https://doi.org/10.18549/PharmPract.2022.1.2613

Original Research

Appropriateness of antifungal prescribing in Oman

Fatima Issa El-Hussain, Abdullah Balkhair, Ibrahim Al-Zakwani, Mohammed Al Za'abi

Received (first version): 20-Dec-2021 Accepted: 18-Jan-2022 Published online: 20-Jan-2022

Abstract

Background: The inappropriate use of antimicrobials has substantially contributed to the development of antimicrobial drug resistance. Appropriate antibacterial prescribing has been emphasised, with minimal focus on appropriate prescribing of antifungals. Evaluation of antifungal use in the clinical setting is essential to prevent unnecessary drug exposure, development of resistance, adverse effects, and high hospitalisation costs. **Objective:** The purpose of this study was to assess the appropriateness of antifungal prescribing among adult patients at the Sultan Qaboos University Hospital (SQUH) in Oman. **Methods:** In this retrospective, observational study, the study population comprised adult patients treated with oral or intravenous antifungals between July 2018 and December 2019. The appropriateness of treatment was assessed using guidelines from the Infectious Diseases Society of America (IDSA) and the National Comprehensive Cancer Network (NCCN), as well as a set of literature-based criteria that were modified by SQUH infectious diseases team to suit local practices. These criteria included indication, dosage, and potential drug interactions. The primary outcome was the frequency of adherence to the treatment guidelines for fungal infections. Descriptive statistics were used for data analysis. **Results:** A total of 400 prescriptions were collected, of which 158 (39.5%) were for empirical therapy, 135 (33.8%) for targeted therapy, 69 (17.3%) for prophylactic therapy, and 38 (9.5%) for pre-emptive therapy. The overall appropriateness was 74.8%. The indication, dosage, and potential for antifungal-drug interactions were considered appropriate in 391 (97.8%), 314 (78.5%), and 381 (95.3%) prescriptions, respectively. Anidulafungin was the most prescribed antifungal agent, with 210 prescriptions (52.5%), followed by fluconazole with 102 prescriptions (25.5%), and voriconazole with 48 prescriptions (12%). Conclusion: In comparison with publised literature, our study revealed appropriate antifungal drug prescribing practices. However, studies with larger sample size in various hospital settings are necessary to confirm our findings on a national scale, and to obtain better statistical inferences and generalisability.

Keywords: Antifungal agents; Inappropriate prescribing; Guideline; Drug resistance; Anidulafungin; Fluconazole; Voriconazole

INTRODUCTION

Antimicrobial drug resistance is a major global concern in clinical medicine. It has been classified by the World Health Organization (WHO) as one of the top ten global public health threats.[1,2] The misuse and overuse of antimicrobials have been identified as major contributors to the development of antimicrobial drug resistance; as a result, emphasis has been placed on appropriate antibacterial prescribing. However, there has been minimal focus on appropriate prescribing of antifungals and antivirals.[3,4] Although acquired resistance to antifungals is less common than resistance to antibiotics, this does not diminish the importance of antifungal resistance, particularly since treatment for fungal infections is limited to only a few classes of antifungal drugs.

Inappropriate antifungal use increases the likelihood of microbial resistance, thereby exposing patients to unnecessary risks, which may cause adverse events and increase hospitalization costs.[5-9] Recent trends in acquired antifungal resistance include increased azole resistance among non-*Candida albicans* isolates, azole resistance in *Aspergillus fumigatus*, and echinocandin resistance in *Candida glabrata* (*C. glabrata*).[5-8] In addition, some fungal species are intrinsically resistant to certain drugs: for example, resistance of *Candidakrusei* to fluconazole and resistance of *Candida lusitaniae* to amphotericin B.[5-8] This is a major concern, particularly for patients who are highly vulnerable to infections, such as immunocompromised patients, cancer patients, organ transplant recipients, and patients undergoing major surgeries.

Studies conducted in various settings have demonstrated that the appropriate use of antifungal drugs ranges from 29% to 62%.[10-14] Nivoix et al. studied the adherence of antifungal prescribing to international antifungal prescribing guidelines in the intensive care unit (ICU) and in the oncology and haematology departments at a tertiary care hospital in France.[10] They reported that the indication and dosage were appropriate in 65% and 62% of cases, inappropriate in 22% and 21% of cases,

Fatima Issa EL-HUSSAIN. MSc. Department of Pharmacology and Clinical Pharmacy, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman. s128706@student.squ.edu.om
Abdullah BALKHAIR. MD. FRCPc. Senior Consultant, Infectious Diseases Unit, Department of Medicine, Sultan Qaboos University Hospital, Muscat, Oman. balkhair@squ.edu.om
Ibrahim AL-ZAKWANI. PhD. Professor, Department of Pharmacology and Clinical Pharmacy, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman. azakwani@squ.edu.om
Mohammed AL ZA'ABI*. MD. PhD. Professor, Department of Pharmacology and Clinical Pharmacy, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman. zaabi@squ.edu.om

www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

https://doi.org/10.18549/PharmPract.2022.1.2613

and debatable in 13% and 17% of cases. Valerio et al. showed that antifungals were inappropriately prescribed in 16% of cases at a tertiary care hospital in Spain in 2017.[11] Inappropriate prescriptions were associated with inadequacies in drug selection (31%) and dosing (16%), not switching from intravenous to oral administration (20%), not adjusting drugs after microbiological results (35%), and unsuitable lengths of therapy (27%).

In a Malaysian tertiary care hospital in 2016, antifungal therapy was found to be appropriate in 44.7% of cases, debatable in 17.9% of cases, and inappropriate in 37.3% of cases.[12] Lachenmayr et al. reported in 2016 that 38% of antifungal drug prescriptions in a German tertiary care hospital were deemed appropriate, while 15.2% and 46.8% of prescriptions were considered debatable and inappropriate respectively.[12]

To the best of our knowledge, there are no studies on the appropriateness of antifungal prescribing in Oman; data is limited to general utilization patterns and surveillance reports.[15,16] In a retrospective analysis of *Candida auris (C. auris)* cases reported nationally to the Oman Antimicrobial Surveillance System in 2019, Al-Rashdi et al. revealed that outbreaks of *C.auris* infections were ongoing and posed a substantial health risk.[16] There were 129 isolates of *C.auris* from 108 inpatients. Of the isolates, 94.8% and 96.1% were non-susceptible to fluconazole and amphotericin, respectively. The mean time from admission to infection was 1.7 months, the mean length of hospital stay was 3.5 months, and the associated mortality rate was 52.5%.

Periodic evaluation of antifungal drug use in the clinical setting is required to optimise patient outcomes and prevent resistance and its associated consequences. The purpose of this study was to assess the appropriateness of antifungal prescribing, in terms of indication, dosage, and drug interactions, among adult patients at Sultan Qaboos University Hospital (SQUH), a tertiary health care facility in Oman.

METHODS

Setting and design

This retrospective, observational study was conducted at SQUH in 2020. Patients aged ≥18 years who were prescribed oral or parenteral antifungals between 1 July 2018 and 31 December 2019 were included in this study. Patients who were prescribed topical or vaginal antifungals were excluded. Ethical approval was obtained from the Medical Research Ethics Committee of Sultan Qaboos University, Muscat, Oman (MREC approval number, 2349).

Evaluation of the appropriateness of antifungal prescribing

The appropriateness assessment was based on criteria previously described by Nivoix et al., that were modified by the SQUH infectious diseases team.[10] These criteria included indication, dosage, and potential antifungal–drug interactions (Table 1). Antifungal use was deemed appropriate when the three evaluation criteria were met, debatable when at least one debatable assessment criterion was present without the presence of any inappropriate assessment criteria, and inappropriate when at least one inappropriate assessment criterion was present.

The indications and dosages were assessed based on the recommendations made by the SQUH infectious diseases team, the Infectious Diseases Society of America (IDSA) guidelines for the diagnosis and management of aspergillosis and candidiasis, and the National Comprehensive Cancer Network (NCCN) guidelines for the prevention and treatment of cancer-

Table 1. Criteria used to assess adherence to antifungal treatment guidelines

Assessment	Indication	Dosage	Antifungal-drug interaction
Appropriate	Follows published guidelines, local protocol, adapted to mycological data, and/or follows infectious diseases team recommendation	Appropriate dose x or underdose or overdose by ≤10% with respect to loading dose when recommended. Also observing the recommended dose limit and dose adjustments for renal dysfunction	Antifungal has no potential interaction with drugs used concomitantly Antifungal presents potential interactions with moderate severity but is subjected to clinical monitoring and/or dose adjustment when required
Debatable	Does not follow protocol, but there is evidence in the literature or there is no suitable alternative	Underdose or overdose x by ≤25% and/or no loading dose and/or no discontinuation or dose adjustment in case of clinically related adverse events	Antifungal presents potential interactions with moderate severity, and clinical monitoring and/or dose adjustment is not performed when required
Inappropriate	Inappropriate antifungal selection with respect to the protocol or mycological data and despite the existence of a suitable alternative	Under or overdose x > 25%; no discontinuation or dose adjustment in case of clinically related adverse event when an appropriate alternative is available	Antifungal presents potential interactions with concomitant medications, including serious or contraindicated interactions. The antifungal is used with concomitant drug therapy and results in failure of the antifungal. Concomitant use of two antifungals of the same classification.

X= According to the drug labelling or guidelines, including dose adjustments according to renal functions.

https://doi.org/10.18549/PharmPract.2022.1.2613

related infections.[17-19] The potential for antifungal–drug interactions and their risk category was assessed using Lexi-Interact Online software (Lexi-Comp Inc., Hudson, Ohio, United States).

Sample size estimation

Previous studies have shown that the rate of appropriate antifungal drug use ranged between 29% and 65%.[10-14] Therefore, for a sample size of 363 patients, a hypothesised appropriate use rate of 40%, a margin of error of 5%, and a confidence interval of 95% were used. The sample size was further increased to 400 to account for any missing data.

Statistical analysis

Descriptive statistics were used to analyse the data collected in this study. Continuous data were described as means and standard deviations (SDs) for normally distributed variables. Categorical data were expressed as frequencies and percentages. Data analysis was performed using the Statistical Package for Social Sciences software version 25 (SPSS, IBM, Chicago, Illinois, USA).

RESULTS

Four hundred patients were enrolled in this study, of whom 58.5% (n=234) were men. The mean age of the study cohort was 52 ± 19 years (range: 18–95 years), and the mean weight and height were 65 ± 19 kg (range: 23–137 kg) and 159 ± 12 cm (range: 75–186 cm), respectively.

Indication for antifungal agents

Among the 400 prescriptions, 227 were prescribed for infections caused by *Candida spp*. (56.8%), 119 for prophylaxis of invasive fungal infection (29.8%), 34 for aspergillosis (8.5%), 6 for mucormycosis (1.5%), 3 for *Pneumocystis jiroveci pneumonia* (0.8%), 1 for a *Cryptococcus sp.* infection (0.3%), and 1 for a *Fusarium sp*. infection (0.3%). Nine (2.3%) prescriptions were indicated for other reasons, such as basidiobolomycosis, *Saccharomyces* infections, tinea pedis, and prophylaxis in patients with human immunodeficiency virus (HIV) (Table 2).

Cultures were isolated from samples retrieved from 279 (69.8%) patients. A positive result was reported in 142 patients (50.9%). Among the positive cultures, 119 were

Table 2. Demographic and clinical characteristics of subjects and prescription (N=400)

Parameter		Mean (SD)	n	(%)
Male			234	58.5
Age, years		52 (19)		
Weight, kg		65 (19)		
Height, cm		159 (12)		
Hospital units	Intensive care		155	38.8
	Haematology		135	33.8
	Oncology		41	10.3
	Other*		69	17.3
Indication	Candida species		227	56.8
	Aspergillusspecies		34	8.5
	Mucorales		6	1.5
	Cryptococcus species		1	0.3
	Fusarium species		1	0.3
	Pneumocystis jirovecii pneumonia		3	0.8
	Invasive fungal infection**		119	29.8
	Others		9	2.3
Microbiological Testing	Candida species		119	83.8
	Aspergillosis species		14	9.9
	Mucorales		4	2.8
	Pneumocystis jirovecii		2	1.4
	Fusarium species		1	0.7
	Others		3	2.1

* Includes: Internal Medicine, Nephrology, Surgery, Gastroenterology, Neurology, Obstetrics and Gynaecology, Pulmonology, Cardiology and Rheumatology.
**Indicates use for prophylaxis for invasive fungal infection.

https://doi.org/10.18549/PharmPract.2022.1.2613

identified as *Candida spp.* (83.8%) and 14 as *Aspergillus spp*. (9.9%). Among the *Candida spp.*, 18 were identified as *C. auris* (15.1%) (Table 2).

Antifungal drugs used

Anidulafungin was prescribed for 210 patients (52.5%), fluconazole for 103 patients (25.8%), voriconazole for 48 patients (12%), liposomal amphotericin B for 18 patients (4.5%), caspofungin for 11 patients (2.8%), posaconazole for 8 patients (2%), and itraconazole for 3 patients (0.8%). Regarding the route of administration, antifungal drugs were administered intravenously to 297 patients (74.3%) and orally to 103 patients (25.8%). Of the 102 patients prescribed fluconazole, 27 (26.5%) had a creatinine clearance of ≤50 ml/min and required dosage adjustments.

The above antifungal drugs were prescribed in different units of the hospital. The ICU was the unit in which antifungals were the most frequently prescribed (155 prescriptions, 38.8%), followed by the haematology units (135 prescriptions, 33.8%), other medical specialties (69 prescriptions, 17.3%), and the oncology unit (41 prescriptions, 10.3%) (Table 2).

Appropriateness of antifungal indications

In this study, the stratification of prescriptions by therapeutic strategy revealed antifungal use as follows: empirical use in 158 patients (39.5%), targeted use in 135 patients (33.8%), prophylactic use in 69 patients (17.3%), and pre-emptive use in 38 patients (9.5%).

Most prescriptions (299, 74.8%) were deemed appropriate. The indication, dosage, and potential for drug interactions were considered appropriate in 391 (97.8%), 314 (78.5%) and 381 (95.3%) prescriptions, respectively. Inappropriateness was mainly associated with prophylactic use (34 out of 69 patients, 49.3%), followed by pre-emptive use (6 out of 38 patients, 15.8%), targeted use (15 out of 135 patients, 11.1%) and empirical use (5 out of 158 prescriptions, 3.2%). The haematology unit recorded the most cases of inappropriate prescribing (36 out of 135 prescriptions, 26.7%), followed by other medical units (13 out of 69 prescriptions, 18.8%), the oncology unit (7 out of 41 prescriptions, 17.1%) and the ICU (4 out of 155 prescriptions, 2.6%) (Table 3).

Table 3. The assessment of antifungal drug prescription appropriateness in relation to indication, dosage, interaction, treatment, and hospital units (N =400)

Parameter		Appropriate, n (%)	Inappropriate, n (%)	Debatable, n (%)
Assessment	Overall	299 (74.8)	41 (10.3)	60 (15)
	Indication	391 (97.8)	4 (1)	5 (1.2)
	Dosage	314 (78.5)	37 (9.2)	49 (12.3)
	Antifungal-drug interaction	381 (95.2)	8 (2)	11 (2.8)
Treatment	Empirical	133 (84.2)	20 (12.7)	5 (3.2)
	Targeted	108 (80)	12 (8.9)	15 (11.1)
	Prophylactic	32 (46.4)	3 (4.3)	34 (49.3)
	Pre-emptive	26 (68.4)	6 (15.8)	6 (15.8)
Hospital units	Intensive care	142 (91.6)	9 (5.8)	4 (2.6)
	Haematology	74 (54.8)	25 (18.5)	36 (26.7)
	Oncology	33 (80.5)	1 (2.4)	7 (17.1)
	Others	50 (72.5)	6 (8.7)	13 (18.8)

Voriconazole and caspofungin were the drugs that were most inappropriately prescribed in terms of indication (5 out of 48 patients (10.4%) and 1 out of 11 patients (9.1%), respectively). Fluconazole and posaconazole were the drugs that were most inappropriately prescribed in terms of dosage (44 out of 102 patients (43.1%) and 1 out of 8 patients (12.5%), respectively) (Table 4).

Potential for drug–drug interactions

The potential for antifungal–drug interactions was found in 76 (19%) prescriptions. Voriconazole had the highest potential for interactions, with 35 potential interactions identified (46.1%), followed by fluconazole with 30 (39.5%), posaconazole with 6 (7.9%), liposomal amphotericin B with 3 (3.9%), and itraconazole with 2 (2.6%). Most of these interactions had a risk rating of C (n=43), a risk rating of D (n=17), or a risk rating of X (n=11). Contraindications for combinations of antifungals were associated with the following combinations: voriconazole and azithromycin, voriconazole and tamsulosin, posaconazole and atorvastatin, posaconazole and tamsulosin, liposomal amphotericin B and foscarnet, itraconazole and domperidone (Table 5).

DISCUSSION

Appropriate and effective antifungal agents are essential for the treatment of fungal infections to ensure successful patient outcomes. Due to the limited number of antifungal drug classes, the emergence

https://doi.org/10.18549/PharmPract.2022.1.2613

Table 4. The assessment of each antifungal drug prescription appropriateness in relation to indication, dosage and interaction (N =400)

Antifungal Drug		**Appropriate (%)**	**Inappropriate (%)**	**Debatable (%)**
Anidulafungin n=210	Overall	86	12	2
	Indication	98	1	1
	Dosage	88	11	1
	Antifungal-drug interaction	100	0	0
Fluconazole n=102	Overall	50	7	43
	Indication	97	2	1
	Dosage	48	8	44
	Antifungal-drug interaction	95	4	1
Voriconazole n=48	Overall	70	13	17
	Indication	91	0	9
	Dosage	92	6	2
	Antifungal-drug interaction	77	8	15
Liposomal amphotericin B n=18	Overall	83	11	6
	Indication	100	0	0
	Dosage	89	11	0
	Antifungal-drug interaction	94	0	6
Caspofungin n=11	Overall	82	9	9
	Indication	91	0	9
	Dosage	91	9	0
	Antifungal-drug interaction	100	0	0
Posaconazole n=8	Overall	75	0	25
	Indication	100	0	0
	Dosage	88	0	12
	Antifungal-drug interaction	75	0	25
Itraconazole n=3	Overall	67	0	33
	Indication	100	0	0
	Dosage	100	0	0
	Antifungal-drug interaction	67	0	33

Table 5. Assessment of antifungal-drug interactions (N= 76)

Antifungal drug	**Interacting drug**	**Frequency**	**Risk rating**
Voriconazole n =35	Esomeprazole	11	C
	Azithromycin	6	X
	Atorvastatin	5	D
	Amlodipine	3	C
	Cyclosporin	3	D
	Others	7	
Fluconazole n=30	Amlodipine	5	C
	Azithromycin	5	C
	Atorvastatin	3	C
	Cyclosporin	3	C
	Moxifloxacin	3	C
	Others	11	
Posaconazole n=6	Esomeprazole	2	D

https://doi.org/10.18549/PharmPract.2022.1.2613

	Cyclosporin	1	D
	Tacrolimus	1	D
	Atorvastatin	1	X
	Tamsulosin	1	X
Liposomal amphotericin B n=3	Foscarnet	1	X
	Colistin	1	D
	Dexamethasone	1	C
Itraconazole n=2	Domperidone	1	X
	Esomeprazole	1	D

Risk Rating C: Monitor therapy. D: Consider therapy modification. X: Avoid combination

of resistance to a single drug class or multiple drugs can substantially complicate patient management.[6-9] Resistance of *Candida* and *Aspergillus* species to azoles, and multidrug resistance of some *Candida spp*., such as *C.glabrata* and *C.auris*, is regarded as a considerable challenge in the management of fungal infections.[6,20] Guidelines have been developed to assist clinicians in appropriate antifungal drug prescribing, and have been demonstrated to be a valuable tool. However, studies have shown that antifungal prescribing guidelines are not consistently adhered to, and inappropriate antifungal prescribing remains a clinical concern, especially in inpatient settings.[10,21,22]

Increasing research is being conducted on the use of antifungal drugs in tertiary care hospitals and adherence to treatment protocols, particularly in relation to IDSA and NCCN guidelines and the appropriate use of antifungal drugs has been reported to range from 29% to 62%.[10-14,23,24] In the present study, we assessed the appropriateness of antifungal prescribing among adult patients at a tertiary health care facility in Oman. We found that over two-thirds (74.8%) of antifungal prescriptions met all the evaluation criteria for appropriate indication, dosage, and potential for drug–drug interactions. The appropriateness rate was 97.8% for indication, 78.5% for dosage, and 95.2% for antifungal-drug interactions. These results are comparable to those of previous studies, in which appropriateness was shown to be in the range of 65–91% for indication, 62–86% for dosage and 46–94% for drug–drug interactions.[10-14,23,24]

Azole antifungals had the lowest rates of appropriate prescribing, which is a finding consistent with previous research.[10-14] The prescribing of azole antifungals was deemed inappropriate due to the lack of dosage reductions in patients with impaired renal function, the lack of loading doses on the first day of therapy, insufficient maintenance dosing, and prescribing in the presence of contraindications or clinically significant drug interactions. It has been shown that patients who receive inappropriate or debatable antifungal treatment have a lower 12-week survival rate (70%) than patients who receive appropriate therapy (81%).[24] Furthermore, Zilberberg et al. demonstrated that inappropriate antifungal therapy had a negative impact on patient outcomes.[25]

In this study, we found a predominance of infections caused by *Candida spp.,* which might explain why anidulafungin and fluconazole were the most frequently prescribed agents. Anidulafungin was prescribed in over half of the prescriptions (52.5%), in addition to fluconazole (25.5%), and voriconazole (12%). In other studies, fluconazole and amphotericin B were the most prescribed antifungal agents.[12,14] A randomised, double-blind trial showed that anidulafungin was more effective than fluconazole in treating systemic Candida infections.[26] Furthermore, a recent pharmacoeconomic analysis reported that anidulafungin was more cost-effective for the treatment of invasive candidiasis caused by *Candida albicans* and non-*albicans Candida* species.[27,28]

In our study, 119 (83.8%) of the positive cultures were identified as *Candida spp*. This finding is consistent with the findings of other studies, in which positive cultures for *Candida spp*. were one of the most common indications for antifungal therapy.[10-14] Over the last decade, the threat of emerging multidrug-resistant *C.auris* has become more prominent worldwide, including in Oman.[16,29,30] In our study, 18 (15.1%) of the 119 isolated *Candida* spp. were identified as *C.auris*, which raises concerns about its spread.

The most common therapeutic strategy identified in our study was empirical (39.5%), followed by targeted (33.8%), prophylactic (17.3%), and pre-emptive (9.5%). Empirical therapy was found to be appropriate in 84% of cases, targeted therapy in 80% of cases, pre-emptive therapy in 68% of cases, and prophylactic therapy in 46% of cases. These findings are in line with the published literature.[10-14] Inappropriateness of prophylactic therapy was attributed to the underdosing of fluconazole in invasive fungal infections (200 mg versus 400 mg daily) and to the prescribing of 200 mg of fluconazole once weekly for the prophylaxis of cryptococcal disease in HIV patients, compared with the recommended dosage of 200–400 mg daily for 6 to 12 months.[18,19,31]

In the current study, we also assessed the appropriateness of antifungal therapies in relation to their interactions

https://doi.org/10.18549/PharmPract.2022.1.2613

with other administered medications. In this regard, the appropriateness was 95%, which is almost identical to the appropriateness reported by Nivoix et al. (94%).[10] In this study, most of the interactions involved azole antifungals (73 out of 76 interactions), which is not surprising given that azoles are well known for their effect on several hepatic cytochrome P450 enzymes and thus, their potential for interactions with a variety of drugs.[32,33]

Our study had a few limitations. First, the generalisability of our results may be limited because this study was conducted at a single tertiary care hospital, therefore, it may be difficult to apply our findings at other hospitals in the country. Second, data were collected via retrospective chart review so were based on electronic patient records; as a result, incomplete or missing information, laboratory tests, or insufficient documentation might have influenced the conclusions. Third, in this study, we were unable to assess the potential outcomes of antifungal drug interactions.

CONCLUSION

In summary, the overall appropriateness rate of antifungal prescribing was 74.8%. The rates of appropriate prescribing for indication, dosage, and potential drug interactions were 97.8%, 78.5%, and 95.2%, respectively. Most of the prescriptions were empiric, and anidulafungin was the most prescribed agent for the treatment of infections caused by *Candida spp*. To further promote appropriate antifungal use, we recommend involving a clinical pharmacist in antifungal prescribing and implementing an antifungal stewardship program across all hospital departments. Studies with larger sample size in various hospital settings are required for better statistical inferences and generalisability.

FUNDING

None.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS (CRediT)

Conceptualization: MA, FIE
Data curation: FIE
Formal analysis: FIE
Methodology: MA, FIE, AB, IA
Supervision: MA, AB, IA
Writing –original draft: MA, FIE
Writing –review & editing: IA, AB, MA

References

1. World Health Organization (2020). " Antimicrobial resistance." WHO, Geneva, Switzerland", Retrieved from https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance. Accessed on December 18, 2021.
2. Minarini LADR, de Andrade LN, De Gregorio E, et al. Editorial: Antimicrobial Resistance as a Global Public Health Problem: How Can We Address It? Front Public Health. 2020;8:612844. https://doi.org/10.3389/fpubh.2020.612844
3. McEwen SA, Collignon PJ. Antimicrobial Resistance: a One Health Perspective. Microbiol Spectr. 2018;6(2). https://doi.org/10.1128/microbiolspec.ARBA-0009-2017
4. Fletcher S. Understanding the contribution of environmental factors in the spread of antimicrobial resistance. Environ Health Prev Med. 2015;20(4):243-52. https://doi.org/10.1007/s12199-015-0468-0
5. Wiederhold NP. Antifungal resistance: current trends and future strategies to combat. Infect Drug Resist. 2017;10:249-259. https://doi.org/10.2147/IDR.S124918
6. Arastehfar A, Gabaldón T, Garcia-Rubio R, et al. Drug-Resistant Fungi: An Emerging Challenge Threatening Our Limited Antifungal Armamentarium. Antibiotics (Basel). 2020;9(12):877. https://doi.org/10.3390/antibiotics9120877
7. Arnold HM, Micek ST, Shorr AF, et al. Hospital resource utilization and costs of inappropriate treatment of candidemia. Pharmacotherapy. 2010;30(4):361-8. https://doi.org/10.1592/phco.30.4.361
8. Hendrickson JA, Hu C, Aitken SL, et al. Antifungal Resistance: a Concerning Trend for the Present and Future. Curr Infect Dis Rep. 2019;21(12):47. https://doi.org/10.1007/s11908-019-0702-9
9. Perlin DS, Rautemaa-Richardson R, Alastruey-Izquierdo A. The global problem of antifungal resistance: prevalence, mechanisms, and management. Lancet Infect Dis. 2017;17(12):e383-e392. https://doi.org/10.1016/S1473-3099(17)30316-X
10. Nivoix Y, Launoy A, Lutun P, et al. Adherence to recommendations for the use of antifungal agents in a tertiary care hospital. J Antimicrob Chemother. 2012;67(10):2506-13. https://doi.org/10.1093/jac/dks256
11. Valerio M, Rodriguez-Gonzalez CG, Muñoz P, et al. Evaluation of antifungal use in a tertiary care institution: antifungal stewardship urgently needed. J Antimicrob Chemother. 2014;69(7):1993-9. https://doi.org/10.1093/jac/dku053
12. Islahudin F, Mohd SFR. Evaluation of appropriate use of antifungal therapy in a tertiary care hospital. Asian J Pharm Clin Res. 2015;8(4):195-9.
13. Lachenmayr SJ, Berking S, Horns H, et al. Antifungal treatment in haematological and oncological patients: Need for quality assessment in routine care. Mycoses. 2018;61(7):464-471. https://doi.org/10.1111/myc.12768

www.pharmacypractice.org (eISSN: 1886-3655 ISSN: 1885-642X)

14. de Souza MC, Dos Santos AG, Reis AM. Drug utilization study of systemic antifungal agents in a Brazilian tertiary care hospital. Int J Clin Pharm. 2016;38(6):1398-1406. https://doi.org/10.1007/s11096-016-0382-6
15. Al Balushi KA, Alzaabi MA, Alghafri F. Prescribing Pattern of Antifungal Medications at a Tertiary Care Hospital in Oman. J Clin Diagn Res. 2016;10(12):FC27-FC30. https://doi.org/10.7860/JCDR/2016/23591.9005
16. Al-Rashdi A, Al-Maani A, Al-Wahaibi A, et al. Characteristics, Risk Factors, and Survival Analysis of Candida auris Cases: Results of One-Year National Surveillance Data from Oman. J Fungi (Basel). 2021;7(1):31. https://doi.org/10.3390/jof7010031
17. Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;63(4):e1-e60. https://doi.org/10.1093/cid/ciw326
18. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2016;62(4):e1-50. https://doi.org/10.1093/cid/civ933
19. Baden LR, Swaminathan S, Angarone M, et al. Prevention and Treatment of Cancer-Related Infections, Version 2.2016, NCCN Clinical Practice Guidelines in Oncology. J Natl ComprCancNetw. 2016;14(7):882-913. https://doi.org/10.6004/jnccn.2016.0093
20. Lone SA, Ahmad A. Candida auris-the growing menace to global health. Mycoses. 2019;62(8):620-637. https://doi.org/10.1111/myc.12904
21. Reslan Z, Lindsay J, Kerridge I, et al. Adherence to Antifungal Guidelines in Malignant Hematology Patients: A Review of the Literature. J Pharm Technol. 2019;35(6):270-280. https://doi.org/10.1177/8755122519859976
22. Poulat C, Nivoix Y, Launoy A, et al. Assessment of high-priced systemic antifungal prescriptions. Med Mal Infect. 2017;47(6):382-388. https://doi.org/10.1016/j.medmal.2017.03.004
23. Vazin A, Davarpanah MA, Ghalesoltani S. Antifungal agent utilization evaluation in hospitalized neutropenic cancer patients at a large teaching hospital. Drug Healthc Patient Saf. 2015;7:97-102. https://doi.org/10.2147/DHPS.S80762
24. Mencarini J, Mantengoli E, Tofani L, et al. Evaluation of candidemia and antifungal consumption in a large tertiary care Italian hospital over a 12-year period. Infection. 2018;46(4):469-476. https://doi.org/10.1007/s15010-018-1139-z
25. Zilberberg MD, Kollef MH, Arnold H, et al. Inappropriate empiric antifungal therapy for candidemia in the ICU and hospital resource utilization: a retrospective cohort study. BMC Infect Dis. 2010;10:150. https://doi.org/10.1186/1471-2334-10-150
26. Reboli AC, Shorr AF, Rotstein C, et al. Anidulafungin compared with fluconazole for treatment of candidemia and other forms of invasive candidiasis caused by Candida albicans: a multivariate analysis of factors associated with improved outcome. BMC Infect Dis. 2011;11:261. https://doi.org/10.1186/1471-2334-11-261
27. Ou HT, Lee TY, Chen YC, et al. Pharmacoeconomic analysis of antifungal therapy for primary treatment of invasive candidiasis caused by Candida albicans and non-albicans Candida species. BMC Infect Dis. 2017;17(1):481. https://doi.org/10.1186/s12879-017-2573-8
28. Auzinger G, Playford EG, Graham CN, et al. Cost-effectiveness analysis of anidulafungin for the treatment of candidaemia and other forms of invasive candidiasis. BMC Infect Dis. 2015;15:463. https://doi.org/10.1186/s12879-015-1143-1
29. Al-Siyabi T, Al Busaidi I, Balkhair A, et al. First report of Candida auris in Oman: Clinical and microbiological description of five candidemia cases. J Infect. 2017;75(4):373-376. https://doi.org/10.1016/j.jinf.2017.05.016
30. Alfouzan W, Dhar R, Albarrag A, et al. The emerging pathogen Candida auris: A focus on the Middle-Eastern countries. J Infect Public Health. 2019;12(4):451-459. https://doi.org/10.1016/j.jiph.2019.03.009
31. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of America. Clin Infect Dis. 2010;50(3):291-322. https://doi.org/10.1086/649858
32. Gubbins PO. Triazole antifungal agents drug-drug interactions involving hepatic cytochrome P450. Expert Opin Drug MetabToxicol. 2011;7(11):1411-29. https://doi.org/10.1517/17425255.2011.627854
33. Gubbins PO, Heldenbrand S. Clinically relevant drug interactions of current antifungal agents. Mycoses. 2010;53(2):95-113. https://doi.org/10.1111/j.1439-0507.2009.01820.x