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ORIGINAL RESEARCH

Impact of a Multifaceted Prevention Strategy on Invasive Fungal Infections in a Surgical Pediatric Cardiac ICU

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Background: Invasive fungal infections were rare but serious complication in pediatric patients following cardiac surgery. Data on the epidemiology, clinical characteristics, and preventive strategies remain limited.

Methods: This was a retrospective before–after study. We reviewed a prospectively maintained database in our pediatric cardiac ICU between 2018 and 2024. All patients who developed invasive fungal infections following cardiac surgery were included. Since our center began the invasive fungal infections prevention bundle in 2021, patients from 2018 to 2020 were included in pre-bundle group, patients from 2021 to 2024 were included in post-bundle group. Our fungal prevention bundle included: 1) Actively providing prophylactic antifungal drugs based on risk stratification. 2) Enhancing hospital acquired infection management. 3) Multi-disciplinary treatment, clinical pharmacists participate in antimicrobial stewardship. 4) Establishing an ICU infection control team to ensure the implementation of the above measures.

Results: In this cohort of 19,761 postoperative pediatric patients, 38 cases (0.19%) of invasive fungal infections were identified, all manifesting as fungal sepsis. Clinical manifestations of infection included fever, an increased leukocyte count, neutrophil percentage, (1,3)-β-D-glucan, C-reactive protein and procalcitonin value. Fourteen patients (37%) exhibited circulatory instability. The median time from surgery to infection was 23 (8, 56) days, with a mortality rate of 24%. Comparative analysis between study periods revealed improvements in infection control measures. Hand hygiene compliance increased from 48% to 61% ($P < 0.001$), antibiotic consumption (defined daily dose) reduced from 32.7 to 27.5 ($P < 0.001$). Following group stratification, the incidence of invasive fungal infections was lower in post-bundle group (0.11%; 12/11,194) than in pre-bundle group (0.3%; 26/8567), $P = 0.002$.

Conclusion: Based on the study findings, the implementation of a multifaceted fungal prevention bundle was associated with a significant reduction in the incidence of invasive fungal infections in pediatric patients after cardiac surgery.

Plain Language Summary: This study found that implementing a bundle of prevention measures significantly reduced the risk of serious invasive fungal infections in children after heart surgery. The strategy included giving antifungal drugs to high-risk children, improving hand hygiene and catheter care, having pharmacists optimize antibiotic use, and creating a dedicated infection control team. As a result, the invasive fungal infections rate dropped from 0.3% to 0.11%, while hand hygiene compliance improved and antibiotic use decreased. This approach provides an effective strategy for protecting children after cardiac surgery.

Keywords: invasive fungal infections, pediatric patients, cardiac surgery, prevention strategies

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Introduction

Invasive fungal infections (IFIs) represent a serious concern in critically ill pediatric patients. Due to advances in perioperative care, the incidence of IFIs remains relatively low, reported between 0.2% and 0.35%.[1] Nevertheless, these infections are linked with considerable mortality, ranging from 10% to 30%.[2]

In pediatric patients undergoing cardiac surgery, numerous factors contribute to an increased risk of postoperative infections, which can compromise the outcomes of congenital heart disease treatment. In the United States, *Candida* species rank as the second most common cause of central line associated bloodstream infections in hospitalized patients, second only to coagulase negative *staphylococci*.[3] Furthermore, Abou and colleagues demonstrated that the mortality rate among patients who develop IFIs postoperatively ranges from 39% to as high as 100%.[4]

Therefore, the early identification of pediatric patients at the highest risk for IFIs is crucial for implementing timely antifungal management. In a single-center, case–control study involving 28 pediatric patients with candidemia and 47 controls, Garcia-San Miguel L et al identified a high Therapeutic Intervention Scoring System score one week after PICU admission and prolonged antibiotic therapy (exceeding 5 days) as significant risk factors. Their findings suggest that shorter antibiotic courses, routine *Candida* surveillance cultures, and preemptive antifungal treatment may improve clinical management.[5] In addition, de Araujo Motta F et al conducted a single-center, case–control study with 30 candidemia patients and 75 matched controls. They demonstrated that a RACHS-1 score ≥3, thrombocytopenia, and acid suppression therapy are independent risk factors for invasive candidiasis in PICU patients with congenital heart defects.[6]

Gardner AH and colleagues evaluated the efficacy of prophylactic fluconazole in reducing the incidence of IFIs. Their study of 261 pediatric patients receiving extracorporeal membrane oxygenation for cardiac indications demonstrated that routine fluconazole prophylaxis was associated with a significant reduction in IFIs.[7] Corroborating this multifaceted approach, Suleyman G and Alangaden GJ highlighted in a review that invasive candidiasis is commonly linked to invasive lines, immunosuppression, and contaminated environments. They concluded that effective control and prevention of IFIs require a comprehensive strategy, which integrates standard infection control measures with targeted antifungal prophylaxis for high-risk patients.[8]

However, the opportunistic nature of IFIs[9] makes management particularly difficult in these immunocompromised pediatric patients following cardiac surgery.[10] Despite the recognized need for comprehensive infection control, there is currently a lack of studies explicitly evaluating the implementation and effectiveness of multifaceted prevention bundles within the specific environment of pediatric cardiac ICUs. To address this gap, this study primarily aims to assess the effectiveness of a four component IFIs prevention and control bundle introduced at our center. Secondarily, it seeks to analyze the epidemiology and clinical features of IFIs in this patient cohort.

Methods

Study Design

We conducted a retrospective analysis using a prospectively maintained database, encompassing all hospital acquired infections in pediatric patients following cardiac surgery at our single center between 2018 and 2024. Our hospital is a tertiary teaching hospital specializing in cardiovascular diseases and serves as national cardiac center of China. All patients receive postoperative care in the ICU, which has 46 beds. The variation in staff numbers correlates with patient volume, with little difference across shifts or over time. The minimum nursing staff never falls below 120, with each nurse responsible for a maximum of two patients. Similarly, the number of physicians remains at least 20, each caring for up to nine patients.

All patients who developed IFIs after surgery were included. IFIs were defined as infections involving the bloodstream, deep tissues, or internal organs, with confirmation based on culture results.[11] As our center implemented an IFI prevention bundle in 2021, patients from 2018 to 2020 were assigned to the pre-bundle group, and those from 2021 to 2024 constituted the post-bundle group for comparative analysis.

We performed blood cultures for patients with fever of unknown origin. Blood was drawn via peripheral venous puncture, with one sample taken each day for two consecutive days.[12]

For patients with fungal sepsis, we monitor for signs of systemic embolism and immune manifestations while performing echocardiography to rule out concurrent infective endocarditis. We also assess for sternal instability, evaluate the nature of mediastinal drainage fluid (if present), and observe for signs of mediastinal swelling. If relevant symptoms are present, we proactively conduct CT scans to investigate possible mediastinitis.

IFIs Bundle Components

1) Proactive administration of prophylactic antifungal drugs (fluconazole 6 mg/kg/day following the 12 mg/kg/day loading dose or caspofungin 50 mg/m^2/day following the 70 mg/m^2/day loading dose) based on risk stratification in patients with any of the following conditions: delayed sternotomy closure, extracorporeal membrane oxygenation support, continuous renal replacement therapy, congenital immunodeficiency syndromes, immunosuppressive therapy, granulocytopenia, long-term corticosteroid use, long-term acid suppressant use, long-term broad spectrum antibiotic use, fungal colonization, or a (1,3)-β-D-glucan result >80pg/mL. Our risk stratification criteria were assigned equal weight. Specifically, prophylactic antifungal therapy was initiated if a patient met any single one of the predefined criteria.

In the pre-bundle group, prophylactic antifungal therapy was administered only in cases of fungal colonization or a (1,3)-β-D-glucan level >80 pg/mL.

2) Enhancing hospital-acquired infection management: Based on adherence to hand hygiene guidelines, environmental health monitoring and surveillance, and the establishment of a comprehensive healthcare associated infection surveillance system, the following additional measures are implemented: chlorhexidine for skin disinfection, ultrasound guided central venous catheter insertion, use of maximal sterile barriers during central venous catheter insertion, daily assessment of catheter necessity and early removal.

3) Multidisciplinary care: clinical pharmacists drive antimicrobial stewardship by stopping surgical prophylaxis within 48 hours, de-escalating empiric therapy according to culture/susceptibility data, eliminating redundant or unnecessary combination regimens, and optimizing treatment duration.

4) Establishing an ICU infection control team to ensure the implementation of the above measures.

Data Collection

Relevant baseline data collected from the medical records included age, gender, weight, primary immune deficiency syndromes, the STAT score,[13] postoperative central venous catheter use, body temperature, hemodynamic status, blood routine, (1,3)-β-D-glucan, c-reactive protein, procalcitonin, PICU stay length, postoperative length of stay, broad spectrum antibiotics use, total parenteral nutrition use, need for continuous renal replacement therapy, delayed sternal closure, extracorporeal membrane oxygenation support, and mortality.

For IFIs, the pathogen species, infection site, and time from surgery to infection onset were recorded. Hand hygiene compliance and antibiotic consumption (defined daily dose) are derived from medical quality control data of our hospital.

Catheter-related bloodstream infection sepsis was defined per Infectious Disease Society of America guidelines.[14]

Crude mortality rate (death rate within 30 days from IFIs) and attributable mortality rate (death within 7 days after candidemia onset and/or with persistent clinical sepsis, or due to IFIs associated complications) were evaluated.[15]

The consistency in the diagnosis of IFIs was ensured by: 1) Adherence to standardized procedures for blood culture collection; 2) Diagnosis and data collection supervised by a specialized ICU infection control team.

Statistical Analysis

Statistical analysis was performed using the SPSS software (version 26.0; IBM Corporation, USA) and R4.5.1 software for Windows. The Kolmogorov–Smirnov test was used to assess the conformity of the continuous variables to the normal distribution. Normal distribution was expressed as the mean plus or minus the standard deviation, whereas a non-normal distribution was expressed as the median accompanied by the interquartile range. Categorical variables are displayed in a numerical form, accompanied by their respective percentages. The Wilcoxon rank-sum test was used for non-normally distributed variables. Categorical variables were analyzed using the chi-squared test, correction for continuity, or Fisher's exact test. We analyzed the effect of the intervention on the antibiotic consumption (defined daily dose) by segmented regression analysis using a Poisson model (before–after intervention). All statistical tests were two tailed and a P value <0.05

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was considered statistically significant. We performed the Durbin–Watson test to assess autocorrelation in antibiotic consumption. A post-hoc power analysis was performed using G*Power software (version 3.1) to evaluate the adequacy of the sample size for the primary outcome (the incidence of IFIs).

Results

The Epidemiology and Clinical Characteristics of IFIs

Among 19,761 pediatric patients who underwent cardiac surgery during 2018–2024, 38 (0.19%) developed IFIs, including *Candida* ×35 (*Candida parapsilosis* ×16, *Candida albicans* ×15, *Candida glabrata* ×1, *Candida portofelicei* ×1, *Candida tropicalis* ×1, *Candida inconspicua* ×1) and *Trichosporon asahii* ×3, all of which were cases of fungal sepsis. Since all 38 cases mentioned in the study presented as "fungal sepsis" and had clear microbiological identification results, according to the EORTC/MSGERC criteria, these cases confirmed by blood culture should be classified as "Proven" invasive fungal disease. All 38 cases in this study were diagnosed with fungal sepsis and did not have concurrent deep-seated infections (eg, endocarditis, mediastinitis).

The pre-bundle group enrolled 8567 pediatric patients, and the post-bundle group enrolled 11,194. There were no statistically significant differences ($p > 0.05$) between the two groups in key demographic characteristics and surgical variables, including age, weight, gender, immune deficiency syndrome, STAT score, postoperative PICU stay, post-operative length of stay, delayed sternal closure, extracorporeal membrane oxygenation support, continuous renal replacement therapy and death. Furthermore, all variables showed a standardized mean difference below 0.2, indicating a high degree of balance between the pre-bundle and post-bundle groups. The details were shown in Table 1.

The median age of these 38 IFIs patients was 16 (5, 71) months, with a median weight of 9.2 (6.1, 17.6) kg. Two patients underwent heart transplantation, 13 underwent palliative surgery for congenital heart disease, and 23 underwent corrective repair, with a median STAT score of 3 (2, 4). The median time from surgery to infection onset was 23 (8, 56) days. At the time of infection, 37 patients were on broad spectrum antibiotics, 29 were receiving total parenteral nutrition infusion, and all had central venous catheters in place, among which 9 were associated with catheter-related bloodstream infections.

Clinical manifestations of IFIs included fever (38.0±0.6°C), a median leukocyte count of 11.4 (9.0–15.7)×10^9/L, a median neutrophil percentage of 78 (69–85)%, a median (1,3)-β-D-glucan value of 103.08 (75.24–108.77) pg/mL, a median C-reactive protein value of 43.5 (37.8–79.9) mg/L, and a median procalcitonin value of 1.39 (0.74–3.23) ng/mL. Fourteen patients exhibited varying degrees of circulatory instability. The median PICU stay was 50 (26–104) days, and the median postoperative length of stay was 75 (44–114) days. Crude mortality rate was 24% (9/38) and attributable mortality rate was 13% (5/38).

Table 1 The Key Demographic Characteristics and Surgical Variables Between the Two Groups

	Pre-Bundle Group (n=8567)	Post-Bundle Group (n=11,194)	*P* value	Standardized Mean Difference
Age (month)	28 (10, 51)	24 (7, 58)	0.337	0.140
Weight (kg)	12.3 (8, 17)	11.4 (7.5, 18)	0.548	0.177
Male (n, %)	4238 (49.5)	5799 (51.8)	0.117	0.046
Immune deficiency syndrome (n, %)	33 (0.4)	51 (0.5)	0.74	0.011
STAT score	2 (2, 3)	2 (2, 3)	0.138	0.062
Postoperative PICU stay (days)	2 (1, 4)	2 (1, 4)	0.91	0.025
Postoperative length of stay (days)	11 (8, 16)	11 (8, 16)	0.253	0.001
Delayed sternotomy closure (n, %)	40 (0.5)	53 (0.5)	0.966	<0.001
Extracorporeal membrane oxygenation support (n, %)	17 (0.2)	24 (0.2)	0.931	0.004
Continuous renal replacement therapy (n, %)	72 (0.8)	99 (0.9)	0.776	0.005
Death (n, %)	47 (0.5)	48 (0.4)	0.521	0.017

Process Variables and Outcome Variables After the Implementation of IFIs Bundles

After implementation of the IFIs bundles, Hand hygiene compliance increased from 48% (435/915) to 61% (735/1210), $P < 0.001$. The quarterly hand hygiene compliance results were shown in Figure 1. Concurrently, antibiotic consumption (defined daily dose) reduced from 32.7 to 27.5 (IRR: 0.842; 95% CI: 0.815–0.970; $P < 0.001$), which were shown in Figure 2. We performed the Durbin–Watson test to assess autocorrelation in antibiotic consumption. The resulting Durbin–Watson value was 2.005, indicating the presence of autocorrelation in these variables. Regarding seasonality, we incorporated a seasonal variable (defining the first and fourth quarters as winter) as a covariate into the Poisson regression model. The analysis yielded a P -value > 0.999 for the seasonal factor, indicating no significant seasonal variation in antibiotic consumption within the study cohort.

In the post-bundle period (2021–2024, n = 11,194), a total of 1016 pediatric patients (9.1%) received antifungal prophylaxis based on the predefined risk stratification criteria. No severe adverse events related to antifungal prophylaxis (fluconazole or caspofungin). No patients discontinued prophylaxis due to drug-related adverse events.

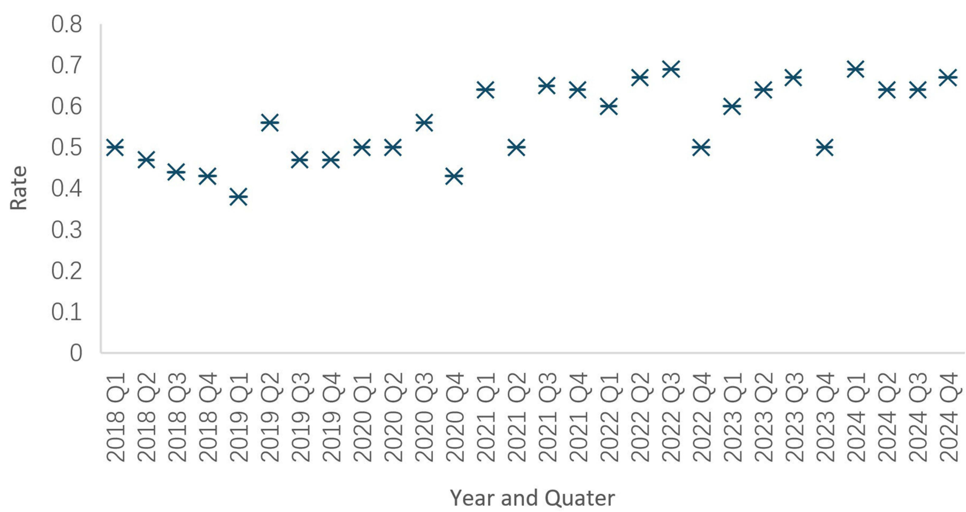

Figure 1 Hand hygiene compliance during the study period. Hand hygiene compliance was calculated as the number of observed hand hygiene actions divided by the total number of opportunities. Data are presented at quarterly intervals from 2018 to 2024.

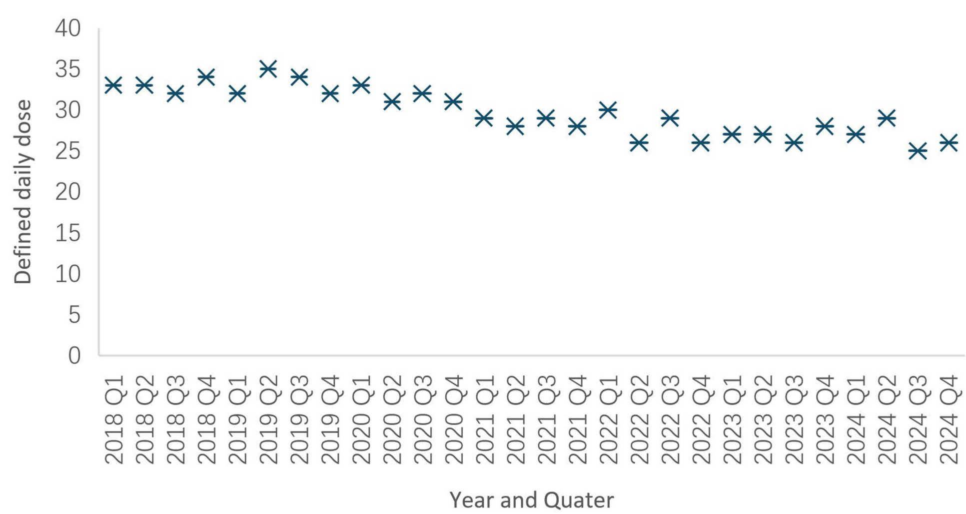

Figure 2 Antibiotic consumption was quantified as the defined daily dose per 100 patient-days. Total doses were calculated by dividing the total grams of each antimicrobial agent by its corresponding WHO-assigned value, then normalized to the total length of stay during the study period. Data are presented at quarterly intervals from 2018 to 2024.

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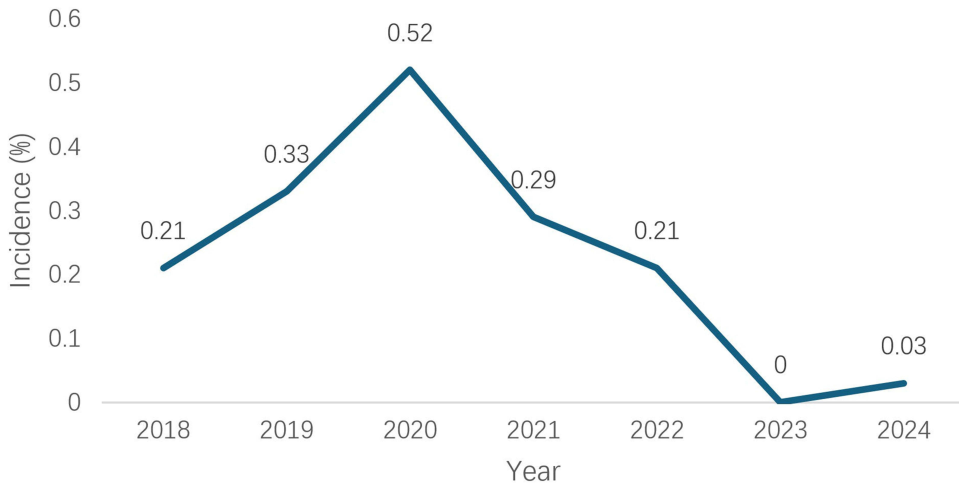

Figure 3 Incidence of invasive fungal infections during the study period. The infection rate was calculated as the number of patients with invasive fungal infections divided by the total number of patients in the same period. Data are presented at yearly intervals from 2018 to 2024.

The incidence of IFIs was lower in post-bundle group (0.11%; 12/11,194) than in pre-bundle group (0.3%; 26/8567), $P = 0.002$. All the 9 catheter-related bloodstream infections occurred in pre-bundle group (35% vs 0, $P = 0.036$). The yearly incidence of IFIs was shown in Figure 3.

A post-hoc power analysis, based on the observed incidence of IFIs and sample sizes, yielded 88.2% power for the primary outcome at a two-sided alpha of 0.05. For the catheter-related infection subgroup, power was 78.5%. This confirms that our study had adequate statistical power to detect the significant clinical improvements observed.

Discussion

This study primarily aimed to evaluate the effectiveness of a multifaceted prevention bundle in reducing the incidence of IFIs within a surgical pediatric cardiac ICU. Our research team previously analyzed 4,776 pediatric patients who underwent cardiac surgery between 2021 and 2022. Among these cases, 10 patients developed IFIs, with a mortality rate of 20%. Additionally, the median postoperative duration of mechanical ventilation was 1,336 hours, and the median length of hospital stay was 112 days. These findings indicate a poor prognosis in patients with postoperative IFIs.[16] Although preliminary research exists, strategies for preventing IFIs after pediatric cardiac surgery remain inadequate. To our knowledge, this is the first study to evaluate the impact of a comprehensive prevention program on IFIs in a pediatric cardiac surgical ICU.

The salient findings of the current study demonstrate that the implementation of a multifaceted bundle was associated with a significant reduction in the incidence of IFIs (from 0.3% to 0.11%, $P = 0.002$) and the complete elimination of catheter-related fungal bloodstream infections (35% vs 0, $P = 0.036$). Concurrently, we observed systemic improvements in key infection control metrics, including enhanced hand hygiene compliance and a significant reduction in antibiotic consumption. These observed improvements collectively signify a holistic advancement in the quality of care and infection control practices within our unit. Furthermore, the comparative analysis revealed no statistically significant differences in demographic or surgical parameters between the pre-bundle and post-bundle groups, suggesting that the reduction in IFIs occurred under comparable risk profiles.

The interpretation of these data is highly relevant to both clinical care and infection control practice. A key component of our strategy was the establishment of a dedicated ICU infection control team. This clinical team, comprising frontline physicians and nurses, was crucial for implementing prevention measures at the bedside. Our experience suggests that the collaboration between this internal ICU team and the central Infection Control Department is essential for sustaining these achievements. This observation, that local clinical leadership combined with external accountability and structured feedback facilitates the long-term maintenance of quality improvement initiatives, aligns

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with current implementation science.[17] While the internal team enhances expertise and immediate execution, the external oversight provides the necessary "pressure" and objective auditing required to achieve optimal outcomes.[18]

In our clinical practice, the dedicated ICU infection control team conducts daily bedside rounds to ensure the rigorous implementation of all bundle components, including hand hygiene. Furthermore, the hospital's central Infection Control Department performs unannounced monthly on-site verifications and data audits. The results of these audits are reported during the hospital's monthly administrative management meetings. Regarding antimicrobial stewardship, clinical pharmacists participate in daily rounds to audit antibiotic data in real-time through the eclectic system, which is also reported at the monthly management meetings. All audit findings are formally documented and archived on the hospital's internal network, where they are accessible to all healthcare staff for transparency and continuous quality improvement. Since these management strategies were implemented as a standard operating procedure for the entire ICU population rather than being restricted to specific high-risk subgroups, the improvements in hand hygiene compliance and antibiotic consumption represent a systemic advancement over time. It is the consistent implementation of an infection prevention and control bundle that determines its optimal efficacy.[19]

This study also represents one of the larger investigations into the epidemiology and clinical characteristics of IFIs following pediatric cardiac surgery. Our findings indicate that IFIs typically present with fever, mildly elevated leukocyte count and procalcitonin, alongside more prominent increases in neutrophil percentage, (1,3)-beta-D-glucan, and C-reactive protein. Although the incidence of IFIs in this population is low (0.19%), its prognosis is poor, often leading to delayed postoperative recovery and a mortality rate of 24%. Mycologically, non-*Candida albicans* species, predominantly *Candida parapsilosis*, were the most common pathogens (16/38, 42%). These findings may facilitate earlier recognition and prompt the initiation of empirical antifungal treatment in clinical practice.

Study Limitations

Due to the potential for a Hawthorne effect, we cannot confirm that hand hygiene compliance remained consistent during unobserved periods. To mitigate this limitation in future studies, a multifaceted approach is recommended. This could include conducting unit culture of safety surveys, reinforcing ongoing training and feedback, evaluating compliance indirectly through the analysis of consumables usage data, and implementing automated electronic hand hygiene monitoring systems.[20] Furthermore, as highlighted by Joseph et al, the development of validated, context-specific monitoring tools and the integration of patient-reported experience measures can further enhance patient safety and quality of care in complex clinical environments.[21]

This study was conducted at a single center. Our patient population may possess distinct clinical characteristics, including a potentially higher proportion of complex congenital heart disease cases compared to other centers. Consequently, the generalizability of our findings is uncertain, and the effectiveness of this preventive program in different settings remains unclear. Furthermore, the specific resources available at our institution, such as a high staff-to-patient ratio and a dedicated infection control team, may not be representative of other hospitals. Therefore, replicating this intervention in resource limited settings may prove challenging. Future multicenter studies are warranted to validate and extend our findings. Nevertheless, there are still valuable lessons to be learned from infection prevention and control experiences in resource-limited settings. In environments where specialized staffing and advanced diagnostics are constrained, a "pragmatic adaptation" strategy is recommended. For instance, risk stratification can be simplified by relying on clinical indicators (eg, STAT score and duration of mechanical support) rather than expensive biomarkers. Furthermore, the "Link Nurse" model, where frontline staff are empowered as infection control champions, can effectively substitute for dedicated IPC teams, a strategy supported by the World Health Organization for improving compliance in resource-limited settings.[22]

This study employed an uncontrolled before and after design. The absence of randomization and a concurrent control group preclude definitive causal conclusions, as the influence of unmeasured confounding factors cannot be ruled out. While the implementation of the multifaceted bundle was the primary intervention, we cannot entirely rule out the influence of secular trends. Over the seven-year study period, incremental improvements in general ICU supportive care, increasing clinical experience of the medical staff, and evolving institutional infection control practices may have also contributed to the observed reduction in IFIs incidence. This limitation constrains the internal validity of our findings. Future research utilizing designs that provide a higher level of evidence, such as randomized controlled trials, is needed to confirm these results.

Conclusion

Based on the findings of this study, the implementation of a multifaceted fungal prevention bundle was associated with a significant reduction in the incidence of IFIs among pediatric patients following cardiac surgery. This strategy was correlated with a decrease in IFI incidence and concurrently observed improvements in key infection control metrics, including hand hygiene compliance and antibiotic stewardship. While these results are encouraging, the retrospective nature of the study suggests that these improvements are associations rather than definitive causal effects. Future efforts should focus on adapting and validating such bundled interventions across diverse healthcare environments to enhance generalizability.

Artificial Intelligence Assistance Statement

The authors declare that no generative AI technologies were used in the generation of the manuscript text, data analysis, or creation of figures. All content was solely prepared by the authors.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author, Xu Wang, upon reasonable request.

Ethical Statement

This study was approved by the Ethics Committee of Fuwai Hospital (ID: 2025-2883). Given the retrospective nature of the study, the requirement for written informed consent from patients to review their medical records was waived by the Ethics Committee. All patient clinical and laboratory data were fully anonymized with all personally identifiable information removed prior to data analysis and interpretation. Patient data were strictly maintained with confidentiality throughout the entire study process, and all relevant data were used exclusively for the purposes of this research only. The study was conducted in accordance with the ethical principles of the 2024 Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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