ORIGINAL ARTICLE

Prevalence and Risk Factors of Multidrug-Resistant Bacterial Infections Among Pediatric Inpatients in Saudi Arabia: A Systematic Review and Meta-Analysis

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ABSTRACT

Background:
Antimicrobial resistance represents a major global public health challenge and poses a particular threat to pediatric populations, who are frequently exposed to broad-spectrum antibiotics, invasive procedures, and prolonged hospitalization. Understanding the burden, pathogen profile, and determinants of multidrug-resistant (MDR) bacterial infections among pediatric inpatients is essential for informing targeted prevention and control strategies.

Objective:
To systematically review and synthesize evidence on the prevalence of multidrug-resistant (MDR) bacterial infections, distribution of MDR pathogens, and associated risk factors among pediatric inpatients in Saudi Arabia.

Methods:
This systematic review and meta-analysis was conducted in accordance with PRISMA 2020 guidelines. PubMed/MEDLINE, Embase, Scopus, Web of Science, Google Scholar, and relevant registers were searched from inception to December 2025. Observational studies reporting MDR bacterial infections among pediatric inpatients (0–18 years) in Saudi Arabia were included. Study quality was assessed using the Newcastle–Ottawa Scale (NOS). A random-effects meta-analysis with Freeman–Tukey double arcsine transformation was used to estimate pooled prevalence. Subgroup analyses were conducted by age group, healthcare setting, geographic region, study design, and study period.

Results:
Seventeen studies comprising 3,512 pediatric inpatients met the inclusion criteria, of which 16 studies were included in the meta-analysis. The pooled prevalence of MDR bacterial infections was 36.0% (95% CI: 22.2%–51.1%), with substantial heterogeneity (I^2 = 98.6%). Gram-negative bacteria predominated, particularly Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii, and Pseudomonas aeruginosa, frequently exhibiting ESBL production and carbapenem resistance. Consistently reported risk factors included prior and broad-spectrum antibiotic exposure, ICU/NICU admission, mechanical ventilation, central venous catheter use, prolonged hospitalization, and underlying comorbidities. Subgroup analyses revealed significant regional variation in MDR prevalence, while differences by age group, healthcare setting, and study period were not statistically significant under random-effects models. Overall study quality was moderate to high, with no studies rated as high risk of bias.

Conclusions:
Multidrug-resistant bacterial infections constitute a substantial burden among pediatric inpatients in Saudi Arabia, driven by antimicrobial exposure, intensive care environments, and patient vulnerability. These findings underscore the need for strengthened antimicrobial stewardship, infection prevention and control measures, and coordinated national surveillance systems targeting pediatric healthcare settings.

KEYWORDS
Multidrug resistance; pediatric inpatients; antimicrobial resistance; Saudi Arabia; systematic review; meta-analysis

INTRODUCTION

Antimicrobial resistance (AMR) is recognized as one of the most serious global public health threats of the 21st century, undermining the effective prevention and treatment of bacterial infections and increasing morbidity, mortality, and healthcare costs worldwide (World Health Organization) (1,2). Multidrug-resistant (MDR) bacterial infections, defined as resistance to at least one agent in three or more antimicrobial classes, have become increasingly prevalent in both community and hospital settings, posing particular challenges for healthcare systems with high antimicrobial consumption and intensive medical care utilization (3,4).

Children represent a uniquely vulnerable population in the context of MDR infections. Pediatric inpatients are frequently exposed to invasive procedures, prolonged hospital stays, broad-spectrum antibiotics, and intensive care environments, all of which contribute to the selection and transmission of resistant pathogens (5). In addition, the immaturity of the immune system in infants and young children, combined with limited antimicrobial options and dosing constraints, further complicates the management of MDR infections in pediatric populations (6). Hospital-acquired infections caused by MDR organisms in children are associated with delayed appropriate therapy, increased length of hospitalization, higher treatment costs, and poorer clinical outcomes (7).

Globally, MDR pathogens such as extended-spectrum β-lactamase (ESBL)–producing Enterobacterales, methicillin-resistant Staphylococcus aureus (MRSA), carbapenem-resistant Acinetobacter baumannii and Klebsiella pneumoniae, and multidrug-resistant Pseudomonas aeruginosa have been increasingly reported among pediatric inpatients (8). However, the epidemiology and risk factors for MDR infections vary substantially across regions, influenced by local antimicrobial prescribing practices, infection prevention and control measures, healthcare infrastructure, and patient characteristics (9).

In the Middle East, and particularly in Saudi Arabia, the burden of AMR has drawn increasing attention due to high rates of antimicrobial use, expanding healthcare services, and the complex patient population served by tertiary and referral hospitals (10). Saudi Arabia has made significant investments in healthcare and has implemented national strategies aligned with the World Health Organization's Global Action Plan on AMR (11). Nevertheless, published evidence suggests a rising prevalence of MDR organisms in hospital settings, including among pediatric patients (12). Despite this concern, data focusing specifically on pediatric inpatients remain fragmented, with many studies combining adult and pediatric populations or focusing on single pathogens rather than providing a comprehensive assessment of MDR infections.

Understanding the prevalence and determinants of MDR bacterial infections among hospitalized children is essential for guiding antimicrobial stewardship programs, optimizing empiric therapy, and strengthening infection prevention and control policies (13). Identifying patient treatment and healthcare related risk factors can support early recognition of high-risk groups and inform targeted interventions aimed at reducing transmission and improving clinical outcomes.

Therefore, this study aimed to assess the prevalence of multidrug-resistant bacterial infections among pediatric inpatients in Saudi Arabia and to identify associated risk factors. By providing context-specific epidemiological evidence, this study seeks to contribute to the development of effective strategies for combating MDR infections in pediatric hospital settings and to support national efforts to mitigate the growing threat of antimicrobial resistance.

MATERIALS AND METHOD

Protocol and registration

This systematic review was conducted and reported in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. To enhance transparency and methodological robustness, the review protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration ID: 0009-0002-3555-4305).

Eligibility criteria

Population: Pediatric inpatients aged ≤18 years, including neonates, infants, children, and adolescents admitted to hospitals in Saudi Arabia.

Exposure: Potential risk factors for multidrug-resistant (MDR) bacterial infection included prior antibiotic exposure, admission to intensive care units (ICUs), use of invasive medical devices, and prolonged duration of hospitalization.

Comparison: Pediatric inpatients without documented MDR bacterial infections or those not exposed to the specified risk factors.

Outcomes: The primary outcomes were (1) the prevalence of MDR bacterial infections and (2) risk factors associated with MDR infections.

Study design: Cross-sectional studies, cohort studies, case–control studies, and hospital- or laboratory-based surveillance reports were eligible for inclusion. Studies were excluded if they were conducted outside Saudi Arabia, involved exclusively outpatient populations, were case reports or case series with fewer than 10 participants, all types of reviews and meta-analysis, lacked extractable data on multidrug-resistant (MDR) bacterial infections, or were published in languages other than English or Arabic.

INFORMATION SOURCES

A comprehensive literature search was conducted across multiple electronic databases, including PubMed/MEDLINE, Scopus, Web of Science, and Embase, to identify relevant studies reporting on the prevalence and risk factors of multidrug-resistant (MDR) bacterial infections among pediatric inpatients in Saudi Arabia. The final search was performed on [10 December 2025], and no restrictions were applied regarding the year of publication.

In addition to database searches, manual searches were undertaken by screening the reference lists of all included studies and relevant review articles to identify additional eligible publications. Citation tracking of key articles was also performed to ensure comprehensive coverage of the available evidence. A grey literature sources, including google scholar, institutional reports and surveillance data, were searched to minimize publication bias.

SEARCH STRATEGY

The search strategy was developed in consultation with review objectives and employed a combination of free-text keywords and controlled vocabulary terms (Medical Subject Headings [MeSH] for PubMed and Emtree terms for Embase). Key search terms included variations of "multidrug-resistant," "antimicrobial resistance," "pediatric," "children," "hospitalized," "inpatients," and "Saudi Arabia." These terms were combined using appropriate Boolean operators ("AND", "OR") to optimize sensitivity and specificity. The search strategy was adapted for each database according to its indexing system and search interface.

STUDY SELECTION

All records retrieved from the electronic database searches were imported into EndNote for reference management, and duplicate citations were removed. The remaining studies

were then uploaded to Rayyan to facilitate the screening process (14). Study selection was conducted in two sequential stages. First, titles and abstracts were independently screened to assess potential eligibility. Second, the full texts of studies deemed potentially relevant were retrieved and independently assessed for final inclusion according to the predefined eligibility criteria.

The screening process was performed independently by two reviewers. Any discrepancies arising during either the title/abstract screening or full-text review were resolved through discussion and consensus. When consensus could not be reached, a third reviewer was consulted to make the final decision.

DATA EXTRACTION

Data extraction was performed using a standardized, pre-piloted data extraction form developed specifically for this review. Two reviewers independently extracted data from all included studies to ensure accuracy and consistency. Extracted information included study characteristics (first author, year of publication, study design, study setting, sample size, and study period), population characteristics (age range, sex distribution), microbiological data (types of bacterial pathogens and definitions of multidrug resistance), and outcome data.

Outcome variables included the prevalence of MDR bacterial infections and quantitative measures of association for potential risk factors (e.g., odds ratios, risk ratios, or hazard ratios), along with corresponding confidence intervals or raw data required for effect size calculation. Any discrepancies in data extraction were resolved through discussion, with arbitration by a third reviewer when necessary.

RISK OF BIAS ASSESSMENT

The methodological quality of the included studies was independently assessed by two reviewers using the Newcastle–Ottawa Scale (NOS). Studies were classified as having a low (7–9 points), moderate (4–6 points), or high (0–3 points) risk of bias, in accordance with established thresholds. For cross-sectional studies, an adapted version of the NOS was applied. Any discrepancies in quality ratings were resolved through discussion, with consultation of a third reviewer when necessary.

DATA SYNTHESIS

Prevalence estimates were pooled using a random-effects meta-analysis based on the DerSimonian–Laird method (15). To stabilize variances, the Freeman–Tukey double arcsine transformation was applied (16). Statistical heterogeneity was evaluated using Cochran's Q test and quantified with the I^2 statistic.

Pooled odds ratios (ORs) for risk factors reported in three or more studies were calculated using random-effects models. Publication bias was assessed through visual inspection of funnel plots and formally evaluated using Egger's regression test when ten or more studies were available.

Pre-specified subgroup analyses were conducted according to age group, healthcare setting, geographic region, pathogen type, and study period. Sensitivity analyses were performed by excluding studies with a high risk of bias and those with small sample sizes ($n < 50$). Statistical significance was defined as a two-sided p value < 0.05. All statistical analyses were conducted using R software (version 4.1.8).

RESULTS

Study Selection

The literature search identified a total of 1,350 records, including 1,200 records retrieved from electronic databases and 150 records identified through registers. Prior to screening, 205 records were removed, comprising 150 duplicate records, 30 records marked as ineligible by automation tools, and 25 records removed for other reasons. Consequently, 1,145 records remained for title and abstract screening.

During the screening stage, 1,065 records were excluded based on irrelevance to the review objectives. Full texts of 80 reports were sought for retrieval, of which 25 reports could not be retrieved. The remaining 55 full-text articles were assessed for eligibility.

Of these, 38 reports were excluded for the following reasons: wrong study population (n = 18), wrong outcome (n = 10), publication in foreign languages (n = 2), and inappropriate study design (n = 8). Ultimately, 17 studies met the predefined eligibility criteria and were included in the systematic review and meta-analysis. The study selection process is illustrated in the PRISMA 2020 flow diagram **(Figure 1).**

Study Characteristics

The 17 studies included in the review were published from 2010 to 2025 and were supported by an aggregate sample of 3512 pediatric inpatients. Studies were conducted across Saudi Arabia, namely in Riyadh (n=8), Jeddah (n=4) and other cities including Najran, Taif, Hail, Jazan, and Al-Qassim (n=1) for each city. The various study designs were cross-sectional studies (n=6), prospective cohorts (n=1), retrospective cohorts (n=6), and surveillance/investigation reports (n=3) and A randomised experimental (n = 1). The sample sizes ranged from 7 to 901 with a median of 129. All studies were conducted in hospital settings across different regions of Saudi Arabia, including tertiary-care hospitals, pediatric wards, neonatal intensive care units (NICUs), and pediatric intensive care units (PICUs). **(Table 1)**

Distribution of MDR pathogens

Across the included studies, gram-negative bacteria predominated among multidrug-resistant (MDR) isolates. Klebsiella pneumoniae was the most frequently reported pathogen, identified in nine studies, and was commonly associated with extended-spectrum β-lactamase (ESBL) production, carbapenem-resistant Enterobacterales (CRE), and carbapenem resistance. Escherichia coli was reported in six studies, predominantly as ESBL-producing and MDR strains. Acinetobacter baumannii and Pseudomonas aeruginosa were each reported in five studies, with resistance profiles characterized by multidrug resistance, extensive drug resistance (XDR), and carbapenem resistance. Other gram-negative organisms included Enterobacter spp. (four studies), Proteus spp. (two studies), Serratia marcescens (two studies), Stenotrophomonas maltophilia (two studies), and Salmonella spp. (one study), with resistance patterns ranging from ESBL production to intrinsic or acquired MDR phenotypes. Additional gram-negative isolates, including Citrobacter spp., Morganella spp., and mixed Enterobacterales, were reported across six studies.

Among gram-positive bacteria, Staphylococcus aureus was reported in seven studies, predominantly as methicillin-resistant S. aureus (MRSA). Enterococcus spp. were identified in four studies, with isolates exhibiting vancomycin resistance (VRE). Coagulase-negative staphylococci, mainly Staphylococcus epidermidis, were reported in four studies as MDR organisms. Streptococcus spp. was reported in two studies, with resistance to penicillin and macrolides, while other gram-positive organisms comprising mixed species were reported in three studies. **(Table 2)**

Risk factors associated with MDR bacterial infections

Across the included studies, a wide range of antibiotic-related, healthcare-related, device-related, microbiological, patient-related, and procedural factors were reported to be associated with multidrug-resistant (MDR) bacterial infections among pediatric inpatients. Antibiotic exposure was one of the most frequently reported domains, with use of broad-spectrum antibiotics identified in eleven studies and prior antibiotic exposure reported in six studies. A prolonged duration of antibiotic therapy exceeding seven days was reported as a risk factor in one study. All antibiotic-related factors were supported by quantitative analyses, including univariate or multivariable regression models.

Healthcare-related factors were consistently reported across studies. Healthcare-associated infection was identified in fourteen studies, while ICU or NICU admission was reported as a risk factor in eleven studies. Prolonged hospitalization, particularly stays exceeding seven days, was reported in eight studies, and previous hospitalization within three months was reported in two studies. These factors were supported by regression analyses or descriptive statistical associations.

Among invasive device-related factors, mechanical ventilation and central venous catheter use were each reported in seven studies, while urinary catheterization was identified in three studies as a potential risk factor. Prior colonization with MDR organisms was reported in seven studies within the microbiological and therapy-related domain.

With respect to patient-related factors, underlying comorbidities were reported in nine studies, immunosuppression in eight studies, and malignancy in six studies. Prematurity or low birth weight was reported less frequently but was identified as a risk factor in neonatal populations. In the procedural and therapeutic domain, surgical procedures were reported in seven studies, and total parenteral nutrition was identified in three studies. All reported risk factors were supported by quantitative analyses, including regression models or clearly reported statistical associations. **(Table 3)**

Direction and consistency of reported risk factors

When examining the direction of association, all reported risk factors demonstrated a consistent positive association with increased risk of MDR bacterial infections across studies. Prior antibiotic exposure was associated with increased MDR risk in six studies, primarily in ICU and NICU settings, based on univariate and multivariable regression analyses. Similarly, broad-spectrum antibiotic use was reported in five studies as increasing MDR risk, particularly in intensive care settings.

Admission to ICU or NICU was associated with increased MDR risk in eight studies, supported by descriptive analyses and regression models. Mechanical ventilation and central venous catheter use were each associated with increased MDR risk in five and four studies, respectively, predominantly in ICU or NICU environments. Prolonged hospitalization was reported in six studies as a risk factor, while previous hospitalization was identified in three studies, mainly through descriptive analyses.

Among patient-related characteristics, prematurity or low birth weight was reported in four studies as increasing MDR risk in NICU settings. Underlying comorbidities were associated with increased MDR risk in six studies across ICU and ward settings. Across all domains, no studies reported protective associations; rather, all identified risk factors were consistently associated with an increased likelihood of MDR bacterial infections. **(Table 4)**

Risk of bias assessment

The methodological quality of the included studies was assessed using the Newcastle–Ottawa Scale (NOS). Overall, the quality of the evidence was moderate to high, with total NOS scores ranging from 5 to 9 out of 9. Of the 17 included studies, 10 studies were assessed as having a low risk of bias (NOS score ≥7), while 7 studies were classified as having a moderate risk of bias (NOS score 4–6). No study was rated as having a high risk of bias.

Across the selection domain, most studies achieved three or four stars, indicating generally adequate representativeness of the study populations and appropriate ascertainment of exposure or outcome. In the comparability domain, several studies received one or two stars, reflecting variable adjustment for potential confounding factors. The outcome domain was generally well addressed, with most studies scoring two or three stars, indicating acceptable outcome assessment and follow-up procedures. Overall, the risk of bias assessment suggests that the majority of included studies were of acceptable methodological quality, supporting the robustness of the findings reported in this review. (Table 5)

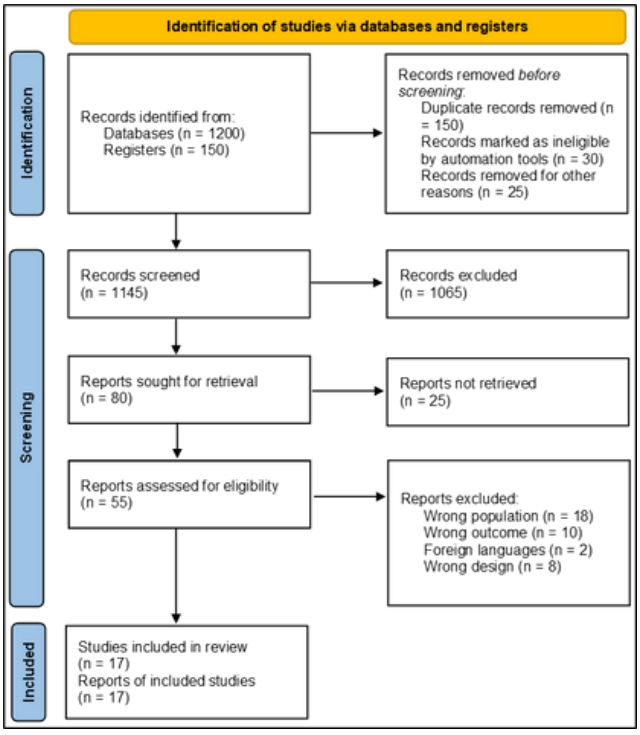

Figure 1: PRISMA 2020 flow diagram illustrating the identification, screening, and inclusion of studies

Pooled Prevalence of MDR Bacterial Infections

A random-effects meta-analysis of 16 studies including 3,512 pediatric inpatients (1,262 MDR cases) estimated a pooled prevalence of multidrug-resistant (MDR) bacterial infections of 36.0% (95% CI: 22.2%–51.1%). Considerable heterogeneity was observed across studies (I^2 = 98.6%, τ^2 = 0.091, Cochran's Q = 1110.50, df = 15, p < 0.0001). **(Figure 2)**

Subgroup Analyses

Subgroup analysis by age group

In subgroup analysis by age group, pooled prevalence estimates were 37.8% (95% CI: 21.3%–55.9%) for pediatric populations (<18/≤14 years; k = 12), 40.8% (95% CI: 6.6%–81.3%) for neonates/mixed neonatal–pediatric samples (k = 2), and 19.9% (95% CI: 12.3%–28.5%) for younger children (<12/<10 years; k = 2). Heterogeneity remained substantial within subgroups (I^2 up to 98.9%), and the test for subgroup differences was not statistically significant (p = 0.175). **(Table 6)**

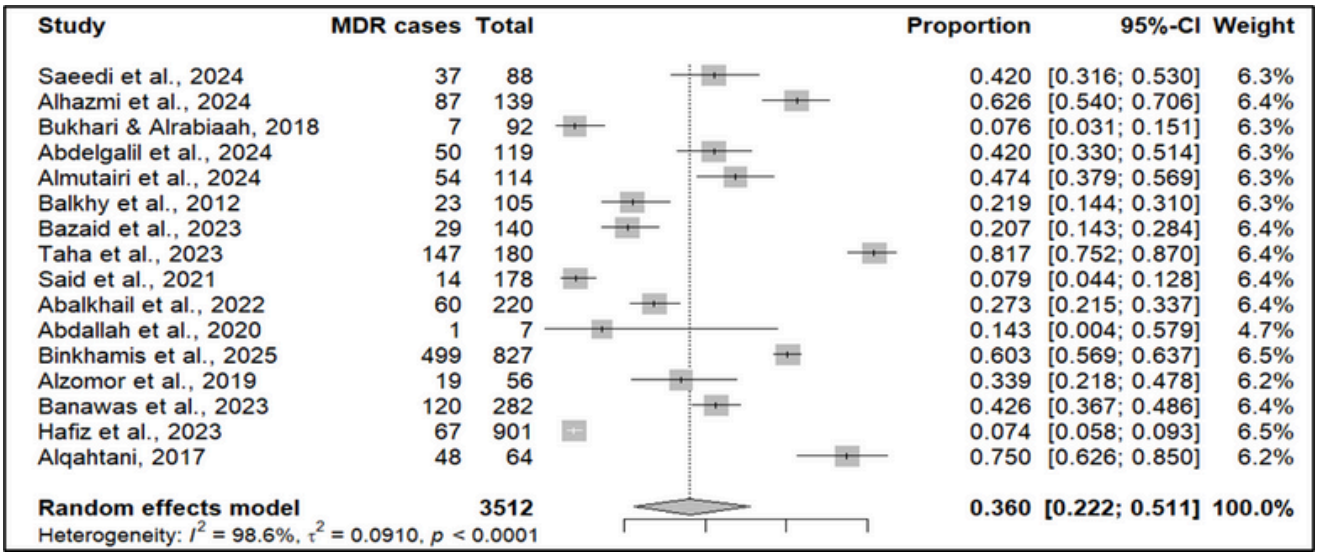

Figure 2: Forest plot of the pooled prevalence of multidrug-resistant bacterial infections among pediatric inpatients in Saudi Arabia

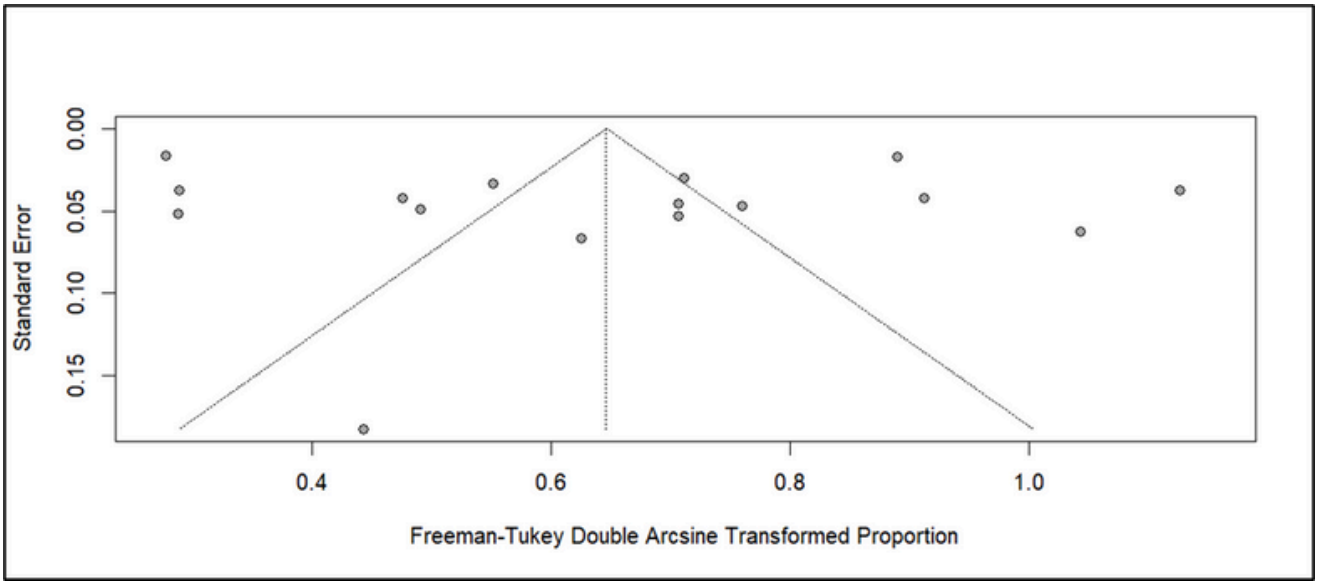

Figure 3: Funnel Plot for Publication Bias Assessment

Subgroup analysis by healthcare setting

When stratified by healthcare setting, the pooled prevalence was 31.0% (95% CI: 18.5%–45.0%) among studies conducted in ICU/NICU/PICU settings (k = 12). Studies categorized as "unclear/mixed" setting showed a higher pooled prevalence (61.3%, 95% CI: 38.3%–82.1%; k = 3). One study conducted in mixed ward and ICU settings reported a prevalence of 42.1% (95% CI: 31.9%–52.6%; k = 1). Subgroup differences were borderline but not statistically significant (p = 0.077). **(Table 6)**

Subgroup analysis by geographic region

Regional subgroup analysis showed significant differences in pooled MDR prevalence (p < 0.0001). The pooled prevalence was 41.7% (95% CI: 16.5%–69.4%) in the Western region (k = 5), 68.2% (95% CI: 55.7%–79.5%) in the Southern region (k = 2), 29.3% (95% CI: 12.4%–49.9%) in the Central region (k = 8), and 7.9% (95% CI: 4.3%–12.3%) in the Northern region (k = 1). Heterogeneity remained high within Western and Central subgroups ($I^2 \geq 97\%$). **(Table 6)**

Subgroup analysis by study design

Subgroup analysis by study design demonstrated statistically significant differences (p < 0.0001). Retrospective/cross-sectional studies reported a pooled prevalence of 43.0% (95% CI: 25.4%–61.5%; k = 12) with substantial heterogeneity (I^2 = 98.9%). Individual study designs represented by a single study yielded prevalence estimates of 7.6% for the prospective cohort study, 7.9% for the surveillance study, 27.3% for the experimental study, and 33.9% for the case–control study. **(Table 6)**

Subgroup analysis by study period

Subgroup analysis by study period showed variation in the pooled prevalence of multidrug-resistant bacterial infections. Studies conducted before 2019 reported a pooled prevalence of 53.7% (95% CI: 21.7%–84.1%, k = 4), while studies conducted during 2020–2022 demonstrated a lower pooled prevalence of 27.9% (95% CI: 15.1%–42.8%, k = 8). More recent studies published in 2023 or later reported a pooled prevalence of 41.4% (95% CI: 13.4%–72.7%, k = 3). However, the test for subgroup differences under the random-effects model was not statistically significant (p = 0.323), indicating that observed differences may be attributable to substantial between-study heterogeneity rather than temporal trends. **(Table 6)**

Sensitivity analysis excluding very small sample study

After excluding the very small-sample study (n < 30), the pooled prevalence remained similar at 37.1% (95% CI: 22.9%–52.5%) across 15 studies, with heterogeneity remaining substantial (I^2 = 98.7%, p < 0.0001).

Publication Bias

Visual inspection of the funnel plot showed an approximately symmetrical distribution of studies around the pooled prevalence estimate. Larger studies clustered near the center of the funnel, while smaller studies demonstrated wider dispersion, which is expected in prevalence meta-analyses. Although no strong evidence of publication bias was observed, interpretation should be cautious due to substantial between-study heterogeneity. (Figure3)

Table 1: Characteristics of included studies reporting the prevalence of multidrug-resistant bacterial infections among pediatric inpatients in Saudi Arabia (12,17-32).

No.	Study	Location	Study Design	Study Period	Setting	Sample Size	Age Group	MDR Cases	Prevalence (%)
1	(Saeedi et al., 2024)	Jeddah	Retrospective cross-sectional	Oct 2021 - Nov 2022	Pediatric wards & ICU	88 pediatric inpatients	<18 years	37 patients (223 MDR cultures)	42.0
2	(Alhazmi et al., 2024)	Jazan	Retrospective	2018–2023	Intensive Care Unit	139	Neonates and children	87	62
3	(Bukhari and Alrabiaah, 2018)	Riyadh	Prospective cohort	2018 and 2023.	ICU	92	Pediatric	7	7.8
4	(Abdelgalil et al., 2024)	Jeddah	Retrospective cross-sectional	January 2018 to December 2022	ICU	119	Children	50	72
5	(Almutairi et al., 2024)	Al-Qassim	cross-sectional	Jan. 2020 to March. 2022	NICU/PICU	114	pediatric (<18 years)	54	47
6	(Balkhy et al., 2012)	Riyadh	A retrospective cohort	October 2001 and December 2007	Pediatric ICU	105	<12 years	23	22
7	(Bazaid et al., 2023)	Jeddah	A retrospective	October 2020 and May 2021	NICU and PICU	140	neonatal and pediatric	29	20
8	(Taha et al., 2023)	Jeddah	Retrospective	Apr 2017 – Mar 2019	KAMC-J & KAUH	180	<18 years	147	82
9	(Mutair et al., 2021)	Riyadh and Qassim	Retrospective	2015 and 2019	ICUs	2838	Children	NR	NR
10	(Said et al., 2021)	Hail	Surveillance	September to December 2020	ICU	178	Young	14	7.8
11	(Abalkhail et al., 2022)	Riyadh	A randomised experimental study	2019 to 2020	ICU	220	Male and female patients (UTIs)	60	27
12	(Abdallah et al., 2020)	Taif	Investigation	NR	NR (Likely clinical/hospital)	7	Patients with UTIs <10 years	1	14
13	(Binkhamis et al., 2025)	Riyadh	A retrospective cross-sectional study	August 2019 and August 2023	NR	827	children aged 14 years and below	499	60
14	(Alzomor et al., 2019)	Riyadh	A retrospective matched case-control	January 2016-2017	ICU	56	pediatric patients	19	33

15	(Banawas et al., 2023)	Riyadh	Investigation	January and December 2020	Intensive Care Unit	282	Pediatric	120	42.5
16	(Hafiz et al., 2023)	Riyadh	Retrospective study	January 2019 to December 2021	Intensive Care Unit	901	Pediatric	67	7
17	(Alqahtani, 2017)	Najran	cross-sectional observational	January 2015 to February 2016	neonatal ICU or pediatric ICU	64	Children	48	75
15	(Banawas et al., 2023)	Riyadh	Investigation	January and December 2020	Intensive Care Unit	282	Pediatric	120	42.5
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* ICU, intensive care unit; NICU, neonatal intensive care unit; PICU, pediatric intensive care unit; MDR, multidrug-resistant; NOS, Newcastle–Ottawa Scale; NR, not reported.

Table 2: Distribution of Multidrug-Resistant (MDR) Pathogens Across Included Studies

Pathogen	Studies Reporting (n)	Resistance Pattern / Phenotype
Gram-negative bacteria		
Escherichia coli	6	ESBL-producing E. coli, MDR
Klebsiella pneumoniae	9	ESBL, CRE, carbapenem-resistant
Acinetobacter baumannii	5	MDR/XDR, carbapenem-resistant
Pseudomonas aeruginosa	5	MDR, carbapenem-resistant
Enterobacter spp.	4	ESBL, MDR
Proteus spp.	2	MDR
Serratia marcescens	2	ESBL/MDR
Stenotrophomonas maltophilia	2	Intrinsic MDR
Salmonella spp.	1	MDR (hospital-acquired cases)
Other Gram-negative	6	Citrobacter, Morganella, mixed Enterobacterales
Gram-positive bacteria		
Staphylococcus aureus	7	MRSA
Enterococcus spp.	4	VRE
Coagulase-negative Staphylococci	4	MDR S. epidermidis
Streptococcus spp.	2	Penicillin- and macrolide-resistant
Other Gram-positive	3	Mixed species

* MDR, multidrug-resistant; ESBL, extended-spectrum β-lactamase; CRE, carbapenem-resistant Enterobacterales; MRSA, methicillin-resistant Staphylococcus aureus; VRE, vancomycin-resistant Enterococcus

Table 3: Frequency of reported risk factors associated with multidrug-resistant bacterial infections among pediatric inpatients in Saudi Arabia

Domain	Risk factor	Studies reporting (n)	Evidence includes OR/regression
Antibiotic exposure	Broad-spectrum antibiotics	(Balkhy et al., 2012; Bukhari and Alrabiaah, 2018; Alzomor et al., 2019; Said et al., 2021; Mutair et al., 2021; Abalkhail et al., 2022; Bazaid et al., 2023; Banawas et al., 2023; Hafiz et al., 2023; Taha et al., 2023; Saeedi et al., 2024)	Yes
	Prior antibiotic exposure	(Balkhy et al., 2012; Alzomor et al., 2019; Banawas et al., 2023; Taha et al., 2023; Saeedi et al., 2024; Alhazmi et al., 2024)	Yes
	Duration >7 days	(Alzomor et al., 2019)	Yes
Healthcare factors	Healthcare-associated infection	(Balkhy et al., 2012; Bukhari and Alrabiaah, 2018; Alqahtani, 2017; Alzomor et al., 2019; Mutair et al., 2021; Said et al., 2021; Abalkhail et al., 2022; Bazaid et al., 2023; Banawas et al., 2023; Hafiz et al., 2023; Taha et al., 2023; Abdelgalil et al., 2024; Almutairi et al., 2024; Saeedi et al., 2024)	Yes
	ICU/NICU admission	(Balkhy et al., 2012; Bukhari and Alrabiaah, 2018; Alqahtani, 2017; Alzomor et al., 2019; Mutair et al., 2021; Said et al., 2021; Abalkhail et al., 2022; Banawas et al., 2023; Taha et al., 2023; Saeedi et al., 2024; Alhazmi et al., 2024)	Yes
	Prolonged hospitalization (>7d)	(Balkhy et al., 2012; Alzomor et al., 2019; Mutair et al., 2021; Said et al., 2021; Bazaid et al., 2023; Banawas et al., 2023; Hafiz et al., 2023; Abdelgalil et al., 2024)	Yes
	Previous hospitalization (3mo)	(Alzomor et al., 2019; Banawas et al., 2023)	Yes
Invasive devices	Mechanical ventilation	(Balkhy et al., 2012; Bukhari and Alrabiaah, 2018; Alzomor et al., 2019; Mutair et al., 2021; Bazaid et al., 2023; Banawas et al., 2023; Saeedi et al., 2024)	Yes
	Central venous catheter	(Balkhy et al., 2012; Alzomor et al., 2019; Mutair et al., 2021; Bazaid et al., 2023; Banawas et al., 2023; Alhazmi et al., 2024; Saeedi et al., 2024)	Yes

Invasive devices	Urinary catheter	(Alzomor et al., 2019; Said et al., 2021; Abalkhail et al., 2022)	Yes
Micro/therapy factors	Prior colonization with MDR	(Balkhy et al., 2012; Alzomor et al., 2019; Mutair et al., 2021; Banawas et al., 2023; Hafiz et al., 2023; Taha et al., 2023; Saeedi et al., 2024)	Yes
Patient factors	Underlying comorbidities	(Balkhy et al., 2012; Alqahtani, 2017; Alzomor et al., 2019; Mutair et al., 2021; Said et al., 2021; Bazaid et al., 2023; Saeedi et al., 2024; Banawas et al., 2023; Alhazmi et al., 2024)	Yes
	Immunosuppression	(Balkhy et al., 2012; Alqahtani, 2017; Alzomor et al., 2019; Mutair et al., 2021; Banawas et al., 2023; Hafiz et al., 2023; Taha et al., 2023; Alhazmi et al., 2024)	Yes
	Malignancy	(Balkhy et al., 2012; Alzomor et al., 2019; Mutair et al., 2021; Banawas et al., 2023; Saeedi et al., 2024)	Yes
	Prematurity/low birth weight	Alhazmi 2024(Alzomor et al., 2019)	Yes
Procedures/therapies	Surgical procedures	(Balkhy et al., 2012; Alzomor et al., 2019; Mutair et al., 2021; Banawas et al., 2023; Hafiz et al., 2023; Taha et al., 2023; Abdelgalil et al., 2024)	Yes
	Total parenteral nutrition	(Balkhy et al., 2012; Alzomor et al., 2019; Banawas et al., 2023)	Yes

Table 4: Frequency of reported risk factors and direction of associated with MDR bacterial infections among pediatric inpatients

Risk Factor	Studies Reporting (n)	Direction of Association	Settings	Evidence Type
Prior antibiotic exposure	**6**	**↑ Increased risk**	**ICU, NICU**	**Multivariable / Univariate**
Broad-spectrum antibiotics	5	↑ Increased risk	ICU	Univariate
ICU/NICU admission	8	↑ Increased risk	ICU/NICU	Descriptive / Regression
Mechanical ventilation	5	↑ Increased risk	ICU/NICU	Regression
Central venous catheter	4	↑ Increased risk	ICU	Regression
Prolonged hospitalization	6	↑ Increased risk	ICU/Ward	Descriptive
Previous hospitalization	3	↑ Increased risk	ICU	Descriptive
Prematurity / low birth weight	4	↑ Increased risk	NICU	Descriptive
Underlying comorbidities	6	↑ Increased risk	ICU/Ward	Descriptive

Table 5: Risk of bias assessment of included studies using the Newcastle–Ottawa Scale

Study	Selection (4)	Comparability (2)	Outcome (3)	Total Score	Risk of Bias
(Balkhy et al., 2012)	★★★	★	★★	**6/9**	**Moderate**
(Bukhari and Alrabiaah, 2018)	★★★★	★	★★	7/9	Low
(Alqahtani, 2017)	★★★	★	★★	6/9	Moderate
(Alzomor et al., 2019)	★★★	★★	★	6/9	Moderate
(Mutair et al., 2021)	★★★★	★	★★★	8/9	Low
(Said et al., 2021)	★★★	★	★★	9/6	Moderate

Study	Selection (4)	Comparability (2)	Outcome (3)	Total Score	Risk of Bias
(Abalkhail et al., 2022)	★★★★	★★	★	**7/9**	**Low**
(Bazaid et al., 2023)	★★★	★	★★	6/9	Moderate
(Banawas et al., 2023)	★★★★	★★	★★★	9/9	Low
(Hafiz et al., 2023)	★★★	★	★★	6/9	Moderate
(Taha et al., 2023)	★★★★	★★	★★	8/9	Low
(Saeedi et al., 2024)	★★★	★★	★★	7/9	Low
(Alhazmi et al., 2024)	★★★★	★★	★★	8/9	Low
(Abdelgalil et al., 2024)	★★★★	★	★★	7/9	Low
(Almutairi et al., 2024)	★★★	★★	★★	7/9	Low
(Abdallah et al., 2020)	★★	★	★★	5/9	Moderate
(Binkhamis et al., 2025)	★★★★	★	★★	7/9	Low

* Selection domain assessed representativeness of the study population, exposure ascertainment, and outcome absence at baseline; Comparability assessed adjustment for key confounders; Outcome domain assessed outcome measurement and adequacy of follow-up. Studies scoring 7–9 were considered low risk of bias, 4–6 moderate risk, and ≤3 high risk.

Table 6: Subgroup analysis of the prevalence of multidrug-resistant bacterial infections among pediatric inpatients

Subgroup	Pooled prevalence	95% CI	I^2/τ^2
Age group			
Pediatric (<18/≤14)	37.80%	21.3–55.9	98.90
Neonates/mixed	40.80%	6.6–81.3	98.10
Children (younger)	19.90%	12.3–28.5	0.00

Setting			
ICU/NICU/PICU	31.00%	18.5–45.0	97.80
Mixed (ward + ICU)	42.10%	31.9–52.6	
Unclear/Mixed	61.30%	38.3–82.1	95.00
Region			
Central	29.30%	12.4–49.9	99.00
Western	41.70%	16.5–69.4	97.30
Southern	68.20%	55.7–79.5	67.00
Northern	7.90%	4.3–12.3	
Design			
Cross-sectional	43.00%	25.4–61.5	98.90
Prospective	7.60%	2.9–14.1	
Experimental	7.90%	4.3–12.3	
Surveillance	27.30%	21.6–33.4	
Retrospective	33.90%	22.0–46.9	
Study period			
≤2019	53.70%	21.7% – 84.1	0.112*
2020–2022	27.90%	15.1% – 42.8	0.049*
≥2023	41.40%	13.4% – 72.7	0.079*

* = τ^2

DISCUSSION

This systematic review and meta-analysis synthesize evidence on the prevalence, pathogen distribution, and risk factors associated with multidrug-resistant (MDR) bacterial infections among pediatric inpatients in Saudi Arabia, integrating data from 17 studies across multiple regions and healthcare settings. The findings reveal a substantial burden of MDR infections, marked heterogeneity across studies, and a consistent set of modifiable and non-modifiable risk factors, all of which align with and expand upon both regional and global evidence on pediatric antimicrobial resistance.

The pooled prevalence of MDR bacterial infections was estimated at 36.0%, indicating that over one-third of pediatric inpatients in Saudi hospitals are affected by MDR organisms. This prevalence is high when compared with reports from high-income countries in Europe and North America, where pediatric MDR prevalence typically ranges from 10% to 25%, but is comparable to estimates reported from the Middle East and other low- and middle-income regions (33). The World Health Organization has highlighted children as a particularly vulnerable population due to frequent antibiotic exposure, immature immune systems, and reliance on invasive medical care, especially in hospital settings (34). The very high heterogeneity observed across studies (I^2 > 98%) is consistent with global prevalence meta-analyses of antimicrobial resistance and likely reflects true contextual variability related to differences in study design, patient populations, healthcare settings, diagnostic capacity, and antimicrobial stewardship practices (2).

Subgroup analysis by age demonstrated higher MDR prevalence among neonates and mixed neonatal–pediatric populations, underscoring the heightened vulnerability of neonates receiving intensive care. Similar patterns have been reported internationally, where neonatal intensive care units (NICUs) represent epicenters for MDR transmission due to prolonged hospitalization, frequent device use, and broad-spectrum antibiotic exposure (35). Stratification by healthcare setting further confirmed that ICU, NICU, and PICU environments are associated with substantially higher MDR prevalence, a finding that aligns with global evidence demonstrating that critically ill pediatric patients face disproportionate MDR risk (36). Intensive care environments are characterized by high antimicrobial pressure and frequent invasive procedures, creating conditions conducive to resistance emergence and transmission.

Geographic subgroup analysis revealed significant regional variation in MDR prevalence within Saudi Arabia, with higher estimates observed in the Southern and Western regions compared with the Central and Northern regions. Similar regional disparities have been reported across the Middle East and are often attributed to differences in referral patterns, infection prevention infrastructure, laboratory capacity, and the implementation of antimicrobial stewardship programs (37). Differences by study design were also notable, with retrospective and cross-sectional studies reporting higher prevalence estimates than prospective or surveillance studies. This pattern has been observed in other systematic reviews and may reflect methodological limitations inherent to retrospective designs, including selection bias and incomplete adjustment for confounding (38). Temporal subgroup analysis suggested fluctuations in MDR prevalence across study periods; however, these differences were not statistically significant under the random-effects model, highlighting the difficulty of inferring clear temporal trends in the presence of substantial heterogeneity and evolving diagnostic practices.

The risk factors identified in this review are highly consistent with international literature. Antibiotic-related factors, particularly prior antibiotic exposure and the use of broad-spectrum agents, emerged as the most frequently reported and robust predictors of MDR infection. These findings reinforce the central role of antimicrobial selective pressure in driving resistance, as repeatedly demonstrated in global studies (39). Healthcare-associated factors, including ICU or NICU admission, healthcare-associated infections, and prolonged hospitalization, were strongly associated with MDR risk, reflecting cumulative exposure to resistant organisms, invasive devices, and repeated antibiotic courses (36). Device-related factors such as mechanical ventilation and central venous catheter use were consistently linked to MDR infections, likely due to biofilm formation and compromised host defenses (35). Patient-related characteristics, including prematurity, immunosuppression, malignancy, and underlying comorbidities, further increased susceptibility to MDR infections, consistent with pediatric studies worldwide (40).

The predominance of Gram-negative organisms, particularly Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumannii, and Pseudomonas aeruginosa, is consistent with global pediatric resistance patterns (8). The high frequency of extended-spectrum β-lactamase (ESBL)-producing and carbapenem-resistant organisms is especially concerning, given their association with limited therapeutic options, increased mortality, prolonged hospitalization, and higher healthcare costs (2). The emergence of carbapenem-resistant Klebsiella pneumoniae and MDR Acinetobacter baumannii in pediatric intensive care settings mirrors trends reported across the Middle East and underscores the urgent need for intensified surveillance and infection control (41,42). Among Gram-positive pathogens, the continued detection of methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant Enterococcus (VRE) highlights persistent gaps in infection prevention and antimicrobial stewardship, even for organisms traditionally considered more controllable (43).

Taken together, these findings emphasize the critical importance of strengthening antimicrobial stewardship programs (ASPs) and infection prevention strategies in pediatric healthcare settings. Evidence from multiple international studies demonstrates that effective ASPs can reduce inappropriate antibiotic use by 20–40% and significantly lower MDR infection rates without compromising patient outcomes (39,44,45). In Saudi Arabia, the high prevalence of MDR infections and substantial regional variability underscore the need for coordinated national surveillance systems, standardized resistance reporting, and targeted stewardship interventions, particularly in ICUs and NICUs (34,37).

Implications for clinical practice and public health

The findings of this review have important implications for pediatric clinical care, infection prevention, and antimicrobial stewardship in Saudi Arabia. The high burden of MDR infections underscores the urgent need for context-specific stewardship programs, particularly in intensive care and neonatal settings. Strategies should prioritize rational antibiotic prescribing, early de-escalation based on culture results, and strengthened infection control measures targeting device-associated infections.

At a policy level, the observed regional variability highlights the need for coordinated national surveillance systems and standardized reporting of antimicrobial resistance in pediatric populations. Integrating MDR surveillance with stewardship and quality improvement initiatives may help reduce the burden of resistance and improve pediatric outcomes.

Strengths and limitations

This review benefits from a comprehensive search strategy, adherence to PRISMA 2020 guidelines, rigorous risk-of-bias assessment, and extensive subgroup and sensitivity analyses. However, limitations include substantial heterogeneity, reliance on predominantly observational study designs, and variability in MDR definitions and laboratory methods across studies. These factors should be considered when interpreting the pooled estimates.

CONCLUSION

This systematic review and meta-analysis demonstrate a substantial burden of multidrug-resistant bacterial infections among pediatric inpatients in Saudi Arabia, with more than one-third of hospitalized children affected. Gram-negative pathogens, particularly ESBL-producing and carbapenem-resistant organisms, predominated, and MDR infections were consistently associated with antibiotic exposure, intensive care admission, invasive device use, prolonged hospitalization, and underlying patient vulnerability. The marked heterogeneity observed across studies highlights important contextual and regional differences in MDR epidemiology. These findings underscore the urgent need for strengthened antimicrobial stewardship, robust infection prevention strategies, and coordinated national surveillance systems targeting pediatric populations, particularly in high-risk hospital settings.

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