

Prescription pattern of Antifungal medicines in a Tertiary Hospital General Practice Clinic, South-South, Nigeria

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ABSTRACT

Background: The increasing threat of antifungal resistance makes fungal diseases an emerging global health concern. Despite this, there is a notable lack of data on antifungal drug utilization in many low and middle-income countries like Nigeria. This study addresses this important gap by evaluating antifungal drug utilization in a tertiary hospital in South-South Nigeria. The objective: of the study was to describe the profile and prescribing trends of antifungal agents in a Tertiary Hospital General Outpatient Clinic South-South Nigeria

Methods: A cross-sectional and descriptive study conducted at the General Practice Clinic (GPC), of the University of Benin Teaching Hospital, Benin City, Edo state, Nigeria from January to December 2021. Dispensed prescription records from the GPC were manually reviewed. Patients who received antifungal agents were included in the study. Antifungal agents were identified using the World Health Organization Anatomical Chemical (ATC) system. The names, route of administration and use of multiple medications were noted. Data is presented descriptively.

Results: A total of 25,258 patients were dispensed prescriptions during the period, and of these, there were 538 (2.1%) patients with prescriptions of antifungal agents. The commonest antifungal monotherapies were fluconazole 284 (41.9%) and clotrimazole 183 (27.0%). Among the 128 patients prescribed multiple antifungal agents, Clotrimazole cream and fluconazole tablet was the commonest combination, 45 (35.2%). Oral formulations were mostly prescribed 350 (51.7%) followed by topical route 310 (45.8%).

Conclusion: This study found a low overall level of antifungal prescriptions. The urgent need for the development and implementation of antifungal stewardship programs cannot be overemphasized

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Keywords: Antifungal agents; Antifungal Stewardship; Drug Utilization review; Prescriptions; Outpatient Clinics; Fluconazole, Nigeria

INTRODUCTION

Fungal infections have increasingly become a serious threat to both human life and the ecosystem. Although the actual prevalence remains uncertain, global estimates suggest these infections affect 1.2 billion people. (Oladele et al. 2020; Denning 2024) Fungal skin infections are the 18th leading cause of the global health burden, accounting for 2% of total outpatient

consultations. (Hay et al. 2014) Typically caused by opportunistic pathogens, fungal infections can range from mild, asymptomatic superficial mycoses to severe, deep systemic diseases.

Citation: Ayinbuomwan SA, Opadeyi AO. (2025). Prescription pattern of Antifungal medicines in a Tertiary Hospital General Practice Clinic, South-South, Nigeria. Nig J Med Dent Educ; 7(2):118-124.

Superficial fungal infections generally affect quality of life and can be easily treated if diagnosed early, however they become life-threatening when they invade internal organs.(Das et al. 2009) The non-specificity of the clinical presentations of fungal infections, and the invasiveness of their diagnostic procedures have historically made early diagnosis challenging. The significant increase in the incidence of fungal infections, particularly in the tropics, is largely attributed to the hot and humid climate, high prevalence of HIV/AIDS and other conditions that can compromise immune defences. Other factors include increased childhood malnutrition, advanced age, the use of invasive monitoring devices, irrational use of broad-spectrum antibiotics, and long-term steroid therapy.(Maschmeyer and Patterson 2014; Oladele et al. 2019) These factors have largely contributed to importance of antifungal drugs to the practice of modern medicine in the last 30 years.

Antifungal drugs are the primary therapy for fungal infections and are a subclass of antimicrobials, which play a significant role in healthcare, especially in low-resource settings in Africa, where infections significantly contribute to morbidity. Undecylenic acid, phenolic dye and weak acid were the earliest available pharmacologic tools for fungal infection treatment. The discovery of griseofulvin in 1939 began the modern era of antifungal therapy in the mid-20th century.(Smith 1990) Over the years, various antifungal agents with different pharmacodynamics have been developed in response to the increased prevalence and rising mortality rates associated with these infections. Antifungal agents are categorized as polyenes, azoles (triazoles, imidazoles,), flucytosine or echinocandins. The addition of Amphotericin B deoxycholate to the therapeutic arsenal marked a major advancement in antifungal development. Two of the antifungal drugs in current use (triazoles and polyenes) had already been introduced into the clinics by 1980. The most recent addition to the antifungal pharmacopeia, the Echinocandins, was developed in 2001. (Butts and Krysan 2012) Most of these agents work by interfering with fungal ergosterol and other cell membrane synthesis, except for echinocandins, which inhibit fungal RNA and DNA synthesis.(Khan and Jain 2000; Odds et al. 2003) However, progress in the development of new antifungals has lagged behind other antimicrobials, partly due to the structural similarity between fungal cell walls and host cells. In addition, this is compounded by the rising trend of antifungal resistance across all categories,

making fungal diseases an emerging global threat. In Africa, irrational and indiscriminate use of antimicrobials is the biggest driver of drug resistance, including overprescribing, multiple prescribing, incorrect prescribing, under-prescribing, and inappropriate prescribing.(Vitiello et al. 2023) The rising threat of antifungal resistance is exacerbating the global challenge of managing infectious diseases. In response to this challenge, global initiatives are promoting the rational use of antimicrobials.(Amane and Priyadarshini 2011) However; the situation is worsening, particularly in developing countries, where widespread misuse of antimicrobials is contributing to the problem at an alarming rate. There is currently a paucity of antifungal drug utilization studies in South-South Nigeria. Evaluating antifungal prescription practices and consumption behaviour in this region can provide valuable insights needed to inform therapeutic decisions and address public health concerns regarding antifungal effectiveness. Therefore, we aimed to understand the profile of antifungal prescriptions in the General Outpatient Department of our institution.

MATERIALS AND METHODS:

This was a cross-sectional and descriptive study conducted at the General Practice Clinic (GPC), of the University of Benin Teaching Hospital, Benin City, Edo state. The clinic is managed by family medicine specialists who also refer patients to other specialists within the hospital. The study covered a period of 12 months, from January to December 2021.

Data Source: The prescription records in the GPC pharmacy were used to identify eligible cases for this study. The dispensed prescription records of all patients who obtained their medications from GPC pharmacy from January to December 2021 were manually reviewed. All patients who received at least one antifungal medication during the study period were included in the analysis. The antifungal medicines were selected using the World Health Organization- Anatomic Therapeutic Chemical (ATC) Classification level 4 and 5. J02-Antimycotics for systemic use; Do1- Antifungals for dermatological use; G01-Gynecological antineoplastic and antiseptics. (World Health Organization Collaborating Centre for Drug Statistics Methodology 2023)

Data analysis : The name of the antifungal agent(s) (generic or trade name), route of administration, and fixed dose combinations were extracted. Data was analyzed using descriptive statistics, including frequencies and proportions.

Ethical considerations: All data was anonymized and confidentiality maintained. The authors assert that all procedures contributing to this work comply with the relevant ethical standards. All procedures involving human subjects/patients data were approved by the University of Benin Teaching Hospital Ethics and Research committee (ADME/E/22/A/VOL.VII/148311668).

RESULTS

There was a total of 25,258 patients who were dispensed prescriptions during the period, and of these, there were 538 (2.1%) patients with prescriptions of antifungal agents. Of which 410 (76.2%) were on monotherapy, and 128 (23.8%) were on multiple antifungal agents. A total of 677 antifungal agents were prescribed in the study and the commonest agents were fluconazole 284 (41.9%) and clotrimazole 183 (27.0%). Fixed-dose combination products, clotrimazole and

metronidazole was prescribed in 21 (3.1%) followed by miconazole hydrocortisone, 5 (0.7%). (Table 1.)

Majority of the medications were administered through the oral route 350 (51.7%), topical route 310 (45.8%), however, the route was not stated for 17(2.5%) medications. The formulations commonly prescribed include oral fluconazole 278 (97.4), topical clotrimazole 116 (63.4%) and clotrimazole pessaries 26(14.2%) (Table 2).

Among the 128 patients prescribed multiple antifungal agents, Clotrimazole cream/Fluconazole tablet was the commonest combination in 45 (35.2%) of the prescriptions, followed by Terbinafine cream/Terbinafine tablet in 16 (12.5%). A couple of patients had 3 antifungal agents dispensed, Clotrimazole cream/Clotrimazole pessaries/Fluconazole tablet was the commonest 7(5.5%).(Table 3.)

Table 1: Antifungal agents dispensed at the UBTH General Practice Clinic

Drug	Frequency(n=677(%))
Fluconazole	284 (41.9)
Clotrimazole	183 (27.0)
Terbinafine	125 (18.5)
Ketoconazole	41(6.1)
Clotrimazole + Metronidazole	21(3.1)
Miconazole	8 (1.2)
Miconazole + Hydrocortisone	5 (0.7)
Itraconazole	4 (0.6)
Tioconazole	3 (0.4)
Clotrimazole + Betamethasone	2 (0.3)
Clotrimazole + Fluconazole	1(0.1)

DISCUSSION

The management of fungal infections in Sub-Saharan Africa faces numerous challenges, including the limited availability of routine diagnostic facilities and a lack of up-to-date, evidence-based treatment guidelines to support the appropriate prescription of antifungal medications. Accurate identification of the causative fungal species and the selection of effective antifungal agents are crucial for successful therapy. However, unlike bacterial infections, fungal infections receive comparatively less research attention—reflected in the scarcity of antifungal consumption studies within the region. Such data are essential for optimizing antifungal use and addressing related public health concerns. In light of this, we set out to evaluate the prescription patterns of antifungal medications in our general practice clinic. In this study, only 2.1% (538) of the 25,258 patients who attended the general practice clinic during the

review period received antifungal prescriptions. This low rate of antifungal prescribing may reflect the limited development and implementation of antifungal management protocols in many developing countries. Compared to other infectious diseases, fungal infections remain largely understudied, underdiagnosed, and undertreated.(Pagano and Fernández 2025) Additionally, most drug utilization studies on antimicrobial use in Africa tend to focus on antibiotics, with little attention given to antifungal agents.(Cole et al. 2017) Fluconazole was the most frequently prescribed antifungal agent in this study. This finding is consistent with previous reports by Valerio et al. (2014), Al Balushi et al. (2016), and Matthew et al. (2023).(Valerio et al. 2014; Al Balushi et al. 2016; Mathew et al. 2023) However, a study by Subashree et al. (2023), (Subashree et al. 2023) which evaluated antifungal prescription patterns in a tertiary care teaching hospital in South India, identified clotrimazole as

the most prescribed antifungal, closely followed by fluconazole. The discrepancy may be due to the relatively short duration of their study, which lasted only two months. Azole antifungals are commonly used in the treatment of fungal infections due to their favorable pharmacokinetic profiles and broad-spectrum activity. They are fungistatic and often employed for long-term management of conditions such as dermatophytosis, pityriasis, candidiasis, onychomycosis, and various systemic mycoses. Additionally, azoles are approved for prophylactic use against candidiasis in immunocompromised patients, including those undergoing cytotoxic chemotherapy, across all age groups. (Allen et al. 2015; Perfect 2017; Fisher et al. 2022) Although

azoles generally exhibit comparable efficacy, immunomodulatory properties, and favorable therapeutic indices, fluconazole is considered the least hepatotoxic among them, with a lower potential for drug interactions and a more favorable adverse effect profile. It is therefore not surprising that various clinical guidelines recommend fluconazole as the first-line treatment for Candida infections. (Pappas et al. 2015) Despite its initial effectiveness, there is a growing trend of resistance to fluconazole in Sub-Saharan Africa. This emerging resistance may be attributed to its widespread overuse in clinical settings, as well as its application as an agricultural fungicide by farmers. (Drakulovski et al. 2023)

Table 2: Formulations of the medications prescribed at the General Practice Clinic of the UBTH

Drug	Formulations	Proportion(%)
Fluconazole (284)	Tablet	141 (49.6)
	Capsule	136 (47.9)
	Cream	3 (1.1)
	Suspension	1 (0.4)
	Not Stated	3 (1.1)
Clotrimazole (183)	Cream.	83 (45.4)
	Vaginal Cream	33 (18.0)
	Pessaries	26 (14.2)
	Tablet	35 (19.1)
	Capsule	1 (0.5)
Terbinafine (125)	Not Stated	5 (2.7)
	Cream	93 (74.4)
	Tablet	31 (24.8)
	Not stated	1 (0.8)
Ketoconazole (41)	Cream	34 (82.9)
	Shampoo	1 (2.4)
	Tablet	1 (2.4)
	Not Stated	5 (13.2)
Clotrimazole + Metronidazole (21)	Vaginal Tablet (pessaries)	21 (100)
Miconazole(8)	Cream	5 (62.5)
	Powder	1 (12.5)
	Not stated	1 (12.5)
	Vaginal cream	1 (12.5)
Miconazole + Hydrocortisone(5)	Cream	5 (100)
Itraconazole(4)	Capsule	1 (25)
	Tablet	1 (25)
Not stated		2 (50)
Tioconazole(3)	Cream	1 (33.3)
	Powder	1 (33.3)
	Tablet	1 (33.3)
Clotrimazole + Betamethasone(2)	Cream	2 (100)
Clotrimazole + Fluconazole(1)	Capsule	1 (100)

In this study, the most common route of administration was oral, however a high proportion (45%) were topical agents. Superficial fungal

infections caused by dermatophytes are the most prevalent type of fungal disease and are typically contracted through direct contact with infected

individuals, particularly in overcrowded and poor hygienic settings. Studies conducted in various African countries have reported a dermatophytosis prevalence ranging from 5% to 31.6%. (Kannan et al. 2006; Osaigbovo 2019; Dogra et al. 2019) Most patients with dermatophytosis initially present to general practice clinics, which may explain the observed prescription patterns in this study. The majority of treatment combinations involved both a topical and an oral antifungal agent, with the combination of fluconazole and clotrimazole being the most frequently prescribed.

Although specific diagnoses were beyond the scope of this study, it is assumed that vaginal candidiasis was a common presentation at the general practice clinic. This therapeutic approach

appears rational and aligns with practices documented by Hamasaki et al. in Tanzania. (Hamasaki et al. 2022) Furthermore, the observed combination of metronidazole and clotrimazole suggests a higher clinical suspicion of vulvovaginal candidiasis and chlamydial infections—conditions that are often challenging to diagnose. This supports the rationale for adopting a syndromic approach to the management of sexually transmitted infections. (Mushi et al. 2022)

This study did not assess the specific indications for the use of these drugs in patients' case records, which would have been valuable in evaluating the rationality of the prescriptions. This will be addressed in future research.

Table 3: Combination Antifungal agents dispensed at the General Practice Clinic UBTH

Antifungal medication Combinations	Proportion /128(%)
Clotrimazole cream/Fluconazole tablet	45(35.2)
Terbinafine cream/Terbinafine tablet	16(12.5)
Clotrimazole cream/Clotrimazole pessaries	12(9.4)
Fluconazole tablets/ Ketoconazole cream	10(7.8)
Fluconazole tablets/ Terbinafine cream	8(6.3)
Clotrimazole cream/Clotrimazole pressaries/Fluconazole tablet	7(5.5)
Fluconazole tablet/Miconazole cream	6(4.7)
Fluconazole tablet/miconazole+hydrocortisone cream	3(2.3)
Clotrimazole+ betamethasone cream/Fluconazole tablet	2(1.6)
Clotrimazole+metronidazole pessaries/clotrimazole cream	1(0.8)
Clotrimazole+metronidazole pessaries/clotrimazole cream/Fluconazole tablet	2(1.6)
Clotrimazole+metronidazole pessaries/Fluconazole tablet	2(1.6)
Clotrimazole cream/ Ketoconazole cream/ itraconazole	1(0.8)
Clotrimazole cream/ Ketoconazole tablet	1(0.8)
Clotrimazole cream/ Terbinafine tablet	1(0.8)
Itraconazole tablet/Clotrimazole cream	2(1.6)
Itraconazole tablet/Ketoconazole cream	1(0.8)
Itraconazole tablet/Terbinafine cream	1(0.8)
Itraconazole tablet/Clotrimazole cream	1(0.8)
Ketoconazole shampoo/Ketoconazole tablet	1(0.8)
Ketoconazole cream Terbinafine tablet	2(1.6)
Tioconazole cream/Fluconazole tablet	1(0.8)
Miconazole/Ketoconazole	1(0.8)
Terbinafine cream/ Terbinafine tablet/ Clotrimazole -metronidazole	1(0.8)

CONCLUSION

In conclusion, this study found a low overall level of antifungal prescriptions, with fluconazole being the most commonly used monotherapy and the combination of fluconazole and clotrimazole the most frequently prescribed combination therapy. The growing issue of antifungal resistance—driven by irrational prescribing practices and further exacerbated by the limited range of antifungal agents available in the pharmacopeia—poses a significant public health challenge, particularly in

Sub-Saharan Africa. The urgent need for the development and implementation of antifungal stewardship programs cannot be overemphasized. Periodic prescription audits may also play a crucial role in addressing these concerns and promoting more rational use of antifungal medications.

Financial support and sponsorship

This work received no specific grant from any funding agency in the public, commercial or not for-profit sectors

Conflicts of interest

The authors declare that they have no conflicts of interest.

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