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Bacterial Profile and Antimicrobial Resistance of Infections Among Hospitalized Burn Patients in Asia: A Systematic Review

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ABSTRACT

Burn injuries cause a considered number of deaths, mainly due to infections. Many low and middle-income countries in Asia lack data on the causes of burn infections and their antimicrobials susceptibility patterns. This systematic review was conducted to analyze Asian studies on the main agents of infection among hospitalized burn patients and their antimicrobials resistance to guide the empirical treatment which is very important for nosocomial infection control.

A literature search was performed in electronic databases to identify related studies between 2013 and 2022. All the finding studies were screened to ensure compliance with including criteria.

After the full screening of the articles, 24 studies were included in this work. The majority of pathogens were gram-negative bacteria (63.5%). The pooled prevalence of isolated bacteria of burn infection revealed that *A. baumannii* (23.8%), *P. aeruginosa* (20%), *S. aureus* (19.7%), and *K. pneumoniae* (11.5%) were the most frequent. According to the pooled results of Antimicrobial Susceptibility Testing (AST) of the included studies, most strains of isolated bacteria were multidrug-resistant (MDR). For gram-negative bacteria, the susceptibility pattern varies greatly according to the genus. The levofloxacin is the only common effective antimicrobial in different percentages. *Methicillin-resistant Staphylococcus aureus* (MRSA) accounted for 70.4% of the isolated S. aureus. Vancomycin and linezolid have a high susceptibility for all gram-positive cocci.

This review suggests that the empirical therapy of hospitalized burn patients in Asia should depend on the combination of antimicrobials that include levofloxacin to prevent increasing MDR emergence in the future. Further studies should be conducted to confirm the clinical effect of these procedures.

1. Introduction

The World Health Organization (WHO) has stated that burn injuries lead to 180,000 deaths annually, and half of these deaths are in southeast Asia (WHO, 2022). Furthermore, 75% of mortalities in burn patients are due to infections (Wang et al., 2010). Damage to the protective skin barrier and immune system, translocation of the bacteria in the gastrointestinal tract, prolonged stay at the hospital, and invasive diagnostic and therapeutic procedures (such as excision, endoscopy, catheter, and surgery) contribute to and accelerate the occurrence of infection among burn patients (Markiewicz-Gospodarek et al., 2022). By reviewing the literature on burn infection, there is continuous evolution in the bacterial profile and antimicrobial resistance (Kulkarni et al., 2015; Nazir et al. 2020; Hameed et al., 2014; Hateet, 2021). Multidrug-resistant (MDR) bacteria which are according to (Magiorakos et al., 2012) non-susceptible to at least one agent of antibacterial in at least three classes of antimicrobials have reported a marked rise in most recent papers. In Iran, 30.3% of *Pseudomonas aeruginosa* were MDR (Hashemzadeh et al., 2022), while in the United States the prevalence of MDR among gram-negative bacteria was 41.3% (Evans et al., 2017), and this rate was higher in Algeria reaching 64% (Tchakal-Mesbahi et al., 2021). MDR has limited choices of treatment and is linked to a high rate of mortality (WHO, 2012). Therefore, the recognition of microbiological profile and antimicrobial susceptibility among burn patients is very important to guide the empirical therapy for preventing the emergence of MDR and reducing morbidity and mortality (WHO, 2012). The proper empirical treatment is very critical, especially, in low and middle-income countries, where the antimicrobial susceptibility test (AST) is not available for all patients, and the bacterial culture/ susceptibility report needs a few days for delivery. One of the most important measures for controlling infectious outbreaks in low and middle-income countries is achieving an antimicrobial stewardship program (Caeiro and Garzón, 2018). Studies have concluded that an improper empirical antimicrobial regimen and the unnecessary use of broad-spectrum antimicrobial can be harmful and increase the resistance (Klinker, 2021). Therefore, the main aim of this work was to present a guide for empirical therapy of hospitalized burn patients in low and middle-income countries in Asia, by continental estimation of the bacterial profile and antimicrobial susceptibility among these patients, based on the analysis of related research which published in the last decade (2013-2022) in Asia.

2. Methods

2.1. Data sources and search strategy

A literature search of PubMed and Google scholar was made from 2013 to 2022 by two team members independently, based on a combination of any keywords related to the subject "burn infection", "bacterial profile", "microbial spectrum", "antibiotic", "antimicrobial", "nosocomial infection", "multidrug-resistance", "*Enterobacteriaceae", "Acinetobacter*", "*Pseudomonas*", "*s. aureus", "Klebsiella"*, and "Asia". Finally, the bibliographies and related articles of each included study were also reviewed for identifying more articles.

2.2. Studies selection

The initial screening was performed based on the title and abstract, then a full-text screening was done of potentially eligible studies based on the availability of the following criteria: the study should be conducted at a hospital in Asia, published after 2012 in a peer-reviewed journal in English, and involve the result of the bacterial profile of burn infection and/ or the result of antimicrobial susceptibility based on the criteria of Clinical and Laboratory Standards Institute (CLSI)

2.3. Data extraction

The name of the first author, country, publication year, study design, sample sources, number of isolated strains, and the methods of identification and antimicrobial susceptibility were extracted from included studies. Data on the frequency of each isolated genus, and the percentage of resistance of each antimicrobial against each

genus were collected from eligible studies through Microsoft Excel for the creation of required charts, tables, and calculations.
The prevalence of each genus and each antimicrobial resistance in Asia was determined based on the median of all the included studies. The presence of outliers data makes the median more accurate than the mean (Von Hippel, 2005).

2.4. Statistical analysis

Data were extracted in Microsoft Excel format, followed by analysis using STATA Version 14.0 statistical software. A random effect model was applied to estimate the pooled estimate and antimicrobial resistance pattern of the isolates. We conducted meta-regression to understand the source of heterogeneity and pooled the estimate using "metaprop" command. The potential source of heterogeneity was investigated by subgroup and meta-regression analysis. The existence of heterogeneity among studies were examined by I^2 heterogeneity test, in which 0–40%, 50–60%, 50–90% and 75–100% represented low, moderate, substantial and considerable heterogeneity, respectively. I2 heterogeneity test of ≥ 50% and a p value of < 0.05 was assured the presence of heterogeneity. Thus, the DerSimonian–Laired random effects model was employed (DerSimonian, 1986).

3. Results

3.1. Search Results

The literature search revealed 3018 articles that had been published between 2013 and 2022, 1879 articles were left after removing duplicates. Out of which, 1505 articles were excluded based on the title, country, and abstract screening. The full text of the 374 remaining articles was further assessed, but 350 were excluded for various reasons such as full text is not available, the articles were not published in English, or the results were not sufficient. Finally, 24 studies were included in this review. (Figure 1)

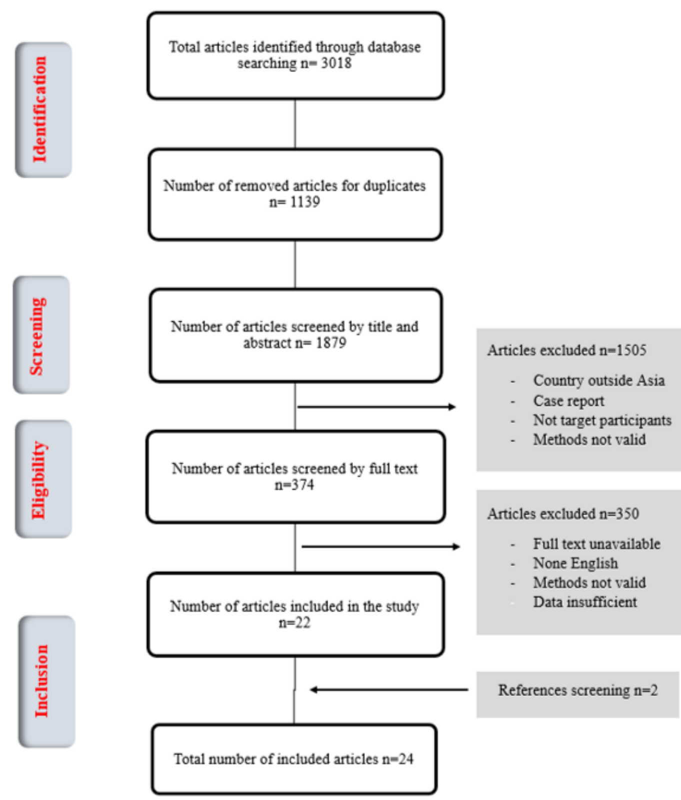

Figure 1. Flow diagram of included studies

3.2. Study Characteristics

The main characteristics of the included studies are presented in Table 1. The twenty-four studies were conducted in 10 countries in Asia. The eligible studies included 18 (75%) studies published between 2013 and 2020, and 6 (25%) studies were published after 2020. All the studies were hospital-based without any age boundary. Half of the studies had a prospective design while the second half had a retrospective design.
The main sample of 70.8% of eligible studies was burn wound swabs, while different clinical samples were collected in the remaining studies although the swab formed more than 75% of the total samples. A total of 18184 bacterial strains were collected from all the included studies.
The culture was the approved method for isolation in all the studies. For the identification, 14 studies applied conventional methods

including gram stain and biochemical tests, 5 studies applied Analytical Profile Index (API), and 5 studies used automated methods (VITEK, Phoenix). The disk diffusion technique was the main method for AST except for five studies that used automated methods.

3.3. Bacterial profile

The majority of pathogens were gram-negative bacteria which accounted for 63.5% (11545/18184 strains), whereas gram-positive bacteria constituted 36.6% (6639/18184 strains). Generally, there were four species that are the most common in all studies, but in different percentages. These species are *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*. There was no agreement between countries or even between studies in the same country on the most predominant bacterial agent of infections among hospitalized burn patients (Table 2). For example, *P. aeruginosa* was the most common in Iraq (Hameed et al., 2014), Bangladesh (Alam et al., 2014), Indonesia (Alam et al., 2017), Iran (Emami et al., 2020), and Pakistan (Saaiq et al., 2015; Chaudhary et al., 2019), whereas *S. aureus* was the most common in China (Cen et al., 2015; Li et al., 2018; Chen et al., 2021), and Iraq (Rashid et al., 2017). *A. baumannii* was the majority of pathogens in China (Wang et al., 2014), Kuwait (ALfadli et al., 2018), and Turkey (Yolbaş et al., 2013), while *coagulase-negative Staphylococcus aureus* (CONS) was the majority in turkey (Asena et al., 2020). After calculating the pooled prevalence of the species in Asian countries, it was found that the most common bacterial species responsible for infections among hospitalized burn patients in Asia were: *A. baumannii* (23.8%), *P. aeruginosa* (20%), *S. aureus* (19.7%), and *K. pneumoniae* (11.5%). (Table 2.)

3.4. Antimicrobial Resistance

The data of AST varied widely between studies, so the pooled of all included studies was calculated for each antimicrobial resistance against each species with a mention of the range. Among gram-negative bacteria **(Table 3),** *A. baumannii* was the most resistant to antimicrobials. By studying the susceptibility of this genus against 20 antimicrobials, more than 68% resistance appeared against 18 antimicrobials, the only exceptions were colistin (2.3%) and levofloxacin (50.2%).

P. aeruginosa and *K. pneumoniae* also showed resistance to most antimicrobials. For *P. aeruginosa* the lowest resistance was for Aztreonam (32%) followed by Piperacillin-tazobactam (34.9%) and Cefepime (35.1%). For *K. pneumoniae* the lowest resistance was for Tobramycin (21.4%) followed by Amikacin (30.5%) and Ceftazidime (34%)

E. coli was more susceptible to antimicrobials than other gram-negative bacteria. The resistance was low to meropenem (10.1%), imipenem (10.5%), and piperacillin-tazobactam (11.6%).

The data for *Proteus spp.* and *Enterobacter spp*. were limited to a few antimicrobials. However, both bacteria had low resistance to meropenem (9.2% and 22.2% respectively), and piperacillin-tazobactam (10% and 14% respectively).

The data of gram-positive bacteria were mainly reported for *S. aureus* with very limited data for CONS and *Enterococcus* (Table 4)**.** CLSI recommends a cefoxitin disk diffusion test for *Methicillin-resistant Staphylococcus aureus* (MRSA) detection (Humphries et al., 2021), so, based on the results of cefoxitin, 70.4% of isolated *S. aureus* were MRSA. The lowest resistance of *S. aureus* was to vancomycin, and linezolid (0%), followed by chloramphenicol (12.8%), while the highest resistance was to ampicillin (98%) followed by penicillin (88%). It is worth noting that vancomycin had a high susceptibility for all gram-positive cocci which cause infection among hospitalized burn patients.

3.5. Heterogeneity

We found a high between-study heterogeneity (I^2 > 85%) in all our analyses (Table 2). Just to identify the sources of heterogeneity, meta-regression was conducted using country, sample source, and sample size as a covariate. The analysis showed that there is no effect of these factors on heterogeneity between studies (Table 5).

Table 1. characteristics of the 24 included studies

Country	design	Sample source	Number of bacterial strains	Methods	Reference
Bangladesh	Prospective	Burn wound swab	53	Culture/ conventional identification/ disk diffusion method	Alam et al., 2014
China	Retrospective	wound secretions, blood, sputum	1914	Culture/ API/ disk diffusion method	Wang et al., 2014
China	Retrospective	wound, respiratory secretion	2212	Culture/ conventional identification/ disk diffusion method	Cen et al., 2015
China	Retrospective	wound, blood, sputum, and urine	1891	Culture/ VITEK/ disk diffusion method	Li et al., 2018
China	Retrospective	wound secretions, blood, sputum	7787	Culture/ VITEK	Chen et al; 2021
India	Prospective	Burn wound swab	96	Culture/ conventional identification/ disk diffusion method	Kulkarni et al., 2015
India	Prospective	Burn wound swab	218	Culture/ conventional identification/ disk diffusion method	Mundhada et al., 2015
India	Retrospective	Burn wound swab	187	Culture/ VITEK	Gupta et al., 2019
India	Retrospective	Burn wound swab	115	Culture/ conventional identification/ disk diffusion method	Sharma, 2020
India	Prospective	Burn wound swab	402	Culture/ conventional identification/ disk diffusion method	Nazir et al., 2020
Indonesia	Retrospective	wound, urine, blood, and sputum	25	Culture/ conventional identification/ disk diffusion method	Wardhana et al., 2017
Iran	Prospective	Burn wound swab	961	Culture/ conventional identification/ disk diffusion method	Haghighifar et al., 2020
Iran	Prospective	wound, urine, sputum, and stool	960	Culture/ conventional identification/ disk diffusion method	Emami et al., 2020
Iraq	Prospective	Burn wound swab	76	Culture/ conventional identification/ disk diffusion method	Hameed et al., 2014
Iraq	Retrospective	blood, urine, burn wounds	500	Culture/ API/ disk diffusion method	Rashid et al., 2017
Iraq	Prospective	Burn wound swab	186	Culture/ API/ disk diffusion method	Hamed et al., 2016
Iraq	Prospective	Burn wound swab	106	Culture/ VITEK / disk diffusion method	Hateet et al., 2021
Kuwait	Retrospective	Burn wound swab	41	Culture/ API/ disk diffusion method	ALfadli et al., 2018
Pakistan	Retrospective	Burn wound swab	100	Culture/ conventional identification/ disk diffusion method	Saaiq et al., 2015
Pakistan	Prospective	Burn wound swab	158	Culture/ conventional identification/ disk diffusion method	Chaudhary et al., 2019
Pakistan	Prospective	Burn wound swab	56	Culture/ API/ disk diffusion method	Basit et al., 2021
Palestine	Prospective	Burn wound swab	53	Culture/ conventional identification/ disk diffusion method	Elmanama et al., 2013
Turkey	Retrospective	Burn wound swab	151	Culture/ Phoenix	Yolbaş et al., 2013
Turkey	Retrospective	Burn wound swab	59	Culture/ conventional identification/ disk diffusion method	Asena et al., 2020

Table 2. Distribution of bacterial causes of infection among hospitalized burn patients in Asian countries

Country	Gram-positive bacteria (%)			Gram-negative bacteria (%)								references
	S. aureus	CONS [a]	Enterococcus spp.	P. aeruginosa	K. pneumoniae	A. baumannii	E. coli	Enterobacter spp.	Proteus spp.	Citrobacter spp.	Others	
Bangladesh	83.3	-	-	93.3	86.7	-	6.7	-	-	-	-	Alam et al., 2014
China	19.3	6.6	3.1	23.7	5.6	24.1	6.6	3.8	-	2.8	-	Wang et al., 2014
China	19.6	6.5	7	11.9	5.6	11.9	6.3	3.3	2.3	-	-	Cen et al., 2015
China	19	8.9	5.2	16.7	7.4	17.6	3.2	3.1	1.5	-	-	Li et al., 2018
China	21.7	9.6	7.6	14.2	4.6	7.1	4.9	5.2	2.3	-	-	Chen et al; 2021
India	41	-	-	43.3	19.3	-	12	-	-	-	-	Kulkarni et al., 2015
India	22.9	-	-	23.9	34.4	2.8	7.3	-	2.8	1.4	-	Mundhada et al., 2015
India	1.6	-	-	45.2	28	14.8	6.6	2.2	1.1	-	1.7	Gupta et al., 2019
India	21.7	-	-	30.4	24.3	10.4	-	4.3	8.7	-	-	Sharma, 2020
India	6.5	-	0.5	33.1	38.3	6.5	4.2	-	10.4	-	-	Nazir et al., 2020
Indonesia	-	16	4	28	8	20	-	12	8	-	4	Wardhana et al., 2017
Iran	10.2	-	0.1	29.8	80	34.9	1.2	3.4	-	-	-	Haghighifar et al., 2020
Iran	6.5	22.2	-	49.9	9.7	7.2	2.7	-	0.4	-	-	Emami et al., 2020
Iraq	3.9	-	-	53.9	3.9	1.3	11.8	25	-	-	-	Hameed et al., 2014
Iraq	53	2	-	17	5	19	1.4	2.2	-	-	-	Rashid et al., 2017
Iraq	7.5	-	-	32.3	17.2	21.5	9.7	5.9	4.8	0.5	-	Hamed et al., 2016
Iraq	17.1	4.8	-	20	6.7	-	7.6	16.2	23.7	-	4.8	Hateet et al., 2021
Kuwait	14.6	-	7.3	14.6	19.5	41.5	-	-	-	-	2.4	ALfadli et al., 2018
Pakistan	18.6	-	-	35.3	20.6	6.9	6.9	-	9.8	-	-	Saaiq et al., 2015
Pakistan	24.1	-	0.6	25	15.2	17.1	8.2	0.6	4.4	-	-	Chaudhary et al., 2019
Pakistan	21.4	-	-	21.4	-	-	14.2	-	-	-	15.7	Basit et al., 2021
Palestine	9	-	-	51	2	2	6	28	-	2	-	Elmanama et al., 2013
Turkey	4.6	-	-	25.8	-	62.3	7.3	-	-	-	-	Yolbaş et al., 2013
Turkey	20.3	37.2	-	-	-	-	11.8	-	-	-	-	Asena et al., 2020
Pooled	19.7	9	5.9	20	11.5	23.8	4.9	4.5	2.6	2.4	4.5	
Heterogeneity												
I^2%	98.4	96.5	98.9	96.4	90.7	96.5	97.1	93.7	89.9	91.2	89.1	
P value	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	

[a] CONS: Coagulase-negative Staphylococcus aureus

Table 3. Pooled Resistance (%) of isolated gram-negative bacteria from hospitalized burn patients to various antimicrobials in Asia between 2013-2022

Antimicrobial	**Pseudomonas spp.**		**Klebsiella spp.**		**Acinetobacter spp.**		**E. coli**		**Proteus spp.**		**Enterobacter spp.**	
	Pooled	Range	Pooled	Range	Pooled	Range	Pooled	Range	Pooled	Range	Pooled	Range
Amikacin	45.2	8.3 - 91.7	30.5	4.7- 90.2	70.7	33.3 - 100	22	0 – 72.7	20.8	0 - 100	33.4	0 – 100
A-C [a]	-	-	38.3	0 - 100	99.6	94.7 - 100	74.6	14.7 - 100	-	-	100	100 – 100
Ampicillin	90.1	0 - 100	98.3	0 -100	96.3	91.5 - 100	92.9	33.3 - 100	-	-	96.1	68.4 – 100
A-S [b]	100	100 - 100	83.1	73 -100	68.9	42.9 - 96	64.1	33.3 - 100	-	-	-	-
Aztreonam	32	15.2 - 100	57.6	39.4 -77.8	95.1	90.8 - 100	62	30.2 - 100	-	-	-	-
Cefepime	35.1	9 - 94.7	45.7	17- 100	81.6	72.5 - 100	61.4	19.4 - 100	-	-	33.8	28 – 100
Cefotaxime	71.6	53.3 - 100	65.9	33.3 - 95	89.2	66.7 - 99	78.4	14.3 - 100	31.5	0 - 100	-	-
Ceftazidime	43.9	16.6 - 94.4	34	18.8 - 94.4	87.1	70.8 - 99	60.9	36.6 - 100	-	-	47.9	24.2 – 69.2
Ceftriaxone	69.2	58.3 - 97.4	60.6	45.2 - 100	90	84.2 - 100	69.8	62.5 - 100	51.7	36.4 - 100	53.7	43.1 – 100
Cefuroxime	91.1	84 - 100	71.1	56 - 100	75.6	50 - 100	73.6	16.7 - 100	-	-	89.5	80.6 – 100
Chloramphenicol	86.2	0 - 95.8	-	-	-	-	46.4	11.1 - 50	-	-	-	-
Ciprofloxacin	59	6.6 - 96.1	61.1	50 - 100	85.8	50 - 100	56	20 - 100	46.4	27.3 - 100	46	23.1 – 100
Colistin	95.7	0 - 100	71.6	0 - 100	2.3	0 - 100	-	-	-	-	-	-
Gentamicin	58.1	6.6 - 100	56.6	30 - 98	83.3	50 - 100	63.9	0 - 86.5	29.7	18.2 - 100	58.6	33.3 – 100
Imipenem	48.2	0 - 100	37.6	1.1- 85	68.7	16.7 - 100	10.5	0 - 100	55.5	0 - 100	19.5	0 – 100
Levofloxacin	39.3	14 - 94.4	34.2	8.6 – 59.3	50.2	39.6 - 84	57.1	20 - 66.7	-	-	-	-
Meropenem	55.8	36.5 - 90.8	44.7	7 - 78.4	68.8	58.5 - 100	10.1	0 – 54.6	9.2	0 - 100	22.2	2.9 – 100
TZP [c]	34.9	3.7 - 96.1	40.3	0 - 88.2	68	36.4 - 100	11.6	0 - 73	10	0 - 50	14	3.6 – 100
Tetracycline	-	-	70.3	56.3 - 72.7	80.9	4 - 90	73.6	40 - 86.4	-	-	-	-
Tobramycin	50.3	16.4 - 100	21.4	0 - 100	75.1	56.9 - 94	57.6	19 - 100	-	-	68.7	24.2-100
TMP-SMX [d]	87.8	67 - 100	61.1	43.3 - 89.8	88.7	50 - 96.3	81.5	33.3 - 92.9	-	-	76.8	48 – 100

[a] Amoxicillin-clavulanate; [b] Ampicillin-sulbactam; [c] Piperacillin-tazobactam; [d] Trimethoprim-sulfamethoxazole

Table 4. Pooled Resistance (%) of isolated gram-positive bacteria from hospitalized burn patients to various antimicrobials in Asia between 2013-2022

Antimicrobial	S. aureus		CONS [a]		Enterococcus spp.	
	Pooled	Range	Pooled	Range	Pooled	Range
Amikacin	75.1	24.3 - 83.3	84.7	0 - 90.9	-	-
Ampicillin	98	85.7 - 100	-	-	-	-
Cefotaxime	77.4	26.4 - 100	-	-	-	-
Cefoxitin	70.4	32 - 98	-	-	-	-
Chloramphenicol	12.8	0 - 71.4	-	-	-	-
Ciprofloxacin	74.9	14.3 - 90.5	46.5	0 - 65.7	59.3	40.2 - 80
Clindamycin	69.1	0 – 90.4	54.7	47.8 - 66.7	-	-
Erythromycin	77.3	47.1 - 94.4	82.1	11.1 – 96.7	78.5	71.1 - 84.6
Gentamicin	65.2	27.7 - 100	39.8	21.7 - 71.4	-	-
Imipenem	65.4	0 - 100	-	11.1- 85	-	-
Linezolid	0	0 - 11.8	-	-	-	-
Oxacillin	52.1	33.3 - 86	59.4	43.4 - 80	-	-
Penicillin	88	63.2 - 100	-	-	43.4	43.1 - 55.5
Rifampin	38.6	35.2 - 41.3	25.1	22.5 - 35.8	-	-
Tetracycline	50.4	0 – 57.1	-	56.3 - 72.7	-	-
TMP-SMX [b]	54.2	12.4 – 79.2	51.3	31.6 - 100	-	-
Vancomycin	0	0 – 20.6	0	0	0	0 -7.4

[a] Coagulase-negative Staphylococcus aureus; [b] Trimethoprim-sulfamethoxazole

Table 5. Meta-regression analysis for some factors assumed to affect between study heterogeneity

Source of heterogeneity	Coefficient	Standard error	P value
Country	0.03	0.019	0.7
Sample source	0.02	0.01	0.1
Sample size	0.0003	0.001	0.5

4. Discussion

This systematic review has addressed the bacterial profile and antimicrobial resistance patterns of infections among hospitalized burn patients in Asia by analyzing 24 eligible studies. The results indicated that any bacterium is a potential pathogen in burn infection. Gram-negative bacteria are more prevalent and more diverse than gram-positive bacteria. According to the findings of previous studies, a prolonged hospital stay is one of the risk factors that contributes to an increased risk of gram-negative bacterial colonization among burn patients (Oncul et al., 2014). Gram-positive bacteria have been reported to survive after burn damage in the depths of sweat glands and hair follicles. In the case of neglecting topical antibacterial, these bacteria significantly colonize the wounds within the first 48 hours post-burn. Therefore, gram-positive bacteria are typically more prevalent during the first week of hospitalization, while gram-negative bacteria mainly appear after a patient has been hospitalized for a longer period of time, typically more than one week of admission (Azzopardi et al., 2014), due to increased use of indwelling devices, intensive diagnostic and therapeutic procedures, and the immunocompromising effects of burns.

There was no consensus among including studies on the leading bacterial isolate of burn infections, this difference is logical and expected as a result of the difference in hospital protocols related to sterilization, disinfection, hygiene measures, and the application of antimicrobials, in addition to differences in socioeconomic status and geographic location. The current review indicated the most isolated bacteria from hospitalized burn patients in Asia after calculating the pooled prevalence of all included studies were *A. baumannii* (23.8%), *P. aeruginosa* (20%), *S. aureus* (19.7%), and *K. pneumoniae* (11.5%). This result is in line with other studies outside of Asia, such as Morocco (El Hamzaoui et al., 2020) in Africa, and Brazil in South America (Zampar et al., 2017). On the other hand, other countries have different genera such as Italy in Europe where *E. coli* and *Proteus spp*. are important pathogens among burn patients (Puca et al., 2021). Also, in Ethiopia (Africa), it turns out that CONS and *Bacillus spp*. which are very common flora on the skin, play an important role in burn infection, indicating poor sterilization, and hygiene procedures (Sewunet et al., 2013). These differences are due to what we previously mentioned about the existence of differences in hospital protocols, in addition to climatic and economic differences.

It was not surprising that *P. aeruginosa* was the first or second cause of infection among hospitalized burn patients in most included studies, this is due to its ability to grow in moist areas, particularly burn wounds, which constitute a typical environment for colonization of this pathogen (Williams et al., 2009). In addition, *P. aeruginosa* requires minimum nutrition, as evidenced by its growth in distilled water and its tolerance to various environmental conditions, making this pathogen well-adapted to hospital environments (Parsnjothi and Dheepa, 2010). Moreover, *P. aeruginosa* is known to form a biofilm that gives long survival benefits and prevents eradication by the immune system of the host or antibacterial treatment (Thi et al., 2020).

Among the eligible studies, *S. aureus* was the first pathogen of infection among burn patients in 5 studies (Cen et al., 2015; Li et al., 2018; Chen et al., 2021; Rashid et al., 2017; Basit et al., 2021) , and the second pathogen in three studies (Kulkarni et ., 2015; Chaudhary et al., 2019; Asena et al., 2020). In general, *S. Aureus* has variant pathogenicity factors that assist host tissue adhesion, immune system response evading, and apoptosis, such as coagulase enzyme, surface protein, and toxins (Issler-Fisher et al., 2015). Furthermore, like *P. aeruginosa, S. aureus* has the ability to make biofilm which is known as a pathogen factor in burn wound infection (Maslova et al., 2021).

K. pneumoniae was recorded as the first pathogen of infection among hospitalized burn patients in three studies (Nazir et al., 2020; Mundhada et al., 2015; Haghighifar and KamaliDolatabadi 2020) and the second pathogen in five studies (Alam., 2014; Gupta et al., 2019; Sharma et al., 2020; ALfadli et al., 2018; Saaiq et al., 2015). This pathogen is among the most dominant causes of nosocomial infections in the United States, it constitutes about 10% of all infections (Magill et al, 2014). The main reservoirs of *K. pneumoniae* that cause nosocomial infections remain unclear, intestinal colonization and healthcare staff's hands have been involved in transmission (Jarvis et al., 1985).

A. baumannii also was recorded as the first pathogen of infection among hospitalized burn patients in three studies (Wang et al., 2014; ALfadli et al., 2018; Yolbaş et al., 2013), while it was the second pathogen in six studies (Cen et al., 2015; Li et al., 2018; Wardhana et al., 2014; Haghighifar and KamaliDolatabadi, 2020; Rashid et al., 2017; Hamed et al., 2016). *A. baumannii* is considered a part of human normal skin flora, and can survive in the hospital environment for a long time because of its resistance to multiple antibiotics, the tendency to humidity, and the ability to cling to inanimate surfaces (Sharma et al., 2014). Nowadays, *A. baumannii* infection is on the rise in hospitals, making it a global threat, particularly, most strains of this genus are multidrug-resistant. Applying invasive procedures such as mechanical ventilation and a urinary catheter in addition to consumption of broad-spectrum antimicrobials are important risk factors for *A. baumannii* infection, and these factors are frequently associated with burn patient management (Towner, 2009).

The model of antimicrobial resistance is very critical for epidemiological and clinical objectives. The findings of this review are really alarming because the most prevalent bacterial isolates were extremely resistant to the routinely used antimicrobials in Asia and considered MDR. The reason for the prevalence of MDR in hospitalized burn patients is that most pathogens are acquired from hospital environments where broad-spectrum antibiotics are frequently used. MDR associates with a high rate of mortality, in addition to the economic burden (WHO, 2012). Continuous training of burn unit staff including hand hygiene, using barriers for physical contact, routine environmental sterilization, and attention to antimicrobial resistance patterns in the unit or at least the region is very important in reducing burn infection, especially MDR strains.

Among gram-negative bacteria, *A. baumannii* showed the highest level of resistance against most tested antimicrobials -which is a special concern- followed by *P. aeruginosa*. The most effective antimicrobials against *A. baumannii* were colistin followed by levofloxacin, this result is consistent with the successful results of combination therapies which include colistin and levofloxacin to treat MDR *A. baumannii* (Wei et al., 2017). *P. aeruginosa* had better susceptibility to antimicrobials, there were five effective, which are aztreonam, piperacillin-tazobactam, cefepime, levofloxacin, and ceftazidime. For *K. pneumoniae* the most effective antimicrobials were tobramycin, amikacin, ceftazidime, levofloxacin, and imipenem. That means levofloxacin is the only common effective antimicrobial in different percentages against the most three prevalent gram-negative bacteria in hospitalized burn patients in Asia. Many studies have proved the efficacy of this antimicrobial in vivo too (Zhang et al., 2020; Yan et al., 2014; Ma et al., 2022). By studying the antimicrobials susceptibility of *Enterobacteriaceae*, we find the common effective antimicrobials among this group are amikacin, piperacillin-tazobactam, and meropenem. Piperacillin-tazobactam is also effective against *P. aeruginosa.* The susceptibility pattern of the gram-negative bacteria varies greatly according to the genus, so the empirical therapy should depend on the combination of antimicrobials with focusing on the most effective. The choice between these antimicrobials would be determined by the clinician according to the clinical situation. Furthermore, combination therapy was recommended by several studies to prevent increasing MDR emergence in the future (Kalligeros et al., 2019; Tschudin-Sutter et al., 2018. High-quality studies should be conducted to detect clinical efficacy.

The majority strains of isolated *S. aureus* were

MRSA (70.4%), which explains the highest sensitivity of *S. aureus* was just to vancomycin, and linezolid, followed by chloramphenicol. Kalligeros et al. analyzed 16 articles related to MRSA acquisition in the burn unit and concluded that the prevalence of MRSA on admission isn't negligible, and the risk of getting this infection during hospitalization increases in the following cases; the absence of decolonization protocols, flame burn, admission to intensive care unit, and inhalation injuries (Liu et al., 2021).

Prophylactic use of systematic antimicrobials isn't suggested as this strategy increases the probability of MDR (Hill et al., 2021). This review found that *S. aureus* (the most common isolated gram-positive bacteria from hospitalized burn patients in the first week) have a high susceptibility to chloramphenicol, so this antimicrobial could be used as topical prophylaxis to prevent burn wound infection. Case-control studies are important to confirm this role.

There are several limitations in this review. First of all, the design of half of the included studies was retrospective, therefore we could not determine the dynamic changes in bacterial profile and antimicrobial resistance during different periods of treatment. Second, most studies presented the results of bacterial identification and antimicrobial susceptibility based on conventional methods and disk diffusion technique. The automated and molecular methods provide more accurate results. Third, lack of data on some antimicrobials against all species, for example, colistin against *E. coli* and *Proteus spp*. Finally, detailed potential risk factors and mortality rates were not available in most studies, therefore, they were not linked in this review.

5.Conclusion

The current review analyzed 24 studies of infections among hospitalized burn patients in Asia during the last decade to provide data on the bacterial profile and antimicrobial resistance pattern. This data would be definitely helpful for clinicians to prescribe appropriate empirical treatment and control the infection, particularly in low and middle-income countries, where the conducting of AST for each case is difficult, and needs a long time which is not allowed by the aggravation of the infection. The majority of pathogens were gram-negative bacteria, and the most predominant isolated species were *A. baumannii, P. aeruginosa, S. aureus,* and *K. pneumoniae*. According to the pooled results of AST of the included studies, the findings of this review are really alarming because the most prevalent bacterial isolates were MDR, and the susceptibility pattern of the gram-negative bacteria varies greatly according to the genus. So, this review suggests that the empirical therapy of hospitalized burn patients in Asia should depend on the combination of antimicrobials to prevent increasing MDR emergence in the future, especially, that includes levofloxacin, which is the only common effective antimicrobial in different percentages against the most three prevalent gram-negative bacteria. This is in addition to the use of topical chloramphenicol as prophylaxis for S. aureus (the most common isolated gram-positive bacteria from hospitalized burn patients). Further studies should be conducted to confirm the clinical effect of these procedures.

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