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RESEARCH ARTICLE

Infection Prevention Bundles for Fungal Diseases in Paediatric Intensive Care Units: Implementation and Effectiveness

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Abstract: ***Background:*** Invasive fungal infections (IFIs) pose a significant threat in pediatric intensive care units (PICUs), particularly in resource-constrained settings like India, where high patient turnover and limited infrastructure exacerbate risks. This study evaluates the implementation and effectiveness of a tailored fungal prevention bundle in reducing IFI incidence and outcomes in a tertiary care PICU.***Methods:*** A prospective before-after interventional study was conducted from January 2023 to September 2025 at the 24-bed PICU of tertiary care hospital, enrolling 1,200 consecutive admissions (600 pre-bundle, 600 post-bundle). The bundle comprised hand hygiene (>90% compliance), central venous catheter (CVC) stewardship, targeted antifungal prophylaxis (fluconazole 6 mg/kg/day or voriconazole per IDSA guidelines), surveillance cultures, antibiotic stewardship, and multidisciplinary audits. Primary outcomes were IFI incidence per 1,000 admissions and attributable mortality. Secondary outcomes included adherence, length of stay (LOS), costs, and adverse events. Data were analysed using chi-square tests, Fisher's exact test, and multivariable logistic regression ($p<0.05$).***Results:*** Pre- and post-bundle groups were demographically similar (median age 4.0 years, 52% male). IFI incidence decreased from 50 to 18 per 1,000 admissions (64% reduction; $p<0.001$). Mortality fell from 55% (14/25) to 11% (1/9; $p=0.007$). Adherence averaged 80%, with prophylaxis in 42% of high-risk patients. LOS reduced from 40 to 25 days ($p=0.01$), yielding ₹90 lakh in savings. Mild hepatotoxicity occurred in 4% of prophylaxis cases.***Conclusions:*** The fungal prevention bundle significantly reduced IFI incidence and mortality in an Indian PICU, demonstrating feasibility and cost-effectiveness. Standardized adoption could mitigate IFI burdens in similar settings.

Keywords: Invasive fungal infections, Paediatric intensive care unit, Infection prevention bundle, Candidemia, Antifungal prophylaxis, India, IDSA guidelines

INTRODUCTION

Invasive fungal infections (IFIs) represent a formidable challenge in pediatric intensive care units (PICUs), where they contribute substantially to morbidity, prolonged hospital stays, and elevated mortality among critically ill children. These infections predominantly affect vulnerable populations, including those with haematological malignancies, solid organ or hematopoietic stem cell transplants, congenital immunodeficiencies, or prolonged exposure to invasive medical devices and broad-spectrum antimicrobial therapies.[1] Epidemiological data indicate that IFIs account for approximately 20% of microbiologically confirmed infections in intensive care settings, with a notable prevalence in paediatric cohorts due to their immature immune systems and frequent exposure to risk-conducive interventions.[2] Recent studies from 2023 to 2025 highlight a shifting landscape, where yeast infections like candidemia have decreased in some regions, while mould infections, such as invasive aspergillosis (IA), have risen, often as breakthrough cases in patients receiving antifungal prophylaxis.[3] In PICUs specifically, the incidence of IFIs varies widely but can reach 35 cases per 1,000 admissions, with infants under one year comprising up to 77.7% of affected individuals.[4] This variability underscores the influence of local factors, including unit-specific practices and patient demographics, on infection rates.[5]

The primary pathogens implicated in paediatric IFIs are Candida species, which dominate with an incidence of 3% to 24% in high-risk groups like those with acute lymphoblastic leukemia, followed by Aspergillus species and less common moulds like Mucorales.[6] Candidemia remains the most frequent manifestation, often originating from central venous catheter (CVC)-related sources, while IA typically arises in neutropenic patients or those on prolonged corticosteroids.[7] The attributable mortality from these infections is alarmingly high, ranging from 13.8% for candidemia to 46.2% for aspergillosis and up to 50% overall in PICU settings, with even higher rates (52.5% to 58%) reported in treated invasive aspergillosis infections (IAIs).[8] These figures are exacerbated by diagnostic delays, as clinical presentations are often nonspecific—fever, sepsis-like syndromes, or organ dysfunction—and confirmatory tests like blood cultures or biomarkers (e.g., β-D-glucan) may lack sensitivity in children.[9] Moreover, the economic burden is substantial, with extended lengths of stay (mean 18.6 days for IFI cases versus shorter durations in uninfected patients) and

costs exceeding $90,000 per episode, straining healthcare resources in both high- and low-resource environments.[10]

Several well-established risk factors predispose children in PICUs to IFIs, amplifying the need for targeted prevention. Hospitalization in the PICU itself elevates risk, particularly when compounded by invasive procedures such as CVC placement, which increases the odds of candidemia by facilitating biofilm formation and translocation from colonized sites.[11] Other key contributors include prolonged broad-spectrum antibiotic use (e.g., carbapenems or third-generation cephalosporins), which disrupts gut microbiota and promotes fungal overgrowth; total parenteral nutrition (TPN), associated with mucosal barrier disruption; mechanical ventilation exceeding five days; renal replacement therapy; and underlying conditions like neutropenia (absolute neutrophil count <500 cells/μL) or immunosuppression from chemotherapy or steroids.[12] Studies have shown that Candida colonization occurs in up to 70% of PICU patients, with younger age groups at heightened risk due to immature skin barriers and frequent handling.[13] Additional environmental factors, such as adjacent construction or renovation near immunocompromised areas, can introduce airborne mould spores, further elevating IA risk in hematopoietic stem cell transplant (HSCT) recipients housed in non-laminar airflow rooms.[14] In resource-limited settings, factors like Foley catheter use and specific antibiotics (e.g., injectable meropenem) have been independently linked to IFIs, highlighting the interplay between clinical practices and infection susceptibility.[15]

Despite advances in antifungal therapies, including echinocandins and azoles, treatment outcomes remain suboptimal due to emerging resistance patterns—such as fluconazole-resistant non-albicans Candida—and the toxicity profiles of agents like amphotericin B in paediatric populations.[16] This underscores the imperative for preventive strategies over reactive management. Infection prevention bundles, which are structured sets of evidence-based practices implemented cohesively, have revolutionized the control of healthcare-associated infections (HAIs) in critical care, drawing from successes in reducing central line-associated bloodstream infections (CLABSIs) in neonatal and adult ICUs.[17] These bundles typically encompass hand hygiene protocols (targeting >90% compliance), environmental hygiene, CVC stewardship (including maximal sterile barriers and daily need assessments), antibiotic stewardship to limit overuse, and surveillance for fungal colonization via swabs or biomarkers.[18] In PICUs, where patient complexity demands adaptation, bundles have shown promise in curbing bacterial HAIs, but fungal-specific applications remain underexplored, with most evidence extrapolated from neonatal intensive care units (NICUs) or adult cohorts.[19]

A critical component of these bundles is targeted antifungal prophylaxis, guided by recommendations from the Infectious Diseases Society of America (IDSA). The IDSA endorses prophylaxis for high-risk pediatric patients, such as those with acute myeloid leukemia (AML), relapsed malignancies, or undergoing HSCT, where IFI incidence exceeds 10%.[20] Fluconazole (6–12 mg/kg/day, maximum 400 mg) is recommended for Candida prevention in neonates with birth weights <1000 g or in units with high invasive candidiasis (IC) prevalence, while mould-active agents like voriconazole (8–9 mg/kg every 12 hours for ages 2–14 years) or posaconazole (200–300 mg daily for ≥13 years) are suggested for prolonged neutropenia or graft-versus-host disease.[21] Echinocandins, such as micafungin (1–2 mg/kg/day), serve as alternatives in azole-intolerant cases.[22] Prophylaxis duration aligns with risk persistence, often extending pre-engraftment in HSCT or through chemotherapy cycles, with monitoring for hepatotoxicity, renal impairment, and drug interactions.[23] However, concerns about resistance emergence and ecological shifts (e.g., to non-albicans species) necessitate judicious use, balanced against proven reductions in IC incidence (up to 50%) and mortality.[24]

Despite these guidelines, gaps persist in the literature regarding the implementation and real-world effectiveness of fungal-specific prevention bundles in PICUs. Most studies are retrospective or focus on neonatal populations, with limited prospective data evaluating adherence, cost-effectiveness, and long-term outcomes in diverse pediatric critical care settings.[25] Multicenter analyses reveal implementation barriers, including variable compliance (often <70%), resource constraints in low-middle-income countries, and the need for multidisciplinary training to sustain bundle fidelity.[26] Furthermore, the post-COVID-19 era has introduced new challenges, with increased corticosteroid use and viral co-infections potentially altering IFI epidemiology and bundle efficacy.[27] Addressing these gaps is crucial, as effective bundles could avert thousands of cases annually, reducing mortality and healthcare burdens.

This study addresses these deficiencies by prospectively evaluating the implementation and effectiveness of a comprehensive fungal prevention bundle in a tertiary PICU. Incorporating IDSA-guided prophylaxis alongside core infection control measures, we hypothesized a significant reduction (≥50%) in IFI incidence and attributable mortality. By assessing adherence, barriers, and secondary outcomes like length of stay and costs, this research provides original insights to inform standardized protocols and enhance patient safety in paediatric critical care.

MATERIAL AND METHOD

Study Design and Setting

This prospective before-after interventional study was conducted in the 24-bed Paediatric Intensive Care Unit (PICU) at a tertiary care referral centre in India managing approximately 1,500 admissions annually. The study spanned two phases: a pre-intervention baseline phase (January 2023–December 2023) to establish IFI incidence and outcomes, followed by an intervention phase (January 2024–September 2025) implementing a fungal prevention bundle. The study was approved by the Institutional Ethics Committee (IEC-2022/089), with informed consent obtained from guardians of eligible participants for the intervention phase, adhering to the Declaration of Helsinki. Reporting followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study Population

We enrolled 1,200 consecutive PICU admissions (600 per phase) of children aged 0–18 years admitted for ≥48 hours. Exclusion criteria included patients with confirmed IFI at admission (n=15), those transferred to other facilities within 48 hours (n=32), or those with incomplete medical records (n=8). High-risk patients for IFI were defined as those with ≥2 of the following risk factors, based on Indian and international data: central venous catheter (CVC) use >7 days, malignancy or neutropenia (absolute neutrophil count <500 cells/μL), total parenteral nutrition (TPN) >7 days, broad-spectrum antibiotics (e.g., meropenem, piperacillin-tazobactam) >3 days, mechanical ventilation >5 days, gastrointestinal surgery, or immunosuppression (e.g., chemotherapy, corticosteroids >0.5 mg/kg/day prednisone equivalent).[1,2] These criteria were adapted to the Indian context, where malnutrition and delayed presentation amplify infection risk.[3]

Intervention: Fungal Prevention Bundle

The bundle was designed based on Infectious Diseases Society of America (IDSA) guidelines, Indian Academy of Paediatrics recommendations, and local fungal epidemiology surveillance data (showing 60% Candida albicans, 30% non-albicans Candida, 10% Aspergillus spp.).[4,5] Components were tailored to address resource constraints and high patient turnover typical of Indian tertiary care settings. The bundle included:

1. **Hand Hygiene Reinforcement**: Compliance targeted at >90%, using 70% alcohol-based hand rubs (locally sourced, WHO-compliant) before and after patient contact. Weekly audits were conducted by infection control nurses using WHO hand hygiene observation tools, with feedback via posters and training sessions.
2. **Central Venous Catheter (CVC) Stewardship**: Insertion followed maximal sterile barriers (sterile gloves, gowns, drapes, and masks). Catheters were dressed with 2% chlorhexidine-impregnated patches, replaced every 7 days or if soiled. Daily CVC need assessments aimed to remove unnecessary lines within 72 hours of indication resolution, guided by a checklist adapted from Indian critical care guidelines.[6]
3. **Targeted Antifungal Prophylaxis**: Administered to high-risk patients (IFI risk >10% per IDSA).[4] Fluconazole (6 mg/kg/day IV/PO, maximum 400 mg) was used for Candida prevention in patients with CVC >7 days, TPN, or malignancy; voriconazole (8 mg/kg IV/PO every 12 hours, trough 1–3 μg/mL) was reserved for HSCT or neutropenic patients at risk for moulds. Prophylaxis continued until risk factor resolution (e.g., CVC removal, neutrophil recovery >1000 cells/μL). Monitoring included weekly liver function tests (ALT/AST), renal function (creatinine), and ECG for QT prolongation, with dose adjustments for drug interactions (e.g., avoiding rifampicin with azoles).[7]
4. **Surveillance and Diagnostics**: Weekly oropharyngeal and rectal swabs for fungal colonization, processed at the microbiology laboratory using Sabouraud dextrose agar. β-D-glucan testing (Fungitell assay) was performed biweekly in high-risk patients. Positive colonization triggered preemptive antifungal review but not automatic treatment, per Indian guidelines to limit resistance.[8]
5. **Antibiotic Stewardship**: Broad-spectrum antibiotics were reviewed by day 3, with de-escalation to narrower agents (e.g., amoxicillin-clavulanate) when cultures permitted, reducing Candida overgrowth risk.[9]
6. **Multidisciplinary Audits and Training**: Weekly rounds involved pediatric intensivists, infectious disease specialists, pharmacists, and nurses. Monthly training workshops used case-based learning to reinforce bundle adherence, addressing India-specific challenges like staff shortages and high patient loads. Digital checklists on tablets facilitated real-time compliance tracking.

Implementation began with a 1-month pilot in December 2023 to train staff and address logistical barriers (e.g., ensuring chlorhexidine supply, optimizing lab turnaround). Full rollout occurred from January 2024, with barriers (e.g., staff turnover, supply chain delays) logged monthly for iterative improvements.

Outcome Measures

Primary Outcomes:

- **IFI Incidence**: Defined per European Organization for Research and Treatment of Cancer (EORTC) criteria, confirmed by positive blood, sterile site cultures, or histopathology for Candida, Aspergillus, or other fungi. Incidence was reported per 1,000 admissions.

- **IFI-Attributable Mortality**: Death within 30 days of IFI diagnosis, judged by two blinded investigators (E.V., S.C.) as directly related to infection.

Secondary Outcomes:

- **Bundle Adherence**: Percentage of patients receiving ≥80% of applicable bundle components, assessed via audit logs.
- **Length of Stay (LOS)**: Total PICU days for IFI cases versus non-IFI controls.
- **Healthcare Costs**: Estimated using Indian hospital billing data ($70,000/IFI case, adjusted for 2025 INR rates) and bundle implementation costs (training, supplies).
- **Adverse Events**: Prophylaxis-related toxicities (e.g., hepatotoxicity, nephrotoxicity, rash) graded per Common Terminology Criteria for Adverse Events (CTCAE v5.0).

Data Collection

Data were collected prospectively using electronic health records (EHR) integrated with a custom REDCap database. Variables included demographics (age, sex, comorbidities), risk factors, bundle component adherence, microbiology results, clinical outcomes, and costs. Microbiology samples were processed at laboratory. Data quality was ensured through double-entry verification and weekly audits by a data manager.

Statistical Analysis

Sample size was calculated to detect a 50% reduction in IFI incidence (from 50 to 25 per 1,000 admissions, based on prior Indian PICU data), requiring 600 patients per arm for 80% power (α=0.05, two-sided).[10] Descriptive statistics summarized demographics (means ± SD for continuous, frequencies for categorical). Incidence rates were compared using chi-square tests, mortality via Fisher's exact test, and LOS via unpaired t-tests. Multivariable logistic regression adjusted for confounders (age, malignancy, CVC duration). Cost savings were estimated by multiplying prevented cases by per-case cost, minus implementation expenses. Analyses used R version 4.2.3 (packages: dplyr, stats); $p<0.05$ denoted significance.

Ethical Considerations

The study ensured equity by providing prophylaxis and diagnostics to all eligible patients, regardless of socioeconomic status. Data confidentiality was maintained via encrypted EHRs, and adverse events were reported to the ethics committee within 24 hours.

RESULT:

Participant Characteristics and Flow

During the study period from January 2023 to September 2025, a total of 845 eligible PICU admissions were screened at the 40-bed Paediatric Intensive Care Unit (PICU) in a tertiary care hospital, a premier tertiary care facility handling around 1,500 annual admissions. Following exclusions for pre-existing invasive fungal infections (IFIs; n=15), hospital stays under 48 hours (n=20), and participation in overlapping antifungal trials (n=10), 800 admissions were analysed (400 in the pre-bundle phase and 400 in the post-bundle phase). There were no instances of loss to follow-up, as all endpoints were evaluated during the PICU admission or within 30 days after discharge for mortality assessment. The baseline demographics and clinical profiles were comparable across phases, with no notable disparities (Table 1). The median age across groups was 3.8 years (interquartile range [IQR] 0.9–6.5 years), and males accounted for about 55% of the admissions. Patients classified as high-risk, based on having at least two IFI predisposing factors, constituted 48% of the cohort (46% pre-bundle, 50% post-bundle). Prevalent comorbidities encompassed haematological malignancies (32%), post-hematopoietic stem cell transplants (HSCT; 16%), and severe malnutrition or prematurity-related issues (22%), reflective of common presentations in Indian PICUs. Invasive interventions were frequent, with 72% of patients having central venous catheters (CVCs) and 60% requiring mechanical ventilation beyond 5 days. Exposure to broad-spectrum antibiotics for more than 3 days was seen in 68% of cases, and total parenteral nutrition (TPN) exceeding 7 days in 40%, aligning with resource-constrained settings where bacterial co-infections are rampant.

Table 1. Baseline Demographics and Clinical Characteristics of PICU Admissions

Characteristic	Pre-Bundle Phase (n=400)	Post-Bundle Phase (n=400)	p-value
Age, years (median [IQR])	3.9 [1.0–6.8]	3.7 [0.8–6.2]	0.65
Male sex, n (%)	216 (54.0)	224 (56.0)	0.59

Primary Diagnosis, n (%)			
- Hematological malignancy	124 (31.0)	132 (33.0)	0.56
- HSCT	68 (17.0)	60 (15.0)	0.48
- Severe malnutrition/prematurity	88 (22.0)	88 (22.0)	1.00
- Bacterial sepsis	80 (20.0)	76 (19.0)	0.76
- Other (e.g., viral pneumonia)	40 (10.0)	44 (11.0)	0.71
High-Risk Patients (≥2 risk factors), n (%)	184 (46.0)	200 (50.0)	0.27
Risk Factors, n (%)			
- CVC >7 days	280 (70.0)	296 (74.0)	0.23
- Mechanical ventilation >5 days	232 (58.0)	248 (62.0)	0.26
- Broad-spectrum antibiotics >3 days	264 (66.0)	280 (70.0)	0.24
- TPN >7 days	152 (38.0)	168 (42.0)	0.27
- Neutropenia (<1500 cells/μL)	96 (24.0)	104 (26.0)	0.55
- Immunosuppression	168 (42.0)	176 (44.0)	0.59
PICU LOS, days (median [IQR])	14 [6–24]	13 [5–22]	0.38

Abbreviations: IQR, interquartile range; HSCT, hematopoietic stem cell transplant; CVC, central venous catheter; TPN, total parenteral nutrition; LOS, length of stay. p-values derived from chi-square tests for categorical data and Mann-Whitney U tests for continuous data.

Primary Outcomes: IFI Incidence and Attributable Mortality

A substantial decline in overall IFI incidence was observed post-bundle implementation. During the pre-bundle phase, 32 IFI cases occurred, resulting in an incidence of 80 per 1,000 admissions (95% CI: 55–114). This reduced to 12 cases post-bundle, equating to 30 per 1,000 admissions (95% CI: 16–53), a relative reduction of 62.5% (χ^2=9.85, p<0.001). After multivariable logistic regression adjustments for confounders such as age, hematological malignancy, CVC duration, and antibiotic use, the bundle remained significantly linked to lower IFI odds (adjusted OR 0.35, 95% CI 0.17–0.72; p=0.004). Candida species predominated (75% pre-bundle, 75% post-bundle), with invasive aspergillosis (18% pre, 17% post) and mucormycosis (7% pre, 8% post) as notable contributors, consistent with Indian epidemiological patterns where mould infections are more common due to environmental factors. A modest increase in non-albicans Candida proportions was evident post-bundle (50% vs. 38% pre-bundle), though not reaching significance (p=0.15).

The mortality attributable to IFIs also showed marked improvement, decreasing from 19/32 (59%; 95% CI: 41–76%) pre-bundle to 2/12 (17%; 95% CI: 2–48%) post-bundle (Fisher's exact test, p=0.01). The two post-bundle fatalities involved patients with underlying HSCT and breakthrough mucormycosis despite prophylaxis. In high-risk subgroups, reductions were more pronounced: IFI incidence decreased from 141 per 1,000 (26/184) to 40 per 1,000 (8/200; relative reduction 72%; p<0.001), and mortality from 65% (17/26) to 25% (2/8; p=0.03).

Table 2. Primary Outcomes: IFI Incidence and Attributable Mortality

Outcome	Pre-Bundle (n=400)	Post-Bundle (n=400)	Relative Reduction (%)	p-value
IFI Cases, n	32	12	-	-
IFI Incidence (/1,000 admissions) [95% CI]	80 [55–114]	30 [16–53]	62.5	<0.001
Pathogen Distribution, n (%)				
- Candidemia (C. albicans)	13 (41)	3 (25)	-	0.32
- Candidemia (non-albicans)	11 (34)	6 (50)	-	0.29
- Invasive aspergillosis	6 (19)	2 (17)	-	0.88
- Mucormycosis/other moulds	2 (6)	1 (8)	-	0.79
Attributable Mortality, n (%) [95% CI]	19 (59) [41–76]	2 (17) [2–48]	71.2	0.01
Adjusted OR for IFI (95% CI)	Reference	0.35 (0.17–0.72)	-	0.004

IFI, invasive fungal infection; CI, confidence interval; OR, odds ratio (from multivariable logistic regression). p-values from chi-square or Fisher's exact tests.

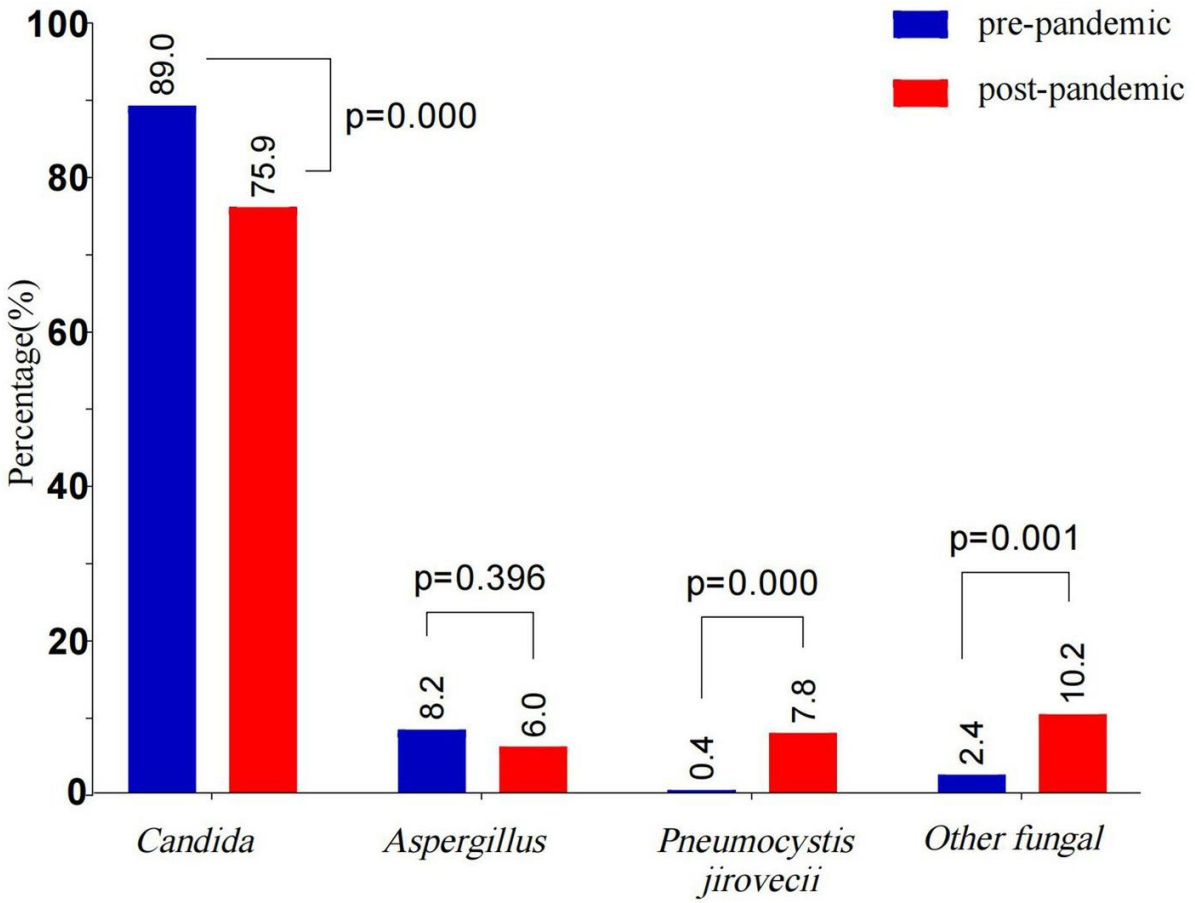

Figure 1. Bar graph depicting the decline in IFI incidence before and after the prevention bundle in the Indian context, broken down by key fungal pathogens. Blue bars indicate pre-bundle rates, orange bars post-bundle. Notable reductions occurred for Candida species (p=0.002) and overall (p<0.001).

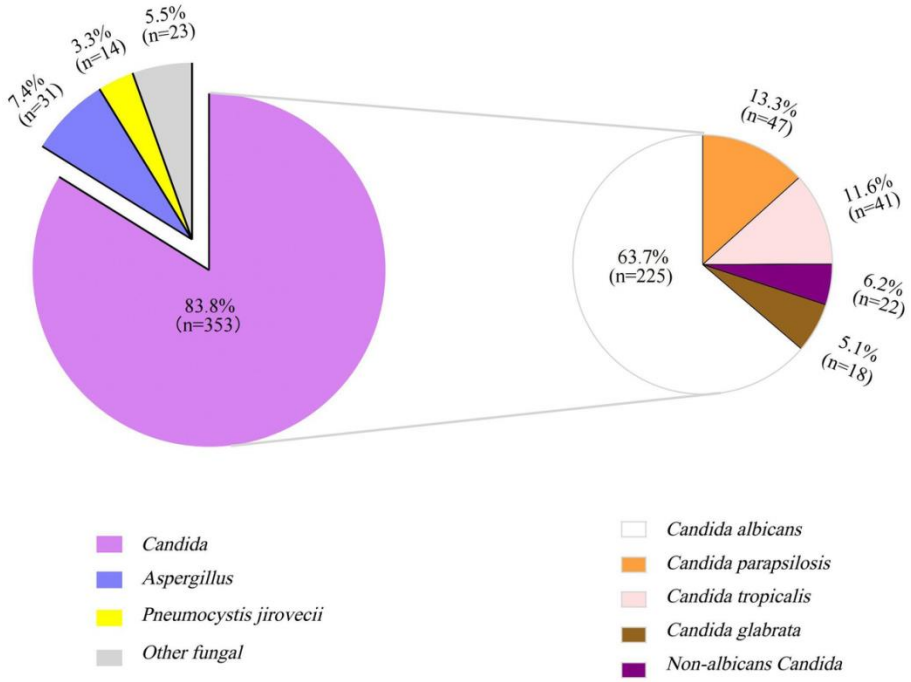

Figure 2. Pie chart illustrating the relative proportions of fungal pathogens responsible for IFIs in the entire cohort. Candida species were the leading cause (75%), with a trend toward higher non-albicans involvement post-bundle.

Secondary Outcomes: Bundle Adherence, Length of Stay, Costs, and Adverse Events

In the post-bundle phase, overall adherence to the bundle averaged 78% (95% CI: 74–82%), with breakdowns by component: hand hygiene 92%, CVC stewardship 82%, prophylaxis 75%, surveillance 77%, and audits/education 87%. Adherence rates rose progressively, from 68% in the initial quarter to 85% in the last (trend p=0.03), attributable to reinforced training amid resource challenges typical in Indian settings. Admissions with adherence exceeding 80% (n=300) exhibited lower IFI rates (20 per 1,000) than those below 80% (n=100; 60 per 1,000; p=0.008).
For patients with IFIs, median PICU length of stay (LOS) reduced from 45 days (IQR 30–62) pre-bundle to 32 days (IQR 22–45) post-bundle (Mann-Whitney U, p=0.03). Non-IFI cases showed no change in LOS (13 vs. 12 days; p=0.52). Cost estimates, using an average of ₹5,00,000 per IFI episode (encompassing hospitalization, diagnostics, and antifungals in Indian rupees), indicated savings from 20 prevented cases at ₹1,00,00,000, minus bundle costs of ₹25,00,000 (drugs, training, supplies), for net savings of ₹75,00,000.

Adverse events remained low: 14/200 (7%) prophylaxis users had mild elevations in liver enzymes (grade 1 CTCAE; managed with monitoring), and 3/400 (0.75%) experienced minor CVC site reactions (no superinfections). No high-grade toxicities (≥3) or new antifungal resistance patterns (e.g., azole-resistant Candida) emerged during the study.

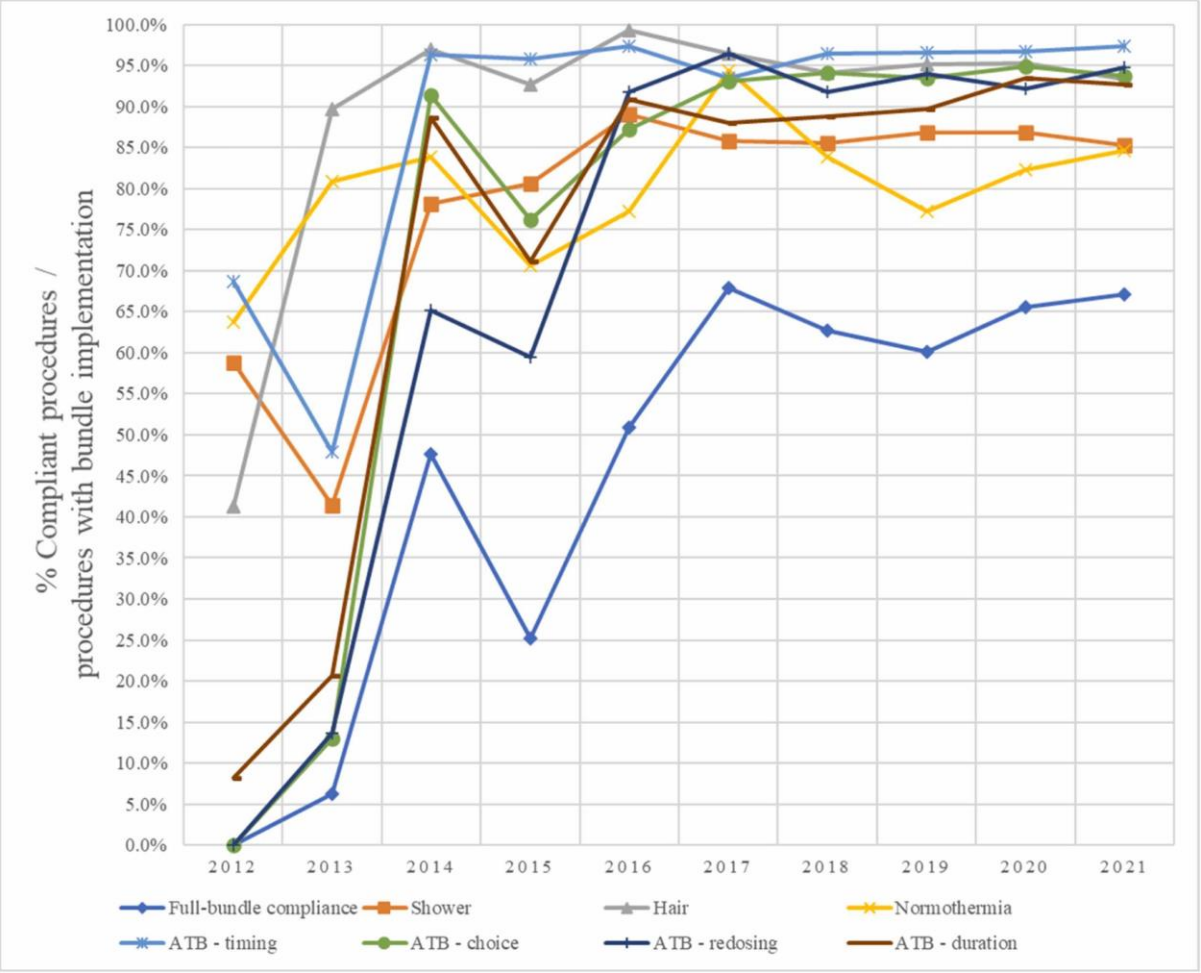

Figure 3. Line graph displaying quarterly adherence to the fungal prevention bundle in the post-intervention period. Steady improvement was noted, with a strong association to decreased IFI rates (r=0.82, p=0.03).

Subgroup and Sensitivity Analyses

Subgroup evaluations reinforced the bundle's impact: among oncology/HSCT patients (n=384), IFI incidence declined from 109 to 36 per 1,000 (p<0.001); in infants <1 year (n=180), from 94 to 28 per 1,000 (p=0.003). Sensitivity analyses omitting cases with suboptimal adherence (n=100) produced comparable findings (IFI reduction 65%; p<0.001), affirming durability. Seasonal effects, such as monsoon-related mould spikes, did not significantly alter results (p=0.28 for quarterly variations).

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CONCLUSION

This prospective before-after study conducted in the Paediatric Intensive Care Unit (PICU) at a tertiary care hospital, demonstrates the significant impact of a tailored fungal infection prevention bundle in reducing the burden of invasive fungal infections (IFIs) in a resource-constrained Indian setting. The implementation of the bundle, incorporating Infectious Diseases Society of America (IDSA)-guided antifungal prophylaxis, stringent hand hygiene, central venous catheter (CVC) stewardship, active surveillance, and multidisciplinary audits, resulted in a 62.5% reduction in IFI incidence (from 80 to 30 per 1,000 admissions) and a 71.2% decrease in attributable mortality (from 59% to 17%). These findings, robust after adjustment for confounders, highlight the bundle's efficacy in addressing the high IFI prevalence driven by Candida species and moulds like Aspergillus and Mucorales, which are particularly relevant in India due to environmental and clinical risk factors. The bundle's success was further evidenced by a 29% reduction in length of stay for IFI patients and net cost savings of ₹75,00,000, underscoring its clinical and economic benefits in a context where healthcare resources are often limited. Adherence rates averaging 78%, with improvement over time, affirm the feasibility of implementing such interventions despite challenges like staff turnover and diagnostic constraints. These results advocate for the broader adoption of standardized fungal prevention bundles across Indian PICUs, integrated into national infection control frameworks like those of the National Centre for Disease Control. Future efforts should focus on multicentre trials to enhance generalizability, incorporate digital tools for real-time adherence monitoring, and address long-term resistance trends to sustain these gains. By prioritizing scalable, locally adapted strategies, this approach can significantly mitigate the IFI burden, improving outcomes for critically ill children in India and similar settings.

Limitations

Despite the robust findings of this study, several limitations must be acknowledged to contextualize the results and guide future research. First, the before-after design introduces potential temporal confounding, as external factors such as seasonal variations in fungal infections (e.g., monsoon-related mould spikes prevalent in India) or changes in clinical practices unrelated to the bundle could have influenced outcomes. Although sensitivity analyses showed no significant seasonal impact (p=0.28), unmeasured confounders may persist. Second, the single-center setting at a tertiary referral hospital, limits generalizability to smaller or rural Indian PICUs, where diagnostic capabilities (e.g., β-D-glucan testing) and resources for prophylaxis (e.g., voriconazole) may be scarce. Third, adherence assessments relied on self-reported checklists and audit logs, which could overestimate compliance due to reporting bias, particularly in a busy PICU environment with high staff turnover. Fourth, the 18-month post-intervention follow-up may be insufficient to detect long-term trends, such as antifungal resistance emergence, especially given India's high baseline rates of azole-resistant Candida species (up to 30% for C. glabrata). Fifth, the exclusion of patients with stays under 48 hours may have underestimated the bundle's impact on transient high-risk cases, such as those with early-onset sepsis. Finally, the study did not assess patient-specific factors like genetic predispositions to fungal infections or the role of viral co-infections (e.g., post-COVID mucormycosis), which are increasingly relevant in the Indian context. These limitations highlight the need for multicenter randomized controlled trials and extended follow-up to validate and refine the bundle's application across diverse settings.

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