



Original Article



Anti-fungal Consumption by Days of Therapy (DOT) Metric in a Teaching Hospital: A Step towards Anti-fungal Stewardship

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ABSTRACT

Background: Anti-fungal stewardship (AFS) remains an under-explored aspect within antimicrobial stewardship programs, particularly in developing nations. Understanding the trend of anti-fungal agent consumption at our institute will assist with implementing an anti-fungal stewardship program (AFSP) soon. This study was carried out to provide benchmarking data on anti-fungal consumption, compare the consumption of anti-fungal agents among various hospital locations, and identify target locations for AFS.

Methods: After the approval of the Institutional Ethics Committee (IEC), a retrospective observational study was conducted at Shree Krishna Hospital, Karamsad. Antifungal consumption was calculated using the Days of Therapy (DOT) metric in adult inpatients in whom systemic antifungal agents (amphotericin B, anidulafungin, caspofungin, fluconazole, flucytosine, and voriconazole) were administered from 2020 to 2022. Data of DOT were captured through the Hospital Information System (HIS) and analysed using Microsoft Excel for Mac version 16.75 (23070901).

Results: Over three years, one patient was prescribed anti-fungal agents per 1000 admissions. Overall anti-fungal consumption in the last three years was 2.96 DOT/1000 Patient Days (PD). The consumption has increased over three years from 2.63 DOT/1000 PD in 2020 to 3.81 DOT/1000 PD in 2022. Fluconazole (2.48 DOT/1000 PD) was the most common anti-fungal agent consumed. The highest anti-fungal use was observed in critical care units (7.48 DOT/1000 PD).

Conclusion: Our study showed increased consumption of antifungal agents over three years. A prospective study is recommended to assess the rationality of antifungal agent prescriptions in locations with high consumption.

KEYWORDS: Anti-fungal; Anti-fungal stewardship; AFSP; Days of therapy; DOT

INTRODUCTION

Fungal infections pose a significant health burden globally. In different geographical locations, the prevalence of fungal diseases differs based on climate, environmental conditions, socioeconomic factors, and

patient-related factors.¹ Fungal infections affect over a billion individuals worldwide and are associated with significant mortality rates. The deaths attributed to fungal diseases are comparable to those caused by

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tuberculosis and exceed those from malaria by more than threefold.² The current population of India is 1,457,001,793 as of Friday, December 20, 2024. This makes India the most populated country in the world, representing 17.78 % of the world population.³ Around 4.4% of India's population suffers from serious fungal diseases.⁴ India, a tropical country, features diverse geographical landscapes such as mountains, plains, plateaus, and numerous rivers. Extensive oceanic boundaries on three sides surround it.¹ All these factors make fungal infections endemic in India, significantly affecting public health.⁵ Anti-fungal medications are essential for treating a broad spectrum of fungal infections, ranging from skin-level (superficial) to deeper tissue infections (subcutaneous) and potentially life-threatening systemic fungal infections throughout the body.⁶ However, due to excessive and improper use of anti-fungal medications, certain fungi have developed resistance to these drugs, making it difficult to treat fungal infections effectively, often requiring alternative treatment strategies or higher doses to combat the resistant strains.⁷

Various factors, including the availability and affordability of medications, healthcare practices, and prescribing patterns, influence the prevalence of anti-fungal use in India.⁸

Unfortunately, a significant proportion of anti-fungal prescriptions are unnecessary or excessive, contributing to the development of anti-fungal resistance.⁷ Moreover, there is a lack of data on antifungals' toxicities and pharmacological interactions, primarily due to limited awareness about anti-fungal usage.⁹

To address these concerns, an anti-fungal stewardship program (AFSP) is essential to ensure the judicious use of antifungals and prevent the development of anti-fungal resistance.¹⁰ A well-structured AFSP can optimise anti-fungal use, minimise the adverse outcomes, and reduce the financial burden of anti-fungal therapy.¹¹ One practical approach for monitoring anti-fungal use is through antimicrobial consumption indicators, such as Days of Therapy (DOT) and Defined Daily Dose (DDD).¹² The Centers for Disease Control and Prevention (CDC) and the National Healthcare Safety Network (NHSN) recommend using DOT as the most accurate and preferred measure of antimicrobial use. This study used the DOT metric to analyse anti-fungal consumption due to its advantages over the DDD method.^{13,14}

This study was done to obtain benchmarking data on anti-fungal consumption by DOT metric, to compare the consumption of anti-fungal agents among hospital

locations, and to identify target locations for anti-fungal stewardship.

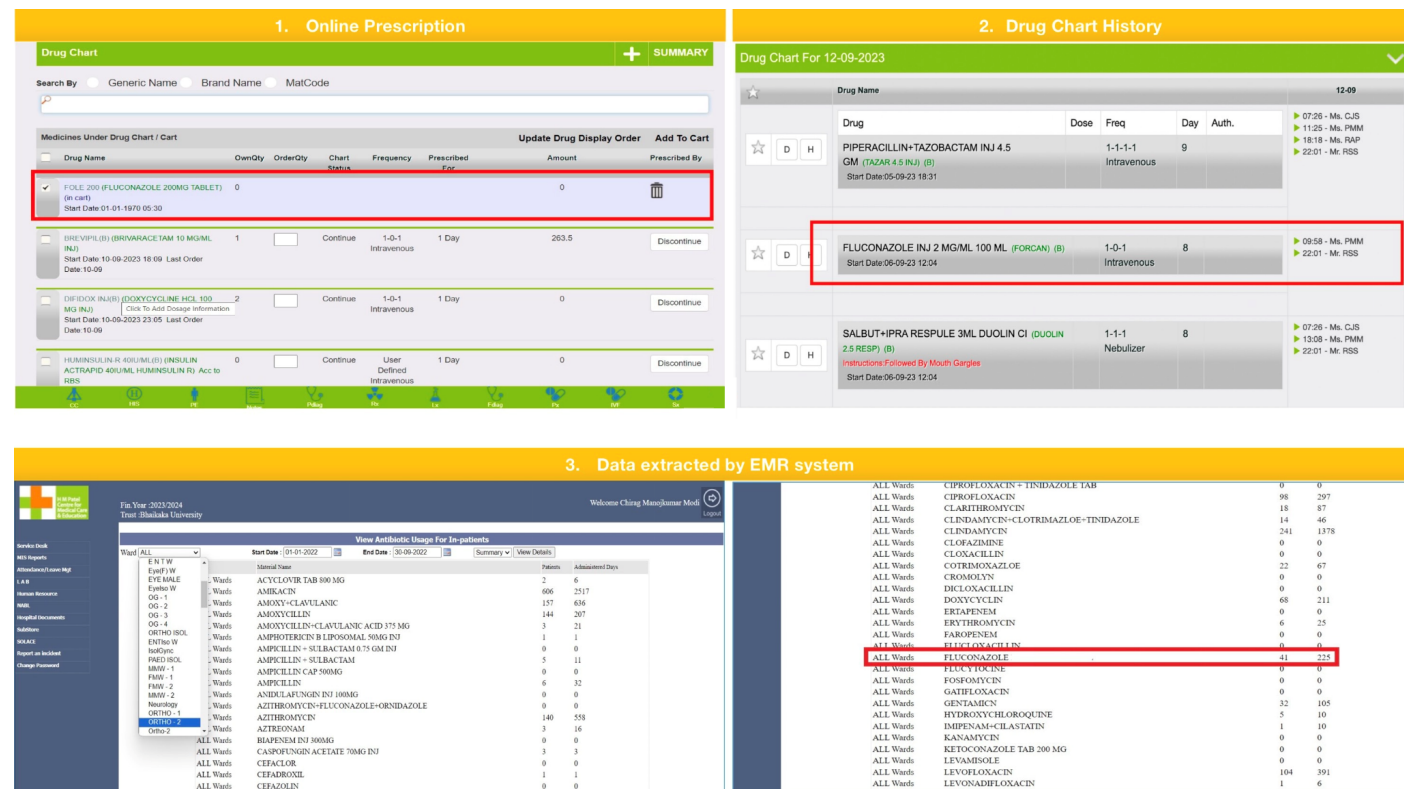
METHODOLOGY

Ethical consideration: The study was approved by the Institutional Ethics Committee, Bhaikaka University, Karamsad, Anand, and individual consent was waived for this retrospective analysis.

Settings: The study was conducted at the Microbiology laboratory of Central Diagnostic Laboratory (NABL accredited), Shree Krishna Hospital (NABH accredited), Bhaikaka University, Karamsad, Gujarat.

Data collection: The retrospective observational study was conducted from January 2020 to December 2022 (3 years). All adult in-patients administered with oral or parenteral anti-fungal agents, namely amphotericin B, anidulafungin, caspofungin, fluconazole, flucytosine and voriconazole, were included in the study. All day-care patients, outpatients, and all pediatric in-patients to whom topical anti-fungal agents were administered were excluded from this study. Data was captured from the Hospital Information System (HIS) of Shree Krishna Hospital, Bhaikaka University, inpatients. Our hospital has an antifungal medical record (EMR) system, antifungal and inpatient services, **SOLACE**, which stands for **Shree Krishna Hospital On-Line Application for Clinical Excellence**. It contains an online prescription and drug administration chart that captures the drug's schedule, date, and time of administration. When a drug was prescribed to a patient by a clinician, it showed up on the drug chart history of that patient, and when a nurse administered it, it was captured in a nursing chart. The antifungal agent's name, number of patients in whom the drug was administered, total administered days, and patient's hospital number according to timeline and location were extracted by the EMR system (Figure 1). With the help of this, we got the anti-fungal consumption data for the years 2020, 2021 and 2022.

Unit of measurement: The DOT metric evaluates the days a patient receives an antimicrobial agent (regardless of dose). Any dose of an anti-fungal agent received for 24 hours represented one (1) DOT. The DOT for a given patient on multiple anti-fungal agents was the sum of DOT for each anti-fungal agent the patient received. DOT is often standardised to 1000 Patient Days (DOT/1000 Patient Days) to compare hospitals or services of different sizes.^{13,14}

Figure 1: Online prescription, drug chart history and data extraction by EMR system

$$\text{DOT} / 1000 \text{ PD} = \frac{\text{Days of therapy with an agent during a period}}{\text{Total number of Patient Days within that period}} \times 1000$$

Patient days were calculated simultaneously by recording the number of patients at the inpatient location by the HIS. At the end of the month, the sum of all days was recorded electronically. At the same time, we could get the Facility-Wide Inpatient Admission Count and Inpatient Location-Specific Admission Count from HIS.^{15,16}

The following formulas were used for the calculations:

1.	Total consumption of anti-fungal agents =
	$\frac{\text{Total DOTs of antifungals in last 3 years}}{\text{Total Patient Days for the last 3 years}} \times 1000$
2.	Yearly consumption of anti-fungal agents =
	$\frac{\text{Total DOTs of anti-fungal agents in a year}}{\text{Total Patient Days for that year}} \times 1000$
3.	Yearly consumption of a particular anti-fungal agent

	$\frac{\text{Total DOTs of that anti-fungal agent in a year}}{\text{Total Patient Days for that year}} \times 1000$
4.	Yearly use of anti-fungal agents
	$\frac{\text{No. of patients (anti-fungal agents administered)}}{\text{Total no. of patients in a year}} \times 1000$
5.	Location-wise use of anti-fungal agents
	$\frac{\text{No. of patients (anti-fungal agents administered)}}{\text{Total no. of patients in a year at that location}} \times 100$

Data analysis: Data was entered and analysed using Microsoft Excel for Mac version 16.75 (23070901).

RESULT

During the study period, 172379 patients were admitted to our hospital. Among them, 183 patients were prescribed anti-fungal agents. Standardising it to 1000 admissions according to formula-4 mentioned above, one patient was prescribed an antifungal agent per 1000 admissions. In the present study, anti-fungal consumption was calculated using a DOT metric. Overall anti-fungal consumption was 2.63, 2.56 and 3.81 DOT/1000 PD, respectively, for 2020, 2021 and 2022 (figure 2).

Figure 2 Pattern of outcomes for de-escalation suggestion made by the antimicrobial stewardship team

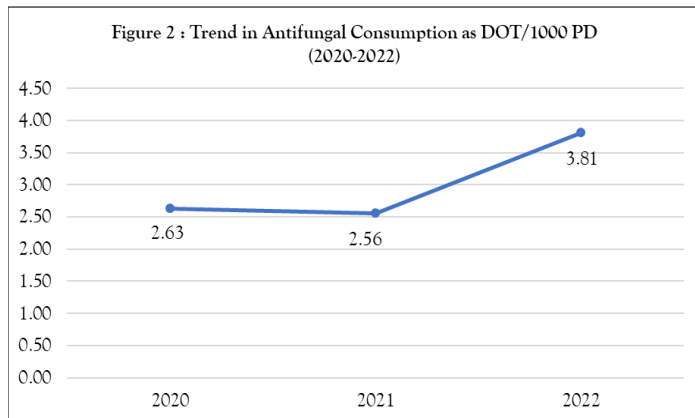


Table 1 shows the yearly consumption of individual anti-fungal agents. Fluconazole was the most consumed anti-fungal agent, having 2.48 DOT/1000 PD. In 2021, amphotericin B, anidulafungin, caspofungin and voriconazole consumption was increased while fluconazole consumption was decreased. In 2022, fluconazole was the most consumed anti-fungal agent (Table 1).

Table 1: Consumption (DOT/1000 PD) of anti-fungal agents (2020-2022)

Anti-fungal agents	2020	2021	2022	Overall
Amphotericin B	0.00	0.16	0.01	0.06
Anidulafungin	0.00	0.03	0.00	0.01
Caspofungin	0.06	0.07	0.06	0.06
Fluconazole	2.21	1.81	3.57	2.48
Flucytosine	0.00	0.00	0.00	0.00
Voriconazole	0.36	0.49	0.18	0.35
Overall	2.63	2.56	3.81	2.96

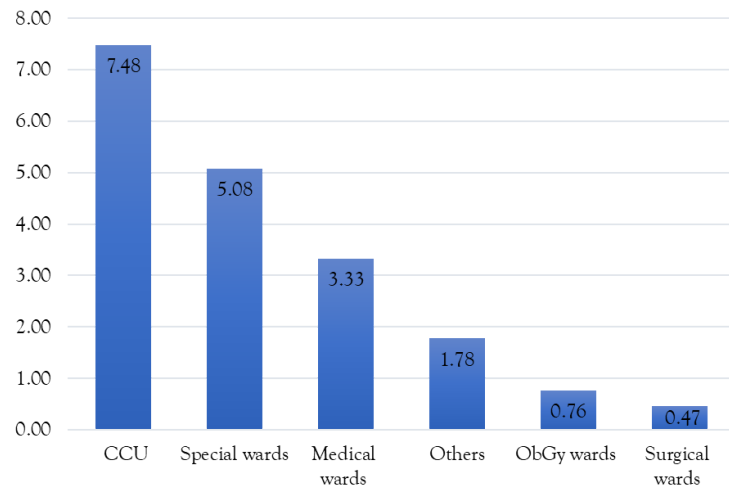
We also analysed location-wise consumption of antifungals, which showed the Critical Care Unit (CCU) (7.48) having the highest consumption, followed by special wards (5.08) and the medical ward (3.33) (figure 3).

DISCUSSION

Our study provides valuable insights into anti-fungal consumption using the DOT metric, which has been

3). Special wards were privileged category wards for patients who wanted to get personalised treatment, including Silver, Gold, Platinum, Deluxe, Super Deluxe and Diamond categories (Figure 3).

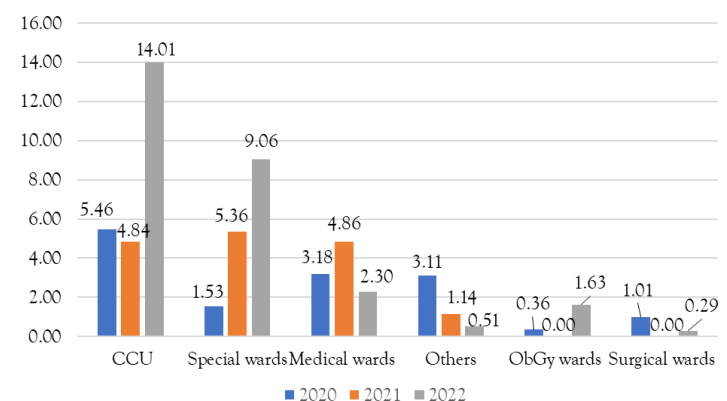
Figure 3 : Location-wise consumption (DOT/1000 PD) of anti-fungal agents



CCU: Critical care unit; Special wards: Silver, Gold, Platinum, Deluxe, Super Deluxe, Diamond category wards; Others: ENT, Ophthalmology, Dermatology, Orthopedic, Oncology, Transplantation unit, Burn unit, Emergency care unit; ObGy wards: Obstetrics and Gynaecology wards; Medical & Surgical wards include male & female wards.

In Figure 4, an increasing trend of antifungal consumption was seen in special wards. In 2020 and 2022, CCU (5.46 and 14.01, respectively) had the highest anti-fungal consumption. However, special wards (5.36) had more consumption in 2021 because they were converted to COVID-19-designated wards (figure 4).

Figure 4: Location specific year-wise consumption (DOT/1000 PD) of antifungal agents



CCU: Critical care unit; Special wards: Silver, Gold, Platinum, Deluxe, Super Deluxe, Diamond category wards; Others: ENT, Ophthalmology, Dermatology, Orthopedic, Oncology, Transplantation unit, Burn unit, Emergency care unit; ObGy wards: Obstetrics and Gynaecology wards; Medical & Surgical wards include male & female wards.

increasingly recognised as a robust and standardised method for monitoring antimicrobial usage. To the best of our knowledge, no Indian study has been found

entirely similar to our study. Our study is the first single-centre study in India demonstrating the versatility of the data on anti-fungal consumption by DOT metric using the EMR system.

In the present study, overall anti-fungal consumption was 2.96 DOT/1000 PD, which was lower than other Indian studies done in 2022 by four single-day point prevalent surveys. In the published study, the overall usage of anti-fungal medications was recorded as 2.71 DDD/1000 PD, with a corresponding figure of 8.96 DOT/1000 PD.¹⁷

Figure 2 illustrates the trend in anti-fungal consumption as DOT/1000 PD at Shree Krishna Hospital from 2020 to 2022. A slight decrease was observed in 2021 (2.56 DOT/1000 PD), followed by a significant rise in 2022 (3.81 DOT/1000 PD). This increase may reflect changes in clinical practices, the expanded use of immunosuppressive therapies, or the rise in COVID-19 and mucormycosis cases in India. The prevalence of Mucormycosis in India was 70 times higher compared to global data.¹⁸ The observed increase in anti-fungal consumption across the study period also aligns with global trends indicating rising anti-fungal use. A study analysed data from 65 countries reported an increase in systemic anti-fungal consumption from 0.50 to 0.92 defined daily doses (DDD) per 1,000 inhabitants per day between 2008 and 2018.⁸

Fluconazole's status as the most commonly consumed anti-fungal agent with 2.48 DOT/1000 PD in our study is consistent with findings from other regions. For example, in Lebanon, fluconazole accounted for 20.99% of total anti-fungal consumption.¹⁹ Its widespread use can be attributed to its broad spectrum of activity, favourable pharmacokinetics, and cost-effectiveness. However, the high usage of fluconazole raises concerns about the possible development of resistance in *Candida* species, which may hamper its effectiveness in treatment.²⁰

The increased use of anti-fungal agents in CCUs (7.48 DOT/1000 PD), as shown in Figure 3, is supported by the published study,²¹ as critically ill patients are more prone to invasive fungal infections. A multisite study found that echinocandins and fluconazole were CCUs' most commonly prescribed antifungals, making up 40% and 38% of total consumption, respectively.²² At our institute, special wards were converted to COVID-19-designated wards in 2021, which might be the reason for the increased consumption (5.36 DOT/1000 PD) compared to CCUs (4.84 DOT/1000 PD) in that particular year. In 2022, there was a notable increase in anti-fungal consumption within CCUs (14.01 DOT/1000 PD), possibly due to patients battling both the severe acute respiratory syndrome coronavirus-2

(SARS-CoV-2) and opportunistic fungal infections like mucormycosis, particularly among those with underlying conditions such as diabetes mellitus, cancer, or those receiving hemodialysis treatment combined with deferoxamine. Other probable factors could be disruptions in implementing infection control guidelines, the widespread use of corticosteroids and antibiotics, and increased hospital crowding.²³ These circumstances highlight the importance of careful anti-fungal management in CCUs, where patients are especially susceptible to these infections.

In our institution, oncology patients are not exclusively admitted to the oncology ward; they are also placed in medical, surgical, special wards, or CCUs based on their comorbid conditions. This admission practice explains the variation in our findings compared to published studies, where significant anti-fungal consumption was reported in dedicated oncology units.^{17,24,25}

Since the late 1960s, when antifungal compounds were first introduced, resistant fungal strains have been identified in numerous countries worldwide. This has led to a steady rise in invasive infections caused by resistant fungi, becoming an increasing concern for healthcare professionals. The development of triazoles and echinocandins in the 1990s expanded treatment options; however, these advancements were soon followed by the emergence of fungal pathogens resistant to these drugs.²⁶ Azole resistance in *Candida* and *Aspergillus* species presents significant clinical challenges alongside echinocandin and multidrug resistance, particularly in *Candida glabrata*. The spread of azole-resistant *Aspergillus fumigatus*, often linked to agricultural use, and the growing threat of multidrug-resistant *Candida auris* is especially concerning.²⁷

In India, infections caused by *Candida albicans* are relatively common, accounting for 37.95% of cases; however, anti-fungal resistance is more prevalent among non-*albicans Candida* (NAC) species. Approximately 10.34% of *Candida albicans* isolates exhibit drug resistance. Resistance to certain azoles, such as fluconazole, is also notable (21.8%).²⁸ Species like *Candida auris* pose a significant challenge due to their high resistance to anti-fungal medications and ability to spread easily in healthcare settings.⁶ Furthermore, 64–71% of multi-triazole-resistant strains have been identified in patients with *Aspergillus* infections, even those without prior exposure to triazole treatments.²⁹

Prolonged or repeated exposure to anti-fungal drugs accelerates fungal adaptation, leading to resistance.

Factors such as low dosages or short treatment durations contribute to the emergence of resistance.⁶ The increasing use of antifungal agents and the accompanying rise in antifungal resistance highlight the need for Anti-Fungal Stewardship (AFS) programs. These initiatives focus on ensuring the appropriate and judicious use of antifungal agents to improve treatment outcomes.

Monitoring the anti-microbial consumption trend in hospitals will serve as an essential intervention in AMSP, and therefore, hospitals need reliable methods to determine the consumption of antimicrobial agents, including antifungal agents. Antimicrobial consumption data using dispensing and procurement criteria cannot be used for DOT calculation, while prescription records/nursing charts/audits & feedback are suitable for DOT analysis. Nursing chart (administration) data is the most accurate data on antimicrobial usage as it records the data of antimicrobials administered to the patients. Therefore, the present study used nursing chart data to calculate DOT. However, it was cumbersome and impossible to compile nursing chart data without electronically maintained data.³⁰ Published studies agreed that Electronic Health Record Systems (EHRS) were the only way to get accurate data on antimicrobial consumption.³¹ Canadian acute care pediatric hospital study stated that Electronic Medication Administration Records (eMAR) was a better source of antimicrobial consumption data than pharmacy dispensing systems.³² Our institute has a well-established HIS, and SOLACE was introduced in 2014. Therefore, it is recommended that each institute try to introduce HIS and explore ways of using it for antimicrobial consumption data and various AMSP initiatives.

Our study had various limitations. This being a retrospective study, the rationality of the prescription couldn't be assessed. Due to the different formats of HIS before 2020, data from more than the last 3 years could not be analysed. The drug chart for pediatric patients was maintained manually due to dose adjustment according to weight; therefore, we could not capture data through SOLACE.

CONCLUSIONS

Our study showed increased consumption of systemic anti-fungal agents in adult inpatients over three years. A prospective study is recommended to measure anti-fungal consumption trends and assess the rationality of anti-fungal agent prescriptions in locations with high anti-fungal consumption. This study will be a pilot study to enhance the anti-fungal stewardship program.

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CONFLICTS OF INTEREST STATEMENT

The authors declare no conflict of interest

SOURCE OF FUNDING

None

ETHICS STATEMENT INCLUDING PATIENT CONSENT

Not applicable

AUTHOR'S CONTRIBUTION

RP: Conceptualization; Methodology; Resources; Data collection; Analysis; Writing the draft

BC: Data collection; Literature review; Analysis; Writing the draft; Review & Editing

CM: Conceptualization; Resources; Data collection; Analysis; Writing the draft; Review & Editing

NP: Conceptualization; Resources; Data collection; Analysis; Writing the draft; Review & Editing

AI DECLARATION

No AI tool was used to generate research data, perform data analysis, interpret findings, formulate scientific conclusions, or make editorial decisions. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript.

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