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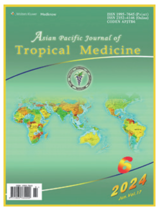

Review Article

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Beta-lactam antibiotic resistance among *Escherichia coli* isolates from patients with urinary tract infections in Vietnam: A systematic review and meta-analysis

Dat T Nguyen✉

Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada

ABSTRACT

Objective: To investigate the evolving patterns of antimicrobial resistance against beta-lactam antibiotics in *Escherichia coli* isolates from urinary tract infection patients in Vietnam, covering the period from 2005 to 2022.

Methods: 29 Descriptive studies published between 2010 and 2022 in English and Vietnamese were included in the analysis. Data on resistance rates to beta-lactam antibiotics, including cephalosporins and carbapenems, were extracted and analyzed. Weighted pooled resistance rates were calculated using random-effects models. Annual trends in resistance were assessed using linear regression analysis.

Results: Among the beta-lactam antibiotics studied, *Escherichia coli* exhibited varying levels of resistance, with cephalosporins showing higher resistance rates compared to carbapenems. Weighted pooled resistance rates were 66% for cefotaxime, 65% for ceftriaxone, 54% for ceftazidime, and 56% for cefepime. In contrast, carbapenems demonstrated lower resistance rates, with weighted pooled resistance rates ranging from 3% to 4% for meropenem, ertapenem, and imipenem. Resistance rates were also observed for amoxicillin/clavulanate (35%), ticarcillin/clavulanate (26%), and piperacillin/tazobactam (12%). Significant annual increases in resistance were noted for imipenem (0.56%, $P<0.001$).

Conclusions: This study highlights the critical issue of antimicrobial resistance in urinary tract infections in Vietnam and emphasizes the importance of prudent antibiotic use and the regular monitoring of resistance patterns. These insights are useful for guiding healthcare professionals in optimizing treatment strategies and for policymakers in formulating evidence-based clinical guidelines to combat antibiotic resistance effectively.

KEYWORDS: Antimicrobial resistance; Urinary tract infection; Vietnam

1. Introduction

Urinary tract infection (UTI) is a prevalent and burdensome communicable disease that would have affected at least 50% of all women before they turn 32 years old[1]. In the Southeast Asia region, the age-standardized incidence rate of UTI was estimated to be 2 494.5 cases per 100 000 in the year 2019[2]. However, little is known about the incidence, etiology, and the efficacy of treatment for UTI in Vietnam[3]. This gap in knowledge arises in part because UTI is typically not reported to public health agencies[4]. Additionally, self-medication is a common practice, because antibiotics can be purchased from pharmacies without prescription[5]. This over-

Significance

Our study had found that the weighted pooled resistance to 3rd and 4th generation cephalosporin exceeded 50%. While the resistance rate to carbapenem was the lowest at around 4%. The resistance to other combinations of beta-lactam antibiotics and beta-lactamase inhibitors ranged between 10% and 40%. These insights are useful for guiding healthcare professionals in optimizing treatment strategies and for policymakers in formulating evidence-based clinical guidelines to combat antibiotic resistance effectively.

✉To whom correspondence may be addressed. E-mail: Datng1997@berkeley.edu

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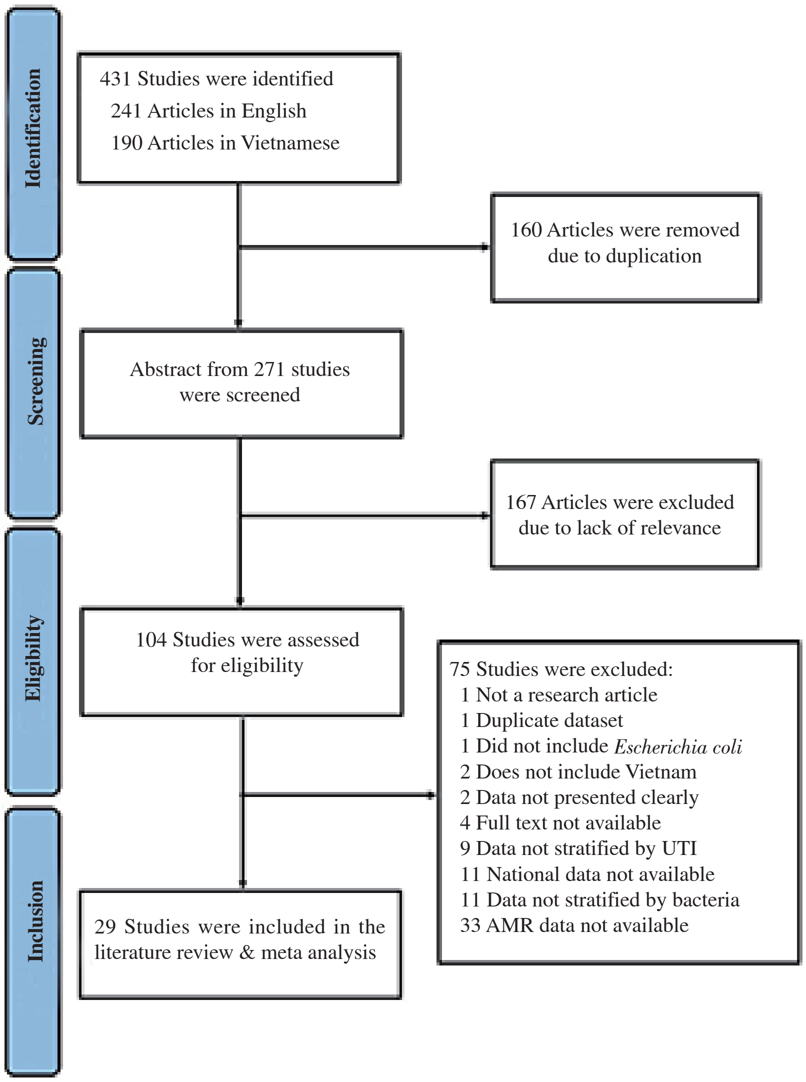

Figure 1. Flow diagram shows the study selection process.

consumption contributes to the development of antimicrobial resistance (AMR), and can partially explain why Vietnam has one of the highest AMR rates in Asia[6]. This increase in resistance rate gradually renders the current treatments for UTI useless. There have been attempts, published both in Vietnamese and English, to survey the susceptibility profile of uropathogens to different antibiotics. However, to the best of our knowledge, there has not been any review conducted to analyze the literature published in Vietnamese scientific journals and aggregate the resistance rate across different studies. The aim of this study is to close the aforementioned knowledge gap by reviewing the current literature and characterize the resistance profile of the most prevalent bacterial etiology of UTI, uropathogenic *Escherichia* (*E.*) *coli*[7], to antibiotics in the beta-lactam class.

2. Materials and methods

Our literature review and meta-analysis was registered with the PROSPERO International Prospective Registers of Systematic Reviews under the ID: CRD42022371917. Our result was reported following the guideline issued by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), specifically the PRISMA 2020 checklist.

2.1. Data sources & search strategy

To find relevant studies, the search was conducted between November and December of 2022 using databases such as EMBASE, PubMed, EBSCO, CitationGate, and the Vietnamese Interlibrary Medical Database. Due to the limited scope of the Vietnamese databases, the search was also conducted on databases of individual

Table 1. Characteristics of studies included in the meta-analysis.

Study	Publication language	Start year	End year	No. of samples	Test method	Standard used	Number of isolates (*n*=5261)	Ref.
Nguyen *et al*. 2022	English	2011	2013	57	VITEK	CLSI	57	[10]
		2018	2022	71			71	
Hoang *et al*. 2017	English	2013	2013	51	Disc diffusion	CLSI	23	[11]
Duong *et al*. 2015	English	2010	2012	143	Disc diffusion	CLSI	115	[12]
Lob *et al*. 2015	English	2011	2013	427	Unclear	CLSI	427	[13]
Tran *et al*. 2014	English	2010	2011	341	Unclear	CLSI	225	[14]
Ramos *et al*. 2012	English	2009	2012	42	VITEK	Unclear	42	[15]
Ramos *et al*. 2011	English	Unclear	Unclear	38	VITEK	Unclear	38	[16]
Cao *et al*. 2012	Vietnamese	2005	2007	2598	Disc diffusion	CLSI	327	[17]
Tran, 2012	Vietnamese	2008	2010	144	Unclear	Unclear	118	[18]
Tran, 2014	Vietnamese	2013	2013	708	Unclear	Unclear	375	[19]
Tran, 2013	Vietnamese	2010	2011	1537	Disc diffusion	CLSI	762	[20]
Tran *et al*. 2013	Vietnamese	2007	2007	457	Unclear	Unclear	212	[21]
		2008	2008	633	Unclear	Unclear	233	
		2009	2009	602	Unclear	Unclear	265	
		2010	2010	732	Unclear	Unclear	363	
		2011	2011	805	Unclear	Unclear	359	
Huynh *et al*. 2014	Vietnamese	2008	2013	58	Unclear	Unclear	43	[22]
Huynh *et al*. 2015	Vietnamese	2013	2013	242	Disc diffusion	CLSI	117	[23]
Nguyen *et al*. 2015	Vietnamese	2012	2013	128	Unclear	Unclear	72	[24]
Tran *et al*. 2019	Vietnamese	2017	2018	91	Unclear	Unclear	57	[25]
Nguyen *et al*. 2021	Vietnamese	2020	2021	100	Unclear	Unclear	61	[26]
Que *et al*. 2021	Vietnamese	2021	2021	473	Disc diffusion	CLSI	182	[27]
Nguyen *et al*. 2018	Vietnamese	2017	2017	183	VITEK	Unclear	76	[28]
Pham *et al*. 2022	Vietnamese	2018	2019	190	Disc diffusion	Unclear	79	[29]
Le *et al*. 2018	Vietnamese	2017	2018	85	Unclear	Unclear	39	[30]
Tran *et al*. 2022	Vietnamese	2020	2022	155	Unclear	Unclear	82	[31]
Nguyen *et al*. 2010	English	2007	2007	128	Disc diffusion	Unclear	59	[32]
Kieu *et al*. 2017	Vietnamese	2014	2016	261	Disc diffusion	Unclear	64	[33]
Tran *et al*. 2016	Vietnamese	2015	2015	319	Unclear	Unclear	136	[34]
Tra *et al*. 2014	Vietnamese	2009	2013	207	Unclear	Unclear	36	[35]
Nguyen *et al*. 2022	Vietnamese	2020	2021	183	VITEK	Unclear	76	[36]
Pham *et al*. 2017	Vietnamese	2017	2017	22	Unclear	Unclear	13	[37]
Cao *et al*. 2018	Vietnamese	2015	2017	98	Unclear	Unclear	57	[38]

CLSI: Clinical and Laboratory Standards Institute.

relevant medical and public health journals. In databases/journals published in English, search was conducted using a combination of 3 keywords: 1) 'Urinary tract infection', or 'cystitis', 'urethritis', 'pyelonephritis'; 2) 'antibiotic resistance' or 'antimicrobial resistance'; 3) 'Vietnam' or 'Viet Nam'. For search conducted in Vietnamese journals and databases, the 3 keywords were localized to become appropriate with local language and medical terminology: 1) 'Nhiễm trùng đường tiểu'; ''Nhiễm trùng đường tiết niệu'; 'Nhiễm khuẩn đường tiểu'; 'Nhiễm khuẩn đường tiết niệu'; 'Nhiễm trùng tiết niệu'; 'Nhiễm khuẩn tiết niệu'; 'Viêm đường tiểu'; or 'Viêm đường tiết niệu'; 2) Đề kháng kháng sinh; 3) Việt Nam.

2.2. Inclusion & exclusion criteria

Our meta-analysis included studies, published between 2000 and 2022, that surveyed the antimicrobial susceptibility profile of *E. coli* isolated from the urine of patients that had been diagnosed with urinary tract infections in Vietnam. Specifically, we focused on studies that assessed the resistance rate to beta-lactam antibiotics such as cephalosporins, carbapenems, and combinations of penicillin plus beta-lactamase inhibitors. Only studies that offered data collected from Vietnam on a national level are included in the studies. Any study that did not offer antimicrobial resistance data, or displayed AMR information in an unclear manner, was excluded. Also, we excluded studies that did not explicitly present the susceptibility profile of *E. coli* or combine the resistance rate of urinary tract infection with other infections.

2.3. Data abstraction & quality assessment

Full text was obtained from the studies, and the following data were retrieved: year of publication, year when data collection was started, year when data collection was ended, which method was used to test resistance, which standard was used as reference, number of *E. coli* isolates assessed in the analysis, and the number of resistant isolates to each type of antibiotics. The quality of the studies was assessed using the checklist for analytical cross-sectional studies published by the Joanna Briggs Institute[8]. The checklist included 8 questions: 1)

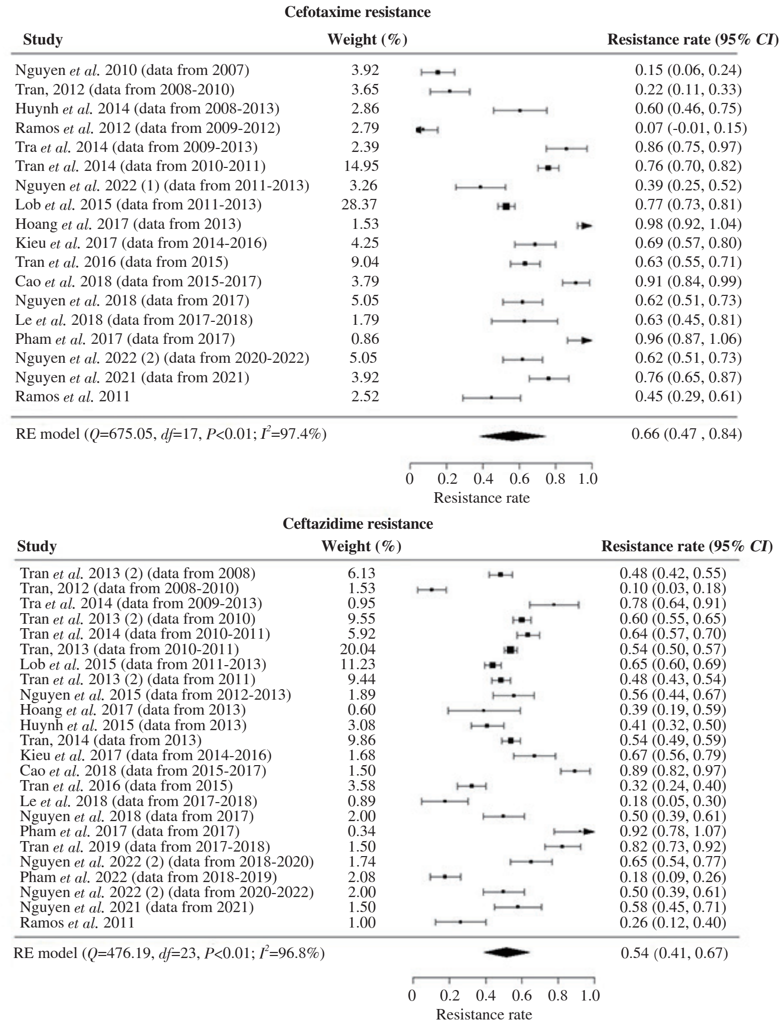

Figure 2. Forest plot displaying the weighted pooled resistance rate of *Escherichia coli* to 3rd generation cephalosporins cefotaxime and ceftazidime.

Were the criteria for inclusion in the sample clearly defined? 2) Were the study subjects and the setting described in detail? 3) Was the exposure measured in a valid and reliable way? 4) Were objective, standard criteria used for measurement of the condition? 5) Were confounding factors identified? 6) Were strategies to deal with confounding factors stated? 7) Were the outcomes measured in a valid and reliable way? 8) Was appropriate statistical analysis used?. Besides the binary options of "Yes" and "No", the questions can also be answered with "Unsure" or "Not Applicable".

2.4. Statistical analyses

In our meta-analysis, we applied the inverse variance heterogeneity model under the assumption of random effects, a more suitable choice than fixed-effect given the significant heterogeneity within our dataset. To gauge the degree of variability within these datasets, we utilized Cochran's Q and I^2 statistics. Our analysis involved the computation of the weighted pooled resistance rate, calculated from the point resistance prevalence reported across multiple studies, and we presented these results using forest plots. Beyond our examination of the weighted pooled resistance rate, our study also aimed to investigate shifts in resistance patterns over time. To accomplish this, we conducted a comprehensive meta-regression analysis, enabling us to explore the development of AMR. The findings of this analysis were visually depicted using bubble plots. To examine the publication bias for the resistance rate against each type of antibiotics, funnel plots were graphed and examined visually. Analysis and visualization was performed using the "metafor"-version 4.2.0-package[9].

3. Results

3.1. Search results

431 Studies were identified from the extracted data; 241 of which were published in English, and 190 articles were written in

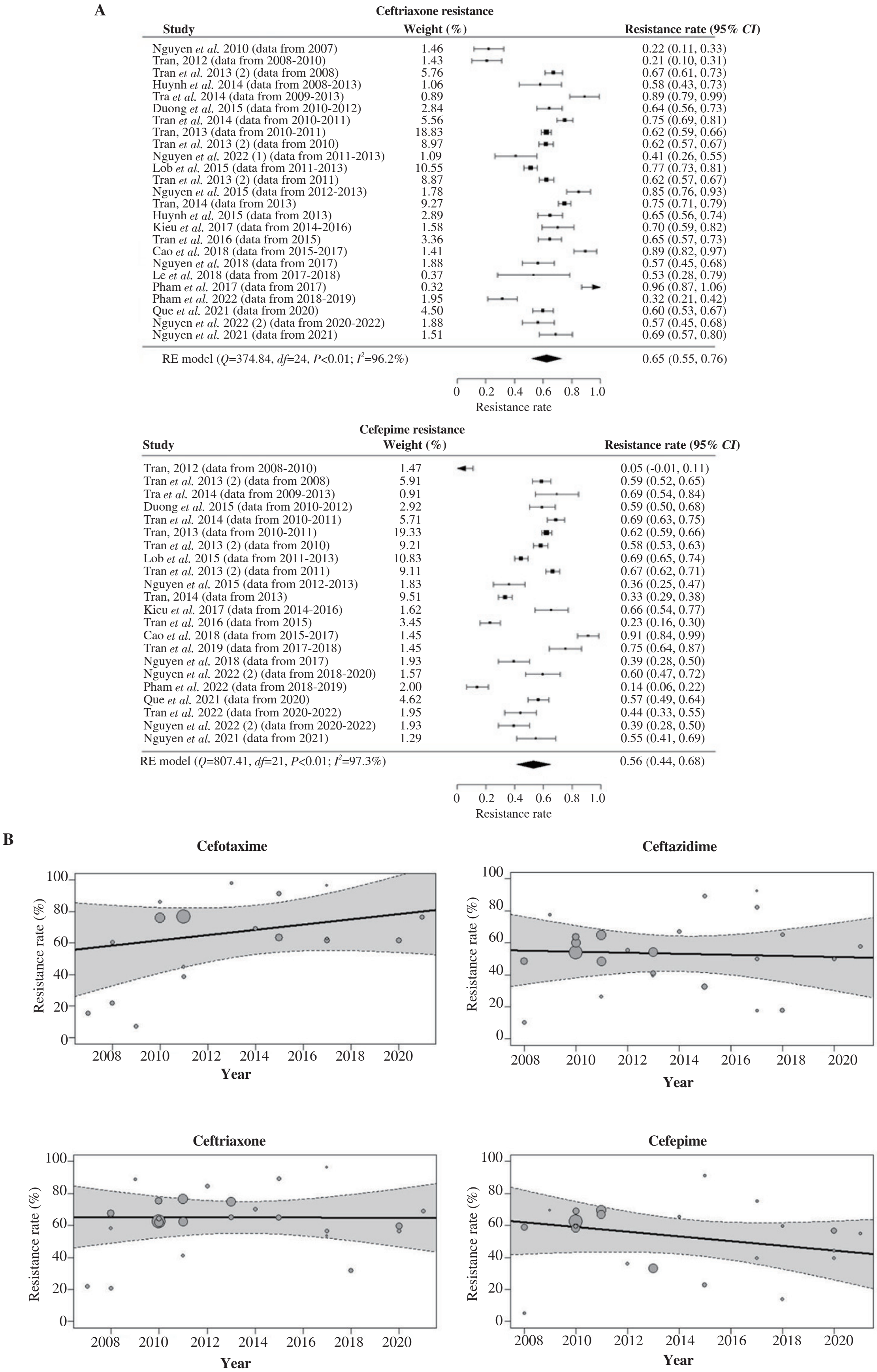

Figure 3. (A) Forest plots displaying the weighted pooled resistance tare uropathogenic *Escherichia coli* to ceftriaxone (3rd generation cephalosporin) & cefepime (4th generation cephalosporin). (B) Meta-regression showing variation in the resistance rate of *Escherichia coli* to cefotaxime, ceftazidime, ceftriaxone, and cefepime between 2005 and 2022.

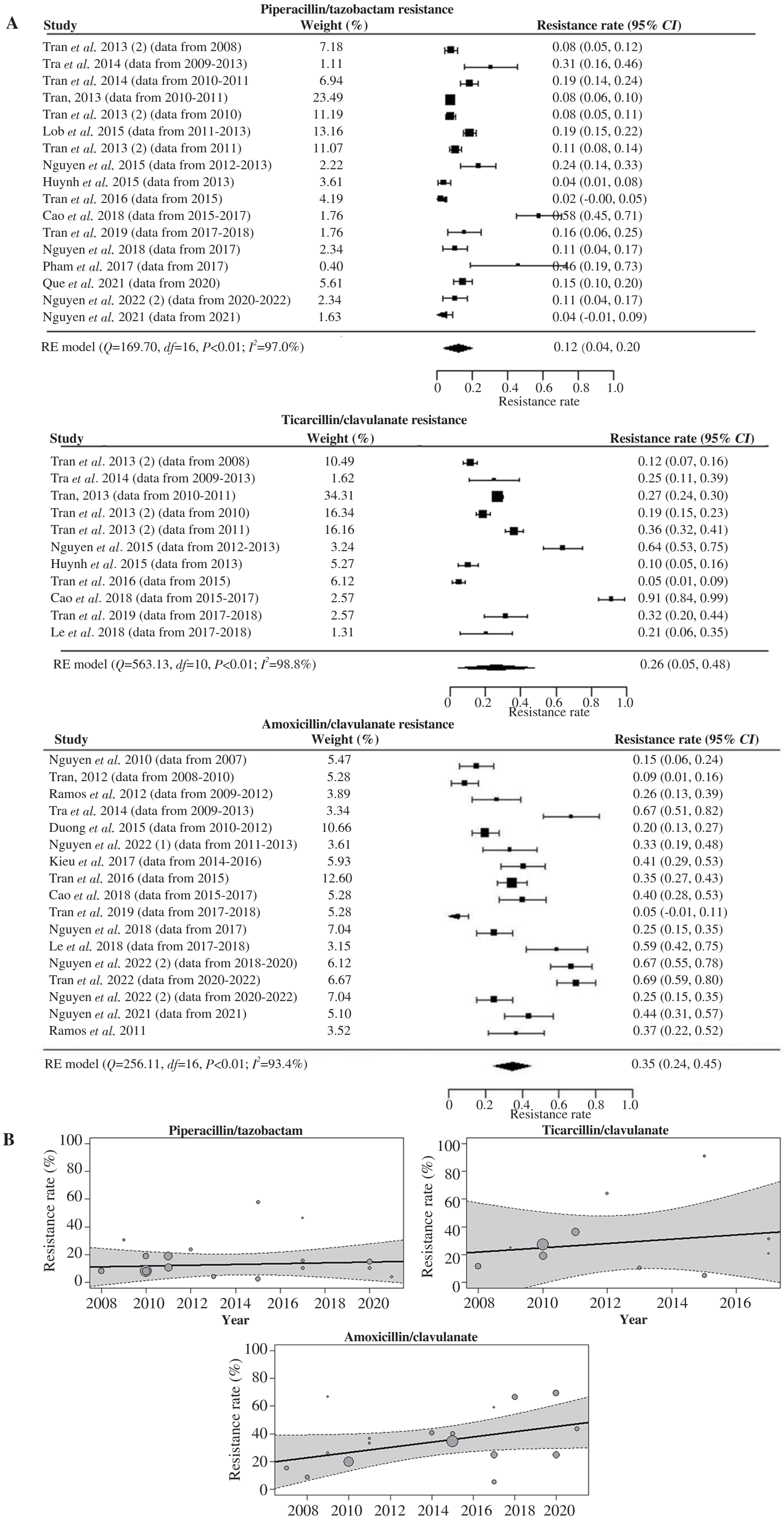

Figure 4. (A) Forest plots displaying the weighted pooled resistance rate of *Escherichia coli* to piperacillin/tazobactam, ticarcillin/clavulanate, and amoxicillin/clavulanate. (B) Meta-regression showing variation in the resistance rate of *Escherichia coli* to piperacillin/tazobactam, ticarcillin/clavulanate, and amoxicillin/clavulanate between 2005 and 2022.

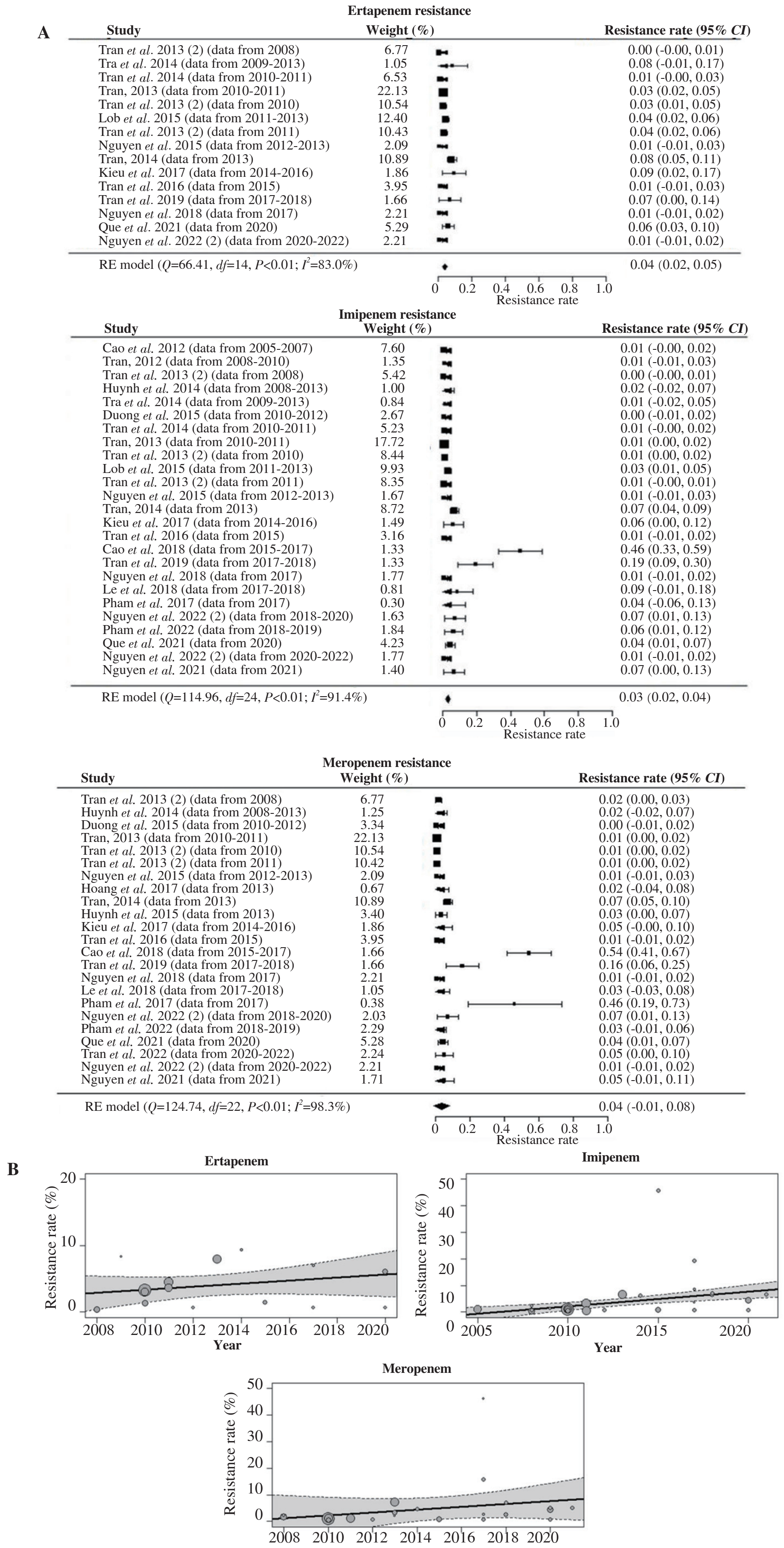

Figure 5. (A) Forest plots displaying the weighted pooled resistance rate of *Escherichia coli* to ertapenem, imipenem and meropenem. (B) Meta-regression showing variation in the resistance rate of *Escherichia coli* to ertapenem, imipenem, and meropenem between 2005 and 2022.

Vietnamese. After duplicates were removed, the title and abstract of 271 studies were screened for relevance. 167 Studies were excluded because neither their title nor abstract indicated that the studies were relevant to our research objective. Full text was obtained from 104 studies to assess for inclusion eligibility. Finally, 29 of them were chosen to be included in the analysis; the reasons behind the exclusion of the 75 eligible studies were stated in Figure 1.

3.2. Characteristics of studies

Our literature review included 29 studies, and their characteristics were summarized in Table 1. These articles were published between 2010 and 2022. 22 Of the 29 studies were published in Vietnamese, and the remaining was written in English. 2 Out of the 29 included studies contained antibiotic resistance data collected from more than 1 time frame; these different sampling periods were treated as individual datasets in our meta-analysis (total datasets: 34). In terms of antibiograms, 14 studies described the method they used. Disc diffusion was utilized in 9 studies, and 5 studies used the VITEK system to characterize antimicrobial resistance. 9 Out of the 29 studies reported the standard they have used to determine susceptibility status; all of them used the standard issued by the Clinical and Laboratory Standards Institute. Cumulatively, the susceptibility profile of 5 261 different isolates of *E. coli* were tested. Quality of these studies were assessed, and the results can be found in Supplementary Table 1.

3.3. Resistance to beta-lactam antibiotics

In our meta-analysis, we investigated the prevalence of antibiotic resistance of *E. coli* to a range of cephalosporin antibiotics: Cefotaxime (3rd generation), ceftazidime (3rd generation), ceftriaxone (3rd generation), and cefepime (4th generation). Visual examination of the funnel plots for these antibiotics indicated the presence of publication bias (Supplementary Figure 1A). The resistance rates and associated statistics for each antibiotic are as follows: Cefotaxime exhibited a weighted pooled resistance (WPR) rate of 66% (95% *CI* 47%-84%) based on 18 datasets. Notably, there was significant heterogeneity among the included datasets (I^2=97.4%), suggesting substantial variation in resistance rates (Figure 2). Ceftazidime showed an overall resistance prevalence of 54% (95% *CI* 41%-67%) across 24 datasets, with a high degree of heterogeneity (I^2=96.8%) (Figure 2). In the case of ceftriaxone, a WPR rate of 65% (95% *CI* 55%-76%) was identified across 25 datasets, along with significant heterogeneity (I^2=96.2%) (Figure 3A). Finally, cefepime showed a WPR rate of 56% (95% *CI* 44%-68%) based on 22 datasets, with significant heterogeneity (I^2=97.3%) (Figure 3A). Meta-regression showed that there was no significant change in WPR of all 4 cephalosporin antibiotics (Figure 3B). These findings showed that the resistance rates were similar between the different cephalosporin antibiotics, with little difference between the generations of class.

Three combinations of beta-lactam antibiotics and beta-lactamase inhibitors were characterized by our analysis: amoxicillin/clavulanate, ticarcillin/clavulanate and piperacillin/tazobactam. Amongst these combinations, piperacillin/tazobactam exhibited the lowest resistance rate, with an overall rate of 12% (95% *CI* 4%-20%) across 17 datasets with significant heterogeneity (I^2=97.0%) (Figure 4A). Ticarcillin/clavulanate followed with a slightly higher resistance rate at 26% (95% *CI* 5%-48%) across 11 datasets, also with significant heterogeneity (I^2=98.8%) (Figure 4A). The combination of amoxicillin/clavulanate had a resistance rate of 35% (95% *CI* 24%-45%) across 17 datasets (I^2=93.4%) (Figure 4A). Our meta-regression analysis indicated a stable trend in antibiotic resistance for all three combinations, although there was a minor but statistically insignificant annual increase of 1.88% in the resistance rate specifically for amoxicillin/clavulanate (P=0.085) (Figure 4B). Inspection of the funnel plots showed publication bias for all three combinations (Supplementary Figure 1B).

Among the three carbapenem antibiotics our study investigated, 15 datasets (I^2=83%) reported the weighted pooled resistance rate to ertapenem was 4% (95% *CI* 2%-5%) (Figure 5A). Imipenem exhibited a similar low resistance rate of 3% (95% *CI* 2%-4%) across 25 datasets, with an I^2 of 91.4% (Figure 5A). Meropenem showed a higher WPR of 4% (95% *CI* 1%-8%) across 23 datasets, with notable heterogeneity (I^2=98.3%) (Figure 5A). Amongst these three carbapenem, only the resistance rate of imipenem had been significantly increased by an annual rate 0.56% (P<0.001) (Figure 5B). In addition, there was publication bias detected from the funnel plots (Supplementary Figure 1C).

4. Discussion

The results of our meta-analysis provide valuable insights into the prevalence and temporal trends of antibiotic resistance of uropathogenic *E. coli* to various beta-lactam antibiotics. These findings significantly enhance our comprehension of the dynamic landscape of antimicrobial resistance in urinary tract infections. Moreover, these insights can serve as a foundational basis for the refinement and development of more effective clinical guidelines, ensuring that healthcare practitioners can make informed decisions when treating patients with urinary tract infections.

In the most recent clinical guideline issued by the Vietnamese Ministry of Health in 2015, cefalexin was recommended as the preferred treatment for cystitis[39]. Other 2nd and 3rd generation cephalosporins, including cefuroxime, cefotaxime, ceftriaxone, and cefoperazone, were suggested for the management of pyelonephritis. Our literature review revealed a scarcity of studies specifically investigating the susceptibility profiles of *E. coli* to 1st and 2nd generation cephalosporins. In contrast, our analysis primarily found an abundant amount of investigation on 3rd and 4th generation cephalosporins, which displayed a pooled weighted resistance rate ranging from 52% to 62%. These rates are significantly higher than those reported in Iran[40], where resistance rates for ceftazidime, ceftriaxone, and cefotaxime were observed at 40%, 35%, and 42%, respectively. In comparison to other neighboring Southeast Asian countries, the resistance rate to cephalosporin was notably higher than the 14% average reported in Thailand[41] and the 30% average in the Philippines[42]. However, the weighted pooled resistance rates that our study obtained from the datasets were relatively similar to the resistance rates reported in China[43] and India[44], where the resistance rates of *E. coli* to ceftriaxone, ceftazidime, cefotaxime, and cefepime, ranging from 50% to 66%. This relatively higher resistance rate to cephalosporins could be attributed to their more extensive usage in clinical settings[45], underscoring the importance of prudent antibiotic use to mitigate the emergence of resistance.

Amoxicillin and clavulanic acid, as a combination therapy, are recommended as first-line treatment options for both cystitis and pyelonephritis[39]. Their favorable safety profile has qualified this medication combination for the management of various infections[46]. Our meta-analysis revealed a weighted pooled resistance rate of 35% against amoxicillin and clavulanate. Interestingly, this resistance rate aligns with that observed in *E. coli* isolates obtained from farm animals[47,48] and clinical isolates from patients with pneumonia[49]. It's noteworthy that amoxicillin and clavulanate can be administered orally and are available over-the-counter in Vietnamese pharmacies, which could potentially contribute to this resistance rate. In contrast, the lower resistance rates observed for ticarcillin/clavulanate and piperacillin/tazobactam may be attributed to their requirement for intravenous administration, limiting their use primarily to hospital settings[50,51]. The higher susceptibility rate to piperacillin/tazobactam is particularly promising, as other studies have reported clinical cure and microbiological eradication rates exceeding 95%[52,53]. These findings suggest that these two antibiotics can effectively be used as treatment in the hospital setting.

Antibiotics belonging to the carbapenem class have not been endorsed by the Vietnamese Ministry of Health in their most recent clinical guidelines[39]. Our meta-analysis indicates that *E. coli* was susceptible to these antibiotics, since their weighted pooled resistance rate was very low—between 3% and 4%. Importantly, carbapenems are exclusively administered intravenously or intramuscularly[54–56], making them a valuable option for treating complicated urinary tract infections in a hospital setting, a recommendation supported by other literature reviews[57,58]. However, as observed in our meta-analysis, there has been a slight but significant increase in the antibiotic resistance rate to imipenem. Thus, it is crucial to exercise caution in their use, as excessive and inappropriate administration can contribute to the development of antimicrobial resistance, as evidenced in studies from surveillance studies conducted in India[59], China[60], and the United States[61]. Therefore, while carbapenems offer a viable treatment option, their judicious use is essential to mitigate the risk of resistance development. As of the present, carbapenems can be considered a last resort treatment option for complicated urinary tract infections. In cases of carbapenem-resistant Enterobacterales, these antibiotics can potentially be used in combination with a beta-lactamase inhibitor. Previous investigations have demonstrated the efficacy of combinations like meropenem & vaborbactam in treating complicated urinary tract infections[62] and other serious carbapenem-resistant Enterobacterales infections[63]. The use of relebactam with imipenem has also yielded beneficial effects[64].

To the best of our knowledge, at the time of our analysis, no prior literature review or meta-analysis had undertaken the task of characterizing the antimicrobial resistance landscape and its temporal trends among bacterial pathogens causing urinary tract infections. Notably, our study represents a pioneering effort in this domain, endeavoring to bridge the gap by including surveillance data published in Vietnamese, a valuable resource often overlooked by the global scientific community due to language barriers.

However, it is crucial to acknowledge certain limitations inherent to our study. Among the 29 studies incorporated into this review, 15 did not explicitly specify the methodology employed for antimicrobial resistance testing, and 20 omitted information regarding the standard utilized in their assessments. This lack of clarity poses a challenge in our attempt to provide a comprehensive analysis and do subgroup analysis to compare any potential variation caused by the different methods of measurement.

In summary, our comprehensive meta-analysis revealed several key findings regarding antibiotic resistance among uropathogenic *E. coli*. Resistance to cephalosporins was found to be the highest, while carbapenems demonstrated the lowest resistance rates, making them candidates for last-resort treatments for hospitalized patients with complicated urinary tract infections. Among the three combinations of beta-lactam and beta-lactamase inhibitors included in our study, piperacillin/tazobactam exhibited the lowest resistance rate. It's important to note that the resistance rates for these antibiotics remained relatively stable, except for significant increases observed in the case of cefotaxime and imipenem. This underscores the importance of conducting antibiograms to determine the most appropriate antibiotic treatment. Future research should expand beyond *E. coli* to investigate resistance rates in other uropathogens and their susceptibility to various antibiotics. Furthermore, a more comprehensive analysis that includes clinical success rates and microbial eradication effectiveness of these antibiotics could provide a more complete understanding of their efficacy. With improved insights, healthcare professionals can offer more effective treatments. Continuous surveillance is essential to provide healthcare providers with the most current and relevant information to treat urinary tract infection effectively.

Conflict of interest statement

The author declares that there is no conflict of interest.

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The authors received no extramural funding for the study.

Author's contributions

DTN developed the theoretical formalism, performed the analytic calculations and performed the numerical simulations.

References

[1] Foxman B, Brown P. Epidemiology of urinary tract infections: Transmission and risk factors, incidence, and costs. *Infect Dis Clin North Am* 2003; **17**(2): 227-241. doi: 10.1016/s0891-5520(03)00005-9.

[2] Zeng Z, Zhan J, Zhang K, Chen H, Cheng S. Global, regional, and national burden of urinary tract infections from 1990 to 2019: An analysis of the global burden of disease study 2019. *World J Urol* 2022; **40**(3): 755-763. doi: 10.1007/s00345-021-03913-0.

[3] Poulsen LL, Bisgaard M, Son NT, Trung NV, An HM, Dalsgaard A. *Enterococcus* and *Streptococcus* spp. associated with chronic and self-medicated urinary tract infections in Vietnam. *BMC Infect Dis* 2012; **12**: 320. doi: 10.1186/1471-2334-12-320.

[4] Okumura J, Wakai S, Umenai T. Drug utilisation and self-medication in rural communities in Vietnam. *Soc Sci Med* 2002; **54**(12): 1875-1886. doi: 10.1016/s0277-9536(01)00155-1.

[5] Huong NM, Gammeltoft T, Rasch V. Strategies for the prevention and treatment of reproductive tract infections among women in Vietnam. *Cult Health Sex* 2008; doi: 10.1080/13691050801932478.

[6] Torumkuney D, Kundu S, Vu GV, Nguyen HA, Pham HV, Kamble P, et al. Country data on AMR in Vietnam in the context of community-acquired respiratory tract infections: Links between antibiotic susceptibility, local and international antibiotic prescribing guidelines, access to medicines and clinical outcome. *J Antimicrob Chemother* 2022; **77**(Suppl 1): i26-i34. doi: 10.1093/jac/dkac214.

[7] Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: Epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol* 2015; **13**(5): 269-284. doi: 10.1038/nrmicro3432.

[8] Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Systematic reviews of etiology and risk. In: Aromataris E, Munn Z, editors. *JBI manual for evidence synthesis;* 2020. [Online]. Available from: https://doi.org/10.46658/JBIMES-24-06. [Accessed on 27 March 2024].

[9] Viechtbauer W. Conducting meta-analyses inrwith the metafor package. *J Stat Software* 2010; **36**(3). doi: 10.18637/jss.v036.i03.

[10]Nguyen SN, Thi Le HT, Tran TD, Vu LT, Ho TH. Clinical epidemiology characteristics and antibiotic resistance associated with urinary tract infections caused by *E. coli*. *Int J Nephrol* 2022; **2022**: 2552990. doi: 10.1155/2022/2552990.

[11]Hoang TAV, Nguyen TNH, Ueda S, Le QP, Tran TTN, Nguyen TND, et al. Common findings of bla CTX-M-55-encoding 104-139 kbp plasmids harbored by extended-spectrum β-lactamase-producing *Escherichia coli* in pork meat, wholesale market workers, and patients with urinary tract infection in Vietnam. *Curr Microbiol* 2017; **74**(2): 203-211. doi: 10.1007/s00284-016-1174-x.

[12]Duong HP, Mong Hiep TT, Hoang DT, Janssen F, Lepage P, De Mol P, et al. Difficultés de prise en charge des infections urinaires fébriles chez l'enfant vietnamien. [Practical problems related to the management of febrile urinary tract infection in Vietnamese children]. *Arch Pediatr* 2015; **22**(8): 848-852. doi: 10.1016/j.arcped.2015.05.010.

[13]Lob S, Hackel M, Biedenbach D, Sahm D, Badal R, Johnson A, et al. Trends in ESBL-production and susceptibility for *E. coli* from urinary tract infections in Southeast Asia: SMART 2010-2013. *Int J Antimicrob Agents* 2015; **45**: S59-S143. doi: 10.1016/s0924-8579(15)30006-6.

[14]Nga TTT, Phuong TL, Phuong TM, Phuong DM, Biedenbach DJ, Narang P, et al. *In vitro* susceptibility of Gram-negative isolates from patients with urinary tract infections in Vietnam: Results from the study for monitoring antimicrobial resistance trends (SMART). *J Glob Antimicrob Resist* 2014; **2**(4): 338-339. doi: 10.1016/j.jgar.2014.04.003.

[15]Ramos NL, Sekikubo M, Dzung DT, Kosnopfel C, Kironde F, Mirembe F, et al. Uropathogenic *Escherichia coli* isolates from pregnant women in different countries. *J Clin Microbiol* 2012; **50**(11): 3569-3574. doi: 10.1128/JCM.01647-12.

[16]Ramos NL, Dzung DT, Stopsack K, Jankó V, Pourshafie MR, Katouli M, et al. Characterisation of uropathogenic *Escherichia coli* from children with urinary tract infection in different countries. *Eur J Clin Microbiol Infect Dis* 2011; **30**(12): 1587-1593. doi: 10.1007/s10096-011-1264-4.

[17]Cao NM, Luc BTV, Nguyen ATT, Vo DTT. Sự đề kháng kháng sinh của các vi khuẩn gây nhiễm khuẩn đường tiết niệu ở người lớn. [The antibiotic resistance of bacteria causing urinary tract infections in adult]. *J Med Ho Chi Minh* 2012; **14**(1): 491-497.

[18]Tran HTM. Đặc điểm lâm sàng và vi khuẩn học trong bệnh nhiễm khuẩn tiểu ở trẻ em. [Clinical and bacteriological characteristics of urinary tract infection in children]. *J Med Ho Chi Minh* 2012; **16**(4): 242-246.

[19]Tran NTT. Tác nhân gây nhiễm trùng tiểu và tình hình đề kháng kháng sinh tại bệnh viện chợ rẫy 2013. [The pathogens urinary tract infection and antimicrobial resistance at choray hospital in 2013]. *J Med Ho Chi Minh* 2014; **18**(4): 119-122.

[20]Tran NTT. Các tác nhân gây nhiễm khuẩn đường tiết niệu thường gặp và đề kháng kháng sinh tạI bệnh viện chợ rẫy n m 2010-2011. [Situation of urinary tract infections antibiotic resistance at cho ray hospital in 2010-2011]. *J Med Ho Chi Minh* 2013; **17**(1): 578-581.

[21]Tran BQ, Tran NTT. Nhiễm trùng tiểu: vi sinh học và tình hình đề kháng kháng sinh tạI bệnh viện chợ rẫy từ 2007-2011. [Urinary tract infection: Microbiology and antimicrobial resistance at cho ray hospital from 2007 to 2011]. *J Med Ho Chi Minh* 2013; **17**(2): 122-127.

[22]Huynh QTV, Tran UNN, Nguyen HTB. Đặc đIểm dịch tễ, lâm sàng, cận lâm sàng và đIều trị nhiễm trùng tiểu ở trẻ em dướI 3 tháng tuổI tạI bệnh viện nhi đồng 2 từ 01/2008-03/2013. [Describing the epidemiological, clinical and laboratory findings, and treatment of urinary tract infection in children under the age of 3 months old, from 01/2008 to 03/2013]. *J Med Ho Chi Minh* 2014; **18**(1): 464-468.

[23]Huynh TM, Tran SX, Nguyen HK, Nguyen YVH, Trinh TT, Vuong NM, et al. Khảo sát phổ vi khuẩn gây nhiễm trùng tiểu và phổ đề kháng kháng sinh của chúng trên bệnh nhân đến khám và đIều trị tạI bệnh viện đạI học y dược thành phố Hồ Chí Minh. [Investigation of bacterial pathogen and antibiotic resistance profiles inpatient diagnosed with urinary tract infection at Ho Chi Minh city university medical center]. *J Med Ho Chi Minh* 2015; **19**(1): 480-485.

[24]Nguyen TTT, Tran HTB. Đặc đIểm lâm sàng và vi trùng học của nhiễm khuẩn đường tiết niệu phức tạp ở người trưởng thành tạI bệnh viện chợ rẫy. [Clinical characteristics and bacteria of adult complicated urinary tract infection at cho ray hospital]. *J Med Ho Chi Minh* 2015; **19**(4): 458-465.

[25]Tran NTK, Hoang TDT, Nguyen MVT. Đặc đIểm vi khuẩn và tình hình đề kháng kháng sinh trong nhiễm khuẩn tiết niệu trẻ em tạI bệnh viện nhi đồng 2 n m 2017-2018. [Characterization and antimicrobial resistance in pediatric urinary tract infection at children's hospital 2]. *J Med Ho Chi Minh* 2019; **23**(3): 184-191.

[26]Nguyen NT, Luu BT. Đặc điểm bệnh nhân nhiễm khuẩn tiết niệu phức tạp điều trị tại bệnh viện trung ương Thái Nguyên. Tạp chí học Việt Nam. [Characteristics of patients with complicated urinary tract infections treated at Thai Nguyen Central Hospital]. *Vietnam Med J* 2021; **508**(2). doi: 10.51298/vmj.v508i2.1580.

[27]Que TA, Le HNM, Tran DA. Nghiên cứu sự kháng kháng sinh của các chủng vi khuẩn gram âm gây nhiễm khuẩn đường tiết niệu phân lập tại bệnh viện hữu nghị đa khoa Nghệ An. [Research of antibiotics resistance of bacteria strains causing urinar tract infections isolated at Nghe An Friendship General Hospital]. *J Clin Med Hue Central Hosp* 2021; **71**: 109-115. doi: 10.38103/jcmhch.2021.71.14.

[28]Nguyen TT, Nguyen MD. Nghiên cứu tỷ lệ và mức độ đề kháng kháng sinh của vi khuẩn gây nhiễm khuẩn đường niệu trên bệnh nhân đặt thông tiểu. [Research antibiotic resistance and rate of bacteria cause urinary tract infections in patients placed urinary catheter]. *108 Institute Clin Med Pharm Sci* 2018; **13**(6): 25-30.

[29]Pham AH, Pham HM. Tình hình kháng kháng sinh của các chủng vi khuẩn gây nhiễm khuẩn tiết niệu tại Bệnh viện Đa khoa Quốc tế Thu Cúc giai đoạn 2018-2019. [The antibiotic resistance situation of pathogenic bacteria causing urinary tract infection isolated at Thu Cuc International General Hospital from 2018 to 2019]. *108 Institute Clin Med Pharm Sci* 2022; **17**(2): 156-163. doi: 10.52389/ydls.v17i3.1201.

[30]Le DK, Le DD, Nguyen KH, Nguyen XM, Vo MN, Nguyen NM, et al. Tình Hình Nhiễm Khuẩn Đường Tiết Niệu tại Khoa Ngoại Tiết Niệu Bệnh Viên Trường Đại Học Y Dược Huế. [Urinary infection at department of urology of hue university of medicine and pharmacy hospital]. *J Med Pharm* 2018; **8**(3): 100-108. doi: 10.34071/jmp.2018.3.16.

[31]Tran PTK, Dang HTV. Đặc điểm bệnh nhân nhiễm khuẩn tiết niệu phức tạp tại bệnh viện bạch mai. [Characteristics of patients with complicated urinary tract infection at Bach Mai Hospital]. *Vietnam Med J* 2022; **518**(2): 279-282. doi: 10.51298/vmj.v518i2.3474.

[32]Nguyen SN, Dang CV. The incidence and causative bacteria of urinary tract infection in children from 2 months to 6 years old in some areas of Hai Phong, Vietnam in 2008. *Hue Univ J Sci: Nat Sci* 2010; **61**: 385-392.

[33]Kieu TC, Le HT, Nguyen AV, Dinh TTT. Nghiên cứu tỷ lệ và tính kháng kháng sinh của các vi khuẩn gây nhiễm khuẩn tiết niệu tạI bệnh viện quân y 103 (2014-2016). [Survey on the antimicrobial resistance of uropathogens isolated from Military Hospital 103 (2014-2016)]. *J Ho Chi*

Minh City Med Assoc 2017; **12**: 20-25.

[34]Tran TTT, Bui CM. Đề kháng kháng sinh của các tác nhân gây nhiễm khuẩn đường tiết niệu tạI bệnh viện an bình n m 2015. [Antibiotic resistance of pathogens urinary tract infections in the laboratory department of An Binh hospital in 2015]. *J Med Ho Chi Minh* 2016; **20**(5): 7-15.

[35]Tra DA, Nguyen PCH. Đánh giá đặc đIểm dịch tễ học và kháng sinh đồ của vi khuẩn trong bệnh l hẹp niệu đạo. [Evaluating epidemiology and antimicrobial susceptibility profiles of bacteria causing urinary tract infections in urethral stricture]. *J Med Ho Chi Minh* 2014; **18**(1): 359-365.

[36]Nguyen HT, Bui LTC, Nguyen DT, Nguyen TT, Dang HT, Doan LNG. Đánh giá tỷ lệ và sự đề kháng kháng sinh của vi khuẩn gây nhiễm khuẩn đường niệu trên bệnh nhân đặt thông tiểu tại Bệnh viện Trung ương Quân đội 108. [Catheter-associated urinary tract infections at the 108 Militay Central Hospital: Investigate the prevalence and antibiotic resistance of bacterial pathogens]. *108 Institute Clin Med Pharm Sci* 2022; **17**: 99-104. doi: 10.52389/ydls.v17idb.1456.

[37]Pham TM, Pham LT, Vo DTM, Nguyen VTH, Ha CTN, Vu CT, et al. Đặc đIểm các trường hợp nhiễm khuẩn niệu liên quan ống thông tiểu tạI bệnh viện đạI học y dược thành phố Hồ Chí Minh. [Characteristics of catheter-associated urinary tract infections at the hcmc university medical center in 2017]. *J Ho Chi Minh City Medical Assoc* 2017; **12**: 26-30.

[38]Cao TX, Phan AD, Nguyen TK, Nguyen TV, Tran TTH. Giám sát nhiễm khuẩn tiết niệu trên người bệnh phẫu thuật tại khoa ngoại tiết niệu bệnh viện TW Huế. [Surveillance of urinary tract infection in surgical patients at the urological hospital of Hue hospital]. *J Clin Med Hue Central Hospital* 2018; **47**: 66-74.

[39]Ministry of Health of the Socialist Republic of Vietnam. *3931/qđ-byt, hướng dẫn chẩn đoán và điều trị một số bệnh về thận-tiết niệu. [3931/QD-BYT Guidance on diagnosis and treatment of kidney and urinary disorders]*; 2015. [Online]. Available from: https://thuvienphapluat.vn/van-ban/The-thao-Y-te/Quyet-dinh-3931-QD-BYT-tai-lieu-chuyen-mon-Huong-dan-chan-doan-dieu-tri-benh-ve-than-tiet-nieu-2015-292501.aspx. [Accessed on 10 October 2023].

[40] Mortazavi-Tabatabaei SAR, Ghaderkhani J, Nazari A, Sayehmiri K, Sayehmiri F, Pakzad I. Pattern of antibacterial resistance in urinary tract infections: A systematic review and meta-analysis. *Int J Prev Med* 2019; **10**: 169. doi: 10.4103/ijpvm.IJPVM_419_17.

[41]Assawatheptawee K, Treebupachatsakul P, Luangtongkum T, Niumsup PR. Risk factors for community-acquired urinary tract infections caused by multidrug-resistant Enterobacterales in Thailand. *Antibiotics (Basel)* 2022; **11**(8): 1039. doi: 10.3390/antibiotics11081039.

[42]Hsueh PR, Hoban DJ, Carmeli Y, Chen SY, Desikan S, Alejandria M, et al. Consensus review of the epidemiology and appropriate antimicrobial therapy of complicated urinary tract infections in Asia-Pacific region. *J Infect* 2011; **63**(2): 114-123. doi: 10.1016/j.jinf.2011.05.015.

[43]Li X, Chen Y, Gao W, Ye H, Shen Z, Wen Z, et al. A 6-year study of complicated urinary tract infections in southern China: Prevalence, antibiotic resistance, clinical and economic outcomes. *Ther Clin Risk Manag* 2017; **13**: 1479-1487. doi: 10.2147/TCRM.S143358.

[44]Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. *Ann Clin Microbiol Antimicrob* 2007; **6**: 4. doi: 10.1186/1476-0711-6-4.

[45]Vu TVD, Do TTN, Rydell U, Nilsson LE, Olson L, Mattias Larsson M, et al. Antimicrobial susceptibility testing and antibiotic consumption results from 16 hospitals in Viet Nam: The VINARES project 2012-2013. *J Glob Antimicrob Resist* 2019; **18**: 269-278. doi: 10.1016/j.jgar.2019.06.002.

[46]MIMS Vietnam. *Amoxicillin+clavulanic acid.* [Online]. Available form: https://www.mims.com/vietnam/drug/info/amoxicillin%20+%20clavulanic%20acid?mtype=generic. [Accessed on 7 October 2023].

[47] Nguyen VT, Carrique-Mas JJ, Ngo TH, Ho HM, Ha TT, Campbell JI, et al. Prevalence and risk factors for carriage of antimicrobial-resistant *Escherichia coli* on household and small-scale chicken farms in the Mekong Delta of Vietnam. *J Antimicrob Chemother* 2015; **70**(7): 2144-2152. doi: 10.1093/jac/dkv053.

[48]Nhung NT, Cuong NV, Campbell J, Hoa NT, Bryant JE, Truc VNT, et al. High levels of antimicrobial resistance among *Escherichia coli* isolates from livestock farms and synanthropic rats and shrews in the Mekong Delta of Vietnam. *Appl Environ Microbiol* 2015; **81**(3): 812-820. doi: 10.1128/AEM.03366-14.

[49]Tran HD, Bach Nguyen YT, Thanh Tran T, Le TTT, Nguyen HTT, Nguyen CM, et al. Community-acquired pneumonia-causing bacteria and antibiotic resistance rate among Vietnamese patients: A cross-sectional study. *Medicine (Baltimore)* 2022; **101**(36): e30458. doi: 10.1097/MD.0000000000030458.

[50]MIMS Vietnam. *Ticarcillin+clavulanic acid.* [Online]. Available form: https://www.mims.com/vietnam/drug/info/ticarcillin%20+%20clavulanic%20acid. [Accessed on 7 October 2023].

[51]MIMS Vietnam. *Piperacillin+tazobactam.* [Online]. Available form: https://www.mims.com/vietnam/drug/info/piperacillin%20+%20tazobactam?mtype=generic. [Accessed on 7 October 2023].

[52] Kaye KS, Belley A, Barth P, Lahlou O, Knechtle P, Motta P, et al. Effect of cefepime/enmetazobactam *vs* piperacillin/tazobactam on clinical cure and microbiological eradication in patients with complicated urinary tract infection or acute pyelonephritis: A randomized clinical trial. *JAMA* 2022; **328**(13): 1304-1314. doi: 10.1001/jama.2022.17034.

[53]Seo YB, Lee J, Kim YK, Lee SS, Lee JA, Kim HY, et al. Randomized controlled trial of piperacillin-tazobactam, cefepime and ertapenem for the treatment of urinary tract infection caused by extended-spectrum beta-lactamase-producing *Escherichia coli*. *BMC Infect Dis* 2017; **17**(1): 404. doi: 10.1186/s12879-017-2502-x.

[54]MIMS Vietnam. *Imipenem*. [Online]. Available form: https://www.mims.com/vietnam/drug/info/imipenem?mtype=generic. [Accessed on 7 October 2023].

[55]MIMS Vietnam. *Meropenem*. [Online]. Available form: https://www.mims.com/vietnam/drug/info/meropenem?mtype=generic. [Accessed on 7 October 2023].

[56]MIMS Vietnam. *Ertapenem*. [Online]. Available form: https://www.mims.com/vietnam/drug/info/ertapenem?mtype=generic. [Accessed on 7 October 2023].

[57]Bader MS, Loeb M, Leto D, Brooks AA. Treatment of urinary tract infections in the era of antimicrobial resistance and new antimicrobial agents. *Postgrad Med* 2020; **132**(3): 234-250. doi: 10.1080/00325481.2019.1680052.

[58]Tan X, Pan Q, Mo C, Li X, Liang X, Li Y, et al. Carbapenems *vs* alternative antibiotics for the treatment of complicated urinary tract infection: A systematic review and network meta-analysis. *Medicine (Baltimore)* 2020; **99**(2): e18769. doi: 10.1097/MD.0000000000018769.

[59]Amladi AU, Abirami B, Devi SM, Sudarsanam TD, Kandasamy S, Kekre N, et al. Susceptibility profile, resistance mechanisms & efficacy ratios of fosfomycin, nitrofurantoin & colistin for carbapenem-resistant Enterobacteriaceae causing urinary tract infections. *Indian J Med Res* 2019; **149**(2): 185-191. doi: 10.4103/ijmr.IJMR_2086_17.

[60]Ding Y, Wang H, Pu S, Huang S, Niu S. Resistance trends of *Klebsiella pneumoniae* causing urinary tract infections in Chongqing, 2011-2019. *Infect Drug Resist* 2021; **14**: 475-481. doi: 10.2147/IDR.S295870.

[61]Zilberberg MD, Nathanson BH, Sulham K, Fan W, Shorr AF. Carbapenem resistance, inappropriate empiric treatment and outcomes among patients hospitalized with Enterobacteriaceae urinary tract infection, pneumonia and sepsis. *BMC Infect Dis* 2017; **17**(1): 279. doi: 10.1186/s12879-017-2383-z.

[62]Kaye KS, Bhowmick T, Metallidis S, Bleasdale SC, Sagan OS, Stus V, et al. Effect of meropenem-vaborbactam *vs* piperacillin-tazobactam on clinical cure or improvement and microbial eradication in complicated urinary tract infection: The TANGO I randomized clinical trial. *JAMA* 2018; **319**(8): 788-799. doi: 10.1001/jama.2018.0438.

[63]Bassetti M, Giacobbe DR, Patel N, Tillotson G, Massey J. Efficacy and safety of meropenem-vaborbactam *versus* best available therapy for the treatment of carbapenem-resistant Enterobacteriaceae infections in patients without prior antimicrobial failure: A *post hoc* analysis. *Adv Ther* 2019; **36**(7): 1771-1777. doi: 10.1007/s12325-019-00981-y.

[64]Sims M, Mariyanovski V, McLeroth P, Akers W, Lee YC, Brown ML, et al. Prospective, randomized, double-blind, phase 2 dose-ranging study comparing efficacy and safety of imipenem/cilastatin plus relebactam with imipenem/cilastatin alone in patients with complicated urinary tract infections. *J Antimicrob Chemother* 2017; **72**(9): 2616-2626. doi: 10.1093/jac/dkx139.

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