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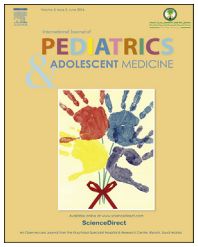

ORIGINAL RESEARCH ARTICLE

Characteristics and risk factors of hospital acquired — Methicillin-resistant *Staphylococcus aureus* (HA-MRSA) infection of pediatric patients in a tertiary care hospital in Riyadh, Saudi Arabia

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KEYWORDS
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Abstract *Background and objectives:* The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections has been steadily increasing. These infections are considered to be either hospital-acquired MRSA (HA-MRSA) or community-acquired MRSA (CA-MRSA). Children are at higher risk of infection than adults. HA-MRSA has been reported to have more serious outcomes than CA-MRSA. However, there are not enough studies in Saudi Arabia to study the characteristics of HA-MRSA in children. We aim to describe the characteristics of HA-MRSA infection, including risk factors, culture site, clinical manifestations, complications, and outcomes among pediatric patients in a tertiary care hospital in Riyadh, Saudi Arabia.
Design and settings: This is a retrospective chart review study. It was conducted in King Abdulaziz medical city in Riyadh.
Patients and methods: The study included all patients 14 years of age or younger who were culture-positive from any site in the body during the period from January 1, 2009 to December 31, 2011. The time of culture compared to admission time was used to differentiate between CA-MRSA (within 72 h of admission) and HA-MRSA (more than 72 h after admission). The final sample size was 39 patients.
Results: We found HA-MRSA to be more common in males and those with risk factors such as previous surgery and previous hospitalization. Patients had a high Pediatric intensive care unit (PICU) admission rate and were commonly septic with positive blood cultures. Seventy-four percent of patients fully recovered, 10% recovered with complications and 15% died.

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Conclusion: HA-MRSA is an infection that can cause serious complications and a high rate of PICU admissions. Clinical manifestations such as shock are associated with higher mortality and morbidity rates. Special care should be given to those admitted to PICU, as they have high rates of mortality and morbidity.

1. Introduction

The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infection has been steadily increasing. This has coincided with an increase in the number of patients presenting with serious invasive disease due to MRSA [1,2]. The causative organisms are defined as *Staphylococcus aureus* strains with an oxacillin minimum inhibitory concentration (MIC) of at least 4 mcg/mL. MRSA is resistant to all beta-lactam agents, including cephalosporins (with the exception of ceftobiprole) [3]. Its resistance is derived from the mecA gene encoding for the low-affinity binding protein PBP-2a, which allows the organism to grow and divide in the presence of methicillin and other beta-lactam antibiotics [4,5]. Due to its high resistance to previously mentioned antibiotics and the appearance of new strains, MRSA infection has become an increasing medical challenge [6–9]. Infections caused by MRSA have been classified as either nosocomial (hospital acquired) or community acquired [2,8,10]. Infection is considered to be HA-MRSA if positive cultures result from samples drawn after 72 h of admission. Cases considered CA-MRSA include those in which positive cultures have been drawn outside the hospital or drawn within 72 h of admission or in cases in which MRSA was diagnosed in an outpatient setting [8,11,12].

Although MRSA infection rates are not significant in countries such as the Netherlands, Denmark, and Sweden [13,14], the threat has increased significantly in many other countries, such as the USA and Western European countries such as Great Britain, in which MRSA infection has become an epidemic [11,12,14,15]. Furthermore, some Middle Eastern countries such as Iran have recorded high numbers of MRSA infections [16]. Children are at risk of acquiring MRSA infections [17–19]. The risk increases more when they have co-morbidities such as malignancies, recent surgeries, autoimmune diseases, previous antibiotic usage, and long-term hospitalization, with resultant exposure to potentially more dangerous strains of HA-MRSA [17,19–21]. Moreover, the threat of MRSA infection has increased in children and has manifested more frequently in neonates and in countries such as the U.S [22,23]. Risk factors for children are the same as for adults, with the addition of genetic diseases such as cystic fibrosis and congenital immunodeficiencies [17,20,24].

The first report of MRSA in Saudi Arabia was published in 1994 by Zaman in the western region in Jeddah. Over a period of three years covering Zaman's report, he found that 7.5% of all *Staphylococcus aureus* infections were MRSA positive [25]. Thereafter, a few reports followed from Madani and others in 2002 in the setting of two tertiary care centers in Saudi Arabia. The studies included patients from adult and pediatric wards (both medical and surgical). They found that 33% of all *Staphylococcus aureus* cultured patients were MRSA positive [11,12]. Despite these data, studies describing MRSA infections in the pediatric population in Saudi Arabia remain limited in number. Only one study [18] exclusively described pediatric MRSA infections in Saudi Arabia. Bukhari et al investigated 80 previously healthy pediatric patients with community acquired MRSA infection and found that 6% (five patients) had invasive CA-MRSA with serious complications that included osteomyelitis, deep vein thrombosis, and subdural empyema [18]. The growing risk of MRSA was reported by Bukharie and Abdelhadi from King Fahd University Hospital in Dammam, Saudi Arabia in a study showing that the prevalence of CA-MRSA infections increased from 9.9 per 10,000 admissions in 2001 to 67 per 10,000 admissions in 2008 [8,13].

Rates of MRSA infection are increasing among the Saudi population, including children. The data on pediatric HA-MRSA are limited, but signs indicate that it is also becoming more frequent [2,6–8,11–13,18,26,27]. These data demonstrates that MRSA infection in the pediatric population needs to be studied further. The aim of this study is to describe characteristics of pediatric HA-MRSA infection in a tertiary care hospital in King Abdulaziz Medical City, Riyadh, Saudi Arabia, and determine possible risk factors, in hope that it will add to the body of knowledge on this important infection in this region.

2. Patients and methods

This is a case series retrospective chart review study that was conducted at King Abdulaziz Medical City in Riyadh, a tertiary care center with approximately 1000 beds. It included all patients who were 14 years of age or younger with a documented culture of MRSA from any site of the body between January 2009 and December 2011. Data on patients with MRSA were retrieved from the database of the Infection Prevention and Control Department at our institution, which performs approximately 900 polymerase chain reaction (PCR) screenings per month. The MRSA policy at KAMC-Riyadh is to screen all patients who are:

- Admitted to the Pediatric intensive care unit (PICU).
- Transferred from another hospital or treated in another hospital within the last six months.
- Undergoing cardiac, orthopedic (including spine) surgery, preoperatively.

- Hemodialysis patients on admission for the first dialysis treatment and for placement of any type of vascular access (i.e.: AV-fistula, permanent catheter, graft, or port access device).
- Patients on continuous ambulatory peritoneal dialysis treatment for the first time when scheduled for catheter placement.
- Known to be previously MRSA positive.
- Roommates of MRSA-positive patients not on isolation precautions.

The sites to screen include:

- Anterior nares.
- Non-intact skin areas (e.g., tracheostomy, pressure sores, or surgical wounds).
- The groin and axillae of neonates and pediatric patients awaiting liver or cardiac surgery.

Presentations of MRSA infection that were included in the study were abscess, signs of shock (hypotension, tachycardia, etc.), discharge from any site of the body, fever, respiratory distress, localized swelling, etc. We considered only the first isolate of bacterial culture results. The time of culture was used to differentiate between CA-MRSA (less than 72 h of admission) and HA-MRSA (more than 72 h after admission). Patient data including age, gender, nationality, risk factors, clinical manifestation, culture site, unit of stay, diagnosis, and outcome were retrieved from patient charts into the data collection sheet. Data were then entered and analyzed using a software statistical package (SPSS version 20). Outcomes were divided into favorable (complete recovery) and unfavorable (recovery with complications or death). Patient confidentiality during data collection and entry was ensured using a coding system that prevented disclosure of names or medical record numbers. Statistical methods used to obtain our objectives included the mean, median, standard deviation, minimum, maximum age, and Chi-Square for categorical data. The results were then transferred to Microsoft Office Excel 2007 to create several charts and diagrams (Table 1, Figs. 1—7).

3. Results

Two hundred patients were documented to have MRSA infection. After analyzing the data, we found that nearly one-quarter (22%, 39 patients) of MRSA-infected patients had HA-MRSA. The majority of patients in our study were males (59%, 23 patients), with 40% females (16 patients) (Table 1). The majority of our sample were Saudis (95%, 37 patients) (Table 1). We categorized the pediatric population studied into three age groups (below one year, between one and five years, and more than five years). Nearly half of the patients were below one year old (46%, 18 patients), with 26% (11 patients) between one and five years, and 28% (10 patients) above five years of age (Table 1). The mean age was 3.1 years of age, with a maximum of 12 years and a minimum of nine days. Most of our population had previous surgery (31%, 12 patients), previous hospitalization (26%, 10 patients), or a cardiac anomaly (23%, nine patients) (Fig. 1). Other co-morbidities included conditions such as asthma, burns, renal failure, or metabolic diseases (Fig. 1). 59% (23 patients) presented with fever. 38% (15 patients) presented with skin and soft tissue infection (SSTI) manifestations. And 23% (9 patients) presented with abscess (Fig. 2). Shock manifestations (hypotension, tachycardia, etc.) were found in 21% (8 patients) (Fig. 2). In 19 infected patients (52%), the site of HA-MRSA isolation was blood in 31% (12 patients), skin and soft tissue in 13% (4 patients), and bone or joint in 8% (3 patients) (Fig. 3). Other less frequently reported sites among our study population included CSF and lumbar drain catheter in two patients (5%) and tip of central venous catheter in one patient (3%) (Fig. 3). We found that 12 patients (31%) were admitted to the PICU, 10 patients (26%) were admitted to the pediatric ward, and five patients each (13% each) were admitted to the burn unit, NICU and cardiac CCU (Fig. 4). Twelve patients (31%) were diagnosed with septicemia, seven patients (18%) had pneumonia, and six patients (15%) had cellulitis (Fig. 5). We attempted to correlate the time of year with the rate of infection, but we were unable to establish a relationship. Twenty-nine (74%) of the studied patients fully recovered (Fig. 6). Among the remaining patients (10%, four patients) recovered with complications such as vision impairment, and six patients (15%) died (Fig. 6). We tried to find an association between unfavorable outcomes and co-morbidities associated with HA-MRSA infection and found that unfavorable outcomes were associated with chronic pulmonary diseases such as asthma *(P-Value = .03)* (Fig. 7). Eighty percent of patients with unfavorable outcomes (eight patients) required PICU care and presented with shock manifestations and/or SSTI manifestations.

Table 1 Patient demographics (n = 39)

	Number	Percent
Age category		
Up to 1 year	18	46%
1 to 5 years	11	28%
5 to 12 years	10	26%
Gender		
Male	23	59%
Female	16	41%
Nationality		
Saudi	37	95%
Non-Saudi	2	5%

4. Discussion

The threat of MRSA infection has been increasing on a national and global basis [2,23]. MRSA infections are considered to be HA-MRSA if positive culture samples are drawn after 72 h of admission. Cases of CA-MRSA infection include patients from whom cultures have been withdrawn outside the hospital or for whom diagnosis occurred in an outpatient setting [8,11,12]. The epidemiological characteristics of HA-MRSA infections vary among geographic regions and from one year to another. A recently published study conducted in Pennsylvania by Casy et al indicated that

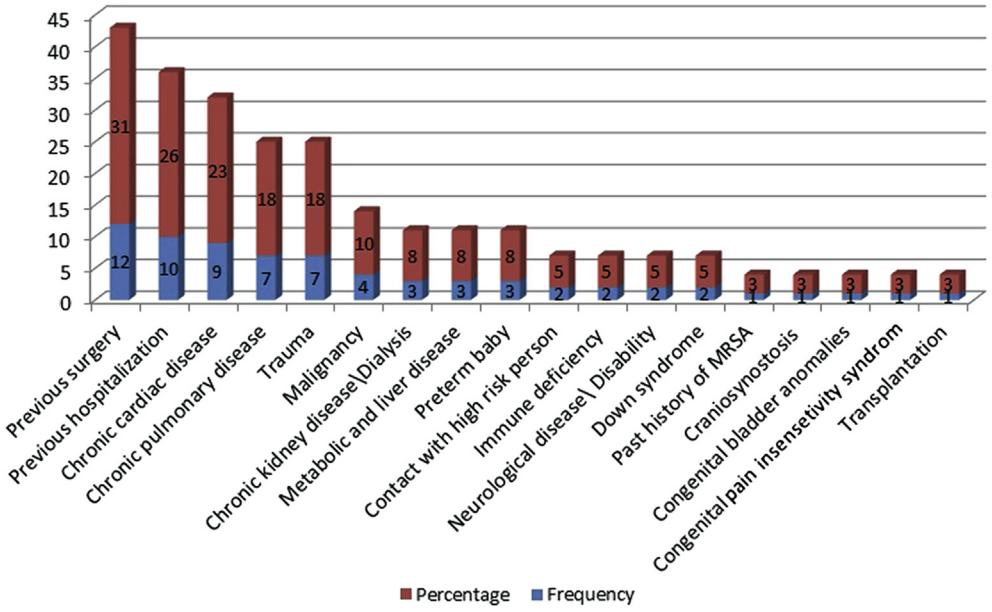

Fig. 1 Comorbidities and associated risk factors.

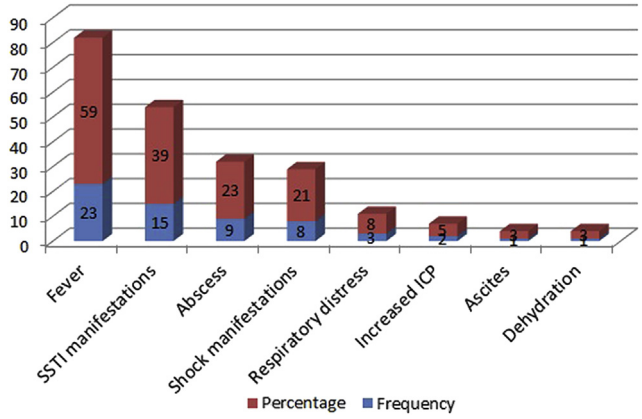

Fig. 2 Clinical presentation (n = 39).

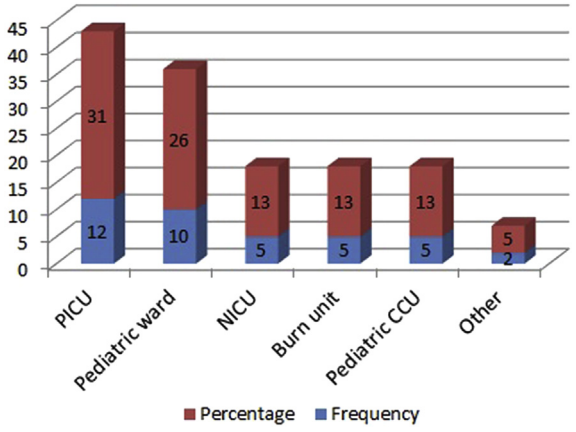

Fig. 4 Unit of stay (n = 39).

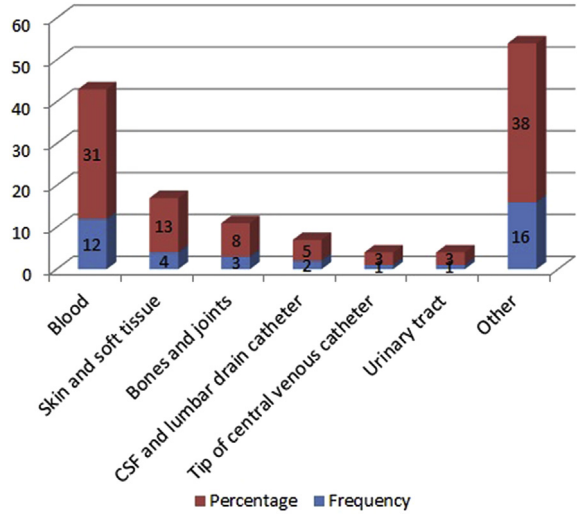

Fig. 3 Site of isolation (n = 39).

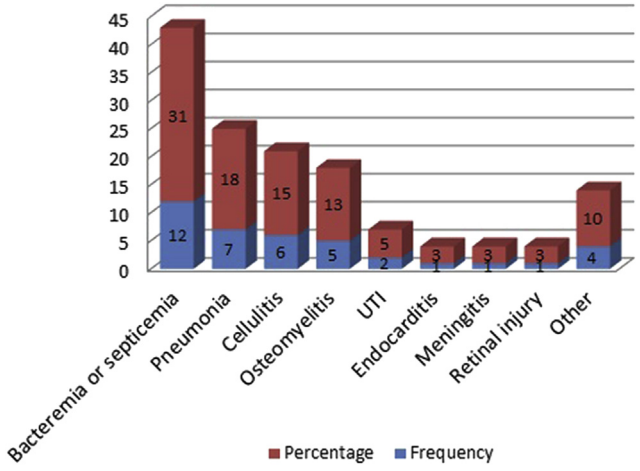

Fig. 5 Presenting diagnosis (n = 39).

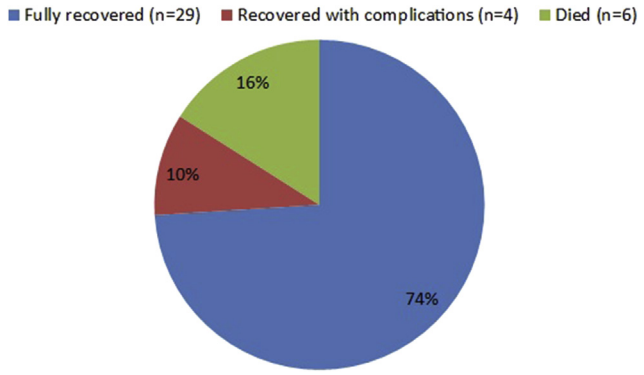

Fig. 6 Outcome (n = 39).

between 2001 and 2010, the annual incidence of HA-MRSA has increased by 7% [28]. We tried to compare some of our research results to other studies conducted at a similar time in other regions. We found that the risk of acquiring HA-MRSA increased with younger age, with a median age of 3.1 years. The finding was correlated with a study conducted in Minnesota, USA, where the mean age of infection was 2.4 years [29].

We found that patients under one year of age had the highest rate of admission due to HA-MRSA (46%, 18 patients) (Table 1). This concurred with the findings of a study conducted by Gutierrez and others in California, USA, indicating that from 1985 to 2009, those under one year of age had a higher hospitalization rate than did children 1—2 years of age (OR 5.6) [23].

The PICU had the highest rate of admission in our study 31% (12 patients) (Fig. 4). This correlated with results of an MRSA review study conducted at Johns Hopkins Hospital in the United States by David MZ et al. This study found that from 2007 to 2008, 6% (72/1674) of patients in their PICU had MRSA colonization [30].

A 2013 study conducted in Pakistan to investigate nasal colonization among septicemia patients found that nasal screening for MRSA colonization can be helpful in determining the cause of septicemia. The same study detected MRSA infections in 100% of those on dialysis or with surgical site infections [31]. We reported that septicemia (31%, 12 patients) and pneumonia (18%, seven patients) were among the most common consequences of HA-MRSA infection in our study (Fig. 5). Similarly, a 2013 study from China by Wu X et al reported that children who acquired HA-MRSA had an aggressive infection course associated most frequently with pneumonia and septicemia. However, the same study indicated that CNS infections were common, whereas in our study, it was rare (6%, two patients) (Fig. 5) [32]. We did not find a correlation between time of year and infection rates in our study. In contrast, a study conducted in the USA to investigate the epidemiological change of MRSA infections found that the infection frequency was highest between the months of June to October. The same study reported that rates of blood stream and pneumonia-related admissions had not changed compared to data they had collected previously. Additionally, most patients in the study had strains of HA-MRSA [33]. Another study, conducted by Leonard M. Mermel et al, reported that children exhibited a seasonal pattern of HA-MRSA infection, whereas adult infections exhibited no such seasonality [34].

We think that the spread of nosocomial can be reduced or even eliminated by implementing and enhancing general infection control and prevention measures, including hand hygiene. Pereira et al published results of a 2014 study that was conducted in Botucatu, Brazil which concluded that improving hygiene practices in high risk areas such as the PICU and NICU would help to prevent infection [35].

5. Conclusion

HA-MRSA is a serious infection with variable epidemiology that presents the need for further investigation within this geographic region. Young children and children with risk factors, especially those involving pulmonary disease, tend

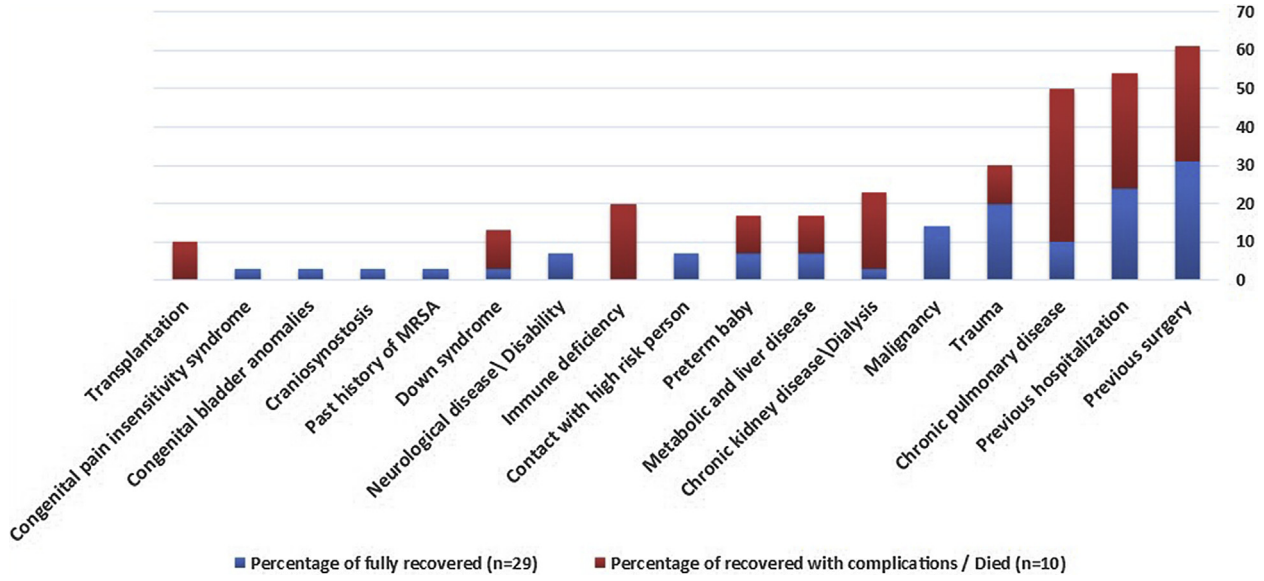

Fig. 7 Corelation between risk factors and outcomes (n = 39).

to have worse prognoses than those who do not. HA-MRSA is responsible for a high number of PICU and NICU admissions. It has been shown in our study to cause serious complications and adverse outcomes, especially for those who require PICU admission. This study emphasizes the need for surveillance of patients who are admitted with HA-MRSA infection. Strict Infection control measures must always be observed when interacting with patients who may be infected with HA-MRSA.

Conflict of interest

None.

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