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Original Research Article

An observational and cross-sectional study of prescribing pattern of antifungal drugs in a tertiary care center of Bihar

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ABSTRACT

Introduction: Fungal infections take a toll on the health of all individuals, irrespective of ages, gender, ethnicity etc. But still major researchers have focused on antibacterial rather than antifungal till recent past, when the limelight has moved to antifungal medicines. Adding to the gravity of the situation, is the growing resistance against these drugs. Keeping these facts in mind, this study was planned to delineate the prescribing pattern of antifungal drugs by the various specialty in a tertiary care center in the eastern part of the country.

Materials and Methods: This was an observational and cross-sectional hospital-based study. The study incorporated 218 patients from various departments of the hospital during the study duration that was from March 2021 to September 2021. Descriptive statistics was performed using SPSS ver 20.0. Results has been depicted in form of text and table.

Result: Antifungal medicines prescribed mostly for leukemia and other immunocompromised status. Most of the patients came from the department of general medicine. Majority of the patients had hematological disorders followed by infections. Anidulafungin was reported to have been prescribed most commonly by the department of surgery in patients with solid tumors. Patients with lung infections also received this drug by physicians. This use can be justified by its action against invasive aspergillosis, oesophageal candidiasis and peritonitis and intraabdominal abscess caused by candida species. Ketoconazole and clotrimazole were the least used antifungal agents in our study. These two agents are mainly indicated for topical use

Conclusion: The current report will aid in understanding antifungal prescription practices. This will also form a basis for future researches and formulating guidelines for rational use of these drugs.

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1. Introduction

Discovery of fungi dates back to around 1500 million years with more than 1.5 million species. Human infections have been documented with around 300 million species of fungus.^{1,2} They have described as an etiological agent of various disease of mankind even before establishing bacteria as a pathogenic agent by David Gruby.³ Despite this fact, most widespread infectious diseases in the 19th century were attributed to bacterial, parasitic, and to viral origins.⁴

Evidence on antibacterial drug has seen an exponential growth since the advent of anti-microbial agents, but the knowledge pool regarding antifungal agents has not witnessed such advancements. This has been justified by the lower prevalence of fungal infections as compared to bacterial ones. However, the last few decades have seen increase in incidence of fungal infections, which has led to aggressive research on new antifungal agents.⁵ The additional reasons to make this a comparatively recent knowledge is the complexity of nature of antifungal agents and long period of research of around 8-10 years for approval of drug.⁶ Nonetheless, detailed knowledge

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regarding the physiology and biochemistry of fungal cells, in addition to other aspects of fungal infections, led to unrevealing of mechanism of action of a wide range of antifungal agents.⁶ The reason behind these necessities and channelization of resources is that recent past has seen many deadly fungal infections that may range from superficial to systemic infections.⁷ From the mid-20th century, the increase in the prevalence of acquired immunodeficiency syndrome (AIDS) along the increased number of organ transplantation, chemotherapy, more invasive procedures, parenteral nutrition, has attributed to increase in incidence of systemic fungal infections. The indiscriminate use of antibiotics added to the worsening of this picture, leading to the installation of fungal infections.⁸

This rampant use of antifungal agents come at a cost, antifungal drug resistance. Moreover, inappropriate use of this group of drugs has worsened the situation. This inevitable process is universal in the microbial world. Although fungal resistance is not at par with bacterial resistance, the economic facets associated with fungal infections remains unacceptably high.¹ These resistance costs the society not only in financial terms but also increases the disease burden.^{9,10}

In spite of all these, data are limited on antifungal use, misuse, overuse and resistance. Such data are essential to address this problem that carries a public health significance.¹¹ This has been more of concern in the developing countries in light of lack of a well-established and proper practice of antifungal management protocols. Moreover, there is a dearth of knowledge on the incidence and prevalence of inappropriate antifungal use and associated risk factors.⁹ This study was planned to address this issue in the eastern part of the country. The main objective of the current study to establish the pattern of use of antifungal agents in a tertiary care center of Bihar.

2. Materials and Methods

A hospital-based cross-sectional study was conducted between March 2021 and September 2021. The study was planned and executed by the Department of Pharmacology, Nalanda Medical College & Hospital, Bihar. Ethical clearance was obtained from the Institutional Ethics Committee. Patients of inpatient and outpatient units of various departments of the hospital were included in the study. Duly signed informed consent forms were obtained from each participant before inclusion. During the total duration of the study, 218 patients of all ages and gender, who were receiving antifungal medication, were included in the study. Data collection was done by detailed interview form that included information like age, gender, body mass index, status, diagnosis, treating department and drugs information (name, route of administration, treatment duration).

Data was compiled and analyzed using The Statistical Package for the Social Sciences (SPSS), Version 20.0 (IBM Corp., Chicago, Illinois, USA). Descriptive statistics was done. Frequencies and percentages were reported for categorical variables, while the mean and standard deviation were used to summarize the data for continuous variables.

3. Results

A total of 218 patients from all the department of the hospital were included in the current study during the whole duration. There was a male preponderance noted with a male female ratio of 1.45. The mean age of the study population was 39.3±17.9 years. The study included patients from 6 months to 88 years. Total number of prescriptions for antifungal medication was 715. Majority patients were outpatients. The range of episodes per patient was 1 to 6. The baseline characteristics of the patients has been shown in [Table 1]. Various departments have been prescribing antifungal drug medications. This distribution has been shown in [Table 2]. The majority of patients prescribed these drugs were diagnosed to have infectious diseases followed by prophylactic use in leukaemia and immunocompromised conditions [Table 3].

3.1. Antifungal drug utilization pattern

The average number of antifungal drugs prescribed per patient was 4.5 with male patients receiving higher average number of prescriptions compared to the female patients (4.2 vs. 3.9). The average number of prescriptions for adults was slightly higher compared to children (3.4 vs. 2.6). The most common route of administration was oral (78.9%) followed by the topical route, then parenteral and then vaginal route. Most common antifungal drug to be prescribed was fluconazole in all the departments for all ages and gender with a little higher than half of the prescriptions. This was followed by nystatin and [Table 4].

4. Discussion

The recent past has seen an increase in the morbidity and mortality of invasive fungal infections (e.g., aspergillosis, candidiasis, histoplasmosis, cryptococcosis). The prevalence is higher among immunocompromised patients and those with comorbidities.^{9,10} To combat this situation, many antifungal drugs have been prescribed and to provide more options for physicians by using drugs with better toxicity profiles.¹¹ Pharmaco-epidemiological studies from developing countries regarding these prescription are very limited. The reason for prescribing antifungal medication may be curative, prophylactic or empirical therapy for their underlying conditions which makes them susceptible to invasive fungal infections. These conditions included leukemia and other immunocompromised status. Most of the patients came from the department of general

Table 1: Distribution of study participants based on their demographic characteristics

| Demographic characteristics | Data |
|---|-------------|
| Total number of antifungal drug prescriptions | 715 |
| Age in years (mean, SD) | 39.3±17.9 |
| Male, n (%) | 128 (58.7%) |
| Body Mass Index in kg/m ² (mean, SD) | 26.2±14.8 |
| Outpatient, n (%) | 468 (65.5%) |
| Total duration of disease, days (mean, SD) | 17.9±22.4 |

Table 2: Prescribing pattern of drugs in the various departments of the hospital

| Department | Prescription | Drugs | | | | | | |
|---------------|--------------|-------|-------|------|-------|-------|------|------|
| | | A | B | C | D | E | F | G |
| Gen Medicine | 86.1% | 36.7% | 21.4% | 9.7% | 13.3% | 12.5% | 2.1% | 4.3% |
| Gen Surgery | 4.1% | 17.1% | 19.4% | - | - | 63.5% | - | - |
| Pediatrics | 7.4% | 5.2% | 23.4% | 5.4% | 65.1% | - | - | 0.9% |
| OBGY | 1.9% | 100% | - | - | - | - | - | - |
| Ophthalmology | 0.5% | 64.2% | 35.8% | - | - | - | - | - |

Table 3: Diagnosis of the patients against their prescriptions for antifungal drugs

| Diagnosis | Prescription | Drugs | | | | | | |
|-------------------|--------------|-------|-------|-------|-------|-------|-------|---|
| | | A | B | C | D | E | F | G |
| Leukemia | 32.3% | 58.9% | 16.7% | 17.7% | 2.8% | 3.9% | - | - |
| Infections | 42.4% | 51.5% | 13.5% | 1.4% | 14.5% | 13.5% | 3.6% | - |
| Solid tumors | 13.4% | - | 58.9% | 14.3% | 13.6% | 24.7% | 13.5% | - |
| Immune deficiency | 8.7% | 87.2% | 6.1% | 0.8% | 5.9% | - | - | - |
| Hematological | 7.3% | 42.1% | 7.8% | 24.7% | 12.8% | 7.9% | 4.1% | - |
| Others | 3.9% | | | | | | | |

Table 4: Distribution of usage of antifungal medications according to their background characteristics

| Drug | Prescription | Age (years) | | Gender | | Patient | |
|------|--------------|-------------|-------|--------|--------|---------|------------|
| | | ≥18 | <18 | Male | Female | Indoor | Outpatient |
| A | 50.4% | 24.6% | 57.5% | 53.1% | 49.5% | 27.8% | 74.5% |
| B | 16.7% | 17.4% | 16.6% | 19.4% | 17.5% | 22.6% | 13.6% |
| C | 12.4% | 14.6% | 13.4% | 10.3% | 14.5% | 16.7% | 5.7% |
| D | 8.4% | 40.2% | 5.7% | 13.4% | 7.1% | 17.7% | 2.4% |
| E | 7.9% | 2.1% | 4.7% | 3.8% | 8.6% | 15.1% | 0.3% |
| F | 3.4% | 0.9% | 1.4% | - | 2.6% | - | 2.0% |
| G | 0.8% | 0.2% | 0.7% | - | - | - | 1.5% |

Drug list: A – Fluconazole, B – Nystatin, C – Voriconazole, D – Amphotericin, E – Anidulafungin, F – Clotrimazole, G – Ketoconazole

medicine. Majority of the patients had hematological disorders followed by infections. In one study, the most common underlying condition was malignancy (42%), followed by hematologic/immunologic deficiency (16%), and cardiovascular condition (15%).¹² This distribution of use of antifungal drugs may be justified by the fact that these infections are a major cause of death in many hospitalization wards.¹³

A large scale study has reported that fluconazole is the most commonly prescribed antifungal agent, alongside increase in the utilization of voriconazole and the echinocandins and a significant dip in the use of conventional amphotericin, itraconazole and flucytosine.^{11,13} This rampant use of Fluconazole is due

to its long half-life, good patient tolerability and minimal associated toxicity. It is now the first line of treatment of oropharyngeal and oesophageal candidiasis. It also has found use in prophylaxis among those undergoing bone marrow transplantation or on cytotoxic chemotherapy.¹³ Though Amphotericin B has proved its efficacy in a variety of systemic fungal infections and in prophylaxis for patients with febrile neutropenia, it has been replaced due to several side effects like nephrotoxicity.^{7,14} Now a days, its use has been limited to the treatment of candidemia and cryptococcal meningitis mainly in immune-compromised patients. Nystatin is a widely used antifungal medication for superficial fungal infections like cutaneous, vaginal and oesophageal candidiasis.¹⁵ Another broad-spectrum

antifungal drug, Voriconazole is used for filamentous fungi and others like *Fusarium* and *Scedosporium* species.¹⁵ It is very commonly used drug in India. But, due to its interactions with digoxin and prednisolone, it should be used with caution.¹⁵ A new drug, echinocandins, has been found to be effective against amphotericin B-resistant fungi. Thus, it may help to manage febrile neutropenia and in combination therapy.¹⁵ In the current study, anidulafungin was reported to have been prescribed. Most common use was seen by the department of surgery in patients with solid tumours. Patients with lung infections also received this drug by physicians. This use can be justified by its action against invasive aspergillosis, oesophageal candidiasis and peritonitis and intraabdominal abscess caused by candida species. Ketoconazole and clotrimazole were the least used antifungal agents in our study. These two agents are mainly indicated for topical use.⁷

5. Conclusion

The prescribing pattern for antifungal drugs has shown similarity to the trend elsewhere, with fluconazole being the most common. There has been an advent of many other newer agents. Due to a dearth of such data in this region of the nation, this report will aid in understanding antifungal prescription practices. This will also form a basis for future researches and formulating guidelines for rational use of these drugs.

6. Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

7. Source of Funding

None.

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