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Hospitalist Impact in Antibiotic Selection in Pediatric Community Acquired *Staphylococcus aureus* Skin Infection

Janie Robles[1*], **Denise I Pinal**[2] **and Charles F Seifert**[1]

[1]*Department of Pharmacy Practice, Texas Tech University Health Sciences Center School of Pharmacy, USA*

[2]*Department of Pharmacy, Cook Children's Medical Center, USA*

[*]**Corresponding author:** Janie Robles, Department of Pharmacy Practice, Texas Tech University Health Sciences Center School of Pharmacy, 3601 4th Street MS 8162, Lubbock, TX 79430, USA, Tel: 8067437643; Fax: 8067434209; E-mail: janie.robles@ttuhsc.edu

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Abstract

Background: Pediatric hospitalist systems continue to increase due to the adoption of these programs within pediatric centers. Pediatric hospitalists provide patient care to hospitalized children for a wide range of conditions with an associated decrease in hospitalization cost and in length of stay. In this study, we aimed to assess empiric antibiotic selection of community acquired *Staphylococcus aureus* (*S. aureus*) skin and soft tissue infections in pediatric patients and the impact on prescribing patterns following the introduction of the pediatric hospitalist service to our institution.

Methods: We conducted a five-year retrospective chart review study from January 2001 to December 2006. One hundred children with positive *S. aureus* cultures, aged 1-18 years were enrolled in the study. Patients who were discharged with the International Classification of Disease, Ninth Revision, Clinical Modification codes for *S. aureus* skin and soft tissue infections were included. Trends in antibiotic selection, infection outcomes, and percent oxacillin resistance *S. aureus* (ORSA)/oxacillin sensitive *S. aureus* (OSSA) were recorded.

Results: One hundred children (5%) of the 1860 patients evaluated, predominately-Hispanic patients, met inclusion criteria. Seventy-seven ORSA and 23 OSSA cultures were identified. Study participants included 55 males and 45 females. Sixty-eight percent of ORSA patients with *S. aureus* strains were susceptible to initial empiric therapy (p=0.0018) vs. 100% of patients with *S. aureus* strains in the OSSA group. No differences were identified in length of stay in the patients that received appropriate treatment vs those that did not (p=0.5511). Among patients with ORSA infections, incidence increased significantly from 2001 to 2006 while susceptible empiric antibiotic regimens reached a low in 2003 and were over 90% in 2006 following the initiation of the hospitalist service.

Conclusion: Pediatric hospitalists improve quality of patient care. In this study, participants had an increase in susceptible empiric antibiotic regimens following the implementation of the pediatric hospitalist service to our facility.

Keywords: *Staphylococcus aureus*; Skin infection; Pediatric; Hospitalist

Abbreviations:

ORSA: Oxacillin Resistance *S. aureus*; OSSA: Oxacillin Sensitive *S. aureus*

Introduction

Pediatric hospitalist systems continue to be introduced into pediatric centers in order to provide care for patients with a wide range of conditions [1,2]. In 1996, Watcher and Goldman introduced the hospitalist concept and recognized the hospitalist role as coordinators to improve inpatient quality of care [3,4]. More recently, hospitalists or generalized inpatient physicians manage the clinical problems of acutely ill patients within healthcare institutions.

Inpatient hospital care has involved traditional models of care until the introduction of hospitalists. Patients with primary care physicians that do not provide inpatient services are one area that has benefited from the hospitalist's model. The incorporation of the hospitalist has allowed for the co-managing of patient care between the hospitalist and the primary care physician. Hospitalists onsite availability allows for the care of patients during acute medical situations and their familiarity with inpatient conditions optimize clinical practices.

Hospitalist literature suggests the impact of the generalized inpatient physician affects several areas within hospital systems. Research indicates the hospitalist model reduced length of stay by 16.6% and costs by 13.4% within health systems [4]. Currently, the impact of pediatric hospitalists within institutions is limited in the medical literature. Existing literature suggests that pediatric hospitalist systems decrease hospital costs, decrease length of stay, and improve quality and efficiency of inpatient care [2,5-9].

In 2006, Landrigan et al. performed an evaluation of the literature to determine the impact of pediatric hospitalists [2]. This report evaluated twenty studies with pediatric hospitalists systems for length of stay (LOS), costs, and quality of care. Researchers found the average decrease in cost (4-16%) and decrease in length of stay (6-15%) was 10%. No data was identified that indicated an increase in costs or LOS with hospitalists. Following their quality of care review, they found inconclusive outcomes on the care delivered. Mussman et al. evaluated pediatric hospitalists systems versus traditional models of care in their effect on quality of patient care and cost [5]. These researchers reviewed 11 studies and found that hospitalists may improve quality and efficiency of inpatient pediatric care. This study also found decreases in the length of stay was seen more often with the hospitalists care in asthma, hematology, and gastroenterology patients, but a few studies found no difference. In spite of the availability of pediatric hospitalist literature, there are limitations in the available data and paucity in the evaluation of cost savings and clinical errors in patient care.

Despite improvement in quality and outcome metrics, the available literature is lacking on the impact of hospitalists on quality and outcomes with relation to common pediatric disease states. Pediatric hospitalists' literature describes pediatric conditions of anemia and the comanagement of pediatric surgical patients, but other illnesses are also detailed [10-12]. Srivastava et al. described three common pediatric diagnoses of asthma, dehydration, and viral illness where the introduction of a pediatric hospitalist service was associated with an improvement in cost and efficiency. Decreases in cost resulted from a reduction in hospitalization by one day with impacts in asthma (9.3%) and dehydration (7.8%) cost per case. In another study of respiratory illnesses in children, Coon and colleagues found discordance in antibiotic prescribing patterns between emergency medicine physicians and pediatric hospitalists' in bacterial respiratory illnesses [13]. They found antibiotics were changed by hospitalists in 93% of patient with a discontinuation of antibiotics in 62% of patients. In our study, we introduce a common pediatric condition, skin and soft tissue infections, that is lacking from the current pediatric hospitalist literature.

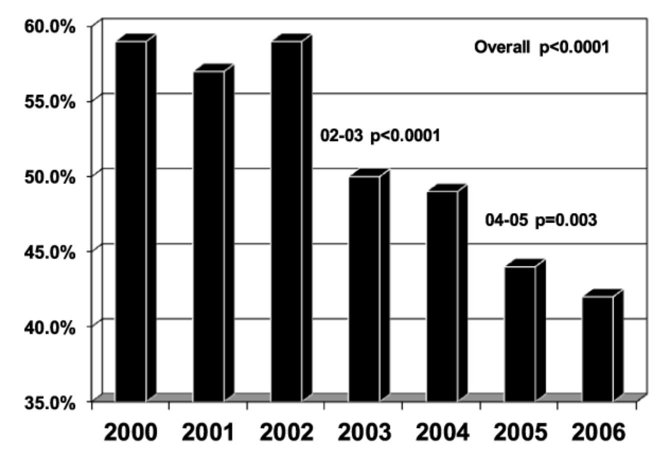

Figure 1: Percent *Staphylococcus aureus* Susceptibility for all Isolates to Oxacillin at TTUHSC/UMC for 2000 through 2006.

Background

Skin and soft tissue infections are associated with community-acquired oxacillin resistant *Staphylococcus aureus* (CA-ORSA). Pediatric CA-ORSA infections are on the rise [14]. At University Medical Center (UMC) Health System, *Staphylococcus aureus* (*S. aureus*) resistance to oxacillin increased from 36% in 1998 to 58% in 2006 (Figure 1) with a 95% susceptibility to tetracycline in 1998 and 96% in 2006 and a 98% susceptibility to trimethoprim/sulfamethoxazole (TMP/SMX) in 1998 and 99% in 2006 (Table 1). This highlights the need for appropriate utilization of antibiotics to limit resistance as well as to prevent unnecessary complications stemming from skin and soft tissue infections.

For over 100 years, *S. aureus* has been well described in the literature with the first report of penicillinase-producing *S. aureus* strains in 1944 following with the emergence and development of oxacillin resistance shortly thereafter [15]. In the early 1980's, CA-ORSA was first reported in adults followed by pediatric cases later that same decade.

CA-ORSA infections are occurring with increasing frequency in the United States and have been observed in healthcare settings in other areas of the world. These infections are a growing cause of concern in children, with reports of 35-75% of CA-ORSA isolates in certain regions [16-18]. In 1999, the Centers for Disease Control and Prevention issued a report that described four pediatric deaths caused by ORSA infections [19]. None of these four children had risk factors for ORSA infection, which prompted investigations into CA-ORSA.

Commonly identified risk factors in CA-ORSA include sports participation, skin trauma, cosmetic body shaving, physical contact with a person who is a carrier of ORSA, and utilizing equipment that has not been cleaned or laundered. Furthermore, CA-ORSA infections have been found to be recurrent in individuals and transmitted between family members and among children in day-care centers. This is a primary concern, especially if the infection is not identified early, due to the potential for further spread.

Current available therapies for *S. aureus* infections include beta-lactam antibiotics, TMP/SMX, clindamycin, tetracyclines, vancomycin, and oxazolidinones [20]. First generation cephalosporins as well as beta-lactams, oxacillin and nafcillin, are commonly used as first-line empiric therapy. CA-ORSA isolates are primarily resistant to beta-lactam antibiotics such as penicillins and cephalosporins. In children, clindamycin has been shown to be effective in treating skin and soft tissue infections caused by CA-ORSA isolates [21]. Isolates expressing the inducible MLS (B) resistance mechanism appear to have susceptibility to clindamycin and resistance to erythromycin, however, clindamycin resistance can be induced in the presence of clindamycin [22]. However, when isolates are D-zone test positive, signifying the inducible macrolide, lincosamide, streptogramin (MLS (B)) phenotype, it is best to avoid this option [22].

The primary aim of this study was to evaluate empiric antibiotic selection in pediatric patients. The secondary aims were to identify percent ORSA vs. OSSA isolates, compare CA-ORSA vs percent initially susceptible to empiric antibiotics, and determine the impact on empiric antibiotic selection following the introduction of the hospitalist service to our institution.

Methods

Study design, statistical methods and data analysis

The Texas Tech University Health Sciences Center Institutional Review Board for the Protection of Human Subjects approved this study. Enrollment in the restrospective January 2001- December 2006 study, consisted of inpatient pediatric patients ages 1- 18 years discharged with a skin and soft tissue infection (*S. aureus*) with the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9) codes along with a postive culture. Participants were excluded from the study if they had history of immune

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dysfunction, human immunodeficiency virus, cancer, splenectomy, transplant, and chronic steroid use. Also excluded were children who were hospitalized prior to the infection. Patients were divided into two groups; patients with CA-ORSA infections and patients with OSSA infections. Differences between the two groups were evaluated concerning the length of stay, complications, and choice of empiric antibiotic.

Organism (# isolates)	AM	A/S	AUG	CFZ	CAX	Cp	CD	E	Gm	LVX	LZD	OX	P	RIF	SYN	T/S	TE	VA
Staph aureus (2597)	7	42	42	42	42	62	80	34	99	65	100	42	7	99	99	99	96	100
AM=Ampicillin; A/S=Ampicillin/Sulbactam; AUG=Augmentin; CFZ=Cefazolin; CAX=Ceftriaxone; CP=Ciprofloxacin; CD=Clindamycin; E=Erythromycin; GM=Gentamicin; LVX= Levofloxacin LZD=Linezolid; OX=Oxacillin; P=Penicillin; RIF=Rifampin; SYN=Synercid; T/S= Trimethoprim/Sulfamethoxazole; TE=Tetracycline; VA=Vancomycin																		

Table 1: 2006 University Medical Center Antibiogram (% Susceptible–Systemic Levels).

From the available medical records, demographic information including age, gender, and ethnicity were extracted. Also identified was the admit date and length of stay. Antibiotic therapy before and during the admission and physician model type (traditional physician or hospitalist) were also collected. Other data analyzed included blood and wound cultures, incision and drainage of abscess, and microbiology.

The data were evaluated using the Excel statistics add-on package Analyze-it v 3.76.1 ã 1997–2015 (Analyze-it Software, Ltd., Leeds, England, United Kingdom) with the a level of significance at 0.05 with a power of 80%. The nominal data were evalauted using chi-square test and Fisher's exact test as appropriate. Continuous data was evaluated for normality with the Shapiro-Wilke test, and all data was determined to be nonparametric. Central tendencies were presented at medians with interquartile range and differences by Mann-Whitney U test.

Results

One thousand eight hundred and sixty children with a positive *S. aureus* culture (5%) were identified of which 100 met study criteria. Subjects were excluded due to incomplete medical records, no positive culture for *S. aureus*, missing cultures, or patients being treated on an outpatient basis. The majority of the participants were Hispanic (57 of 100 (57%)). Study participants were similar with 55% male (55 of 100) and 45% female (45 of 100). Of those included in the study, 77 had ORSA and 23 had OSSA. Baseline characteristics are provided in (Table 2).

Children with ORSA were 68.8% susceptible to initial empiric therapy (p=0.0018) vs. 100% of patients in the OSSA group (Figure 2). Cefazolin was the most commonly prescribed antibiotic in ORSA patients that was not susceptible. The incidence of ORSA in pediatric skin and soft tissue infections increased significantly from 2001 to 2006 while susceptible empiric antibiotic regimens reached a low in 2003 and were over 90% in 2006 (Figures 3 and 4) shows higher empirically sensitive antibiotic choices after the pediatric hospitalist service was implemented in 2005 (83.1% vs. 65%, p=0.0397). Significantly higher incidence of ORSA was noted in children >3 years of age (100%) than children £3 years of age (70.9%, p=0.0115) (Figure 5).

No differences were noted in the length of stay between patients who were treated with appropriate antibiotics and those who were not (p=0.5511); both groups had a median length of stay of three days. Furthermore, incision and drainage plus antibiotics vs. antibiotics alone did not affect length of stay (median length of stay of three days). One interesting find of the study identified only 35% of patients initially started on inappropriate empiric therapy were switched to appropriate therapy during their hospital stay.

Mean age	2 (1-16)
Gender; Male (%)	55 (55%)
Ethnicity; n (%)	
Hispanic	57 (57%)
Caucasian	28 (28%)
African American	9 (9%)
Other	6 (6%)
Length of stay; Median (days)	3 (1-14)
Season of year	
Fall	29 (29%)
Winter	26 (26%)
Spring	23 (23%)
Summer	22 (22%)
Culture	
ORSA	77 (77%)
OSSA	23 (23%)

Table 2: Baseline patient characteristics (N=100).

Discussion

This study reports on the findings of an evaluation of empiric antibiotic selection in pediatric patients. Several implications regarding this study were identified including the affected study population's initial susceptibility to empiric antibiotics, % ORSA vs % initial susceptibility to empiric antibiotics in 2006, % initially susceptible to empiric antibiotics following the implementation of the pediatric hospitalist service, and a lack of the change in length of stay in patients with antibiotics and incision and drainage vs antibiotics alone.

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Our study clearly showed that the prevalence of ORSA among *S. aureus* isolates in our patients had seen a significant increase from 2001 to 2006, which is in accordance with our institution's antibiogram as well as national numbers. In addition to this, we found that empiric antibiotic selection appeared to be progressively improving from 2003-2006 in our pediatric population, probably due to physician awareness of the prevalence of ORSA in our patients and the increasing use of clindamycin as initial drug of choice therapy for skin and soft tissue infections due to susceptibilities.

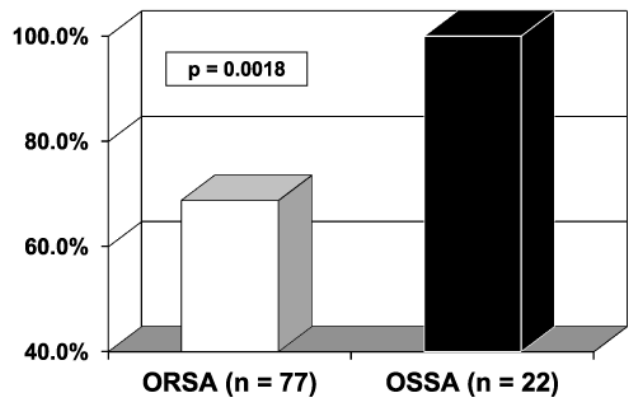

Figure 2: Percent of Community Acquired Skin & Soft Tissue Infections Initially Susceptible to Empiric Antibiotics.

For initially susceptible ORSA, antibiotics included: clindamycin, TMP/SMX, & vancomycin; for initially resistant ORSA, antibiotics included: cefazolin, ceftriaxone, piperacillin/tazobactam, ampicillin, ampicillin/sulbactam, cefoxitin, ticarcillin/tazobactam and nafcillin.

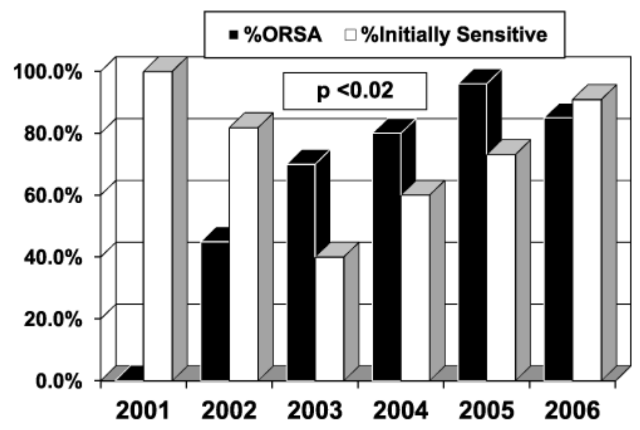

Figure 3: Percent CA- ORSA vs. Percent Initially Susceptible to Empiric Antibiotics by Year.

This study failed to show that incision and drainage altered the hospital length of stay despite patients receiving an inpatient course of antibiotic therapy. No significant difference was noted in all patients on length of stay between patients who were treated with appropriate antibiotics and those who were not (p=0.5511). Only 35% of patients initially started on inappropriate empiric therapy were switched to appropriate therapy during their stay. This study suggests that neither isolate nor antibiotic selection is a strong predictor of hospital length of stay in children.

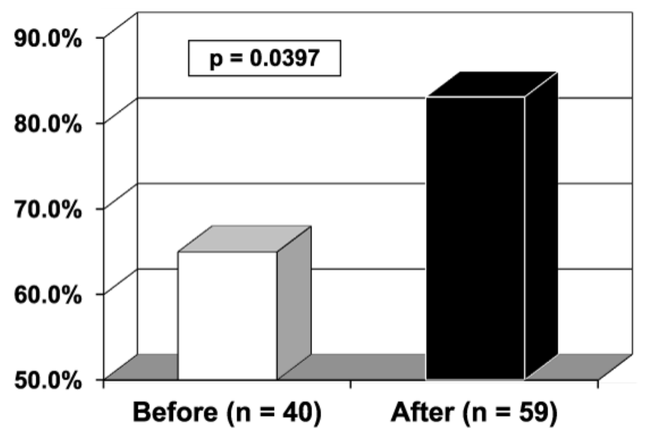

Figure 4: Percent of Staph Aureus Community Acquired Skin & Soft Tissue Infections Initially Susceptible to Empiric Antibiotics Before & After Implementation of the Pediatric Hospitalist Service.

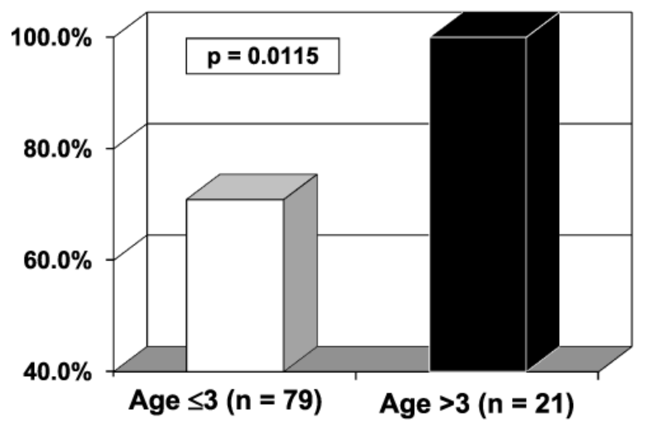

Figure 5: Percent ORSA in patients >3 vs Patients ≤3.

Antibiotic therapy selection requires consideration of bacterial characteristics including antibiotic resistance. Variability among CA-ORSA strains remains an issue, with some strains expressing resistance. TMP/SMX and clindamycin are among the oral antibiotics that have been used with success in treating infections caused by CA-ORSA [23]. At UMC, the percent of all systemic *S. aureus* isolates that are resistant to oxacillin increased from 36% in 1998 to 58% in 2006 (Figure 1). Thus, it is imperative to understand the susceptibility patterns of isolates as well as to possess awareness of the local antimicrobial susceptibility patterns, especially with increasing incidences of resistance, in order to make a sound therapeutic decision when prescribing antibiotic therapy.

Pediatric hospitalist services positively influence efficiency of inpatient care and help decrease hospital related costs, but there is a lack of data on the impact with common diseases [2,6]. Limitations that pediatric physicians face include the lack of guidelines for treating

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many common conditions, but also patients with chronic complex conditions [24]. Coon et al. found discordance in antibiotic prescribing patterns between emergency medicine physicians and pediatric hospitalists in a study of 181 children with respiratory illnesses (P<0.001) [13]. We describe in our study the impact on a common condition, skin and soft tissue infections, that is not currently available in the literature.

At the time of this study, the Infectious Diseases Society of America guidelines for the treatment of ORSA infections in adults and children were not available and our institution did not have a formulary restriction or a treatment guide with a full choice of antibiotic selection by prescribers. However, the availability of the guidelines may have been beneficial to guide antibiotic selection and to avoid inappropriate empiric treatment that was not changed following the availability of susceptibilities. Possibilities exist that due to a wide selection of antibiotics the choice of antimicrobial may have been inappropriate due to resistance. Despite the lack of an antibiotic selection resource, our hospitalist model implemented in 2005 selected appropriate empiric antibiotics 83% vs. 65% in the traditional model. The differences suggest the hospitalist implementation may have contributed to the differences in prescribing patterns.

Despite the positive impact of hospitalist's services, some considerations regarding their differences in effect are important to discuss. Mussman et al. evaluated 11 pediatric hospitalist studies for improved quality of care and efficiency of inpatient care [5]. They found the influence of hospitalists is not universal as related to quality and efficiency of care. Consistent practices or guidelines are required in facilities with pediatric hospitalist services to ensure the impact is widespread. At our institution, the pediatric hospitalist service employed a single individual to provide care of patients. During the hospitalist coverage, the quality and efficiency of care may have been variable when compared with multiple providers that only covered during the weekends. Elliott et al. found that an increasing hospitalist workload is associated with an increase in cost and length of stay [25]. This evidence suggests the evaluation of the facility should occur to prevent an impact on efficiency and cost of care with an increase in hospitalist workload. Due to having only one pediatric hospitalist providing care at our facility, it would be expected that this individual would experience increased workload; however, we did not explore increase in workload and length of stay further in our study.

Our study has several limitations. The major limitation is related to the restrictions of a retrospective chart review. A prospective study to evaluate the impact of the pediatric hospitalist on empiric antibiotic selection in children would improve upon these results to help minimize some of the current limitations in the data. In addition, the hospitalist model was not evaluated for a longer period to determine its impact on length of stay and antibiotic selection since some pediatric hospitalists literature have not found differences in length of stay and efficiency of care. Also, we did not evaluate the role of interdisciplinary healthcare professionals to determine the impact if any that they had in this study such as laboratory specialists or pharmacists that also contribute to patient care. In our study, there were a small percentage of positive cultures for *S. aureus* in addition to a small sample size. Selection bias may have occurred due to OSSA patients being more likely to be treated as outpatients, leaving the ORSA patients as the only subjects presenting to the hospital. Additionally, there may have been different prescribing patterns between surgery and pediatric services, with pediatrics being more likely to prescribe antibiotics and surgery being more likely to perform incision and drainage. Finally, recurrences and relapses in this setting are difficult to account for due to having an open-system.

Conclusions

Our five-year retrospective study suggests that following the implementation of a hospitalist service, there was an improvement in the selection of pediatric empiric antibiotics in skin and soft tissue infections. Overall, we found significant increases in CA-ORSA, a lack of impact on length of stay by isolate selection, or treatment with incision and drainage. Although hospitalist selection of susceptible empiric antibiotic regimens improved, future studies of hospitalist impact in the care of pediatric patients are warranted.

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