Original Article

Epidemiology of burn-related infections in the largest burn unit in Saudi Arabia

Mohammed E. Mater, MBBS, *Ayman E. Yamani,* MBBS, FRCSC, *Ahmad A. Aljuffri,* MBBS, *Sumayah A. Binladen,* MBBS.

ABSTRACT

الأهداف: أولاً وصف البيانات الوبائية للحروق، بما في ذلك أنواع الحروق والعدوى المرتبطة بالحروق لدى المرضى البالغين والأطفال. ثانيًا، تحديد تأثير المكورات العنقودية الذهبية المقاومة للميثيسيلين (MRSA) على مدة الإقامة في المستشفى، وثالثًا، لتحديد ما إذا كان المظهر الميكروبيولوجي يختلف في المرضى الذين يعانون من حروق شديدة وغير شديدة.

المنهجية: أجريت هذه مراجعة مخطط بأثر رجعي تم فيها مراجعة السجلات الطبية لجميع مرضى الحروق المقبولين في مستشفى النور التخصصي، مكة المكرمة، المملكة العربية السعودية خلال الفترة من يناير 2016م ويناير 2017م للبيانات الديموغرافية والميكروبيولوجية وبيانات الحروق باستخدام ورقة تجميع بيانات. لم يكن من الضروري التوزيع العشوائي حيث تم ادراج جميع المرضى. أجرينا إحصاءات وصفية واستدلالية على البيانات التي تم جمعها.

النتائج: من بين 250 مريضاً، كان 53.6% من مرضى الأطفال و 68.4% من المرضى الذكور. كان المكورات العنقودية الذهبية أكثر الكائنات شيوعًا في الدم وجروح الحروق الطفيفة. كان تردد المكورات العنقودية الذهبية المقاومة للميثيسيلين 82.5%. زادت مدة الإقامة في المرضى الذين يعانون من إصابات الحروق المصابة.

الخلاصة: سجل الأطفال أكثر عدد إصابة بالحروق، مما يمثل حافزًا لبرامج الوقاية التعليمية الأكثر تركيزًا في تلك المجموعة. بالإضافة إلى ذلك، تحمل التهابات الحروق مرض أكثر، وترتبط بإقامة أطول في المستشفى. يمكن أن تساعد هذه البيانات في تنفيذ برامج الوقاية المختلفة.

Objectives: To first describe the epidemiological data of burns, including burn types and burn-related infections, in adult and pediatric patients. Second, to determine the effect of *Methicillin-Resistant Staphylococcus aureus* (MRSA) on length of hospital stay and, third, to determine if the microbiological profile differs in patients with severe and non-severe burns.

Methods: This is a retrospective chart review in which medical records of all burn patients admitted to Al-Noor Specialist Hospital, Makkah, Kingdom of Saudi Arabia between January 2016 and January 2017 were reviewed for demographic, microbiological, and burn data using a data-collection sheet. No randomization was necessary as all patients were included. Descriptive and inferential statistics were performed on the collected data.

Results: Of 250 patients, 53.6% were pediatric patients and 68.4% were male patients. The most common organism in blood and wound cultures of minor burns was *Staphylococcus aureus*. *Methicillin-resistant Staphylococcus aureus* (MRSA) frequency was 82.5%. Length of stay increased in patients with infected burn injuries.

Conclusion: The pediatric population had a high frequency of burn injuries, representing an incentive for more focused educational prevention programs in that group. Additionally, burn infections carry significant morbidity, and are associated with longer hospital stay. These data can help implement various prevention programs.

Keywords: burns, wound infection, sepsis, epidemiology, *Methicillin-resistant staphylococcus aureus*

Saudi Med J 2020; Vol. 41 (7): 726-732
doi: 10.15537/smj.2020.7.25141

From the Department of Plastic Surgery (Mater, Yamani), Burns Unit, Al-Noor Specialist Hospital, Makkah; Department of Pediatric Surgery (Aljuffri), King Abdulaziz Medical City, Ministry of National Guard Hospital; and from the College of Medicine (Binladen), King Saud Bin Abdulaziz University, Jeddah, Kingdom of Saudi Arabia.

Received 7th January 2020. Accepted 30th May 2020.

Address correspondence and reprint request to: Dr. Mohammed E. Mater, Department of Plastic Surgery, Burns Unit, Al-Noor Specialist Hospital, Makkah, Kingdom of Saudi Arabia. E-mail: Mohammedmater@outlook.com
ORCID ID: https://orcid.org/0000-0001-6229-2190

Burns are among the most devastating injuries, and lead to great mortality and morbidity. The fourth most common type of trauma worldwide, the World Health Organization (WHO) has estimated that burn injuries result in 265,000 deaths annually and roughly 11 million burn patients needed medical attention in 2004.[1] Burn rates within the east Mediterranean region have increased to an annual incidence of 518/100,000 from 112/100,000, with a mean mortality rate that ranges from 5-37%, in the years from 1989 to 2006.[2] However, one systematic review showed a decrease in mortality, length of stay (LOS), incidence and burn severity in burn patients worldwide.[3] A systematic review of severe burn injuries showed that a common cause of death in severe burn patients was sepsis, accounting for 2-14% of deaths.[4] Infections are a great source of mortality and morbidity in burn patients, with burn wounds and the bloodstream being frequent sites of infection. Various bacteria are implicated in burn-related infections. A study showed that *Acinetobacter baumannii*, followed by *Pseudomonas aeruginosa*, are the most common organisms in the burn intensive care unit (ICU). *Staphylococcus aureus*, followed by *Pseudomonas aeruginosa*, are the most common organisms in the regular burn unit.[5] A systematic review of burn wound infections showed that Gram-negative organisms are the most common organisms in burn wounds, with *Pseudomonas aeruginosa* being the most common organism overall.[6] In severe burn patients (≥40% TBSA), *Acinetobacter baumannii*, *Pseudomonas*, and *Methicillin-resistant Staphylococcus aureus* (MRSA) were predominant in burn-related infections.[7] There is a local data of burn wound infections from Taif, Saudi Arabia that showed a predominance of *Staphylococcus aureus* organism, followed by *Klebsiella*.[8]

A matter of great concern is the emergence of drug-resistance in Gram-positive organisms. *Methicillin-resistant Staphylococcus aureus* accounts for 98% of all *Staphylococcus aureus* infections within the burn ICU, and 67% in non-intensive care burn unit patients. Burn ICU patients have increased rates of drug resistant strains of Gram-negative organisms when compared to those in the regular burn unit.[5] Recent studies show that *Multidrug-resistant organisms* (MDRO) are associated with a greater number of surgical procedures, longer duration of mechanical ventilation, prolonged antibiotic therapy and longer hospitalization.[9] One study; however, showed that MRSA, when compared to *Methicillin-sensitive Staphylococcus aureus* (MSSA), did not increase LOS or mortality. Furthermore, another study showed that multi-drug resistant *Pseudomonas*, when compared to multi-drug sensitive *Pseudomonas*, did not increase mortality and LOS.[10] Due to the obvious lack of local data about the common burn infection organisms and their impact on burn prognosis, this research was conducted to illustrate the microbiological data of burn victims based on results from the largest burn unit in Saudi Arabia, and their sequelae in order to guide future research efforts in burn management.[11]

The objectives of this study are to first describe the epidemiological data of burns, including burn types and burn-related infections, in adult and pediatric patients. Second, to determine the effect of MRSA on length of hospital stay and, third, to determine if the microbiological profile differs in patients with severe and non-severe burns.

Methods. A retrospective chart review was conducted of all burn patients who were admitted and treated at Al-Noor Specialist Hospital, Riyadh, Saudi Arabia, between January 2016 and January 2017. The burn unit at Al-Noor specialist hospital is considered the largest in Saudi Arabia in terms of capacity.[11] It contains 21 beds and has an average admission rate of 200-250 patients per year. All acute burn patients from all age groups and both genders, with or without blood or wound cultures, admitted during the specified period, were included. Patients with chronic burn wounds and patients transferred from other hospitals were excluded, in order not to affect the microbial profile. Patients with incomplete medical charts were also excluded, making the total excluded patients 13. The pediatric age group was defined as patients <14 years old. Wound cultures were only taken when there were local and systemic signs of infection, such as increasing burn wound depth, erythema, and fever. The wound was copiously irrigated with saline and a swab was taken from the burn wound, not the donor sites. With regards to blood cultures, they were only drawn when patients exhibited systemic signs of infection, such as fever, and a change in white blood cell and platelet counts. The distinction between colonized versus infected wounds on culture results depended on 2 factors. The first factor is the clinical findings of the patient, whether he or she were having an infection or not. The second factor is the quantitative microbiology of the wound swab taken. A wound swab with a microbial load of $\geq 10^5$ CFU/g was considered

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

infected.[12] Systemic antibiotics were administered as soon as patients showed signs of infection only. The data were collected using a validated data collection form which included the patients' demographics (age and gender) and burn-related data (type of burn, total burn body surface area, culture results and length of hospital stay). All data were reviewed, organized, and tabulated in a spreadsheet format, which were then encoded into IBM SPSS Statistics (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Quantitative data were represented by mean, median and interquartile range. On the other hand, qualitative data were represented by frequencies and percentages. Comparisons among the groups were conducted using the Mann-Whitney test, student t-test and Chi-square test. Results were deemed significant when $p<0.05$. This study was conducted in compliance with the declaration of Helsinki and granted ethical approval by the Institutional Review Board (IRB) at the hospital.

Results. In total, 250 burn patients were included. A description of patients' demographics can be seen in **Table 1**. The majority of patients were males (171; 68.4%) and pediatric (134; 53.6%). The mean age was 19.79 years. The majority of burns were scald burns in the pediatrics age group (85; 63.4%), which is statistically significant when compared to the adult age group ($p<0.001$). In the adult age group, flame burns were the most common (n=70; 60.3%) ($p<0.001$.) Overall, scald burns were the most common (n=103; 41.2%), followed by flame burns (n=79; 38.8%).

Figure 1 summarized the overview of burns type. The mean total burned body surface area (TBSA) was 16.5% (SD 19.98), while the mean length of hospital stay was 16.18 days (SD 16.71). A TBSA burn of ≥40% was more common in adults (19.4%) compared to pediatrics (4.1%) ($p<0.001$.).

Blood cultures were drawn from 25.6% of our population, with only 39% being positive for infectious organisms. In addition, 33.2% of burn wounds were cultured with 57.8% returning positive for infection. For blood cultures, the majority were positive in adults (51.4%), whereas only 24.2% were positive in

Table 1 - Demographic characteristics of all burn patients who were admitted and treated at Al-Noor Specialist Hospital, Riyadh, Saudi Arabia between January 2016 and January 2017 (N=250).

Demographic characteristics	n (%)	Mean	Median	Interquartile Range
Age (years)		19.79	10	31
TBSA (%)		16.54	8	10
Length of stay (days)		16.18	12	17
Gender				
Male	171 (68.4)			
Female	79 (31.6)			
Mortality	12 (4.8)			

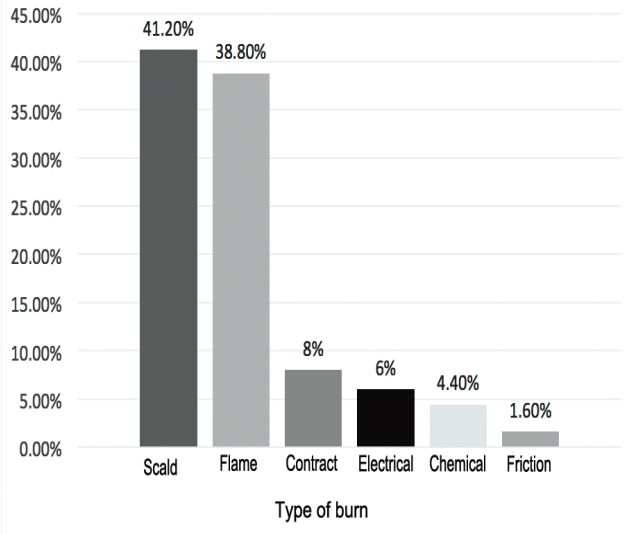

Figure 1 - Frequencies of different burn types.

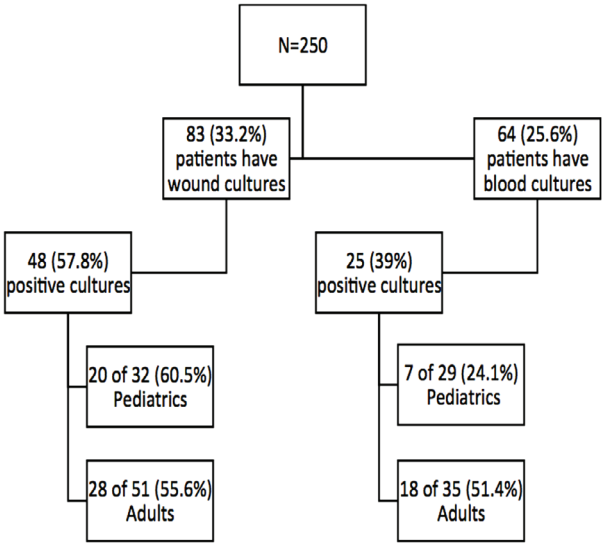

Figure 2 - Frequency of cultures.

the pediatric age group. As for burn wound cultures, 55.6% were positive in adults and 60.5% were positive in pediatrics (**Figure 2**).

Blood and wound cultures in pediatrics were 100% positive when TBSA was ≥40%. A TBSA of ≥40% predicted a positive blood culture in both the adult ($p \leq 0.041$) and pediatric population, ($p \leq 0.025$). On the other hand, it could not predict a positive wound culture in either group ($p \leq 0.431$ and $p \leq 0.486$).

Table 2 highlights the organisms isolated from blood and wound cultures. The most common isolated organisms in blood cultures were MRSA and coagulase-negative *Staphylococci* (both 26.5%), followed by *Klebsiella pneumoniae* (17.7%). For burn wound cultures, the most common isolated organism was MRSA (36.4%), followed by *Pseudomonas aeruginosa* (22.7%). In patients with ≥40% TBSA burns, wound cultures showed *Staphylococcus aureus* (n=7; 33.3%) to be the most common organism, followed by *Pseudomonas aeruginosa* (n=5; 24%), *Acinetobacter baummanii* and *Enterobacter cloacae* (**Figure 3**).

Acinetobacter baumannii was significantly more frequent in wounds in patients with ≥40% TBSA versus <40% (19% versus 2%) (p=0.005). Other organisms failed to show statistical significance. On the other hand, blood cultures in patients with ≥40% burn TBSA showed *Staphylococcus aureus* and coagulase negative *Staphylococcus species* to be the most common organisms (25%), followed by *Klebsiella pneumoniae* (20%), and *Acinetobacter baumannii* (15%) (**Figure 4**). In all cultures drawn, total MSSA was 6 (9.6%), with total MRSA being 33 (45.2%). Of all cultures positive for *Staphylococcus aureus*, MRSA was higher than MSSA (82.5% versus 17.5%). Positive blood cultures were polymicrobial in 16% and wound cultures were polymicrobial in 17% of the cases.

The student t-test was used to analyze the effect of

Table 2 - Microorganism profile of wound and blood cultures.

Microorganism	Burn wound cultures	Blood cultures
MRSA	36.36	26.47
MSSA	7.58	5.88
Enterobacter cloacae	12.12	5.88
Klebsiella pneumoniae	7.58	17.65
Proteus Mirabilis	1.52	Nil
Haemophilus influenzae	Nil	2.94
Acinetobacter baumannii	7.58	8.82
Candida albicans	1.52	2.94
Pseudomonas aeruginosa	22.73	2.94
Coagulase-negative *Staphylococcus*	3.03	26.47

Values are presented as number and percentage (%). MRSA: *Methicillin-resistant Staphylococcus aureus*, MSSA: *Methicillin-sensitive Staphylococcus aureus*

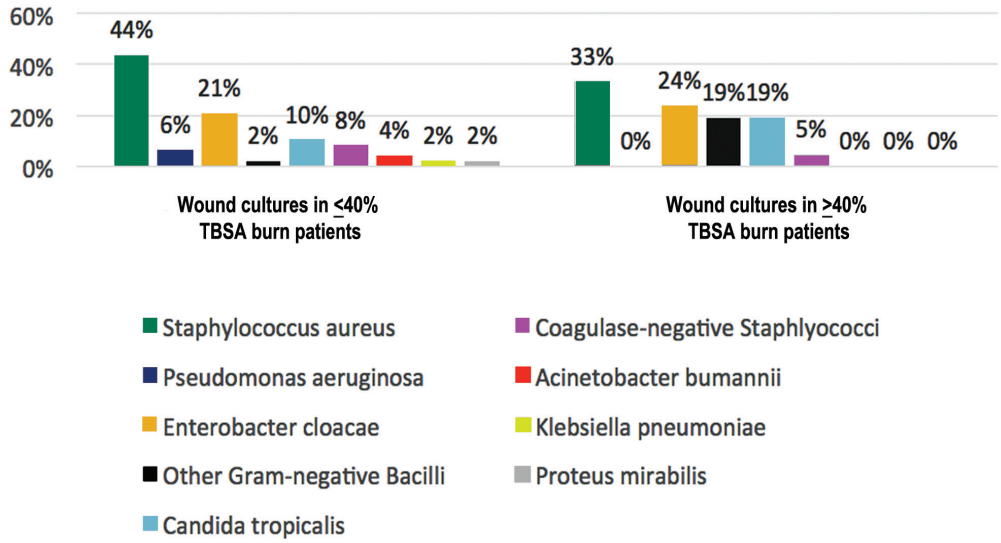

Figure 3 - Wound cultures based on total body surface area (TBSA).

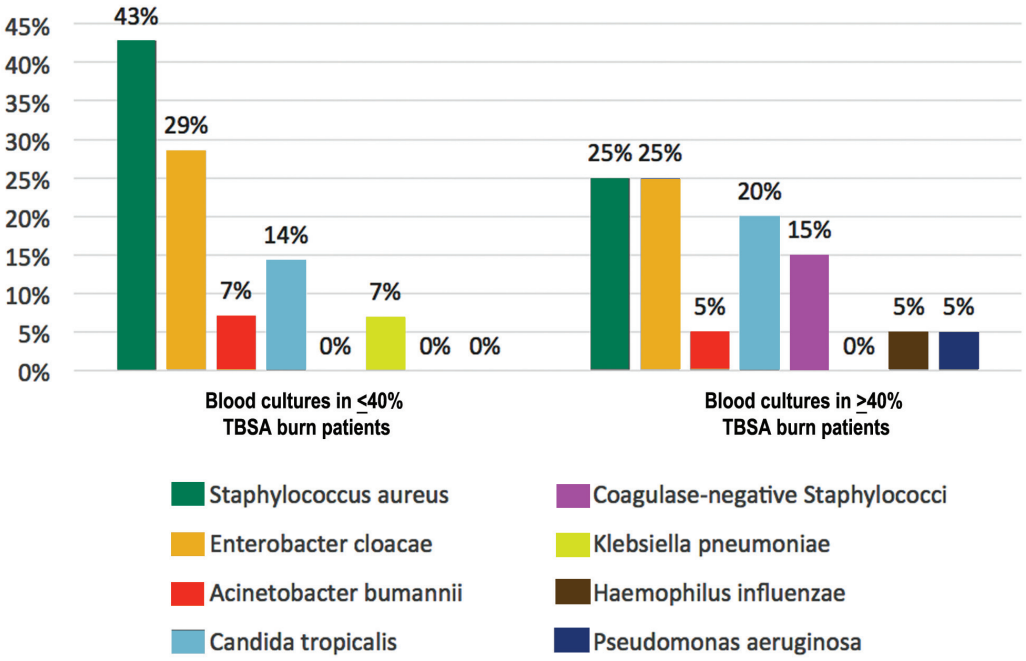

Figure 4 - Blood cultures based on total body surface area (TBSA).

positive cultures on length of stay. Patients with positive blood cultures had a significantly longer hospital stay (p<0.001) (95% CI: 12.72-33.47), as did patients with positive burn wound cultures (p=0.04) (95% CI: 0.97-19.58). In addition, the higher the TBSA the longer the hospital stay (p<0.001). *Methicillin-resistant Staphylococcus aureus* had no significant effect on length of hospital stay (p=0.71) (95% CI: -19.71-6.03), nor did MSSA (p=0.77) (95% CI: -15.87-25.58).

Discussion. Patients with serious burn injuries require immediate care in an exceedingly specialized burn unit to reduce morbidity and mortality. Although survival rates for burn patients have improved substantially within the past few decades because of advances in modern medical care in specialized burn centers, nosocomial infections still present a significant challenge for burn physicians treating burn patients and are known to cause over 50% of burn-related deaths.[8] Burns to adult males occur mostly in outdoor or work settings, while burns to adult females occur mostly at home.[13,14] In this study, more adult men (74.2%) than women (25.8%) suffered from burns. This may be due to the fact that men operate more machinery and drive cars while women did not at the time of the study. This is in concordance with a study by Al-Aali et al[8] in which males represented 72.2% and females 27.7% of burn injuries. Results published by the WHO differ, showing women have slightly higher rates of burns than men.[15]

In the literature, the consensus is that burns remain more common in the pediatric age group than adults and our study concurs with this.[16] Scald burns were the most common type of burns, followed by flame burns, contact burns, electrical burns, chemical burns and friction burns (**Figure 1**), slightly different in this study population than the East Mediterranean region.[2] In this study, scald burns (63.4%) were the most common in the pediatric age group while flame burns (60.3%) were the most common type of burn in the adult age group. A European systematic review reported a similarly high rate of scald burns in pediatrics at 30-80%.[4]

Heggers et al[17] mentions that burn wounds become infected due to the immunosuppressed state of the host and the wound environment, which are ideal for the proliferation of infecting organisms. Infections are a major source of mortality and morbidity in burn patients, with blood and burn wounds being common sources of infections.[5] There is a directly proportional association between TBSA and positive cultures in both the pediatric and adult populations. Blood and wound culture rates were found to be higher when the TBSA was ≥40% and were positive more commonly in

pediatrics (both 100%) than in adults (76.4%, 68.7% respectively). However, the percentages were lower when the TBSA was <40% with positive blood cultures in adults being 38.8% and 11.11% in pediatrics. The most common organisms isolated from burn wounds were MRSA (36.4%) followed by *Pseudomonas aeruginosa* (22.7%) (**Table 2**). Other studies also showed a high prevalence of *Staphylococcus* (27.6% and 20%, respectively) and *Pseudomonas aeruginosa* (12.3% and 39.5%, respectively) isolated from burn wounds.[5,8] The most common organisms isolated from blood cultures were MRSA (26.5%), coagulase-negative *Staphylococci* (26.5%) and *Klebsiella pneumoniae* (17.7%) (**Table 2**). Reports from Bahemia et al[8] also showed a high prevalence of *Staphylococcus* and Gram-negative bacteria in blood cultures. In severe burn patients with TBSA ≥40%, the most common isolated bacteria from burn wounds were *Staphylococcus aureus* (33%), *Psuedomonas aeruginosa* (24%), *Acinetobacter baumannii* and *Enterobacter cloacae* (each 19%) **(Figure 3).** Burn ICU patients have the same predominance of Gram-negative bacteria.[5]

The emergence of drug-resistant Gram-positive bacteria is a global crisis. The prevalence of MRSA infections worldwide is 13%-74%.[18] A study of the prevalence of MRSA in the Gulf Corporation Council Countries (GCC), also showed that Saudi Arabia reported the highest rate of MRSA (39%) and the lowest rate was reported in Kuwait (3.3%).[19,20] This study supports the previous study and reports a high rate of MRSA (82.5%). Of all cultures positive for *Staphylococcus aureu*s, MRSA was more common than MSSA (82.5% versus 17.5%). *Methicillin-resistant Staphylococcus aureus* frequency in burn infections was 98% of all *Staphylococcus aureus*-infected patients in the burn ICU, while the frequency decreased to 67% in the regular burn unit patients which is comparable to the results of our study.[5] Such high levels can be due to administering antibiotics after clinical decisions only, without further diagnostic investigations or general abuse of antibiotics.[19] Similar to other literature reports, MRSA did not affect the length of hospital stay.[10] There is a recent study that mentions reducing the use of fluoroquinolones and third generation cephalosporins (which have been associated with an increased rate of MRSA) as a potentially useful control measure in patient populations where MRSA is prevalent.[21] Similarly, a case-control study carried out in the United Kingdom stated that the higher the number of antimicrobial agents used, the higher the risk for MRSA with fluoroquinolones having the highest risk.[22]

Study limitations. This study was limited by 2 points which must be noted. First, data was collected over one year only (2016). Second, cultures data were restricted to blood and burn wound cultures, since they are the most frequently taken, and no data on antibiotics usage was recorded. No data was collected on any use of invasive devices, as it was not the scope of our study. However, the center we collected data from is the largest burn center in Saudi Arabia, and the sample represented all age groups.[11]

In conclusion, the pediatric population has an increased frequency of burn injuries which is an incentive for more focused educational prevention programs. Additionally, burn infections carry significant morbidity, and are associated with a longer hospital stay. Moreover, this study shows that MRSA rates are significantly high in burn infections, which can be attributed to the misuse of antibiotics. This should prompt better antibiotic stewardship and limit the use of fluoroquinolones and cephalosporins in particular as resistance has also shown to develop during therapy, especially in the pediatric age group.[23,24] Minimizing the use of these antibiotics can reduce the rate of MRSA infection.[25] More effective prevention of transmission by enforcing strict contact precautions is also useful. This data can be helpful to implement local and national programs aimed at the prevention of MRSA infection.

Acknowledgment. *The authors wish to acknowledge Yousef B. Abalkhail and Assal K. Al Amoudi for their contributions to this study, and PageCure (pagecure.com) for editing the language of the paper.*

References

1. Mathers C, Fat DM, Boerma JT. The global burden of disease: 2004 update. Geneva (SW): World Health Organization; 2008.
2. Othman N, Kendrick D. Epidemiology of burn injuries in the East Mediterranean Region: a systematic review. ***BMC Public Health*** 2010; 10: 83.
3. Smolle C, Cambiaso-Daniel J, Forbes AA, Wurzer P, Hundeshagen G, Branski LK, et al. Recent trends in burn epidemiology worldwide: A systematic review. ***Burns*** 2017; 43: 249-257.
4. Brusselaers N, Monstrey S, Vogelaers D, Hoste E, Blot S. Severe burn injury in Europe: a systematic review of the incidence, etiology, morbidity, and mortality. ***Crit Care*** 2010; 14: R188.
5. Yali G, Jing C, Chunjiang L, Cheng Z, Xiaoqiang L, Yizhi P. Comparison of pathogens and antibiotic resistance of burn patients in the burn ICU or in the common burn ward. ***Burns*** 2014; 40: 402-407.
6. Azzopardi EA, Azzopardi E, Camilleri L, Villapalos J, Boyce DE, Dziewulski P, et al. Gram negative wound infection in hospitalised adult burn patients-systematic review and metanalysis. ***PLoS One*** 2014; 9: e95042.

7. Bahemia IA, Muganza A, Moore R, Sahid F, Menezes CN. Microbiology and antibiotic resistance in severe burns patients: A 5 year review in an adult burns unit. ***Burns*** 2015; 41: 1536-1542.
8. Al-Aali KY. Microbial profile of burn wound infections in burn patients, Taif, Saudi Arabia. ***Arch Clin Microbiol*** 2016; 7: 2.
9. van Langeveld I, Gagnon RC, Conrad PF, Gamelli RL, Martin B, Choudhry MA, et al. Multiple-Drug Resistance in Burn Patients: A Retrospective Study on the Impact of Antibiotic Resistance on Survival and Length of Stay. ***J Burn Care Res*** 2017; 38: 99-105.
10. Sen S, Palmieri T, Greenhalgh D. Review of burn research for the year 2013. ***J Burn Care Res*** 2014; 35: 362-368.
11. Ministry of Health, Al Noor Specialist Hospital. Plastic Surgery 2017 [cited 2020]. Available from: http://www.nsh.med.sa/Pages/Plastic-surgery.aspx.
12. Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. ***Clin Microbiol Rev*** 2001; 14: 244-269.
13. Davies JW. The problems of burns in India. ***Burns*** 1990; Suppl 1: S1-S24.
14. Hemeda M, Maher A, Mabrouk A. Epidemiology of burns admitted to Ain Shams University burns unit, Cairo, Egypt. ***Burns*** 2003; 29: 353-358.
15. World Health Organization. Burns. [cited 2016 September]. Available from: https://www.who.int/news-room/fact-sheets/detail/burns
16. Fekih Hassen A, Ben Khalifa S, Daiki M. Epidemiological and bacteriological profiles in children with burns. ***Burns***. 2014; 40: 1040-1045.
17. Heggers JP, McCoy L, Reisner B, Smith M, Edgar P, Ramirez RJ. Alternate antimicrobial therapy for vancomycin-resistant enterococci burn wound infections. ***J Burn Care Rehabil*** 1998; 19: 399-403.
18. Köck R, Becker K, Cookson B, van Gemert-Pijnen J, Harbarth S, Kluytmans J, et al. *Methicillin-resistant Staphylococcus aureus* (MRSA): burden of disease and control challenges in Europe. ***Euro Surveill*** 2010; 15: 19688.
19. Adam KM, Abomughaid MM. Prevalence of Methicillin-resistant Staphylococcus Aureus in Saudi Arabia Revisited: A Meta-analysis. ***Open Public Health J*** 2018; 11: 584-591.
20. Aly M, Balkhy HH. The prevalence of antimicrobial resistance in clinical isolates from Gulf Corporation Council countries. ***Antimicrob Resist Infect Control*** 2012; 1: 26.
21. Byrne FM, Wilcox MH. MRSA prevention strategies and current guidelines. ***Injury*** 2011; 42 Suppl 5: S3-S6.
22. Schneider-Lindner V, Delaney JA, Dial S, Dascal A, Suissa S. Antimicrobial drugs and community-acquired methicillin-resistant Staphylococcus aureus, United Kingdom. ***Emerg Infect Dis*** 2007; 13: 994-1000.
23. Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, et al. EMERGEncy ID Net Study Group. *Methicillin-resistant S. aureus* infections among patients in the emergency department. ***N Engl J Med*** 2006; 355: 666-674.
24. Trucksis M, Hooper DC, Wolfson JS. Emerging resistance to fluoroquinolones in staphylococci: an alert. ***Ann Intern Med*** 1991; 114: 424-426.
25. Tacconelli E, De Angelis G, Cataldo MA, Pozzi E, Cauda R. Does antibiotic exposure increase the risk of *Methicillin-Resistant Staphylococcus aureus* (MRSA) isolation? A systematic review and meta-analysis. ***J Antimicrob Chemother*** 2008; 61: 26-38.