalized and immunocompromised patients. The use of specific culture media for mycotic pathogens will increase the positivity of the mycological examination.

*Corresponding Author: Zafindrasoa Domoina Rakotovao-Ravahatra ✉ ravahatradomoina@yahoo.fr

Introduction

Mycotic pulmonary infections are becoming more and more common in hospitals (Chabasse *et al.*, 2009). Among these mycotic infections, nosocomial candidiasis is becoming more and more frequent. Indeed, 14% of nosocomial pneumopathies in intensive care would be due to yeasts, mainly *Candida* (Azoulay *et al.*, 2001). In Madagascar, few studies concerning pulmonary candidiasis have been performed. In Abidjan, 17.6% of parasitic and mycotic infections were found in bronchial aspiration fluids (Adou-Bryn KD *et al.*, 1999). *Candida* nosocomial pneumopathies are also reported in diabetics or alcoholics, patients with frequent buccal and yeast pharyngeal colonization. Nosocomial pneumopathies to *Candida* also affect subgroups of patients with common factors such as immunosuppression, hospitalization in intensive care or postoperative. In cancer patients on chemotherapy, patients with hematological malignancies, organ transplant recipients, or those infected with HIV, *Candida* pneumonia is a marker of severe damage of the immune system and a particular sensitivity opportunistic infections. The associated contributing factors are represented by therapeutic aplasia, the presence of central catheters, undernutrition or corticosteroid therapy (Azoulay *et al.*, 2001). This study highlights the importance of mycological examination of pulmonary specimens especially in hospitalized and immunocompromised patients. The objectives of this study were to determine the incidence of yeast *Candida spp* in pulmonary samples, to describe the clinical and socio-demographic characteristics of these pulmonary infections and to propose suggestions to clinicians and biologists who analyze these pulmonary samples.

Materials and methods

Type and period of study

This is a prospective and descriptive study at the laboratory of Joseph Raseta Befelatanana University Hospital for a period of one year from April 2018 to March 2019.

Inclusion criterion

This study includes all pulmonary samples of patients who have applied for cyto-bacteriological examination. These pulmonary samples are either sputum, or bronchial aspiration fluids or bronchoalveolar fluids.

Exclusion criterion

This study excludes any non-compliant pulmonary specimens such as salivary specimens and pulmonary specimens contained in a transport medium other than the laboratory vial (sterile red cap vial).

Criterion of positivity

The presence of *Candida spp* colonies in culture and the demonstration of the filamentation of *Candida albicans* yeasts constitute the criterion of positivity of this study.

Dependent and independent variables

The dependent variable is constituted by the positivity of the culture showing yeasts *Candida spp*. The independent variables consist of the type of pulmonary sampling, the gender, the age, the clinical information, the departments, the result of the cyto-bacteriological examination of the pulmonary specimen, the result of the mycological examination of the pulmonary specimen, the result of the filamentation test to differentiate between *Candida albicans* and *non-albicans Candida*.

Limit of the study

This study is limited to biological examinations available in the laboratory of Joseph Raseta Befelatanana University Hospital. Indeed, the culture media used for the mycological examination are the same as for the bacteriological examination. The use of special culture media for mycological examination may increase the positivity rate of *Candida* pulmonary infections. This study was authorized by the Director of Establishment of the University Hospital of Befelatanana and the Department Head of the laboratory before its implementation.

This study respected the notion of anonymity and confidentiality. Data entry and processing has done on the Epi-Info 3.5.2 software.

Results

For a period of one year, 17 of the 107 pulmonary sampling (15.90%) were positive for yeasts of the genus *Candida* (Fig. 1). Of these yeasts, 82.4% are represented by the species *Candida albicans*.

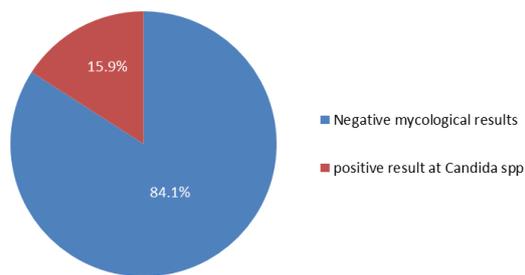


Fig. 1. Incidence of yeasts of the genus *Candida* in pulmonary samples from April 2018 to March 2019.

Concerning the distribution of pathogens found in pulmonary samples, bacteriology and mycology results showed a predominance of *Acinetobacter* bacteria and *Candida albicans* (Fig. 2).

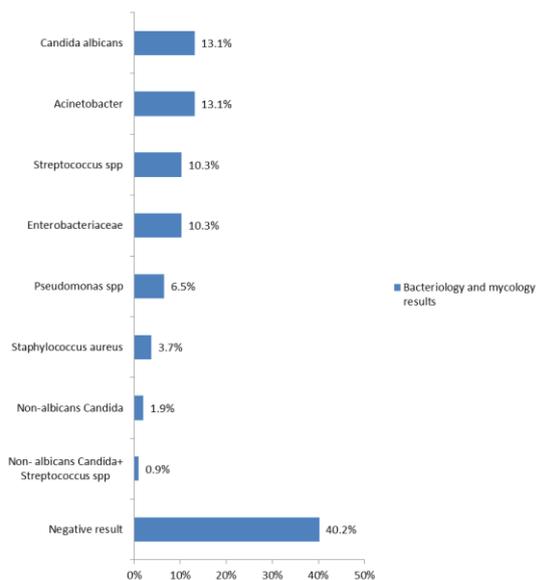


Fig. 2. Distribution of Pathogens found in pulmonary samples from April 2018 to March 2019.

Regarding the distribution of pathogens according to study parameters, the patients aged 40 and over (8.4%), the men (8.4%), the patients with pneumopathy (10.3%) and the patients hospitalized in the surgical resuscitation department (7.5%) were most affected by *Candida albicans* (Fig. 3, 4, 5 and table 1).

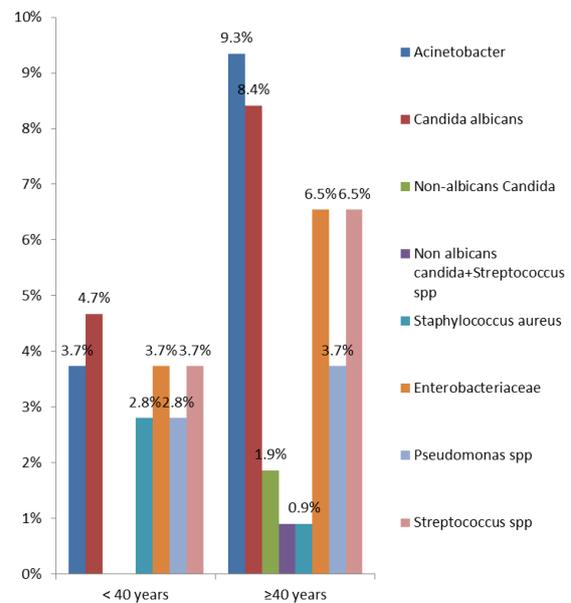


Fig. 3. Distribution of Pathogens found in pulmonary samples by age from April 2018 to March 2019.

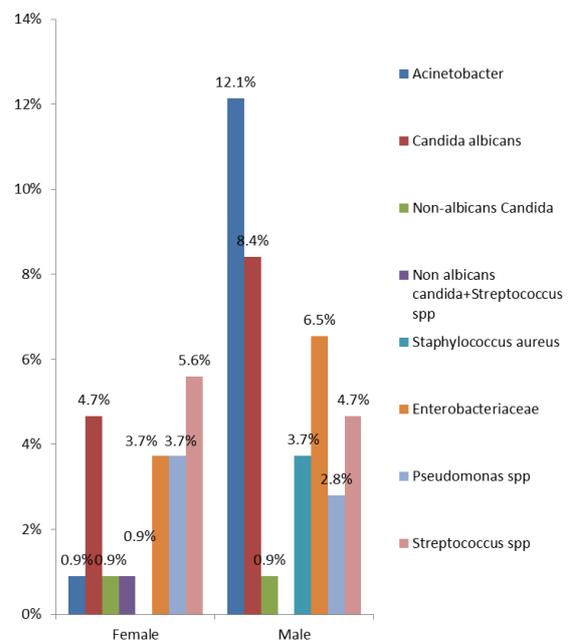


Fig. 4. Distribution of Pathogens found in pulmonary samples by gender from April 2018 to March 2019.

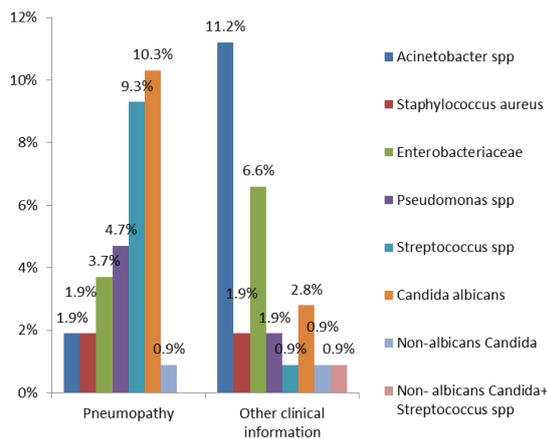


Fig. 5. Distribution of Pathogens found in pulmonary samples by clinical information from April 2018 to March 2019.

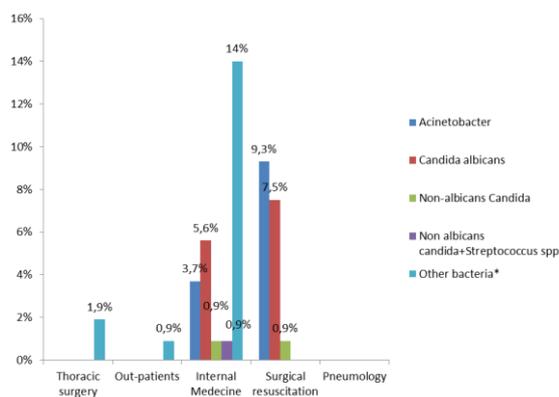


Fig. 6. Distribution of Pathogens found in pulmonary samples by department from April 2018 to March 2019.

*Other bacteria: *Staphylococcus aureus*, *Enterobacteriaceae*, *Pseudomonas spp*, *Streptococcus spp*.

Discussion

This study showed a high incidence of 15.9% of yeasts of the genus *Candida* in lung sample. The incidence of pulmonary candidiasis in our study is comparable to another study in Nepal that found 12.2% of pulmonary candidiasis (Jha *et al.*, 2006). It is true that most yeasts found in pulmonary samples come from tracheobronchial colonization of mycoses from the digestive tract. Nevertheless, in the intensive care unit, *Candida*-positive pulmonary specimens are frequently found beyond the thresholds and are validated to distinguish bronchopulmonary colonization and

infection (Azoulay *et al.*, 2001). Similarly, pulmonary candidiasis are common in immunocompromised patients or on broad-spectrum and extended antibiotics. According to the authors, their presence in lung samples represents either a nosocomial bronchopulmonary infection or a colonization of the tracheobronchial tree which is a risk factor for deep candidiasis and whose repeated research at several sites should be systematic (Zarrinfar *et al.*, 2016).

In this study, the species *Candida albicans* is the most common (82.4% of *Candida spp*). However, other studies currently report the emergence of *Candida non-albicans* that are responsible for nosocomial infections resistant to antifungals such as *Candida auris* (70% *Candida albicans* and 30% *non-albicans Candida*) (Jha *et al.*, 2006). This difference is due to the use of specific culture media such as the specific Sabouraud Dextrose Agar medium that increase the positivity of the culture. Indeed, in our study, we used blood agar, chocolate agar and uriselect. If the Befelatanana laboratory uses specific media for yeasts, the prevalence of *Candida albicans* and non-albicans *Candida* will increase significantly.

Simultaneously, *Acinetobacter spp* was the frequently isolated bacterium in our study and was represented in 13,1% of cases. In other studies, *Haemophilus influenzae* was most represented in 24.79% of cases (Jha *et al.*, 2006). The bacterial etiology may vary from country to country depending on their geographical characteristics.

Regarding age groups, older subjects are more affected by *Candida albicans*. The high frequency of candidiasis in older subjects is probably due to several factors. Indeed, as the age increases, many diseases appear and the patient begins to take drugs that are lifelong drug treatments for some people. These treatments can modify the oropharyngeal flora resulting in the proliferation of yeasts (Laurent *et al.*, 2011).

Similarly, very old people are often immunocompromised and are more vulnerable to metabolic, cancerous and other diseases leading to yeast overgrowth.

Regarding gender, men are more affected than women in this study. This result is similar to another study that also showed a male predominance in 60% of cases. This male predominance is probably due to other conditions associated with candidiasis, which are more common in men (Mjabber *et al.*, 2010).

Regarding clinical information, patients with pneumopathy are most affected by *Candida albicans*. First, the bacterial etiology of pneumopathy must always be diagnosed. Nevertheless mycotic etiology should not be underestimated. The definitive diagnosis is mainly given by histological examination revealing parenchymal invasion by *Candida albicans*. It is true that pulmonary candidiasis is still rare. Nevertheless, a diagnostic error is dangerous for the patient. In fact, pulmonary candidiasis can be complicated by systemic candidiasis, which is very difficult to treat and can be fatal for the patient (Cateau *et al.*, 2012). Otherwise, *Candida*-positive specimens are common in immunocompromised patients or on broad-spectrum and extended antibiotics. Thus, mycological examinations of pulmonary specimens should always be performed for these patients.

Regarding hospitalization services, this study showed that patients hospitalized in the surgical intensive care unit frequently have positive *Candida albicans*. Moreover, various studies confirm that fungal infections are common and represent the third leading cause of documented sepsis in intensive care unit (18% of documented sepsis) (Vincent *et al.*, 2006 and Vincent *et al.*, 2009). This could be due to the more or less severe alteration of the immune system. Similarly, invasive procedures in the intensive care unit such as tracheobronchial intubations

can promote tracheobronchial colonization by yeasts and increase the frequency of pulmonary candidiasis (Gauzit *et al.*, 2001).

In the laboratory of Joseph Raseta Befelatanana University Hospital, medical biologists always validate the mycological findings for pulmonary samples since *Candida albicans* pneumopathies are serious and are found mainly in immunocompromised patients. It is true that most of the yeasts found in lung samples are due to tracheobronchial colonization of mycoses from the digestive tract. Nevertheless, in intensive care, *Candida* positive pulmonary specimens are frequently found beyond the thresholds and are validated to distinguish colonization and nosocomial bronchopulmonary infection (Azoulay *et al.*, 2001).

This study highlights the importance of mycological examination of pulmonary specimens, especially in hospitalized and immunocompromised patients. Clinicians should always prescribe mycological examination of pulmonary specimens. Indeed, other fungal infections can also be responsible for pneumopathy such as pulmonary aspergillosis which can be fatal for the patient in the absence of early management. For some laboratories that do not practice mycology such as the laboratory of Joseph Raseta Befelatanana University Hospital, the use of a more specific culture medium for fungal infections is necessary to improve the diagnosis of pulmonary mycosis. This is Sabouraud-Chloramphenicol agar (Agban *et al.*, 2013). The use of this culture medium could increase the frequency of detection of yeasts and other fungi causing lung disease in hospitalized and immunocompromised patients. In short, the results of this study are likely results. Indeed, the positivity rate can be increased if specific culture media have been used.

Conclusion

This study has highlighted the importance of a mycological examination of the pulmonary

specimen because *Candida* spp infections are common, especially in hospitalized and immunocompromised patients. This is nosocomial pulmonary candidiasis in the majority of cases. Pulmonary candidiasis must be treated quickly because it can be complicated by systemic candidiasis, which is very difficult to treat and can be fatal for the patient. The use of specific culture media for fungal infections in laboratories that analyze lung specimens could improve the diagnosis of pulmonary candidiasis and improve patient management.

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References

Adou-Bryn KD, Ouhon J, Assoumou A, Kassi EA, Kone M. 1999. Fungi and parasites isolated on examination of 142 bronchial aspiration fluids in Abidjan. *Médecine d'Afrique Noire* **46**, 363-365.

Agban A, Gbogbo KA, Hoekou YP, Atchou K, Tchacondo T, et al. 2013. Evaluation of the antifungal activity of extracts of *Cassia alata* L. and *Piliostigma thonningii* (Schumach.) Milne Redh. (Fabaceae) on *Candida albicans*. *International Journal of Biological and Chemical Sciences* **7**, 1041-1047.

Azoulay E, Limal N, Mayaud C, Schlemmer B. 2001. *Candida* positive lung sampling: nosocomial infection or colonization? *Reanimation* **10**, 323-328.

Cateau E, Rodier MH, Imbert C. 2012. Could antifungal lock be useful in the management of candidiasis linked with catheters? *Medecine Science* **28**, 740-745.

Chabasse D, Pihet M, Bouchara JP. 2009. Emergence of new pathogenic fungi in medicine. *Revue Francophone des Laboratoires* **416**, 71-86.

Gauzit R. 2001. Epidemiology and risk factors of systemic candidiasis in intensive care. *Annales françaises d'anesthésie et de réanimation* **20**, 394-399.

Jha BJ, Dey S, Tamang MD, Joshy ME, Shivananda PG. 2006. Characterization of *Candida* species isolated from cases of lower respiratory tract infection. *Kathmandu University Medical Journal* **4**, 290-294.

Laurent M, Gogly B, Tahmasebi F, Paillaud E. 2011. *Oropharyngeal candidiasis* of elderly patients. *Geriatric et Psychologie Neuropsychiatrie du vieillissement* **9**, 21-28.

Mjabber A, Moutaouakil A, El Aziz S, Chadli A, El Ghomari A, Farouqi A. 2010. P137 Candidiasis and diabetes. *Diabetes & Metabolism* **36**, A71.

Vincent JL, Rello J, Marshall J, Silva E, Anzueto A. 2009. International study of the prevalence and outcomes of infection in intensive care units. *Journal of the American Medical Association* **302**, 2323-2329.

Vincent JL, Safr Y, Sprung C, Ranieri VM, Reinhart K. 2006. Sepsis in European intensive care units: result of the SOAP study. *Critical Care Medicine* **34**, 344-353.

Zarrinfar H, Kaboli S, Dolatabadi S, Mohammadi R. 2016. Rapid detection of *Candida* species in bronchoalveolar lavage fluid from patients with pulmonary symptoms. *Brazilian Journal of Microbiology* **47**, 172-176.