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REVIEW

Antifungal Stewardship in the Pediatric Intensive Care Unit: Time is of the Essence

Elisavet Chorafa, Elias Iosifidis, Christina Tzika, Anastasia-Izampella Papathanasiou, Emmanuel Roilides

Infectious Diseases Unit, 3rd Department of Pediatrics, Aristotle University and Hippokration General Hospital, Thessaloniki, 54642, Greece

Correspondence: Emmanuel Roilides, 3rd Department of Pediatrics, Hippokration General Hospital, Konstantinoupoleos 49, Thessaloniki, 54642, Greece, Tel +2310 892444; +6937442644, Email roilides@auth.gr

Abstract: Invasive fungal infections (IFIs) represent a significant cause of morbidity and mortality in critically ill children admitted to pediatric intensive care units (PICUs). Despite the variation of the incidence of candidemia and invasive candidiasis (IC) and *Candida* species distribution between different PICU settings, increasing rates of non-*albicans Candida* species and emerging antifungal resistant strains are observed. Antifungals are prescribed in PICUs mainly for empiric treatment, with limited use of diagnostic-driven strategies despite availability of fungal biomarkers in many settings. Data on antifungal prophylaxis in PICU outside traditional high-risk populations are scarce with no official guidance on administration of prophylaxis and to which patients. Diagnostic challenges, heterogeneity and complexity of PICU patients, and the absence of specific guidelines on prophylaxis contribute to increased and/or inappropriate antifungal use. Although antifungals are frequently used in PICU, antifungal stewardship (AFS) activities reported particularly in this population remain limited. Shift from empiric to pre-emptive treatment, systematic use of therapeutic drug monitoring, new diagnostic tests and fungal biomarkers and limiting the group of patients outside the high-risk groups on prophylaxis are the key targets for AFS in critically ill children. Only nine AFS interventions including PICU patients were found in the English literature; seven were part of hospital-wide stewardship programs and only three were targeted to antifungals. Audit with feedback was mainly used as a strategy, while various designs and outcomes were observed. Antifungal stewardship programs are essential to optimize antifungal use in PICUs; however, standardized frameworks tailored to these settings should be developed. This review describes the epidemiology of IFIs in PICUs, current antifungal prescribing practices, and summarizes AFS interventions implemented in PICUs up to now in order to propose recommendations for future antifungal stewardship initiatives in these patients.
Keywords: pediatrics, amphotericin B, azoles, echinocandins, prescriptions, antifungal stewardship program

Introduction

Invasive fungal infections (IFIs) are a significant concern for critically ill children hospitalized in pediatric intensive care units (PICUs).[1] The main host-related risk factors for developing IFIs include immunosuppressive therapy, hematopoietic stem cell transplantation (HSCT), solid organ and tissue transplantation (SOT), as well as primary or secondary immunodeficiencies. PICU patients represent a heterogeneous population that, in addition to severe underlying conditions, are exposed to multiple ICU-related factors increasing the risk for IFIs, including prolonged hospitalization, the presence of invasive devices, administration of broad-spectrum antibiotics and parenteral nutrition, mechanical ventilation, and frequently performed invasive procedures.[2–5]

IFIs are associated with substantial morbidity and mortality in critically ill children, particularly when the initiation of targeted antifungal therapy is delayed.[1,6,7] In the PICU setting, timely diagnosis of IFIs remains challenging due to non-specific clinical manifestations and the limited sensitivity of currently available diagnostic tools. In addition, the lack of well-defined guidelines on antifungal prophylaxis in PICU patients further complicates clinical decision-making and contributes to an increased and/or inappropriate prescription of antifungal agents.[8–10] Moreover, current evidence suggests that early administration of appropriate antifungal therapy with the proper duration of the right drug at the

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right dose is crucial for achieving favorable clinical outcomes. Therefore, the development and implementation of antifungal stewardship programs as a coordinated approach to optimizing the antifungal use are necessary to improve patients' outcomes, reduce toxicity, limit antifungal resistance, and manage excessive healthcare cost.[11,12] In this context, a discussion focused on the prudent, timely, and appropriate use of antifungal therapy in critically ill children admitted to the PICU is warranted.

The current article is a narrative review that aims to discuss the antifungal prescribing patterns in PICU patients, to summarize antifungal stewardship programs implemented in PICUs to date and highlight key considerations for future antifungal stewardship activities in critically ill children. We searched PUBMED using the following keywords: "antifungal stewardship AND pediatric intensive care unit", "antifungal stewardship AND children", "antifungal prescribing AND pediatric intensive care unit", "antifungal prescribing AND children", "antifungal use AND pediatric intensive care unit", "antifungal use AND children" until September 2025.

Epidemiology of IFIs in PICU Patients

Candida spp. are the predominant causes of IFIs in critically ill children admitted to PICUs accounting for approximately 9–15% of bloodstream infections (BSIs).[3] In contrast, invasive mold diseases caused predominantly to *Aspergillus* or *Mucorales* remain rare, in this setting and affect mainly patients with hematologic malignancies or those who have undergone transplantation.[1,13] According to a review by the Centers for Disease Control and Prevention (CDC) on pediatric hospital-acquired infections (HAIs) reported to the National Healthcare Safety Network between 2018 and 2021, *Candida* spp. were the fifth most frequent cause of central line-associated bloodstream infections (CLABSI) in PICUs, accounting for 9.8% of cases in US hospitals.[14] Similarly, the European Centre for Disease Prevention and Control (ECDC) point prevalence survey (PPS) conducted in 2011–2012 reported a prevalence of 6% of HAIs due to *Candida* spp. in hospitalized neonates and children.[15] In European PICUs, the incidence rate for invasive candidiasis (IC) varies between 3.5 to 7 per 1000 admissions;[16] whereas, in US PICUs, it is estimated at approximately 3.5 per 1000 admissions.[2] In a recently published 12-week lasting weekly PPS of antifungal use in European PICUs (CALYPSO study), 19 out of 101 recorded antifungal courses were prescribed for *Candida* infections.[17]

Incidence of IC and the distribution of *Candida* species vary considerably between countries and among individual PICUs, reflecting differences in case mix (ie, PICUs caring for HSCT patients, or cardiothoracic patients), antifungal prophylaxis policies, and local clinical practices[16,18] Although *Candida albicans* remains the leading species causing IFIs in PICU patients, there is an increasing proportion of invasive infections caused by non-*albicans Candida* species.[1,13,18] In a multinational prospective study of pediatric and neonatal invasive candidiasis conducted by the International Pediatric Fungal Network (IPFN), Steinbach et al found that while *C. albicans* was the most common cause of candidemia, non-*albicans Candida* spp. accounted for 56% of cases among pediatric patients.[19] Similarly, in a multicenter retrospective European study (EUROCANDY study), *C. albicans* remained the most frequently isolated species in PICUs; however, it accounted for only 50.5% of invasive candidiasis cases.[6] Non-*albicans Candida* species were responsible for nearly half of all infections, with *C. parapsilosis* being the predominant non-albicans species and accounting for 31% of cases, a finding which is consistent with the epidemiology reported in other single-center PICU studies.[4,7] An even higher percentage of non-*albicans Candida* species (60%) was observed among European PICU patients in the more recent CALYPSO study, further underscoring the evolving epidemiology of invasive candidiasis in this pediatric population.[17]

Although invasive aspergillosis (IA) occurs less frequently in pediatric patients admitted to PICUs compared with invasive candidiasis, it remains a life-threatening infection in selected high-risk populations. Children with acute myelogenous leukemia (AML), high-risk acute lymphoblastic leukemia (ALL), relapsed leukemia, aplastic anemia and children undergone HSCT are at high risk for developing IA.[1] In children with hematologic malignancies or post-transplant immunosuppression, the combination of profound immune dysfunction, prolonged neutropenia, corticosteroid exposure, and critical illness substantially increases vulnerability to invasive mold infections such as IA; nevertheless, data specifically describing the epidemiology and outcomes of IA in PICU populations remain scarce, as most available studies include these patients within broader hematology–oncology or transplant cohorts.[1,13,20]

Both IC and IA are associated with increased burden of disease such as prolonged length of stay in the PICU and in hospital, increased morbidity and excess mortality.[2,13,21,22] In a US hospital study, PICU patients with candidemia had significantly longer PICU and hospital stays, as well as a higher 30-day mortality rate (44% vs 14%) compared with patients without candidemia.[22] Similarly, mortality rates ranging from 16.7% to 18.2% have been reported in single-centre or multicentre national studies for IC,[4,21,23] whereas a higher mortality rate of 27.8% was observed among PICU patients in the European EUROCANDY study.[6] Overall, these findings emphasize the significant burden of IFIs in critically ill children and reflect the substantial variability in reported mortality among different healthcare settings and study populations.

In recent years, almost all European countries have reported isolated cases or outbreaks of candidemia caused by *Candidozyma auris* (previously named as *Candida auris*) in healthcare settings mainly in adult wards and adult ICU's, while the number of countries where *C. auris* has become endemic continues to increase.[24] In pediatric populations, premature neonates and children hospitalized in neonatal and pediatric ICU's are mainly affected by the emergence of *C. auris* as documented in several observational studies and case series.[25–28] In the global NeoObs study of neonatal sepsis, conducted mainly in low- and middle-income countries, *C. auris* was identified as the third most common pathogen among neonates with invasive candidiasis.[26] Similarly, in a multicentre Indian study of children with ICU-acquired candidemia including neonates, *C. auris* accounted for 4.5% of candidemia episodes,[25] and was associated with a high mortality rate of 33%. Furthermore, in a systematic review of IFIs caused by *C. auris* in neonates and children, Ashkenazi-Hoffnung et al, reported that bloodstream infection was the most common clinical presentation, approximately one third of cases occurred in NICU patients, and overall mortality approached 40%[27]. Although reports of *C. auris* infections in PICU patients remain scarce, its rapid patient-to-patient transmission, diagnostic challenges with currently available laboratory methods, and distinctive antifungal resistance profile represent major therapeutic and infection control challenges in pediatric ICUs.

Along with the increasing incidence of IC caused by non-*albicans Candida* species, a shift in antifungal susceptibility patterns has been observed, as several of these species may exhibit intrinsic or acquired resistance to commonly used antifungal agents. Inappropriate antifungal use, increase in use of antifungal prophylaxis and additional environmental and healthcare-related factors further contribute to the emergence and spread of antifungal-resistant fungi.[29] Although there are limited data specifically reporting antifungal susceptibility patterns of *Candida* species in PICU patients, multicentre surveillance studies in adult populations provide important insights. These data report low resistance rates to fluconazole among *C. albicans* isolates, in contrast to increasing resistance among *Nakaseomyces glabratus* (formerly named as *Candida glabrata*) and *C. parapsilosis* isolates, with resistance rates of 12% and 17% in European centers in 2018 and 5% and 7.5% in US centers between 2017 and 2021, respectively.[29] A single PICU study from Egypt reported high fluconazole resistance among *N. glabratus* isolates 29%, lower resistance among *C. parapsilosis* 9% and a notable fluconazole resistance rate of 11% among *C. albicans*. In contrast, other pediatric studies not limited to PICU settings have reported fluconazole resistance rates up to 5% for *C. albicans*.[7,30] Over the last years, *C. auris* with its almost universal resistance to fluconazole and relatively high resistance to amphotericin B is emerging and spreading at first to adult and subsequently to pediatric settings as well, and has contributed to the growing burden of antifungal resistance.[27,29,30]

Antifungal Prescribing in PICU Patients

Antifungal prescribing patterns in PICU patients have been described in a limited number of studies,[4,17,23,31–34] most of which primarily focus on the types of antifungals agents used for empiric therapy. According to current guidelines for critically ill pediatric patients, both liposomal amphotericin B (LAMB) and echinocandins are recommended for empiric treatment in suspected candidiasis of moderate to high severity. In contrast, fluconazole should be reserved for mild infections, in patients without risk factors for resistant isolates and without prior azole exposure.[8,9]

In the recently published CALYPSO study, which investigated antifungal prescribing practices in 18 European PICUs, fluconazole was the most frequently prescribed antifungal overall (42%).[17] This finding is consistent with results

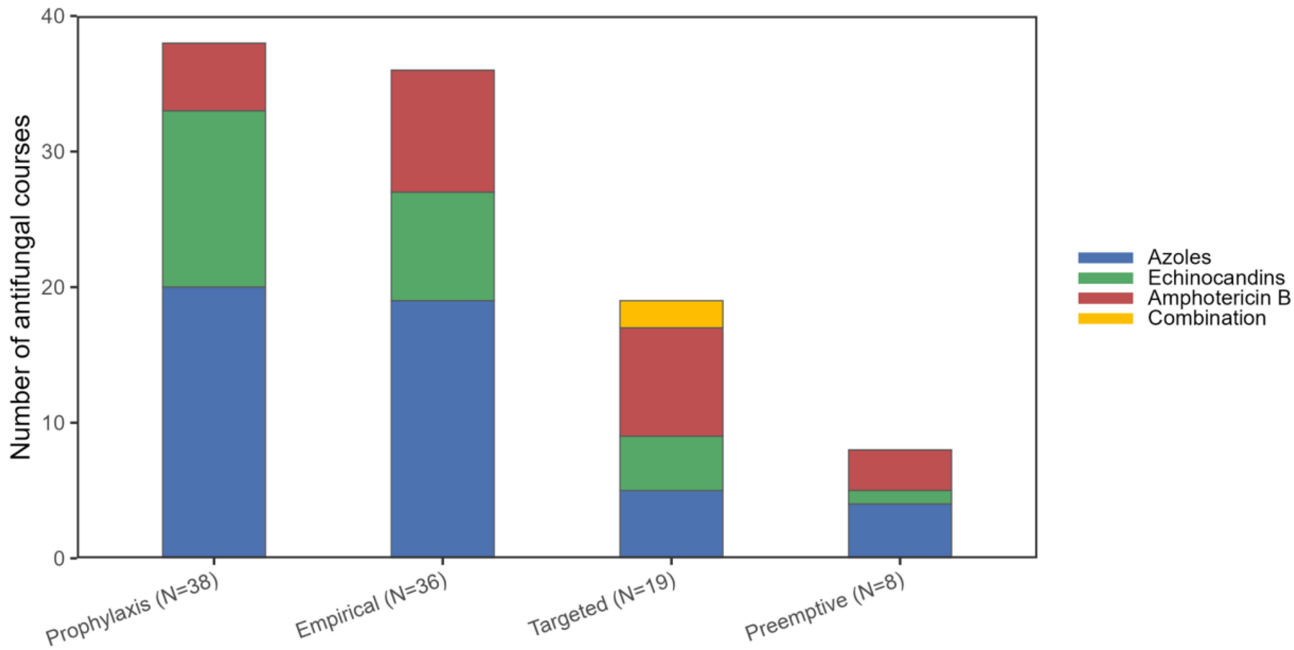

Figure 1 Antifungal prescriptions (N=101) by indication in European PICUs (modified from CALYPSO study[17]), Azoles: Fluconazole, Posaconazole, Voriconazole, Isavuconazole, Echinocandins: Anidulafungin, Micafungin, Caspofungin, Amphotericin (B) Amphotericin B lipid complex, Liposomal Amphotericin B, Combination: combinations of 2 antifungals.

from studies conducted in pediatric hospitals in Türkiye and in the US.[33,35] Conversely, LAMB was reported as the main antifungal agent used for treatment in a multicenter study from the UK and in a single-center study from Spain that also included PICU patients. When antifungal prescribing was analyzed according to treatment indication, amphotericin B accounted for the largest proportion of courses prescribed for targeted treatment (37%) of *Candida* infections within the CALYPSO network (Figure 1). This is in contrast with other national studies of pediatric candidemia in PICU settings, where fluconazole accounted for approximately 60% of prescriptions.[4,36] Among prescriptions for empirical and preemptive treatment, azoles (53%) was the most commonly used agent followed by LAMP (25%); whereas for prophylaxis, azoles was used in 53% prescriptions and echinocandins in 34% (Figure 1).

The majority of antifungal prescriptions in European PICUs were administered for treatment purposes, mostly for empiric indications (36%) whereas only a small proportion (8%) were prescribed for preemptive or diagnostic-driven indications (Figure 1).[17] These prescribing patterns may reflect the diagnostic challenges associated with IFIs combined with the clinical complexity of PICU patients, which increase the tendency of physicians to initiate antifungal therapy even with low suspicion for fungal infection.

The implementation of newer diagnostic tools and fungal biomarkers, when appropriately interpreted, may facilitate the prompt diagnosis of IFIs and support a shift toward pre-emptive or diagnostic driven antifungal strategies, ultimately enabling more targeted treatment.[35,37] In the multinational BIOPIC study performed by the IPFN to evaluate fungal biomarkers in hospitalized pediatric patients with suspected IC, the T2Candida assay (T2Biosystems, Inc., Wilmington, MA, USA) demonstrated high sensitivity (79.2%) and specificity (97.1%), supporting its potential use either alone or in combination with other biomarkers, such as Platelia Candida Ag Plus (BIORAD, Hercules, CA, USA) for IC.[37] Although most European PICUs reported having access to some of those diagnostics modalities in the CALYPSO study, their routine use in clinical practice remains limited.[17]

Data on the use of antifungal prophylaxis in critically ill pediatric patients outside the well-recognized high-risk groups of oncology and transplant recipients remain very limited. There is only one non-randomized pediatric study with historical controls exploring the benefit of antifungal prophylaxis in PICU patients.[3,38] In this single-center study, oral amphotericin B was administered as prophylaxis to mechanically ventilated critically ill children hospitalized in the PICU for more than seven days. Although this strategy was associated with a lower incidence of *Candida* bloodstream infections compared with historical controls, the retrospective design, and lack of randomization substantially limit the generalizability of these findings. Consequently, the most recent European Confederation for Medical Mycology (ECMM)/International Society of Human and Animal Mycology (ISHAM)/American Society for Microbiology (ASM) 2025 guidelines for candidiasis, do not provide specific recommendations regarding the administration of antifungal prophylaxis or the identification of PICU subgroups that may benefit from this strategy.[9,10,39] A risk stratified approach guided by individual risk factors and local epidemiology should be used for prophylaxis in non-oncology and non-transplant patients. Also, a shift from prophylaxis practices to preemptive treatment with the help of new diagnostic biomarkers is needed. Prolonged administration of broad-spectrum antibiotics, presence of central venous catheters, parenteral nutrition, colonization with Candida spp and abdominal surgery are factors associated with high risk both in adult and pediatric studies. In clinical practice, PICU patients with multiple of these risk factors hospitalized in hospitals with high *Candida* incidence could be benefit from prophylaxis or preemptive antifungal therapy if new diagnostic tools and fungal biomarkers are available.

A Cochrane systematic review (2016) including both adult and pediatric critically ill populations found moderate-quality evidence that untargeted antifungal treatment is not associated with a significant reduction in all-cause mortality compared with no antifungal treatment or placebo.[40] Although untargeted antifungal therapy was associated with a reduction in invasive fungal infections, the quality of evidence supporting this finding was low, with high heterogeneity among studies and a high risk of publication bias. However, real-world practices suggest high use of antifungal prophylaxis in PICU settings. In detail, Chorafa et al in the European multicentre CALYPSO study reported that 40% of PICU patients received antifungal prophylaxis, a rate higher than previously described, with 63% of these patients belonging to oncology and transplant populations[17,33] In addition, among European PICUs, approximately half of the participating reported local antifungal prophylactic policies extending beyond immunocompromised patients to include patients undergoing abdominal surgery, those with long-term central venous lines or those receiving prolonged parenteral nutrition, despite the absence of international or national guideline recommendations for these patient groups. Overall, the decision to administer antifungal prophylaxis in the PICU setting should be individualized, carefully balancing patient-specific risk factors, diagnostic challenges, local epidemiology and the potential risks with unnecessary antifungal exposure.[18,41]

Time is of the Essence

Timely management is crucial in the treatment of IFIs in critically ill pediatric patients hospitalized in PICUs. Delayed initiation of antifungal therapy in cases of suspected or confirmed IFIs has been consistently associated with increased mortality, a finding well documented for both invasive *Candida* and mold infections.[3,16,42] Conversely, inappropriate early antifungal therapy, probably due either to resistance of the causative agent or inadequate drug exposure resulting from suboptimal dosing, may similarly be associated with poor outcomes and increased mortality. At the same time, unnecessary or inappropriate antifungal drug prescribing in the absence of microbiological or diagnostic evidence, as well as irrationally prolonged duration of empiric or targeted therapy may contribute to the emergence of antifungal resistance, expose patients to avoidable drug-related toxicity and increase healthcare costs. Therefore, achieving a timely yet judicious balance between prompt initiation and rational use of antifungal agents is essential for the optimal management of the critically ill young patients.

Antifungal Stewardship Programs in PICU

The implementation of antifungal stewardship programs (AFS) represents a well-established strategy to optimize antifungal use. AFS programs aim to ensure that antifungal agents are prescribed only when clinically indicated, while promoting the appropriate selection of antifungal agent, dosing regimen, route, timing of initiation and duration of therapy.[11,12] Despite the frequent use of antifungal agents in critically ill children, antifungal stewardship in the ICU setting remains an area that has received limited attention, particularly in neonatal and pediatric populations. In a multicentre survey conducted in US hospitals on AFS practices and perceptions among physicians and pharmacists related to hospital antibiotic stewardship program (ASP), almost half of responders acknowledged inappropriate

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antifungal use at their institution despite the implementation of prospective audit and feedback strategies in 63% of hospitals.[43]

Kourti et al highlighted key challenges and emerging opportunities in antifungal stewardship among immunocompromised children and neonatal intensive care patients emphasizing the optimal use of available diagnostic tools to facilitate a shift from empiric to pre-emptive antifungal therapy as well as the need for broader implementation of therapeutic drug monitoring (TDM)[44] These antifungal stewardship elements are equally relevant for PICU patients and represent readily actionable targets for AFS implementation. Moreover, the lack of evidence-based guidelines for antifungal prophylaxis and the absence of standardized step-down and de-escalation strategies represent important knowledge gaps and priorities for future research in the PICU setting.

Critically ill children differ substantially from other hospitalized patients of similar age or from adults, particularly with regard to disease complexity and severity as well as pharmacokinetic and pharmacodynamic characteristics. Considering the non-specific clinical signs and symptoms of IFIs and the challenges of early diagnosis, administration of empiric antifungal therapy is a common clinical practice. One of the main targets of AFS in PICUs should be to facilitate a shift from empiric to pre-emptive or targeted antifungal treatment. The broader implementation of novel diagnostic tests for IFIs and fungal biomarkers has the potential to increase the use of preemptive and targeted strategies and reduce unnecessary or prolonged empiric treatment. In this context, close collaboration between intensivists and microbiology teams, regarding the use of cultures and other diagnostic tests may enable early notification, prompt de-escalation of therapy and minimization of drug-related toxicity and antifungal resistance.

Another key target for AFS in PICUs is the use of antifungal prophylaxis in patients outside well-recognized high-risk groups, such as oncology or transplant recipients, patients undergoing abdominal surgery, or those with neutropenia or immunosuppression. Given the lack of formal guideline recommendations and the absence of clear evidence demonstrating a reduction of IFIs in these populations, a careful assessment of individual patient risk factors is warranted. In addition, surveillance of local IFIs incidence and antifungal drug resistance patterns by the AFS team may help guide both the prompt initiation and timely discontinuation of antifungal prophylaxis. Education in combination with other stewardship strategies is an essential part of every stewardship program, particularly in AFS. Persistent knowledge gaps in antifungal prescribing, including indications for prophylaxis and empiric therapy, first-line treatment of IA and IC, and appropriate duration of therapy, have been reported in multiple studies.[43,45]

The foundational core recommendations for antifungal stewardship were initially defined for adult populations by the Mycoses Study Group Education and Research Consortium (MSGERC), providing a structured framework encompassing leadership and accountability, multidisciplinary collaboration, diagnostic stewardship, optimization of antifungal selection and dosing, therapeutic drug monitoring, and audit with feedback.[11] These principles were subsequently adapted to pediatric populations by Evangelidis et al, who tailored antifungal stewardship core elements to the specific epidemiological, pharmacokinetic, and organizational characteristics of children[46] Within this pediatric framework, stewardship is conceptualized not as a restrictive intervention, but as a clinical support system enabling timely, appropriate, and patient-centered antifungal decision-making. Application of these pediatric-adapted core elements to the PICU setting is supported by data from PICU-focused studies, including the CALYPSO network and other reports (Table 1), which highlight both the feasibility of implementation and the persistent gaps in systematic antifungal stewardship across European PICUs.

Although key principles for effective organization and implementation of stewardship programs (either antifungal or antibiotic) have been clearly defined both by MSGERC and IDSA accordingly, there are many barriers in their application in everyday clinical practice.[55] Difficulties in patients' data systems, lack of sufficient time allocated to stewardship are the main barriers reported in the systematic review of Rzewuska et al[56] Identification of specific barriers and facilitators in each institution in order to apply the appropriate behavioral change strategies is a key part of an AFS' success and sustainability.

Table 1 Summarized Studies Describing Antifungal Stewardship Programs That Involved Patients Admitted to PICUs

First Author, Year, Ref	Study Type	Country-City-Institution	Intervention Period	Study Population	Intervention	Study Findings
Wassef, 2020,[47]	Single-center Prospective study	Egypt, Pediatric Hospital of Cairo University, PICU	Pre-intervention April-September 2016 Intervention: October-December 2016 Post-intervention: January-June 2017	PICU patients	Education, facility-specific treatment policy based on national guidelines and local antimicrobial susceptibilities, establish PICU specific antibiogram, pre-authorization for targeted antibiotics (Amphotericin B and Fluconazole included)	Decrease in Amphotericin B and Fluconazole use (DOTs)
Velasco- Arnaiz, 2020,[48]	Single-center, prospective study	Spain, Barcelona, Hospital Sant Joan de Deu	Pre Intervention (2015–2016) Intervention period (2017–2018)	Pediatric patients including PICU patients	Post-prescription feedback Electronic clinical chart informing prescribers whether prescription is "optimal" or "non-optimal". For "non-optimal" prescriptions, recommendations to discontinue or to modify were provided by the ASP in face-to-face or by phone	Total antifungal use remained stable A slight increase of optimal prescriptions
Mendoza-Palomar, 2021,[31]	Prospective, observational, single-center study	Spain, Barcelona, Hospital, Universitari Vall d'Hebron	July to October 2018	Pediatric patients including PICU patients	Evaluation of prescriptions by an AFS team as: "necessary" (clinical situation required the use of an AF) "appropriate" (drug active against the causative microorganism), and "adequate" (correct dose, duration and route while in concordance with local or international protocols)	Of 219 prescription evaluations, 195 (89%) were considered optimal. Reasons for non-optimal prescriptions were lack of indication and disagreement with protocols In PICU, 58.3% non-optimal prescriptions
Scardina, 2021,[49]	Retrospective, single-center study	Lurie Children's Hospital of Chicago, USA	2013–2018	Pediatric patients including PICU patients	TDM of AF agents in patients who received combination AF therapy	TDM resulted in timely discontinuation of combination AF therapy 74% (26/35 of combination therapy courses were discontinued after therapeutic antifungal concentrations were achieved

(*Continued*)

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Table 1 (Continued).

First Author, Year, Ref	Study Type	Country-City-Institution	Intervention Period	Study Population	Intervention	Study Findings
Goff, 2022,[50]	Prospective observational cohort study	Australia, Perth, Perth Children's Hospital	2014–2018	Pediatric patients including PICU patients	Evaluation of AMS including AFS, Investigation of AF therapy appropriateness and compliance with prescribing guidelines	37% reduction in AF expenditures
Villaverde, 2023,[51]	Prospective, single-center, longitudinal study	Spain, Madrid, Hospital Universitario 12 de Octubre	Period 1: 2014–2015 Period 2: 2016–2017	Pediatric patients including PICU patients	PID review and consultation on targeted antimicrobial and antifungal prescriptions	Decrease in both the DOT among AF prescribed and total costs after the initiation of the stewardship program
Bio, 2023,[52]	Retrospective cohort study	Lucile Packard Children's Hospital, Stanford, USA	2020–2022	Pediatric patients including PICU patients	Prospective audit and feedback by the ASP team	Recommendations for the 25% of AF prescriptions in PICU performed with an acceptance rate of 26% by the treating physicians
Fan, 2024*,[53]	Single center, retrospective study	China, Beijing, Beijing Children's Hospital	Control period: 2016–2018 Intervention period: 2018–2020	Pediatric patients with severe pneumonia	Education on the rational use of antimicrobials and audit of prescriptions	A significant decrease in AF agents' prescriptions by 27.4%
Soni, 2024,[54]	Single-center, retrospective study	South-West England, Bristol, teaching hospital	1 January to 31 December 2022	Adults and pediatric pts including PICU	Audit of prescriptions by the AFS team including TDM	Decrease of antifungal consumption by 25.1% and expenditure by 59.9%

Note: *The ASP program was mainly focused on antimicrobials.
Abbreviations: PICU, Pediatric Intensive Care Units; ASP, Antibiotic Stewardship Program; AFS, Antifungal Stewardship; TDM, Therapeutic Drug Monitoring; AF, antifungal; PID, Pediatric Infectious Disease; DOT, Days of Therapy.

Summary of Antifungal Stewardship Interventions in PICU Patients

Antifungal stewardship programs are usually part of hospitals' antibiotic stewardship programs that serve both adult and pediatric populations; and are only rarely tailored to the specific needs of critically ill pediatric patients. Among the 18 European PICUs participating in the CALYPO study, only 7 PICUs (39%) reported having an AFS in place. However, there are few studies reporting AFS interventions in PICU settings or having outcomes measured separately for PICU patients. In a recent systematic scoping review of antimicrobial stewardship programs in PICUs including 18 studies, only two reported outcomes were related to antifungal use.[57]

Table 1 summarizes published AFS programs involving pediatric patients admitted to PICUs. Among the nine studies identified, seven described hospital-wide AFS programs that also included patients admitted to PICUs as well,[31,48–52,54] whereas one study focused exclusively on the PICU setting,[47] and another included only PICU patients with severe pneumonia.[53] Three programs were exclusively dedicated to antifungal stewardship,[31,49,54] while the remaining studies reported antibacterial and antifungal stewardship interventions.[47,48,50–53] One additional study describing an AFS intervention based on educational bundles in a university hospital was not included in Table 1 as outcomes were not reported separately for pediatric patients or for PICU patients.[58]

The majority of AFS programs (7/9) implemented prospective audit with feedback as their primary intervention in combination with facility-specific clinical practice guidelines in some cases;[31,48,51,53,54] mirroring strategies frequently used in antimicrobial stewardship programs across PICUs.[57,59] Less frequently reported interventions included pre-authorization (one study) and the use of TDM as a primary stewardship tool (two studies).[47,49,54]

Conclusion

Antifungal stewardship programs represent an essential framework to optimize antifungal use in PICUs along with enhanced diagnostic strategies for IFIs and infection control practices. Key priorities integrated in AFS in PICU patients include reducing unnecessary empiric treatment while facilitating preemptive and targeted therapy, integrating TDM, rationalizing antifungal prophylaxis based on local epidemiology and patient-specific risk factors, and strengthening education on antifungal prescribing. Future research should focus on the development of standardized AFS protocols specifically tailored to pediatric critical care settings and the evaluation of their impact through robust, multicenter studies.

Disclosure

The authors report no conflicts of interest in this work.

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