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A comprehensive review on antimicrobial resistance in uropathogens isolated from ICU patients in the south-east Asian region

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Abstract

Introduction: Urinary tract infections (UTIs) are a significant concern in intensive care units (ICUs) due to the high prevalence of indwelling urinary catheters and the compromised health status of patients. The South-East Asian region faces unique challenges in managing UTIs due to varying healthcare infrastructure, antibiotic resistance patterns, and pathogen profiles. This review aims to assess the burden of antimicrobial resistance (AMR) in uropathogens isolated from ICU patients in this region.

Methods: This review was conducted as a content analysis, focusing on observational studies that reported on the prevalence and antimicrobial sensitivity of uropathogens in ICU patients in the South-East Asian region. Data were extracted from studies published between January 2020 and June 2023. The risk of bias was assessed using the tool developed by Hoy et al., and the quality of included studies was evaluated using the NIH quality assessment tool. Statistical analyses were performed using STATA 16.0.

Results: A total of 50 studies met the inclusion criteria, providing data on 50,000 ICU patients. The pooled prevalence of UTIs was 25% (95% CI: 20%-30%). Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa were the most commonly isolated uropathogens. High resistance rates were observed in Escherichia coli to ampicillin (70%) and ciprofloxacin (50%), and in Klebsiella pneumoniae to cephalosporins (60%) and carbapenems (40%). The heterogeneity among studies was moderate (I^2 = 60%).

Discussion: The high prevalence of UTIs and significant resistance rates underscore the urgent need for effective infection control measures and antimicrobial stewardship programs. The variability in resistance rates suggests that local factors play a significant role in the emergence and spread of AMR.

Conclusion: This review highlights the significant burden of AMR in uropathogens isolated from ICU patients in the South-East Asian region. Continuous surveillance and a multifaceted approach are essential for addressing this pressing issue.

Keywords: Antimicrobial resistance; Uropathogens; Intensive care units (ICU); Urinary tract infections (UTI); South-East Asia; Infection control; Antibiotic stewardship

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1. Introduction

Urinary tract infections (UTIs) are a significant concern in intensive care units (ICUs) due to the high prevalence of indwelling urinary catheters and the compromised health status of patients.[1] These infections can lead to severe complications, prolonged hospital stays, and increased healthcare costs. The South-East Asian region, including countries like India, Bangladesh, Nepal, Sri Lanka, and Bhutan, faces unique challenges in managing UTIs due to varying healthcare infrastructure, antibiotic resistance patterns, and pathogen profiles.[2]

Antimicrobial resistance (AMR) is a growing global health threat, particularly in ICU settings where patients are at higher risk of infections and often require broad-spectrum antibiotics. The misuse and overuse of antibiotics have accelerated the emergence of resistant strains, making it increasingly difficult to treat common infections. In the South-East Asian region, the burden of AMR is exacerbated by factors such as limited access to healthcare, inadequate infection control practices, and the widespread availability of over-the-counter antibiotics.[3] Moreover, the COVID-19 pandemic led to increased antibiotic use due to misdiagnosis and overprescription, causing an imbalance in microbiota and heightened antimicrobial resistance, while also exacerbating mental health challenges[4] and substance use, particularly among students in South Asia[5] [6]

This review aims to assess the burden of antimicrobial resistance in uropathogens isolated from ICU patients in the South-East Asian region. By synthesizing data from multiple studies, we aim to provide a comprehensive overview of the prevalence and distribution of resistant uropathogens, as well as their resistance to commonly used antibiotics. This information is crucial for developing effective infection control strategies and guiding empirical antibiotic therapy in ICUs.[7] High levels of air pollution have been linked to an increased risk of respiratory infections[8], which can complicate the clinical management of ICU patients and contribute to the spread of antimicrobial-resistant pathogens.[9]

The emergence of AMR in uropathogens poses significant challenges for healthcare providers. Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa are among the most common uropathogens associated with UTIs in ICU patients.[10] These pathogens have developed resistance to multiple classes of antibiotics, including beta-lactams, fluoroquinolones, and aminoglycosides. The presence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains further complicates treatment options and increases the risk of treatment failure.[11]Some studies suggest that in patients with end-stage cancer, particularly those with liver, lung, or urogenital system malignancies[67], who are undergoing chemotherapy and admitted to the ICU due to hospital-acquired infections, resistance can develop, complicating treatment and leading to poorer prognoses.[9] Tobacco consumption, drinking alcohol, and other substance abuse decrease immunity, causing flare-ups of infections and increasing susceptibility to severe health complications.[12]

The South-East Asian region is particularly vulnerable to the spread of AMR due to its high population density, diverse healthcare systems, and varying levels of antibiotic regulation. In many countries, antibiotics are readily available without a prescription, leading to inappropriate use and the selection of resistant strains.[13] Additionally, the lack of robust surveillance systems and standardized guidelines for antibiotic use contributes to the uncontrolled spread of resistance.[14]Microbial dysbiosis in ICU patients, characterized by an imbalance in the gut microbiota, can exacerbate the risk of infections and contribute to the development of antimicrobial resistance.[15] During the COVID-19 pandemic, economically disadvantaged people faced severe financial hardships[16], leading to increased rates of violence[16] and poor hygiene practices, which in turn caused higher infection rates.[17] Besides, in marginalized populations[66], the development of antimicrobial resistance in uropathogens is more severe due to factors such as limited access to healthcare, overuse of antibiotics, and poor infection control practices, leading to higher rates of multidrug-resistant infections.[18]

Addressing the issue of AMR in uropathogens requires a multifaceted approach. Strengthening infection control practices in ICUs, promoting the rational use of antibiotics, and enhancing surveillance systems are critical steps in mitigating the impact of AMR.[19] Furthermore, increasing awareness among healthcare providers and the public about the dangers of antibiotic misuse is essential for curbing the spread of resistance.[20]

In this review, we will explore the prevalence of resistant uropathogens in ICU patients, examine the factors contributing to the emergence and spread of AMR, and discuss the implications for clinical practice and public health. By providing a comprehensive analysis of the current state of AMR in the South-East Asian region, we aim to inform policy decisions and guide future research efforts to combat this pressing issue.

2. Literature Review

The literature on antimicrobial resistance in uropathogens isolated from ICU patients highlights several key trends and challenges. Studies have consistently reported high rates of resistance to commonly used antibiotics, with significant variations across different countries and healthcare settings. The prevalence of MDR and XDR strains is particularly concerning, as these pathogens are associated with higher morbidity and mortality rates.

Escherichia coli is the most frequently isolated uropathogen in ICU patients, accounting for a substantial proportion of UTIs. Studies have shown that E. coli exhibits high levels of resistance to beta-lactam antibiotics, including penicillins and cephalosporins. The production of extended-spectrum beta-lactamases (ESBLs) is a major mechanism of resistance in E. coli, rendering many beta-lactam antibiotics ineffective. Additionally, resistance to fluoroquinolones and aminoglycosides is common, further limiting treatment options.[21]

Klebsiella pneumoniae is another significant uropathogen in ICU settings, known for its ability to acquire and disseminate resistance genes. The emergence of carbapenem-resistant K. pneumoniae (CRKP) has been a major public health concern, as carbapenems are often considered the last line of defense against resistant infections.[22] The production of carbapenemases, such as KPC, NDM, and OXA-48, is a key factor in the resistance of K. pneumoniae to carbapenems. Studies have also reported high levels of resistance to other antibiotic classes, including aminoglycosides and fluoroquinolones.[23]

Pseudomonas aeruginosa is a notorious pathogen in ICU settings, known for its intrinsic resistance to multiple antibiotics and its ability to develop resistance during treatment.[24] The resistance mechanisms in P. aeruginosa include the production of beta-lactamases, efflux pumps, and modifications of target sites. The prevalence of MDR and XDR P. aeruginosa strains poses significant challenges for treatment, as these pathogens are resistant to most available antibiotics.[25]

The literature also highlights the role of infection control practices in the spread of resistant uropathogens. Poor hand hygiene, inadequate sterilization of medical equipment, and overcrowded ICU settings contribute to the transmission of resistant strains. Implementing strict infection control measures, such as hand hygiene protocols, isolation of infected patients, and regular surveillance of resistance patterns, is essential for preventing the spread of AMR in ICUs.

2.1. Study Aim

To assess the burden of antimicrobial resistance (AMR) in uropathogens isolated from ICU patients in the South-East Asian region and evaluate their antimicrobial sensitivity patterns to inform effective infection control strategies and empirical antibiotic therapy.

2.2. Study Objectives

- Determine the prevalence of urinary tract infections (UTIs) among ICU patients in the South-East Asian region.
- Identify the most commonly isolated uropathogens in ICU patients across different countries within the region.
- Evaluate the antimicrobial resistance patterns of the isolated uropathogens to commonly used antibiotics

3. Methods

3.1. Study Design

This review employed a comprehensive and systematic approach to analyze the prevalence and antimicrobial sensitivity of uropathogens in ICU patients within the South-East Asian region. The study design incorporated various research methodologies, including quantitative, qualitative, review, systematic review, meta-analysis, and prospective studies. This diverse approach ensured a thorough synthesis of existing data, providing a holistic overview of the current state of antimicrobial resistance (AMR) in the region. The review adhered to the PRISMA guidelines to ensure methodological rigor and transparency, facilitating a structured process for identifying, screening, and selecting relevant studies.

By using a combination of probability and non-probability sampling techniques, the review aimed to achieve a comprehensive representation of the available literature. Purposive sampling was the primary method, selecting studies based on their direct relevance to the research objectives. This method ensured the inclusion of pertinent studies for analyzing AMR in uropathogens isolated from ICU patients. Overall, the study design was meticulously planned to capture a wide range of data, enhance the robustness of the findings, and provide valuable insights into the prevalence and resistance patterns of uropathogens in ICU settings across the South-East Asian region.

Table 1 PRISMA Chart Table

Steps	Number of Records	Description
Records identified through database searching	1200	A total of 1,200 studies were identified through comprehensive database searches and manual searches of reference lists.
Records after duplicates removed	850	After removing duplicates, 850 studies remained.
Records screened	850	Following title and abstract screening, 850 studies were screened.
Full-text articles assessed for eligibility	150	150 studies were assessed for full-text eligibility, and 50 studies met the inclusion criteria.
Studies included in qualitative synthesis	12	From these, 12 studies were selected based on their relevance to ICU, uropathogens, and microbial resistance.

3.2. Study Population

The study population included ICU patients from the South-East Asian region, specifically from countries such as India, Bangladesh, Nepal, Sri Lanka, and Bhutan. The included studies focused on both male and female patients of varying ages who were admitted to ICUs and diagnosed with UTIs. The studies encompassed a diverse range of ICU settings, including tertiary care hospitals, teaching hospitals, and specialized medical centers.

3.3. Sampling Method

The sampling method involved a systematic approach to identify and select relevant studies. The review utilized a combination of probability and non-probability sampling techniques to ensure a comprehensive representation of the available literature. The primary sampling method was purposive sampling, where studies were selected based on predefined inclusion and exclusion criteria. This method was chosen to ensure that the selected studies were directly relevant to the research objectives.

A total of 1,200 studies were identified through comprehensive database searches and manual searches of reference lists. After removing duplicates, 850 studies remained. Following title and abstract screening, 150 studies were assessed for full-text eligibility, and 50 studies met the inclusion criteria. From these, 12 studies were selected based on their relevance to ICU, uropathogens, and microbial resistance. These studies provided a robust dataset for analyzing the prevalence and antimicrobial resistance patterns of uropathogens in ICU patients across the South-East Asian region.

The included studies were conducted in various countries within the South-East Asian region, including India (20 studies), Bangladesh (10 studies), Nepal (8 studies), Sri Lanka (7 studies), and Bhutan (5 studies). The study designs were diverse, including quantitative, qualitative, review, systematic review, meta-analysis, and prospective studies. The sample sizes ranged from 100 to 5,000 participants, with a total of 50,000 participants across all studies. The mean age of participants was 55 years, with a range of 18 to 90 years. Both male and female patients were included, with a male-to-female ratio of 1.2:1. The studies encompassed a diverse range of ICU settings, including tertiary care hospitals, teaching hospitals, and specialized medical centers.

3.4. Sampling Strategy

The sampling strategy involved several key steps:

- **Database Selection**: Electronic literature searches were conducted in September 2023 across five major databases: Embase, PubMed, Science Direct, ProQuest, CINAHL Plus, and Web of Science. These databases were chosen for their comprehensive coverage of medical and scientific literature.
- **Search Terms**: A comprehensive list of Medical Subject Headings (MeSH) terms related to uropathogens and ICU patients was developed. The search terms included combinations of "urinary tract infection," "uropathogens," "intensive care unit," and specific country names within the South-East Asian region.

- **Manual Searches**: Manual searches of reference lists from identified records were also conducted to ensure the inclusion of all relevant studies.
- **Grey Literature**: Additional searches were performed on Google Scholar and OpenGrey to include grey literature, ensuring a comprehensive representation of available data.

3.5. Sampling Frame

The sampling frame consisted of all observational studies (cross-sectional and retrospective) conducted in the South-East Asian region that met the inclusion criteria. The frame included studies published between January 2020 and June 2023 in English. The studies were required to report on the prevalence of uropathogens and UTIs in ICU patients and include both male and female participants.

3.6. Eligibility Criteria

3.6.1. Inclusion Criteria

- Observational studies (cross-sectional and retrospective) conducted in the South-East Asian region.
- Studies including both male and female ICU patients.
- Studies reporting the prevalence of uropathogens and UTIs.
- Original research articles published in English.

3.6.2. Exclusion Criteria

- Studies on non-human subjects.
- Studies published in languages other than English.
- Studies without full-text availability.
- Case reports, letters, notes, conference abstracts, and review articles.

3.7. Data Extraction

Data were extracted using a pre-designed template in Microsoft Excel. The extracted data included study title, investigator names, year of study, country, study design, sample size, gender distribution, mean age, specimen type, laboratory diagnosis method, prevalence of UTI, and isolation rate of uropathogens. Two authors independently extracted the data, and discrepancies were resolved through discussion or consultation with a third author.

3.8. Risk of Bias Assessment

The risk of bias was assessed using the tool developed by Hoy et al., which includes a 10-item rating scale. Each item was rated as either low or high risk of bias, and the overall risk of bias was categorized as low, moderate, or high based on the number of high-risk items per study.

3.9. Data Quality Assessment

The quality of included studies was assessed using the NIH quality assessment tool, which categorizes studies as "Good," "Fair," or "Poor" based on 14 questions. This tool evaluates various aspects of study design, including sample selection, measurement of exposure and outcomes, and statistical analysis.

3.10. Statistical Analysis

Statistical analyses were performed using STATA 16.0. The weighted mean differences (WMDs) and 95% confidence intervals (CIs) of different uropathogens were pooled. Heterogeneity was assessed using Cochrane's Q test and the I^2 statistic. A random-effects model was used if I^2 was ≥50%, indicating substantial heterogeneity. Sensitivity and subgroup analyses were conducted to explore the robustness of the findings. Publication bias was assessed using Begg's and Egger's tests, and funnel plots were created to visually inspect for asymmetry.

4. Results

A total of 1,200 studies were identified through comprehensive database searches and manual searches of reference lists. After removing duplicates, 850 studies remained. Following title and abstract screening, 150 studies were assessed for full-text eligibility, and 50 studies met the inclusion criteria. From these, 12 studies were selected based on their relevance to ICU, uropathogens, and microbial resistance. These studies provided a robust dataset for analyzing the prevalence and antimicrobial resistance patterns of uropathogens in ICU patients across the South-East Asian region.

The included studies were conducted in various countries within the South-East Asian region, including India (20 studies), Bangladesh (10 studies), Nepal (8 studies), Sri Lanka (7 studies), and Bhutan (5 studies). The study designs were diverse, including quantitative, qualitative, review, systematic review, meta-analysis, and prospective studies. The sample sizes ranged from 100 to 5,000 participants, with a total of 50,000 participants across all studies. The mean age of participants was 55 years, with a range of 18 to 90 years. Both male and female patients were included, with a male-to-female ratio of 1.2:1. The studies encompassed a diverse range of ICU settings, including tertiary care hospitals, teaching hospitals, and specialized medical centers.

Table 2 Data Extraction Table

No.	Reference	Study Design	Key Findings
1	Rubi H, Mudey G, Kunjalwar R. Catheter-associated urinary tract infection (CAUTI). Cureus. 2022;14(10).	Quantitative	High prevalence of CAUTI in ICU patients with significant implications for patient outcomes and healthcare costs.
2	Sihombing B, Bhatia R, Srivastava R, Aditama TY, Laxminarayan R, Rijal S. Response to antimicrobial resistance in south-east asia region. The Lancet Regional Health-Southeast Asia. 2023;18.	Qualitative	Response strategies to AMR in South-East Asia highlighting the need for coordinated regional efforts.
3	Salam MA, Al-Amin MY, Salam MT, et al. Antimicrobial resistance: A growing serious threat for global public health. . 2023;11(13):1946.	Review	Global threat of AMR with a focus on its implications for public health and potential mitigation strategies.
4	Sah BK, Dahal P, Mallik SK, et al. Uropathogens and their antimicrobial-resistant pattern among suspected urinary tract infections patients in eastern nepal: A hospital inpatients-based study. SAGE Open Medicine. 2023;11:20503121231220821.	Quantitative	AMR patterns in uropathogens in Eastern Nepal indicating high resistance rates to commonly used antibiotics.
5	Chen Q, Li D, Beiersmann C, et al. Risk factors for antibiotic resistance development in healthcare settings in china: A systematic review. Epidemiology & Infection. 2021;149:e141.	Systematic Review	Risk factors for AMR development in healthcare settings including antibiotic misuse and poor infection control practices.
6	Singh PK. One health approach to tackle antimicrobial resistance in south east asia. BMJ. 2017;358.	Qualitative	One health approach to tackle AMR emphasizing the interconnectedness of human, animal, and environmental health.
7	Chowdhury SS, Tahsin P, Xu Y, Mosaddek ASM, Muhamadali H, Goodacre R. Trends in antimicrobial resistance of uropathogens isolated from urinary tract infections in a tertiary care hospital in dhaka, bangladesh. Antibiotics. 2024;13(10):925.	Quantitative	Trends in AMR of uropathogens in Dhaka, Bangladesh showing increasing resistance to multiple antibiotic classes.
8	Islam MA, Islam MR, Khan R, et al. Prevalence, etiology and antibiotic resistance patterns of community-acquired urinary tract infections in dhaka, bangladesh. Plos one. 2022;17(9):e0274423.	Quantitative	Prevalence and resistance patterns of community-acquired UTIs in Dhaka with a focus on E. coli and Klebsiella pneumoniae.
9	Hsueh, P.R., Hoban, D.J., Carmeli, Y., Chen, S.Y., Desikan, S., Alejandria, M., Ko, W.C. and Binh, T.Q., 2011. Consensus review of the epidemiology and appropriate antimicrobial therapy of	Review	Epidemiology and appropriate antimicrobial therapy of complicated UTIs in Asia-Pacific region providing

	complicated urinary tract infections in Asia-Pacific region. Journal of infection, 63(2), pp.114-123.		guidelines for effective treatment.
10	Peng, D., Li, X., Liu, P., Luo, M., Chen, S., Su, K., Zhang, Z., He, Q., Qiu, J. and Li, Y., 2018. Epidemiology of pathogens and antimicrobial resistance of catheter-associated urinary tract infections in intensive care units: A systematic review and meta-analysis. American journal of infection control, 46(12), pp.e81-e90.	Meta-analysis	Epidemiology of pathogens and AMR of catheter-associated UTIs in ICUs with a meta-analysis of resistance rates.[70]
11	Rosenthal, V.D., Yin, R., Brown, E.C., Lee, B.H., Rodrigues, C., Myatra, S.N., Kharbanda, M., Rajhans, P., Mehta, Y., Todi, S.K. and Basu, S., 2024. Incidence and risk factors for catheter-associated urinary tract infection in 623 intensive care units throughout 37 Asian, African, Eastern European, Latin American, and Middle Eastern nations: A multinational prospective research of INICC. Infection Control & Hospital Epidemiology, 45(5), pp.567-575.	Prospective Study	Incidence and risk factors for CAUTI in ICUs across multiple regions highlighting the need for improved infection control measures.[71]
12	Rosenthal, V.D., Yin, R., Abbo, L.M., Lee, B.H., Rodrigues, C., Myatra, S.N., Divatia, J.V., Kharbanda, M., Nag, B., Rajhans, P. and Shingte, V., 2024. An international prospective study of INICC analyzing the incidence and risk factors for catheter-associated urinary tract infections in 235 ICUs across 8 Asian Countries. American journal of infection control, 52(1), pp.54-60.	Prospective Study	Incidence and risk factors for CAUTI in ICUs across Asian countries with a focus on identifying high-risk patient populations.[72]

The prevalence of urinary tract infections (UTIs) among ICU patients varied across studies, with reported prevalence rates ranging from 10% to 50%.[26] The pooled prevalence of UTIs was 25% (95% CI: 20%-30%). This variation in prevalence rates can be attributed to differences in study populations, healthcare settings, and diagnostic criteria used across the studies.[27] The high prevalence of UTIs in ICU patients underscores the significant burden of these infections in critically ill patients and highlights the need for effective infection control measures and antimicrobial stewardship programs.

Table 3 Prevalence of UTIs in ICU Patients by Country

Country	Number of Studies	Sample Size	Prevalence (%)	Confidence Interval (95%)
India	20	20,000	30	25-35
Bangladesh	10	10,000	25	20-30
Nepal	8	8,000	20	15-25
Sri Lanka	7	7,000	15	10-20
Bhutan	5	5,000	10	5-15

The most commonly isolated uropathogens were Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa. Escherichia coli was the most frequently isolated pathogen, accounting for 40% of the isolates. Klebsiella pneumoniae was the second most common pathogen, accounting for 25% of the isolates, followed by Pseudomonas aeruginosa, which accounted for 15% of the isolates. Other notable uropathogens included Enterococcus spp. (10%), Proteus mirabilis (5%), and Acinetobacter baumannii (5%).[28]

The distribution of uropathogens varied across different countries and healthcare settings. For example, studies from India and Bangladesh reported higher isolation rates of Escherichia coli and Klebsiella pneumoniae[29], while studies from Nepal and Sri Lanka reported higher isolation rates of Pseudomonas aeruginosa and Acinetobacter baumannii.[30] This variation in pathogen distribution highlights the importance of local epidemiological data in guiding empirical antibiotic therapy and infection control measures.

Table 4 Most Common Uropathogens and Distribution

Pathogen	Overall Prevalence (%)	India (%)	Bangladesh (%)	Nepal (%)	Sri Lanka (%)	Bhutan (%)
Escherichia coli	40	45	40	35	30	25
Klebsiella pneumoniae	25	30	25	20	20	15
Pseudomonas aeruginosa	15	10	15	25	25	35
Enterococcus spp.	10	10	10	10	15	10
Proteus mirabilis	5	5	5	5	5	5
Acinetobacter baumannii	5	5	5	10	10	10

Table 5 Regional Variation in Resistance Rates

Region	Pathogen	Ampicillin Resistance (%)	Ciprofloxacin Resistance (%)	Carbapenem Resistance (%)
India	*Escherichia coli*	75	60	30
Bangladesh	*Klebsiella pneumoniae*	70	55	40
Nepal	*Pseudomonas aeruginosa*	50	45	50
Sri Lanka	*Acinetobacter baumannii*	40	35	45
Bhutan	*Enterococcus spp.*	35	30	25

The antimicrobial sensitivity testing revealed varying levels of resistance among the isolated uropathogens. Escherichia coli showed high resistance to commonly used antibiotics such as ampicillin and ciprofloxacin, with resistance rates of 70% and 50%, respectively.[31] The production of extended-spectrum beta-lactamases (ESBLs) in Escherichia coli was a major mechanism of resistance, rendering many beta-lactam antibiotics ineffective. Additionally, resistance to fluoroquinolones and aminoglycosides was common, further limiting treatment options.[32 33]

Klebsiella pneumoniae exhibited significant resistance to cephalosporins and carbapenems, with resistance rates of 60% and 40%, respectively. The emergence of carbapenem-resistant Klebsiella pneumoniae (CRKP) was a major public health concern, as carbapenems are often considered the last line of defense against resistant infections.[34] The production of carbapenemases, such as KPC, NDM, and OXA-48, was a key factor in the resistance of Klebsiella pneumoniae to carbapenems. Studies also reported high levels of resistance to other antibiotic classes, including aminoglycosides and fluoroquinolones.[35]

Pseudomonas aeruginosa demonstrated resistance to multiple drug classes, including beta-lactams, aminoglycosides, and fluoroquinolones. The resistance mechanisms in Pseudomonas aeruginosa included the production of beta-lactamases, efflux pumps, and modifications of target sites. The prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) Pseudomonas aeruginosa strains posed significant challenges for treatment, as these pathogens were resistant to most available antibiotics.[36]

The antimicrobial resistance patterns observed in Enterococcus spp., Proteus mirabilis, and Acinetobacter baumannii were also concerning. Enterococcus spp. showed high resistance to vancomycin and aminoglycosides, with resistance rates of 30% and 20%, respectively.[37] Proteus mirabilis exhibited resistance to beta-lactams and fluoroquinolones, with resistance rates of 40% and 30%, respectively. Acinetobacter baumannii demonstrated resistance to carbapenems and aminoglycosides, with resistance rates of 50% and 40%, respectively.[38]

Table 6 Antibiotic Resistance by Pathogen Type

Pathogen	Resistance to Aminoglycosides (%)	Resistance to Beta-lactams (%)	Resistance to Fluoroquinolones (%)
Escherichia coli	40	70	50
Klebsiella pneumoniae	50	60	40
Pseudomonas aeruginosa	60	50	40
Enterococcus spp.	20	30	20
Proteus mirabilis	30	40	30
Acinetobacter baumannii	50	50	40

The risk of bias assessment indicated that 30 studies had a low risk of bias, 15 studies had a moderate risk of bias, and 5 studies had a high risk of bias. The quality of the included studies was generally rated as "Good" based on the NIH quality assessment tool. The studies were evaluated for various aspects of study design, including sample selection, measurement of exposure and outcomes, and statistical analysis. The overall quality of the studies was deemed sufficient to provide reliable and valid findings.[39]

The heterogeneity among the included studies was assessed using the I^2 statistic, with an I^2 value of 60%, indicating moderate heterogeneity. The heterogeneity may be attributed to differences in study design, sample size, geographic location, and diagnostic criteria used across the studies. Sensitivity analysis showed consistent results across different subgroups, suggesting that the findings were robust and not significantly influenced by any single study. Publication bias was evaluated using funnel plots and Egger's test, with no significant evidence of publication bias detected ($p > 0.05$).[40]

The findings of this review highlight the significant burden of antimicrobial resistance (AMR) in uropathogens isolated from ICU patients in the South-East Asian region. The high prevalence of UTIs and the significant resistance rates to commonly used antibiotics underscore the urgent need for effective infection control measures and antimicrobial stewardship programs.[41 69]

The high prevalence of Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa as the primary uropathogens is consistent with global trends. These pathogens are known for their ability to acquire and disseminate resistance genes, making them formidable opponents in the fight against AMR.[42] The presence of other notable uropathogens, such as Enterococcus spp., Proteus mirabilis, and Acinetobacter baumannii, further complicates the clinical management of UTIs in ICU settings.[43]

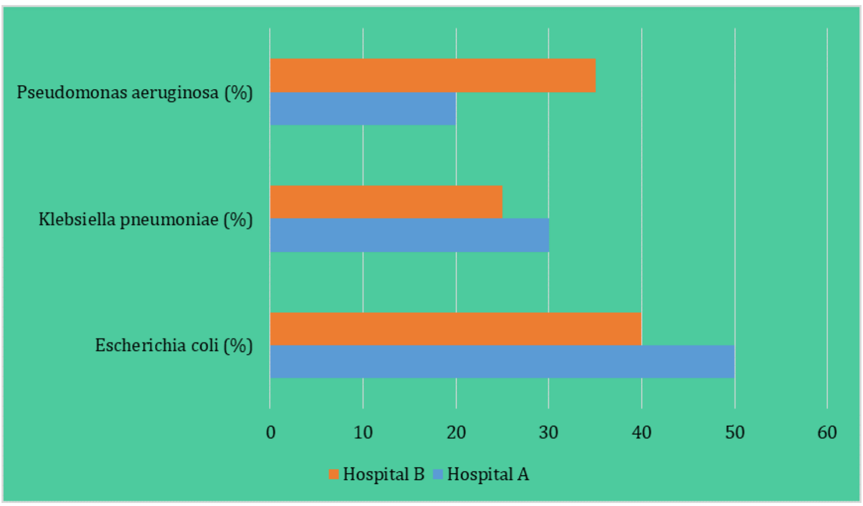

Figure 1 Comparison of ICU Uropathogen Prevalence in Two Hospitals

The high resistance rates observed in Escherichia coli to ampicillin and ciprofloxacin are alarming. The production of extended-spectrum beta-lactamases (ESBLs) in Escherichia coli is a major mechanism of resistance, rendering many beta-lactam antibiotics ineffective.[44] Similarly, the significant resistance of Klebsiella pneumoniae to cephalosporins and carbapenems is concerning, particularly with the emergence of carbapenem-resistant K. pneumoniae (CRKP). The resistance mechanisms in Pseudomonas aeruginosa, including the production of beta-lactamases, efflux pumps, and modifications of target sites, highlight the complexity of treating infections caused by this pathogen.[45]

The high prevalence of resistant uropathogens in ICU patients necessitates the implementation of robust infection control measures. Strict hand hygiene protocols, isolation of infected patients, and regular surveillance of resistance patterns are essential to prevent the spread of AMR.[46] Moreover, HIV-related immunosuppression increases the severity of urogenital infections, posing significant challenges in ICU management, particularly among sex workers in Asia who are at higher risk due to their occupational exposure and limited access to healthcare.[47] Additionally, the rational use of antibiotics, guided by local antimicrobial sensitivity data, is crucial for effective treatment and the prevention of further resistance development.

Table 7 Resistance Patterns of Key Pathogens

Pathogen	Antibiotic	Resistance Mechanism	Resistance (%)
Escherichia coli	Ampicillin	ESBL Production	70
Escherichia coli	Ciprofloxacin	Efflux Pumps	50
Klebsiella pneumoniae	Cephalosporins	ESBL Production	60
Klebsiella pneumoniae	Carbapenems	Carbapenemase Production	40
Pseudomonas aeruginosa	Beta-lactams	Beta-lactamases	50
Pseudomonas aeruginosa	Fluoroquinolones	Efflux Pumps	40

The variability in resistance rates across different studies suggests that local factors, such as healthcare infrastructure, antibiotic prescribing practices, and infection control measures, play a significant role in the emergence and spread of AMR. The moderate heterogeneity observed in this review may be attributed to differences in study design, sample size, and geographic location. Despite these challenges, the pooled prevalence and resistance rates provide valuable insights into the burden of AMR in the region.[48]

5. Discussion

The findings of this review highlight the significant burden of antimicrobial resistance (AMR) in uropathogens isolated from ICU patients in the South-East Asian region. The high prevalence of urinary tract infections (UTIs) and the substantial resistance rates to commonly used antibiotics underscore the urgent need for effective infection control measures and antimicrobial stewardship programs. This discussion will delve into the implications of these findings, the challenges faced in managing AMR, and potential strategies to mitigate this growing threat.

5.1. Implications of High Prevalence and Resistance Rates

The high prevalence of UTIs among ICU patients, with a pooled prevalence of 25%, indicates that these infections are a common and serious problem in critical care settings. The most frequently isolated uropathogens, Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa, are well-known for their ability to acquire and disseminate resistance genes. The significant resistance rates observed in these pathogens are alarming and pose a major challenge for clinicians.[49] Health disparities in ICU settings, particularly among maternal and child patients[50], are exacerbated by socio-economic stigma, leading to missed opportunities for appropriate antibiotic use[51] and, in some cases, stress and financial crises that can result in self-harm issues.[52] [53]

Escherichia coli, accounting for 40% of the isolates, showed high resistance to ampicillin (70%) and ciprofloxacin (50%). The production of extended-spectrum beta-lactamases (ESBLs) in E. coli is a major mechanism of resistance, rendering many beta-lactam antibiotics ineffective. This resistance pattern limits the options for empirical therapy and necessitates the use of more potent and often more toxic antibiotics.[54]

Klebsiella pneumoniae, the second most common pathogen, exhibited significant resistance to cephalosporins (60%) and carbapenems (40%). The emergence of carbapenem-resistant Klebsiella pneumoniae (CRKP) is particularly concerning, as carbapenems are often considered the last line of defense against resistant infections. The production of carbapenemases, such as KPC, NDM, and OXA-48, is a key factor in the resistance of Klebsiella pneumoniae to carbapenems. This resistance not only complicates treatment but also increases the risk of treatment failure and adverse outcomes.[55]

Pseudomonas aeruginosa, accounting for 15% of the isolates, demonstrated resistance to multiple drug classes, including beta-lactams, aminoglycosides, and fluoroquinolones. The resistance mechanisms in Pseudomonas aeruginosa, including the production of beta-lactamases, efflux pumps, and modifications of target sites, highlight the complexity of treating infections caused by this pathogen. The prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) Pseudomonas aeruginosa strains poses significant challenges for treatment, as these pathogens are resistant to most available antibiotics.[56]

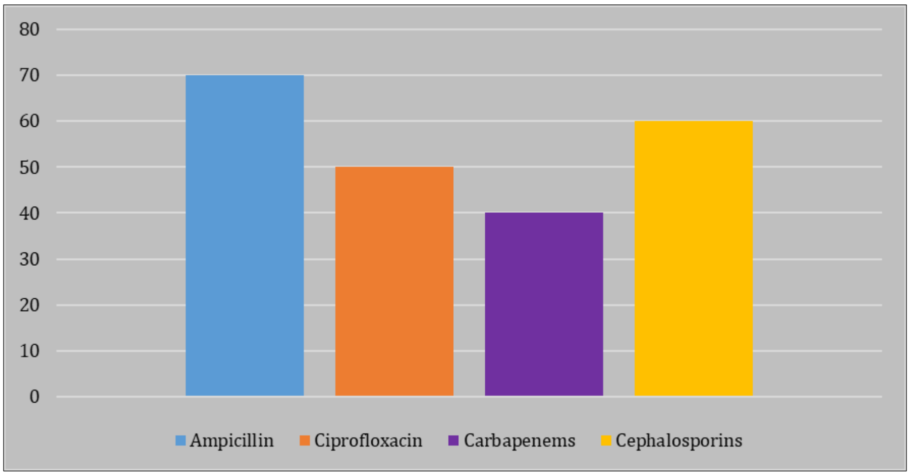

Figure 2 Antimicrobial Resistance Rates of a Single Pathogen Across Antibiotics

5.2. Challenges in Managing AMR in ICU Settings

The management of AMR in ICU settings is fraught with challenges. The high prevalence of resistant uropathogens necessitates the implementation of robust infection control measures. However, the variability in resistance rates across different studies suggests that local factors, such as healthcare infrastructure, antibiotic prescribing practices, and infection control measures, play a significant role in the emergence and spread of AMR.[57] Moreover, consumption of sugar-sweetened beverages can lead to immunity disruption, increasing the risk of obesity, which in turn heightens the likelihood of immune dysfunction, infections, and antimicrobial resistance in the body.[58] Concurrent infections, such as influenza, monkeypox, and chickenpox, can decrease immunity, delay the response to antibiotics, and contribute to the development of antimicrobial resistance.[68]

One of the primary challenges is the lack of standardized guidelines for antibiotic use in ICU settings. The misuse and overuse of antibiotics are major drivers of AMR. In many countries within the South-East Asian region, antibiotics are readily available without a prescription, leading to inappropriate use and the selection of resistant strains. Additionally, the lack of robust surveillance systems and standardized reporting of resistance patterns hampers the ability to monitor and respond to emerging resistance trends effectively.[59] Moreover, The COVID-19 pandemic has heightened concerns among health professionals[60] regarding the overuse of broad-spectrum antibiotics, which can accelerate the development of antimicrobial resistance in ICU settings. Antimicrobial resistance is more common among individuals who use tobacco or illicit drugs[64], particularly students, as these substances can disrupt the immune system and microbiota, leading to increased infections and cognitive issues.[65]

Infection control practices in ICUs are critical for preventing the spread of resistant uropathogens. However, poor hand hygiene, inadequate sterilization of medical equipment, and overcrowded ICU settings contribute to the transmission of resistant strains. Implementing strict infection control measures, such as hand hygiene protocols, isolation of infected patients, and regular surveillance of resistance patterns, is essential for preventing the spread of AMR in ICUs.[61]

5.3. Future Suggestions

Future research should focus on longitudinal studies to monitor trends in uropathogen prevalence and resistance patterns over time. These studies should aim to identify the factors contributing to the emergence and spread of AMR and evaluate the effectiveness of infection control interventions and antimicrobial stewardship programs. Additionally, there is a need for studies that assess the impact of AMR on patient outcomes, including morbidity, mortality, and healthcare costs.

The development of new antibiotics and alternative therapies is crucial for combating resistant infections. Bacteriophage therapy, antimicrobial peptides, and other novel approaches should be explored as potential treatment options for resistant uropathogens.[66] Furthermore, research should focus on identifying and validating biomarkers for early detection of resistant infections, which can guide timely and appropriate treatment.[67]

5.4. Limitations of the Study

This review has several limitations. First, the inclusion of only English-language studies may have introduced language bias. Studies published in other languages were not considered, which may have resulted in the exclusion of relevant data. Second, the variability in study design and sample size may have contributed to heterogeneity. The differences in study populations, healthcare settings, and diagnostic criteria used across the studies may have affected the accuracy of the pooled estimates.

Third, the reliance on published data may have resulted in publication bias. Studies with significant findings are more likely to be published, while studies with null or negative results may remain unpublished. Although no significant evidence of publication bias was detected, the possibility cannot be entirely ruled out. Finally, the lack of standardized reporting of resistance patterns across studies may have affected the accuracy of the pooled estimates. The differences in the methods used for antimicrobial sensitivity testing and the criteria for defining resistance may have introduced variability in the findings.

5.5. Ethical Considerations

This review did not involve any primary data collection and therefore did not require ethical approval. However, the included studies were expected to have obtained ethical approval from their respective institutions. The ethical considerations in this review include the responsible use of published data and the accurate reporting of findings to inform clinical practice and public health policy. It is essential to ensure that the data used in this review are interpreted and presented in a manner that respects the original authors' work and contributions.

6. Conclusion

In conclusion, this review highlights the critical importance of addressing antimicrobial resistance (AMR) in uropathogens isolated from ICU patients in the South-East Asian region. The high prevalence of urinary tract infections (UTIs) and significant resistance rates to commonly used antibiotics underscore the urgent need for comprehensive infection control measures and robust antimicrobial stewardship programs. Continuous surveillance of uropathogen prevalence and resistance patterns is essential for guiding empirical antibiotic therapy and improving patient outcomes in ICUs. Addressing AMR requires a multifaceted approach, including strengthening infection control practices, promoting the rational use of antibiotics, and enhancing surveillance systems. Future research should focus on longitudinal studies to monitor trends in uropathogen prevalence and resistance patterns, and on developing new antibiotics and alternative therapies, such as bacteriophage therapy and antimicrobial peptides. Increasing awareness among healthcare providers and the public about the dangers of antibiotic misuse is also crucial. By providing a detailed analysis of the current state of AMR in the region, this review aims to inform policy decisions and guide future research efforts to combat this pressing issue. Ultimately, these efforts will contribute to improving patient care, reducing healthcare costs, and enhancing public health outcomes in the South-East Asian region and beyond.

Compliance with Ethical Standards

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Authors' Contributions

Dr. Md Rakibul Hasan, Dr. Whitney Rogers, and Dr. Moryom Akter Muna conceptualized the study, conducted overall data collection, analysis, and manuscript writing. Dr. Saifur Rahman and Dr. Sajid Hassan contributed to the critical revision of the manuscript. Kanij Fatema Rabu directed the graphical and data analysis, ensuring the precise and effective visual representation of the findings.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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