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Epidemiological Profile of Opportunistic Fungal and Parasitic Infections at a Tertiary Care Hospital in Fez, Morocco

Adadi Soukaina*, Azzine Zineb, Ben-Saghroune Hayat and Tlamçani Zineb

Parasitology and Mycology Department, Central Laboratory of Medical Analysis, Hassan II University Hospital, Sidi Mohamed Ben Abdellah, Fez, Morocco

Corresponding Author: Adadi Soukaina, Parasitology and Mycology Department, Central Laboratory of Medical Analysis, Hassan II University Hospital, Sidi Mohamed Ben Abdellah, Fez, Morocco.

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Abstract

Introduction: Fungal and parasitic infections due to opportunistic pathogens have increased dramatically in recent decades. This increase is associated with high morbidity and mortality, and is directly related to the increase in populations at risk of developing severe fungal and parasitic infections. The objective of this prospective study is to elucidate the prevalence and spectrum of common infections in presumed immunocompromised patients followed at a tertiary care hospital.

Materials and Methods: Clinical samples were received from different departments of a tertiary care hospital in Fez, Morocco, taken from immunocompromised patients of all age groups and both sexes and submitted to a mycological or parasitological study. The identification of fungal and parasitic isolates was performed according to the recommended standard methods. The various fungi and parasites were confirmed by special staining whenever necessary.

Results: 238 fungal and parasitic isolates were isolated, including 19 parasitic cases and 219 fungal infections. For the fungal isolates identified, *Candida* sp (74.4%) was the most common, of which *Candida albicans* was the dominant species, followed by *Pneumocystis jirovecii* (7.1%), *Aspergillus* sp (5%), *Cryptococcus neoformans* (4.2%), and *Trichosporon* sp (1.3%). For parasitic isolates *Cryptosporidium* sp (4.6%) was the most prevalent species followed by *Cyclospora* sp (3.4%).

Conclusion: The awareness of clinicians to the diagnosis and early treatment of these infections, helping in the proper management of patients, especially in resource-limited countries like ours.

Keywords: *Fungal; Parasitic; Immunocompromised; Opportunistic Infection*

Introduction

Fungal and parasitic infections are an important cause of morbidity and mortality in immunocompromised individuals. The incidence of these infections is increasing, largely because of the growing number of immunocompromised patients, including those with neutropenia, human immunodeficiency virus, chronic immunosuppression, and those taking immunosuppressive therapy. Pathogens include mycotic organisms such as *Candida* sp and *Aspergillus* sp, *Cryptococcus neoformans*, *Pneumocystis jirovecii*, and parasitic organisms including intestinal coccidiosis and microsporidia.

Materials and Methods

This is a retrospective and descriptive study conducted at the laboratory of parasitology- mycology of a tertiary care hospital in Fez, Morocco, from January 2016 to December 2021. The cases to be studied were selected among the patients frequenting the different services of medicine, hematology, infectious diseases, nephrology, oncology and pediatrics, over a period of 5 years (January 2016 - December 2021). 238 immunocompromised patients of different categories, such as HIV positive individuals, patients with hematological malignancies undergoing chemotherapy with a total leukocyte count below 4000, chronic hemodialysis patients and patients receiving immunosuppressive drugs were included in the study.

Various samples were collected according to symptoms and clinical presentations and underwent mycological or parasitological study according to universal recommendations.

Population and study design

Two hundred and thirty-eight patients (n = 238) of all age groups and both sexes admitted to the different medical departments of a tertiary care hospital in Fez, Morocco, were studied. All patients were evaluated according to a pre-established protocol covering personal data, history including the nature of immunosuppression, presenting complaints and physical examination.

Microscopy, culture and identification

Based on the clinical symptoms and the organs involved, clinical specimens were collected following all universal precautions. The samples were submitted for mycological or parasitological study depending on the type of sample and the suspected infection in the patient.

Samples received for mycological study were processed in 2 steps: direct examination in the fresh state, after mounting with potassium hydroxide (KOH) (30% potash), after staining (May Grunwald Giemsa or toluidine blue), or after preparation with India ink. Then, a systematic culture in three media (Sabouraud simple, Sabouraud with added chloramphenicol and Sabouraud with added cycloheximide) is performed. A sample is considered positive when a fungus is detected on direct examination and on culture when it is a superficial sample. Deep samples are considered positive when direct examination and/or culture are positive.

The isolation and identification of fungal elements were based on morphological (macroscopic aspect and microscopic examination), phenotypic (the filamentation test), biochemical (the use of sugar assimilation tests (galleries)) and immunological (agglutination tests of latex particles sensitized by monoclonal antibodies), as well as the use of direct and indirect diagnostic methods to detect invasive mycoses, which are often fatal in immunocompromised patients. These include the enzyme-linked immunosorbent assay of galactomannan antigen for the diagnosis of invasive aspergillosis and indirect immunofluorescence testing of bronchoalveolar lavage and sputum samples for pneumocystis cysts.

For the parasitological examination, it concerned especially the stool samples, they were examined directly in the fresh state with and without staining (lugol 2%, Merthiolate-Iode- Formol...) and after concentration in formalin-ether. A modified Ziehl-Neelsen stain was used to detect severe and chronic intestinal parasitosis in immunocompromised patients.

Statistical analysis

Statistical analysis was performed using epi info software version 7.2.5.0. Descriptive statistics were given as numbers and percentages for categorical variables and as means, standard deviations, minimum and maximum values for numerical variables.

Results

During the study period, we collected 238 cases out of a total of 9647 specimens, representing an overall prevalence of 2.46%. The annual distribution of cases shows two peaks, in 2016 and 2020 (Figure 1).

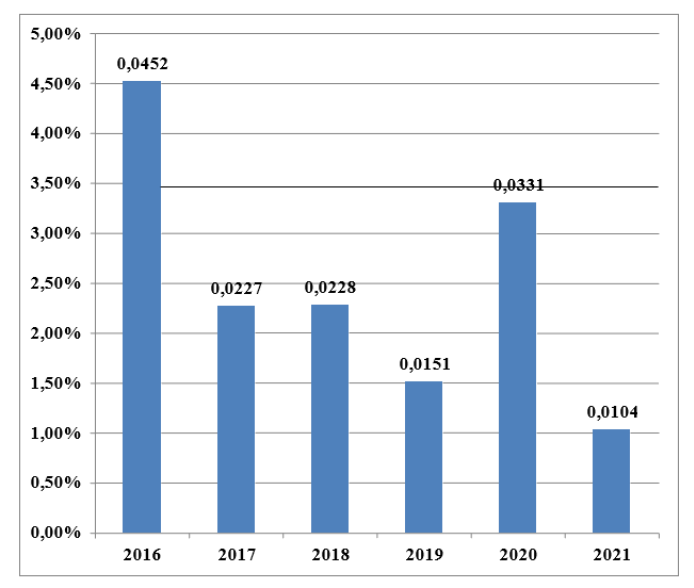

Figure 1: *Annual distribution of opportunistic infections between January 2016 and December 2021.*

Women were in the majority with a sex ratio of 1.10. The mean age was 40.15 years with extremes of 0 and 86 years. The maximum number of cases of opportunistic infections was observed in the age group between 41 and 50 years (18.9%) (Table 1).

Age Group	Male		Female		Total	
	n	%	n	%	n	%
0-10	22	9,2%	10	4,2%	32	13,4%
11-20	12	5%	11	4,6%	23	9,6%
21-30	11	4,6%	13	5,4%	24	10%
31-40	18	7,5%	15	6,3%	33	13,8%
41-50	17	7,2%	28	11,7%	44	18,9%
51-60	15	6,3%	14	5,8%	29	12,1%
61-70	9	3,7%	24	10%	33	13,7%
71-80	6	2,5%	6	2,5%	12	5%
81-90	3	1,2%	4	1,6%	7	2,8%
Total	113	47,5%	125	52,5%	238	100%

Table 1: *Distribution of patients by age and gender (n = 238).*

Different states of immunosuppression were found, dominated by neutropenic patients followed for a hematological malignancy receiving chemotherapy (34.5%), patients under immunosuppressive treatment (17.2%), and HIV-positive persons (13%) (Table 2).

Type of immunosuppression	Number	%
Hemopathy under chemotherapy	82	34,5%
Immunosuppressants	41	17,2%
HIV	31	13%
Diabetes	28	11,8%
Solid cancer under chemotherapy	25	10,5%
Long-term corticosteroid therapy	15	6,3%
Chronic hemodialysis	9	3,8%
Radiotherapy	4	1,7%
Tuberculosis	3	1,3%
Total	238	100%

Table 2: *Distribution of the immunodepression states found.*

A total of 238 samples were collected and processed. The detailed distribution of different fungal and parasitic isolates among various clinical specimens and the underlying immunosuppression are presented in table 3-5. *Candida* sp (74.8%) being the most common, followed by *Pneumocystis jirovecii* (7.1%), *Aspergillus* sp (5%), *Cryptosporidium* sp (4.6%), *Cryptococcus* sp (3.8%), *Cyclospora* sp (3.4%), and *Trichosporon* sp (1.3%).

Isolates n = 238	N	% of total	Type of immunodepression (n)
Candida sp	178	74,8%	78 under chemotherapy 32 on immunosuppressants 28 Diabetes 12 HIV 03 Tuberculosis 04 under radiotherapy 15 under corticosteroid therapy 05 chronic hemodialysis
Pneumocystis jirovecii	17	7,1%	08 under chemotherapy 04 HIV 04 on immunosuppressants 01 chronic hemodialysis
Aspergillus sp	12	5%	11 under chemotherapy 01 HIV
Cryptococcus sp	09	3,8%	09 HIV
Trichosporon sp	3	1,2%	01 HIV 01 on immunosuppressants 01 chronic hemodialysis

Cryptosporidium sp	11	4,6%	05 under chemotherapy 03 on immunosuppressants 02 chronic hemodialysis 01 HIV
Cyclospora sp	8	3,4%	05 under chemotherapy 02 HIV 01 on immunosuppressants

Table 3: *Distribution of different fungal and parasitic isolates according to the type of immunosuppression.*

Isolates n=238	% of total
Candida sp:	74,8%
Candida albicans	41,2%
Candida tropicalis	8%
Candida glabrata	6,3%
Candida parapsilosis	2,1%
Candida krusei	1,7%
Candida dubliniensis	1,3%
Candida lusitanae	0,4%
Candida sake	0,4%
Candida inconspicua	0,4%
Candida guillermondi	0,4%
Candida famata	0,4%
Autre non-albicans *Candida*	11,7%
Pneumocystis jirovecii	7,1%
Aspergillus sp:	5%
Aspergillus sp	4,6%
Aspergillus flavus	0,4%
Cryptococcus sp:	3,8%
Cryptococcus neoformans	3,8%
Trichosporon sp	1,2%
Cryptosporidium sp	4,6%
Cyclospora sp	3,4%

Table 4: *Distribution of different fungal and parasitic isolates by species.*

Clinical samples	Number		Isolates	
Oropharyngeal	15	6,3%	15 *Candida* sp	6,3%
Blood	43	18%	26 *Candidas* sp	10,9%
			11 *Aspergillus* sp	4,6%
			06 *Cryptococcus* sp	2,5%
CSF	03	1,2%	02 *Cryptococcus* sp	0,8 %
			01 *Candida* sp	0,4%
Respiratory	70	29,4%	52 *Candida* sp	21,8%
			17 *Pneumocystis jirovecii*	7,2%
			01 *Aspergillus* sp	0,4%
Skin and phanera	56	23,5%	52 *Candida* sp	21,8%
			03 *Trichosporon* sp	1,3%
			01 *Cryptococcus* sp	0,4%
Uro-genital	07	3%	07 *Candida* sp	3%
Puncture fluid	15	6,3%	15 *Candida* sp	6,3%
Ophthalmological	03	1,3%	03 *Candida* sp	1,3%
Stool	19	8%	11 *Cryptosporidium* sp	4,6%
			08 *Cyclospora* sp	3,4%
Total	238	100%	238	100%

Table 5: *Distribution of different fungal and parasitic isolates among various clinical samples.*

Among the *Candida* isolates, *Candida albicans* (n = 98) was the most prevalent species, followed by *Candida tropicalis* (n = 19), *Candida glabrata* (n = 15), *Candida krusei* (n = 4), *Candida dubliniensis* (n = 4), and only 1 case each of *Candida lusitaniae*, *Candida parapsilosis*, *Candida sake*, *Candida inconspicua*, and *Candida famata*. The infectious complications found related to these different species were fungemia and invasive candidiasis.

Aspergillus sp was isolated from 12 patients and was responsible in 11 cases for invasive aspergillosis, with only one case of *Aspergillus flavus* isolated in a respiratory sample.

Among *Cryptococcus* sp, *Cryptococcus neoformans* was isolated from all cases (n = 10). However, 17 cases of *Pneumocystis jirovecii* and 3 of *Trichosporon* sp were identified (Table 3).

For parasitic isolates, two parasites were isolated, *Cryptosporidium* sp in 11 cases, and *Cyclospora* sp in 8 cases (Table 3).

Discussion

The increase in the incidence of mycoses and opportunistic parasitosis is one of the major facts of infectious pathology during the last decades. This phenomenon corresponds essentially, on the one hand, to the increase in the number of mycotic infections related to candidiasis, aspergillosis, cryptococcosis, and to the emergence of new fungi unknown or considered as common contaminants, and on the other hand, to the increase of infections secondary to opportunistic intestinal protozoa.

The opportunism of these pathogens is closely related to the appearance of increasingly severe states of immunodepression [1-4], therefore the organism takes advantage of the opportunity offered by a weakened immune system, which will expose it to several infections called, opportunistic, having the potential to cause serious morbidity and mortality [4].

In immunocompromised patients, the etiologic agent and type of infection differ according to the nature of the immune deficiency and the terrain. Severe neutropenia is the main factor predisposing to fungal infections, and is notably encountered during acute leukemia and its treatment, and hematopoietic stem cell allografts. In the latter situation, the risk of fungal infection exists both during the initial neutropenia and at a later stage, when a graft- versus-host reaction requires an increase in immunosuppressive treatment, in particular through the addition of prolonged corticosteroid therapy. In this context, opportunistic fungal infections are mainly due to *Candida* sp and *Aspergillus* sp [5]. Deficiencies in cellular immunity are another predisposing factor for fungal infections, including HIV-induced deficiencies, which are now a major contributor to mortality from fungal diseases worldwide. Although the advent of antiretroviral therapy has resulted in a marked decrease in their incidence in treated patients, mycotic infections remain a frequent mode of onset and cause of death during human immunodeficiency virus infection. However, *Pneumocystis jirovecii* pneumonia is the most common cause of respiratory infection, and cryptococcal meningitis now accounts for the majority of deaths from HIV-related fungal infection worldwide, primarily in sub-Saharan Africa. In addition, the current HIV pandemic has led to the emergence of new opportunistic infections in the context of endemic fungal infections [6,7].

Other immunosuppressive conditions causing acquired deficits in cellular immunity may cause fungal infections, including degenerative or metabolic diseases, mainly lymphoma, solid tumors, renal failure, and diabetes, as well as immunosuppression related to immunosuppressive therapy and long-term corticosteroid therapy [8].

Opportunistic mycoses show distinct incidence patterns worldwide and may have different epidemiological characteristics, depending on the geographical region, however the burden of opportunistic fungal infections in Morocco is unknown with only few epidemiological data and case reports available. In our study, *Candida* species (74.8%) were the most frequent, followed by *Pneumocystis jirovecii* (7.1%), *Aspergillus* sp (5%) and *Cryptococcus* sp (3.8%), which is consistent with the results of different studies [9-12].

Given the complexity of patients at risk for infection and the diverse and growing array of fungal pathogens, opportunistic mycoses pose considerable diagnostic and therapeutic challenges. Although *Candida* sp and *Aspergillus* sp continue to be the most common pathogens causing invasive fungal disease in immunocompromised individuals [4].

Invasive fungal diseases continue to take a significant toll on human health and are associated with excessive morbidity and mortality. *Candida* sp continues to be the most common cause of invasive fungal infections in most immunocompromised patient populations, *Candida albicans* remains the most isolated species in this study, followed by *Candida tropicalis, Candida glabrata*, and *Candida parapsilosis*. This distribution of species has been consistent in different studies from Brazil, Argentina, and Chile [11], however other studies from Algeria and Thailand have shown a different pattern with *Candida parapsilosis* as the most common [13,14]. Blood cultures are the mainstay of the diagnosis, but only give positive results in 50 - 60% of disseminated infections [15].

Aspergillus infections rank second in frequency of fungal infections (after *Candida* sp infections) and first in severity. It is recognized as the most common acquired pulmonary fungal infection in severely immunocompromised patients, particularly those with hematologic malignancies receiving chemotherapy [16,17]. A three-year prospective study conducted in Tunisia in patients with hematologic malignancies revealed that among 105 neutropenic patients, 29 were diagnosed with invasive aspergillosis [12]. Another study from northern Algeria describes a 7.7% rate of invasive aspergillosis in neutropenic patients [12], which is confirmed by our study in which *Aspergillus* sp was isolated from 12 neutropenic patients out of 15 identified cases of aspergillosis.

Serological diagnosis of invasive opportunistic fungal infections is a real necessity to allow early and rational implementation of antifungal treatment and to prevent mortality, but, because of the humoral immunity deficit secondary to the deep immunosuppression linked to the underlying pathology or its treatment, serum antibody detection techniques are often of little help during the acute phase of the infection, On the other hand, they are good prognostic markers [18], so the diagnosis of invasive infection relies mainly on the detection and assay of parietal polysaccharide components specific to certain fungal genera or species, mannans for *Candida* or galactomannan for *Aspergillus*, which are currently valuable tools used almost routinely in clinical mycology. A positive blood test is a major biological argument for the diagnosis of invasive fungal infection, especially in neutropenic patients, as these antigens can be detected early before mycological examinations and sometimes even before the appearance of clinical and/or radiological signs of the disease [18].

Regarding pneumocystis, a deep-seated mycosis caused by a cosmopolitan fungus, *Pneumocystis jirovecii*, developing mainly in the lung of profoundly immunocompromised patients [19]. The infection usually occurs when T-cell function is suppressed, it is a common opportunistic infection in HIV-infected patients, Thus, it is observed in various clinical entities, such as solid organ transplants, autoimmune diseases and patients undergoing chemotherapy [20], as shown in our study. However, a single-center study conducted at the Mohammed VI University Hospital in Marrakech, Morocco, found that pneumocystis was indicative of HIV infection in 80% of cases [21], a second Cameroonian study reported a high prevalence of detection of *Pneumocystis jirovecii* in healthy HIV patients, while another also reported an increased frequency of the disease in African children [22]. Nevertheless, chemoprophylaxis with trimethoprim-sulfamethoxazole (TMP- SMX) taking into account the immune status of the patient and the underlying disease is still necessary to prevent infection [19].

The rise of *Cryptococcus* sp has completely modified the epidemiology of cerebrospinal diseases in sub-Saharan Africa, where 70% of HIV/AIDS infections are located. Cryptococcal neuromeningitis (CNM) is the highest form of this infection. Mortality remains high and death is unavoidable in the absence of antifungal treatment. The frequency of this condition ranges between 2% and 30% in patients with HIV [9]. Nevertheless, all cases with cryptococcosis identified in our series were seropositive, which is compatible with the literature, particularly in Algeria and sub-Saharan Africa where more than 70% of cryptococcosis cases are seropositive [13,23].

Detection of subclinical or asymptomatic infection by testing for serum cryptococcal antigenemia in patients with advanced HIV infection, and administering antifungal therapy to those who test positive, can prevent the development of neuromeningeal cryptococcosis (NCM). The cryptococcal antigen is identifiable on average 22 days before clinical onset [24], and has been shown to be 100% significant in terms of predicting the occurrence of CNM during the first year of antiretroviral therapy [25]; it is further linked to CNM and mortality [26].

Trichosporonosis, as an infection of immunocompromised individuals, is gradually being identified as an opportunistic disease with the potential to cause invasive and fatal disseminated infections. It is considered the second most common cause of yeast infection after *Candida*. It has also been reported in AIDS patients and critically ill patients without other underlying immunosuppression. Skin and nail lesions are quite common, such as the cases mentioned above, and may serve as a diagnostic clue to invasive *Trichosporon* sp infection [27].

Given the potential risk of certain intestinal parasites in immunocompromised individuals, early screening for intestinal parasitic infections is highly recommended, which will contribute to the management and improved quality of life of these persons [28]. *Cryptosporidium* sp and *Cyclospora* sp were found to be the major agents of intestinal parasitic infection in the present series with rates of 4.6% and 3.4% respectively, similar results have been obtained in Morocco [29] and in other parts of Africa, such as Nigeria and Tanzania [30], these two parasites, coccidian protozoa, continue to be the most common etiological agents of diarrhea in immunocompromised patients, especially HIV-infected patients [31]. Diagnosis is usually made by microscopically identifying the presence of oocysts in the stool of infected individuals by acid-fast staining (modified Ziehl-Neelsen method) on unconcentrated fecal smears, where oocysts stain pink on a blue counter-stain background [32].

Conclusion

Epidemiologic changes in the occurrence of fungal and parasitic infections in an immunocompromised patient population present a real challenge to the clinician. The increased morbidity and mortality related to these infections persists despite the increasing spectrum of antifungal drug therapy. Perhaps the best approach to controlling these pathogens is to develop at least less invasive therapies that represent a source of immunosuppression to prevent the development of these infections.

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Bibliography

1. Bnelhaj H. "Mycoses opportunistes et immunodepression". Universite´ mohammed V faculte´ de medecine et de pharmacie de rabat – Maroc (2010).
2. Koehler P., *et al*. "Epide´miologie de l'aspergillose invasive et de la re´sistance aux azoles chez les patients atteints de leuce´mie aigue: l'e´tudeSEPIA". *International Journal of Antimicrobial Agents* 49 (2017): 218-223.
3. Teng JC., *et al*. "E' pide´miologie des maladies fongiques invasives dans les troubles lymphoprolife´ratifs". *He´Matologique* 100 (2015): e462-e466.
4. Jerez Puebla LE. "Infections fongiques chez les patients immunode´prime´s". *Immunode´Ficience* (2012).
5. Sophie De Guibert., *et al*. "Indications des antifongiques syste´miques, spe´cialite´ par spe´cialite". *Me´Decine The´Rapeutique* 16.4 (2010): 296-312.
6. Gaborit B., *et al*. "Infections fongiques au cours de l'infection par le virus de l'immunodéficience humaine". EMC (2018).
7. Limper AH., *et al*. "Fungal infections in HIV/AIDS". *The Lancet Infectious Diseases* 17.11 (2017): e334-e343.
8. Dropulic LK and Lederman HM. "Overview of Infections in the Immunocompromised Host". *Microbiology Spectrum* (2016).
9. Koffi D., *et al*. "Estimates of serious fungal infection burden in Co^ te d'Ivoire and country health profile". *Journal of Medical Mycology* 31.1 (2021): 101086.
10. Bassiri Jahromi S and Khaksar AA. "Deep-seated fungal infections in immunocompromised patients in iran". *Iranian Journal of Allergy, Asthma and Immunology* 4.1 (2005): 27-32.
11. Marcio Nucci., *et al*. "Epidemiology of Opportunistic Fungal Infections in Latin America". *Clinical Infectious Disease* 51.5 (2010): 561-570.
12. Kmeid J., *et al*. "Epidemiology and burden of invasive fungal infections in the countries of the Arab League". *Journal of Infection and Public Health* 13.12 (2020): 2080-2086.

13. Chekiri-Talbi M and Denning DW. "Estimation des infections fongiques en Alge´rie". *Journal de Mycologie Me´dicale* 27.2 (2017): 139-145.

14. Monica A Slavin and Arunaloke Chakrabarti. "Opportunistic fungal infections in the Asia- Pacific region". *Medical Mycology* 50.1 (2012): 18-25.

15. Cuenca-Estrella M., *et al*. "Ligne directrice ESCMID* pour le diagnostic et la prise en charge des maladies a` Candida 2012: proce´dures de diagnostic". *Clinical Microbiology and Infection* (2012): 18.

16. Kimura S. "[Invasive Aspergillosis in Hematological Patients]". *Medical Mycology Journal* 57.2 (2016): 77-88.

17. Ardi P., *et al*. "Study on invasive aspergillosis using galactomannan enzyme immunoassay and determining antifungal drug susceptibility among hospitalized patients with hematologic malignancies or candidates for organ transplantation". *Microbial Pathogenesis* 147 (2020): 104382.

18. En ligne Bertholom C. "Le diagnostic des infections fongiques invasives". *Option/Bio* 20.417 (2009): 18-19.

19. Salzer HJF., *et al*. "Clinical, Diagnostic, and Treatment Disparities between HIV-Infected and Non- HIV-Infected Immunocompromised Patients with Pneumocystis jirovecii Pneumonia". *Respiration* 96.1 (2018): 52-65.

20. Wei KC., *et al*. "Pneumonie a` Pneumocystis jirovecii chez des patients atteints d'un lymphome non hodgkinien non infecte´s par le VIH et traite´s par rituximab". *Rapports Scientifiques* 8.1 (2018).

21. Elannaoui M. "La pneumocystose pulmonaire chez les patients vivant avec le VIH au CHU mohammed VI-Marrakech". Faculte´ de me´decine et de pharmacie de Marrakech- Maroc (2021).

22. Ocansey BK., *et al*. "Estimated Burden of Serious Fungal Infections in Ghana". *Journal of Fungi* 5.2 (2019): 38.

23. Rajasingham R., *et al*. "Global burden of disease of HIV-associated cryptococcal meningitis: an updated analysis". *The Lancet Infectious Diseases* 17.8 (2017): 873-881.

24. Ssebambulidde Kenneth., *et al*. "Symptomatic Cryptococcal Antigenemia Presenting as Early Cryptococcal Meningitis with Negative Cerebral Spinal Fluid Analysis". *Clinical Infectious Diseases: an Official Publication of the Infectious Diseases Society of America* 68.12 (2019): 2094-2098.

25. JN Jarvis., *et al*. "Harrison Screening for cryptococcal antigenemia in patients accessing an antiretroviral treatment program in South Africa". *Clinical Infectious Diseases* 48 (2009): 856-862.

26. DB Meya., *et al*. "Cost-effectiveness of serum cryptococcal antigen screening to prevent deaths among HIV-infected persons with a CD4+ cell count < or = 100 cells/microL who start HIV therapy in resource-limited settings". *Clinical Infectious Diseases* 51 (2010): 448-455.

27. Wan J., *et al*. "Plaques purpuriques et de couleur cre`me chez une personne immunode´prime´e: un cas de trichosporonose disse´minee". *JAAD Case Reports* 2.3 (2016): 275-277.

28. Heydari A., *et al*. "Investigating the Prevalence of Intestinal Parasites in Immunocompromised Patients in Bushehr Province, Southwest Iran: A Conventional and Molecular Study". *Türkiye Parazitoloji Dergisi* 45.2 (2021): 121-127.

29. Badaoui L and G Dabo HL. "Parasitoses opportunistes digestives chez les adultes infecte´s par le VIH: Aspects e´pide´miologiques Opportunistic digestive parasitic infections in adults infected with HIV: epidemiological expression". *Journal Marocain des Sciences Me´dicales* 19.2 (2014).

30. Samie A., *et al*. "Prevalence of intestinal parasitic and bacterial pathogens in diarrhoeal and non-diarroeal human stools from Vhembe district, South Africa". *Journal of Health, Population and Nutrition* 27.6 (2009): 739-745.

31. Liu H., *et al*. "Prevalence and genetic characterization of *Cryptosporidium, Enterocytozoon, Giardia* and *Cyclospora* in diarrheal outpatients in China". *BMC Infectious Diseases* 14 (2014): 25.

32. Bhattachan B., *et al*. "Detection of *Cryptosporidium parvum* and *Cyclospora cayetanensis* infections among people living in a slum area in Kathmandu valley, Nepal". *BMC Research Notes* 10.1 (2017): 464.

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