Antimicrobial resistance from one health perspective in the Middle East: A systematic review

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Abstract

Background: Antimicrobial resistance (AMR) is recognized globally as a significant health challenge, but its extent remains unclear in many regions. It is crucial to prioritize a foundational evaluation of AMR prevalence to facilitate the implementation of laboratory-based surveillance. Adopting a One Health perspective, this study outlines the present AMR status in the Middle East.

Aim: To synthesize the current state of knowledge on AMR in the Middle East, delineate the contributions of different sectors (human health, animal health, and environment), and discern the effectiveness of One Health interventions in mitigating AMR.

Methods: An exhaustive literature search was conducted via PubMed, ScienceDirect, and Google Scholar. Potential articles were screened and assessed for eligibility based on prescribed eligibility criteria. Data synthesis was done, and the results were reported and discussed thematically.

Results: Twenty-three studies were included in the study and published between 2019 and 2023. Most studies reveal substantial challenges in treating infections, with a significant prevalence of resistance in critical care units, particularly against extended-spectrum beta-lactamases and carbapenem-resistant Gram-negative bacteria. Colistin and imipenem resistance in pediatric populations further emphasize the urgency of understanding and addressing diverse resistance mechanisms in the region. Studies on urinary pathogens, bacteremia, and biofilm formation highlight the multifaceted challenge of AMR. The emergence of resistance to key antibiotics emphasizes the urgency for tailored treatment strategies.

Conclusion: Given the interconnectedness of human, animal, and environmental health, a One Health perspective is imperative. The diverse challenge demands coordinated efforts, including innovative interventions and public health policies. Bridging existing gaps through future research is crucial for evidence-based and context-specific strategies in combating AMR in the region.

Keywords: Antimicrobial resistance, One Health, Middle East.

Introduction

Antimicrobial resistance (AMR) is a global public health emergency, challenging our ability to combat bacterial infections. In their pursuit of improving health and agricultural productivity, middle-income countries often misuse antimicrobials, contributing to widespread resistance (Tadesse *et al.*, 2017). The lack of awareness among farmers and the extensive use of food-producing animals are vital factors (Tadesse *et al.*, 2017). In our interconnected world, AMR can swiftly spread across humans, animals, plants, and the environment, undermining infection treatment and causing economic repercussions. The escalating threat of AMR requires a One Health approach, recognizing the interdependence of humans, animals, and the environment (Adisasmito *et al.*, 2022).

Our investigation centers on the One Health paradigm, acknowledging human, animal, and environmental health links. Rudolf Virchow's concept of "zoonosis" in the 19th century and Calvin Schwabe's "one medicine" underscored these connections (Schwabe, 1964).

In the Middle East, unique socio-economic factors contribute to the complexity of AMR, requiring region-specific interventions. This study explores the interplay between One Health and AMR in the Middle East, aiming to uncover patterns, identify gaps, and provide insights for targeted interventions. Our systematic review will offer stakeholders and policymakers a robust foundation for informed decision-making in the fight against AMR in this region.

What is the current state of AMR in the Middle East, and how do different sectors, including human health,

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animal health, and the environment, contribute to the development and spread of AMR? Furthermore, what evidence exists regarding the effectiveness of One Health interventions in mitigating AMR in the Middle East? Hence, the primary objectives are to synthesize the current state of knowledge on AMR in the Middle East, delineate the contributions of different sectors (human health, animal health, and environment), and discern the effectiveness of One Health interventions in mitigating AMR.

Materials and Methods

This study followed preferred reporting items for systematic review and meta-analysis (PRISMA) 2020 guidelines (Page *et al.*, 2021).

Identification and selection of studies
Search strategy
The search strategy involved a combination of keywords in different combinations including antimicrobial, antibiotic, drug, Gram-negative, Gram-positive, one-health, and Middle East. In addition, specific infections and countries in the Middle East were included in the search strings.

Eligibility criteria
Inclusion criteria
All studies had to meet the following pre-defined inclusion criteria:
- Studies conducted in the Middle East.
- Research focusing on AMR in humans, animals, and the environment.
- Publications from a specified time range from 2019 to November 2023.

Exclusion criteria
Studies that satisfied the following criteria were excluded:
- Studies not adopting a one-health approach.
- Comments, editorials, conferences, paper commentaries, non-full-texts, discussions, reports, reviews, and meta-analysis.
- Studies combining data, e.g., aggregating resistance rates in broad categories such as "Gram-negative organisms," "Gram-positive organisms," or "Enterobacteriaceae."
- Studies on animals, environment, overall resistance rates, and those without information on total bacteria isolates.

Data selection and extraction
Information was collected from each study using a form and a database specifically created for this study, utilizing a Microsoft Excel spreadsheet. Data extracted included article information (Author, year of publication, study design, country, total number of participants, and outcomes).

Methodological quality assessment
The Cochrane Organization's Risk of Bias 2 tool was employed to evaluate the quality of the study (Sterne *et al.*, 2019). The risk of bias graph and summary plot were generated using the Robvis visualization tool. In addition, the National Institutes of Health quality assessment tool for observational cohort and cross-sectional studies was employed to evaluate the quality of the study (Armijo-Olivo *et al.*, 2012).

Data analysis
Data were systematically extracted and organized using Microsoft Excel 2021. The extracted data are presented in Table 1, showing the author (s), study design, sample size, and outcomes.

Ethical approval
Not needed for this study.

Results

Study selection
Initially, 625 articles were retrieved through the search process. After applying eligibility criteria during the screening process, 547 articles were excluded. The remaining 57 articles underwent a full-text review, and 34 were excluded as they did not fully meet the eligibility criteria. It is essential to highlight that some articles were excluded for multiple reasons. Ultimately, only 23 articles m*et al*l the inclusion criteria and were included in the study. Figure 1 represents the PRISMA flowchart summarizing the subsequent data screening procedure.

Methodological quality assessment results
Figures 2 and 3 show the quality assessment results.

Data selection and extraction
Data were systematically extracted and presented in Table 1.

Study characteristics and thematic analysis of outcomes
The investigation into AMR in Middle Eastern healthcare settings reveals complexity, as demonstrated by a study at King Faisal Hospital in Saudi Arabia (Kabrah, 2022). In this cross-sectional study of 298 patients with central venous catheters, a substantial challenge emerged in treating intensive care unit infections. Notably, 175 patients exhibited resistance to extended-spectrum beta-lactamases (ESBL) and carbapenem-resistant Gram-negative bacteria (GNB), highlighting the difficulty in managing such infections and the urgent need for effective strategies in critical care settings. Colistin resistance, explored by Nawfal Dagher *et al.* (2020) through rectal swabs, exposed the prevalence of resistance as all eight clinical strains isolated exhibited resistance to colistin. This finding emphasizes the urgency of understanding diverse resistance mechanisms present in the region. A study by Rahbar *et al.* (2020) on the investigation into urinary pathogens highlighted the potential of temocillin in treating infections caused by ESBL-producing *Escherichia coli* and *K. pneumoniae*, advocating for exploring alternative treatments for common infections in the region. Pediatric populations, as explored by Sahib Abdul-Mohammed *et al.* (2022), showcased a concerning trend of imipenem resistance. Among identified isolates, *A. baumannii*, *P. aeruginosa*, and *K. pneumoniae* exhibited resistance, with *A. baumannii* prevalent in both blood and urine samples, underlining the diverse sources of resistant bacteria in pediatric

Table 1. *Study descriptor table.*

Reference	Study design	Country	Sample size	Outcomes
Akhavizadegan *et al.*, 2021	Cross-sectional study	Iran	300	Recommend imipenem and amikacin over traditional first-line therapy (fluoroquinolone and sulfamethoxazole-trimethoprim) for hospitalized urinary tract infection patients. Most effective antibiotics for Gram-negative uropathogens: imipenem (6.0% overall resistance), amikacin (6.3%), and nitrofurantoin (10.3%).
Al Benwan and Jamal 2022	Retrospective study	Kuwait	N/A	Enterobacterales exhibited high resistance against ampicillin, cephalothin, nitrofurantoin, amoxicillin/clavulanic acid, and trimethoprim-sulfamethoxazole. ESBL-producing *E. coli* and *K. pneumoniae* prevalence was 26% and 55%, respectively. Most effective antibiotics for Gram-negative organisms: meropenem, amikacin, gentamicin, and piperacillin/tazobactam. For Gram-positive organisms: vancomycin, ampicillin, linezolid, and nitrofurantoin.
Albert *et al.*, 2019	Randomized controlled trial	Kuwait	61	Low infection, mortality, and multidrug resistance rates, with a relatively high prevalence of gastrointestinal infection. Selected *S. typhimurium* and *S. enteritidis* isolates characterized by whole-genome sequencing, offering insights into phylogeny, virulence, and resistance.
Almutawif and Eid, 2023	Randomized controlled trial	Saudi Arabia	3,937	*Enterococcus* spp. exhibited high resistance rates (>62.3%) to ciprofloxacin, gentamicin, and tetracycline, while *Streptococcus* spp. demonstrated significant resistance rates (>76.6%) to colistin and trimethoprim/sulfamethoxazole.
Al-Tawfiq *et al.*, 2020	Longitudinal study	Saudi Arabia	N/A	No change in antibiotic resistance among *P. aeruginosa* and *E. coli* was observed over time (2013–2018), with a consistently high rate of ESBL-producing *E. coli* and *K. pneumoniae*.
Alzahrani *et al.*, 2021	Cross-sectional study	Saudi Arabia	102	High rates of methicillin-resistant *S. aureus* colonization were observed among center residents (24.7%) and employees (15.8%). Long-term residence in the correctional institution and poor hand hygiene were identified as significant risk factors. Antibiogram results categorized isolated strains into six phenotypes, predominantly featuring two antibiotic-resistant patterns, indicating potential cross-contamination and local dissemination foci.
Dargahi *et al.*, 2022	Randomized controlled trial	Iran	96	Isolated GPB included coagulase *Staphylococcus* (16%) and *S. aureus* (14%). Among GNB, *Klebsiella* spp. (16%), *A. baumannii* (22%), and *P. aeruginosa* (35%) were identified. Thirty-two percent of strains were MDR, and 29% were XDR. Seventy-two percent exhibited biofilm formation, indicating a high prevalence of biofilm producers.
Gordon *et al.*, 2019	Longitudinal study	Israel	427	Out of 427 events 284 (66%) were Health associated (HA), 64 (15%) were MRSA and 9 (2%) were CA-MRSA. Increased 1-year mortality in children with HA bacteremia (hazard ratio (HR) 4.1, 95% confidence interval (CI) 1.3–12) and prior chronic disease (HR 3.4, 95% CI to 9.0).
Hafiz *et al.*, 2023	Longitudinal study	Saudi Arabia	152	*Klebsiella pneumoniae* exhibited concerning resistance rates: amoxicillin-clavulanate and cefuroxime (72%), ceftazidime (68%), cephalothin (76.3%), and Carbapenems (36%). The impact of *K. pneumoniae* bloodstream infection extended beyond individual patients, affecting the community with multi-drug resistant infections.

Continued

Reference	Study design	Country	Sample size	Outcomes
Hammour *et al.*, 2023	Retrospective cross-sectional study	Jordan	1,043	The predominant carbapenem-resistant bacteria were *Acinetobacter baumannii* (93.3%), *K. pneumoniae* (59.2%), and *P. aeruginosa* (41.9%). *Escherichia coli* (6.9%) and *Proteus mirabilis* (3.3%) showed lower prevalence. Overall, carbapenem-resistant Gram-negative isolates constituted 41.2% (430 out of 1,043).
Lillie *et al.*, 2019	Prospective cohort study	Jordan	195	Empirical antibiotics (cephalexin) exhibited *in-vitro* resistance in 30.9% of cases. Among fifty patients with unavoidable healthcare-related bloodstream infections (BSIs), *E. coli* BSI showed significant mortality, with limited modifiable risk factors for mortality or prolonged hospital stay.
Mostafavi *et al.*, 2021	Cross-sectional study	Iran	1,180	*Escherichia coli* (68.1%), *E.* spp. (8.8%), and *K. pneumonia* (8.0%) were the main pathogens. Isolated bacteria showed high susceptibility to imipenem (94.9%), meropenem (92.2%), amikacin (91.9%), gentamicin (64.4%), cefepime (52.6%), and ceftazidime (47.2%). Lowest susceptibility was seen with ceftriaxone (41.8%), cefotaxime (40%), ciprofloxacin (38.6%), and trimethoprim-sulfamethoxazole (31.3%). Imipenem, meropenem, and amikacin are recommended for empiric therapy in complicated hospitalized patients with community-acquired UTI.
Rahbar *et al.*, 2020	Cross-sectional study	Iran	500	Temocilin exhibited high activity with a 95% susceptibility rate and ranked as the fourth most active antibiotic at 65%, based on urinary and systemic breakpoints.
Sahib Abdul-Mohammed *et al.*, 2022	Prospective cohort study	Iraq	100	Imipenem-resistant organisms included *K. pneumonia* (*n* = 21), *P. aeruginosa* (*n* = 19), and *Acinetobacter baumannii* (*n* = 16). *Klebsiella pneumonia* was more prevalent in males (*n* = 57) than females (*n* = 43), followed by *P. aeruginosa* and *A. baumannii*, especially within the 1–3 day range.
Nawfal Dagher *et al.*, 2020	Randomized controlled trial	Lebanon	23	All isolates were resistant to colistin. They had MICs for colistin that ranged from 8 to 30 mg/l. This study highlights the presence of colistin-resistant GNB in a Lebanese hospital, and urgent research needs to be conducted to avoid the spread of such bacteria.
Kabrah, 2022	Cross-sectional study	Saudi Arabia	298	Among the samples, 36 were ESBL-producing GNB, and 139 were carbapenem-resistant GNB, all displaying multidrug resistance. Imipenem was identified as an effective antibiotic against ESBL-producing GNB. Implementing antibiotic utilization measures seems crucial in controlling the emergence of multidrug-resistant pathogens, including ESBL and carbapenem-resistant GNB.
Rahimzadeh *et al.*, 2023	Prospective cohort study	Iran	N/A	Cefepime resistance was observed in 51% of isolates, followed by amikacin at 47.76%. There is an increasing trend in resistance to *P. aeruginosa*.
Merhi *et al.*, 2023	Cross-sectional study	Lebanon	59	Out of 41 isolates resistant by Etest and 18 susceptible, multilocus sequence typing determined clonality. Based on average nucleotide identity (ANI), 80% were E. hormaechei, 18% were *K. aerogenes*, and 2% were *E. cloacae*.
Arafa *et al.*, 2022	Qualitative study	Saudi Arabia	1,000	60% of the isolates showed resistance to ampicillin and no resistance to the other three.

Reference	Study design	Country	Sample size	Outcomes
Araj *et al.*, 2020	Qualitative study	Lebanon	299	C/T showed similar efficacy against *E. coli* and *K. pneumonia* isolates (MIC90 values 1 and 1.5 ug/ml). However, its activity was lower against MDR isolates (*E. coli* MIC90: 256 ug/ml, *K. pneumoniae* MIC90: 96 ug/ml). For non-MDR *P. aeruginosa*, MIC90 was 3 ug/ml, while for MDR *P. aeruginosa*, it was ≥256 ug/ml. Overall, C/T demonstrated comparable or higher susceptibility compared to routine antimicrobials.
Islam *et al.*, 2022	Qualitative study	Qatar	Rodents	Poorly managed mixed-species animal farming poses a higher risk of zoonoses. Urbanization and climate change can impact ecosystems, vectors, and vector-borne diseases. The One Health framework is recommended to monitor and mitigate potential spillover or epidemics of rodent-borne zoonoses.
Qasemi *et al.*, 2022	Cohort study	Iran	265	The high prevalence of biofilm and β-lactamase-producing UPEC strains in Zahedan suggests a potential influence of socioeconomic status and environmental factors on the pathogenicity of these strains.
Sheikh *et al.*, 2022	Single-centre retrospective study	Bahrain	4,715	High incidences of ESBL *E. coli* and ESBL *K. pneumoniae*, along with alarming increases in *P. aeruginosa* resistance to carbapenems, necessitate suitable oral antibiotics such as amoxicillin-clavulanate, cefixime, and cefuroxime for empirical treatment.

patients. A cross-sectional study by Mostafavi *et al.* (2021) on community-acquired urinary tract infections emphasized *E. coli* as the predominant pathogen, with imipenem, meropenem, and amikacin identified as effective choices for severe cases, reinforcing the importance of tailored empirical therapy.

A retrospective study by Hammour *et al.* (2023) identified *A. baumannii*, *K. pneumoniae*, and *P. aeruginosa* as the most prevalent carbapenem-resistant bacteria, necessitating targeted interventions to address antibiotic resistance in the population. A study by Hafiz *et al.* (2023) assessment of *K. pneumoniae* bacteremia in Saudi Arabia revealed the impact at the patient and community levels, emphasizing the broader implications of multidrug-resistant infections. Research by Gordon *et al.* (2019) on *Staphylococcus aureus* bacteremia in children insisted on the association between Methicillin-resistant *Staphylococcus aureus* (MRSA) and increased long-term mortality in healthcare-associated cases. Biofilm formation in endotracheal tubes, as studied by Dargahi *et al.* (2022), revealed the prevalence of biofilm-producing Gram-positive bacteria (GPB), with colistin and linezolid identified as effective antibiotics against resistant GNB and GPB isolates. In a detention center, Alzahrani *et al.* (2021) found high rates of MRSA colonization among residents and employees, attributing it to poor personal hygiene and inadequate infection control measures.

A cross-sectional study by Akhavizadegan *et al.* (2021) on antibiotic resistance in uropathogens indicated higher resistance rates in inpatient samples, emphasizing

the importance of tailored treatment strategies. Araj *et al.*'s (2020) findings on Ceftolozane/Tazobactam (C/T) revealed high activity against ESBL-producing *E. coli* and *K. pneumoniae*, indicating its potential as a minimally toxic and resistance-reducing alternative treatment. These results underscore the pressing need for coordinated efforts to address AMR in the Middle East, adopting a One Health perspective to tackle this critical public health challenge.

In the quantitative analysis of mortality outcomes across the included studies, varying mortality rates were observed, as shown in Table 1. Albert *et al.* (2019) reported a mortality rate of 6.56%, with 4 out of 61 patients succumbing to the antibiotic therapy. Similarly, Gordon *et al.* (2019) reported a mortality rate of 17.56%. Hafiz *et al.* (2023) reported the highest mortality rate among the studies, with 48 deaths out of 148 patients, yielding a mortality rate of 32.43%. Lillie *et al.* (2019) reported a mortality rate of 23.40%.

Discussion

This study of AMR from a One Health perspective in the Middle East reveals a complex landscape marked by resistance patterns in various clinical settings. The comprehensive exploration of diverse studies emphasizes the urgent need for coordinated efforts to address this region's multifaceted challenge of AMR. The prevalence of resistance observed in critical care units, as demonstrated by Kabrah (2022) is a stark reminder of the urgent need for tailored treatment strategies in these high-stakes environments. This
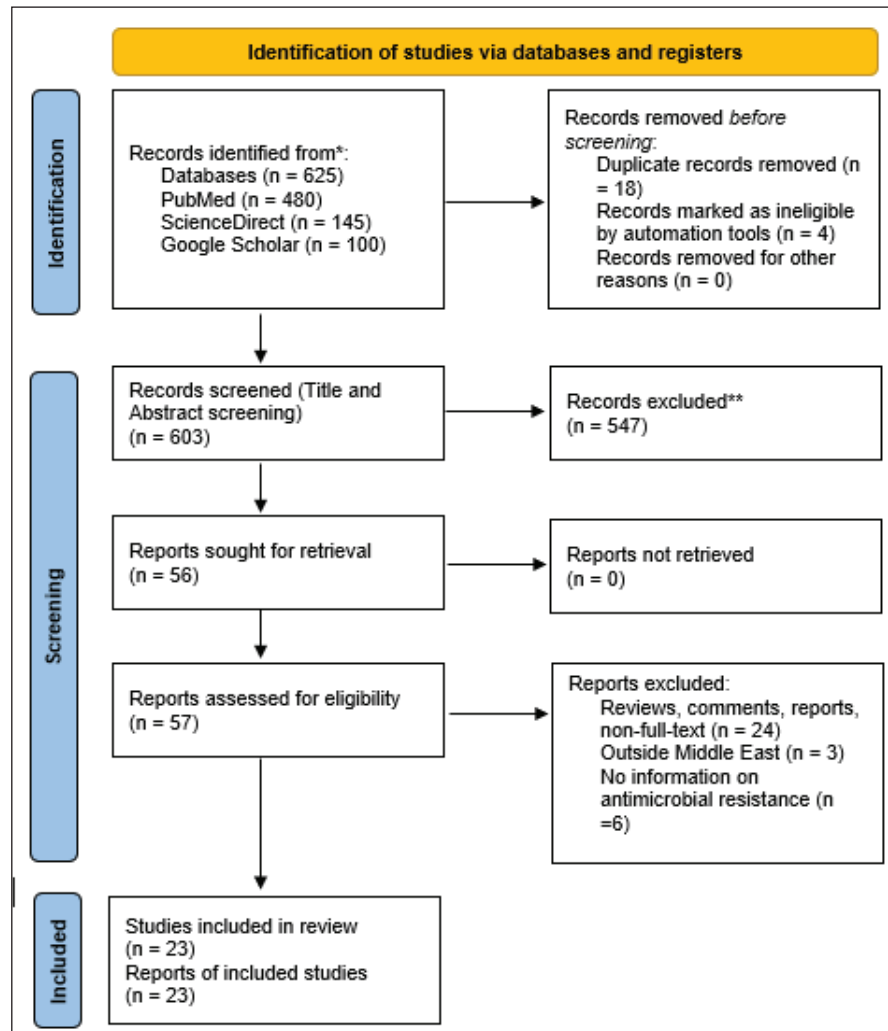
Fig. 1. *PRISMA flow diagram showing results of the study selection (Page et al., 2021).*

finding emphasizes the critical role of targeted interventions in managing infections within intensive care units. Moreover, the widespread resistance, exemplified by colistin-resistant isolates (Nawfal Dagher *et al.*, 2020), raises significant concerns about the efficacy of current therapeutic approaches. Colistin resistance, often considered a last-resort antibiotic, highlights the challenges in treating infections caused by multidrug-resistant strains. The potential implications for patient outcomes and the broader healthcare system further emphasize the urgency to address these challenges.

Comparing our findings with existing literature brings to light the distinctive patterns of resistance observed in the Middle East. The noteworthy carbapenem resistance rates across various bacteria, as evidenced by Hammour *et al.* (2023), set the region apart globally. This highlights the necessity for tailored strategies, acknowledging the unique challenges and contributing factors specific to the Middle East. Furthermore,

the community-level impact of multidrug-resistant infections, exemplified in *K. pneumoniae* bacteremia (Hafiz *et al.*, 2023), emphasizes the need for comprehensive interventions beyond individual patient care. The authors' assessment of *K. pneumoniae* bacteremia aligns with broader literature emphasizing the community-level impact of multidrug-resistant infections. A study by Nordmann *et al.* (2009) further emphasizes the wider societal implications, urging a comprehensive response to curb the spread of resistance.

Gordon *et al.*'s (2019) study on *S. aureus* bacteremia aligns with research by Quezada *et al.* (2013) emphasizing the long-term mortality associated with MRSA in healthcare-associated cases. The study by Dargahi *et al.* (2022) on biofilm formation aligns with a survey by Fadl (2018), highlighting the prevalence of biofilm-producing GPB and identifying effective antibiotics against resistant isolates. Akhavizadegan *et al.* (2021) study on antibiotic resistance in

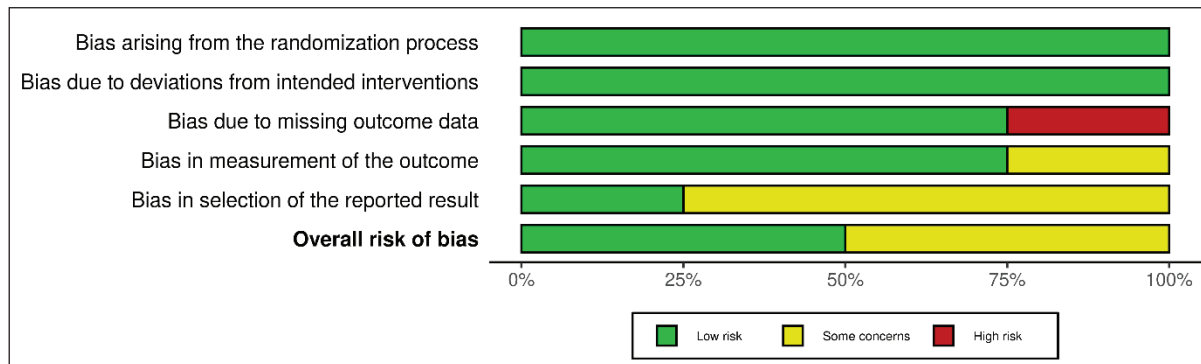**Fig. 2.** *Traffic lights plot of the risk of bias assessment.*

Fig. 3. *Risk of bias summary plot.*

uropathogens aligns with a study by Kot (2019), indicating higher resistance rates in inpatient samples and emphasizing the importance of tailored treatment strategies. Findings by Araj *et al.* (2020) on C/T align with Giacobbe *et al.* (2018), suggesting its potential as an alternative treatment with minimized toxicity and bacterial resistance.

Mostafavi *et al.* (2021) study on community-acquired urinary tract infections aligns with a study by Kallen *et al.* (2006), emphasizing the importance of tailored empirical therapy. The identification of *E. coli* as the predominant pathogen and the effectiveness of imipenem, meropenem, and amikacin in severe cases aligns with global trends outlined by Giamarellos-Bourboulis *et al.* (1997). Hammour *et al.*'s (2023) study on carbapenem-resistant bacteria echoes the global concern highlighted by Gupta *et al.* (2011).

The socio-economic, cultural, and healthcare system dynamics specific to the Middle East may play pivotal roles in shaping observed resistance trends. Understanding these variation factors becomes paramount as we seek to develop effective interventions tailored to the unique challenges presented by the region. Adopting a One Health perspective is critical in addressing the multifaceted challenge of AMR in the Middle East. When analyzing the observed resistance patterns, human, animal, and environmental health interconnectedness becomes evident. Integrating efforts across these domains will be essential for developing comprehensive and sustainable strategies to mitigate resistance effectively. Recognizing the interplay between different health sectors emphasizes the need for collaborative, cross-disciplinary approaches to combat the growing threat of resistance.

Conclusion

This study explores AMR in the Middle East from a One Health perspective. The synthesis of findings paints a vivid picture of resistance challenges across diverse clinical settings. Resistance prevalence in critical care units underscores the need for tailored treatment in intensive care. The emergence of colistin resistance and diverse strains underscores the urgency in understanding and addressing resistance mechanisms. Temocillin's potential and alternative interventions highlight the need to explore strategies against common infections. Pediatric resistance trends emphasize the need for targeted interventions. The

prevalence of carbapenem-resistant bacteria and the impact of multidrug-resistant infections underscore the urgent need for coordinated efforts.

The association of MRSA with increased long-term mortality and biofilm-producing bacteria prevalence adds complexity to managing infections. High colonization rates in detention centers highlight societal implications and the role of hygiene and infection control. Given these comprehensive findings, a coordinated, One Health approach is imperative to address the complex challenge of AMR in the Middle East.

Conflict of interest

The author declares that there is no conflict of interest.

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Data availability

All used data were presented in the manuscript.

Reference

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