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Risk Factors for Pulmonary Mycosis in Immunocompromised Patients in Surakarta, Indonesia

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ABSTRACT

Introduction: Recent evidence shows that there is an increase in the incidence of pulmonary mycosis globally. In clinical settings, pulmonary mycosis is commonly misdiagnosed as pulmonary tuberculosis (PTB). Identifying risk factors can ease the diagnosis of pulmonary mycosis. This study aimed to determine the risk factors for pulmonary mycosis in immunocompromised patients in Surakarta.
Methods: This was an analytic observational study with a retrospective cohort study method. This study used purposive sampling technique on 218 medical records of immunocompromised patients during January 2019–September 2022 at a referral hospital in Surakarta. The correlation of sociodemographic, health status, health behavior, history of diseases, medications, and transplantations with the incidence of pulmonary mycosis was analyzed using Chi-Square test or Fisher's exact test as its alternative.
Results: There was a significant correlation between educational level (p=0.018), nutritional status (p=0.001), smoking habit (p=0.000), history of corticosteroid use (p=0.031), history of antibiotic use (p=0.006), history of chemotherapy (p=0.003), history of PTB (p=0.047), and history of chronic obstructive pulmonary disease (COPD) (p=0.001) with the incidence of pulmonary mycosis. Meanwhile, there was no significant correlation between occupation (p=0.057), neutrophil level (p=1.000), history of human immunodeficiency virus (HIV) infection (p=1.000), history of diabetes mellitus (DM) (p=0.070), and history of organ transplantation (p=1.000) with the incidence of pulmonary mycosis.
Conclusion: Low educational level, malnutrition, smoking habit, history of pulmonary diseases, and medications are the risk factors for pulmonary mycosis in immunocompromised patients in Surakarta. It is important to identify these risk factors when examining patients with respiratory disorder symptoms.

Keywords: immunocompromised; pulmonary mycosis; risk factors

INTRODUCTION

Pulmonary mycosis is a systemic fungal infection that causes pulmonary and/or airway disorders. Clinical symptoms include fever, malaise, chest pain, shortness of breath, a protracted and productive cough with mucoid or purulent sputum, and hemoptysis. In recent years, the incidence of this disease has increased, jeopardizing people's health all around the world. This condition coincides with an increase in immunocompromised and chronic lung disease patients[1]. The most commonly reported types of pulmonary mycosis cases are pulmonary candidiasis, pulmonary aspergillosis, pulmonary histoplasmosis, pulmonary cryptococcosis, and pneumocystis carinii pneumonia (PCP)[2].

One of the biggest challenges in dealing with pulmonary mycosis in Indonesia nowadays, besides the increasing incidence rate, is conducting early diagnosis and proper treatment for pulmonary mycosis patients[1]. Pulmonary mycosis is commonly misdiagnosed as pulmonary tuberculosis (PTB) in daily clinical practice. This is due to the lack of information on the pathognomonic clinical symptoms and radiological characteristics of pulmonary mycosis to differentiate it from PTB, and moreover, both often occur as co-infections[3,4]. The mycology laboratory examination is one of the most important parts in diagnosing pulmonary mycosis.[5] However, the facilities for mycology laboratory examinations in several areas of Indonesia are still insufficient, resulting in the late diagnosis of pulmonary mycosis[6]. This condition can be harmful to patients because they may not obtain appropriate therapy for their ailment, resulting in greater morbidity and mortality rates[7].

To improve the quality of pulmonary mycosis management in Indonesia in the future, it is important to improve clinicians' knowledge and awareness of epidemiology as well as the diagnosis of pulmonary mycosis[3]. Thus, a further comprehension of pulmonary mycosis epidemiology, pathogenesis, and risk factors is necessary[2]. Risk factors can be an important part of easing the diagnosis of pulmonary mycosis. Previous studies have shown various risk factors related to pulmonary mycosis, such as older age, residential areas, smoking behaviors, low CD4+ and CD8+ T cell counts, prolonged use of antibiotics and corticosteroids, organ transplantation, and underlying respiratory illnesses[8–10]. Based on this information, it is known that sociodemographic, health behavior, health status, history of diseases, medications, and transplantations can be considered potential risk factors for pulmonary mycosis; thus, further research is required to analyze these factors.

In Indonesia, there have been no recent studies about the risk factors for pulmonary mycosis. Hence, the authors are intrigued to conduct a study that aims to determine the risk factors for pulmonary mycosis in immunocompromised patients in Surakarta, Indonesia.

METHOD

This was an analytic observational study with a retrospective cohort study method. The study was conducted by obtaining secondary data from the medical records of immunocompromised patients during January 2019–September 2022 at a referral hospital in Surakarta. The immunocompromised patients in this study mainly referred to patients with malnutrition status, neutropenia status, history of human immunodeficiency virus (HIV) infection, history of diabetes mellitus (DM), history of corticosteroid use (more than four weeks), history of antibiotic use (more than two weeks), history of chemotherapy (within the past year), or history of organ transplantation. The data from immunocompromised patients with pulmonary mycosis was compared to the data from a control group without pulmonary mycosis. Patients with incomplete medical records were excluded from the study.

The medical records were collected using the purposive sampling technique. After collecting samples from the case group via purposive sampling, the samples from the control group were identified by manually matching the sex and age of the patients in both groups. Based on our calculations using the hypothesis test for an odds ratio, the minimal sample size was 33 medical records for each group, for a total of 66 medical records.

The pulmonary mycosis cases that were analyzed as the dependent variables in this study were pulmonary candidiasis, pulmonary aspergillosis, and PCP. They were diagnosed based on the diagnostic criteria, which consisted of possible, probable, and proven. In the diagnosis of pulmonary mycosis, the mycological culture test was performed to confirm the diagnosis of probable cases by using sputum or bronchoalveolar lavage (BAL) fluid as the specimen, and the biopsy was performed to confirm the diagnosis of proven cases by using lung or bronchial tissue as the specimen. On the other hand, the suspected risk factors of pulmonary mycosis, such as patients' sociodemographic (occupation and educational level), health behavior (smoking habit), health status (nutritional status and neutrophil

level), disease history (HIV infection, DM, PTB, and chronic obstructive pulmonary disease (COPD)), medication history (antibiotic, corticosteroid, and chemotherapy), and organ transplantation history, were analyzed as the independent variables in this study.

The obtained data were analyzed using the Chi-Square test to show the correlation between the incidence of pulmonary mycosis and its suspected risk factors. The Fisher's exact test was performed as an alternative when the data did not meet the requirements of the Chi-Square test. The tests were performed using IBM Statistical Package for the Social Sciences (SPSS) version 24.0 for Windows. This study obtained ethical clearance from the Health Research Ethics Committee of Dr. Moewardi General Hospital with number 1.091/VIII/HREC/2022.

RESULTS

Table 1. Characteristics of Immunocompromised Patients at a Referral Hospital in Surakarta based on Sex and Age (n=218)

Characteristics	n	%
Sex		
Male	152	69.7
Female	66	30.3
Age (years)		
≤ 20	2	0.9
21 – 30	4	1.8
31 – 40	20	9.2
41 – 50	64	29.4
51 – 60	52	23.9
≥ 61	76	34.9

Patients Characteristics

During our observation, there were 218 medical records of immunocompromised patients that met the inclusion criteria (complete medical record). The patients consisted of 152 males (69.7%) and 66 females (30.3%). Most of the patients were aged ≥ 61 years (34.9%) (Table 1).

Table 2. Characteristics of Pulmonary Mycosis Cases at a Referral Hospital in Surakarta during January 2019-September 2022

Characteristics	n	%
Diagnostic Criteria (n=109)		
Possible	11	10.1
Probable	93	85.3
Proven	5	4.6
Specimen (n=98)		
Sputum	63	64.3
BAL fluid	30	30.6
Bronchial tissue	1	1.0
Lung tissue	4	4.1
Causative Agents (n=98)		
Candida spp.	2	2.0
Candida albicans	44	44.9
Candida glabrata	6	6.1
Candida tropicalis	31	31.6
Candida parapsilosis	3	3.1
Candida lusitaniae	1	1.0
Candida guilliermondii	1	1.0
Aspegillus spp.	9	9.2
Pneumocystis carinii	1	1.0

Pulmonary Mycosis Cases Characteristics

The incidence of pulmonary mycosis among 109 immunocompromised patients during January 2019–September 2022 at a hospital in Surakarta included 93 probable (85.3%), 11 possible (10.1%), and 5 proven (4.6%) cases. Thus, there were only 98 fungi that could be identified from the probable and proven cases. The most common cause of pulmonary mycosis in the hospital was Candida spp. (89.8%), with Candida albicans (44.9%) as the most common species, followed by Candida tropicalis (31.6%) (Table 2).

Table 3. Correlation between Risk Factors and The Incidence of Pulmonary Mycosis

Risk Factors	Pulmonary Mycosis				Total		p-value
	Positive		Negative				
	n	%	n	%	n	%	
Occupation							
Farmer	26	23.9	15	13.8	41	18.8	0.057
Non-farmer	83	76.1	94	86.2	177	81.2	
Educational Level							
Primary education	59	54.1	62	56.9	121	55.5	
Secondary education	44	40.4	30	27.5	74	33.9	0.018*
High education	6	5.5	17	15.6	23	10.6	
Nutriniotal Status							
Underweight	46	42.2	26	23.9	72	33.0	
Ideal	48	44.0	44	40.4	92	42.2	0.001*
Overweight	13	11.9	29	26.6	42	19.3	
Obese	2	1.8	10	9.2	12	5.5	
Smoking Habit							
Non-smoker	57	52.3	92	84.4	149	68.3	
Light smoker	11	10.1	3	2.8	14	6.4	0.000*
Moderate smoker	23	21.1	11	10.1	34	15.6	
Heavy smoker	18	16.5	3	2.8	21	9.6	
Neutrophil Level							
Neutropenia	1	0,9	2	1.8	3	1.4	1.000
Not neutropenia	108	99.1	107	98.2	215	98.6	
History of HIV Infection							
Yes	6	5.5	6	5.5	12	5.5	1.000
No	103	94.5	103	94.5	206	94.5	
History of DM							
Yes	35	32.1	48	44.0	83	38.1	0.070
No	74	67.9	61	56.0	135	61.9	
History of Organ Transplantation							
Yes	1	0.9	0	0	1	0.5	1.000
No	108	99.1	109	100	217	99.5	
History of Corticosteroid Use							
Yes	14	12.8	5	4.6	19	8.7	0.031*
No	95	87.2	104	95.4	199	91.3	
History of Antibiotic Use							
Yes	74	67.9	54	49.5	128	58.7	0.006*
No	35	32.1	55	50.5	90	41.3	
History of Chemotherapy							
Yes	9	8.3	25	22.9	34	15.6	0.003*
No	100	91.7	84	77.1	184	84.4	
History of PTB							
Yes	45	41.3	31	28.4	76	34.9	0.047*
No	64	58.7	78	71.6	142	65.1	
History of COPD							
Yes	20	18.3	4	3.7	24	11.0	0.001*
No	89	81.7	105	96.3	194	89.0	

The Analysis of Risk Factors

The bivariate analysis was performed by using the Chi-Square test and Fisher's exact test to provide an analysis of risk factors for the incidence of pulmonary mycosis. The results showed that several risk factors, such as educational level (p=0.018; Chi-Square test), nutritional status (p=0.001; Chi-Square test), smoking habit (p=0.000; Chi-Square test), history of corticosteroid use (p=0.031; Chi-Square test), history of antibiotic use (p=0.006; Chi-Square test), history of chemotherapy (p=0.003; Chi-Square test), history of PTB (p=0.047; Chi-Square test), and history of COPD (p=0.001; Chi-Square test), were significantly correlated with the incidence of pulmonary mycosis. Meanwhile, occupation (p=0.057; Chi-Square test), neutrophil level (p=1.000; Fisher's exact test), history of HIV infection (p=1.000; Chi-Square test), history of DM (p=0.070; Chi-Square test), and history of organ transplantation (p=1.000; Fisher's exact test) were not significantly correlated with the incidence of pulmonary mycosis (Table 3).

DISCUSSION

In our study, it was found that most of the immunocompromised patients with pulmonary mycosis were male and elderly. This finding is similar to previous studies that showed older age was one of the pulmonary mycosis risk factors[8,9]. It is the immunosenescence process that makes the elderly more susceptible to respiratory tract infections[11]. However, sex and age were not included in our analysis of risk factors for the incidence of pulmonary mycosis.

The most prevalent case of pulmonary mycosis found in this study was pulmonary candidiasis, which was caused by *C. albicans*. It corresponds with previous studies that showed *C. albicans* as the most common causative agent of pulmonary mycosis[10,12]. Unfortunately, the examination equipment in the hospital's mycology laboratory has limitations in its ability to diagnose pulmonary mycosis. As a result, it was unclear if the fungus discovered and identified in the medical records was commensal or opportunistic.

There were two sociodemographic aspects that were analyzed as risk factors for pulmonary mycosis: educational level and occupation. The educational level was significantly correlated with the incidence of pulmonary mycosis, similar to a previous study conducted in Banjar Regency, Indonesia[13]. This implies that the more educated a person is, the better their disease prevention will be. Otherwise, occupation was not significantly correlated with the incidence of pulmonary mycosis. It does not correspond with our references, which stated that farmers had a higher susceptibility to endemic pulmonary mycoses caused by pathogenic fungi such as *Histoplasma capsulatum, Paracoccidioides brasiliensis, and Paracoccidioides lutzi*[14,15]. Based on an epidemiological study in Latin America, those three pathogenic fungi are endemic to the Americas[16]. Thus, most farmers in Indonesia have very low exposure to these three fungal pathogens, and so the risk of developing the pulmonary mycosis caused by these three fungal pathogens is also very low, making our finding reasonable.

The health status also shared similar results with the sociodemographic aspects in this study. The nutritional status was significantly correlated with the incidence of pulmonary mycosis. This finding is in accordance with a study conducted at a hospital in Wisconsin[17]. Malnutrition in an individual can lead to immune system dysfunction known as nutritional-acquired immune deficiency syndrome (NAIDS), making them more susceptible to various infections, especially opportunistic fungal infections[18]. Meanwhile, the neutrophil level was not significantly correlated with the incidence of pulmonary mycosis. A cross-sectional study in Kolkata, India, showed that neutropenia that lasted for more than 10 days was the risk factor for invasive fungal infection (IFI) in patients with hematological malignancies, which was different from our result[19].

The analysis of smoking habit showed a significant correlation with the incidence of pulmonary mycosis. This finding corresponds with a systematic review and meta-analysis that stated that there was an increased risk of invasive fungal disease (IFD) in smokers compared to non-smokers[20]. An experimental study conducted in Canada also supports our findings. The study showed that there was a significant correlation between the smoke condensate of cigarettes and the adhesion, growth, and biofilm formation of *C. albicans*, thus increasing their ability to develop opportunistic infections[21].

This study showed that the history of medications, such as corticosteroid, antibiotic, and chemotherapy, had a significant correlation with the incidence of pulmonary mycosis. A study in Japan revealed that the administration of prednisolone with an equivalent steroid dose of 55 mg/kg cumulatively for the first 4 weeks in patients with severe acute graft-versus-host disease (GVHD) showed a significant correlation with the increase in the incidence of fungal infections, similar to our findings[22]. Another study in Nigeria also corroborates our finding; the study showed that long-term use of antibiotics had a significant correlation with the incidence of pulmonary mycosis in non-TB patients[10]. Corticosteroid and antibiotic impair the innate and adaptive immune systems, making the individual more susceptible to opportunistic fungal infections in the respiratory tract[10,22]. Regarding chemotherapy, our finding is in accordance with a cross-sectional study in Kolkata, India, which stated the induction chemotherapy was one of the risk factors for the incidence of IFI[19]. Similar to the effects of corticosteroid and antibiotic, chemotherapy can lead to a weakened epithelial barrier and dysfunction of both the innate and adaptive immune systems, making it more susceptible to opportunistic infections by fungi[23].

The history of pulmonary diseases, such as PTB and COPD, also had a significant correlation with the incidence of pulmonary mycosis in this study. It is in accordance with a cross-sectional study in Brazil that showed that cavities in the lung tissue had a significant correlation with pulmonary mycosis in PTB patients[24]. In PTB patients, the cavities that are formed in the lungs contain adequate oxygen and necrotizing tissue to provide a suitable place for various organisms, including fungi, to grow and cause an infection[25]. The finding about COPD is also consistent with a cohort study in South Korea, which showed that COPD was one of the pulmonary disease histories that had a significant correlation with the increase in pulmonary aspergillosis risk in bronchiectasis patients[26]. COPD patients commonly get long-term corticosteroid therapy, which leads to a reduction in alveolar macrophage activity that inhibits the function of neutrophils in destroying *Aspergillus spp.* fungal components. Thus, increasing the colonization of *Aspergillus spp.* in COPD patients[1].

The history of HIV infection, the history of DM, and the history of organ transplantation were not significantly correlated with the incidence of pulmonary mycosis. This finding is not in accordance with the previous studies[27–29]. This is due to the fact that the onset and duration of these factors were not considered in our study, so that possible complications such as pulmonary mycosis might not have occurred in many patients with these factors. This is true for the neutrophil level in our study as well. Furthermore, the background of these factors, such as the degree of neutropenia, the stage of HIV infection (based on CD4+ T cell counts), the blood glucose level of DM patients, and the type of transplanted organ, was not analyzed in our study. In this case, the severity of each underlying condition was not considered in our study, so the results regarding these factors are not very detailed.

There are also other limitations in this study. The data of patients in this study was only derived from one hospital, making generalizations difficult for every incidence of pulmonary mycosis in Indonesia. The population in this study was also too broad in scope, so the data and results obtained for each immunocompromised factor were less representative. Furthermore, the other risk factors that may be correlated with the incidence of pulmonary mycosis, such as sex, age, genetic factors, environmental conditions, economic conditions, personal hygiene, and history of autoimmune diseases, were not included in the analysis. Further studies on these factors need to be conducted for better comprehension of pulmonary mycosis risk factors.

CONCLUSION

This study concludes that low educational level, malnutrition, smoking habit, history of pulmonary diseases, and medications are risk factors for pulmonary mycosis in immunocompromised patients in Surakarta. A thorough anamnesis is necessary for the identification of these risk factors, especially when screening patients with respiratory illness symptoms such as chest pain, shortness of breath, and a protracted cough. Identification of these risk factors can aid in the early diagnosis of pulmonary mycosis, resulting in more successful patient treatment.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest from this submitted work.

REFERENCES

1. Rozaliyani A, Jusuf A, Soepandi PZ, Burhan E, Handayani D, Widowati H, et al. Infeksi jamur paru di Indonesia: situasi saat ini dan tantangan di masa depan. J Respir Indo. 2019;39(3):210–4, https://doi.org/10.36497/jri.v39i3.69
2. PDPI. Mikosis paru: pedoman diagnosis dan penatalaksanaan di Indonesia. Jakarta: Fakultas Kedokteran Universitas Indonesia; 2017.
3. Amiri MRJ, Siami R, Khaledi A. Tuberculosis status and coinfection of pulmonary fungal infections in patients referred to reference laboratory of Health Centers Ghaemshahr City during 2007-2017. Ethiop J Health Sci. 2018;28(6):683–90, https://doi.org/10.4314/ejhs.v28i6.2
4. Njovu IK, Musinguzi B, Mwesigye J, Kassaza K, Turigurwa J, Nuwagira E, et al. Status of pulmonary fungal pathogens among individuals with clinical features of pulmonary tuberculosis at Mbarara University Teaching Hospital in Southwestern Uganda. Ther Adv Infect Dis. 2021;8:1–11, https://doi.org/10.1177/20499361211042477
5. Sutton DA. Basic mycology. In: Hospenthal DR, Rinaldi MG, editors. Diagnosis and treatment of human mycoses. 1st ed. Totowa: Humana Press; 2007. p. 15–20, https://doi.org/10.1007/978-1-59745-325-7_2
6. Setiyawati D, Situmeaang SMF. Identifikasi jamur pada pasien penderita tuberkulosis paru di RSUP H. Adam Malik Medan. J Kesmas Prima Indo. 2021;3(2):47–51, https://doi.org/10.34012/jkpi.v3i2.2042
7. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. Bull World Health Organ. 2011;89(12):864–72, https://doi.org/10.2471/BLT.11.089441
8. Guo M, Tong Z. Risk factors associated with invasive pulmonary mycosis among severe influenza patients in Beijing City, China. Int J Gen Med. 2021;14:7381–90.
9. Lin J, Feng B, Tang H, Xu H, Tang Y. A systematic review and meta-analysis: pulmonary mycosis pathogen distribution. Ann Palliat Med. 2021;10(7):7919–32, https://doi.org/10.21037/apm-21-1388

10. Sani FM, Abdullahi IN, Animasaun OS, Ghamba PE, Anka AU, Salami MO, et al. Prevalence and risk factors of pulmonary fungal pathogens among symptomatic patients with or without tuberculosis at Gombe, Nigeria. J Med Microbiol Infect Dis. 2020;8(3):76–83.

11. Wasityastuti W, Dhamarjati A, Siswanto. Imunosenesens dan kerentanan populasi usia lanjut terhadap coronavirus disease 2019 (covid-19). J Respir Indo. 2020;40(3):182–91, https://doi.org/10.36497/jri.v40i3.115

12. Ogba O, Abia-Bassey L, Epoke J. Prevalence of symptomatic opportunistic respiratory mycoses and mycobacterium tuberculosis among human immunodeficiency virus positive patients in Calabar Nigeria. Int J Innov Med Heal Sci. 2013;1:6–13, https://doi.org/10.13070/rs.en.1.726

13. Azizah M, Fahrurazi, Qoriaty NI. Tingkat pengetahuan dan pendidikan ibu balita dengan kejadian penyakit pneumonia pada balita di Kelurahan Keraton Kecamatan Martapura Kabupaten Banjar. An-Nadaa. 2014;1(1):1–4.

14. Ghosh UC, Hazra K. Fungal infection in the lung. In: Bansode BR, editor. Medicine update. 12th ed. Mumbai: The Association of Physicians of India; 2017. p. 232–5.

15. Salzer HJF, Burchard G, Cornely OA, Lange C, Rolling T, Schmiedel S, et al. Diagnosis and management of systemic endemic mycoses causing pulmonary disease. Respiration. 2018;96(3):283–301, https://doi.org/10.1159/000489501

16. Sifuentes-Osornio J, Corzo-León DE, Ponce-de-León LA. Epidemiology of invasive fungal infections in Latin America. Curr Fungal Infect Rep. 2012;6(1):23–34, https://doi.org/10.1007/s12281-011-0081-7

17. Schulte DM, Sethi A, Gangnon R, Duster M, Maki DG, Safdar N. Risk factors for Candida colonization and co-colonization with multi-drug resistant organisms at admission. Antimicrob Resist Infect Control. 2015;4(46):1–9, https://doi.org/10.1186/s13756-015-0089-9

18. Duggal S, Chugh TD, Duggal AK. HIV and malnutrition: effects on immune system. Clin Dev Immunol. 2012;2012:784740, https://doi.org/10.1155/2012/784740

19. Mitra AN, Pramanik P, Bhattacharya R. Invasive fungal infections in acute haematological malignancies : a cross-sectional study. J Clin Diagnostic Res. 2023;17(1):7–13, https://doi.org/10.7860/JCDR/2023/60309.17271

20. Pourbaix A, Rapnouil BL, Guéry R, Lanternier F, Lortholary O, Cohen JF. Smoking as a risk factor of invasive fungal disease : systematic review and meta-Analysis. 2020;71(4):1106–19, https://doi.org/10.1093/cid/ciaa001

21. Semlali A, Killer K, Alanazi H, Chmielewski W, Rouabhia M. Cigarette smoke condensate increases C. albicans adhesion, growth, biofilm formation, and EAP1, HWP1 and SAP2 gene expression. BMC Microbiol. 2014;14(61):1–9, https://doi.org/10.1186/1471-2180-14-61

22. Matsumura-kimoto Y, Inamoto Y, Tajima K, Kawajiri A, Tanaka T, Hirakawa T, et al. Biology of blood and marrow transplantation association of cumulative steroid dose with risk of infection after treatment for severe acute graft-versus-host disease. Biol Blood Marrow Transplant. 2016;22(6):1102–7, https://doi.org/10.1016/j.bbmt.2016.02.020

23. Teoh F, Pavelka N. How chemotherapy increases the risk of systemic candidiasis in cancer patients: current paradigm and future directions. Pathogens. 2016;5(1):1–16,

https://doi.org/10.3390/pathogens5010006

24. Matsuda JDS, Wanke B, Balieiro AADS, Santos CSDS, Cavalcante RCDS, Muniz MM, et al. Prevalence of pulmonary mycoses in smear-negative patients with suspected tuberculosis in the Brazilian Amazon. Rev Iberoam Micol. 2021;38(3):111–8, https://doi.org/10.1016/j.riam.2020.12.004

25. Soedarsono, Widoretno ETW. Aspergilloma pada tuberkulosis paru. J Respi. 2017;3(2):58–65, https://doi.org/10.20473/jr.v3-I.2.2017.58-65

26. Yang B, Kim T, Ryu J, Park HY, Hwangbo B, Kong SY, et al. Increased incidence and associated risk factors of aspergillosis in patients with bronchiectasis. J Pers Med. 2021;11(5):422, https://doi.org/10.3390/jpm11050422

27. Aguilar CA, Hamandi B, Fegbeutel C, Silveira FP, Verschuuren EA, Ussetti P, et al. Clinical risk factors for invasive aspergillosis in lung transplant recipients: results of an international cohort study. J Heart Lung Transplant. 2018;37(10):1226–34, https://doi.org/10.1016/j.healun.2018.06.008

28. Rooku KC, Adhikari S, Bastola A, Devkota L, Bhandari P, Ghimire P, et al. Opportunistic respiratory infections in HIV patients attending Sukraraj Tropical and Infectious Diseases Hospital in Kathmandu, Nepal. HIV AIDS (Auckl). 2019;11:357–67, https://doi.org/10.2147/HIV.S229531

29. Udeani TK, Asogwa VN, Ezenwaka U. Assessment of systemic fungal infections among diabetic patients in Enugu, Nigeria. J Infect Dis Epidemiol. 2018;4(2):1–5, https://doi.org/10.23937/2474-3658/1510051