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Review Article

Resistance Patterns of Gram-Negative Bacteria and Surgical Site Infections Across the Middle East: A Systematic Review and Meta-Analysis

Meer Kamal[1], Mohammad Al-Tamimi[2], Ayman D. Alsheikh[3], Imdat Kilbas[4], Khaled M. Aboshanab[5], Muhammad Yasir[6], Mutasim E. Ibrahim[7], Shnya R. Hamalaw[8], Suhaib H. Kakamad[9], Hussein M. Hamasalih[10], Hawdang A. Sidiq[10], Shvan L. Ezzat[11], Yasemin Çağ[12], Berun A. Abdalla[1,13]*

1. *Department of Scientific Affairs, Smart Hospital, Madam Mitterrand Street, Sulaymaniyah, Iraq*
2. *Department of Microbiology, Pathology and Forensic Medicine, Faculty of Medicine, The Hashemite University, Zarqa, Jordan*
3. *Department of Medical Laboratory Sciences, Faculty of Allied Medical Sciences, Zarqa University, Zarqa, Jordan*
4. *Dental Prosthesis Technology Program, Vocational School of Health Services, Fenerbahce University, Istanbul, Türkiye*
5. *Department of Microbiology and Immunology, Faculty of Pharmacy, Ain Shams University, Cairo, Egypt*
6. *Pathological Sciences Department-MBBS Program, Fakeeh College for Medical Sciences, and Fakeeh Care Group, Jeddah, Saudi Arabia*
7. *Department of Microbiology and Clinical Parasitology, College of Medicine, University of Bisha, Bisha, Saudi Arabia*
8. *College of Medicine, University of Sulaimani, Madam Mitterrand Street, Sulaymaniyah, Iraq*
9. *Department of Medical Laboratory Technology, Faculty of Health Sciences, Qaiwan International University, Sulaymaniyah, Iraq*
10. *Department of Quality, Smart Hospital, Madam Mitterrand Street, Sulaymaniyah, Iraq*
11. *Department of Laboratory, Smart Hospital, Madam Mitterrand Street, Sulaymaniyah, Iraq*
12. *Department of Infectious Diseases and Clinical Microbiology, Istanbul Medeniyet University Faculty of Medicine, Istanbul, Türkiye*
13. *Kscien Organization for Scientific Research (Middle East Office), Azadi Mall, Hamdi Street, Sulaymaniyah, Iraq*

***Corresponding author:** berun.anwer95@gmail.com (B. A. Abdalla). Zargatay Taza, House number 54, Zip code: 46001, Sulaymaniyah, Iraq*

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Abstract

Introduction

Surgical site infections (SSIs) are a leading healthcare-associated infection, driven by multidrug-resistant Gram-negative bacteria. Regional data from the Middle East remain limited. This meta-analysis aimed to estimate pooled antimicrobial resistance (AMR) profiles of Gram-negative isolates (GNI) recovered from SSIs.

Methods

PubMed/MEDLINE and Google Scholar were searched in January 2026 for studies reporting AMR in SSI GNI. Eligible studies were English-language reports from the Middle East presenting AMR patterns of Gram-negative bacteria recovered from SSIs. Case reports, laboratory and animal studies, conference papers, and abstract-only publications were ineligible. Proportions were pooled using DerSimonian-Laird random-effects models with Freeman-Tukey double-arcsine transformation, heterogeneity assessed by I^2.

Results

Twenty-three studies from 8 countries were included. GNI comprised 71.9% (95% CI 60.5-82.2) of all culture-positive isolates and, when restricted to SSI-confirmed specimens, 86.4% (95% CI 63.6-99.3). *Escherichia coli* was most frequent (27.9%), followed by *Pseudomonas aeruginosa* (25.8%) and *Klebsiella pneumoniae* (21.3%). Resistance exceeded 65% for ampicillin in *E. coli* and for ceftriaxone in both *E. coli* and *K. pneumoniae*, with resistance to the remaining third-generation cephalosporins (cefotaxime, ceftazidime) ranging from 46.5% to 85.9%.

Conclusion

Gram-negative SSI isolates in the Middle East showed high resistance across many agent classes, with substantial multidrug resistance, carbapenem resistance, and ESBL production. This regional resistance profile reinforces the need for local, SSI-specific surveillance and antimicrobial stewardship.

1. Introduction

Surgical site infections (SSIs) are among the most frequent and challenging complications following surgical procedures, significantly impacting patient outcomes, hospital costs, and quality of care worldwide. They are the most frequent healthcare-associated infection in low- and middle-income countries (LMICs) [1]. The proportion of SSIs is reported to be up to 27% of healthcare-associated infections in LMICs [2]. The pooled incidence of SSIs in LMICs is reported to be 5.9 per 100 surgical operations and 11.2 per 100 surgical patients, with rates reaching 11.7% after caesarean section [1].

Even though SSIs were historically dominated by Gram-positive organisms, current epidemiological data show the emergence of multidrug-resistant Gram-negative bacteria (MDR-GNB), which is clinically significant in various healthcare settings. The most commonly reported GNBs were *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp. [3].

Despite the use of perioperative antibiotics, SSIs continue to burden postoperative patients, a problem attributed to the emergence of antimicrobial resistance (AMR) [4]. Globally, AMR is a dire health threat [4]. It is estimated to be responsible for approximately five million deaths annually [5]. In the United States, a significant number of pathogens contributing to the SSI were reported to be resistant to standard prophylactic antibiotics [6]. The problem of AMR is particularly pronounced in developing countries [7]. To address this threat, the World Health Organization (WHO) prioritizes antibiotic-resistant bacteria to guide research and control strategies. In its 2024 Bacterial Priority Pathogens List, GNB dominate the critical tier [8].

Despite this global attention, robust regional data regarding resistance patterns in SSI from the Middle East remain scarce [6]. Continuous surveillance is therefore needed and requires a systematic approach that accounts for patient-, procedure-, and environment-related risk factors [9].

This systematic review and meta-analysis aimed to estimate the regional pooled antibiotic-resistance profiles of Gram-negative isolates (GNI) recovered from SSI.

2. Methods

2.1 Study Protocol

This systematic review and meta-analysis study was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement guidelines.

2.2 Data Sources and Search Strategy

A comprehensive systematic search was conducted in PubMed/MEDLINE and Google Scholar in January 2026 to identify published studies reporting antibiotic resistance patterns of GNI from SSIs in the Middle East. The search strings were as follows. PubMed/MEDLINE: ("Antimicrobial Resistance"[tiab] OR "Antibiotic Resistance"[tiab] OR MDR[tiab] OR "multidrug-resistant"[tiab]) AND ("Surgical Wound Infection"[Mesh] OR "Surgical Site Infection"[ti] OR SSI[ti] OR "Postoperative Wound Infection"[ti]) AND ("Gram-Negative Bacteria"[Mesh] OR Enterobacteriaceae[tiab] OR "Escherichia coli"[tiab] OR "Klebsiella pneumoniae"[tiab] OR "Pseudomonas aeruginosa"[tiab] OR "Acinetobacter baumannii"[tiab]). Google Scholar: allintitle: "Gram negative" OR Enterobacteriaceae OR "Escherichia coli" OR "E coli" OR Klebsiella OR Pseudomonas OR Acinetobacter "Wound Infection" OR "Surgical Wound Infection" OR "Surgical Site Infection". Manual citation searching of all retrieved articles was performed for additional relevant studies.

2.3 Eligibility Criteria

Studies were included if: (1) they were published in English; (2) reported human clinical samples of GNI recovered from SSIs; (3) reported AMR patterns for SSI GNI; (4) were conducted in the Middle East, which for this review was defined as the transcontinental region comprising the Arabian Peninsula, the Levant, Iraq, Iran, Türkiye, and Egypt; and (5) for studies that sampled mixed clinical specimens, SSI-specific isolates and their antimicrobial-susceptibility data could be extracted separately.

Studies were excluded if they: (1) had insufficient data on bacterial species identification, antimicrobial susceptibility testing, or confirmation of SSI; (2) were case reports, in vitro or animal studies, or conference papers; (3) were abstract-only publications; or (4) were in non-recommended journals/publishers [10].

2.4 Study Selection Process

Two reviewers independently screened the titles and abstracts of all studies to identify studies meeting the eligibility criteria. Retrieved eligible articles underwent full-text review by both reviewers. A third reviewer was enlisted to cast the deciding vote and resolve discrepancies by evaluating conflicting data and reaching a consensus. Duplicate records were removed manually.

2.5 Data-Collection Process

Two reviewers independently extracted data using a structured Microsoft Excel spreadsheet. Discrepancies in extracted data were resolved by consulting a third reviewer. Data extracted from eligible studies included: (1) study characteristics (first author, year

of publication, country, study design, study period, and sample size); (2) patient characteristics included demographic variables (age, sex), type of surgery, surgical urgency (elective and emergency), surgical wound classification (clean, clean contaminated, contaminated, dirty), and SSI classification (superficial incisional, deep incisional, organ/space); (3) microbiological profile included total clinical sample counts, culture-positive isolate counts, microbial growth patterns (monomicrobial and polymicrobial), the total number of Gram-negative isolates (GNI), and the number of GNI recovered specifically from SSIs (SSI-specific GNI, i.e., defined by specimen source rather than by species); (4) susceptibility of antimicrobials for SSI-specific GNI across the following antibiotic classes: aminoglycosides (gentamicin, amikacin), carbapenems (imipenem, meropenem), cephalosporins (cefotaxime, ceftazidime, ceftriaxone, cefepime, cefoxitin, cefuroxime), fluoroquinolones (ciprofloxacin, levofloxacin), folate pathway inhibitors (co-trimoxazole), beta-lactam beta-lactamase inhibitors (ampicillin/sulbactam, piperacillin/tazobactam, amoxicillin/clavulanate), penicillins (ampicillin) and monobactams (aztreonam); and (5) antibiotic resistance patterns: MDR, extended-spectrum beta-lactamase (ESBL) and carbapenem resistance (CR). For studies reporting mixed clinical specimens, only data that could be specifically attributed to surgical site infections were extracted for SSI-specific resistance analyses.

2.6 Outcomes

The primary outcome was the AMR profile of GNI recovered from SSIs. For each species, this comprised the pooled proportion of resistance to each individual antimicrobial agent, together with the pooled proportions of isolates classified as MDR, CR, and ESBL-producing.

Secondary outcomes were (i) the pooled proportion of GNI among all culture-positive isolates recovered by the included studies (the all-isolate denominator), (ii) the pooled proportion of GNI among isolates confirmed to derive from SSIs (the SSI-restricted denominator), and (iii) the pooled prevalence of each individual species among SSI GNI. These outcomes characterize the organisms that underlie the resistance estimates.

Pooled proportions of MDR, CR, and ESBL production were analyzed only when these categories were classified and reported by the primary studies themselves; they were not derived from agent-level resistance percentages. Accordingly, the number of studies and isolates contributing to the MDR, CR, and ESBL estimates may differ from those contributing to agent-level resistance estimates.

2.7 Quality Assessment

Methodological quality was appraised using design-specific Joanna Briggs Institute critical appraisal checklists [11]. Studies were assessed using the checklist corresponding to their design: cross-sectional (8 items), case-control (10 items), cohort (11 items), or case series (10 items). These appraisals informed the risk-of-bias domain of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) certainty assessment.

2.8 Data Analysis

Data were analyzed using the meta package in R version 4.6.0. Proportions were pooled using a DerSimonian-Laird random-effects model with the Freeman-Tukey double-arcsine transformation to stabilize variances and to accommodate studies reporting proportions of 0% or 100%.

Each bacterium-antibiotic combination (and likewise each species and resistance-pattern outcome) was pooled only when at least two studies contributed data. Between-study heterogeneity was assessed using Cochran's Q test and quantified using the I^2 statistic and the between-study variance (τ^2). Each species-level prevalence was pooled independently across its own set of contributing studies; the resulting estimates are therefore not mutually exclusive partitions of a common denominator and are not expected to sum to 100%.

To explore geographical variation, resistance was further analyzed in subgroups by country. A formal between-country comparison (Cochran's Q test between subgroups) was performed only when at least two countries each contributed at least two studies, and the corresponding p-value is reported for these analyses.

Temporal trends were explored using random-effects meta-regression of the logit-transformed proportion of resistance on publication year for each bacterium-antibiotic combination. As sampling periods were inconsistently reported, publication year served as a proxy for collection year. These regressions are reported as the odds ratio for resistance per year with 95% confidence intervals, and were carried out only for combinations with at least six studies; significant trends ($p < 0.05$) were confirmed by leave-one-out analysis and considered robust only if significance persisted after removal of any single study.

2.9 Certainty of Evidence

The certainty of evidence for each pooled estimate was rated with the GRADE approach adapted for prevalence data [12]. As all included studies were observational, every outcome began at low certainty and was rated down for risk of bias, inconsistency, indirectness, imprecision, and publication bias. Inconsistency was judged from the I^2 statistic, imprecision from the width of the pooled confidence interval and the number of contributing isolates, and risk of bias from the JBI appraisal; publication bias could not be formally assessed.

3. Results

3.1 Study Selection

A total of 543 records were identified through electronic searches (PubMed/MEDLINE and Google Scholar) and backward citation searching. After 20 duplicates were removed, 523 records underwent title and abstract screening, of which 422 were excluded.

The remaining 101 reports were sought for retrieval; 3 could not be retrieved. The 98 reports assessed for eligibility underwent full-text screening, after which 75 were excluded, leaving 23 included studies (Figure 1) [6,9,13–33].

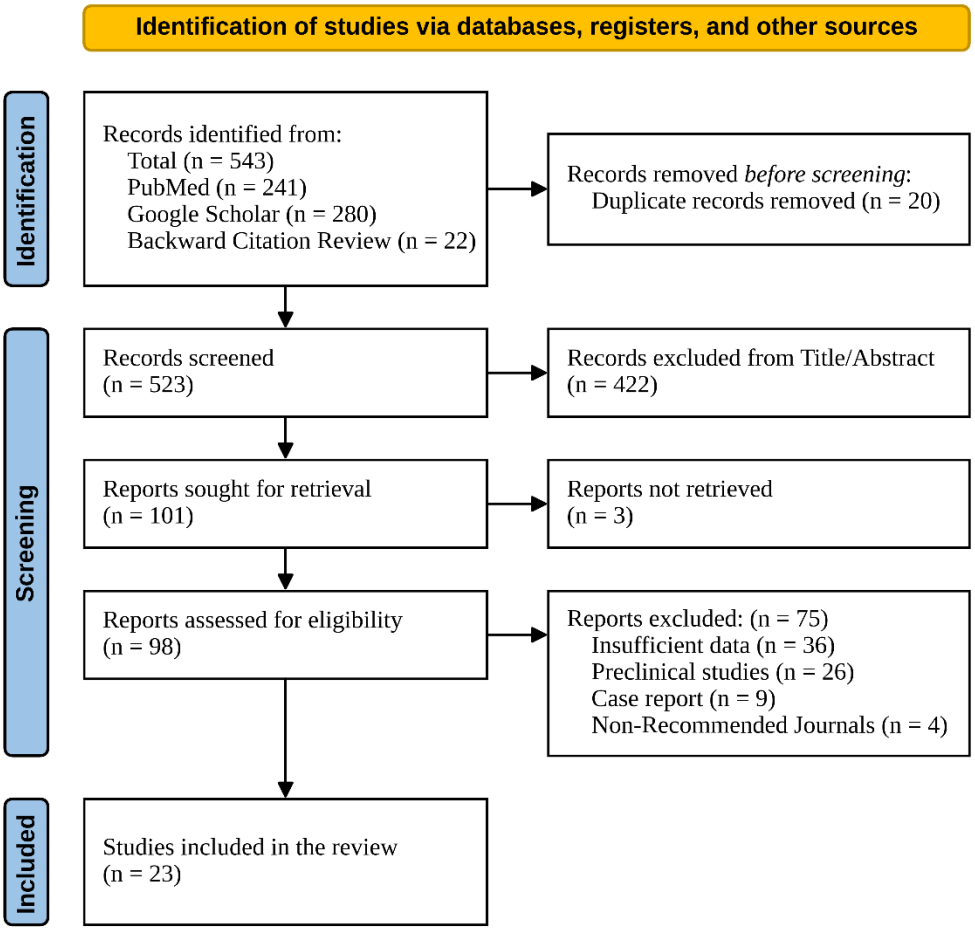


Figure 1. *PRISMA 2020 flow diagram illustrating the study selection process.*

3.2 Study and Patient Characteristics

The included studies were published between 2005 and 2026. They were conducted across 8 countries, most frequently Egypt (n = 6), Iraq (n = 4), Türkiye (n = 4), Iran (n = 3), and Saudi Arabia (n = 3). Most included studies were cross-sectional in design (n = 17), followed by prospective cohort studies (n = 3), case-control studies (n = 2), and one case series. Study duration varied and ranged from 4 to 120 months. The combined sample comprised 5,413 patients.

Sex distribution was reported for 3,694 patients, with 1,866 males (50.51%) and 1,828 females (49.49%). Patient age was reported with a pooled weighted mean of 44.57 (SD 20.32). Seventeen studies (n = 4,027; 74.39%) sampled SSIs exclusively, while six (n = 1,386; 25.61%) included mixed clinical specimens (Table 1 & Table 2). Methodological quality, assessed using the Joanna Briggs Institute critical appraisal checklist, was generally good across the four designs (Table S1).

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Table 1. Characteristics of the included studies.

Author(s)	Ref	Year	Country	Study Design	Duration (months)	Age (Mean ± SD)	Sample size	Male	Female	Hospital stays (d)	Infection type	JBI
Kawtharani et al.	[25]	2026	Lebanon	Cross-sectional	9	57.0 ± 21	63	23	40	N/A	SSI	8/8
Ramadan et al.	[13]	2025	Egypt	Cross-sectional	6	42.0 ± 14.2	130	76	54	N/A	SSI	6/8
Anwar et al.	[17]	2025	Iraq	Cross-sectional	12	50.1 ± 20.7	128	67	61	4	Mixed Clinical	5/8
Muhammed et al.	[23]	2024	Iraq	Cross-sectional	6	41.7 ± 18.8	61	31	30	N/A	SSI	7/8
Alruways et al.	[22]	2023	Saudi Arabia	Cross-sectional	12	N/A	31	21	10	N/A	Mixed Clinical	6/8
Heidari et al.	[14]	2022	Iran	Cross-sectional	6	N/A	115	63	52	N/A	Mixed Clinical	8/8
Elnagar	[16]	2021	Egypt	Cross-sectional	12	49.2 ± 13	186	117	69	6.7	SSI	7/8
Ali and Al-Jaff	[28]	2021	Iraq	Cross-sectional	12	N/A	133**	49	64	N/A	SSI	7/8
Hemmati et al.	[33]	2020	Iran	Cross-sectional	24	49.0 ± 19.6	78	54	24	16.6	SSI	5/8
El-Saed et al.	[6]	2020	Saudi Arabia	Cross-sectional	120	49.5 ± 18	403*	120	280	N/A	SSI	6/8
Raouf et al.	[30]	2020	Egypt	Prospective Cohort	24	40.9 ± 13.1	57	27	30	12.6	SSI	5/11
Metwally and Aamir	[26]	2020	Egypt	Cross-sectional	10	42.0 ± 13	135	84	51	7.7	SSI	7/8
Abdulqader and Saadi	[31]	2019	Iraq	Prospective Cohort	6	45.8 ± 15.2	31	20	11	1.87	SSI	8/11

Table 1. Continued….

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El-Kholy et al.	[18]	2018	Egypt	Case-control	12	51.0 ± 21.7	33	24	9	13	SSI	9/10
Al-Awaysheh	[9]	2018	Jordan	Cross-sectional	12	55.1 ± 10	102	47	55	N/A	SSI	7/8
Nasiri et al.	[19]	2018	Iran	Cross-sectional	N/A	43.0 ± 22.1	369	164	205	19.9	Mixed Clinical	7/8
Helal et al.	[32]	2015	Egypt	Cross-sectional	N/A	N/A	100	N/A	N/A	≥7.0	SSI	7/8
Namıduru et al.	[24]	2013	Türkiye	Prospective Cohort	4	40.6 ± 22.4	1,397	706	691	17.9	SSI	3/11
Khan et al.	[20]	2012	Qatar	Case series	24	44.0 ± 14.7	6	5	1	N/A	SSI	10/10
Khairy et al.	[29]	2011	Saudi Arabia	Cross-sectional	9	45.4 ± 12.7	131	93	38	N/A	SSI	8/8
Bayram and Balci	[21]	2006	Türkiye	Cross-sectional	12	N/A	615	N/A	N/A	N/A	Mixed Clinical	6/8
Akıncı et al.	[27]	2005	Türkiye	Case-control	9	53.1 ± 20.8	128	75	53	19.5	Mixed Clinical	9/10
Surucuoglu et al.	[15]	2005	Türkiye	Cross-sectional	60	N/A	981	N/A	N/A	N/A	SSI	7/8

**Sex reported for 400 patients. **Sex reported for 113 patients.*
Abbreviations: N/A, not reported. JBI, Joanna Briggs Institute critical appraisal score.

Table 2. Summary of patient characteristics and Gram-negative isolate distribution.

Variable	Total no. (%)*
Patients	**5,413 (100.00%)**
Mean Age	**44.57** [a]
Male	1,866 (50.51%) [b]
Female	1,828 (49.49%) [b]
Isolate Source	**5,413 (100.00%)**
SSI	4,027 (74.39%)
Mixed Clinical	1,386 (25.61%)
Surgical Wound Classification	**2,523 (100.00%)** [c]
Clean-contaminated	1,602 (63.50%)
Clean	490 (19.42%)
Contaminated	331 (13.12%)
Dirty	100 (3.96%)
SSI Classification	**998 (100.00%)** [c]
Superficial incisional	613 (61.42%)
Deep incisional	330 (33.07%)
Organ-Space	55 (5.51%)
Surgical Urgency	**698 (100.00%)** [c]
Emergency Surgery	411 (58.88%)
Elective Surgery	287 (41.12%)
Types Of Surgery	**2,130 (100.00%)** [c]
General/Gastrointestinal Surgery	774 (36.34%)
Orthopedic	445 (20.89%)
Obstetrics/Gynecology	271 (12.72%)
Cardiovascular & Thoracic	225 (10.56%)
Pediatric surgery	65 (3.05%)
Neurosurgery	39 (1.83%)
Plastic surgery	35 (1.64%)
Urological surgery	12 (0.56%)
Other/unspecified	264 (12.39%)
Microbial Growth Pattern	**312 (100.00%)** [c]
Monomicrobial	188 (60.26%)
Polymicrobial	124 (39.74%)
Susceptibility Test Method	**23 (100.00%)**
Disc Diffusion	19 (82.61%)
Automated systems (VITEK)	2 (8.70%)
Mixed methods	2 (8.70%)
Microbial Profile among GNB Isolates	**2,122 (100.00%)** [c]
Pseudomonas aeruginosa	637 (30.02%)
Escherichia coli	480 (22.62%)
Klebsiella pneumoniae	375 (17.67%)
Acinetobacter baumannii	269 (12.68%)

Table 2. Continued....

Enterobacter species	161 (7.59%)
Proteus mirabilis	109 (5.14%)
Citrobacter species	25 (1.18%)
Other gram negatives**	66 (3.11%)
SSI Gram-Negative Bacteria Isolates	**1,322 (62.30%)**
Non-SSI Gram-Negative Bacteria Isolates	**800 (37.70%)**
Microbial Profile among SSI GNB Isolates	**1,322 (100.00%)** [c d]
Escherichia coli	332 (25.11%)
Pseudomonas aeruginosa	320 (24.21%)
Klebsiella pneumoniae	280 (21.18%)
Acinetobacter baumannii	113 (8.55%)
Enterobacter species	99 (7.49%)
Proteus mirabilis	90 (6.81%)
Citrobacter species	23 (1.74%)
Other gram negatives**	65 (4.92%)

**Percentages may not add up to 100 due to rounding.*
***Other GNB isolates include* Stenotrophomonas maltophilia*:* Serratia *spp.:* Providencia *spp.:* Salmonella *Typhimurium:* Burkholderia cepacia*:* Morganella morganii*:* Bacteroides fragilis*:* Proteus vulgaris*.*
[a]*: Number reported is pooled weighted mean across 17 studies.*
[b]*: Sex distribution was reported in 20 studies (n = 3,694).*
[c]*: Totals for each section correspond to the number of relevant cases and isolates.*
[d]*: This total is a crude count of all Gram-negative isolates. Species prevalences are pooled estimates drawn only from studies reporting each species, so their denominators are study-dependent and lower than this total.*
Abbreviations: SSI, Surgical site infection; GNB, Gram-negative bacteria.

3.3 Surgical Wound and Procedure Characteristics

The majority of surgical wounds were clean-contaminated, 1,602 (63.50%), followed by clean, 490 (19.42%), contaminated, 331 (13.12%), and dirty, 100 (3.96%). The three most frequent surgery types were general/gastrointestinal surgery, 774 (36.34%), orthopedic surgery, 445 (20.89%), and obstetrics/gynecology, 271 (12.72%). A large proportion of the SSIs were superficial incisional, 613 (61.42%), followed by deep incisional, 330 (33.07%), and organ-space, 55 (5.51%). Microbial growth patterns were monomicrobial in 188 (60.26%) and polymicrobial in 124 (39.74%). The most common susceptibility test method was disc diffusion, 19 (82.61%) (Table 2).

3.4 Main Outcomes

3.4.1 Antimicrobial Resistance Estimates

Cefoxitin demonstrated the peak pooled resistance in *E. coli* at 82.4% (95% CI 41.5-100.0), with ampicillin-sulbactam recording the next highest at 74.8% (95% CI 48.1-93.9). *K. pneumoniae* isolates showed the highest resistance to cefoxitin at 88.3% (95% CI 64.7-99.6), closely trailed by cefotaxime at 85.9% (95% CI 65.1-98.1). Among clinically relevant anti-pseudomonal agents, the greatest resistance level for *P. aeruginosa* was observed against ceftazidime, 59.1% (95% CI 33.7-82.0), followed by gentamicin, 46.7% (95% CI 28.5-65.3). Among clinically relevant agents, *A. baumannii* showed the highest resistance to cefepime at 84.9% (95% CI 70.2-95.2), followed by ampicillin-sulbactam at 84.2% (95% CI 55.5-99.2). Among the antibiotics tested against *P. mirabilis*, ciprofloxacin yielded the top resistance rate of 45.8% (95% CI 15.7-77.6), followed by ceftazidime, 44.9% (95% CI 10.4-82.6). Finally, *Enterobacter* spp. exhibited a top pooled resistance of 52.0% to ceftazidime (95% CI 23.2-80.1) and a subsequent 49.6% to ciprofloxacin (95% CI 21.9-77.3). Resistance to imipenem and meropenem was 13.9% (95% CI 4.3-27.7) and 7.7% (95% CI 1.2-18.8) in *E. coli*, 22.2% (95% CI 9.8-37.9) and 23.3% (95% CI 9.6-40.8) in *K. pneumoniae*, and 34.1% (95% CI 16.0-54.9) and 31.7% (95% CI 14.0-52.6) in *P. aeruginosa* (Table 3).

3.4.2 Multidrug Resistance, Carbapenem Resistance, and ESBL Production

The pooling for MDR ranged from 27.0% in *P. aeruginosa* (95% CI 5.5-54.9) to 55.2% in *A. baumannii* (95% CI 25.5-83.4). Carbapenem resistance peaked in *A. baumannii* at 87.0% (95% CI 55.5-100.0); in *K. pneumoniae* it was at 57.4% (95% CI 41.8-72.3). The pooling for ESBL production in *K. pneumoniae* was 45.8% (95% CI 15.9-77.2) and for *P. mirabilis* 60.3% (95% CI 25.9-90.6). Several pools rested on a few studies and showed wide confidence intervals (Table 4).

3.4.3 Microbiological Profile of Surgical Site Infections

The pooled proportion of GNI among all culture-positive isolates was 71.9% (95% CI 60.5-82.2); when restricted to isolates confirmed to derive from SSIs, it was 86.4% (95% CI 63.6-99.3). Both estimates showed very high heterogeneity (I^2 = 98.1% and 99.3%, respectively). Among GNI recovered from SSIs, *E. coli* was the most frequently isolated species, with a pooled prevalence of 27.9% (95% CI 23.1-33.0, I^2 = 69.1%, k = 18, n = 1,267), followed closely by *P. aeruginosa* at 25.8% (95% CI 18.4-34.0, I^2 = 89.0%, k = 19, n = 1,293) and *K. pneumoniae* at 21.3% (95% CI 16.0-27.1, I^2 = 79.7%, k = 18, n = 1,267).

Table 3. Pooled resistance estimates for individual antimicrobial agents among Gram-negative bacterial species isolated from surgical site infections

Antibiotic drug	Resistant (n)	Sample (n)	Pooled resistance (%) *	95% CI	I^2 (%)	P-value**
Escherichia coli						
Amikacin	36	139	25.6	4.1 - 57.3	93.2	<0.001
Gentamicin	68	183	42.9	21.4 - 65.9	89.9	<0.001
Imipenem	20	158	13.9	4.3 - 27.7	77.9	<0.001
Meropenem	13	161	7.7	1.2 - 18.8	77.3	<0.001
Cefuroxime	31	83	54.2	6.3 - 97.1	95.7	<0.001
Cefepime	42	60	73.9	35.6 - 98.0	89.7	<0.001
Cefotaxime	35	78	46.5	26.5 - 67.1	71.9	0.014
Ceftazidime	51	111	67.4	20.8 - 98.6	96.0	<0.001
Ceftriaxone	42	59	73.8	56.2 - 88.1	50.4	0.109
Cefoxitin	36	45	82.4	41.5 - 100.0	89.1	<0.001
Ciprofloxacin	57	91	69.8	44.0 - 90.3	84.6	<0.001
Levofloxacin	26	48	64.9	26.6 - 94.4	87.2	<0.001
Co-trimoxazole	65	129	52.7	39.5 - 65.8	52.9	0.060
Aztreonam	19	92	38.8	7.9 - 76.1	91.3	<0.001
Amoxicillin-clavulanate	55	126	55.3	33.5 - 76.1	82.2	<0.001
Ampicillin-sulbactam	34	45	74.8	48.1 - 93.9	68.9	0.040
Piperacillin-tazobactam	5	62	16.2	0.0 - 80.7	94.4	<0.001
Ampicillin	65	117	71.2	36.8 - 95.5	92.4	<0.001
Klebsiella pneumoniae						
Amikacin	57	125	31.4	9.0 - 59.7	90.1	<0.001
Gentamicin	66	127	49.6	26.1 - 73.2	86.1	<0.001
Imipenem	31	125	22.2	9.8 - 37.9	71.1	0.001
Meropenem	35	121	23.3	9.6 - 40.8	74.6	<0.001
Cefepime	45	66	60.2	38.1 - 80.2	65.8	0.020
Cefotaxime	62	71	85.9	65.1 - 98.1	72.8	0.012
Ceftazidime	86	125	62.5	38.4 - 83.7	85.9	<0.001
Ceftriaxone	67	79	80.9	61.8 - 94.4	68.1	0.024
Cefoxitin	50	56	88.3	64.7 - 99.6	78.1	0.010
Ciprofloxacin	45	86	41.9	13.1 - 74.2	88.4	<0.001
Levofloxacin	28	47	56.1	38.1 - 73.3	28.2	0.243
Co-trimoxazole	52	79	67.5	42.3 - 88.2	79.0	<0.001
Aztreonam	21	64	31.0	10.2 - 57.0	73.3	0.011
Amoxicillin-clavulanate	85	113	74.4	47.3 - 94.0	88.0	<0.001
Ampicillin-sulbactam	31	36	64.2	8.2 - 100.0	89.6	<0.001
Piperacillin-tazobactam	38	92	33.7	5.3 - 71.5	92.0	<0.001
Ampicillin	63	67	89.9	69.6 - 99.6	72.5	0.006
Pseudomonas aeruginosa						
Amikacin	46	139	30.9	11.8 - 54.2	86.4	<0.001
Gentamicin	67	156	46.7	28.5 - 65.3	80.9	<0.001
Imipenem	44	140	34.1	16.0 - 54.9	82.8	<0.001
Meropenem	43	147	31.7	14.0 - 52.6	84.2	<0.001
Cefepime	30	71	39.4	20.9 - 59.7	63.7	0.011

Table 3. Continued....

Ceftazidime	69	136	59.1	33.7 - 82.0	88.2	<0.001
Ciprofloxacin	56	134	44.9	24.0 - 66.8	83.5	<0.001
Levofloxacin	13	29	44.7	27.8 - 62.1	0.0	0.525
Aztreonam	34	100	34.6	21.5 - 49.0	47.2	0.108
Piperacillin-tazobactam	39	124	32.4	8.3 - 63.2	91.2	<0.001
Acinetobacter baumannii						
Amikacin	50	75	69.9	47.8 - 88.0	73.3	<0.001
Gentamicin	49	73	66.4	55.6 - 76.4	0.0	0.568
Imipenem	48	76	67.7	39.4 - 90.3	83.9	<0.001
Meropenem	39	60	74.8	44.1 - 95.8	82.9	<0.001
Cefuroxime	33	45	82.4	51.5 - 99.1	80.7	0.001
Cefepime	45	52	84.9	70.2 - 95.2	39.6	0.127
Cefotaxime	15	19	79.1	46.4 - 98.3	60.8	0.078
Ceftazidime	45	60	79.0	59.9 - 93.0	61.7	0.011
Ceftriaxone	36	37	95.1	86.2 - 99.6	0.0	0.806
Ciprofloxacin	37	62	64.2	23.8 - 95.1	90.8	<0.001
Levofloxacin	12	17	68.5	43.5 - 88.8	17.7	0.303
Co-trimoxazole	31	60	57.8	20.5 - 90.6	89.3	<0.001
Amoxicillin-clavulanate	15	15	95.9	81.4 - 100.0	0.0	0.939
Ampicillin-sulbactam	24	28	84.2	55.5 - 99.2	65.5	0.055
Piperacillin-tazobactam	42	66	63.6	31.9 - 89.8	85.4	<0.001
Proteus mirabilis						
Amikacin	14	45	29.5	2.6 - 69.4	87.1	<0.001
Gentamicin	16	41	42.9	10.5 - 79.2	83.3	<0.001
Imipenem	7	23	31.5	15.1 - 50.6	0.0	0.474
Meropenem	3	31	14.0	1.6 - 35.7	48.1	0.123
Ceftazidime	15	37	44.9	10.4 - 82.6	83.3	<0.001
Ciprofloxacin	17	41	45.8	15.7 - 77.6	78.0	0.001
Aztreonam	11	31	32.3	1.6 - 77.9	85.0	0.001
Piperacillin-tazobactam	6	27	24.4	10.7 - 41.5	0.0	0.702
***Enterobacter* species**						
Amikacin	10	35	33.0	9.1 - 63.0	60.0	0.029
Gentamicin	14	34	49.2	20.5 - 78.2	59.8	0.041
Imipenem	4	32	27.5	2.0 - 67.1	73.6	0.004
Meropenem	3	32	21.4	1.5 - 55.2	65.3	0.021
Ceftazidime	14	35	52.0	23.2 - 80.1	59.4	0.031
Ciprofloxacin	11	32	49.6	21.9 - 77.3	49.5	0.095
Piperacillin-tazobactam	1	28	7.2	0.0 - 30.7	46.6	0.154

**Certain agent-organism combinations reflect intrinsic resistance and were not interpreted as acquired resistance (K. pneumoniae: ampicillin. A. baumannii: amoxicillin-clavulanate, cefuroxime, cefotaxime, ceftriaxone). Pooled values for these combinations derive from primary studies that inconsistently tested or reported these agents and do not represent acquired resistance. They are shown for completeness and were not interpreted.*
***P value from Cochran Q test.*
Abbreviations: CI, Confidence interval; I^2, Heterogeneity; n, Number.

Table 4. Pooled prevalence of resistance patterns (MDR, carbapenem resistance, and ESBL production) among Gram-negative SSI isolates

Resistance pattern	Bacterial species	Resistant isolates (n)	Total isolates (n)	Pooled resistance (%)	95% CI	I^2 (%)	P-value*
MDR	*Acinetobacter baumannii*	35	57	55.2	25.5-83.4	70.6	0.002
	Klebsiella pneumoniae	35	96	36.4	6.7-71.9	87.5	<0.001
	Escherichia coli	29	104	29.0	12.3-48.8	70.8	0.008
	Pseudomonas aeruginosa	18	124	27.0	5.5-54.9	74.3	0.004
Carbapenem resistance	*Acinetobacter baumannii*	23	29	87.0	55.5-100.0	65.8	0.020
	Enterobacter species	3	5	67.5	10.3-100.0	0.0	0.412
	Klebsiella pneumoniae	61	106	57.4	41.8-72.3	54.0	0.054
	Pseudomonas aeruginosa	33	58	56.2	13.3-94.6	91.0	<0.001
	Escherichia coli	23	86	26.2	16.9-36.5	1.7	0.397
	Proteus mirabilis	5	24	16.7	0.0-47.1	55.5	0.106
	Proteus mirabilis	6	10	60.3	25.9-90.6	0.0	0.633
ESBL	*Escherichia coli*	39	100	53.2	8.3-95.2	95.4	<0.001
	Klebsiella pneumoniae	21	51	45.8	15.9-77.2	78.6	0.003

**P value from Cochran Q test*

Abbreviations: MDR, Multi-drug resistant; ESBL, Extended-spectrum β-Lactamases; CI, Confidence interval; I^2, Heterogeneity; SSI, Surgical-site infection; n, Number.

Less frequently isolated species included *A. baumannii*, 13.0% (95% CI 8.1-18.6, I^2 = 79.5%, k = 16, n = 1,071), *P. mirabilis*, 8.6% (95% CI 6.3-11.2, I^2 = 90.5%, k = 12, n = 1,099), *Enterobacter* spp., 7.9% (95% CI 4.5-12.0, I^2 = 72.4%, k = 11, n = 945) and *Citrobacter* spp., 4.5% (95% CI 1.7-8.5, I^2 = 61.0%, k = 6, n = 469).

3.5 Variation in Resistance Between Countries

For *P. aeruginosa*, imipenem resistance differed markedly between countries (p < 0.001): Egypt 56.7%, Iran 77.2%, Iraq 7.4%, and Türkiye 10.1%; a similar geographic pattern was seen for amikacin (p < 0.001), meropenem (p = 0.029), and gentamicin, although the gentamicin difference was not significant (p = 0.130). Ceftazidime resistance (p = 0.003) was 95.6% in Egypt, 53.6% in Iran, 62.0% in Iraq, and 32.5% in Türkiye. For *K. pneumoniae*, ceftazidime resistance varied significantly between countries (p < 0.001), at 89.8% in Egypt, 42.5% in Iraq, and 23.5% in Türkiye; amikacin (p = 0.013) and meropenem (p = 0.035) also differed significantly. For *E. coli*, amikacin resistance differed between countries (p = 0.039), at 54.8% in Egypt, 18.7% in Iraq, and 17.6% in Türkiye (Table S2).

3.6 Temporal Trends in Antimicrobial Resistance

Resistance was positively associated with publication year (2005-2026) for *K. pneumoniae* against ceftazidime, OR 1.2 per year (95% CI 1.1-1.3; p < 0.001), for *Enterobacter* spp. against ceftazidime, OR 1.2 per year (95% CI 1.1-1.4; p = 0.006), and for *A. baumannii* against imipenem, OR 1.3 per year (95% CI 1.1-1.5; p = 0.007). *P. aeruginosa* resistance to piperacillin-tazobactam declined over the period (2017-2024), OR 0.5 per year (95% CI 0.4-0.8; p < 0.001) (Table S3).

3.7 Certainty of Evidence

The GRADE certainty of evidence was very low for 138 of the 139 graded analyses, driven by high between-study heterogeneity and wide confidence intervals in the pooled proportions. The only exception was carbapenem resistance in *E. coli*, rated low certainty (Table S4).

4. Discussion

Perioperative antibiotic prophylaxis is a key part of SSI prevention, with cephalosporins recommended as standard agents for most clean and clean-contaminated procedures [3]. The rising number of GNB resistant to cephalosporins and beta-lactam beta-lactamase inhibitor combinations is therefore relevant to the Gram-negative-directed component of prophylaxis in contaminated procedures and, more directly, to empirical treatment of established SSIs, since agents chosen from older susceptibility data may no longer match the Gram-negative organisms actually recovered [15]. This is a greater concern in regions where local resistance patterns are poorly described, leaving prophylactic and empirical choices to rely on outdated or unrepresentative data [6].

Enterobacterales are a major cause of SSIs worldwide [34]. In this meta-analysis, *E. coli* was the most frequently isolated Gram-negative species from SSIs (27.9%), followed by *P. aeruginosa* (25.8%) and *K. pneumoniae* (21.3%), with *A. baumannii*, *P. mirabilis*, *Enterobacter* spp., and *Citrobacter* spp. less common. The predominance of *E. coli* is consistent with the meta-analysis by Chelkeba et al., which reported *E. coli* at 17.0%, with *K. pneumoniae* and *P. aeruginosa* both at 11.0%, in Ethiopian wound infections [35]. *E. coli* is thus consistently the most common Gram-negative species across these settings. The higher absolute proportions in the present analysis may partly reflect differences in case mix and sampling: Chelkeba et al. drew on broader wound infections rather than SSIs specifically [35].

Resistance to aminopenicillins and cephalosporins in the current meta-analysis was high, with pooled resistance exceeding 65% to ampicillin in *E. coli* and to ceftriaxone in both *E. coli* and *K. pneumoniae*, and reaching up to 85.9% for other third-generation cephalosporins, alongside substantial fluoroquinolone and aminoglycoside resistance. Ampicillin resistance was high, with pooled *E. coli* resistance of 71.2% in the present meta-analysis, broadly consistent with the high rate reported in the Northeast Indian SSI series by Deka et al. (92.2%) [36]. Resistance to imipenem and meropenem in this pooled analysis was comparatively low in *E. coli* (13.9% and 7.7%), in line with the low rate pooled by Monk et al. (6.0%), although that estimate derived from a broader compartment of wound, skin, soft-tissue, and surgical site infections across Africa rather than SSIs specifically [37]. Third-generation cephalosporin and fluoroquinolone resistance in the present analysis ran markedly higher (*E. coli* ceftriaxone 73.8%, ciprofloxacin 69.8%), exceeding the 42% and 35% reported in Ethiopian wound isolates by Chelkeba et al. [35]. In *E. coli* and *K. pneumoniae*, carbapenems showed comparatively lower resistance than the beta-lactam alternatives tested, with imipenem and meropenem resistance below every such alternative; this floor was firm for *E. coli* but only relative for *K. pneumoniae*, whose 22.2-23.3% sat well above the 8.0% reported by Monk et al., and is itself of concern given the WHO critical-priority status of carbapenem-resistant *K. pneumoniae* [8,37]. Because carbapenems are reserve rather than prophylactic agents, this preserved carbapenem activity does not offset the high resistance to other agents described above.

P. aeruginosa in this analysis reached pooled imipenem and meropenem resistance of 34.1% and 31.7%, several-fold higher than *E. coli* and above *K. pneumoniae*. This sits slightly above the meropenem-resistant *P. aeruginosa* pooled by Gobezie et al. in Ethiopia, at 25% for wound and 28% for hospital-acquired infections, although neither category was SSI-specific [38], and also sits above the anti-pseudomonal CR of 21% reported in African wound and SSI isolates [37]. The broader anti-pseudomonal profile was close to or above these comparators, with ceftazidime resistance of 59.1% in the current analysis against 41% that reported by Monk et al. [37], consistent with the WHO designation of carbapenem-resistant *P. aeruginosa* as a high-priority pathogen [8].

Against the National Healthcare Safety Network (NHSN) SSI surveillance, the regional excess was consistent and large across agents [39]. In the current meta-analysis, pooled *E. coli* ceftriaxone and ciprofloxacin resistance (73.8% and 69.8%) exceeded NHSN extended-spectrum-cephalosporin and fluoroquinolone nonsusceptibility (18.2% and 32.1%), *K. pneumoniae* imipenem and meropenem resistance (22.2-23.3%) ran roughly sevenfold above the NHSN figure for CR (3.1%), and *P. aeruginosa* imipenem and meropenem resistance (34.1% and 31.7%) roughly threefold above it (9.1%). Because NHSN reports nonsusceptibility (resistant or intermediate), whereas the present estimates capture resistance alone, this comparison applies a stricter threshold to the regional figures and therefore likely understates rather than overstates the difference [39].

The same excess held for MDR. In this pooled analysis, proportions (*E. coli* 29.0%, *K. pneumoniae* 36.4%, *P. aeruginosa* 27.0%, *A. baumannii* 55.2%) exceeded the corresponding NHSN SSI figures (*E. coli* 7.4%, *Klebsiella* spp. 6.3%, *P. aeruginosa* 4.5%, *Acinetobacter* spp. 26.5%) [39], by roughly four- to sixfold for the Enterobacterales and *P. aeruginosa*, consistent with a high-income regional study by El-Saed et al. that independently found MDR Enterobacterales significantly more frequent than in NHSN hospitals [6].

Resistance varied markedly between countries across the included studies, as shown by *P. aeruginosa* imipenem resistance of 56.7% in Egypt and 77.2% in Iran against 7.4% in Iraq and 10.1% in Türkiye ($p < 0.001$). Variation of this magnitude has been reported across comparable regions, including the Middle East and Southern Asia [40] and Eastern

Europe [41], and is commonly attributed to differences in antibiotic consumption, stewardship maturity, infection-prevention capacity, and surveillance infrastructure [41,42]. Antibiotic consumption has correlated with rising Gram-negative resistance, but the present data associate resistance with country rather than measuring these drivers. A complementary explanation is that countries differ in which resistance mechanisms predominate, as specific enzymes tend to cluster in certain regions, so the resistance burden also reflects local molecular epidemiology [41]. Within the Middle East, El-Saed et al. attributed high Gram-negative resistance in Saudi surgical isolates to mechanisms including New Delhi Metallo-beta-lactamase, Oxacillinase-48, carbapenemases, mgrB-mediated colistin resistance, and porin loss, though such mechanisms were not characterized in the present analysis [6]. Whichever predominates, these factors can still be addressed through surveillance and stewardship, which supports country-specific empirical guidance as the practical way to drive change.

Our meta-analysis has several limitations. First, heterogeneity was high across most pooled estimates (I^2 frequently >80%), and several rested on few studies and small isolate counts with wide confidence intervals; reflecting these issues, the GRADE certainty of evidence was very low for 138 of the 139 pooled analyses (the only exception being carbapenem resistance in *E. coli*, rated low certainty), which substantially limits confidence in the pooled estimates and should be considered when interpreting the overall findings. Second, because MDR and CR were extracted only where primary studies reported them, the pattern-level pools derive from partly different study sets than the per-drug analyses and may not describe the same isolates. Third, the temporal analysis used publication year as a proxy for sampling year and is exploratory, indicating direction rather than magnitude. Fourth, the data associate resistance with country rather than measuring antibiotic use, stewardship, or molecular epidemiology directly, so proposed drivers remain inferential. Fifth, susceptibility testing in the included studies relied predominantly on phenotypic disc diffusion (82.61%), and genotypic confirmation of resistance determinants (e.g., blaCTX-M, blaKPC, blaNDM) was not reported in any study. Phenotypic methods may underestimate ESBL- and carbapenemase-mediated resistance, as co-produced enzymes can mask their expression and low-level producers may test as susceptible. Finally, restriction to published, predominantly English-language, and tertiary-center studies may have introduced publication and referral bias.

5. Conclusion

Across the Middle East, the Gram-negative organisms recovered from surgical-site infections carried extensive resistance that reached even carbapenems in *K. pneumoniae.* Given the very low certainty of the evidence, these estimates are best read as a signal of the regional resistance burden and reinforce the need for local, SSI-specific surveillance and antimicrobial stewardship.

Declarations

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