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Clinical insights into invasive aspergillosis among immunosuppressed patients: A single-centre experience from Argentina

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ABSTRACT

Background: Invasive aspergillosis poses a significant threat to immunocompromised individuals. Diagnostic criteria incorporating biomarkers and imaging have improved diagnosis, and treatment options have expanded. However, in Argentina, diverse patient demographics and environmental factors add complexity to managing this infection.
Aims: This study aims to explore the epidemiology, diagnostic methods, and treatment of invasive aspergillosis in an Argentine hospital setting.
Methods: We collected data from patients with suspected invasive aspergillosis at a tertiary care hospital in Central-Northern Argentina. Variables included demographics, underlying conditions, diagnostic criteria, treatment, and outcomes.
Results: With a median age of 44.5 years and a 51% of male patients, our institution conducted invasive aspergillosis screenings on 192 patients, many of whom were battling malignancies (90%). One third of them had the infection set as probable or possible. Imaging (31%) and positive microbiological results (16%) were examples of diagnostic evidence. With an overall mortality rate of 15%, half of the patients got antifungal treatment for a median of seven days. Mortality among the diagnosed patients was 22%. Patients without stem-cell transplantation had a high death rate (31%), although this difference was not statistically significant; in patients having pulmonary nodules (15%) the death rate was not statistically significant either. There were no discernible variations in mortality according to the type of treatment received.
Conclusions: Our study reveals that invasive aspergillosis remains a significant issue in high-risk patients, and has a notable mortality rate, particularly among those patients with pulmonary nodules. Computed tomography provides a high diagnostic yield.

Perspectivas clínicas sobre la aspergilosis invasiva en pacientes inmunodeprimidos: experiencia de un centro en Argentina

Palabras clave:
Aspergilosis invasiva
Pacientes inmunodeprimidos

RESUMEN

Antecedentes: La aspergilosis invasiva representa una amenaza significativa para las personas inmunodeprimidas. Los criterios diagnósticos que incluyen biomarcadores y estudios por imágenes han mejorado su diagnóstico, y las opciones terapéuticas se han ampliado. Sin embargo, en Argentina, la diversidad demográfica de los pacientes y los factores ambientales añaden complejidad al manejo de esta infección.

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Objetivos: Este estudio tiene como objetivo explorar la epidemiología, los métodos diagnósticos y el tratamiento de la aspergilosis invasiva en un hospital argentino.
Métodos: Se recopilaron datos de pacientes con sospecha de aspergilosis invasiva de un hospital terciario ubicado en el centro-norte de Argentina. Las variables incluyeron datos demográficos, condiciones subyacentes, criterios diagnósticos, tratamiento y resultados.
Resultados: Con una mediana de edad de 44,5 años y un 51% de pacientes de sexo masculino, se realizaron cribados de aspergilosis invasiva en 192 pacientes, la mayoría con neoplasias malignas (90%). Un tercio de los casos fueron clasificados como probables o posibles. Técnicas de imagen (31%) y resultados microbiológicos positivos (16%) aportaron las evidencias diagnósticas. La tasa de mortalidad global fue del 15%, y la mitad de los pacientes recibió tratamiento antifúngico durante una mediana de siete días. La mortalidad entre los pacientes diagnosticados fue del 22%. Los pacientes sin trasplante de progenitores hematopoyéticos presentaron una alta tasa de mortalidad (31%), aunque esta diferencia no fue estadísticamente significativa. En los pacientes con nódulos pulmonares (15%) la tasa de mortalidad tampoco fue significativa estadísticamente. No se observaron variaciones discernibles en la mortalidad según el tipo de tratamiento recibido.
Conclusiones: Los hallazgos revelan que la aspergilosis invasiva sigue siendo un problema relevante en pacientes de alto riesgo, a pesar de la profilaxis, y se asocia con una notable tasa de mortalidad, especialmente entre aquellos pacientes con nódulos pulmonares. La tomografía computarizada aporta un alto rendimiento diagnóstico.

Invasive aspergillosis is a serious fungal infection caused by fungi within the *Aspergillus* genus, most commonly *Aspergillus fumigatus*.[2,16] This condition mainly affects immunocompromised patients. The immunological vulnerability of these individuals facilitates the colonization and tissue invasion by the fungus, which can trigger an uncontrolled inflammatory response and, in severe cases, lead to the systemic dissemination of the infection, with potentially fatal consequences.[12] In recent years, some diagnostic criteria, including the detection of biomarkers such as galactomannan,[6] a polysaccharide released by the cell wall of *Aspergillus* during the active replication of the fungus, and the interpretation of tomographic images, which can reveal characteristic signs of the disease, such as nodular lesions, pulmonary cavitation or vascular invasion,[4] have been set up. In addition, there are new antifungal treatment options.[10]

In the hospital context of Argentina, invasive aspergillosis represents a multifaceted and significant clinical challenge. The diversity of the patient population, along with the country's own environmental conditions, contributes to the complexity of managing this fungal infection.[5,14] The high prevalence of immunocompromised patients, including those undergoing solid organ or bone marrow transplants, as well as patients with malignant haematological diseases such as leukaemia and lymphoma, is a favourable scenario for the development of invasive aspergillosis.[14] In addition, the increasing incidence of chronic diseases, such as diabetes mellitus and chronic obstructive pulmonary disease in the general population, increases the population at risk of contracting this invasive aspergillosis.[14] The diverse geography of Argentina, marked by latitudinal values ranging from subtropical to sub-Antarctic regions, influences the distribution and environmental load of *Aspergillus* spores, which can vary significantly depending on the geographical location of the hospital centre. Local weather conditions, such as humidity and temperature, can favour the proliferation of fungi in the hospital environment, thus increasing the risk of exposure and acquisition of the fungus in susceptible patients.[8] In addition, the infrastructure, infection control practices, or access to diagnostic and treatment techniques can vary among different hospital centres, affecting the implementation of preventive measures and the clinical management of invasive aspergillosis cases.[13]

In this manuscript, our aim was to explore the epidemiology, risk factors, diagnostic methods, and therapeutic options for invasive aspergillosis in an Argentinian hospital centre, providing an updated and practical vision for the effective management of this mycotic infection in our clinical setting.

1. Methods

Information regarding patients with suspected invasive aspergillosis, based on clinical symptomatology, was systematically collected over a 18-month period to thoroughly examine the treatment approaches at Sanatorio Allende, a tertiary care centre located in Central-Northern Argentina. The institution is a tertiary hospital with 232 beds, primarily serving patients undergoing allogeneic stem-cell transplantation. As this study was retrospective and cross-sectional, it was determined that no ethical clearance, nor informed consent, was required in accordance with the regulations set forth by the local ethics committee of Sanatorio Allende (Córdoba, Argentina).

A comprehensive array of variables was documented for our analysis, encompassing demographic details such as sex and age, the primary underlying condition predisposing patients to invasive aspergillosis, additional predisposing factors for invasive aspergillosis beyond malignancy, the status and last treatment history of malignancies preceding invasive aspergillosis (if applicable), radiological indicators of invasive aspergillosis, mycological evidence (including identification of the pathogenic fungus, when available), site of infection, ongoing antifungal prophylaxis, treatment specifics, as well as 30 days post-invasive aspergillosis diagnosis mortality.

Patients included in the analysis were categorized as having proven, probable, or possible invasive fungal infection (IFI) according to the European Organization for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) criteria.[6] If patients were not eligible within the abovementioned categories (patients with underlying conditions, symptoms and mycological evidence suggesting IFI, but without supportive imaging procedures), they were considered as having putative IFI.

We did not estimate a-priori sample size for this exploratory study. To examine and compare the demographics and clinical characteristics of patients, categorical variables are presented as frequencies and percentages, with comparisons in mortality proportion made using the chi-squared test or Fisher's exact test, as appropriate. Continuous variables are described using medians and

interquartile ranges (IQRs), with comparisons performed using the Mann–Whitney *U* test. Data processing and analysis were performed using the Statistical Package for the Social Sciences (SPSS®) version 27.0, developed by IBM Corp. in Chicago, IL, United States.

2. Results

Over a period of 18 months, our hospital admitted 192 patients for screening due to suspicion of invasive aspergillosis. Among these patients, 51% (98/192) were male, and the median overall age was 44.5 years (IQR 30–60, range 0–76). A vast majority, 89.6% (172/192), were battling malignancies during the screening process. Non-mould active antifungal prophylaxis was administered to 76.6% (147/192) of the patients, primarily fluconazole (99.3%, 146/147) (Table 1).

Out of the total patients screened for invasive aspergillosis, 33.9% (65/192) were finally diagnosed with the infection. The diagnoses were distributed as follows: 3.1% (2/65) proven, 36.9% (24/65) probable, 52.3% (34/65) possible, and 7.7% (5/65) putative invasive aspergillosis (Table 1).

In terms of diagnostic evidence, 16.1% (31/192) of the cases had positive microbiological results, while 31.3% (60/192) had imaging procedures supporting invasive pulmonary aspergillosis. Antifungal treatment was received by 51% (98/192) of the patients, with a median duration of 7 days (IQR 4–13, range 2–21). The overall mortality rate among the screened patients was 14.6% (28/192) (Table 1).

Focusing on the 65 patients diagnosed with invasive aspergillosis, all in the lungs, 64.6% (42/65) were male, and the median age was 44.5 years (IQR 30–60, range 0–76). A high percentage, 87.7% (57/65), had an underlying malignancy, primarily haematological. These malignancies were predominantly treated with either allogeneic (59.6%, 34/57) or autologous (31.6%, 18/57) hematopoietic stem-cell transplantation (HSCT). The median duration of neutropenia before invasive aspergillosis diagnosis was 12 days (IQR 8–14, range 3–30). Non-mould active prophylaxis before invasive aspergillosis diagnosis was observed in 73.8% (48/65) of the patients (Table 1).

In terms of diagnostic tests, serum galactomannan tests were positive in 38.5% (25/65) of the patients, 6.2% (4/65) had positive bronchoalveolar lavage (BAL) galactomannan tests, and two patients (3.1%) were diagnosed through lung biopsy. In 92.3% (60/65) patients computed tomography scan images supporting the diagnosis were obtained. Among them, 81.5% (53/65) showed pulmonary nodules suggestive of invasive pulmonary aspergillosis, and 21.5% (14/65) showed cavitation signs (Table 1).

Liposomal amphotericin B was the primary antifungal, administered to 72.3% (47/65) of the patients, either alone (60%, 39/65) or in combination with triazoles (12.3%, 8/65). Voriconazole was the preferred option for 15.4% (10/65) of the patients. The median duration of the antifungal treatment was 7 days (IQR 4–13, range 2–21) (Table 1).

The overall mortality rate among patients with invasive aspergillosis was 21.5% (14/65). This rate was similar for both males (21.4%, 9/42) and females (21.7%, 5/23), $p = 1$. Mortality in patients without HSCT (30.8%, 4/13) was higher compared to those with allogeneic HSCT (23.5%, 8/34), or autologous HSCT (11.1%, 2/18); however, the difference was not statistically significant, $p = 0.41$. No significant differences were observed either in mortality depending on the EORTC/MSG level of invasive aspergillosis (proven 50%, 1/2; probable 20.8%, 5/24; possible 14.7%, 5/34; putative 60%, 3/5), $p = 0.08$. However, patients with pulmonary nodules (15.1%, 8/53) had a significantly higher mortality compared to those without pulmonary nodules ($p = 0.016$), while this difference was not observed in patients with cavitations (42.9%, 6/14, $p = 0.06$). No statistically significant differences were observed in patient mortality based on the received treatment: liposomal amphotericin B (27.7%, 13/47, $p = 0.052$), triazoles (16.7%, 3/18, $p = 0.736$), echinocandins (0%, 0/3, $p = 1$) (Table 1).

3. Discussion

Over a span of 18 months, we retrospectively screened the clinical history of 192 patients that might have suffered invasive aspergillosis. Males were predominant (51%), with a median age of 44.5 years, and many of the patients had the underlying burden of malignancies (89.6%). Among our cohort, approximately one third (33.9%) received a final diagnosis of invasive aspergillosis, predominantly falling under the EORTC/MSG categories of probable or possible cases. Diagnostic confirmation hinged upon positive microbiological findings (47.7%) and diagnostic imaging results (92.3%). Almost all (92.3%) of the diagnosed patients underwent antifungal treatment for a median duration of 7 days. In the overall sample of screened patients, the mortality rate was 14.6%. Within the subset of invasive aspergillosis cases, mortality was notably higher (21.5%), with discernible correlation observed with pulmonary nodules, but not with cavitations or specific treatment modalities.

Echoing the findings in existing literature,[7] our study underscores a noteworthy sex discrepancy among patients, with a higher prevalence of invasive aspergillosis observed in males. However, the comparable mortality rates between both genders suggest that gender might not have exerted a significant influence on patient outcomes in the context of invasive aspergillosis. Furthermore, the median age (44.5 yers) of the affected individuals, with an interquartile range spanning from 30 to 60 years, suggests a wide age distribution, with higher mortality rate in middle-aged individuals.

The heightened mortality rate observed in patients with underlying malignancies, mainly haematological malignancies, although not statistically significant in our sample, aligns with previous reports emphasizing the pivotal role of immune status in prognostication.[9] Additionally, the median duration of neutropenia preceding invasive aspergillosis diagnosis, 12 days in our sample, concurs with existing literature, further highlighting prolonged neutropenia as a notable risk factor for invasive aspergillosis development.[11]

Diagnostic assessments revealed positive serum galactomannan tests in 38.5% of the patients, with additional positive findings from BAL galactomannan tests (6.2%) and lung biopsies (3.1%). Notably, 92.3% of patients exhibited positive computed tomography scan results suggestive of invasive aspergillosis, with pulmonary nodules identified in 81.5% of cases and cavitations in 21.5%. This underscores the pivotal role of imaging in invasive aspergillosis diagnosis, notwithstanding potential discrepancies between microbiological and imaging evidence, indicative of the current diagnostic limitations necessitating more refined clinical tools.[1,3,15]

Antifungal therapy was administered to 92.3% of patients, primarily involving liposomal amphotericin B (72.3%) either as monotherapy or in combination with triazoles, while voriconazole was preferred for 23.1% patients, aligning moderately with prevailing treatment guidelines, which recommend isavuconazole or voriconazole as first line treatment options.[1,3,15] The limited access to certain antifungals at our institution may be viewed as the primary constraint in providing the antifungals that are strongly recommended.[13] In parallel, in the majority of cases, the treatment administered was empirical. At that stage, microbiological evidence was unavailable, so a broader-spectrum antifungal, such as liposomal amphotericin B, was preferred in our institution.

Table 1
Clinical data of the enrolled patients.

	Screened sample		Invasive aspergillosis						
			Overall		Alive		Dead		*p* value
	n	%	*n*	%	*n*	%	*n*	%	
Sex									
Female	94	49.0%	23	35.4%	18	78.3%	5	21.7%	1.000
Male	98	51.0%	42	64.6%	33	78.6%	9	21.4%	
Age (years)	44.5 (30–60) [0–76]		44.5 (30–60) [0–76]		38 (20–56) [2–74]		43 (35–64) [0–69]		
Underlying conditions									
Haematological malignancy	163	84.9%	54	83.1%	44	81.5%	10	18.5%	
Solid tumour	10	5.2%	4	6.2%	4	100.0%	0	0.0%	
Diabetes mellitus	3	1.6%	1	1.5%	0	0.0%	1	100.0%	0.166
Solid transplantation[*]	5	2.6%	2	3.1%	1	50.0%	1	50.0%	
Other underlying conditions	9	4.7%	4	6.2%	2	50.0%	2	50.0%	
No underlying condition	2	1.0%	0	0.0%	0	0.0%	0	0.0%	
HSCT									
alloHSCT	80	41.7%	34	52.3%	26	76.5%	8	23.5%	
alloHSCT non-related	11	5.7%	8	12.3%	7	87.5%	1	12.5%	0.410
alloHSCT related	61	31.8%	24	36.9%	18	75.0%	6	25.0%	
alloHSCT NOS	8	4.2%	2	3.1%	1	50.0%	1	50.0%	
autoHSCT	67	34.9%	18	27.7%	16	88.9%	2	11.1%	
Neutropenia	177	92.2%	60	92.3%	48	80.0%	12	20.0%	0.292
Length in days	12 (8–14) [3–30]		12 (8–14) [3–30]		12 (9–16) [5–30]		13 (6–20) [5–23]		
Antifungal prophylaxis, yeast active	147	76.6%	48	73.8%	38	79.2%	10	20.8%	1.000
Fluconazole	146	76.0%	47	72.3%	37	78.7%	10	21.3%	
EORTC/MSG criteria									
No IFI	127	66.1%	–	–	–	–	–	–	
Putative IA	5	2.6%	5	7.7%	2	40.0%	3	60.0%	0.080
Possible IA	34	17.7%	34	52.3%	29	85.3%	5	14.7%	
Probable IA	24	12.5%	24	36.9%	19	79.2%	5	20.8%	
Proven IA	2	1.0%	2	3.1%	1	50.0%	1	50.0%	
Mycological evidence									
No positive result	161	83.9%	34	52.3%	29	85.3%	5	14.7%	
Positive BAL GM	4	2.1%	4	6.2%	4	100.0%	0	0.0%	0.172
Positive lung biopsy, histopathology	2	1.0%	2	3.1%	1	50.0%	1	50.0%	
Positive serum GM	25	13.0%	25	38.5%	17	68.0%	8	32.0%	
Imaging procedures									
Negative	132	68.8%	5	7.7%	2	40.0%	3	60.0%	
Positive	60	31.3%	60	92.3%	49	81.7%	11	18.3%	
Pulmonary nodules	53	27.6%	53	81.5%	45	84.9%	8	15.1%	0.016
Cavitation	14	7.3%	14	21.5%	8	57.1%	6	42.9%	0.060
Antifungal treatment									
Liposomal amphotericin B	82	42.6%	47	72.3%	34	72.3%	13	27.7%	0.052
Liposomal amphotericin B alone	73	38.0%	39	60.0%	29	74.4%	10	25.6%	
Liposomal amphotericin B + itraconazole	1	0.5%	1	1.5%	1	100.0%	0	0.0%	
Liposomal amphotericin B + posaconazole	2	1.0%	2	3.1%	1	50.0%	1	50.0%	
Liposomal amphotericin B + voriconazole	6	3.1%	5	7.7%	3	60.0%	2	40.0%	
Anidulafungin	1	0.5%	1	1.5%	1	100.0%	0	0.0%	
Caspofungin	2	1.0%	2	3.1%	2	100.0%	0	0.0%	
Fluconazole	1	0.5%	0	0.0%	0	0.0%	0	0.0%	
Voriconazole	12	6.3%	10	15.4%	10	100.0%	0	0.0%	
No treatment[**]	94	49.0%	5	7.7%	4	80.0%	1	20.0%	
Length of antifungal treatment (days)	7 (4–13) [2–21]		7 (4–13) [2–21]		10 (5–15) [2–21]		10 (7–21) [3–21]		
30-Day mortality	28	14.6%	14	21.5%	0	0.0%	14	100.0%	

BAL, bronchoalveolar lavage; EORTC/MSG, European Organization for Research and Treatment of Cancer/Mycoses Study Group; GM, galactomannan; HSCT, hematopoietic stem-cell transplantation; IA, invasive aspergillosis; IFI, invasive fungal infection; NOS, not otherwise specified.

[*] Solid transplantation: renal ($n = 3$), heart ($n = 1$), and liver ($n = 1$).

[**] The patient who neither received treatment nor survived was diagnosed post-mortem.

The overall mortality rate among all screened patients was 14.6% (28 out of 192). Notably, the mortality rate among invasive aspergillosis patients stood at 21.5% (14 out of 65), with no significant disparities noted across different variables. Nonetheless, the significantly elevated mortality observed in patients with pulmonary nodules underscores the potential prognostic value of this radiological finding.[5]

Despite the nature of this study, several limitations warrant acknowledgment. Firstly, its retrospective design inherently imposes constraints regarding data completeness and potential bias in patient follow-up. Additionally, the study was conducted at a single centre, which may limit the generalizability of the findings to broader patient populations. Furthermore, the reliance on diagnostic criteria for invasive aspergillosis, which are subject to

interpretation and evolving standards, may introduce variability in case ascertainment. The relatively small sample size, along with the use of mortality as the sole outcome measure, may also limit the generalizability of the results, including a full survival in patients receiving voriconazole. Moreover, the study's focus on hospitalized patients may overlook cases managed in outpatient settings, potentially underestimating the true burden of invasive aspergillosis in the community. Variability in clinical practices, such as antifungal prophylaxis regimens (the prophylaxis provided to our patients did not include mould-active regimens) and treatment modalities, may introduce confounding factors that influence outcomes. Lastly, the study's retrospective nature precludes the ability to establish causal relationships between exposures and outcomes, emphasizing the need for prospective investigations to elucidate the mechanisms underlying disease progression and treatment responses.

Despite these limitations, this study provides valuable insights into the epidemiology, clinical characteristics, and outcomes of invasive aspergillosis, laying the groundwork for future research endeavours aimed at addressing these knowledge gaps and refining clinical management strategies. Our study highlights the persistent challenge of invasive aspergillosis in high-risk patients. Diagnostic reliance on computed tomography scans and the moderate sensitivity of serum galactomannan tests underscores the need for a multifaceted approach to diagnosis. While treatment with liposomal amphotericin B moderately aligns with guidelines, mortality remains a concern, particularly in patients with pulmonary nodules, emphasizing the need for improved prophylactic and therapeutic strategies within our institution.

CRediT authorship contribution statement

FeRi and JSG made substantial contributions to the study concept and design, data verification, the statistical analysis and interpretation of data, and drafted the manuscript. FeRi, JC, CB, FeRo, BP, LLA, MM, and JSG made substantial contributions to the acquisition of data for the work, and critically reviewed the manuscript and gave the final approval for publication.

Consent for publication

Not applicable.

Ethics approval and consent to participate

As the data collection for this study was retrospective in nature, it was determined that no ethical clearance, nor informed consent, was required in accordance with the regulations set forth by the local ethics committee of Sanatorio Allende (Córdoba, Argentina).

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Declaration of competing interest

The authors declare no conflicts of interest related to the submitted manuscript. All authors had full access to the data and had the final responsibility when submitting them for publication.

Data availability

Data will be shared upon reasonable request after contacting the corresponding author.

References

1. Budin S, Salmanton-Garcia J, Koehler P, Stemler J, Cornely OA, Mellinghoff SC. Validation of the EQUAL Aspergillosis Score by analysing guideline-adherent management of invasive pulmonary aspergillosis. J Antimicrob Chemother. 2021;76:1070–7.
2. Cadena J, Thompson GR 3rd, Patterson TF. Aspergillosis: epidemiology, diagnosis, and treatment. Infect Dis Clin North Am. 2021;35:415–34.
3. Cornely OA, Koehler P, Arenz DSCM. EQUAL Aspergillosis Score 2018: an ECMM score derived from current guidelines to measure QUALity of the clinical management of invasive pulmonary aspergillosis. Mycoses. 2018;61:833–6.
4. de Oliveira VF, Silva GD, Taborda M, Levin AS, Magri MMC. Systematic review and meta-analysis of galactomannan antigen testing in serum and bronchoalveolar lavage for the diagnosis of chronic pulmonary aspergillosis: defining a cutoff. Eur J Clin Microbiol Infect Dis. 2023;42:1047–54.
5. Dignani MC, Davel G, Refojo N, Mazza M, Córdoba S, Hevia AI, et al. The epidemiology of mould infections in Argentina: review and experience. Curr Fungal Infect Rep. 2012;6:336–45.
6. Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis. 2020;71:1367–76.
7. Egger M, Hoenigl M, Thompson GR 3rd, Carvalho A, Jenks JD. Let's talk about sex characteristics – as a risk factor for invasive fungal diseases. Mycoses. 2022;65:599–612.
8. Giusiano GE, Piontelli E, Fernandez MS, Mangiaterra ML, Cattana ME, Kocsube S, et al. Biodiversity of species of *Aspergillus* section Fumigati in semi-desert soils in Argentina. Rev Argent Microbiol. 2017;49:247–54.
9. Henao-Martinez AF, Corbisiero MF, Salter I, Chastain DB, Thompson GR. Invasive pulmonary aspergillosis real-world outcomes: clinical features and risk factors associated with increased mortality. Med Mycol. 2023;61:myad074.
10. Hoenigl M, Arastehfar A, Arendrup MC, Bruggemann R, Carvalho A, Chiller T, et al. Novel antifungals and treatment approaches to tackle resistance and improve outcomes of invasive fungal disease. Clin Microbiol Rev. 2024;37:e0007423.
11. Koehler P, Salmanton-Garcia J, Grafe SK, Koehler FC, Mellinghoff SC, Seidel D, et al. Baseline predictors influencing the prognosis of invasive aspergillosis in adults. Mycoses. 2019;62:651–8.
12. Lionakis MS, Drummond RA, Hohl TM. Immune responses to human fungal pathogens and therapeutic prospects. Nat Rev Immunol. 2023;23:433–52.
13. Riera F, Caeiro JP, Cornely OA, Salmanton-Garcia J, Argentinian IFI Diagnostic and Treatment Capacity Group. The Argentinian landscape of mycological diagnostic capacity and treatment accessibility. Med Mycol. 2023;61:myad058.
14. Riera FO, Caeiro JP, Denning DW. Burden of serious fungal infections in Argentina. J Fungi (Basel). 2018;4:51.
15. Ullmann AJ, Aguado JM, Arikan-Akdagli S, Denning DW, Groll AH, Lagrou K, et al. Diagnosis and management of *Aspergillus* diseases: executive summary of the 2017 ESCMID-ECMM-ERS guideline. Clin Microbiol Infect. 2018;24 Suppl. 1:e1–38.
16. Yerbanga IW, Nakanabo Diallo S, Rouamba T, Denis O, Rodriguez-Villalobos H, Montesinos I, et al. A systematic review of epidemiology, risk factors, diagnosis, antifungal resistance, and management of invasive aspergillosis in Africa. J Mycol Med. 2023;33:101328.