

Prescription Practices of Antifungal Agents at Gynaecology and Oncology Departments of a Tertiary Hospital in Mwanza, Tanzania: A Retrospective Study

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ABSTRACT

Introduction: Irrational antifungals prescription results in inappropriate use of antifungals, leading to emergence of antifungal resistance.

Aim: To determine the prescription patterns of antifungal agents in Gynaecology and Oncology Departments of the tertiary hospital in Tanzania.

Materials and Methods: This was a retrospective hospital-based study involving files of patients who attended Gynaecology and Oncology Department of Bugando Medical Centre between January 2017 to December 2017. All files of patients with fungal infections were analysed. The analysis of the data was done from January 2018 to August 2018. Checklist was used to collect information such as clinical diagnosis, age, name of antifungal, number of antifungals, dosage form and dose frequency. Descriptive analysis was done using STATA version 13.0.

Results: A total of 1,070 files of patients who attended Gynaecology and Oncology Departments in the year 2017 were retrieved, of

which 860 (80.4%) were from patients who attended Gynaecology Department. A total of 156 (14.6%) files out of 1,070 were of patients with fungal infections. Of the patients from gynaecology 116 (n=860, 13.48%) had fungal infection. While of the patients from oncology 40 (n=210, 19.1%) had fungal infection. The most common fungal infection diagnosed were vaginal candidiasis 112 (96.6%) and oral candidiasis 33 (82.5%) from gynaecology and oncology department, respectively. Common antifungal prescribed were azoles (clotrimazole 56.9% in gynaecology and fluconazole 30% in oncology). The prevalence of irrational antifungal prescription in gynaecology and oncology departments was 22.4% (26/116) and 20% (8/40), respectively.

Conclusion: About one in five antifungal prescriptions for vaginal candidiasis in gynaecology and oral candidiasis in oncology are irrational as evidenced in standard treatment guideline. Clinicians should adhere to the national standard treatment guidelines in order to reduce irrational prescriptions of antifungal agents.

Keywords: Clotrimazole, Fluconazole, Oral candidiasis, Vaginal candidiasis

INTRODUCTION

Antifungal stewardship program are crucial in guiding, monitoring and directing the appropriate use of antifungal agents for best clinical outcome of patients [1]. The demand of antifungal stewardship program increases with the increase in prevalence of fungi infections worldwide [2-4]. Trends of opportunistic fungal infections in different countries of Africa have been documented to increase from about 18% (documented from 1999 to 2000) [5,6] to over 60% (between 2011 and 2014) [7-9], in patients with different immunocompromised conditions. The growing burden of fungi infections is associated with the use of broad spectrum antibiotics, anticancer therapy, immune suppressive therapy and increased prevalence of immune suppressive conditions such as malignancy [10,11]. The consequences of increased prevalence of fungal infections include the increased use and misuse of antifungal agents. Irrational prescription of antifungal agents is one of the major misuses of antifungal agents that can lead to the development of antifungal drug resistance.

According to World Health Organisation (WHO) rational or good prescription of drug is based on five crucial elements: (i) Appropriate indication, (ii) Appropriate drug (based on efficacy, safety, suitability and cost), (iii) Appropriate patient without contraindications or likelihood of developing adverse reactions, (iv) Patients should be provided with appropriate, accurate relevant clear information about their conditions and the medications to be used, and (v) Appropriate monitoring of all anticipated and expected effect of

the medications [12,13]. The irrational prescription of antifungal agents is a broad term which includes prescription with either of the following; wrong drug, wrong formulation, wrong dosage, wrong route of administration, wrong duration of therapy or unnecessarily expensive drug for the clinical condition of the patients in question [14,15]. Irrational prescription further includes prescription of the antifungal agents using a brand name instead of generic name which might lead to dispensing errors, increase treatment costs, reduce drug availability and influence the pharmaceutical companies [16]. With the antifungal stewardship program the correct prescription will be promoted together with optimal use of antifungal agents by careful selection of agents based on the patients profile, targeted pathogens, agents' toxicity, cost and local resistance profile [17].

Empirical treatment by antifungal agents without having the epidemiological susceptibility data in low-and middle-income countries is one of the major factor that leads to irrational prescription of antifungal agents [18]. The WHO estimates 50% of the prescribed drugs include antifungal agents are irrational [19], the situation might be worse in low-and middle-income countries like Tanzania. Gynaecology and Oncology Departments are among the wards with significant number of fungal infections ranging from superficial infections like dermatophytosis to serious systemic infection like invasive fungal infection [20-22]. Here, authors report the prescription practices of clinicians in gynaecology and oncology departments. Furthermore, the patterns of irrational prescription in these departments have been detailed.

MATERIALS AND METHODS

This was a retrospective hospital-based study conducted in the Gynaecology and Oncology Departments of Bugando Medical Centre in Tanzania. The protocol to conduct this study was approved by the joint CUHAS/BMC research ethics and review committee (CREC) with certificate number CREC 576/2018. Permission to conduct the study was requested from the Director General of the BMC.

The hospital serves a population of 18 million people from eight different surrounding regions and is attended by around 300,000 patients each year from north western Tanzania. The oncology department caters for around 50-150 cancer patients from nine different regions of the Lake zone per month. The gynaecology department serves more than 500-1000 patients in a year.

From the medical records unit, files of patients who attended or were admitted in gynaecology and oncology departments from January 2017 to December 2017 were retrieved and reviewed if they had antifungal prescriptions or not. The analysis of the data was done from January to August 2018. Data were extracted from all files with antifungal prescription using structured checklist. The extracted data included demographic (like age, gender, and clinical parameters like ward, diagnosis and antifungal prescribed) data of the patients with antifungal prescription.

Case definitions: Fungal infection in this study was based on the clinical diagnosis (symptomatic diagnosis) made by the clinician attending the respective patient. Polypharmacy in the current study was defined as prescription of more than two antifungal agent in one file. Furthermore, the irrational prescription was defined as prescription with either of the following wrong drug, wrong formulation, wrong dosage, and wrong route of administration, wrong duration of therapy or unnecessarily expensive drug for the clinical condition of the patients in question.

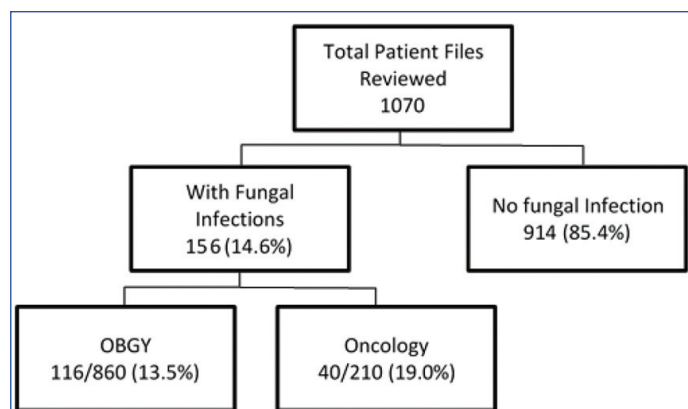
STATISTICAL ANALYSIS

Data were entered in Microsoft excel sheet for cleaning and coding before being transferred to STATA version 13.0 for analysis. Categorical data like clinical condition, type of antifungal prescribed were summarised as proportions while continuous variables were summarised as median with interquartile ranges.

RESULTS

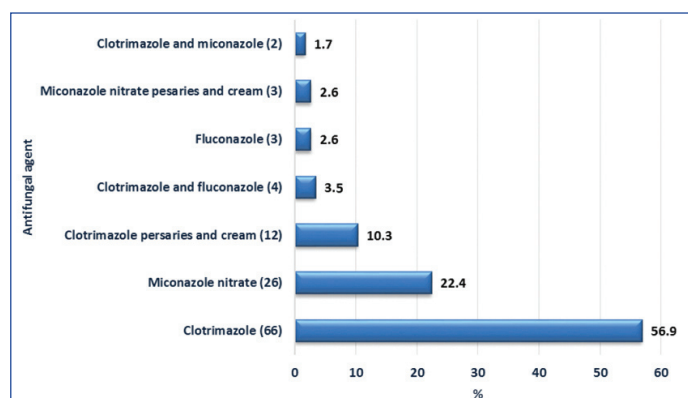
A total of 1,070 files of patients who attended in both departments for the year 2017 were retrieved, majority were from gynaecology department 860 (80.4%). Out of 1070, 156 (14.6%) files had diagnosis of fungal infections [Table/Fig-1]. The overall median age of patients with fungal infections were 31 IQR (24-38) years. A total of 116 (n=860, 13.48%) and 40 (n=210, 19.1%) files from gynaecology and oncology departments had fungal infection diagnosis, respectively. Of the studied files, only three files from gynaecology department and one file from oncology department had laboratory request for fungi diagnosis. A total of 34 (21.8%) files had irrational antifungal prescription from both gynaecology and oncology departments.

Gynaecology department: The median age of patients with fungal infections in gynaecology department was 33 IQR (27-38.5) years. The most common fungal infection diagnosed in gynaecology department was vaginal candidiasis 112 (n=116, 96.6%). Three (n=112, 2.7%) patients with vaginal candidiasis had recurrent vaginal candidiasis (clinical diagnosis as indicated in the file). Other fungal infections documented in gynaecology department included two cases of Tinea pedis, one case of oral candidiasis and one case of cutaneous candidiasis.



[Table/Fig-1]: Flow chart diagram of the studied files. OBGY: Obstetrics and gynaecology

In gynaecology department, a total of 137 antifungals were prescribed to 116 patients. The average number of antifungals prescribed per file was 1.2 (137/116). Two different types of antifungals were prescribed in 21 (n=116, 18.1%) patients. The most commonly prescribed antifungals were clotrimazole either pessaries or cream to 66 (56.9%) patients, followed by miconazole nitrate either pessaries or cream to 26 (22.4%) patients as shown in [Table/Fig-2].



[Table/Fig-2]: Antifungals prescribed in gynaecology department. values in bracket are the number of patients to which these antifungals were given

Irrational prescription of antifungal at gynaecology department:

In this department, the irrational prescription of antifungal was found in 26 (22.4%) files. Polypharmacy was the most frequently documented cause of irrational prescription in 20 (n=26, 76.9%). Miconazole nitrate 10 (n=26, 38.5%) was the most frequently antifungal agents prescribed with wrong duration, frequency or combination of wrong duration and frequency [Table/Fig-3].

Oncology department: The age of patients with fungal infection from oncology department ranged from 1 year to 56 years. The median age was 21.5 years with IQR (4-34) years. The most common fungal infection documented from oncology department was oral candidiasis 33 (82.5%). Other fungi infections included vaginal candidiasis 5 (12.5%), Tinea corporis 1 (2.5%) and Tinea capitis 1 (2.5%).

A total of 46 antifungal were prescribed to 40 patients with different fungi infections in oncology department. The average number of antifungals prescribed per file was 1.2 (46/40). Majority of patients were prescribed with one type of antifungal agent 36 (78.2%). One patient with oral candidiasis was prescribed with three different types of antifungal agents (miconazole nitrate, fluconazole, clotrimazole). Fluconazole tablets to 12 (n=40, 30%) patients were most frequently prescribed in the oncology department [Table/Fig-4]. A total of 8 (20%) files from oncology department had irrational prescription mainly polypharmacy and wrong drug duration [Table/Fig-3].

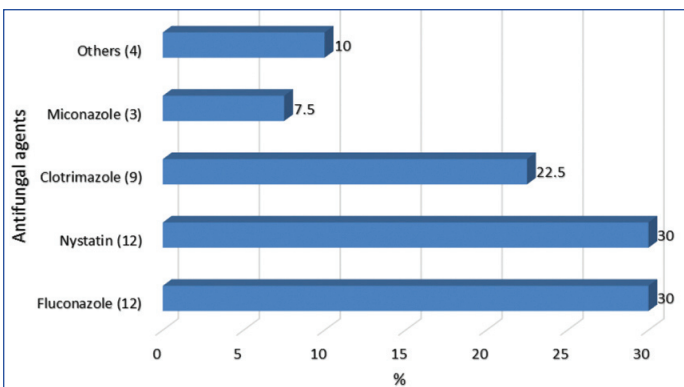
S. No.	Clinical case	Name of drug used	Dosage form	Dose frequency and duration	Dose
Polypharmacy/duration in gynaecology department					
1.	Recurrent vaginal candidiasis	Clotrimazole Fluconazole	Pessaries Tablets	OD for 6/7 OD for 10/7	400 mg 200 mg
2.	Vaginal candidiasis	Clotrimazole Ketoconazole	Tablet Topical	OD for 6/7 BD for 2/52	500 mg 200 mg
4.	Vaginal candidiasis	Miconazole nitrate Clotrimazole	Topical Pessaries	BD for 7/7 OD for 6/7	2%, 500 mg
5.	Vaginal candidiasis	Clotrimazole Fluconazole	Topical Tablet	BD for 10/7 OD for 10/7	1% 150 mg
6.	Vaginal candidiasis	Clotrimazole Fluconazole	Topical Tablet	BD for 14/7 Stat	1% 150 mg
7.	Vaginal candidiasis	Miconazole nitrate Clotrimazole	Topical Tablets	BD for 14/7 OD for 6/7	2% 500 mg
8.	Vaginal candidiasis	Miconazole nitrate	Pessaries Topical	BD for 3/7 BD for 7/7	2% 400 mg
9.	Vaginal candidiasis	Miconazole nitrate	Pessaries Topical	T. nocte for 3/7 BD for 7/7	2% 400 mg
10.	Vaginal candidiasis	Miconazole nitrate	Pessaries Topical	OD for 3/7 BD for 7/7	2% 400 mg
11.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	T. nocte for 3/7 BD for 7/7	1% 500 mg
12.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 14/7	1% 500 mg
13.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 10/7	1% 500 mg
14.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 14/7	1% 500 mg
15.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 10/7	1% 500 mg
16.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 14/7	1% 500 mg
17.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 10/7	1% 500 mg
18.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 10/7	1% 500mg
19.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 10/7	1% 500 mg
20.	Vaginal candidiasis	Clotrimazole	Pessaries Topical	OD for 6/7 BD for 14/7	1% 500 mg
Wrong dose duration/frequency in gynaecology department					
21.	Vaginal candidiasis	Fluconazole	Tablet	BD for 7/7	150 mg
22.	Recurrent vaginal candidiasis	Miconazole nitrate	Topical	BD for 14/7	2%
23.	Vaginal candidiasis	Miconazole nitrate	Topical	BD for 10/7	400 mg
24.	Vaginal candidiasis	Miconazole nitrate	Topical	BD for 10/7	400 mg
25.	Vaginal candidiasis	Miconazole nitrate	Topical	BD for 10/7	2%
26.	Vaginal candidiasis	Miconazole nitrate	Topical	BD for 10/7	2%
Oncology department					
1.	Tinea capitis	Fluconazole Ketoconazole	Tablet Shampoo	OD for 2/52 OD for 2/52	200 mg
2.	Vaginal candidiasis	Fluconazole	Tablet	OD for 2/52	200 mg
3.	Oral candidiasis	Fluconazole	Tablet	OD for 2/52	200 mg
4.	Oral candidiasis	Miconazole nitrate Fluconazole Clotrimazole	Tablet Topical	BD for 1/52 TDS 1/12	2%, 200 mg
5.	Oral candidiasis	Fluconazole	Tablet	OD for 14/7	200 mg
6.	Oral candidiasis	Fluconazole	Tablet	OD for 14/7	150 mg
7.	Oral candidiasis	Fluconazole Nystatin oral	Tablet Syrup	OD for 7/7 TDS 1/52	100000U
8.	Oral candidiasis	Clotrimazole, ketoconazole	Tablet	OD for 6/7 BD for 2/52	500 mg 200 mg

[Table/Fig-3]: Irrational prescribed antifungal in gynaecology and oncology department.
OD is once daily, BD is 'bis en die or twice a day, TDS is three times a day, T. nocte is one tablet at night

DISCUSSION

Irrational use of antifungal agents significantly contributes to the global burden of antifungal resistance. On the other hand antifungal resistance is the major factor that led to the shift of the fungi

pathogens causing invasive fungal infections, persistent infections and increased treatment cost [23]. In the current study, irrational prescription of antifungal agents was documented in 20% and 22.4% files from the Oncology department and Gynaecology



[Table/Fig-4]: Antifungal agents prescribed at oncology department.

Others include Clotrimazole and ketoconazole (1), fluconazole and ketoconazole (1), fluconazole and nystatin (1) and miconazole, Clotrimazole and fluconazole (1)

Values in b bracket are the number of patients to which these antifungals were given

department, respectively. This was higher than previously reported in a tertiary hospital in Madrid Spain back in 2014 when they were advocating for the need of having antifungal stewardship program [2]. The observed difference is contributed by the limited use of fungal diagnosis services as evidenced in the current study were only 2.5% of files had documentation of laboratory diagnosis request. Accurate and timely diagnosis of fungi infection has been documented to be critical in the reduction of unnecessary use and ultimate reducing the antifungal resistance [24].

In the current study fungal infections like dermatophytosis, vaginal and oral candidiasis were the only documented type of infections in 156 files studied. This has also been documented in previously studies [25,26]. Nevertheless, in recent decades upsurge documentation of invasive fungal infections in patients with underlying diseases like cancer has been observed [20,27]. In the current study no clinical diagnosis of invasive fungal infection was observed justifying low use of laboratory investigations for fungi infections in the study. Cutaneous and mucocutaneous fungi infections have wrongly been taken as simple infections that do not require laboratory diagnosis such as culture and sensitivity as a results this has led to recurrent and disseminated infections [28].

Azole antifungal agents like fluconazole was documented to be the leading agent used for fungal infections like oral candidiasis in sub-Saharan Africa, including Tanzania [25,29,30]. This has also been observed as the most prescribed antifungal for oral candidiasis in the current study. Our previous study on over the counter medication of antifungal agents in Mwanza observed fluconazole as one of the most dispensed antifungal agent among patients with vaginal candidiasis in the similar study settings [25]. The easy availability, low toxicity, easily administering and ability to cover a broad range of fungi pathogens is among the reasons for fluconazole being more used [31].

This study has found one in every five files with antifungal prescription from gynaecology or oncology department had irrationally antifungal prescription. This irrational prescription is alarming and of public health importance as the rational use of antifungal agents has been documented to be usefully in preserving antifungal agents, reduce antifungal resistance development and adoption of essential drug list [32].

Limitation(s)

Not having files with invasive fungi infections might overestimate the underuse of laboratory investigations for fungi infections.

CONCLUSION(S)

About one in five antifungal prescriptions for vaginal candidiasis in gynaecology and oral candidiasis in oncology are irrational as evidenced in standard treatment guideline. This is enhanced by the underuse of mycological investigations available like culture

and sensitivity. Clinicians should adhere to the national standard treatment guidelines in order to reduce irrational prescriptions of antifungal agents.

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