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Review Article

Nosocomial Infections in Iranian Pediatric Patients With Burn Injuries: A Review

Mohammad Sadegh Rezai[1,*] and Soheila Shahmohammadi[1]

[1]Mazandaran Pediatric Infectious Diseases Research Center, Bouali Sina Hospital, Mazandaran University of Medical Sciences, Sari, IR Iran

*Corresponding author: Mohammad Sadegh Rezai, Mazandaran Pediatric Infectious Diseases Research Center, Bouali Sina Hospital, Mazandaran University of Medical Sciences, Sari, IR Iran. Tel/Fax: +98-1133342334, E-mail: drmsrezaii@yahoo.com

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Context: Nosocomial infections (NIs) are the most common life-threatening complications and leading cause of morbidity and mortality in pediatric patients with burn injuries. It is estimated that annually two million infections, 90000 deaths, and 4.5 billion USD in excess healthcare costs are imposed by NIs. Herein, we reviewed the articles related to NIs in Iranian pediatric patients with burn injuries.

Evidence Acquisition: A review of epidemiologic studies on NI in pediatric patients with burn injuries in Iran was performed by searching studies indexed in PubMed, Google scholar, Iranmedex, Magiran, SID databases, published in English language in 2014. Keywords for searching included "Nosocomial Infections", "Hospital- acquired infection", "Healthcare- associated infections", "burn", "children", "pediatric", and "Iran". All articles related to NIs in pediatric patients with burn injuries or about general population with burn injuries, which included pediatric population up to the age 18 years in Iran, were included. Articles out of the definition for age group or lack of significant data, outpatients, and patients selected for reconstructive surgeries were excluded.

Results: Of 43 reviewed articles, nine eligible articles were selected. The male to female ratio was 1.6:1. The age ranged from birth to 18 years with the mean of 3.4 years. Overall incidence of NIs was 20.94%. *Pseudomonas aeruginosa* (30.39%), *Klebsiella pneumonia* (17.54%), *Acinetobacter* (17.47%), and *Staphylococcus aureus* (14.98%) were the most common prominent isolates with high antibiotic resistance isolated from the cultures of different sites of infections including burn wound. Vancomycin was highly specific antibiotic against Gram-positive bacteria isolates. All spices of *Acinetobacter* were multidrug resistant. The mean of mortality rate was 8.75%.

Conclusions: In spite of higher incidence of NIs in children with burn injuries, there are no well-described benchmark rates in this population. Further epidemiologic studies to identify knowledge gap regarding NIs in pediatric patients with burn in Iran is recommended.

Keywords: Nosocomial Infections; Burns; Pediatric; Iran

1. Context

Nosocomial infections (NIs), defined by national healthcare safety network (NHSN), are localized or systemic conditions caused by adverse reaction to the presence of an infectious agent(s) or its toxin(s), which was not present on admission. The typical incubation period for bacterial hospital-acquired infections (HAIs) is usually ≥ 48 hours after admission. Additionally, each infection should be assessed individually due to variation of incubation periods by the type of pathogen and patient's underlying diseases (1).

The NIs are also remained the most common cause of morbidity and mortality in hospitalized patients, with higher risk among patients admitted in burn care unit and a majority of these patients population is composed of children, most of whom are younger than four years (2-4). In Iran, burn has been reported the second most common cause of death following traffic accidents in individuals < 15 years old (5).

Both risk and causative microorganisms of burn wounds infection are related to the size of burn wound and the time of infection onset. Wound infections in patients with burn injuries can develop from either endogenous organisms frequently causing colonization of the wound or exogenous organisms. Burn wound colonization is essentially produced by Gram-positive organisms, antibiotic-susceptible Gram-negative organisms, and fungal agents. In burned patients with total body surface area (TBSA) less than 30%, Gram-positive cocci, composed of methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* (MRSA), were reported to be the most common causes of wound infections, while in patients with extensive burns with TBSA more 30%, Gram-negative bacteria, particularly *Pseudomonas aeruginosa,* were more common cause of infection (6). Although, over the last two decades *Pseudomonas* spp. and other Gram-negative bacteria were the most common organisms causing burn wound infection, they obviously declined due to improvements in the isolation of patients (7). According to a report by Mozingo and Pruitt (8), the most common microorganisms causing burn wound infection were mold species, principally *Aspergillus* spp. as a non-bacterial pathogen. They demonstrated that patients who had received broad-spectrum antimicrobial agents preoperatively or for treatment of complications following blood stream infections, or those with prolonged burn wounds opening were at higher risk of burn wound colonization or infection by non-bacterial pathogen such as yeasts, fungi, and multiple-drug resistant (MDR) bacteria (8). However, according to the previous epidemiologic studies in Iran, the majority of organisms such as *P. aeruginosa* and *S. aureus* associated with NIs in patients with burn injuries are MDR, and cause increasing length of hospital stay, prolonged therapy, and increased costs (9-11).

There are few epidemiologic studies related to NIs in pediatric population in Iran, and most of the epidemiologic studies are not specific for children, especially about pediatric with burn injuries (2, 12-16).

In spite of the progress made in the surveillance of HAIs or NIs by national nosocomial infection surveillance system (NNIS), a well-described benchmark rates for NIs definitions in pediatric patients with burn injuries are not available (17, 18).

Because the surveillance systems are the first step in developing infection control programs, performing epidemiologic studies to identify risk factors that predispose occurrence of burn injuries and feedback of collected data to healthcare providers for early detection of problems can be effective to develop preventive programs, improve outcome, and achieve effective NIs control strategies. Herein, we performed a retrospective review of epidemiologic studies on NIs among Iranian pediatric patients with burn injuries to identify the prevalence of NIs in this high-risk group of patients, to improve our knowledge regarding current epidemiologic status for a better planning, to provide the best care for this population, and to determine the accuracy of diagnosis of NI based on burn infection criteria as well as to distinguish between the primary and secondary bloodstream infection defined by center of control and prevention of diseases (CDC) and national health-care safety network (NHSN) surveillance systems.

2. Evidence Acquisition

A review of epidemiologic studies on NIs among Iranian pediatric patients with burn injuries was performed by searching of studies indexed in PubMed, Google scholar, Iranmedex, Magiran, and SID databases, published in English language. Keywords for searching articles were "nosocomial infection", "hospital-acquired infection", "healthcare-associated infections", "burn", "children", "pediatric", and "Iran." All articles concerning epidemiologic studies on NIs in pediatric patients with burn injuries or general population with burn, which included pediatric patients with up to 18 years in Iran, were included. Data such as number of patients, gender, age, cause of burn injury, location of burn wound, TBSA, time of burn wound infection, causes of infection, type of NI, antibiogram results, therapeutic agents, length of hospital stay, rational of antibiotic therapy, encoding gene, length of follow-up, and outcome were extracted. We excluded articles that had included patients out of the definition age group, lacked significant data, or concerned outpatients and patients selected for reconstructive surgeries. Flow Diagram for the studies included in review is demonstrated in Figure 1.

The NIs definitions in burn infections used in our review followed those of the CDC/NHSN surveillance definitions for specific types of infections modified in 2014 (19). The CDC/NHSN infection criteria, modified in 2014, was also used to distinguish between the primary and secondary nature of a blood steam infection (BSI), along with the definition of "matching organisms", important notes, and reporting instructions (19). Data were analyzed by SPSS 16 (SPSS Inc, Chicago, Illinois, the United States) through descriptive statistics and missing data were handled by weighting techniques.

3. Results

A total of 43 eligible articles were found. After excluding duplicates, independent titles and abstracts, or studies with inadequate data, and screening done by two independent reviewers, nine articles were selected. Four studies had described epidemiologic features of pediatric burn injuries, three were descriptive retrospective studies performed on NIs in general populations including pediatrics age group, and one had compared the effect of silver sulfadiazine dressing and nitrofurazone as topical therapy in pediatrics with burn injuries. None of the selected articles met all inclusion criteria for the review. Summary of data from the final nine reviewed articles are shown in Table 1.

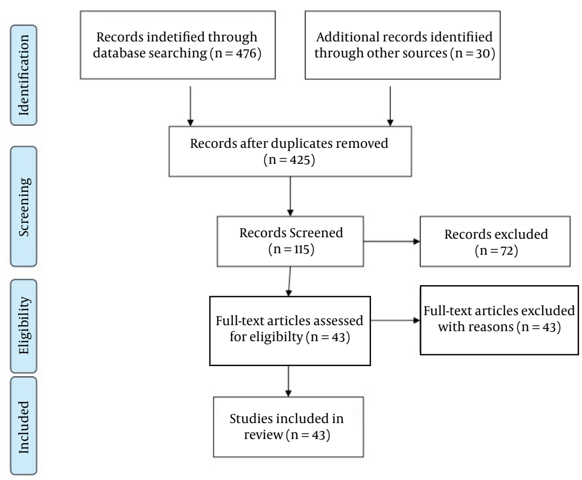

Figure 1. Flow Diagram for the Studies Included in Review

Table 1. Summary of Data Derived From the Final Nine Reviewed Articles [a]

Authors	Year	Study Design	Time of Burn Wound Infection	Categorization on of Nosocomial Infections and Causative Agents					Therapeutic Agents		Length of Hospital Stay	Outcome
				CVC	VAP	Urine	Sepsis	Burn Wound	Topical Antimicrobial	Systemic Antimicrobial		
Alaghehbandan et al. (20)	2001	Descriptive	-					+		-	1 - 156, 12.7 - 22.9 (Mean, 15.8) days	Overall MR, 16%; < 3y/o MR, 21.1%
Azimi et al. (2)	2011	Descriptive	First 48 hours				+ (Positive culture for *Pseudomonas aeruginosa* and/or *Acinetobacter*)	+ (Positive culture results for *Pseudomonas aeruginosa* and/or *Acinetobacter* at 1 week = 67%, 2 week 81%, 3 weeks 84%, 4 weeks)	Mupirocin 2%		At least 2 weeks	Overall MR, 12%
Rafii et al. (14)	2012				-	+					1 - 62 days (Mean, 7.5)	5.6 %
Rouzbahani et al. (12)	2004	Secondary data analysis	-		-	-	-	-	-	-	Mean, 10.6 days	Overall 6.9%, (5.5% in < 10 y/o; 10.8% in 6 - 10 y/o)
Behzadnia et al. (13)	2014	Retrospective cross-sectional			+ (*Pseudomonas* spp., 33.33%; *Escherichia coli,* 44.44%)	+ (*Pseudomonas* spp., 30.76%, *Acinetobacter,* 46.15%)		+ (*Pseudomonas* spp., 40%; *Acinetobacter,* 33/33%),			2 - 35 days (mean, 7 days)	

Darvishpour et al. (21)	2006	Semi-experimental	-				+	SS/daily dressing, Nitro/daily dressing	6.736 ± 11 (SS); 4.105 ± 10.6 (Nitro)	Similar therapeutic effect
Ekrami et al. (15)	2010	Descriptive	-		*Staphylococcus* spp., *Enterobacter* spp., *Escherichia coli*	*Pseudomonas aeruginosa, Acinetobacter baumannii, Proteus* spp. *baumannii, Proteus* spp.	*Pseudomonas aeruginosa*		1 - 311 (14 days), (< 7 days = 429 patients), (7 - 14 days = 323 patients)	MR, 8%
Alavi et al. (22)	2011	Descriptive		+		+				MR (7 (4%) = sepsis in 6 (86%); Respiratory infection in 1(14%)) with TBSA > 40%
Yousefi-Mashouf and Street (16)	2006	Retrospective				*Pseudomonas aeruginosa* (26.9%), *Klebsiella pneumonia* (30.4%), *Staphylococcus. aureus, Streptococcus. epdermidis, Escherichia coli* (28.6%), others	*Pseudomonas aeruginosa* (32.7%), *Klebsiella pneumonia* (28.1%), *Staphylococcus aureus* (21.2%), *Streptococcus epdermidis, Proteus mirabilis, Escherichia coli, Klebsiella oxytoca, Enterobacter ogglomerous, Proteus vulgaris, Enterococci* spp., others, *Proteus mirabilis, Escherichia coli, Klebsiella, Citrobacterfreu oxytoca*			

[a] Abbreviations: CVC, central venous catheter; VAP, ventilator-associated pneumonia; MR, mortality rate; SS, silver sulfadiazine; Nitro, nitrofurazone.

Out of 55314 hospitalized patients with burn injury, 6257 were ≤ 18 years old. Excluding 324 children not differentiated for sex, about 3649 patients (61.5%) were boys and 2284 (31.5 %) were girls. The male to female ratio was 1.6:1. The age ranged from birth to 18 years with the mean of 3.4 years.

As shown in Table 2, scalds were the most common type of burn injuries (50.23%), followed by flame and fire (28.8%), and other causes of burn (20.07%). The TBSA of the burned patients ranged from 1% to 100% with a median of 45%. Mean TBSA was 26.6% based on four of the selected articles that reported the values. However, the mean TBSA for the three articles, which included length of hospitalization, was 30.97%. The range of hospital stay was one to 311 days. Mean of the length of hospital stay, based on reports by three out of nine reviewed articles, was 13.47 days.

Burn wound infections as one of the most common types of NIs was reported in seven of the nine reviewed articles. Ventilator-associated pneumonia (2 studies), blood stream infections (2 studies), and urinary tract infections (2 studies) were the others common NIs in our review. The most common isolates from the clinical specimens and site of NIs were derived from four of the nine reviewed articles is shown in Table 3. The overall incidence of NIs was 20.94%. *Pseudomonas aeruginosa* (30.39%), *Klebsiella pneumonia* (17.54%), *Acinetobacter* (17.47%), and *Staphylococcus aureus* (14.98%) were the most common prominent isolates with high antibiotic resistance, isolated from the cultures of different sites of infections including burn wound (Table 4).

The most effective antibiotics against both Gram-positive and Gram-negative isolates were ciprofloxacin, ceftizoxime, and amikacin. Vancomycin was highly specific for Gram-positive bacteria isolates. High resistance to ampicillin, tetracycline, and carbenicillin were found. Table 5 shows the antibiotic susceptibility patterns of some isolates from wound infections reported in two out of nine reviewed articles by 14-year intervals (1998 - 2012). As shown in Table 5, all spices of *Acinetobacter* are MDR. Silver sulfadiazine and Nitrofurazone dressings were the topical antibiotic used for second- and third-degree burn wound infection. Mupirocin 2% was used as prophylactic topical antimicrobial agent for prevention and treatment of sepsis in patients with second- and third-degree burns. The mean of mortality rate, derived from six of total nine articles, was 8.75%, but the mean of mortality rates obtained by the two of the nine studies in pediatric patients with burn injuries aging < 10 years was 12.46%. Except one, none of the reviewed articles included data about rational of antibiotic therapy and length of follow-up, and none of them had mentioned encoding gene.

4. Discussions

This review of nine observational studies on NIs among Iranian pediatric patients with burn injuries revealed the knowledge gap in previous epidemiologic studies regarding the prevalence of NIs in this high-risk group of patients. It emphasized on the needs to provide the best care for this population and to develop a well-described benchmark to determine the accuracy of diagnosis of NIs based on burn infection criteria, and distinguish between the primary and secondary bloodstream infection defined by CDC/NHSN surveillance systems.

We found report about neither the exact prevalence and type of NIs nor the main isolates causing NIs among children with burn injuries aging < 18 years in Iran. Because in most of the reviewed articles children were as a part of the studied general population, the results of previous epidemiologic studies were not the real representative of Iranian pediatric patients with burn injuries in the general population (2, 12-16).

The mean age of the patients in our review was also about 3.4 years and most of them were male, which was in agreement with the five of the nine selected studies (12, 14, 15, 20, 22).

Related to burned TBSA and length of hospitalization, a significant association between mean age, sex, mean burned TBSA, and length of hospital stay was reported by the four of the reviewed articles ($P < 0.0001$) (12, 15, 16, 20). Normal skin as a barrier against penetration of microorganisms is lost following burn injury, and a serious cross-infection provided by drug-resistant microorganisms such as *P. aeruginosa* and MRSA in patients with burned TBSA of > 30% was reported (16, 23). Overall, we could find no correlation between mean burned TBSA and mean of length of hospitalization for our review due to lack of data. However, based on the three articles, in cases of burned TBSA of > 30%, prolonged length of hospitalization of > 10 days increases the risk of NIs and costs for patients and healthcare services.

Regarding etiologies of burn wound infection, a high resistance of *P. aeruginosa,* as a causative agent of NI, to the most of antimicrobial agents was reported (20, 24, 25). Azimi et al. (2) identified more than one bacteria from the wounds in 95% of samples. In their study, in first 48 hours of admission, results of 40% of cultures were positive without *Pseudomonas* and *Acinetobacter* species (differentiation of present on admission and Nis). At the end of the first week, 67% of patients had at least one *Pseudomonas* and/or *Acinetobacter* isolate in their cultures that increased gradually in the second (81%), third (84%), and fourth (98%) weeks. Blood samples were positive in 29% of cases. Of the positive results, 85% were *Pseudomonas* and 15% were *Acinetobacter* species (Secondary BSI). They believed that replacement of positive cultures and colonization of negative cultures can show changing of different genus and species of bacteria in positive and negative cultures that reveal NI in burn wound. From the similarity between isolates from the wound and blood culture, presence of second BSI can be concluded (2). The most common bacteria isolated by Behzadnia et al. (13) from the burn wound were also *P. aeruginosa* and *Acinetobacter species*. Similar results were found in other studies and the results of our review (26-28). Behzadnia et al. (13) also found underlying diseases including diabetes mellitus and use of steroids, as established risk factors for NIs, among pediatric patients with burn injuries.

Table 2. Demographic Characteristics of Pediatric Burned Studied Population [a]

Authors	Year	Total Number of Patients (Children and Adults)	Total Number of Children	Gender		Age Range	Mean Age, y	Causes of Burn, %	Site of Burn Injuries, %	TBSA	MR
				Male	Female						
Alaghehbandan et al. (20)	2001	3341	1454	1056	398	≤ 1 mo to 15 y	5.3	Flame (35.7), Scalds (56), Electrical l (3.9), Chemical (0.5)	-	1% - 100%; over all Mean, 25.9%; TBSA < 40%, 945 (65%)	16% (overall), (MR in < 3 y/o = 21.1%)
Azimi et al. (2)	2011	164	32	-	-	1 - 18 y	-	-	-	8%-100%	12% (overall)
Rafii et al. (14)	2012	2229	1014	610	404	0 - 15 y (most age range, 3-6 y; < 6, 593 (58.7%))	-	Hot water & Scald (51.8); Electrical (1.8)	-	≤ 10% to ≥ 41%	5.6%
Rouzbahani et al. (12)	2004	1085	541	315	226	0 - 18, y (< 5 y, 23%)	-	Scald (62); Fire and Gas (17); Electrical (1.7); Others (19.3)	-	1% - 100% (Mean, 28.3%)	Overall 6.9 %, (in < 10 y/o = 5.5%; in 6 - 10 y/o = 10.8%)
Behzadnia et al. (13)	2014	34556	34	-	-	1 d to 12 y	6 ± 4.32	-	-	-	-
Darvishpour et al. (21)	2006	60	60	-	-	0 - 14 y	-	Hot water and Scald	All parts of body except face and perineal area	≤ 20% (II and III degree)	-
Ekrami et al. (15)	2010	6082	2786	1594	1192	0 - 18 y	-	Fire, hot fluid (71.5); electrical, others	-	1% - 100% (mean, 38.7%)	8%
Alavi et al. (22)	2011	7341	138	74	64	20 d to 14 y	3.76	Scald (79); chemical (4); flame & fire (12); electrical (5)	Trunk (23); extremities, (5); head and neck (6); face (18); others	1% - 90% (II = 79%), (III = 43%); Mean TBSA, 13.7%	%4
Yousefi-Mashouf and Street (16)	2006	456	198	-	-	0 - 18 y	-	Scald (boiled water, hot liquids) (26.5); fire and flame (25.6); chemical (8.9); electrical (0.9)	Head & neck, trunk, extremities, others	1% to > 30%	-

[a] Abbreviations: MR, mortality rate; TBSA, total body surface area.

Table 3. The Most Common Isolates From the Clinical Specimens and Site of Nosocomial Infections Derived From Four of the Nine Reviewed Articles [a]

Author/Date	Year	Time of Burn Wound Infection	Gram Negative [b]					Gram Positive [b]			Fungal	Most Isolate
			Pseudomonas spp.	*Acinetobacter* spp.	*Pseudomonas* + *Acinetobacter*	*Klebsiella* spp.	*Escherichia coli*	*Staphylococcus aureus*	*Streptococcus epidermidis*	*Enterobacter* spp.	*Candida albicans*	
Azimi et al. (2)	2011	-, First 48 h, end of 1st week (67%), 2nd week (81%), 3rd week (84%), 4th week (98%)	325 (40), 4 (16), 49 (55.5), 61 (33.3), 37 (40.6), 26 (30.9)	132 (16), 1 (4), 9 (9.2), 19 (10.3), 2 (2.1), 6 (7.1)	-, -, 6 (6.1), 28 (15.3), 13 (14.2), 15 (17.8)	215 (27), -, -, -, -	-, -, -, -, -	-, -, 15 (15.4), 17 (9.2), 5 (5.4), 1(1.2)	-, -, -, -, -		-, -, -, -, -	*Pseudomonas* (40%), *Acinetobacter* (17%), *Staphylococcus aureus* (16%)
Behzadnia et al. (13)	2014	-	57 (36.84), W = 12 (40), U = 3 (33.33), Vap = 4 (30.76)	16 (28.07), W = 10 (33.33), U = 0, Vap = 6 (46.15)	-, -, -, -	3 (5.26), W = 0, U = 0, Vap = 2 (15.38)	4 (7.01), W = 0, U = 4 (44.44)	2 (3.50), W = 2 (6.66), U = 0, -	3 (5.26), W = 2 (6.66), U = 0, -	-, W = 2 (6.66), U = 1 (20), -	2 (3.50), W = 0, U = 0, Vap = 2 (22.22)	*Pseudomonas* (36.84%), *Acinetobacter* (28.02%)
Ekrami et al. (15)	2010	-	W = 51.4, U = 14.2, BSI = 41.1	W = 2.4, U = 5.8, BSI = 3.6	-	-	W = 8.6, U = 24.8, BSI = 12.3	W = 23.3, U = 24.8, BSI = 29.4	-	W = 12.6, U = 24.8, BSI = 12.3	-	*Pseudomonas* (47.7%)
Yousefi-Mashouf and Street (16)	2006	-	W = 176 (32.7), -, BSI = 36 (26.9)	-, -, -	-, -, -	W = 117 (21.8), -, BSI = 40 (30.4)	W = 21 (3.9), -, BSI = 22 (16.5)	W = 114 (21.2), -, BSI = 8 (6.2)	W = 279 (5.1), -, BSI = 16 (12.1)	W = 10 (1.6), -, -	-, -, -	*Pseudomonas aeruginosa* (32.7%), *Klebsiella* (21.8%), *S. aureus* (21.2%)

[a] Abbreviations: BSI, blood stream infection; VAP, ventilatory associated infection ; W, wound; U, urine.
[b] Values are presented as No. (%) or %.

Table 4. Distribution of Most Common Isolate and Type of Nosocomial Infections Derived From Four of Nine Reviewed Articles [a,b]

Type of NIs	*Pseudomonas aeruginosa*	*Acinetobacter*	*Staphylococcus aureus*	*Klebsiella pneumonia*	Total Mean
Wound infection	40.0, 40.0, 51.4, 32.7	16.00, 33.33, 2.4, NR	7.8, 6.66, 23.3, 21.2	27, NR, NR, 21.8	
Mean wound infection	41.02	17.24	14.74	24.35	24.35
UTI	NR, 33.33, 14.2, 0.0	NR, 0.0, 5.8, NR	NR, 0.0, 24.8, NR	NR, 0.0, NR, NR	
Mean UTI	15.84	2.9	12.4	0.0	13.59
VAP	NR, 30.76, NR, NR	NR, 46.15, NR, NR	NR, NR, NR, NR	NR,15.38, NR, NR	
Mean VAP	30.76	46.15	-	15.38	30.8
BSI	NR, NR, 41.1, 26.9	NR, NR, 3.6, NR	NR, NR, 29.4, 6.2	NR, NR, NR, 30.4	
Mean BSI	34	3.6	17.8	30.4	15

[a] Abbreviation: BSI, blood stream infection; NIs, nosocomial infections; NR, not reported; UTI, urinary tract infection; VAP, ventilator-associated pneumonia

[b] Values are presented as %.

Table 5. Antibiotic Susceptibility Patterns of Some Isolates Resistant to Antibiotics From Wound Infections Reported in Two Out of Nine Reviewed Articles With Fourteen Years Intervals (1998 - 2012) [a,b]

Used Antibiotics	Year	*Staphylococcus saprophyticus* (R)	*Staphylococcus aureus* (R)	*Klebsiella* spp. (R)	*Enterobacter* (R)	*Escherichia coli* (R)	*Acinetobacter* spp. (R)	*Pseudomonas* spp. (R)
Behzadnia et al. (13) [c]	2014							
AM		100	100	100	66.6	100	100	57.14
TE		66	100	-	100	100	100	71.42
CF		-	-	-	-	-	-	-
CB		33	100	-	66.6	100	100	42.85
CT		100	-	-	-	66.6	100	42.85
GM		-	-	66.6	100	100	100	42.85
AN		-	-	-	-	-	100	50
CP		100	100	-	100	100	100	99.4
Yousefi-Mashouf and Street (16)	2006							
AM		-	96	93	81	82	-	100
TE		-	94	25	68	81	-	86
CF		-	78	47	52	58	-	62
CB		-	53	16	71	68	-	88
CT		-	18	87	26	14	-	21
GM		-	32	28	18	39	-	79
AN		-	38	70	22	64	-	32
CP		-	11	92	11	9	-	12

[a] Abbreviations: AM; Ampicillin, AN; amikacin, CB; carbenicillin, CF; cephalexin, CT; Ceftizoxime, CP; ciprofloxacin; GM; gentamicin; R, Resistant; TE; Tetracycline.

[b] Data are presented as %.

[c] The burn and surgical wounds infections in this study was not discriminated from each other. No common isolates or no common antibiotic were used.

They reported that *Pseudomonas* species isolated from clinical samples in their study were highly resistant to third-generation of cephalosporins, aminoglycosides, and fluoroquinolones. Enterobacteriaceae species showed high level of resistance to antibiotics. In recent years, true fungi have replaced bacteria as the most common microorganisms causing burn wound infection (8, 29). Fungal infection was reported only in one from the reviewed articles. Mozingo et al. (23) reported mold species, principally *Aspergillus* species, as nonbacterial pathogens (29). We conclude that lake of controlling of fungal infection by routine culture can be the cause of low fungal infection among our studied population (13). Although herpes simplex viral infection in burn infections was reported by Kagan et al. (30), we found no herpes simplex viral infection in our review. Similar to Ekrami et al. (15), Sengupta et al. (31) reported *Acinetobacter baumanni* as a rapid emerging MDR germ; as skin flora, these strains have been reported to be easily transmitted due viability in a hospital environment as an MDR isolates. In epidemiological study conducted by Yousefi- Mashouf and Street (16), *P. aeruginosa* was the most prevalence isolated Gram negative microorganism similar to other study (32) and *Klebsiella pneumonia* was the second cause of infections of burn wound in dissimilar to report by others (32-35).

Regarding type of NIs, infection at the other sites of burn wound, predominantly the lungs as the clinical manifestations of the systematic immunosuppressive effects of burn injury remains the most common cause of morbidity and mortality among patients with severe burned injury (36). Although VAP was reported in two of the 9 reviewed articles, but due to non- selective pediatric patients with burn injuries as an exact studied population, we could not obtain the exact estimation of VAP among Iranian pediatrics burned patients population (13, 22). Behzadnia et al. (13) reported that among their pediatric patients with burn injuries, wound infection was the most common type of NI, followed by urinary tract infection and respiratory tract infection. The NIs with urine, blood, and wound sources were also detected by Ekrami et al. (15) in hospitalized patients with burn injuries including pediatric patients of up to 18 years of age.

In a study by Weber et al. (17) about NI in pediatric patients with burn injuries, a modified NI surveillance system was introduced. They revised the CDC definition of burn wound infection that allowed categorizing the infected burn wound into the colonized, noninvasive infected, and invasive infected burn wound subcategories (17). While the standard CDC definition of burn infection only defined invasive infection, and did not included colonization (13). Colonization as a category of noninvasive infected burn wound was reported in the two articles of reviewed articles (2, 21). Darvishpour et al. (21) reported discrepancy between clinical diagnosis of burn wound infections and microbiological findings. They concluded that although the laboratory results were positive due to colonization not invasive wound infection, the clinical features of patients were good and epithelial tissues were presented at the site of burn wounds. Swab contamination was another reason explained by the authors (21). Colonization of negative cultures isolated from infected burn wound was also reported by Azimi et al. (2) as a cause of NI in patients with burn injuries.

Related to morbidity and mortality rate of burn victims, occurrence of invasive burn infection and the rate of morbidity and mortality due to infection have significantly reduced by development of wound care over the four past decays, such as using effective topical antimicrobial chemotherapy, prompt surgical excision, and timely closure of the burn wound (23). The fatality rate reported by Alaghehbandan et al. (20) was higher than the case fatality reported by our review and others (37-40). Rafii et al. (14) reported that better diagnosis, management, and referring the patients to specialized center could be contributed to lowering trend in the mortality rate. They also found that the incidence of burn was higher in urban area than in rural area, but flame and fire were more common causes of burn in rural area that could be related to their lifestyle (13). The lowest mortality rate was 10.8%, reported by Rouzbahani et al. (12) in children aged six to ten years. The mortality rate among children <10 years was 5.5% of the total mortality rate in their study. They concluded the low mortality rate in those < 10 years of age was due to minor burns with low burned TBSA caused by scalds (12). Ekrami et al. (15) believed that high mortality rate could be due to old hospital structure, insufficient personnel, and large number of admitted patients. This result has shown similarity with the result of our review.

With regard to treatment of burn wound, both topical and systemic antimicrobial therapies are used for prevention and control of burn wound infections. The three most common used topical antimicrobial agents for care of burn wound are silver sulfadiazine, Mafenide acetate, applied on the burn wound as topical creams, and silver nitrate as a 0.5% solution (41, 42). The gold standard of topical burn wound treatment is silver sulfadiazine (43). Although in Azimi et al. (2) study neither type of administered topical antiseptic agent nor the effectiveness of this therapy was reported, based on decreasing the mortality rate compared to the previous studies, from 19% in Tehran and 34.45% in southwest of Iran to 12% in their study, it can be concluded that use of topical antimicrobial agents was effective (2, 10, 44). They also, reported that 2% mupirocin ointment was effective equally in decreasing bacterial counts in local burn wound and preventing of systemic infection (2). By comparing the dressing of 1% silver sulfadiazine cream, as a gold standard, with nitrofurazone topical antimicrobial agents for care of the wound in pediatric patients with burn injuries, Darvishpour et al. (21) reported that the efficacy of the two agents were equal and stated that only frequent use of a therapeutic agents could not be the reason of its efficacy. In this review, systemic antibiotic therapy was reported in two reviewed articles (13, 16). The most common antibiotics were ampicillin, tetracycline, cephalexin, carbenicillin, ceftizoxime, gentamicin, amikacin, and ciprofloxacin. In cases of fungal burn wound infections, if fungal infection invades the underlying viable tissue or is associated with systemic signs of sepsis, parental administration of amphotericin B should be started (23).

Prevention of burn wound infection is emphasized in general care of the patients with severe burn injuries by preventing infection complications, mainly through environmental control to minimize cross-contamination such as single-bed rooms isolation for prevention of patient-to-patient contact, airflow patterns of the isolation rooms including positive airflow design to delay colonization by HAI flora and negative airflow design for patients with airborne route infections, and application of topical antimicrobial prophylaxis for the burn wound. The typically colonization surveillance program introduced by Mozingo and Pruitt (23) was composed of twice-weekly cultures of sputum and the burn wound surface, and twice-weekly cultures of urine and stool. Antibiotic sensitivity test for the predominant isolates or targeted organisms can be helpful to recognize the cross-contamination problems and MDR bacteria in the units' normal flora, and more importantly, to avoid administration of unnecessary and inappropriate antibiotics to minimize the emergence of microbial resistant (45, 46).

Despite higher incidence of NIs in children with burn injuries, there are no well-described benchmark rates in this high-risk population. The NIs in pediatric patients with burn injuries result in increasing mortality and high costs for patients' families and healthcare centers, and require special attention in controlling and prevention of infection complications. Providing a NI surveillance system for pediatric patients with burn injury is recommended to identify the risk factors, to evaluate current treatments, to identify signs of infections, and more importantly, to identify knowledge gap regarding the NIs in this high-risk group of patients with burn in Iran.

Authors' Contributions

Both of the two authors have been contributed in all stages to provide the review article.

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