

A
Summer Internship Project Report
On
TO UNDERSTAND PRESCRIPTION PATTERN OF
ANTIFUNGALS IN ICU SETUP

In partial fulfillment for award of
Masters in Business Administration- Pharmaceutical Management

Submitted By
Kush Dua
MBA-Pharmaceutical Management
2014-2016

Under the guidance of
Mr. Hemant Kothawade
Product Manager, Bharat Serums and Vaccines Ltd.

Dr. Sandeep Narula
Associate Professor, IIHMR University

Institute of Health Management Research
Jaipur, Rajasthan

Certificate

This is to certify that **Mr. Kush Dua**, student of Masters in Business Administration Pharmaceutical Management 6th Batch, IIHMR University, Jaipur has successfully completed his project titled **"To Understand Prescription Pattern of Anti-Fungals in ICU Setup"** as a part of his Summer Internship project at Bharat Serums and Vaccines Ltd. from 1st April 2015 to 31st May 2015.

The project was field work and was carried out independently with a sincere, scientific and analytical approach under my supervision and guidance.

I wish him all the success and luck in his future endeavors.



Col. (Dr.) Ashok Kaushik

Dean (Academic and Students Affairs)

IIHMR University, Jaipur



Dr. Sandeep Narula

Associate Professor

IIHMR University, Jaipur



BHARAT SERUMS AND VACCINES LIMITED

(CIN: U24236MH1971PLC018134)

Registered Office : 17th Floor, Hoechst House, Nariman Point, Mumbai - 400021, India

Tel. : +91-22-6656 0900 / 6656 0980

Fax : +91-22-6656 0901 / 6656 0903

E-mail : corporate@bharatserums.com

Website : www.bharatserums.com

INTERNSHIP CERTIFICATE

June 16, 2015

To whom-so-ever it may concern

This to certify that, Mr. Kush Dua, has successfully completed a two month Internship in our Marketing Department beginning April 1, 2015 and submitted a project report titled, 'To Understand the prescription pattern of Antifungals in ICU setup'.

During this period, he was found to be sincere, pro-active, creative and diligent. His performance was satisfactory.

We wish him success in his future career.

Sincerely,

For Bharat Serums and Vaccines Limited

Akhilesh Mishra
Vice President- Human Resources.

Acknowledgement

The satisfaction and euphoria that accompany the successful completion of the project would be incomplete without the mention of the people who made it possible.

First of all, I express my sage sense of gratitude and indebtedness to our Director, Dr. S.D.Gupta, IIHMR University.

I would like extend my sincere and heartfelt thanks to MR. Rakesh Dave, Vice-President, Bharat Serums and Vaccines Ltd. For providing me an opportunity learn and develop professionally.

I would also like to express my deep sense of gratitude to my corporate mentor Mr. Hemant Kothawade and my faculty mentor Dr. Sandeep Narula. I am greatly indebted to both of them for providing their valuable guidance at all stages of the study, their advice, constructive suggestions, positive and supportive attitude and continuous encouragement, without which it would have not been possible to complete the project.

To place on record, I owe a debt of gratitude to all my teachers for grooming me and my classmates for the inspiration needed to work with dedication and motivation throughout as an Intern at Bharat Serum and Vaccines Ltd.

A sincere thanks to the respondents for sparing their valuable time, support and providing relevant information.

I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards the industry in coming future.

List of Tables

Table 1: Commonly used Antifungals in Invasive fungal Infections	14
Table 2: Summary of IDSA Guidelines for Treating Invasive Candidiasis and Aspergillosis	15
Table 3: Number of patients Vs percentage response (per week)	18
Table 4: Number of patients Vs percentage response of doctors for different infections (per week).....	20
Table 5. Percentage response of intensivists with respect to type and number of patients .	22
Table 6: Percentage of intensivists and choice of anti-fungal	24

List of Figures

Figure 1: Choice of Anti-Fungal for treatment of confirmed Candida and Aspergillus infections (per week)	9
Figure 2: Classification of Anti-Fungal Agents.....	13
Figure 3: Total Number of patients Vs Percentage response (per week).....	18
Figure 4: Immunocompromised patients Vs Percentage response (per week).....	19
Figure 5: Patients on anti-Fungal Therapy Vs Percentage response (per week)	19
Figure 6: Patients suffering from Candida Infection Vs Percentage response (per week)	20
Figure 7: Patients suffering from Aspergillus Infection Vs Percentage response (per week).....	21
Figure 8: Patients suffering from Mucorales Infection Vs Percentage response (per week)	21
Figure 9: Percentage response of intensivists with respect to number of patients and type of patients (per week)	22
Figure 10: Percentage of intensivists Vs choice of drugs (per week).....	23
Figure 11: Percentage of Intensivists Vs choice of Anti-Fungal (per week)	24
Figure 12: Choice of Anti-Fungal for treatment of confirmed Candida and Aspergillus infections (per week)	25
Figure 13: Percentage of intensivists not in favor of combination therapy (per week)	26
Figure 14: Percentage response of intensivists Vs Number of Patients of Febrile Neutropenia (per week)	27
Figure 15: Choice of Anti-Fungal for Febrile Neutropenia (per week)	27
Figure 16: Choice of Diagnostic Tests Vs Percentage response of Intensivists (per week)	28

Table of contents

Contents

Executive Summary	8
Company Profile	11
Vision.....	11
Presence	11
Introduction.....	13
Background.....	13
Rationale	15
Objectives	16
Methodology	17
Research Design:	17
Sampling Design:.....	17
Sampling	17
Sample population:	17
Sample area:.....	17
Sample Size.....	17
Findings and Interpretation	18
Objective 1	Error! Bookmark not defined.
Objective 2:.....	Error! Bookmark not defined.
Objective 3.....	Error! Bookmark not defined.
Objective 4.....	Error! Bookmark not defined.
Findings based on opinions	29
Limitations to the study.....	29
Suggestions	30
Implications.....	30
Way ahead.....	30
Annexure.....	31

Executive Summary

The project assigned was “To understand the prescription pattern of Anti-Fungals in ICU setups” with primary objectives being:

- ✓ To study the incidence of Antifungals in Intensive Care Units;
- ✓ To identify the most prescribed Antifungal in Invasive Fungal Infections
 - Prophylactic Treatment
 - Empirical Therapy
 - Treatment of confirmed infection
- ✓ To identify the choice of Antifungal in Febrile Neutropenia patients
- ✓ To determine the current unmet medical need in case of Invasive Fungal Infection

The project was carried out in 3 stages:

First stage was to carry out secondary research on Antifungals used in ICU and preparation of questionnaire followed by second stage which involved meeting the intensivists and conducting the survey. The final stage was to move ahead with data analysis and conclusion.

Stage 2 was carried out in various ICU's namely Medical, Surgical, Cardiac, Neuro, Neonatal, Transplant, and Medical Oncology in hospitals across Delhi-NCR.

After meeting the intensivists, following findings were observed:

- ✓ **Incidence of Anti-Fungals**
 - Approximately 40% of the total ICU patients required antifungal therapy which has increased majorly in last decades;
 - Candida was found in 85% of the patients requiring antifungals followed by Aspergillus;
 - 94% of intensivists were in opinion that Mucorales was rare;
 - Majorly post-surgery patients' required antifungal therapy due to their decreased immunity followed by hospital acquired infection patients, patients on multiple drug therapy and cancer patients.
- ✓ **Most prescribed Anti-Fungal**
 - Fluconazole was the choice of 84% intensivists as far as prophylactic treatment was concerned, another 10% were not in favor of giving prophylactic treatment;
 - For empirical therapy of Candida, Fluconazole was preferred by 75% intensivists and for Aspergillus Voriconazole was choice of 53% intensivists followed by 41% for Amphotericin B and its formulations.
 - Echinocandins like Caspofungin and Micafungin were gaining importance among intensivists for empirical therapy but it was true only for Private hospitals

- For confirmed *Candida* infection cases, Caspofungin was choice of 47% intensivists followed by Fluconazole at 30%. However it was different for confirmed *Aspergillus* infection cases where Liposomal Amphotericin B was preferred by 42% intensivists and 39% preferred Voriconazole.

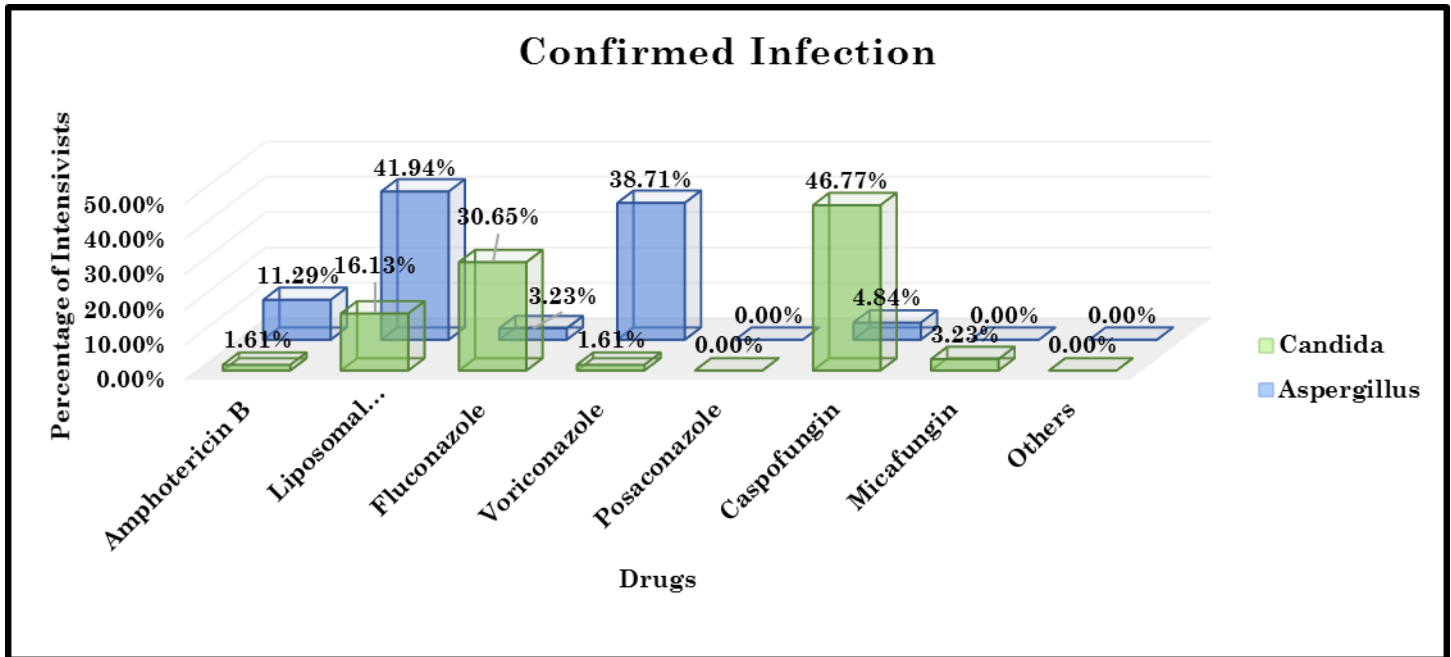


Figure 1: Choice of Anti-Fungal for treatment of confirmed *Candida* and *Aspergillus* infections (per week)

- Fluconazole was most preferred due its low cost and least side effects and part of hospital formulary in various hospitals
- Though major side effects encountered with Amphotericin B was Nephrotoxicity, Hepatotoxicity, still it was considered safe for use if dosage was effectively monitored.
- 82% of intensivists were not in favor of administering combination therapy for *Candida*. Of the remaining 5% preferred **Fluconazole+Caspofungin**.
- 69% of intensivists did not support combination therapy for *Aspergillus* infection. Of the remaining, **Liposomal Amphotericin B+Voriconazole** was preferred by 13% intensivists and **Amphotericin B+Voriconazole** by 8%.

✓ Febrile Neutropenia

- Though 90% of intensivists examined 0-5 patients with Febrile Neutropenia every week, the number of cases were increasing as per intensivists
- Caspofungin was the choice of drug for Febrile Neutropenia for 37% intensivists followed by Fluconazole and Liposomal Amphotericin B

✓ Unmet Medical Need

- Need for newer antifungals with better efficacy and less side effects.
- Need for economical antifungals
- Need for newer, quicker and reliable diagnostic tests.

The study draws attention to the fact that antifungals command the largest share (17.8%) in Indian Pharmaceutical market, stand at US\$6.82bn and is growing at 26.9%. Further investigations reveals that future scope of Antifungals is vast due to:

- Widespread use of broad-spectrum antibiotics;
- Increased number of individuals with reduced immune responses caused by acquired immunodeficiency syndrome or cancer chemotherapy agents
- As more patients undergo transplant surgeries, the incidence of fungal sepsis will increase.
- Also, with higher age-wise longevity, more disposable income and better diagnostic facilities, more patients will get diagnosed with fungal infection at the right time and would get treated in the right way to improve survivability.

The report also provides a way ahead for the organization with Fluconazole being the molecule to venture into due to its low cost and figures showing FORCAN (Cipla) is the choice of Antifungal in Prophylactic and Empirical therapy and having a sales of approximate 68Lac in Delhi-NCR.

Also investing in R&D sector to improve existing Amphotericin B molecule may prove a growth driver.

Also due to increasing population and income levels, demand for high-end drugs in India is expected to reach US\$8billion by 2015(ibef.org), venturing into Echinocandins may prove to be a productive option.

Company Profile

Bharat Serums and Vaccines Limited (BSV) is one of the fastest growing biopharmaceuticals companies in India and has been ranked amongst the top Indian Biopharmaceutical companies. With its inception in 1971 by Dr. Gautam and Bharat Daftary, the company has 2 manufacturing units in Ambarnath, Maharashtra, 3 independent R&D facilities and a horse farm in outskirts of Maharashtra and over 900 employees.

With its 75% of business coming from domestic markets, its international business is slated to grow exponentially.

Vision

To Be An Innovative, Caring And Trustworthy Partner In Bringing Life To Life

- Mitigating the anguish and suffering of millions.
- Underlying fairness and transparency in dealings with all stakeholders including employees and business partners.
- The Group is driven by an informal culture fostering cohesion and innovation

Presence

Domestic

Products are sold through 6 specialized divisions and has over 25 brands.

- **DIVA:** prime division of BSV, operating in Gynaecology and Obstetrics segment
 - Flagship Brand: Rhoclone and Hucog
- **ASPIRE:** A complete solution in AST (Assisted reproductive Technology)
 - Flagship Brand: Foligraf
- **ELITE:** A tender division of BSV, operating in hospital based emergency medicine and casualty
 - Flagship Brand: Tetglob, Equirab and ASVS
- **ALTIUS:** Second largest division of the company and operating in Critical Care segment
 - Flagship Brand: Gamma IV and Albumin
- **ANAGEN:** Offering corner stone therapies in Transplantation and Aplastic Anemia
 - Flagship Brand: Thymogam and Ampholip
- **UROCARE:** Offering corner stone therapies in Urological problems
 - Flagship Brand: Luprodex

International

- With a zest born out of the desire to improve health and quality of life globally, BSV started its international business operations in early 2000. The international business operation got a major boost with the commissioning of the new Ambernath plant in 2003.
- The Company's products are registered in more than 45 countries and its manufacturing facilities are accredited and certified by various regulatory authorities from Asia, Latin America, Middle East, Africa , etc
- The company also has global subsidiaries namely
 - BSV BIOSCIENCES, INC (United States)
 - BSV BIOSCIENCE,GMPH (Germany)

Introduction

Background

Invasive Fungal Infections is well documented complication of many conditions and procedures that result immunosuppression, including transplantation, Human Immunodeficiency Virus (HIV) infection, and treatment of malignancy. During the past several decades, opportunistic fungi have emerged as serious nosocomial threats, particularly among patients in Intensive Care Unit (ICU). According to national surveillance efforts coordinated through the Centers for Disease Control and Prevention and institutional reports, there has been a greater than 10-fold rise in invasive infections among critically ill patients since the 1980's (1)

The pathogens involved are mainly yeasts and moulds of *Candida* and *Aspergillus*. *Candida* species account for > 80% of all fungal isolates causing nosocomial infection whereas the rest are *Aspergillus* species. (2)

Classification

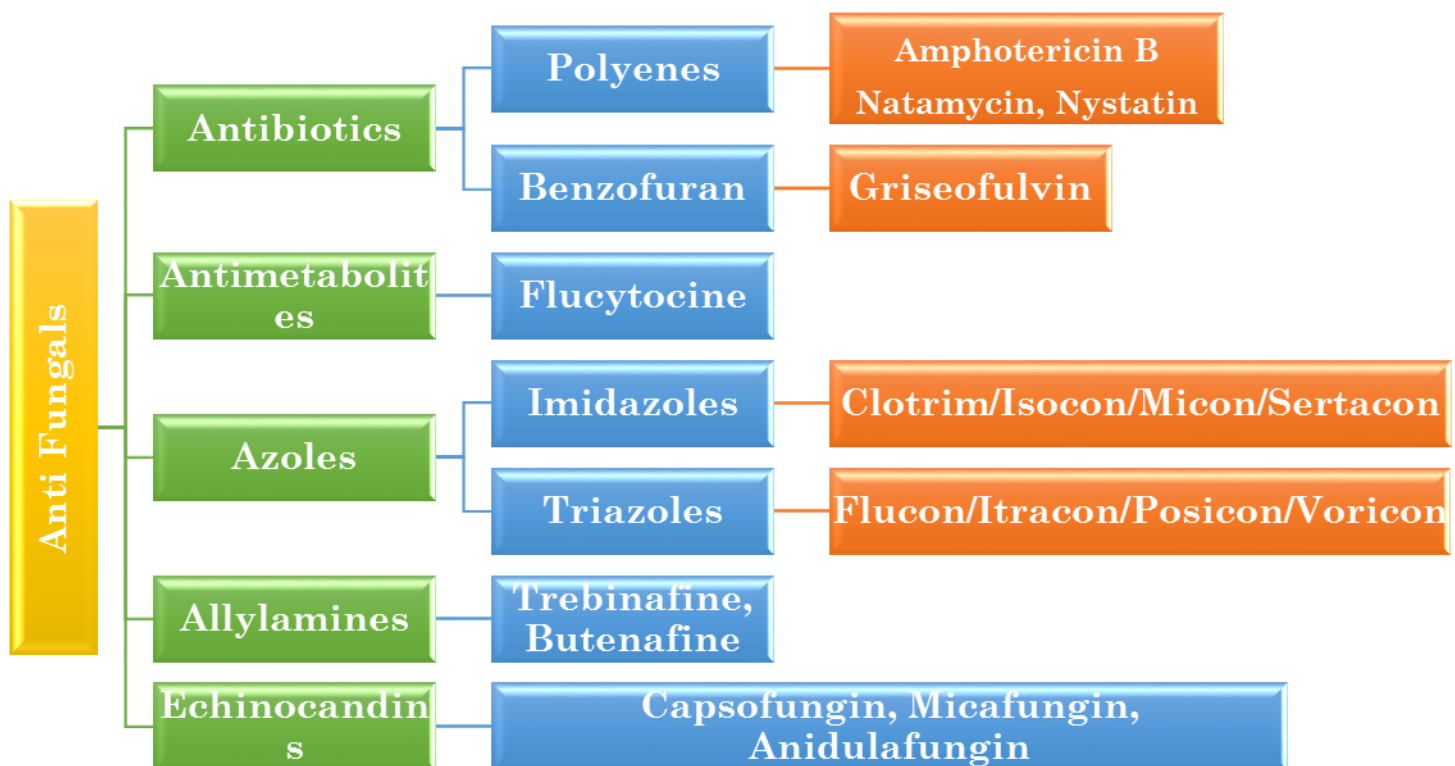


Figure 2: Classification of Anti-Fungal Agents

Majorly used Antifungals in treatment of Invasive Fungal Infections are given in Table 1

Drug	Effective against	Side Effects	Top Brands
Amphotericin B (AmB)	Candida, Cryptococcus, Aspergillus, Blastomyces, some yeast	Nephrotoxicity, Hepatotoxicity, Anemia	FUNGISOME(Lifecare), AMPHOTRET(BSV),
Lipid Amphotericin B (LipAmB)- ABLC, ABCD	---Do---	Less severe than AmB	PHOSOME(Cipla), AMPHONEX(BSV)
Fluconazole	Candida	unusual bruising or bleeding, loss of appetite, pain in the upper right part of the stomach	FORCAN(Cipla), ZOCON(FDC), SYSCAN(Torrent)
Voriconazole (2 nd Gen Azole)	Candida, Aspergillus, Fusarium	Reversible visual disturbances, Confusion, Hallucinations, Hepatitis	VORAZE(Natco Pharma), VORIZE
Posaconazole (2 nd Gen Azole) given with fatty meal	Candida, Aspergillus, Cryptococcus, Mucorales		
Echinocandins Caspofungin, Micafungin, Anidulafungin	<i>Candida, Saccharomyces,</i> <i>Pneumocystis carinii, Aspergillus</i>	fever, phlebitis, rash and chills, electrolyte imbalance	CANCIDAS(Merk), CASPERCID(Sanofi), MYCAMINE(GSK)

Table 1: Commonly used Antifungals in Invasive fungal Infections

IDSA (Infectious Disease Society of America) has issued guidelines for treatment of Invasive Candidiasis and Aspergillosis

Summary of IDSA Guidelines for Treating Invasive Candidiasis and Aspergillosis

Disease State	First-Line Treatment	Alternative Regimen(s)
Invasive aspergillosis	Voriconazole 6 mg/kg IV q12h for 2 doses; then 4 mg/kg IV q12h or 200 mg PO q12h	Lipid amphotericin B 3–5 mg/kg IV q24h Caspofungin 70-mg IV loading dose; then 50 mg/day IV Micafungin 100–150 mg/day IV Posaconazole 800 mg/day PO in 2–4 divided doses Itraconazole dose depends on formulation
Candidemia (non-neutropenic patient; moderate-severe illness)	Caspofungin 70-mg IV loading dose; then 50 mg/day IV Micafungin 100 mg/day IV Anidulafungin 200-mg IV loading dose; then 100 mg/day IV	Fluconazole 800-mg IV loading dose; then 400 mg/day IV or PO
Candidemia (neutropenic patient)	Caspofungin 70-mg IV loading dose; then 50 mg/day IV Micafungin 100-mg IV daily Anidulafungin 200-mg IV loading dose; then 100 mg/day IV	Fluconazole 800-mg IV loading dose; then 400 mg/day IV/PO Voriconazole, if mold coverage desired Voriconazole 6 mg/kg IV q12h for 2 doses; then 4 mg/kg IV q12h or 200 mg PO q12h
<i>Candida glabrata</i>	Echinocandin (see above)	Fluconazole or voriconazole with susceptibility testing
<i>Candida parapsilosis</i>	Fluconazole	Echinocandin, if already responding to therapy
Solid-organ transplant recipient (prophylaxis)	Fluconazole 200–400 mg/day IV/ PO for 7–14 days	Liposomal amphotericin B 1–2 mg/kg/day IV for 7–14 days
ICU prophylaxis (high-risk patients only)	Fluconazole 400 mg/day IV/PO	

ICU = intensive care unit; IDSA = Infectious Diseases Society of America; IV = intravenous; PO = by mouth; q12h = every 12 hours; q24h = every 24 hours.

Table 2: Summary of IDSA Guidelines for Treating Invasive Candidiasis and Aspergillosis

Rationale

Fungal infections are an increasing cause of morbidity and mortality in immunocompromised and critically ill patients. As we treat an increasingly aging population, prolong life with immunosuppressive therapy for a variety of disorders and administer broad spectrum antibiotics, the risk of fungal infections increases. An increasing incidence of invasive candidiasis, aspergillosis and zygomycosis has been reported from India. Therefore it has become the need of hour to understand the underlying indications of patients requiring Anti-Fungal therapy in ICU's and identify the unmet medical need in case of Invasive Fungal Infections.

The study has provided insights on:

- ✓ Market scenario of Antifungals in respect to Intensive Care Unit i.e. which are the majorly encountered infections, what are the underlying indications for fungal infections and which are the most commonly prescribed Antifungals for Invasive Fungal Infections(IFI)
- ✓ Most commonly prescribed Antifungals for IFI's in Prophylactic treatment, Empirical therapy and in cases of confirmed Candida/Aspergillus infection
- ✓ Most prescribed combination therapy for Candida/Aspergillus infections
- ✓ Choice of drug in Febrile Neutropenia patients
- ✓ Most preferred diagnostic tests for fungal infection detection
- ✓ Unmet Medical Need in case of Invasive Fungal Infections
- ✓ A future scope for Anti-Fungals in ICU setups

Objectives

- ✓ To study incidence of Antifungals in Intensive Care Units;
- ✓ To identify the most prescribed Antifungal in Invasive Fungal Infections
 - Prophylactic Treatment
 - Empirical Therapy
 - Treatment of confirmed infection
- ✓ To identify the choice of Antifungal in Febrile Neutropenia patients
- ✓ To determine the current unmet medical need in case of Invasive Fungal Infection

Methodology

Research Design:

Descriptive study (Cross-sectional).

Sampling Design:

Sampling

Non probability Purposive sampling

Sample population:

HOD Critical Care

Intensivists

Senior Consultants (Critical Care)

Consultants (Critical Care)

Sample area:

Delhi-NCR

Sample Size

Hospitals- 30

Respondents- 62

Findings and Interpretation

Incidence of Antifungals in Intensive Care Units

Number of patients

It was found out that approximately 42% of intensivists examined a total of 21-30 patients in a week followed by 30.65% in the range 31-40. However around 84% of intensivists responded that though they examined higher number of patients in ICU/week, the number of Immunocompromised patients was less than 10 and 82% of doctors responded that the number of patients requiring anti-fungal therapy was even lesser than that of Immunocompromised patients.

It was found out that approximately 40% of the total patients in ICU required Anti-Fungal Therapy.

Table 3 gives a comparison of number of patients and percentage of intensivists' response in each range.

Patients	Total	Immunocompromised	Anti-Fungal
0-10	0 %	83.87 %	82.26 %
11-20	11.29 %	14.52 %	17.84 %
21-30	41.94 %	1.62 %	0 %
31-40	30.65 %	0 %	0 %
Above 40	16.13 %	0 %	0 %

Table 3: Number of patients Vs percentage response (per week)

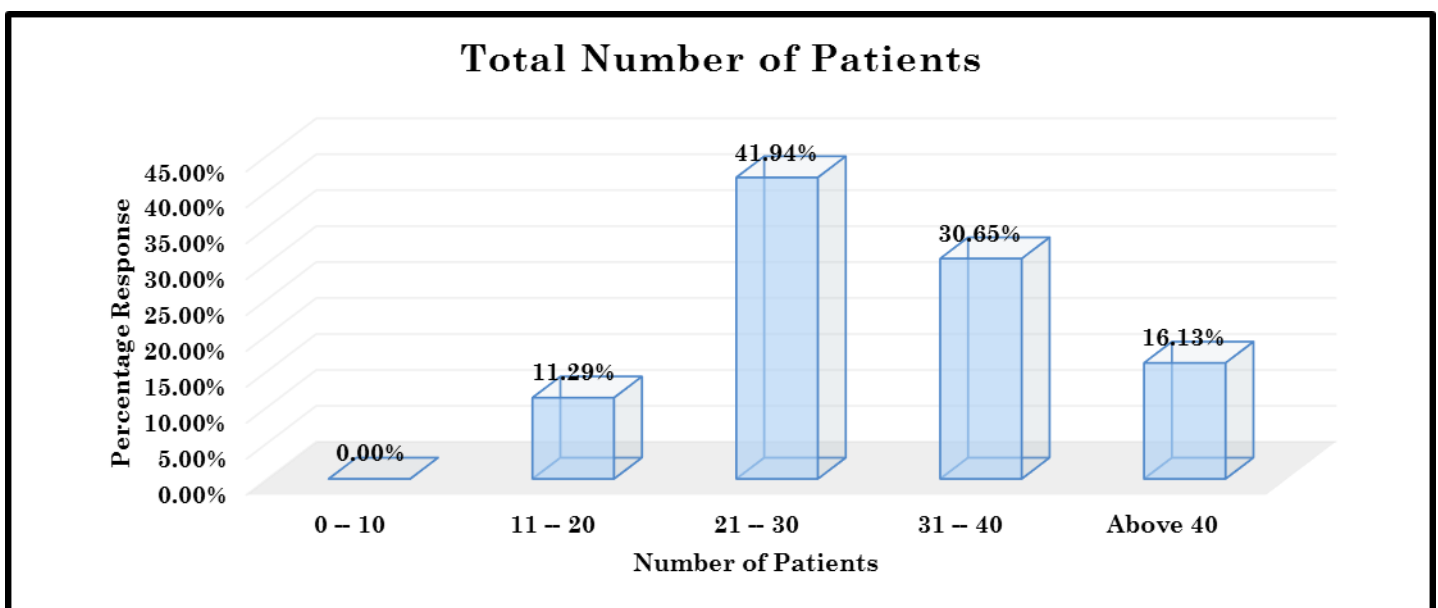


Figure 3: Total Number of patients Vs Percentage response (per week)

Immunocompromised patients

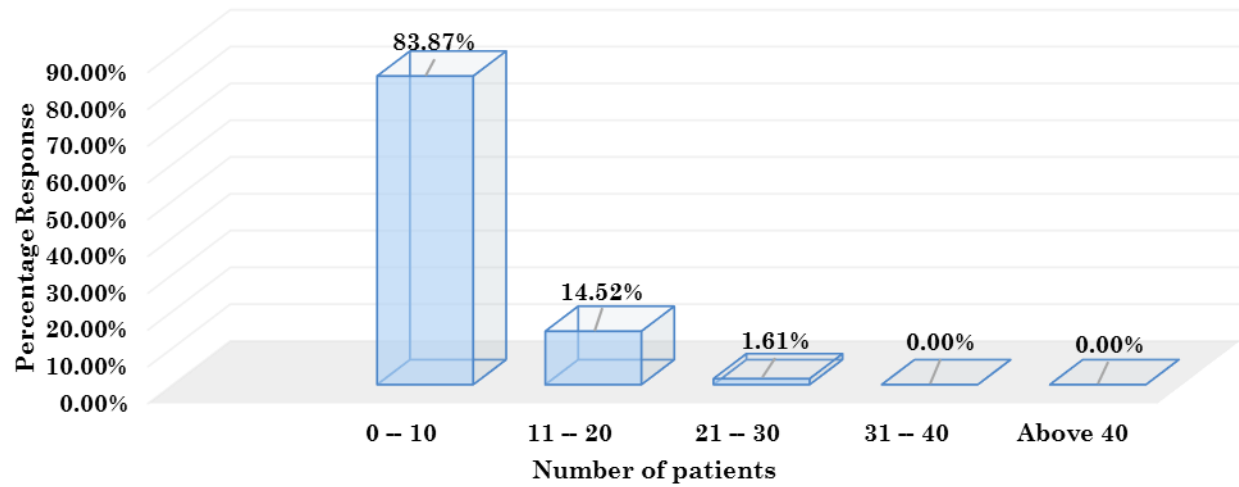


Figure 4: Immunocompromised patients Vs Percentage response (per week)

Antifungal Therapy

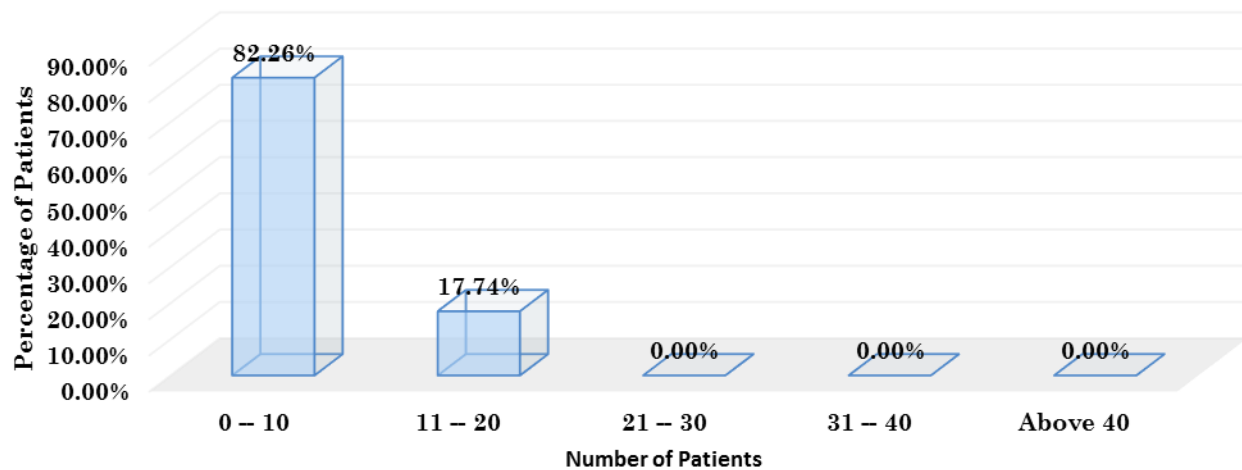


Figure 5: Patients on anti-Fungal Therapy Vs Percentage response (per week)

Type of Infections

It was found from the survey that around 85% of the intensivists encountered 0-5 patients per week suffering from Candida infection while 77% encountered Aspergillus infection while 21% found Aspergillus infection rare. When enquired about Mucorales, 94% of intensivists found it rare. When further enquired, it was also found out that Non-Albican species was major species causing Candida infection.

Table 4 and figures 6, 7 and 8 show representation of percentage response and number of patients for different infections encountered.

Patients	Candida	Aspergillus	Mucorales
0-5	85.48 %	77.42 %	6.45 %
6-10	12.90 %	1.61 %	0 %
11-15	1.61 %	0 %	0 %
16-20	0 %	0 %	0 %
Above 20	0 %	0 %	0 %
Rare	0 %	20.97 %	93.55 %

Table 4: Number of patients Vs percentage response of doctors for different infections (per week)

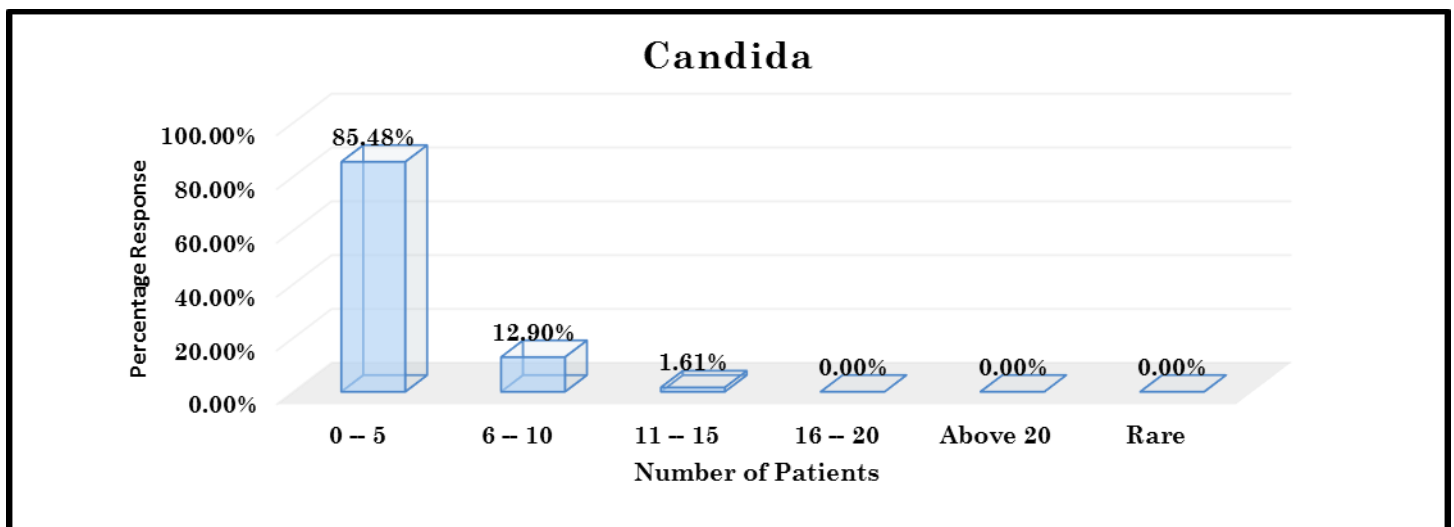


Figure 6: Patients suffering from Candida Infection Vs Percentage response (per week)

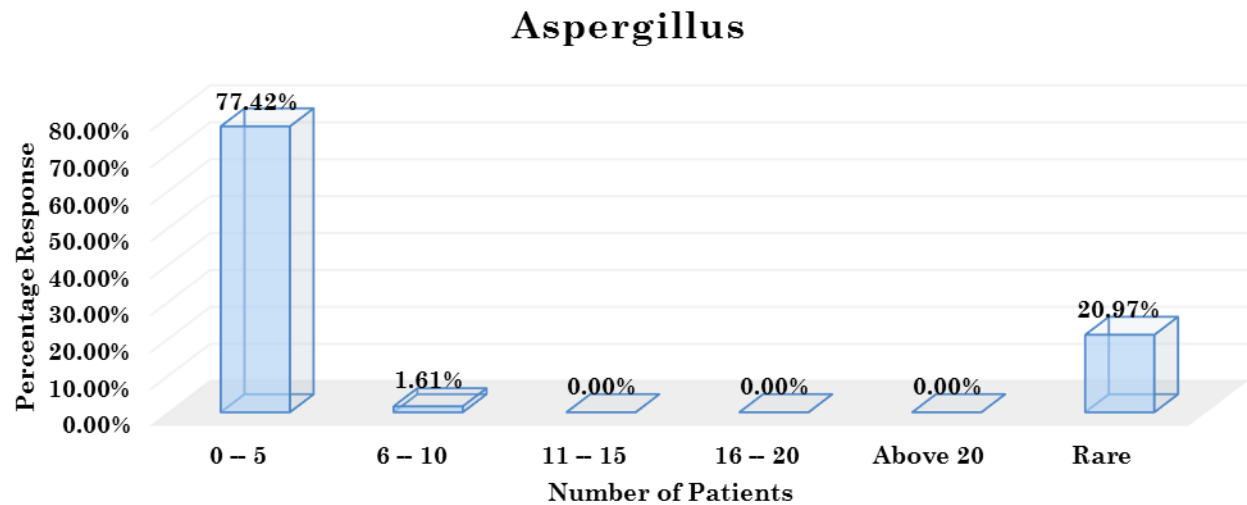


Figure 7: Patients suffering from Aspergillus Infection Vs Percentage response (per week)

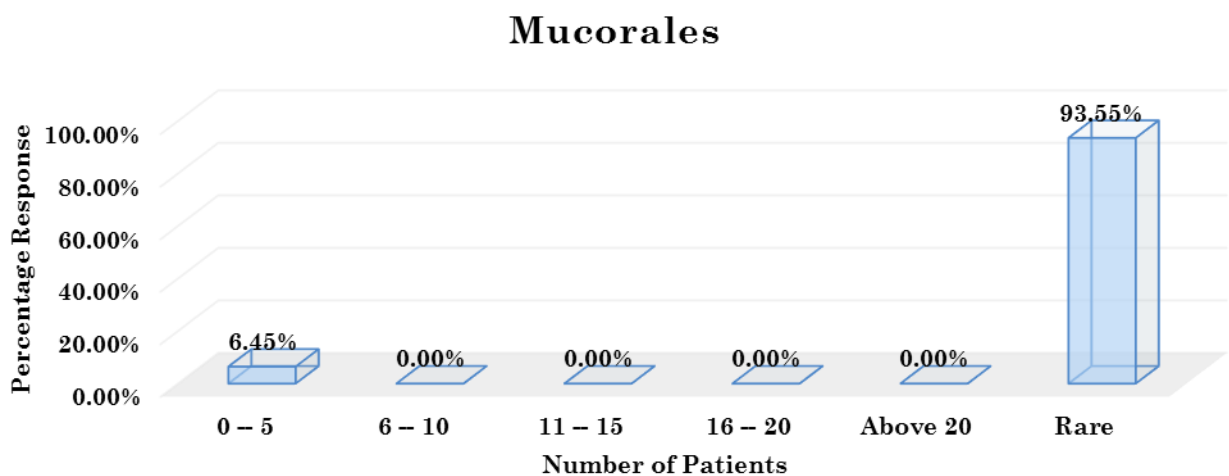


Figure 8: Patients suffering from Mucorales Infection Vs Percentage response (per week)

Underlying Indications

Patients in ICU requiring Anti-fungal therapy are very less (0-5) per week and majority of intensivists i.e. 75% examined/administered anti-fungal in “others” category of patients which primarily includes post-operative/surgery patients. Only 40% of intensivists administered anti-fungal therapy in AIDS patients.

The following table (Table 5) and chart (Table 9) give a brief description about the number of patients and type of patients and percentage response.

Type/Number	0 – 5	6 – 10	11 – 15	16 – 20	Above 20	Rare
Cancer	54.84%	11.29%	1.61%	0.00%	0.00%	32.26%
Transplant	56.45%	3.23%	0.00%	0.00%	0.00%	40.32%
Drug Related	62.90%	8.06%	0.00%	0.00%	0.00%	29.03%
AIDS	40.32%	1.61%	0.00%	0.00%	0.00%	58.06%
Hospitalized	67.74%	19.35%	0.00%	0.00%	0.00%	12.90%
Others	75.00%	21.43%	0.00%	0.00%	0.00%	14.29%

Table 5. Percentage response of intensivists with respect to type and number of patients

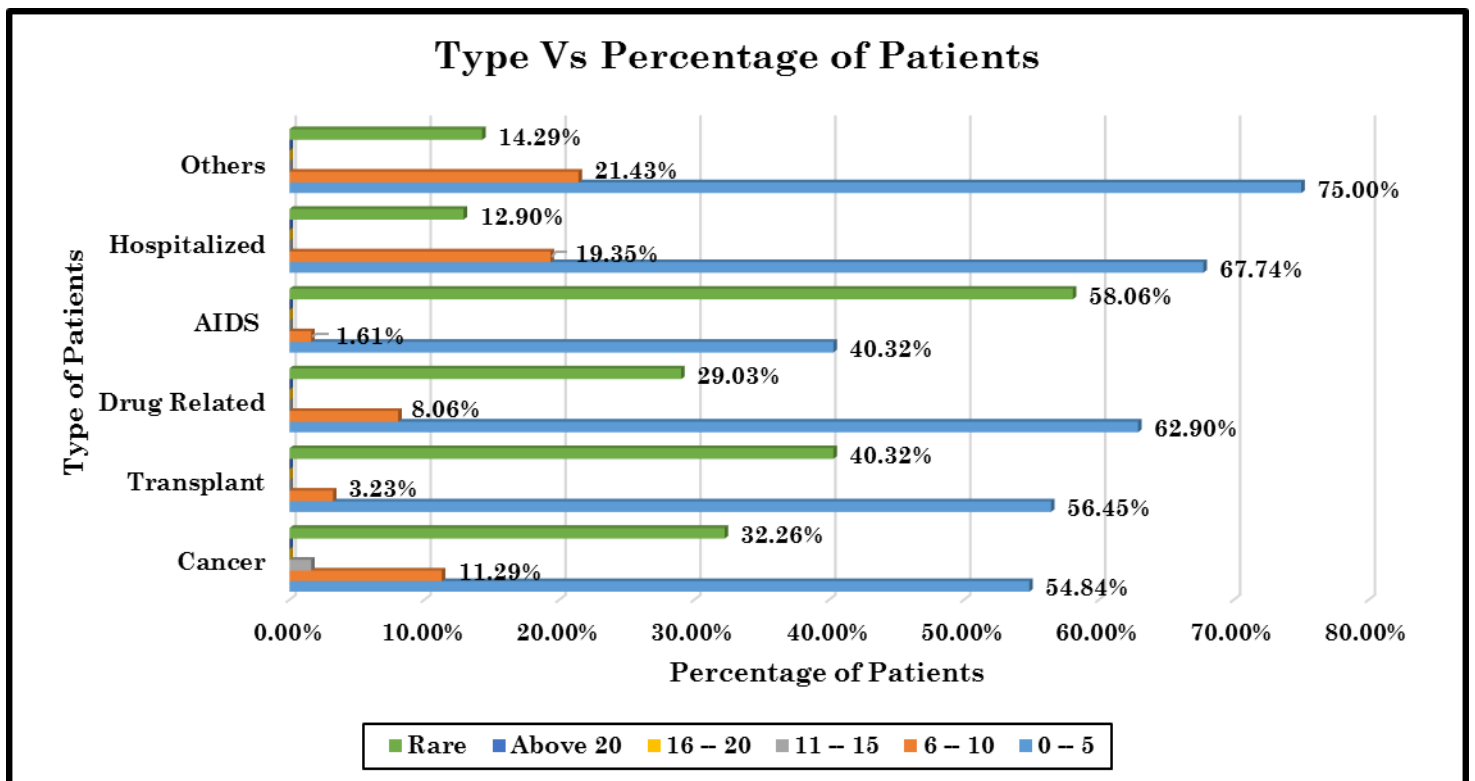


Figure 9: Percentage response of intensivists with respect to number of patients and type of patients (per week)

Most prescribed Anti-Fungal in Invasive Fungal Infection

1. Prophylactic Therapy

When questioned about prophylactic treatment, around 84% of intensivists preferred Fluconazole and around 10% responded that they were not in favor of giving prophylactic treatment. Figure 10 gives a graphical representation of Percentage of intensivists Vs Anti-fungal drugs.

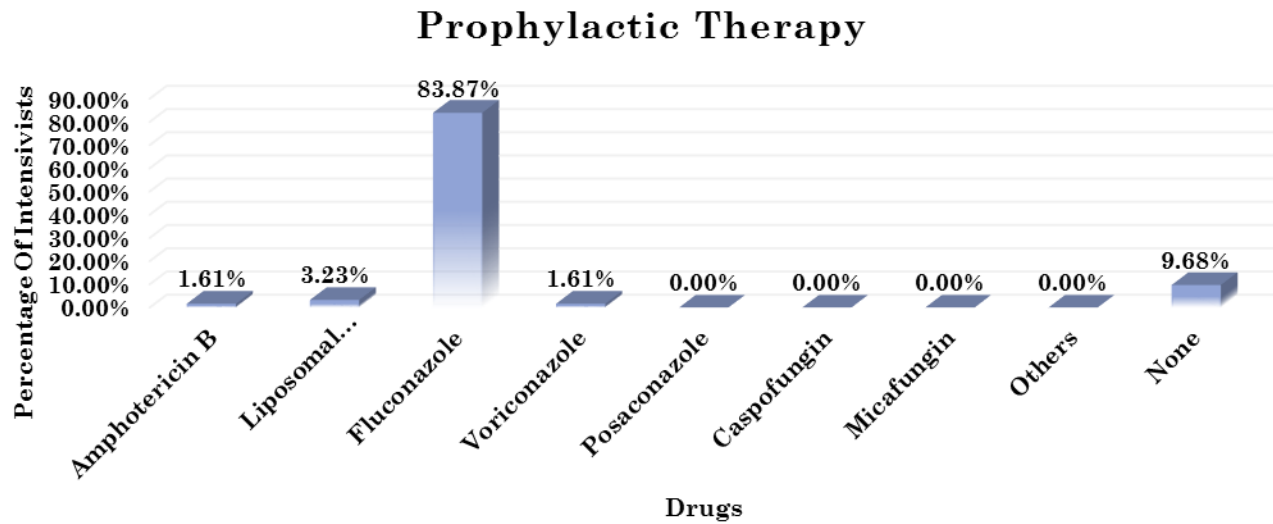


Figure 10: Percentage of intensivists Vs choice of drugs (per week)

The most common prescribed brand was Forcan (Cipla) and prescribed dose was found out to be 400mg OD and average number of days was found to be 9.27 days.

Following calculations were performed to find out average sales of FORCAN injection in ICU's
Packing: 100ml bottle (2mg/1ml)

Cost: 118.50INR

Dose: 400mg OD

Therefore, to administer 400mg, 2 bottles of FORCAN are required.

Average Sales per month: Cost of 1 bottle*Number of bottles*Av. Number of days*Av. Number of patients* Number of weeks*Number of doctors(Figure 10)

$$=118.5*2*9.27*5*4*84$$

$$=36,90,943.20\text{INR(as per MRP)}$$

This implies that FORCAN has an average sales of around **37 Lac** per month in Delhi-NCR as far as Prophylactic Treatment is concerned.

2. Empirical Therapy

For empirical therapy, Fluconazole (75.81%) was the choice of drug for Candida Infection with its closest competitor Amphotericin B at 11.29%.

Empirical therapy for Aspergillus shows a different trend with Voriconazole being the market leader at 53% followed by Liposomal Amphotericin B at 24% and conventional Amphotericin B at 19%. Table 6 and figure 11 give a representation of choice of Anti-Fungal among doctors in Empirical Therapy

Drug/ Infection	Candida	Aspergillus
Amphotericin B	11.29%	19.35%
Liposomal Amphotericin B	3.23%	24.19%
Fluconazole	75.81%	0.00%
Voriconazole	0.00%	53.23%
Posaconazole	0.00%	0.00%
Caspofungin	9.68%	3.23%
Micafungin	0.00%	0.00%
Others	0.00%	0.00%

Table 6: Percentage of intensivists and choice of anti-fungal

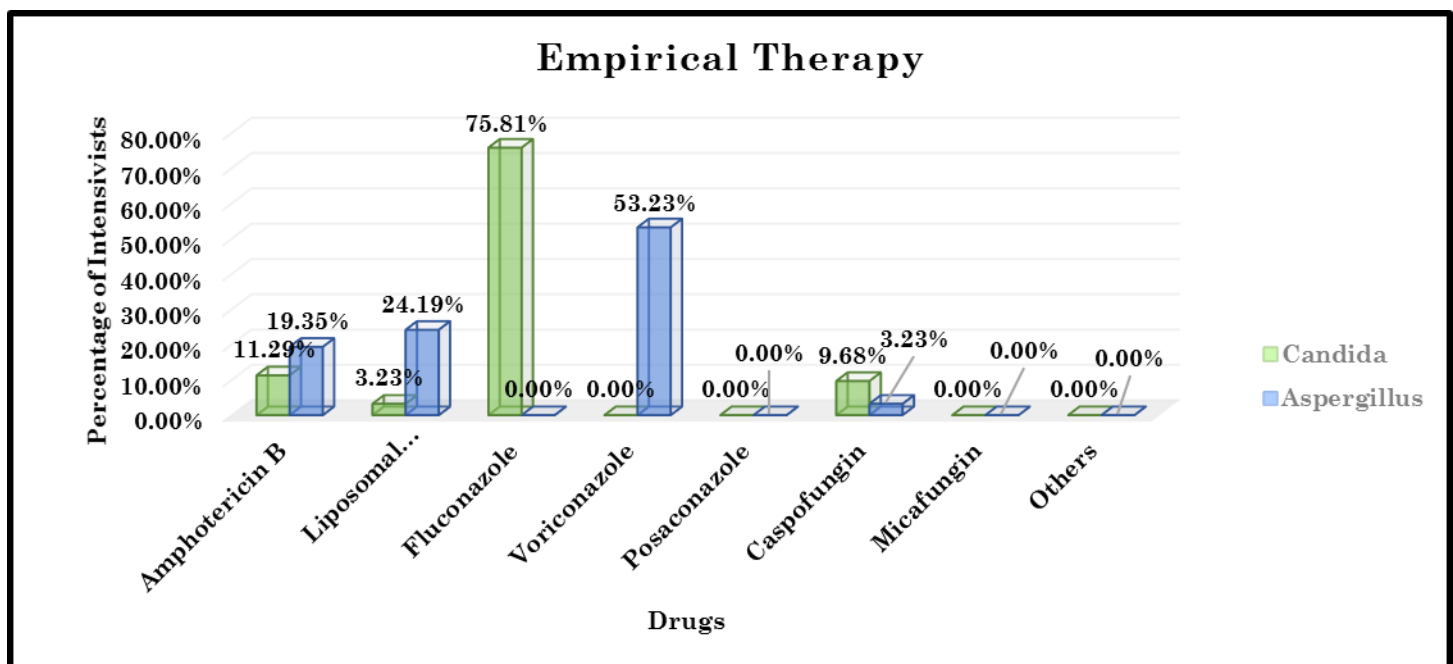


Figure 11: Percentage of Intensivists Vs choice of Anti-Fungal (per week)

Average duration for therapy for Candida was found out to be 13.57 days and that for Aspergillus was 14 days.

Again if calculate sales of FORCAN,

Prescribed dose: 800mg loading followed by 400mg OD

Average sales per month: $118.5 \times (4 \times 1 + 2 \times 12.57) \times 3 \times 4 \times 76$

=31,49,218.08INR (as per MRP)

That is an average sale of approximately 31.5Lac per month.

The study also shows that Echinocandins are gaining importance. Also quite a few intensivists were in favor that as ICU patients are critically ill Amphotericin B and its type and Echinocandins are preferred due to their effective response and also few major side effects which can be managed by dose regulation.

3. Confirmed Infection

For treatment of Candida infection, Caspofungin was the choice of anti-fungal for 47% intensivists followed by Fluconazole and Liposomal Amphotericin B at 31% and 16% respectively.

However for treatment of Aspergillus, 42% intensivists preferred Liposomal Amphotericin B followed by Voriconazole being the choice of 39% intensivists. (Figure 12)

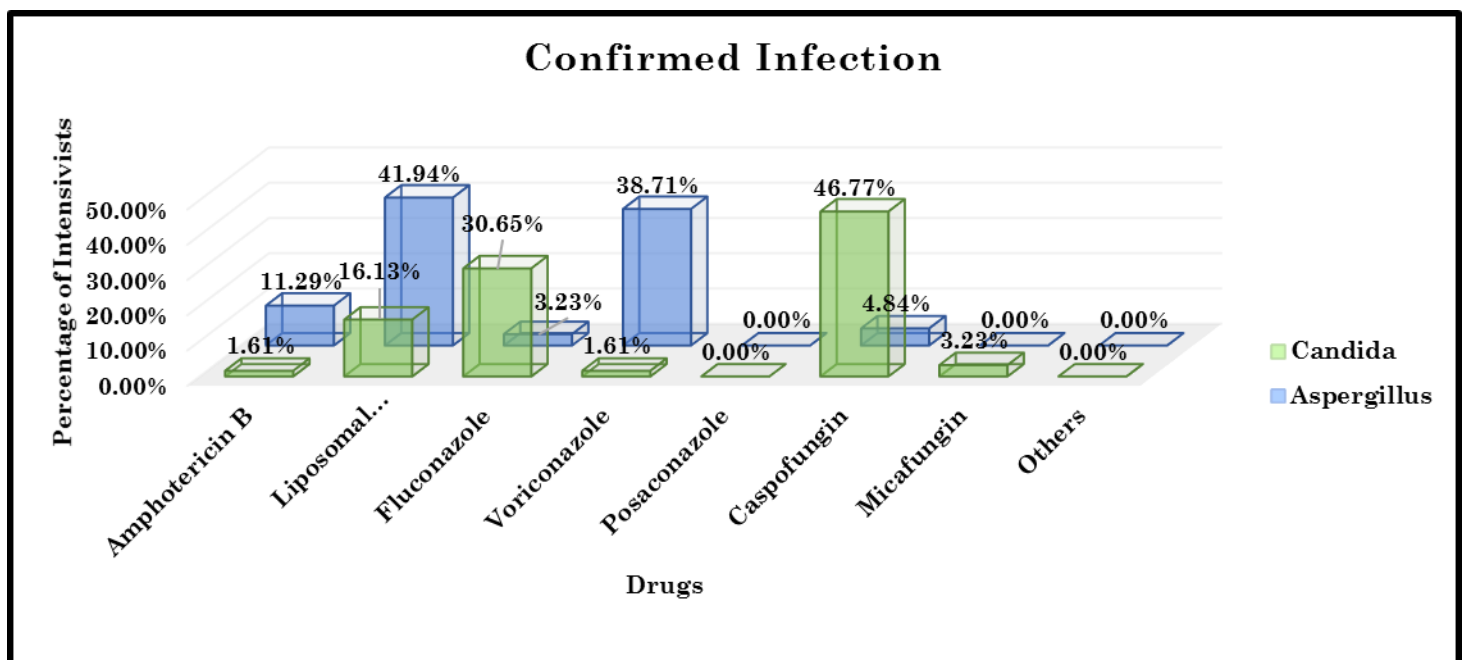


Figure 12: Choice of Anti-Fungal for treatment of confirmed Candida and Aspergillus infections (per week)

Various intensivists were in doubt when asked about treatment of Candida infection. They gave the information that choice of Anti-Fungal for treatment of Candida differs with respect to species and site of infection.

Combination Therapy

When asked about combination therapy, 82% of intensivists were in opinion of not giving any combination therapy for Candida infection. Same was the choice of 69% intensivists for Aspergillus infection. (Figure 13)

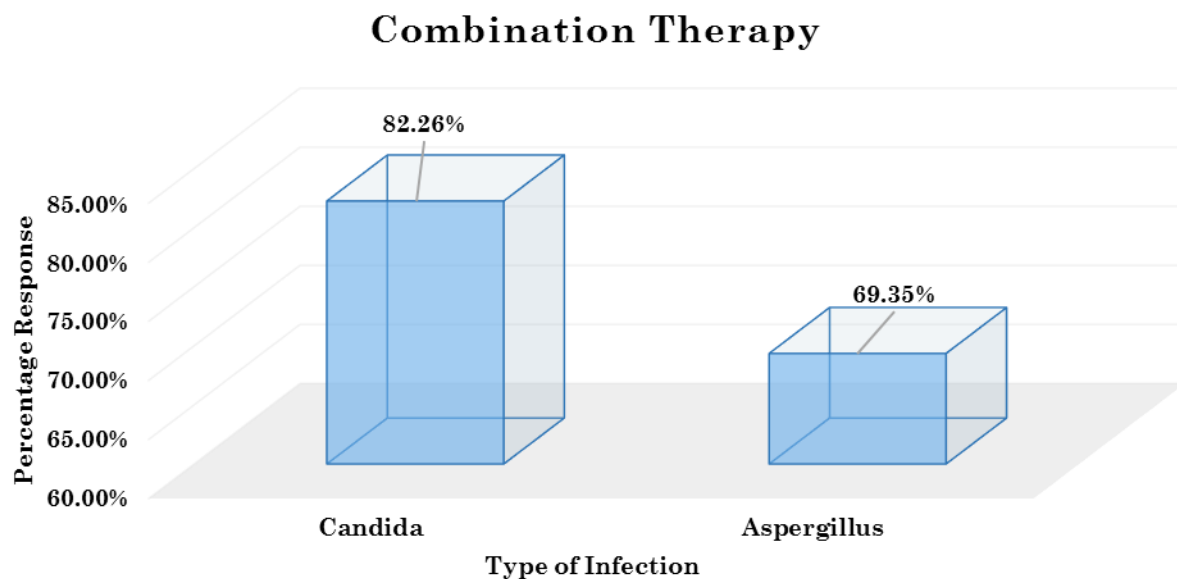


Figure 13: Percentage of intensivists not in favor of combination therapy (per week)

The most prescribed combination for treatment of Candida infection was **Fluconazole + Caspofungin** which was a choice of 5% intensivists. Whereas for Aspergillus infection, it was **Liposomal Amphotericin B + Voriconazole** which was a choice of 13% intensivists followed by **Amphotericin B + Voriconazole** at 8%

Choice of drug for Febrile Neutropenia patients

Figure 13 clearly shows that 90% of the intensivists responded that examine 0-5 patients with Febrile Neutropenia with Caspofungin being the choice of 37% intensivists followed by Fluconazole and Liposomal Amphotericin B being the choice of 21% and 15% respectively. Average duration of the therapy was around 14 days.

3% of intensivists who responded NA were of Neonatal ICU.

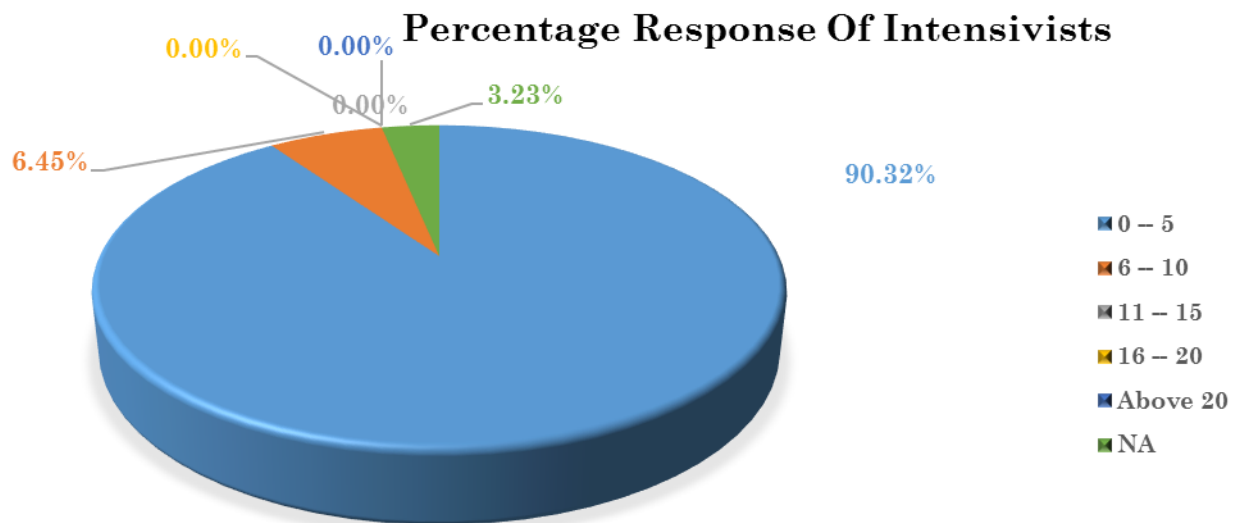


Figure 14: Percentage response of intensivists Vs Number of Patients of Febrile Neutropenia (per week)

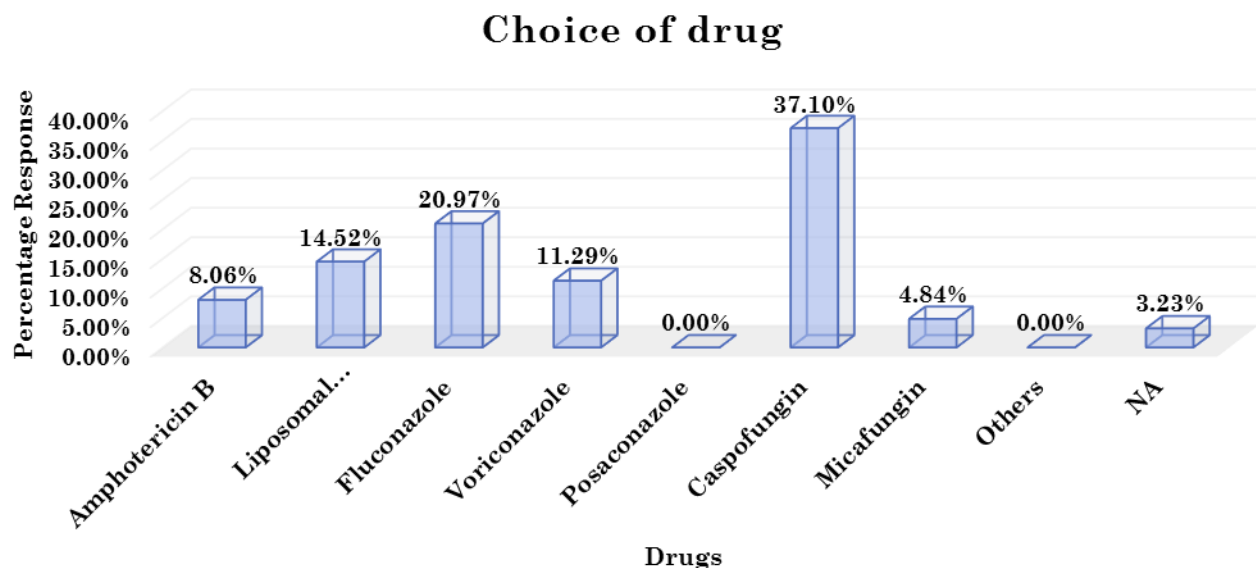


Figure 15: Choice of Anti-Fungal for Febrile Neutropenia (per week)

Diagnostic Tests

For Candida detection, Culture test remained the choice of 87% intensivists whereas for Aspergillus it was Galactomannan Test for 42% intensivists and Culture Test for 32%. Also 23% intensivists favored CT Scan for Aspergillus detection. Figure 16 shows choice of diagnostic tests for infection detection.

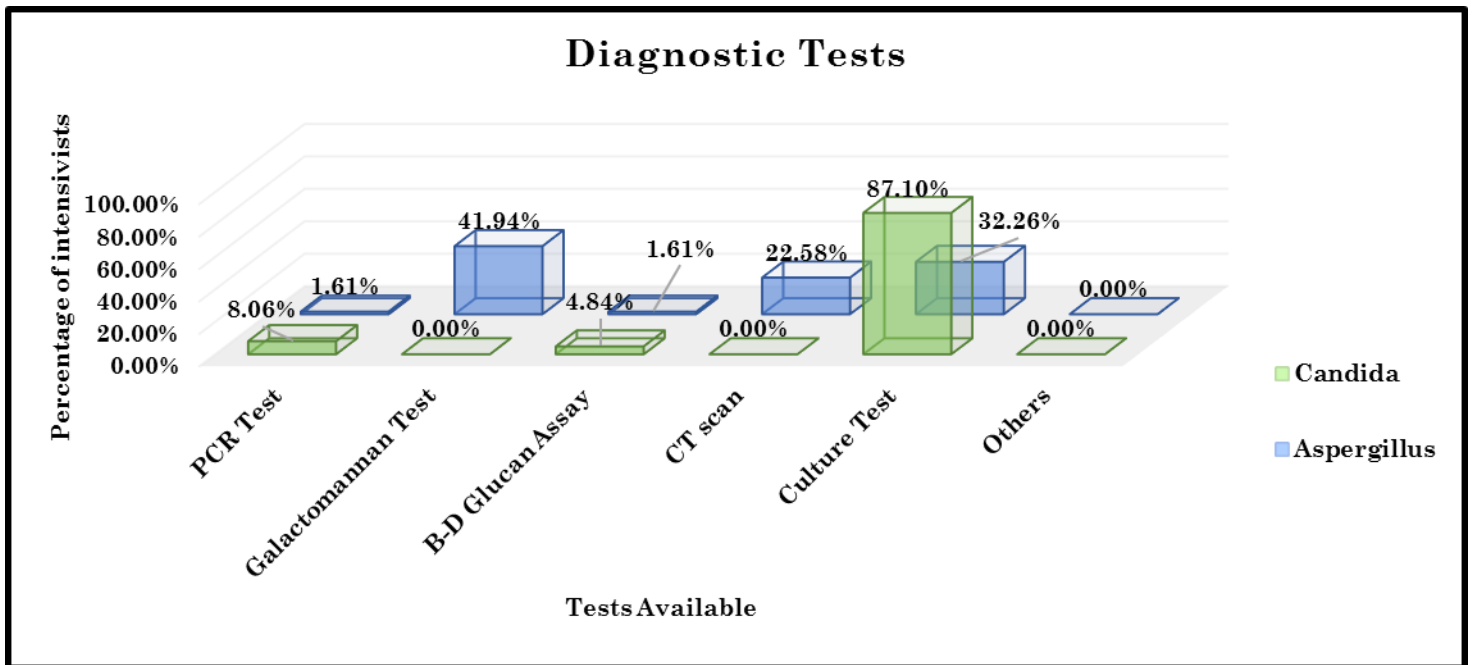


Figure 16: Choice of Diagnostic Tests Vs Percentage response of Intensivists (per week)

Current unmet medical need in case of Invasive Fungal Infection

Most of the intensivists had an opinion that:

- ✓ There is a need for newer, quicker and reliable diagnostic tests;
- ✓ Better Anti-Fungals available in the market are expensive;
- ✓ No ideal Antifungal;

Some of the senior Intensivists also claimed that though Echinocandins were the latest and best in therapy, they were not suitable for severely ill patients, Amphotericin B is the choice of drug for those patients.

Findings based on opinions

Findings based on opinions of the intensivists were:

1. Prescribing Anti-Fungals depends on Sensitivity Test, Type of Species causing infection and Site of infection;
2. Prescribing Anti-Fungals also depends upon economic status of the patient;
3. A significant difference was observed in Private and Government Hospitals, in Private Hospitals all Anti-Fungals are being prescribed whereas in Government Hospitals main stress is given on Fluconazole as it is economical and has least side effects;
4. Though Fluconazole is the market leader and here to stay due to economic reasons and least side effects, Liposomal Amphotericin B and Echinocandins are gaining importance;
5. Number of patients with Fungal Infections are increasing providing an opportunity to discover newer and better Anti-Fungals;
6. Non-Albicans may be a major species causing Candida Infection;
7. Number of patients requiring Anti-Fungal Therapy in Cardiac Critical Care/Apex Coronary Care are very few (2-3 patients/month);
8. Many fungal species are becoming resistant towards Anti-Fungals;
9. Noticeable low use of Posaconazole was observed;
10. Diagnostic Tests need attention;

Limitations to the study

- Species specification i.e. Albicans and Non-Albicans could have been included in the questionnaire;
- Site specification for Candida Infection could have been added included;
- Sample size could have been increased to get more accurate result.

Suggestions

Implications

The study gives quite a clear picture about the prescription trends of Anti-Fungals in ICU setup. The study shows a way ahead to proceed. It provides complete information about

Which antifungal is being neglected?

Which antifungal has a greater scope?

Doctors' opinion about antifungals.

Areas where BSV can venture into.

This information can be used to and worked upon to increase the market share in Anti-Fungals and generate more revenue.

Way ahead

- Amphotericin B and its types have a good potential in Anti-Fungal market provided they are used wisely i.e. proper dose and duration. Its price is one of the major reasons for its low popularity. In view of some intensivists, if a formulation of Amphotericin B better than its Liposomal form and low cost is discovered, it can easily be a market leader.
- Echinocandins also have a greater importance in the market due to their wide spectrum of action and minimal side effects.
- As India falls in Low-Middle income group countries, with a fairly large population not being financially strong, Fluconazole has a good market potential as revealed by study. The data shows that FORCAN (Cipla), favorite Fluconazole of intensivists and consultants have an average sales of around **68Lac** in Delhi-NCR per month. Therefore, Fluconazole is one molecule where a company can venture into.
- Also improving the existing Amphotericin B preparations i.e. R&D is another area where a company can venture into.
 - Echinocandins also have a greater importance in the market due to their wide spectrum of action and minimal side effects. Caspofungin is another molecule which provides an opportunity for a company to capture the Anti-Fungal market.

Annexure

Questionnaire

S.No.

Date: _____

Name: _____ Location: _____

Q1. How many patients do you examine weekly?

	Total	Immunocompromised	Anti-Fungal Therapy
0-10			
11-20			
21-30			
31-40			
Above 40			

Q2. How many cases of following infection do you encounter weekly?

	Candida	Aspergillus	Mucorales	Others
0-5				
6-10				
11-15				
16-20				
Above 20				

Q3. What is the underlying indication for patients requiring antifungal therapy?

	0-5	6-10	11-15	16-20	Above 20
Cancer					
Transplant					
Drug related					
AIDS					
Hospitalized					
Others					

Q4. Which antifungal do you prefer for prophylactic treatment?

	Tick the preferred	Dose	Duration	Vials
Amphotericin B				
Liposomal Amphotericin B				
Fluconazole				
Voriconazole				
Posaconazole				
Caspofungin				
Micafungin				
Others				

Q5. Which antifungal you prefer in empirical therapy?

	Candida				Aspergillus			
	Tick the preferred	Dose	Duration	Vials	Tick the preferred	Dose	Duration	Vials
Amphotericin B								
Liposomal Amphotericin B								
Fluconazole								
Voriconazole								
Posaconazole								
Caspofungin								
Micafungin								
Others _____								

Q6. Which is the most preferred diagnostic test for diagnosis of fungal infection? (Tick the appropriate)

	Candida	Aspergillus
PCR Test		
Galactomannan Test		
B-D Glucan Assay		
CT scan		
Culture Test		
Others _____		

Q7. Which drug do you prefer for confirmed **Candida** infection?

	Tick the preferred	Dose	No. of Days	Vials	Major Side Effects	Management of Side Effects
Amphotericin B						
Liposomal Amphotericin B						
Fluconazole						
Voriconazole						
Posaconazole						
Caspofungin						
Micafungin						
Others						

Q8. Which is the preferred combination therapy for above?

Combination	Dose	Duration

Q9. Which drug do you prefer for confirmed **Aspergillus** infection?

	Tick the preferred	Dose	No. of Days	Vials	Major Side Effects	Management of Side Effects
Amphotericin B						
Liposomal Amphotericin B						
Fluconazole						
Voriconazole						
Posaconazole						
Caspofungin						
Micafungin						
Others _____						

Q10. Which is the preferred combination therapy for above?

Combination	Dose	Duration

Q11. How many patients with **Febrile Neutropenia** do you examine weekly?

0-5	6-10	11-15	16-20	Above 20

Q12. What is your choice of drug for treatment of Febrile Neutropenia?

Drug	Dose	Duration

Q13. According to your opinion, what is the current unmet medical need in treatment of IFIs?
