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***Staphylococcus aureus* infections among Children Receiving a Solid Organ Transplant: Clinical features, epidemiology and antimicrobial susceptibility**

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Abstract

Background—*S. aureus* is among the most common causes of healthcare-associated infection (HAI) in the United States. Patients who have received a solid organ transplant (SOT) represent a unique population for the acquisition of HAIs given their preoperative organ failure, immunosuppression and need for invasive procedures. However, limited literature is published on *S. aureus* infections among children with SOT. We describe the epidemiology, antimicrobial susceptibility and clinical features of *S. aureus* infections among pediatric SOT recipients.

Design—An ongoing prospective *S. aureus* surveillance database was searched from 2001 to 2012 for infections in patients with a history of SOT at Texas Children's Hospital (TCH). Medical records and antibiotic susceptibility profiles were reviewed; specific attention was applied to the time since transplantation to infection.

Results—Thirty-eight pediatric SOT recipients developed 41 *S. aureus* infections out of the total of 696 transplants performed during the study period; the highest incidence of infection was among heart recipients. Overall, the most common infectious diagnoses were skin-and-soft-tissue infections (66.1%) followed by bacteremia (15.3%). Among isolates in SOT patients, 47.5%, 16.9% and 6.7% were resistant to methicillin, clindamycin or mupirocin, respectively. Three infections (7.3%) occurred in the early post-transplant period (< 1 mo), all of which were bacteremia ($p=0.007$) and all due to methicillin-susceptible *S. aureus* MSSA). The majority of infections (90.2%) occurred in the late post-transplant period (> 6 months). In 10 cases (16.9%), *S. aureus* infection was associated with graft rejection in the same admission.

Conclusions—*S. aureus* represents an important cause of morbidity in pediatric SOT recipients. While the majority of infections occurred late after transplant (>6 months), those acquired in the

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early post-transplant period were more often invasive and due to MSSA in our hospital. Physicians caring for SOT recipients should be aware of the risks posed by this pathogen and the potential concomitant morbidity including graft rejection.

Keywords

Staphylococcus aureus; pediatric; transplant

Introduction

Staphylococcus aureus is among the most common causes of healthcare-associated infection (HAI) in adults and children in the United States. Patients who have received a solid organ transplant (SOT) represent a unique population for the acquisition of HAIs given their preoperative organ failure, need for surgery and often prolonged hospitalization, and immunosuppression. SOT is a known risk factor for *S. aureus* bacteremia in adult patients (1). *S. aureus* infection occurs in 18% of adult lung recipients in the first 90 days post-transplant and is associated with an increased length of hospital stay, risk of subsequent CMV disease, organ rejection and mortality (2). Methicillin-resistant *S. aureus* (MRSA) is known to be increasing in frequency as a pathogen among adult lung recipients (2). Furthermore, MRSA colonization is a risk factor for invasive staphylococcal infection in adult liver recipients (3).

There is, however, very little published literature on *S. aureus* infections among pediatric SOT patients. The few published series primarily discuss *S. aureus* as among the prominent pathogens in the early post-transplant period. Work from France and Japan has shown that *S. aureus* is among the most common bacterial pathogens encountered early after pediatric liver transplantation, accounting for 20–32% of all infections (4, 5). It is unclear, however, if the risk or clinical features of infection vary by the organ transplanted. Furthermore, it is uncertain if staphylococcal infections in pediatric SOT recipients are less susceptible to antimicrobials and antiseptics than those among the general pediatric population which may necessitate an alteration in empiric treatment.

We sought to describe the clinical features, antimicrobial susceptibility and molecular epidemiology of *S. aureus* infections among pediatric SOT patients at Texas Children's Hospital. We hypothesized that infections in SOT recipients would be resistant to multiple antimicrobials as a result of empiric antibiotic and antiseptic exposure (6) and associated with a complex clinical course.

Methods

Patients and Clinical Isolates

Patients and isolates were identified from a prospective *S. aureus* surveillance study that has been ongoing at Texas Children's Hospital (TCH) since 2001 (7). TCH is a tertiary care teaching hospital in Houston, Texas with 639 licensed inpatient beds and active heart, lung, liver and kidney transplantation programs. Small bowel transplantation was not performed at TCH during the study period; however, patients who received small bowels at other

institutions may have followed up at TCH due to proximity to their place of residence. *S. aureus* isolates are identified during the routine course of clinical care by the TCH clinical microbiology laboratory; isolates are subcultured, stored in horse blood at -80°C in the Infectious Diseases Research Laboratory and basic clinical and demographic data are recorded on a standardized form. Sputum and tracheal aspirate cultures were not routinely collected by the surveillance study. The study database was searched for patients with a *S. aureus* infection and a past medical history significant for SOT from 2001 to 2012. Identified study patients were included regardless of whether they received inpatient or outpatient treatment. Medical records for all patients were reviewed; medication, laboratory and vital sign data was recorded from the time of onset of signs/symptoms of infection until resolution. Medication review included immunosuppressive agents that patients were taking at the time of the *S. aureus* infection. Screening for MRSA colonization of SOT recipients was at the discretion of their transplant physician and was not performed routinely during the study period; thus, this data was not included in this study. This study was approved by the Institutional Review Board of Baylor College of Medicine.

Definitions

Fever was regarded as a body temperature $\geq 100.4^{\circ}\text{F}$. Hemodynamic instability was defined as clinical signs of tachycardia, hypotension or poor perfusion prompting the need for fluid resuscitation or vasopressor support by the clinician of record. Skin-and-soft-tissue infection (SSTI) was regarded as skin and soft tissue abscesses, cellulitis, folliculitis, pustulosis, impetigo and lymphadenitis. Surgical site infections (SSI) were defined as a positive culture from a surgical site + signs/symptoms of infection (egg. fever, erythema, fluctuance, drainage etc.) without an alternate diagnosis (8). Superficial SSIs were those limited to the skin and subcutaneous tissues at the site of an incision; those extending below the subcutaneous tissues were regarded as deep SSIs (8). For purposes of this study, we used the diagnosis of central-line-associated bloodstream-infection (CLA-BSI) to describe those patients who had ≥ 1 positive blood culture obtained via central venous catheter plus signs/symptoms of infection and without an alternative source of bacteremia (9). Invasive infections included bacteremia, deep SSI, pneumonia and osteoarticular infection. Timing of infection post-transplantation was defined as follows: early (≤ 30 days), intermediate (31–180 days), late (≥ 181 days) (10). Hospital-acquired infection was considered if infection developed > 72 hours after hospital admission (11). Duration of hospitalization for patients with infection already in the hospital was counted from the time of *S. aureus* isolation until the time of discharge from the hospital (12). Prior antibiotic exposure was regarded as documentation of any antibiotic receipt in the three months prior to the infection of interest (13). Complications were considered those as a result of infection or treatment and included metastatic infection, thrombosis at time of infection, secondary infections and antibiotic related side-effects (6). Acute kidney injury (AKI) was defined as a doubling of the baseline serum creatinine. Relapse was defined as a *S. aureus* infection with an identical susceptibility pattern that developed following clinical resolution of a previous infection requiring additional antimicrobial therapy or a drainage procedure within one month of the original infection. Graft rejection was based on the presence of characteristic histologic features on biopsy obtained at the time of an active *S. aureus* infection; grading of rejection

was based upon published criteria (14) as reported by the pathologist of record. Biopsies were not re-reviewed for this study.

Antimicrobial Susceptibility and Molecular Studies

Susceptibility to oxacillin, vancomycin, clindamycin and trimethoprim-sulfamethoxazole was determined by the TCH clinical microbiology laboratory in the routine course of care. All isolates further underwent mupirocin susceptibility testing by E-test (BioMérieux), PCR for the antiseptic tolerance gene *smr* using previously published primers (13) and analysis by pulsed-field gel electrophoresis (15). The *smr* gene has previously been associated with elevated minimum bactericidal concentrations to chlorhexidine and other antiseptics (13).

Statistical Analyses

The TCH Transplant Infectious Diseases Service (FMM) provided information on the total number of organs transplanted during the study period (2001–2012) and this was used as the denominator in incidence calculations; patients transplanted prior to the study period or transplanted at another institution were excluded from incidence calculations. For patients with more than one infection, only the first episode of *S. aureus* infection was used for comparisons of clinical data and outcomes. In examining the timing of infection after transplantation, patients who had received their transplant prior to the start of the surveillance period (before 2001) or who had received transplantation at another institution were similarly excluded from these analyses. Continuous variables were examined with the ANOVA, student's *t* and Mann-Whitney *U* tests and dichotomous variables with χ^2 and Fisher exact tests; analyses were performed using STATA ver. 12 (STATA corp., College Station, TX). Two-tailed *p*-values < 0.05 were considered statistically significant.

Results

Patients, Demographics and Diagnoses

During the study period 60 *S. aureus* infections were identified in 56 unique patients with a history of SOT in the microbiologic database. Only one infection (MSSA empyema in the early-post-transplant period diagnosed by pleural fluid culture) was identified in a lung recipient and, given that sputum cultures were excluded from the surveillance study, this patient was excluded from subsequent analyses. This resulted in 59 infections in 55 transplant recipients included in the study (Table 1). The median age of patients was 11.8 years (interquartile range (IQR): 6.2–15.3). The organs most frequently transplanted in this series were heart (26/55, 47.2%) followed by kidney (13/55, 23.6%) and liver (12/55, 21.8%); four patients (7.2%) had received a second transplant after failure of a previous graft. The most common infectious diagnoses were skin-and-soft-tissue infection (SSTI, 39/59, 66.1%) followed by bacteremia (9/59, 15.3%); most cases of bacteremia were central-line associated (8/9, 88.9%). Overall, eleven patients (20%) had positive blood cultures (eight were CLA-BSI, one case of primary bacteremia and one case each of secondary bacteremia associated with osteomyelitis and a soft tissue abscess, respectively). Forty-five infections (74.6%) resulted in hospital admission for a median of 7 days (IQR: 4–10 days); eight cases (13.6%) resulted in intensive care admission or transfer for a median of 2.5 days (IQR: 1–6.5 days). Nine episodes were associated with hemodynamic instability

(15.3%). Seven infections (11.7%) were hospital-acquired and the remainder developed signs/symptoms of infection as outpatients. Eight patients (14.3%) were deceased at the time of study completion; however, no deaths were directly attributable to *S. aureus* infection.

Antimicrobial Susceptibility and Molecular Studies

Methicillin-resistance was noted in 28 (47.5%) isolates. MRSA was more often associated with skin-and-soft-tissue infections than MSSA (23/28, 82.1%, vs. 15/31, 48.4%, $p=0.007$). Clindamycin-resistance was noted in ten isolates (16.9%) and mupirocin resistance was noted in four isolates (6.7%); no isolate was resistant to trimethoprim-sulfamethoxazole. There was a tendency for both clindamycin resistance (6/28, 21.4% vs. 4/31, 12.9%, $p=0.4$) and mupirocin-resistance to be more common among MRSA than MSSA isolates (4/28, 14.3%, vs. 0/31, $p=0.04$). Infections due to MSSA were more often invasive (10/31, 32.3%, vs. 1/28, 3.6%, $p=0.006$) and associated with indwelling central venous lines (CVLs) than those due to MRSA (8/31, 25.8%, vs. 0/28, $p=0.005$).

Fifty-six isolates were available for molecular analyses. The most common PFGE type was USA300 accounting for 26/56 (46.4%) of isolates; the USA300 PFGE type was more common among MRSA (18/26, 69.2%) than MSSA (8/30, 26.7%, $p=0.003$). In addition, SSTIs made up a larger proportion of USA300 infections (22/26, 84.6%) than non-USA300 infections (15/30, 50%, $p=0.006$). Overall 17 isolates (30.3%) possessed the *smr* gene of which 7/17 (41.2%) belonged to the USA300 pulsotype and 10/17 (58.8%) were MRSA.

Incidence and Features of *S. aureus* Infection by Transplanted Organ

During the study period (2001–2012), 179 heart, 316 liver and 201 kidney transplants were performed at TCH. Forty-one *S. aureus* infections developed in 38 patients who received an organ in the study period, for an overall incidence of 5.8 *S. aureus* infections per 100 transplants in the study period. The highest incidence of *S. aureus* infection was among heart recipients at 10.1 per 100 transplants (Figure, $p=0.01$).

The features of *S. aureus* infection were compared by the organ transplanted (Table 2). SSTIs were more common among heart recipients than any other organ. By contrast, the highest proportion of invasive infections was seen among liver transplant patients (33.3%, $p=0.3$). More of the liver recipients also had CVLs in situ at the time of infection (3/9, 33.3%), however, this did not achieve statistical significance. There was no temporal trend in the incidence of *S. aureus* infections by organ. The proportion of patients that were transplanted from 2001–2012 and who were receiving cyclosporine at the time of their *S. aureus* infection declined in the study period (4/13, 30.7%, patients from 2001–2006 compared to 0/25 patients from 2007–2012, $p=0.01$); there were no other statistically significant trends in immunosuppression use in the study population.

The majority of infections occurred in the late-post-transplant period (37/41, 90.2%); only three *S. aureus* infections occurred in the early-post-transplant period (3/41, 7.3%) and one in the intermediate-post-transplant period (1/41, 2.4%). When infections are compared by the time period since transplantation, a number of differences become apparent (Table 3). Infections in the early period were more often invasive than those occurring in the late

period (3/3, 100% vs. 5/37, 13.5% $p=0.005$). Additionally, early infections were more likely to be associated with fever on presentation (3/3, 100%, vs. 5/37, 21.6%, $p=0.005$) and indwelling CVLs than late infections (3/3, 100%, vs. 2/37, 5.9%, $p=0.002$). None of the early infections were a result of MRSA; however, more of the patients with *S. aureus* infection in the early period received empiric vancomycin (3/3, 100% vs. 13/27, 35.1%, $p=0.05$) than those with infection in the late period.

Treatment, Outcomes and Complications

The majority of patients were admitted to the hospital and received intravenous antibiotics (39/59, 66.1%) for at least a portion of their therapy. The most commonly used intravenous antibiotic for empiric therapy was vancomycin (20/39, 51.3%); in fourteen cases vancomycin was administered along with another agent (13/20, 65%). The median duration of IV therapy was 7 days (IQR: 4–10 days). Following a course of IV therapy, 28/39 (71.8%) patients were discharged home on oral antibiotics to complete a median total duration of therapy of 10 days (IQR 10–14 days). AKI developed in three patients during treatment with vancomycin (3/20, 15%); no cases of treatment associated *Clostridium difficile* disease were observed with any antibiotic. Thirty-eight infection episodes (64.4%) were managed with the assistance of a surgical or bedside drainage procedure.

Fifteen patients (25.4%) received oral antibiotics alone; four of these had mild superficial surgical site infections. The most commonly used oral antimicrobial was clindamycin ($n=8$) followed by trimethoprim-sulfamethoxazole ($n=2$) and cephalexin ($n=2$). Two patients were prescribed mupirocin alone. None of the patients on oral or topical therapy alone developed relapse of infection on discontinuation of antibiotics; one patient was admitted as a result of poor response to outpatient therapy. Three patients with minor skin abscesses received incision and drainage alone.

Six patients developed relapse of infection following discontinuation of therapy; five of these patients had positive blood cultures (83.3%). One patient was in the early post-transplant period while all others were >180 days post-transplant. There were no differences in duration of antibiotic therapy or antibiotic choice among patients who relapsed and those who did not. MSSA was more commonly isolated among those patients who relapsed compared to those that did not (6/6, 100%, vs. 25/53, 47.2%, $p=0.02$). The risk of relapse was higher among infections associated with a positive blood culture than among those without (5/11, 45.5%, vs. 1/29, 2%, $p<0.001$). Three of the cases of relapsed bacteremia were CLA-BSIs initially managed with antibiotics and line retention. Additional complications included three patients developing secondary infection with other organisms during therapy and one patient with bacteremia who was diagnosed with *S. aureus* pyomyositis during treatment.

In ten cases (16.9%) the infection was associated with a diagnosis of graft rejection in the same admission; eight cases were heart recipients and one case each in a kidney recipient and a liver recipient. In seven cases, rejection was diagnosed concomitantly with a *S. aureus* SSTI; one case each occurred in the early and intermediate post-transplant periods with the others being in the late period. The proportion of cases by the grade of acute cellular rejection is as follows: mild ($n=2$), moderate ($n=5$) and severe ($n=2$). One biopsy was

reported by the pathologist as consistent with acute cellular rejection however no grade was assigned; one additional patient underwent biopsy and was found to have no evidence of rejection.

Discussion

S. aureus is a common pathogen among both healthy and immunocompromised children and is known to be a predominant cause of HAI (16). While the clinical features and epidemiology of *S. aureus* have been described in children with malignancy (6, 17) and HIV (18, 19), little data is available in the pediatric SOT population. We describe a series of *S. aureus* infections among pediatric SOT recipients with an overall prevalence of 5.8/100 new transplants. Furthermore, we noted similar proportion of cases due to MRSA and MSSA in this population, in contrast to previous studies of pediatric oncology patients at our institution which have shown a predominance of MSSA (6).

A study of 192 adult heart recipients found that *S. aureus* accounts for up to 30% of bacterial infections after transplant (20). We observed the highest incidence of *S. aureus* infections to occur among pediatric heart recipients (10.1/100 transplants). The full reasons for the higher rate of *S. aureus* infection in heart recipients are unclear, however, it is notable that these patients also had higher rates of corticosteroid use. Corticosteroid use has previously been associated with increased incidence of *S. aureus* infection in adults without SOT (21, 22); this could potentially have contributed to the higher incidence among heart recipients in our study. Given that all transplant patients were not reviewed, we cannot fully evaluate the potential impact of different immunosuppression regimens over time or by transplanted organ on *S. aureus* infection. Notably, however, we did observe an overall decline in cyclosporine use in our population consistent with data from the Scientific Registry of Transplant Recipients (23).

While the largest number of infections occurred among heart recipients, the majority of these infections were minor soft-tissue infections. By contrast, there was a trend for infections in liver recipients to be more often invasive. Previous studies of pediatric liver recipients have noted that *S. aureus* accounts for 20–32% of bacterial pathogens in early post-transplant infections and are often associated with an invasive phenotype (4, 5). In a study of adult liver recipients from Spain, *S. aureus* accounted for approximately 13% of all cases of early bacteremia and was an independent risk factor for mortality (24). Studies including both adult and pediatric lung recipients have shown that *S. aureus* infection complicates as many as 18% of transplants in the first 90 postoperative days (2). Furthermore, nearly 80% of children >6 years old with cystic fibrosis (CF) have *S. aureus* in their sputum (25) and CF is among the principal indications for pediatric lung transplantation (23). Given that our surveillance study does not capture *S. aureus* from respiratory specimens, we were not able to accurately account for infections in lung recipients. While one early-onset invasive infection was noted in a lung recipient, this patient was excluded from subsequent analyses in order to not provide a biased view of disease in lung recipients. Notably, however, our study design would have identified any lung recipients with blood stream, surgical site or soft-tissue infections and none were found.

While the overwhelming majority of infections in our series (90.2%) occurred in the late post-transplant period, those that did occur in the early period were significantly more likely to be invasive. This is consistent with the work of numerous investigators suggesting the high risk for invasive bacterial infection of any cause occurring in the early- to intermediate-post-transplant periods (4, 26, 27). Singh et al. reported substantial reductions in the incidence of *S. aureus* infection in the first month following liver transplantation through active screening for nasal/rectal colonization, cohorting and decolonization with nasal mupirocin (28). While complete colonization data was not available for this study, it is unclear that active screening or decolonization in the early period would have been cost effective or beneficial given that the majority of infections occurred late after transplantation. Other agents utilized to decrease the incidence of HAIs include the use of chlorhexidine baths, oral rinses and swabs for CVL care (29–31). A number of genes have been described in *S. aureus* associated elevated MBCs to antiseptics including chlorhexidine. Notably there was a high prevalence of the chlorhexidine tolerance gene *smr* among isolates from transplant patients with 30.3% of isolates being positive for this gene; this likely reflects the exposure to this agent during hospitalization or other encounters with healthcare providers. Johnson et al, as well as similar work at our own institution, have reported that approximately 14% of *S. aureus* isolates from a general pediatric population possess *smr* (13, 32). Taken together, this suggests that complex medical conditions may predispose to infection with antiseptic tolerant organisms compared to the general pediatric population.

There is limited published data from which to draw conclusions regarding the management of SOT patients with staphylococcal infection. For patients transplanted at our center with early-onset *S. aureus* infection, the inclusion of an anti-staphylococcal β -lactam along with vancomycin should be considered in empiric therapy based on the high prevalence of MSSA. While the majority of the patients in the current study were admitted to the hospital and received IV antibiotics, however, 25% were treated successfully as outpatients. Thus, for patients with minor soft tissue infections and good follow-up, oral antimicrobial therapy may be reasonable. Notably, however, *S. aureus* can cause substantial morbidity in the SOT population. Six infections (10.2%) were associated with relapse of staphylococcal disease at the end of therapy and this was particularly the case for those patients with CLA-BSI. This emphasizes the importance of aggressively treating invasive infections in this immunocompromised population including the prompt removal of infected CVLs. Notably, Infectious Diseases Society of America (IDSA) guidelines for the management of intravascular catheter infections originally published in 2001 and revised in 2009 recommend removal of CVLs if *S. aureus* is the identified pathogen (33); our findings help to illustrate the importance of this recommendation.

In addition, infection can occur coincident with graft rejection in SOT patients. Acute and chronic rejection is well described with viral infections such as CMV (34) but has been described associated with bacterial pathogens as well (2). Over 16% of patients in this series were diagnosed with graft rejection concurrently with *S. aureus* infection, including patients with seemingly minor soft tissue infection. These data emphasize that practitioners should be vigilant for the development of this complication in transplant recipients with

staphylococcal infection. It is notable, however, that our study design did not take into account the impact of confounding factors on graft rejection (such as serum immunosuppressant levels or concomitant viral infections such as CMV) and thus the data on graft rejection must be interpreted cautiously.

We acknowledge that the sample size and retrospective design of this study limit the degree to which certain variables can be associated with clinical outcomes. Given that screening for colonization was not routinely performed, we cannot assess the degree to which colonization could have contributed to the risk for infection. However, given that most infections occurred in the late post-transplant period, and that all the infections in the early post-transplant period were associated with MSSA, the utility of pre-transplant screening for MRSA colonization appears to be limited in our population. In addition, as sputum cultures were not routinely collected by our surveillance study, we likely underestimated the incidence of staphylococcal respiratory infections, especially in lung recipients (2). Finally, it is difficult to formulate firm treatment recommendations in addition to those routinely applied in the management of *S. aureus* infections based on this work.

In conclusion, *S. aureus* accounts for significant morbidity among pediatric SOT recipients. The prevalence of disease is higher among heart recipients than other organs, albeit the majority of disease is noninvasive. Early-onset infections were characterized by a predominance of MSSA infection and invasive disease. Further work is needed to explore the specific management of staphylococcal infection in this vulnerable population.

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Figure. Incidence of *S. aureus* infection by organ transplanted

From 2001–2012, 179 heart, 316 liver and 201 kidney transplants were performed at TCH. Forty-one infections occurred among the patients who received organs during this period (overall incidence of 5.8/100 transplants).

Table 1

Demographics and Diagnoses

N = 59 Infections, 55 Patients (%)	
Median Age, years (IQR)	11.8 (6.2–15.3)
Female Gender	19 (34.5)
African-American Race	7 (12.7)
Hispanic Ethnicity	29 (52.7)
Methicillin-Resistant	28 (47.5)
Clindamycin-Resistant	10 (16.9)
Mupirocin-Resistant	4 (6.7)
<i>smr</i>-Positive	17 (30.3)
Transplanted Organ	
Heart[*]	26 (47.2)
Kidney	13 (23.6)
Liver	12 (21.8)
Liver-Kidney	1 (1.8)
Liver-Small Bowel	2 (3.6)
Small Bowel	1 (1.8)
Re-transplant	4 (7.2)
Infectious Diagnosis	
Skin and Soft Tissue Infection	39 (66.1)
Bacteremia	9 (15.3)
Central-Line Associated	8 (88.9)
Surgical Site Infection	5 (8.5)
Superficial Surgical Site Infection	4 (80)
Chronic otitis/sinusitis	4 (6.8)
Osteomyelitis	1 (1.7)
Hospital Admission	44 (74.6)

* Underlying conditions leading to transplantation are listed. Among heart recipients: congenital heart disease (n=13), dilated cardiomyopathy (n=8), restrictive cardiomyopathy (n=2), anthracycline toxicity (n=2) and parvovirus myocarditis (n=1). Among kidney recipients: focal segmental glomerulosclerosis (n=4), obstructive uropathy (n=2), vasculitis (n=1), hyperoxaluria type 2 (n=1), Alport Syndrome (n=1) and unknown (n=4). Among liver recipients: biliary atresia (n=4), ornithine transcarbamylase deficiency (n=2) and one patient each with bile duct paucity, neurogenin 3 mutation, hemochromatosis, carbamoyl phosphate synthetase deficiency, succinyl acid lyase deficiency, and progressive familial intrahepatic cholestasis. The patient who received a liver-kidney transplant had Caroli disease. The liver-small bowel recipients had TPN cholestasis secondary to necrotizing enterocolitis and intestinal atresia, respectively. The small bowel recipient had a history of gastroschisis.

Table 2

Features of *S. aureus* Infection Among Patients who Received a Transplant at Texas Children's Hospital, 2001–2012

	Heart (n=18)	Liver (n=9)	Kidney (n=11)	P value
Median Age, Years	11.8 (6.3–15.3)	3.2 (2.3–13)	13.4 (11.3–19.3)	0.002
Time Since Transplant, Months	29 (23–41)	35(25–41)	36(9–56)	0.7
CVL in situ	1 (5.6)	3 (33.3)	2 (18.2)	0.1
MRSA	9 (50)	3 (33.3)	4 (36.6)	0.7
Early Period	1 (5.6)	0	2 (18.1)	0.4
Intermediate Period	1 (5.6)	0	0	0.9
Late Period	16 (88.9)	9 (100)	9 (81.8)	0.5
SSTI	14 (77.8)	1 (11.1)	6 (54.5)	0.004
Bacteremia	1 (5.6)	2 (22.2)	2 (18.1)	0.4
Surgical Site Infection	0	2 (22.2)	1 (9.1)	0.07
Invasive Infection	2 (11.1)	3 (33.3)	2 (18.1)	0.3
Hospital Admission	13 (72.2)	4 (44.4)	8 (72.7)	0.3
Hospital Duration	7 (4–7)	6 (5–17)	7 (4–7)	0.3
Total Treatment Duration, d	10 (10–14)	10 (6–13.5)	10 (7–14)	0.9
Immunosuppression				
Cyclosporine	2 (11.1)	0	8 (72.7)	<0.001
Tacrolimus	9 (50)	0	8 (72.7)	0.002
Mycophenolate	10 (55.6)	3 (33.3)	5 (45.5)	0.5
Prednisone	15 (83.3)	1 (11.1)	8 (72.7)	0.001
Rejection	4 (22.2)	1 (11.1)	1 (9.1)	0.7

Table 3Features of *S. aureus* infection in relation to time after transplantation

	Early Period*, n=3	Intermediate Period, n=1	Late Period, n=37	P value
MRSA	0	0	18 (48.6)	0.06
Clindamycin-resistance	0	0	9 (24.3)	0.9
CVL in situ	3 (100)	0	3 (8.1)	0.002
Fever on Presentation	3 (100)	1 (100)	8 (21.6)	0.005
Hospital Duration, days	7 (2–35)	4	7 (4–11)	0.6
PICU Admission	1 (33.3)	0	4 (10.8)	0.4
WBC on presentation, 10³/μl	10.1 (9.6–16.8)	15.6	8.7 (6.3–13.6)	0.7
IV# Therapy	3 (100)	1 (100)	22 (59.4)	0.3
Duration of IV Treatment, days	10 (7–14)	4	7 (4–10)	0.4
Total Duration of Treatment, days	10 (7–14)	10	10 (7–14)	1
Empiric Treatment				
Vancomycin	3 (100)	0	13 (35.1)	0.05
Anti-staphylococcal β-lactam	0	0	4 (10.8)	0.9
Clindamycin	0	1 (100)	15 (40.5)	0.1
Bacteremia	3 (100)	0	3 (8.1)	0.002
Duration of Bacteremia	3 (2–3)	n/a	2 (1.5–2.5)	0.5
Surgical Site Infections	0	0	4 (10.8)	0.9
SSTI	0	1	20 (54)	0.1
Any Invasive Infection	3 (100)	0	5 (13.5)	0.005

* The early post-transplant period was considered 30 days since receipt of an organ, the intermediate period was considered 31–180 days following transplantation and the late period was defined as 181 days beyond transplant.

IV, intravenous