



Distribution of Nosocomial Pathogens and Antimicrobial Resistance among Patients with Burn Injuries in China: A Comprehensive Research Synopsis and Meta-Analysis

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ABSTRACT

Introduction: Over the past decade, numerous studies have described the types of pathogens and their antibiotic resistance patterns in patients with burn injuries in China; however, the findings have generally been inconsistent. We conducted a literature search and meta-analysis to summarize the infection spectra and antimicrobial resistance patterns in patients with burn injuries.

Methods: We searched the PubMed, Embase, Web of Science, China National Knowledge

Infrastructure, China Biomedical Literature, Wanfang, and Weipu databases for relevant articles published between January 2010 and December 2023. The DerSimonian–Laird random-effects model was used to estimate the proportions and 95% confidence intervals (CIs) of pathogens among Chinese patients with burn injuries. Meta-regression analyses were performed to explore differences in the proportions of pathogens among different subgroups and their resistance patterns. This study was registered with PROSPERO (CRD42024514386). **Results:** The database searches yielded 2017 records; after removing duplicates and conducting initial screening, 219 articles underwent full-text screening. Ultimately, 60 studies comprising a total of 62,819 isolated strains reported the proportions of pathogens in patients with burn injuries and were included in this meta-analysis. Meta-analyses were conducted on 18 types of

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pathogens. The most common pathogens causing infections in Chinese patients with burn injuries were *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Staphylococcus epidermidis*. Similar results were observed in the subgroup analysis focusing on wound infections. Since 2015, there has been a significant decrease in the proportion of *Pseudomonas aeruginosa* ($R^2=4.89\%$) and a significant increase in the proportion of *Klebsiella pneumoniae* ($R^2=9.60\%$). In terms of antibiotic resistance, there has been a significant decrease in the resistance of *Staphylococcus aureus* to multiple antibiotics and an increasing trend in the resistance of *Klebsiella pneumoniae*.

Conclusions: We systematically summarized the epidemiological characteristics and antibiotic resistance patterns of pathogens among individuals suffering from burns in China, thus providing guidance for controlling wound infections and promoting optimal empirical antimicrobial therapy. The observed high levels of antibiotic resistance underscore the need for ongoing monitoring of antibiotic usage trends.

Keywords: Burns; Pathogens; Antimicrobial resistance; Meta-analysis; China

Key Summary Points

Why carry out this study?

Infection is the most common complication among individuals suffering from burns and one of the contributing factors to mortality in patients with burns, more than half of the deaths can be attributed to various infectious complications.

Comprehensive research synopses of the infection spectra and antimicrobial resistance patterns among individuals suffering from burns in China are lacking.

What was learned from this study?

The five most frequently detected pathogens in patients with burn injuries were *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Staphylococcus epidermidis*.

Both the proportion and resistance of *Klebsiella pneumoniae* have significantly increased, warranting attention in clinical practice.

Acinetobacter baumannii generally exhibits high resistance to multiple antibiotics (>50%), which thus highlights the necessity for long-term monitoring efforts.

INTRODUCTION

Burn injuries are a global public health concern, with an estimated 120,000 related deaths occurring annually worldwide. The majority of burn-related deaths occur in low- and middle-income countries [1, 2]. China has a high incidence of burn injuries, as evidenced by research indicating that there were 1,079,000 patients with burn injuries in mainland China in 2019, accounting for 12% of the global incidence cases and ranking first worldwide among all countries. With 11,000 deaths, China ranks second globally in terms of burn-related mortality after India, with 26,000 deaths [3]. Burn injuries can result in varying degrees of damage to the skin, which is the body's largest organ and primary physical barrier against external pathogens [4]. Consequently, both endogenous and exogenous pathogenic microorganisms readily colonize burn wounds, leading to severe infections that endanger patient lives [5]. Infection is the most common complication among individuals suffering from burns and one of the contributing factors to mortality in patients with burns, with approximately 50–75% of deaths attributed to various infectious complications [6, 7]. Hence, effective prevention, control, and treatment of burn infections present urgent challenges for all healthcare institutions.

The pathogens causing infections in patients with burn injuries are predominantly bacteria, with the species composition changing

dynamically over time. For instance, although gram-positive bacteria appear earlier than gram-negative bacteria, their duration of persistence is shorter [8]. Research indicates that within the first 5 days of hospitalization, *Staphylococcus aureus* is the most common pathogen, whereas *Pseudomonas aeruginosa* becomes predominant after 5 days of admission [9, 10]. Gram-negative bacteria constitute the primary causative agents of infections in patients with burn injuries, accounting for approximately 70% of cases, with notable species including *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*. Gram-positive bacteria account for approximately 30% of cases, with *Staphylococcus aureus* and *Enterococcus* spp. being common [11, 12]. The colonization patterns of pathogens that cause burn infections may vary owing to differences in geographical, climatic and environmental factors, hospital management practices and the duration of hospitalization. A study conducted in Morocco identified *Acinetobacter baumannii* and *Pseudomonas aeruginosa* as the most common pathogens among patients with burn infection, while studies in China revealed that *Staphylococcus aureus* and *Staphylococcus epidermidis* were the most prevalent pathogens isolated from patients with burn injuries [13, 14].

The continuous increase in antibiotic resistance is primarily attributable to the irrational or excessive use of antibiotics. The decreased sensitivity of bacteria to conventional antibiotics has significantly complicated the management of burn infections. The emergence and transmission of multidrug-resistant (MDR) bacteria represent major challenges to global health care systems. The World Health Organization (WHO) estimates that by 2050, an increase in antibiotic resistance could lead to 10 million deaths [15, 16].

As the initial use of antibiotics in patients with burn injuries relies mainly on local microbial epidemiology [17], it is crucial to determine the distribution of pathogens and their resistance characteristics among individuals suffering from burns in China. Clinicians must rationally prescribe antibiotics and formulate strategies to avoid antimicrobial resistance in patients with burn injuries. Although the regional compositions of burn infection

pathogens and antibiotic resistance have been studied in China, comprehensive reports on the overall situation with pathogen infections and resistance among individuals suffering from burns in China are lacking [13, 18]. This study aimed to evaluate and summarize the pathogen infection status among individuals suffering from burns in China and provide a synopsis of our current understanding of the infection spectrum and antimicrobial resistance patterns in patients with burn injuries.

METHODS

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [19] and was registered in PROSPERO (CRD42024514386) before the systematic review was performed.

Search Strategy

A comprehensive search was conducted in the PubMed, Web of Science, China Biomedical Literature, China National Knowledge Infrastructure, Wanfang, and Weipu databases (Table S1) using a combination of free text and controlled vocabulary (i.e., MeSH terms). This study focused on analyzing the distribution and antimicrobial resistance characteristics of nosocomial pathogens among individuals suffering from burns over the past decade. Therefore, the search was limited to articles published between 1 January 2010 and 30 November 2023. The search terms included “cross infection,” “nosocomial infection,” “hospital infection,” “wound infection,” “bacteria,” “pathogens,” “burns,” and “China.” The retrieved literature was managed using EndNote (version 20), and duplicates were removed. Relevant conference papers were manually searched in the Army Medical University Library journal database, and all references included in the studies were reviewed.

Selection Criteria

The inclusion criteria for the meta-analysis were as follows: (1) studies on nosocomial infections in patients with burn injuries, (2) sample collection started in 2010 or later, (3) a study population comprising Chinese individuals, and (4) sufficient data available to calculate the proportion or antimicrobial resistance rates of pathogens with corresponding 95% confidence intervals (CIs). The exclusion criteria were as follows: (1) abstracts, reviews, or communications; (2) studies with a total number of bacterial isolates fewer than 200; (3) insufficient information, including incomplete or inaccessible study data; and (4) studies based on data from the National Nosocomial Infection Surveillance System.

Data Extraction and Risk of Bias Assessment

The data were extracted independently by two researchers using a data extraction form. The following data were extracted: author, publication year, study region, hospital level, number of patients with burn injuries, total number of pathogens detected, common pathogens isolated from patients with burn injuries, and antibiotic-resistant strains. Disagreements in the data extracted were resolved through consultation with a third party. For duplicate publications, only studies with the highest quality and the most complete or informative data on pathogen strain detection were included. If the study data could be divided into datasets before and after 2015, they were extracted separately.

A predetermined checklist, adapted from previous case series scales and consisting of ten items was used to assess the quality of the included studies [20]. The checklist included two dimensions (external validity and internal validity) with four and six items, respectively. A score of 1 was assigned if the literature was judged to have a low risk of bias for each item by answering yes or no to the questions. The total score ranged from 0 to 10 points, with higher scores indicating higher quality. A risk of bias summary plot was generated using the R 4.1.3 software, with scores ≤ 5 indicating a high risk

of bias, scores 6–7 indicating a moderate risk of bias, and scores ≥ 8 indicating a low risk of bias.

Data Analysis

All the statistical analyses were performed using R 4.1.3. Statistical tests were two-tailed, and $P < 0.05$ was considered to indicate statistical significance, unless otherwise stated. Formulas from previously published articles were used to calculate the proportions of pathogenic and antibiotic-resistant strains in patients with burn injuries in each study [21]. Freeman–Tukey double arcsine transformation was used to stabilize the variance in proportions [22]. The DerSimonian–Laird random-effects model was used to estimate the pooled proportions of pathogens across studies and their 95% CIs [23]. The Cochran Q test was used to analyze heterogeneity among studies, with the Q statistic approximately following a χ^2 distribution with $k-1$ (where k is the number of studies), and $P < 0.10$ indicates significant heterogeneity. The magnitude of heterogeneity was quantitatively assessed by the Higgins I^2 value, which ranged from 0% to 100%, with higher values indicating greater heterogeneity. Heterogeneity is typically considered significant if I^2 exceeds 50% [24]. Funnel plots were used to assess potential publication bias in the included literature, and Egger's test was employed to evaluate the asymmetry of funnel plots [25].

Subgroup analyses and univariate meta-regression were performed to explore differences in pathogen proportions and resistance rates between studies. In univariate meta-regression analysis, the dependent variable was the proportion or resistance data of pathogens, while the independent variables included the study time (dummy variable: 2015 or after), hospital level (dummy variable: tertiary), risk of bias (dummy variable: high), region (dummy variable: eastern region), and sample size (dummy variable: < 500 isolates). The restricted maximum likelihood method was used to estimate the variance between studies in the meta-regression analysis, and the proportion of variance explained by any meta-regression model was estimated using the R^2 statistic [26].

RESULTS

Literature Overview

A total of 2017 relevant articles were initially identified. After removing duplicates, we screened the titles and abstracts of 1373 articles, resulting in the exclusion of 1154 studies. Further screening of the abstracts and full texts led to the exclusion of an additional 159 articles. Among these, 47 studies had a total number of isolated pathogenic strains fewer than 200, 45

articles were not related to infections in patients with burn injuries, 26 studies lacked sufficient data, 19 studies focused on nonhuman subjects, 10 were case reports, 7 were duplicate publications, and 5 were reviews or abstracts. Ultimately, 60 articles meeting the inclusion criteria were identified (Fig. 1). Among the 60 included studies, 1 had a longer time span. To explore the impact of time on pathogen colonization patterns and antimicrobial sensitivity, this study was divided into two parts according to the time (before and after 2015).

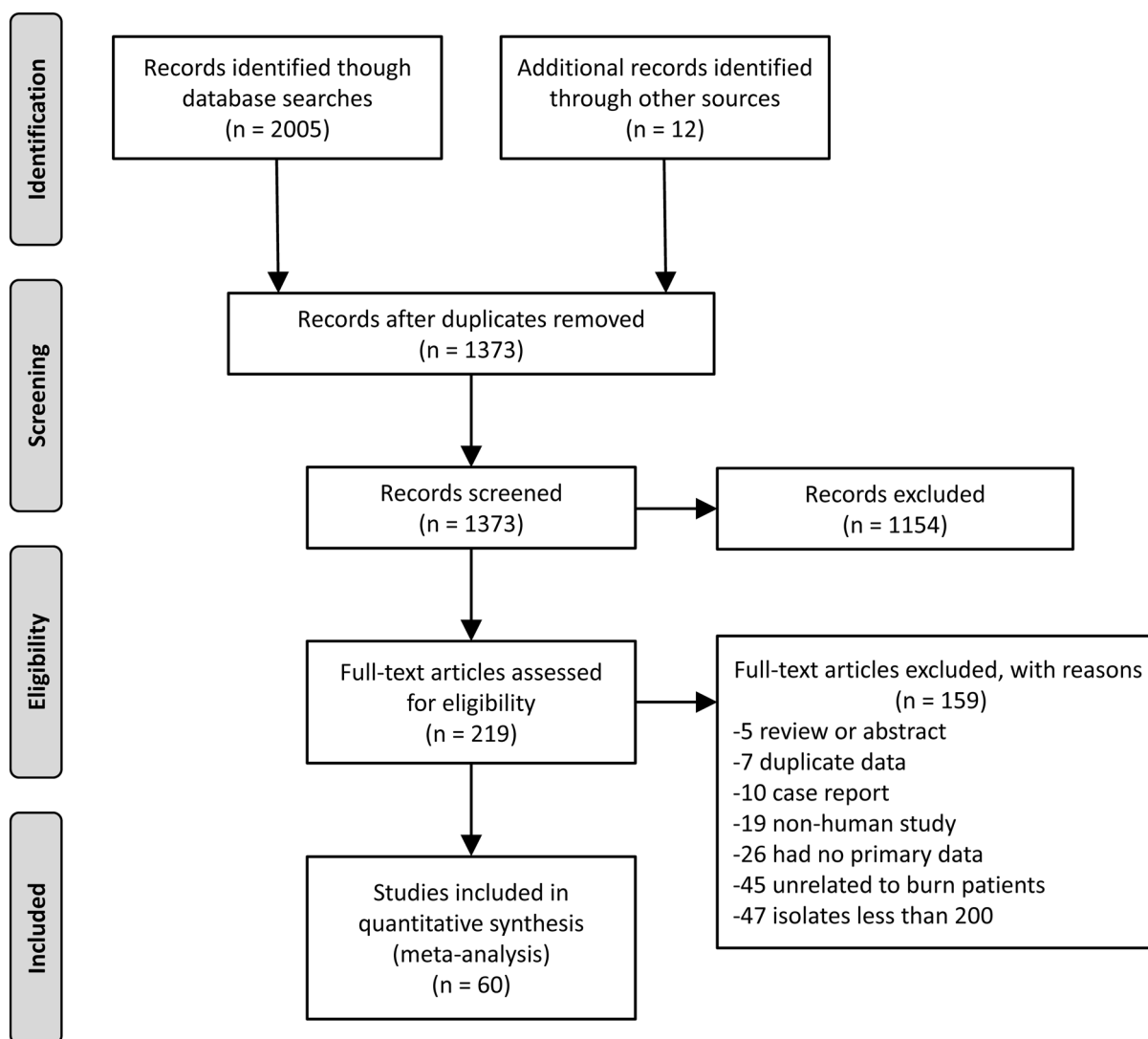


Fig. 1 Literature inclusion and exclusion processes

Study Characteristics and Risk of Bias Assessment

The characteristics of the 60 eligible studies are presented in Table 1. A total of 62,819 pathogen isolates were identified, with the number of isolates per study ranging from 209 to 4624. All studies were conducted between 2010 and 2023 and represented 24 provinces out of 34 in China. Specifically, 17 studies were from the western region, 11 from the central region, and 32 from the eastern region. The results of the risk of bias assessment are depicted in Fig. 2, with detailed information provided in Table S2. Individual studies obtained scores ranging from 5 to 9, with 18 studies classified as having high quality (score ≥ 8).

Distribution of Nosocomial Pathogens

In total, 18 pathogens were reported in 10 or more studies (Table 2), and meta-analyses were conducted for these pathogens. They included five gram-positive bacteria, eight gram-negative bacteria, and five fungi. Significant heterogeneity was observed among the studies in the pooled estimates, with Higgins I^2 values ranging from 87.2% to 98.2% (Q test $P < 0.001$). The five pathogens with the highest proportions were *Staphylococcus aureus* (18.3%, 95% CI 16.3–20.4), *Pseudomonas aeruginosa* (16.2%, 95% CI 14.2–18.5), *Acinetobacter baumannii* (13.7%, 95% CI 11.7–15.9%), *Klebsiella pneumoniae* (7.4%, 95% CI 6.2–8.7%), and *Staphylococcus epidermidis* (5.9%, 95% CI 4.5–7.4%; Table 2, Fig. 3a). The main type of burn infection was wound infection, with pathogen data from 22 studies all sourced from wounds. Among these, the five most frequently detected pathogens in wound infections were consistent with the results derived from clinical samples of all types. However, their rankings varied slightly, with the respective proportions as follows: *Staphylococcus aureus* (17.8%, 95% CI 14.4–21.5), *Pseudomonas aeruginosa* (16.0%, 95% CI 12.6–19.8), *Acinetobacter baumannii* (11.8%, 95% CI 8.8–15.2), *Staphylococcus epidermidis* (8.6%, 95% CI 5.7–12.0), and *Klebsiella pneumoniae* (6.2%,

95% CI 4.3–8.4) (Table 2; Fig. 3b). Egger's test revealed no evidence of publication bias in the pooled proportions ($P > 0.05$; Fig. S1).

Subgroup analyses and univariate meta-regression were used to examine the sources of heterogeneity for the top five pathogens using several covariates: the study time, hospital level, risk of bias, region, and sample size. Studies conducted after 2015 reported a significantly lower estimated proportion of *Pseudomonas aeruginosa* (13.5%, 95% CI 10.9–16.3) than those conducted before 2015 (17.9%, 95% CI 15.1–20.9) ($R^2 = 4.89\%$, Table 3). In contrast, there was an increasing trend for *Klebsiella pneumoniae* ($R^2 = 9.60\%$, Fig. 4), whose proportion increased from 6.2% (95% CI 5.1–7.4) before 2015 to 9.7% (95% CI 7.0–12.7) after 2015. According to the subgroup analysis at the hospital level, the proportion of *Staphylococcus epidermidis* was significantly greater in nontertiary hospitals ($R^2 = 9.24\%$). In the subgroups based on different sample sources, the proportion of *Acinetobacter baumannii* in bloodstream infections (25.5%, 95% CI 16.3–35.9) was significantly greater than that in wound infections (11.8%, 95% CI 8.8–15.2). However, the proportion of *Staphylococcus epidermidis* in wound infections (8.6%, 95% CI 5.7–12.0) was significantly greater than that in the pooled results from multiple sample sources (4.6%, 95% CI 3.3–6.1). Univariate meta-regression analysis revealed significant differences in the proportions of *Staphylococcus aureus* ($R^2 = 8.04\%$), *Acinetobacter baumannii* ($R^2 = 9.37\%$), and *Staphylococcus epidermidis* ($R^2 = 25.65\%$) among the risk of bias subgroups. However, the proportions of pathogens did not differ by region or sample size. Nevertheless, in the subgroup analysis by province, we found that the proportions of *Staphylococcus aureus* exceeded 30% in three provinces (Fig. 5a), namely, Shaanxi Province at 37.0% (95% CI 29.8–44.6), Liaoning Province at 33.4% (95% CI 25.9–41.4), and Qinghai Province at 30.9% (95% CI 28.1–33.8). Furthermore, the proportions of *Pseudomonas aeruginosa* exceeded 30% in two provinces (Fig. 5b), namely, Anhui Province at 33.0% (95% CI 29.1–37.0) and Sichuan Province at 32.5% (95% CI 27.3–37.9). The detailed results for each subtype can be found in Tables S3–S7.

Table 1 Main characteristics of the included studies

Study ID	Year	Province	Hospital level	Num-ber of patients	Num-ber of isolates	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>	<i>Acinetobacter baumannii</i>	<i>Klebsiella pneumoniae</i>	<i>Staphylococcus epidermidis</i>	Risk of bias
Zhang et al. [27]	2016–20	Henan	Tertiary	Unclear	1902	584	278	69	137	124	7
Zhou et al. [13]	2021	Shanghai	Tertiary	348	649	102	55	69	69	92	8
Han et al. [28]	2010–23	Shaanxi	Tertiary	216	245	101	54	33	8	-	6
Hu and Lu [29]	2020–22	Jiangsu	Tertiary	Unclear	1167	215	292	192	247	-	6
Han and Zhang [30]	2015–20	Chongqing	Tertiary	833	833	134	103	65	63	49	7
Li et al. [31]	2018–20	Shaanxi	Tertiary	249	527	177	62	86	41	-	8
Liu et al. [32]	2015–20	Beijing	Tertiary	Unclear	456	44	104	39	27	50	8
Wang et al. [33]	2016–19	Jiangsu	Tertiary	3475	250	64	41	31	39	-	7
Xu et al. [34]	2014–19	Liaoning	Tertiary	750	2113	791	499	154	126	-	7
Jin et al. [18]	2020	Zhejiang	Tertiary	16	400	13	37	91	45	3	5
Yang et al. [35]	2016–20	Yunnan	Tertiary	245	367	42	74	73	15	11	8
Yu et al. [36]	2019–21	Guizhou	Tertiary	Unclear	2136	575	196	127	85	-	7
Zhu et al. [37]	2015–20	Zhejiang	Nontertiary	Unclear	2437	709	156	101	131	434	8
Liao a [38]	2011–15	Jiangxi	Tertiary	674	1568	181	289	376	289	63	6
Liao [38]	2016–20	Jiangxi	Tertiary	502	1114	115	132	321	199	42	6
Zheng et al. [39]	2015–19	Beijing	Tertiary	83	2235	355	537	427	433	24	7

Table 1 continued

Study ID	Year	Province	Hospital level	Num- ber of patients	Num- ber of isolates	<i>Staphy- lococcus aureus</i>	<i>Pseu- domonas aeruginosa</i>	<i>Acinetobac- ter bauman- ni</i>	<i>Klebsiella pneumo- niae</i>	<i>Staphylococ- cus epider- midis</i>	Risk of bias
Hu et al. [40]	2013–18	Zhejiang	Tertiary	136	225	42	22	51	41	0	7
Liu et al. [41]	2014–19	Multiple regions	Tertiary	478	304	84	124	–	6	–	7
Wu et al. [42]	2015–18	Zhejiang	Tertiary	576	883	190	77	–	–	95	7
Chen et al. [43]	2015	Taibei	Tertiary	37	335	40	34	63	17	–	7
Chang et al. [44]	2014–18	Qinghai	Nontertiary	Unclear	1019	315	119	182	76	–	7
Liu et al. [45]	2015–17	Shanghai	Tertiary	534	1219	136	183	176	203	–	7
Ouyang et al. [46]	2018	Jiangxi	Tertiary	367	578	83	54	108	79	16	7
Wu et al. [47]	2015–17	Fujian	Tertiary	97	297	59	42	23	11	0	7
Xu et al. [48]	2016–17	Shanghai	Tertiary	548	1053	210	142	137	218	–	7
Fu et al. [49]	2015–16	Shandong	Tertiary	1842	209	29	8	71	15	8	7
Yang et al. [50]	2014–17	Yunnan	Tertiary	Unclear	2073	430	482	128	122	196	8
Zhang et al. [51]	2012–17	Chongqing	Tertiary	1310	2183	567	316	281	92	–	8
Li et al. [52]	2013–15	Fujian	Tertiary	1449	1891	–	316	332	139	69	7
Lin et al. [53]	2015	Taiwan	Tertiary	52	645	57	68	222	22	–	7
Tang et al. [54]	2014	Shanghai	Tertiary	177	323	22	30	63	45	–	7
Chen [55]	2010–14	Hebei	Nontertiary	888	888	203	326	56	73	36	7

Table 1 continued

Study ID	Year	Province	Hospital level	Num-ber of patients	Num-ber of isolates	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>	<i>Acinetobacter baumannii</i>	<i>Klebsiella pneumoniae</i>	<i>Staphylococcus epidermidis</i>	Risk of bias
Fan et al. [56]	2014–15	Tianjin	Tertiary	453	981	138	271	109	66	97	8
Lu [57]	2015–17	Sichuan	Nontertiary	100	302	66	98	63	–	26	8
Sun [58]	2013–15	Hubei	Nontertiary	100	277	52	44	16	11	–	6
Tan et al. [59]	2011–14	Guizhou	Tertiary	711	348	143	76	24	9	6	7
Wang [60]	2013–15	Henan	Nontertiary	375	295	49	60	56	7	39	8
Xu et al. [61]	2011–14	Shanghai	Tertiary	750	2399	489	447	369	175	206	7
Zhang et al. [62]	2011–16	Gansu	Tertiary	2423	2197	583	305	341	89	183	7
Zhang et al. [63]	2013–16	Ningxia	Nontertiary	161	421	31	103	0	15	82	6
Dai et al. [64]	2013–15	Fujian	Tertiary	541	298	68	37	31	12	22	6
Li [65]	2012–14	Shandong	Tertiary	Unclear	594	113	36	103	48	29	7
Wang et al. [66]	2013–15	Jiangsu	Tertiary	117	215	22	23	91	33	9	5
Yan [67]	2013–15	Jiangsu	Tertiary	389	564	81	158	36	27	26	9
Yin et al. [68]	2013–14	Jiangsu	Tertiary	20	1892	384	216	505	226	–	6
Zhang et al. [69]	2012–14	Yunnan	Tertiary	245	245	24	26	47	26	1	7
Zhu [70]	2012–14	Jiangsu	Tertiary	Unclear	4624	992	1077	835	293	80	7
Zha et al. [71]	2010–14	Anhui	Tertiary	Unclear	542	39	179	125	19	–	7
Sun and Wang [72]	2010–13	Henan	Tertiary	280	212	44	48	10	30	–	8

Table 1 continued

Study ID	Year	Province	Hospital level	Num- ber of patients	Num- ber of isolates	<i>Staphy- lococcus aureus</i>	<i>Pseu- domonas aeruginosa</i>	<i>Acinetobac- ter bauman- nii</i>	<i>Klebsiella pneumo- niae</i>	<i>Staphylococ- cus epider- midis</i>	Risk of bias
Tang et al. [73]	2012–14	Hubei	Tertiary	Unclear	710	78	48	79	43	58	8
Wang et al. [74]	2012–14	Guizhou	Tertiary	150	217	26	37	38	20	11	9
Yin et al. [75]	2011–13	Ningxia	Tertiary	Unclear	2587	556	112	168	91	246	7
Cen et al. [76]	2011–13	Zhejiang	Tertiary	1942	2212	276	197	169	72	72	7
Chen et al. [77]	2012–13	Zhejiang	Tertiary	100	520	300	200	10	0	10	7
Chen and Jiang [78]	2010–12	Shandong	Nontertiary	Unclear	1325	152	113	132	87	126	8
Dong et al. [79]	2011–13	Hebei	Tertiary	278	307	49	32	57	11	58	8
Liu [80]	2010–12	Yunnan	Tertiary	Unclear	2105	321	733	–	–	–	7
Peng et al. [81]	2010–14	Hubei	Nontertiary	1004	360	36	82	–	–	13	8
Wang et al. [82]	2010–12	Jiangsu	Tertiary	Unclear	310	25	22	27	11	61	8
Xu et al. [83]	2011–13	Liaoning	Tertiary	Unclear	1242	366	385	118	64	102	7
Gong et al. [84]	2011–12	Chongqing	Tertiary	298	1994	302	333	577	209	–	7

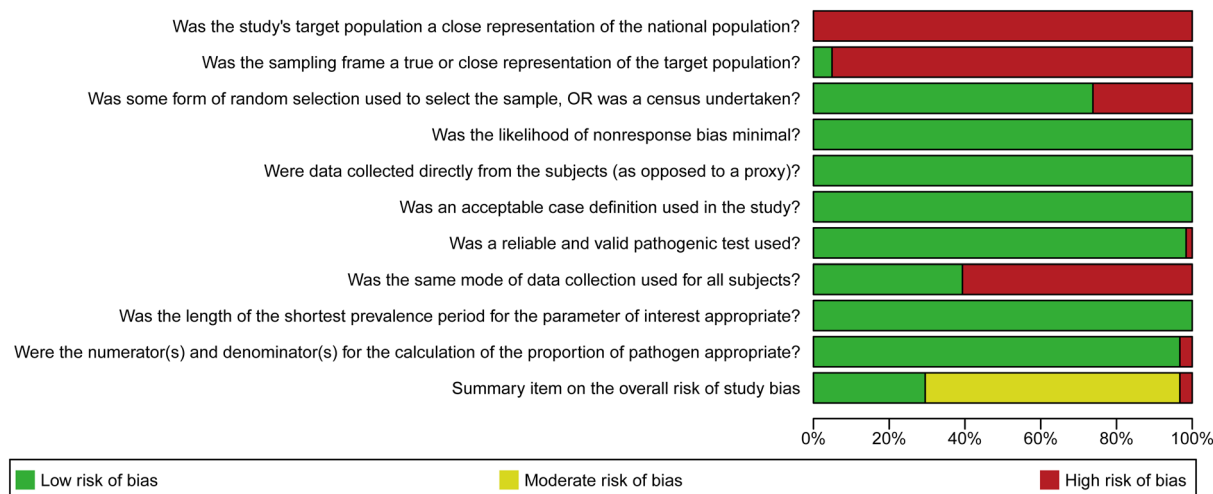


Fig. 2 Results of the risk of bias assessment

Antimicrobial Resistance

We further analyzed the resistance of the top five pathogens to different antibiotics, conducted meta-analyses of antibiotics reported in ten or more studies, and compared resistance rates before and after 2015 (Tables S8–S12). After 2015, *Staphylococcus aureus* (Fig. 6a) exhibited significantly reduced resistance to clindamycin ($R^2=18.63\%$), erythromycin ($R^2=25.98\%$), gentamycin ($R^2=15.35\%$), penicillin ($R^2=23.56\%$), and tetracycline ($R^2=44.26\%$). The resistance of *Pseudomonas aeruginosa* to aztreonam significantly decreased ($R^2=16.28\%$). However, *Acinetobacter baumannii* showed significantly increased resistance to piperacillin ($R^2=30.67\%$). With the exception of minocycline and tigecycline, *Acinetobacter baumannii* exhibited high resistance (>50%) to the remaining 19 antibiotics. After 2015, *Klebsiella pneumoniae* (Fig. 6b) showed significantly increased resistance to several antibiotics, including cefepime ($R^2=22.48\%$), ciprofloxacin ($R^2=24.71\%$), imipenem ($R^2=34.54\%$), levofloxacin ($R^2=29.77\%$), meropenem ($R^2=33.82\%$), piperacillin-tazobactam ($R^2=16.18\%$), and trimethoprim-sulfamethoxazole ($R^2=41.74\%$). There was a significant decrease in the resistance of *Staphylococcus epidermidis* to ciprofloxacin ($R^2=60.94\%$) and gentamycin ($R^2=31.07\%$).

DISCUSSION

This systematic review summarized data from 60 studies involving a total of 62,819 strains of pathogens. Among the five most frequently detected pathogens in nosocomial infections among individuals suffering from burns, two were gram-positive bacteria (*Staphylococcus aureus* and *Staphylococcus epidermidis*), while three were gram-negative bacteria (*Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*). The resistance rates of both gram-positive bacteria showed decreasing trends, while the three gram-negative bacteria continued to exhibit relatively high levels of resistance, with *Klebsiella pneumoniae* showing a trend toward increasing resistance, thereby warranting special attention.

Infection is a common complication of burns, with infected individuals suffering from burns having a three times greater mortality than that of uninfected patients [85]. Studies have shown that pathogens causing nosocomial infections in patients with burn injuries change over time. Gram-positive bacteria tend to appear earlier than gram-negative bacteria, possibly because burn wounds are initially sterile, and gram-positive bacteria remaining in the skin glands or hair follicles quickly colonize the surface of burn wounds. However, over time, endogenous

Table 2 Proportions of pathogens causing nosocomial infections in patients with burn injuries

Pathogens	All types of clinical samples									
	Wounds					Wounds				
	Number of studies	Total number of isolates	Number of specific pathogen isolates	Proportions	I^2	Number of studies	Total number of isolates	Number of specific pathogen isolates	Proportions	I^2
<i>Enterococcus faecalis</i>	38	45,145	1230	2.5% (1.9–3.2)	94.9	10	10,048	272	2.4% (1.1–4.1)	95.5
<i>Enterococcus faecium</i>	31	39,005	691	1.6% (1.1–2.1)	93.4	9	7556	142	2.1% (0.9–3.9)	94.6
<i>Staphylococcus aureus</i>	60	60,928	12,474	18.3% (16.3–20.4)	97.7	22	19,838	4018	17.8% (14.4–21.5)	97.6
<i>Staphylococcus epidermidis</i>	41	42,278	2875	5.9% (4.5–7.4)	97.5	17	14,689	1401	8.6% (5.7–12.0)	97.8
<i>Staphylococcus haemolyticus</i>	34	35,548	1161	2.0% (1.2–2.9)	96.9	14	11,813	549	2.8% (1.3–4.9)	96.9
<i>Acinetobacter baumannii</i>	57	59,167	8283	13.7% (11.7–15.9)	98.2	20	18,595	2326	11.8% (8.8–15.2)	97.8
<i>Enterobacter cloacae</i>	47	45,643	2079	3.6% (2.9–4.4)	94.7	19	15,062	695	3.7% (2.6–5.0)	92.8
<i>Escherichia coli</i>	58	60,968	3243	5.8% (4.9–6.7)	95.4	21	18,955	1024	5.4% (4.1–6.9)	94.4
<i>Klebsiella pneumoniae</i>	57	59,169	4807	7.4% (6.2–8.7)	97.0	20	18,595	1475	6.2% (4.3–8.4)	96.9
<i>Proteus</i> spp.	37	39,900	1410	2.7% (1.9–3.7)	96.4	14	9785	377	2.7% (1.1–4.9)	96.8
<i>Pseudomonas aeruginosa</i>	61	62,819	10,750	16.2% (14.2–18.5)	98.1	22	19,838	3184	16.0% (12.6–19.8)	97.9
<i>Serratia</i> spp.	15	9366	245	2.0% (0.8–3.7)	95.8	6	3189	76	1.9% (0.5–4.0)	92.3
<i>Stenotrophomonas maltophilia</i>	27	22,517	457	1.7% (1.0–2.7)	95.6	10	8297	183	1.5% (0.7–2.7)	91.9

Table 2 continued

Pathogens	All types of clinical samples						Wounds					
	Number of studies	Total number of isolates	Number of specific pathogen isolates	Proportions	<i>I</i> ²	<i>I</i> ²	Number of studies	Total number of isolates	Number of specific pathogen isolates	Proportions	<i>I</i> ²	
<i>Aspergillus</i> spp.	16	12,443	111	0.3% (0.0–0.8)	92.0	92.0	8	8093	103	0.5% (0.0–1.4)	94.7	
<i>Candida albicans</i>	25	24,287	463	1.6% (1.0–2.3)	93.0	93.0	9	8250	137	1.7% (0.6–3.4)	94.9	
<i>Candida glabrata</i>	17	17,582	137	0.5% (0.2–0.8)	88.7	88.7	5	4253	12	0.2% (0.0–0.7)	80.0	
<i>Candida parapsilosis</i>	15	12,912	88	0.3% (0.1–0.7)	87.3	87.3	6	5491	41	0.3% (0.0–0.9)	88.3	
<i>Candida tropicalis</i>	24	24,882	220	0.6% (0.4–1.0)	87.2	87.2	7	7726	40	0.3% (0.1–0.6)	76.8	

or exogenous gram-negative bacteria from the gastrointestinal or respiratory tract gradually colonize the wound surface and replace gram-positive bacteria [8, 86]. Owing to differences in antibiotic sensitivity among different types of pathogens, understanding the types of pathogens causing nosocomial infections in patients with burn injuries and their resistance patterns is of paramount importance for the early prevention of such infections.

In this study, *Staphylococcus aureus* was the most common pathogen, with a proportion of 18.3%, which was slightly lower than the prevalence rates reported in Pakistan (24.05%) and Iran (20.2%) but comparable to those reported in India (18.11%) and Turkey (18.5%) [87–90]. *Staphylococcus aureus*, with its various surface proteins that facilitate binding to host proteins, such as fibronectin in the extracellular matrix [91, 92], is highly likely to infect wounds, including burns and surgical incisions [93, 94]. In addition, *Staphylococcus epidermidis* was the second most common gram-positive bacterium causing infections in patients with burn injuries. Although *Staphylococcus epidermidis* is a member of the normal microbiota of the human skin and actively initiates skin immune responses to maintain skin homeostasis, it becomes pathogenic when the skin is damaged [95]. In this study, the proportion of *Staphylococcus epidermidis* was 5.9%, which is consistent with findings in South Korea (4.4%) [96]. However, in a study conducted in the eastern region of China, the proportion of *Staphylococcus epidermidis* (0.75%) was significantly lower [18]. This difference may be owing to different causative factors.

This study conducted a meta-analysis of the antibiotic resistance of *Staphylococcus aureus* and *Staphylococcus epidermidis* and revealed an overall decreasing trend in the resistance of both gram-positive bacteria. *Staphylococcus aureus* showed significantly reduced resistance to tetracycline, gentamycin, and ampicillin, which is consistent with findings at the Beijing Children’s Hospital in China [97]. This phenomenon may be attributed to clone replacement leading to decreased antibiotic resistance. Several studies have demonstrated that community-acquired methicillin-resistant *Staphylococcus aureus* has rapidly spread to hospitals and become predominant, leading

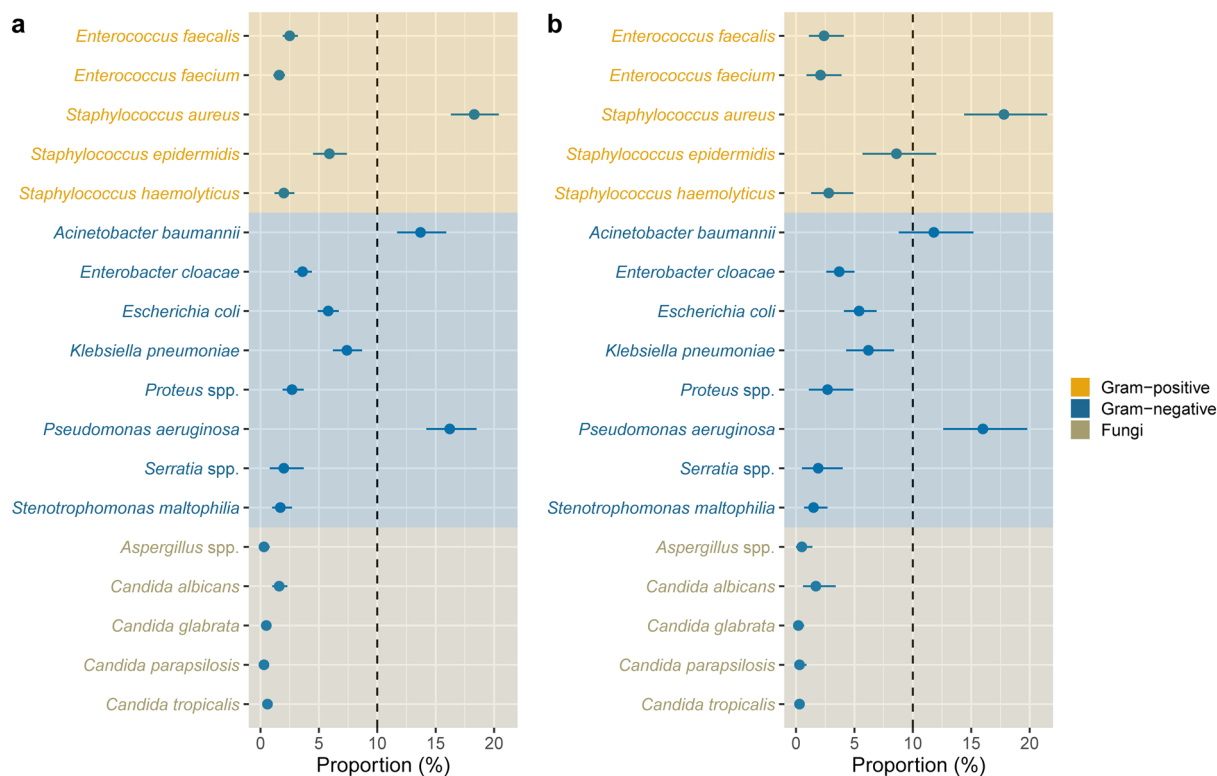


Fig. 3 Distribution of pathogens causing nosocomial infections in patients with burn injuries. **a** Meta-analyses using data for all types of clinical samples. **b** Meta-analyses using data for wounds

to a decrease in the detection rate of hospital-acquired methicillin-resistant *Staphylococcus aureus*. Since the resistance of community-associated methicillin-resistant *Staphylococcus aureus* has not significantly changed under the selection pressure of antibiotics, the overall trend is a decrease in the resistance of *Staphylococcus aureus* [98–100]. Similarly, the resistance of *Staphylococcus epidermidis* to tetracycline, gentamycin, and clindamycin significantly decreased. Furthermore, this study showed that both *Staphylococcus aureus* and *Staphylococcus epidermidis* remained fully sensitive to vancomycin, indicating its effectiveness in treating nosocomial infections caused by these two bacteria. Another reason for the overall decreasing trend in resistance of both gram-positive bacteria may be the National Action Plan to Contain Antimicrobial Resistance (2016–2020); the National Action Plan was issued in 2016 by multiple departments in response to the World Health Organization’s (WHO’s) Global Action Plan on Antimicrobial

Resistance [101], and implemented comprehensive governance measures at the national level to address bacterial resistance [102].

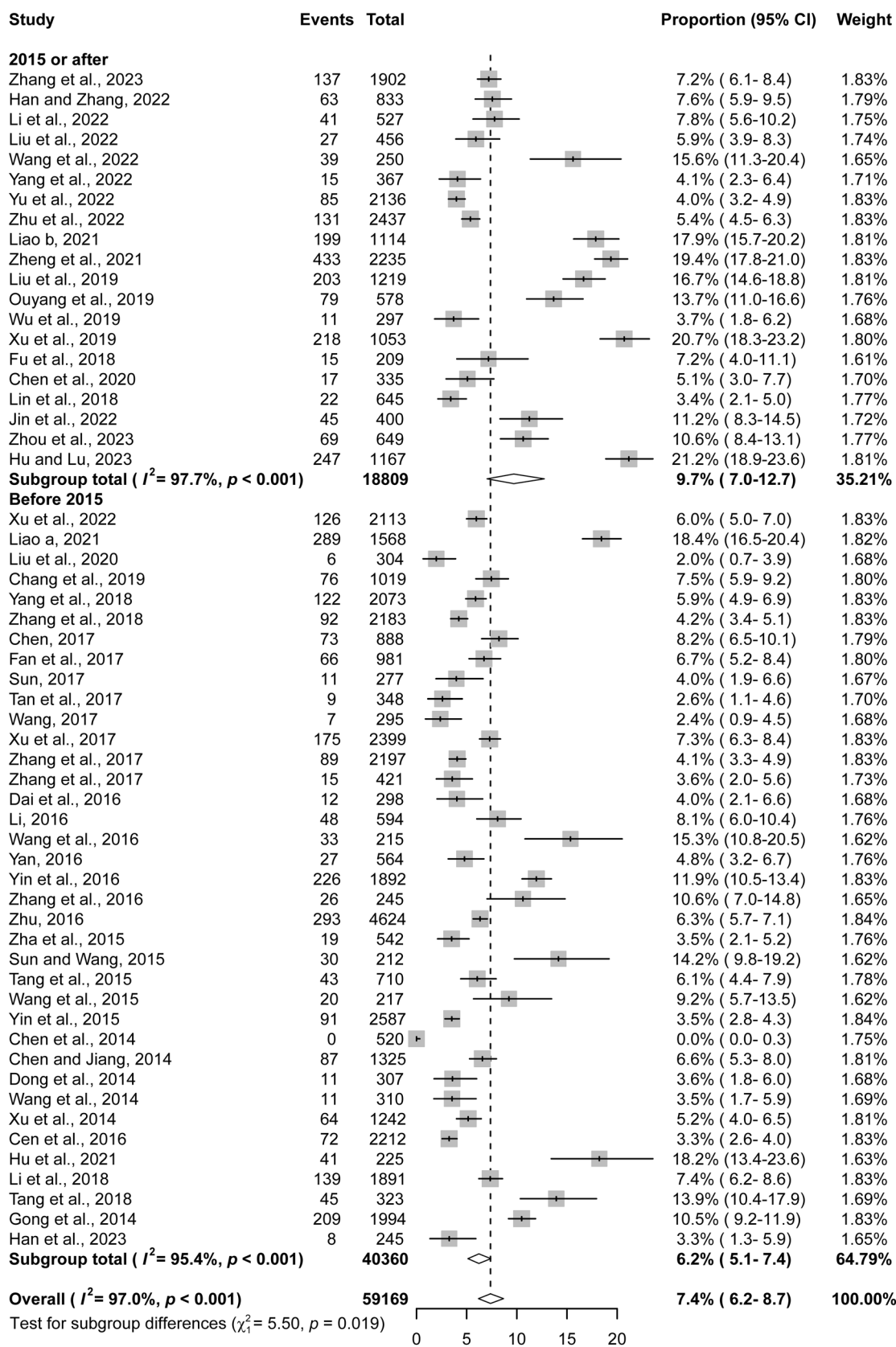
Gram-negative bacteria are the most common pathogens causing nosocomial infections in patients with burn injuries. In this study, three of the top five detected bacteria were gram-negative, namely, *Pseudomonas aeruginosa* (16.2%), *Acinetobacter baumannii* (13.7%), and *Klebsiella pneumoniae* (7.4%). Although *Pseudomonas aeruginosa* ranks second in the detection rate among pathogens causing nosocomial infections in patients with burn injuries, the composition of pathogens causing burn infections may vary because of differences in regional climates and hospital types. Honnegowda et al. conducted a survey at the Manipal Burns Centre in India and reported that *Pseudomonas aeruginosa* was the most common pathogen (35.3%) in samples from patients with burns [89]. Similarly, Saaiq et al. reported that *Pseudomonas aeruginosa* had the highest proportion (35.29%) in

Table 3 Pooled proportions of the top five pathogens causing nosocomial infections in patients with burn injuries across time subgroups

Subgroup	Proportions of pathogens			Estimate	<i>I</i> ²	Univariate meta-regression		
	Number of studies	Total number of isolates	Number of specific pathogen isolates			Coefficient (95% CI)	<i>P</i> value	<i>R</i> ²
<i>Staphylococcus aureus</i>								
2015 or after	22	19,994	3999	17.1% (13.9–20.5)	97.4	Ref	Ref	< 0.01
Before 2015	38	40,934	8475	19.0% (16.4–21.7)	97.9	0.025 (–0.039 to 0.089)	0.445	
<i>Pseudomonas aeruginosa</i>								
2015 or after	22	19,994	2773	13.5% (10.9–16.3)	96.8	Ref	Ref	4.89
Before 2015	39	42,825	7977	17.9% (15.1–20.9)	98.4	0.061 (0.001–0.121)	0.047	
<i>Acinetobacter baumannii</i>								
2015 or after	21	19,111	2554	15.1% (11.2–19.3)	98.4	Ref	Ref	< 0.01
Before 2015	36	40,056	5729	12.9% (10.6–15.5)	98.1	–0.030 (–0.099 to 0.038)	0.386	
<i>Klebsiella pneumonia</i>								
2015 or after	20	18,809	2096	9.7% (7.0–12.7)	97.7	Ref	Ref	9.60
Before 2015	37	40,360	2711	6.2% (5.1–7.4)	95.4	–0.064 (–0.114 to –0.014)	0.012	
<i>Staphylococcus epidermidis</i>								
2015 or after	14	12,662	974	5.3% (2.7–8.8)	98.3	Ref	Ref	< 0.01
Before 2015	27	29,616	1901	6.2% (4.7–7.9)	96.9	0.019 (–0.052 to 0.090)	0.604	

Pakistan [7]. *Acinetobacter baumannii* possesses strong adhesion and colonization capabilities, can resist dry and humid environments, and is widely distributed in nature [103]. Owing to its significantly increased isolation, infection, and resistance rates, infection control has become challenging. In this study, the proportion of *Acinetobacter baumannii* ranked third after *Pseudomonas aeruginosa*; this finding is consistent with the findings of Gupta et al. at a tertiary

hospital in India, where *Acinetobacter baumannii* was the third most common pathogen (14.83%) causing infections in patients with burn injuries [104]. Owing to differences in hospital management among different regions, the proportion of *Acinetobacter baumannii* also significantly differed. A study by Bayram et al. in Turkey showed that *Acinetobacter baumannii* was the most common pathogen (23.6%) isolated from patients with burn infection [105]. *Klebsiella pneumoniae*



◀Fig. 4 Proportions of *Klebsiella pneumoniae* in patients with burn injuries across different time subgroups

has gradually become one of the main causes of nosocomial infections in recent years [106]. Although in a study by Chaudhary et al. carried out at a tertiary hospital in Pakistan [87] *Klebsiella pneumoniae* ranked the same, the detection rate (15.9%) was significantly greater than that observed in our study (7.2%).

Gram-negative bacteria possess multiple mechanisms of resistance. For example, their double membrane structure confers intrinsic resistance to many antibiotics, while efflux pumps, in conjunction with the double membrane, increase resistance and encode various antibiotic-hydrolysing enzymes [107]. Owing to multiple resistance mechanisms, the resistance rates of gram-negative bacteria have been continuously increasing in recent years, posing a global challenge to the accurate and effective treatment of gram-negative bacterial infections. Therefore, understanding the resistance of gram-negative bacteria causing hospital infections is highly important for guiding the selection of appropriate antibiotics during the process of preventing infection. The results of this study show a decreasing resistance trend of *Pseudomonas aeruginosa* to certain antibiotics. However, its resistance to some other antibiotics, such as ampicillin, cefazolin, and cefotaxime, remains relatively high, which is consistent with the findings of Chaudhary et al. [87]. Among the antibiotics included in the analysis, *Acinetobacter baumannii* had high resistance (>50%) to all antibiotics, except minocycline and tigecycline, with resistance rates exceeding 90% for ampicillin, amikacin, cefazolin, and cefotaxime, which is consistent with multiple previous studies [87, 96, 105]. Notably, this study revealed a significant increase in the resistance of *Klebsiella pneumoniae*, for example, to trimethoprim-sulfamethoxazole, meropenem, and imipenem, which is consistent with the findings of multiple studies [104, 105, 108]. These results indicate the need for strict management of antibiotic use when treating gram-negative bacterial infections to prevent further increases in antibiotic resistance. The study findings also suggest the need

to introduce new antibiotics or other infection control measures in the treatment of gram-negative bacterial burn infections.

Fungi, including *Candida albicans* (1.6%), *Candida tropicalis* (0.6%), and *Candida glabrata* (0.5%), can also cause nosocomial infections in patients with burn injuries. Although fungal infections account for a small proportion of infections, infections caused by fungi in patients with burn injuries have no obvious specificity, unlike bacterial infections, thus making them difficult to distinguish and leading to misdiagnosis and delayed treatment [109, 110]. Some fungi, such as *Aspergillus* and *Zygomycetes*, are prone to invading blood vessels and spreading to internal organs after infection, often resulting in a poor prognosis and high mortality [111, 112]. Therefore, careful identification of pathogens causing infections in patients with burn injuries is necessary. Previous studies have shown that *Candida albicans* is the most common fungus that causes burn infections. However, in recent years, both domestic and foreign studies have shown a significant increase in the proportion of non-*Candida albicans* fungi, such as *Candida tropicalis* and *Candida glabrata*, among the detected fungi [113–115]. The reason for this phenomenon may be differences in the detection methods for fungi among different regions or even among countries.

Although there was a decreasing trend in the resistance of gram-positive bacteria observed in this study, we must remain vigilant. Moreover, owing to the persistently high levels of resistance in gram-negative bacteria, it is urgent to find solutions to this problem. The emergence of multidrug-resistant bacteria poses a significant threat to the life and health of patients. Therefore, effective prevention and treatment are crucial for improving patient outcomes [116]. Prior to initiating antibiotic therapy, strict microbial surveillance should be conducted, and efforts should be made to avoid the use of inappropriate medications [117, 118]. Additionally, the microbial composition of burn wounds is dynamic, and regular assessments by physicians are required to identify the primary pathogens and their resistance patterns, thus enabling the formulation of optimal treatment strategies for burn infections.

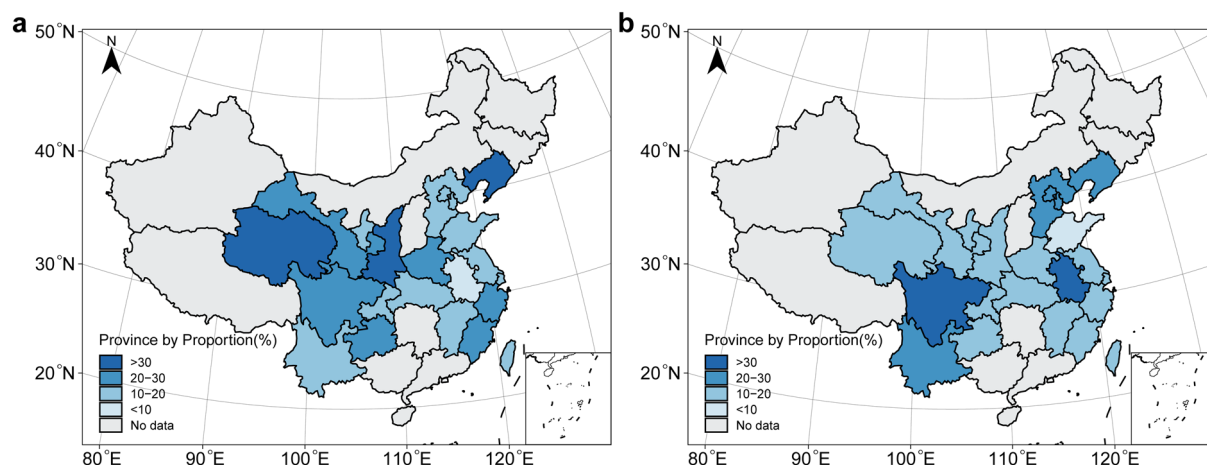


Fig. 5 Geographical distribution of proportions of **a** *Staphylococcus aureus* and **b** *Pseudomonas aeruginosa* in patients with burn injuries

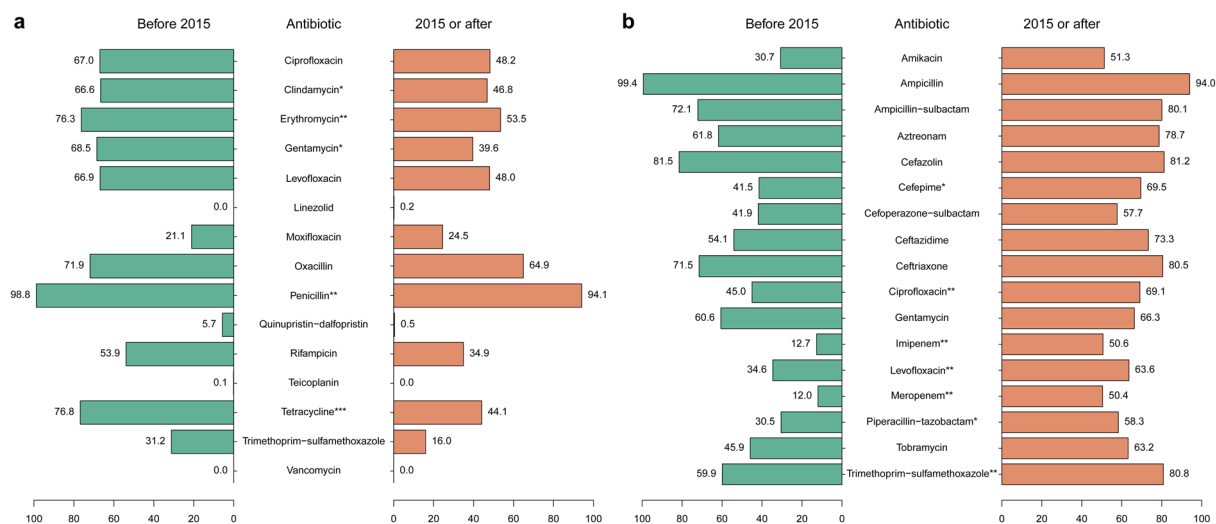


Fig. 6 Antibiotic resistance rates for *Staphylococcus aureus* and *Klebsiella pneumoniae* in different year subgroups (* $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$)

Despite the strict adherence to the PRISMA guidelines in this study, certain limitations need to be considered. First, considerable heterogeneity among the included studies was observed, and subgroup analyses and meta-regression analysis could not fully explain the sources of heterogeneity. Second, because small-sample studies are prone to chance results, studies with fewer isolated pathogens associated with burn infection were excluded

from the analysis, resulting in missing detection data for some provinces. Third, the data used for the meta-analysis were retrieved from public databases, which provide limited clinical information, such as patient injury factors, burn sites, burn areas, and burn depths, making it impossible to analyze potential factors affecting the distribution of pathogens in patients with burn injuries.

CONCLUSIONS

The results of this study indicate that, in China, the most common gram-positive bacteria involved in burn infections are *Staphylococcus aureus* and *Staphylococcus epidermidis*, while the most common gram-negative bacteria are *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*. Wound infections are the most common type of infections in patients with burn injuries. The common pathogens observed in wound infections of patients with burn injuries were consistent with those from clinical samples of all types, with a slight difference in the ranking, such that the detection rate of *Staphylococcus epidermidis* was greater than that of *Klebsiella pneumoniae*. Additionally, we found that the analyzed pathogens exhibited very high levels of resistance to penicillin antibiotics and some cephalosporin antibiotics. Therefore, infections caused by these bacteria may have a high incidence and lead to high mortality, highlighting the critical importance of effective prevention and treatment strategies to improve the prognosis of individuals suffering from burns. There is an urgent need to develop more effective antibiotics to address potential infections in patients with burn injuries. Moreover, effective management of the clinical environment to reduce the quantity of environmental pathogens can effectively lower the incidence of nosocomial infections. Notably, the proportion and resistance of *Klebsiella pneumoniae* have significantly increased, which warrants attention in clinical practice to prevent infection outbreaks among individuals suffering from burns.

Author Contributions. Gaoming Li, Yu Luo, and Wei Qian conceived and designed the study. Yuhui Yang and Qingling Zeng performed the literature search. Zhenkun Wang, Lang Zhou, and Aibo He worked on the data extraction and collection. Gaoming Li, Yuhui Yang, Guangyun Hu, and Zongyue Chen analyzed and interpreted the data. Yuhui Yang and Qingling Zeng wrote the initial draft of the report. Gaoming Li, Yu Luo, and Wei Qian critically revised subsequent

versions of the report. All authors reviewed and approved the final report.

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Data Availability. All the raw data from the 60 analyzed studies are available in the main text and Supplementary Material; further inquiries can be sent to the corresponding author.

Declarations

Conflict of Interest. Yuhui Yang, Qingling Zeng, Guangyun Hu, Zhenkun Wang, Zongyue Chen, Lang Zhou, Aibo He, Wei Qian, Yu Luo, and Gaoming Li declare no competing interests.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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