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Mapping antimicrobial susceptibility of community-acquired uropathogenic Escherichia coli across low, middle and high-income countries highlights significant differences: insights for empiric treatment

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ABSTRACT

Objectives: Rising antimicrobial resistance (AMR) in *Escherichia coli* urinary tract infections (UTI) poses a global challenge. Evidence-based treatment of cystitis requires local resistance data. The DASH to Protect Antibiotics (https://dashuti.com/), a multi-regional group, supports centers in generating and sharing focused antibiograms to guide stewardship in community UTIs. This multi-country study aimed to describe antimicrobial susceptibility patterns of community-acquired *E. coli* isolates in low, middle, and high-income countries (LMICs and HICs).
Methods: The study was conducted in 37 representative centers across 13 countries in Asia (Middle East and Indian Subcontinent), Africa, Europe, and North America. A rigorous comparative analysis of the antimicrobial susceptibility of *E. coli* isolated from cases of simple cystitis presenting in outpatient or emergency departments was carried out. The impact of gross domestic product, climate, and population density per km^2 on *E. coli* susceptibility profile was analyzed using the Kruskal-Wallis test and two-way analysis of variance.
Results: Antimicrobial susceptibility varied significantly between LMICs and HICs, with nitrofurantoin (89%) and fosfomycin (96%) emerging as empiric choices globally. Across most centers, susceptibility to other oral antimicrobials was low: co-trimoxazole <60%, amoxicillin-clavulanic acid <70%, first-generation cephalosporins <50%, fluoroquinolones <60%. Injectable antibiotics fared better: piperacillin-tazobactam >70%, amikacin and meropenem >80%. Higher susceptibilities were noted in countries with high gross domestic product ($P < 0.001$) and humidity ($P = 0.002$).

Conclusion: Marked geographical differences in *E. coli* susceptibility patterns support the need for localized antibiograms and tailored empirical therapy. This study reinforces the utility of nitrofurantoin and fosfomycin as first-line agents and discourages the use of fluoroquinolones and third-generation cephalosporins.

Introduction

Management of *Escherichia coli* urinary tract infections (UTI), one of the most common community-acquired infections worldwide, is becoming increasingly challenging due to rising antimicrobial resistance (AMR) [1,2]. Evidence-based treatment of cystitis requires local susceptibility data, as resistance to nitrofurantoin, fosfomycin, amoxicillin-clavulanic acid, third-generation cephalosporin, trimethoprim-sulfamethoxazole (TMP-SMX), fluoroquinolones, and carbapenems is highly region-dependent [3].

Studies mapping susceptibility rates of *E. coli* across different geographic and economic regions are needed to assess regional patterns and develop local solutions. A multicenter comparative study of the antimicrobial susceptibility rates of uropathogenic *E. coli* was conducted by Diagnostic and Antimicrobial StewardsHip (DASH) to Protect Antibiotics (http://dashuti.com) across 13 countries (eight low and middle-income countries [LMICs] and five high-income countries [HICs]) with the objective of understanding both local and regional variation in *E. coli* susceptibility rates in cystitis. The participating countries were located in the Indian subcontinent (IS): India, Pakistan, Bangladesh; the Middle East (ME): Oman, Iran, Qatar, and the Kingdom of Saudi Arabia; two countries from Africa: Egypt, Benin; Ukraine, England, and Canada. All countries prescribed nitrofurantoin, trimethoprim-sulfamethoxazole, ampicillin, a fluoroquinolone (ciprofloxacin), an aminoglycoside (gentamicin, amikacin), third-generation cephalosporins (ceftriaxone and ceftazidime), beta-lactam/beta-lactamase inhibitors (amoxicillin-clavulanic acid and piperacillin-tazobactam), and carbapenems (meropenem, imipenem), making comparisons possible. The exception was fosfomycin, which was tested and prescribed only in the ME.

Antibiotic use and misuse, climate change, and economic factors contribute to rising AMR. A recent study on *Klebsiella pneumoniae* cystitis by this group reported that antimicrobial susceptibility was directly linked to geographic regions, log gross domestic product (GDP), humidity, and low and high temperatures [4]. The diverse socio-economic, demographic, and climatic profiles of the participating countries prompted us to explore the potential influence of these variables on AMR. Analysis of these variables may provide insight into our understanding of the complex factors driving AMR.

Local recommendations are essential to address the specific needs of each country, as governance, healthcare infrastructure, and environmental factors differ significantly. Our study aims to inform public health policies and empiric management of UTI in communities, as well as in traveling individuals, as the multi-regional UTI antibiograms spanning LMICs and HICs will go a long way in strengthening travel medicine.

Understanding how the environmental and economic factors interact with *E. coli* susceptibility trends will contribute valuable insights to our efforts to contain AMR and can inform global discussions on AMR.

Methods

Recruitment of centers

Fifty-five centers were approached in 2022, of which 37 tertiary-care public and private hospitals joined. Five countries participated from the ME (Oman, Iran, Qatar, Saudi Arabia), four from the IS (India, Pakistan, Bangladesh, and Maldives), two from Africa (Egypt and Benin), and three from the temperate climate: Ukraine, England, and Toronto. The geographic location of the sites is shown in Figure 1a. Seventeen centers were academic, while the remaining were non-academic. The recruitment process is outlined in a previous study [1]. The period of study was from 1st May 2022 to 31st December 2022.

Geographic distribution and climate of the centers

The geographic spread and climate of these sites from East to West is as follows: Dhaka, Bangladesh (one site, tropical monsoon-type climate); India (seven centers): three in North (N.) India, characterized by a subtropical climate (Delhi, Gurugram, Lucknow), one in central (C.) India, (Bhopal, Madhya Pradesh), two in East (E.) India, (Kalyani, West Bengal, and Bhubaneswar, Orissa), and one in the West (W.) India (Jaipur, Rajasthan; hot climate); Pakistan (five centers, with temperate climate, three in Peshawar and one each in Lahore and Karachi); Iran (three centers, two in Sari, (with humid subtropical climate and one in Tehran, hot arid climate); Oman, eight tertiary-care centers, (four in Muscat, and one each in Suhar, Ibri and Rustaq) and 55 linked health centers.

There was one center each in Qatar (Al Wakra), the Kingdom of Saudi Arabia (KSA, Buraydah), and Egypt (Cairo). The climate in these countries is a hot subtropical desert type. More geographically distant centers included: Benin (West Africa, tropical); Male, Maldives (equatorial monsoon, in the Indian Ocean); and three centers in the temperate region: Dnipro (Ukraine), London (United Kingdom), and Toronto (Canada). Among these, five were high-income countries (Oman, Qatar, KSA, the United Kingdom, and Canada) while the others were LMICs. GDP data were taken from the World Bank. (https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups).

Temperature and humidity were accessed from https://www.visualcrossing.com/weather-data. Details are shown in Table S1.

Sample processing

Mid-stream urine samples from patients with cystitis (frequency, dysuria, and urgency, with or without hematuria and abdominal pain) presenting in the outpatient or emergency department were processed as per standard guidelines in 2023 [1]. Antimicrobial susceptibility testing was performed according to Clinical & Laboratory Standards Institute (CLSI) guidelines M100-Ed33, 2022 [5]. Twenty-three sites primarily used disc diffusion testing, while 14 used automated systems; 11 sites used a combination of both approaches. Quality control was practiced by all laboratories.

Data collection

Antimicrobial susceptibilities of uropathogenic *E. coli* isolates were analyzed across the 38 sites (32 sites in the IS and ME, and one site each in the Maldives, Egypt, Benin, Ukraine, UK, and Canada). Antimicrobial susceptibility data from a minimum of 30 non-duplicate *E. coli* isolates per site were collated into site-wise antibiograms. Only routinely tested antimicrobial agents were included. CLSI guideline M39A4E (CLSI 2022) was used by all centers to prepare the antibiograms [6,7]. Buraydah (KSA) sent combined outpatient and inpatient data.

Statistical analysis

The harmonic mean was calculated using the pooled averages. The mean proportion of *E. coli* susceptibility to each drug was calculated based on the GDP of the countries. The Kruskal-Wallis test was used to compare susceptibility means between antimicrobials and GDP groups. A two-way analysis of variance was conducted to simultaneously analyze the impact of the antimicrobial and GDP on the proportion of susceptible *E. coli* while adjusting for other variables (low and high temperature, humidity, and population density per km^2). Data analysis was carried out using SPSS 29, and a significance level of P <0.05 was established.

Results

Antimicrobial susceptibility profile of E. coli

The susceptibility rates across all sites are shown in Table 1. Regional rates by centers for major antibiotics are shown in Figure 1b. Table S2 shows the range and harmonic mean of susceptibilities by broad regions. A clear trend is observed in the susceptibility rates to common antimicrobials across countries (Figure 2). Susceptibility rates of intravenous antimicrobial groups in ME and North Africa (MENA), IS, and temperate sites are shown in Figure S1, and those of countries with multiple sites (Oman, India, Pakistan, and Iran) in Figure S2. Table 1 delineates susceptibility rates across various sites.

A significant difference in susceptibility ($P < 0.05$) was observed when comparing each drug within the three GDP groups (Figure 3 and Table 3), except for fosfomycin ($P = 0.432$) and ceftriaxone ($P = 0.081$). The post hoc analysis revealed significant susceptibility differences between lower-middle and high-income countries across all drugs ($P < 0.05$), except for the two mentioned drugs before.

Fosfomycin

Two centers in Muscat, Oman, tested fosfomycin; one reported 100% and the other 96% susceptibility. Al Wakra, Qatar reported 96%. India (91–100%) and Pakistan (84–100%) reported overall susceptibility of 96%, Maldives: 99%, Cairo: 89%, Benin: 95%, Dnipro: 82%, and London: 97%.

Nitrofurantoin

In the HIC ME, the susceptibility ranged from 96–98%, in Oman, 97% in Al Wakra, and 92% in Buraydah. In MENA LMICs, it was 86% in Tehran and Cairo, and 91% in Sari. In the IS, susceptibility in decreasing order was: 95% in the Maldives, 86% in Bangladesh, 85% (73–100%) in India, and 83% (77–97%) in Pakistan. In HIC temperate countries, London had higher susceptibility (99%) than Toronto (88%), while Ukraine, an LMIC, had 85%.

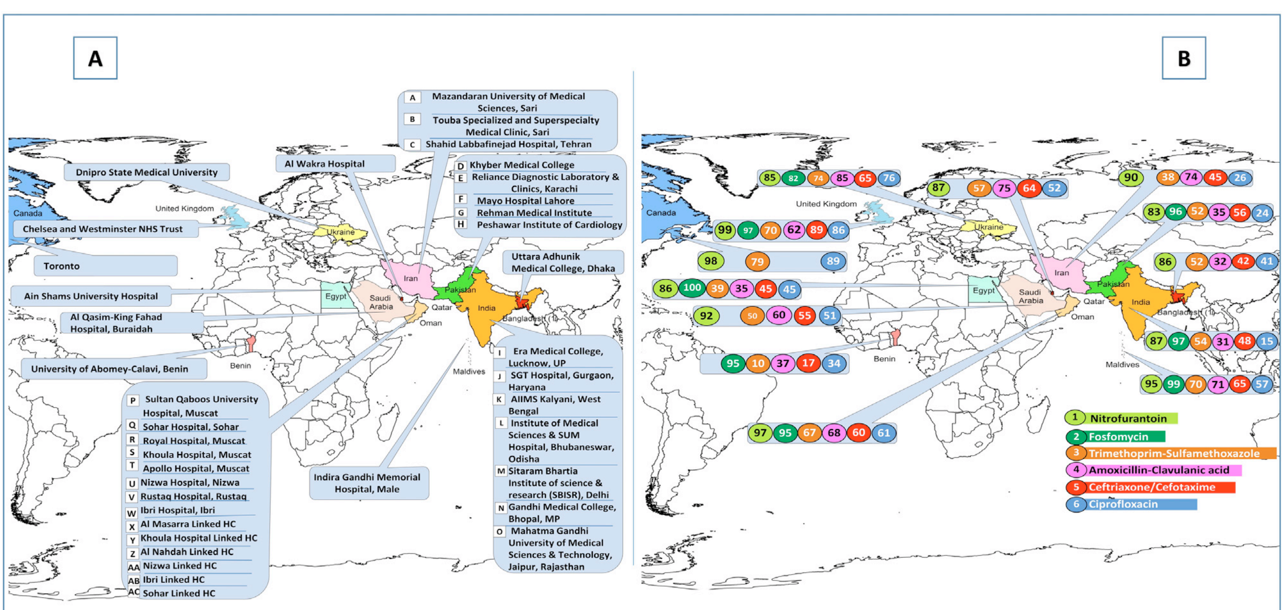

Figure 1. a and b. Geographic location of participating centers and susceptibility profile of *Escherichia coli* to commonly prescribed antimicrobials.

Table 1
Susceptibility profile of *E. coli* across sites located in the Indian subcontinent, MENA and temperate countries.

	Country	Institution	Total	Nitrofurantoin	Fosfomycin	Sulfamethoxazol	Ampicillin	Cefazolin	Cefuroxime	Ceftazidime	Ceftriaxone	Cefepime	Gentamicin	Amikacin	Ciprofloxacin	Amoxicillin-Clavulanic acid	Piperacillin-Tazobactam	Imipenem	Meropenem
Middle East + Africa (18 centers)	Oman	Sultan Qaboos University Hospital, Muscat, Oman	200	96%	100%	71%	30%	36%	57%	63%	62%	68%	88%	100%	63%	79%	98%	100%	100%
		Sohar Hospital, Suhar, Oman	69			72%	43%		67%		79%		94%	100%	83%	62%	96%	100%	100%
		Royal Hospital, Muscat, Oman	604	97%		61%	25%			50%	49%	53%	81%	99%	48%	61%	94%	98%	98%
		Khoula Hospital, Muscat, Oman	25	96%		56%	28%	60%	60%	65%		69%	80%	100%	60%	86%	92%	100%	100%
		Apollo Hospital, Muscat, Oman	117	96%	95%	68%						64%	82%	97%	61%		88%		95%
		Rustaq Hospital, Rustaq, Oman	376	98%		76%					74%		87%	100%	74%		94%		100%
		Ibri Hospital, Ibri, Oman	281	97%		72%	28%	55%	59%	68%	57%	82%	84%	85%	51%	53%	89%	100%	100%
		Al Masarra Linked HC (8), Oman	142	97%		66%	35%	57%	62%	78%	69%	80%	88%	100%	63%	82%	97%	100%	100%
		Khoula Linked HC (23), Oman	60	98%		63%	40%	60%	62%	68%	68%	73%	90%	100%	66%	95%	100%	100%	100%
		Al Nahdah Linked HC (24), Oman	255	98%		60%	30%	35%	51%	61%	57%	63%	89%	98%	57%	85%	98%	99%	99%
		Ibri Linked HC (17), Oman	596	98%		74%	36%	69%	72%	78%	74%	86%	90%	93%	59%	67%	90%	100%	100%
		Nizwa Hospital, Nizwa, Oman	262	88%		66%	31%			49%	47%	67%	83%	88%	67%	78%	88%	99.5%	97%
		Nizwa Linked HC (24) , Nizwa, Oman	1024	92%		73%	33%			46%	43%	75%	86%	98%	73%	82%	93%	100%	97%
	Saudi Arabia	Al Qassim- King Fahad Hospital, Buraidah, Saudi Arabia	198	92%		50%	28%			55%	55%	57%	80%	97%	51%	60%	75%	97%	97%
	Qatar	Al Wakra Hospital, Qatar	100	97%		57%	30%		58%	80%	64%	83%	85%	99%	52%	75%	92%	97%	100%
	Iran	Emam Khomeini Sari, Iran	94	91%		50%	20%	23%	25%	50%	73%	78%	82%	89%	48%	74%	92%		
		Toba, Sari, Iran	140	92%		51%	18%	22%	25%	55%	76%	81%	84%	89%	46%	75%	94%		
		Shahid Labbafinejad Hospital, Tehran, Iran	235	86%		26%					25%	33%	41%	66%	14%		72%		91%
	Egypt	Ain Shams University Hospital, Egypt	100	86%	100%	39%	9%	45%	50%	47%	45%	50%	79%	94%	45%	35%	67%	86%	85%
	Benin	Abomey- Calavi University Hospital	282		95%	10%				20%	17%		47%		34%	37%		91%	91%
	Harmonic mean			94%	97%	44%	25%	35%	46%	53%	49%	40%	77%	94%	47%	61%	88%	99%	98%

(*continued on next page*)

Table 1 (*continued*)

Indian Subcontinent (14 centers)	India	Era Medical College, Lucknow, UP, India	105	94%						67%	82%	84%	94%	100%	52%		87%	97%	
		SGT Hospital, Gurgaon, Haryana, India	75	74%	91%	65%	50%		62%	65%	63%	69%	42%	66%	40%	58%	70%	84%	82%
		AIIMS Kalyani, West Bengal, India	452	97%	98%	60%	23%	31%			45%	58%	75%	92%	39%	59%	87%	91%	91%
		Institute of Medical Sciences & SUM Hospital, Bhubaneswar, Orissa, India	182	85%	99%	51%	18%			55%	36%		87%	92%	16%	48%	65%		
		Sitaram Bhartia Institute of science & research (SBISR), Delhi, India	185	91%	97%	53%			35%	69%	74%		85%	91%	27%	66%	87%	96%	95%
		Gandhi Medical College, Bhopal, MP, India	815	73%		51%	16%						48%	55%	9%	10%	40%	58%	56%
		Mahatma Gandhi University of Medical Sciences & Technology, Jaipur, Rajasthan, India	191	100%	100%	47%			24%	52%	49%	58%	69%	88%	5%	43%	72%	83%	82%
	Pakistan	Pakistan Khyber Medical College, Pakistan	137	86%	100%	23%	16%			74%	80%	82%	80%	86%	30%	33%	88%	96%	96%
		Reliance Diagnostic Laboratory Karachi, Pakistan	30	97%	100%	37%	30%				50%	53%		87%	47%	67%	77%	90%	
		Mayo Hospital Lahore, Pakistan	32	77%	85%	22%							43%	85%	15%		41%	85%	85%
		Rehman Medical Institute, Pakistan	38	80%	96%	84%	38%		30%	32%	52%		68%	74%	35%	49%	82%	90%	90%
		Peshawar Institute of Cardiology, Pakistan	79	79%	100%	71%			18%	20%	52%		60%	71%	17%	35%	57%	93%	92%
	Bangladesh	Uttara Adhunik, Bangladesh	244	86%		52%			19%	36%	42%	58%	85%	92%	41%	42%	77%		100%
	Maldives	Indira Gandhi Memorial Hospital, Maldives	477	95%	99%	70%	37%			83%	65%	75%	86%	97%	57%	71%	90%	94%	94%
	Harmonic mean			86%	97%	45%	24%	31%	25%	45%	51%	60%	66%	80%	19%	19%	68%	76%	78%
Temperate centers (3)	Ukraine	Dnipro State Medical University, Ukraine	34	85%	82%	74%	9%	33%	52%	65%	65%	68%	88%	88%	76%	71%	85%	88%	88%
	United Kingdom	Chelsea and Westminster NHS Trust, United Kingdom	1559	99%	97%	70%		88%		89%	87%		93%	100%	86%	62%	86%		99%
	Canada	Toronto, Canada	273881	98%		79%									89%				

Co-trimoxazole

Susceptibility was 64% (range 56–72%) in Oman, 57% in Al Wakra, 50% in Buraydah, 42% in Iran (range 51%–26%), 39% in Cairo, and 10% in Benin. In the IS, Maldives was high at 70%, India: 55%; Bangladesh: 52%; Pakistan: 34% (22–84%); In temperate regions, susceptibility was: Toronto: 79%, Dnipro: 74%, London 70%.

Ampicillin

Susceptibility in Oman was 32% (17–50%), 30% in Al Wakra, 22% in India (25–43%), 19 % in Iran, 17% in Pakistan, and 9% in both Cairo and Dnipro.

First- and second-generation cephalosporins and cephamycins

Cefazolin susceptibility was 44% in Oman (35–69%), 22% in Iran, 45% in Cairo, 31% in Kalyani, 33% in Dnipro, and was high in London at 65%.

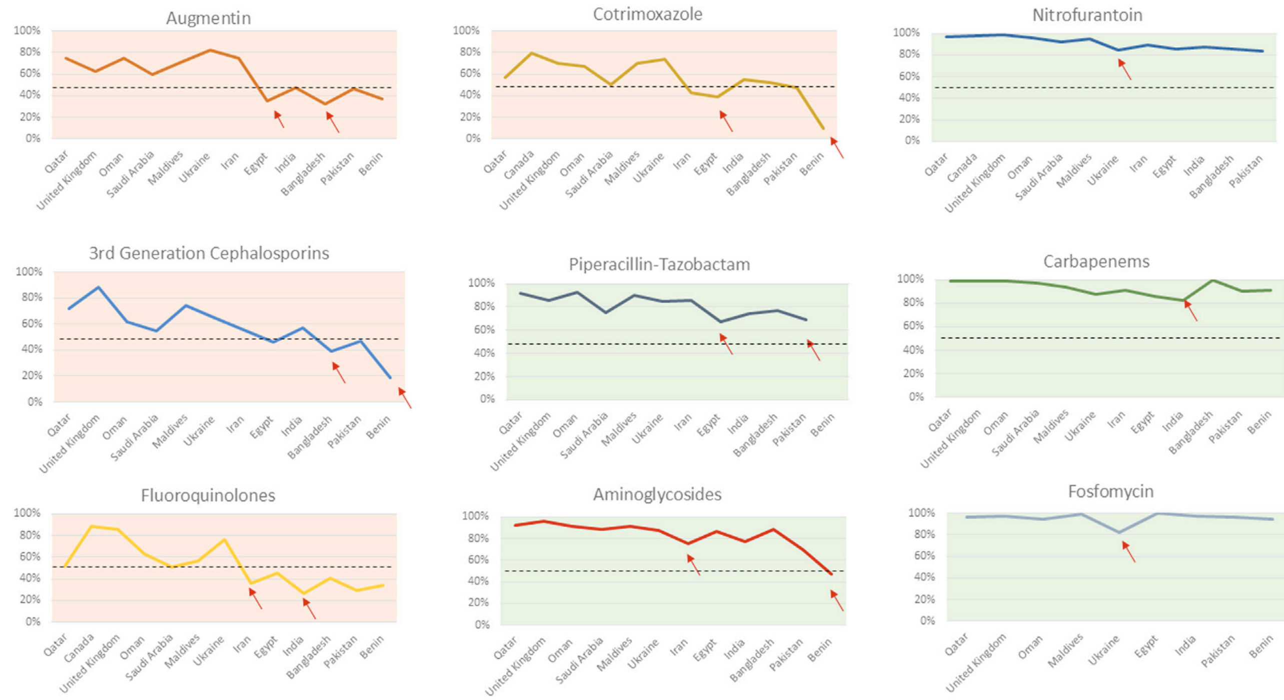

Figure 2. Susceptibility rates of *Escherichia coli* to common antibiotics across the participating countries.

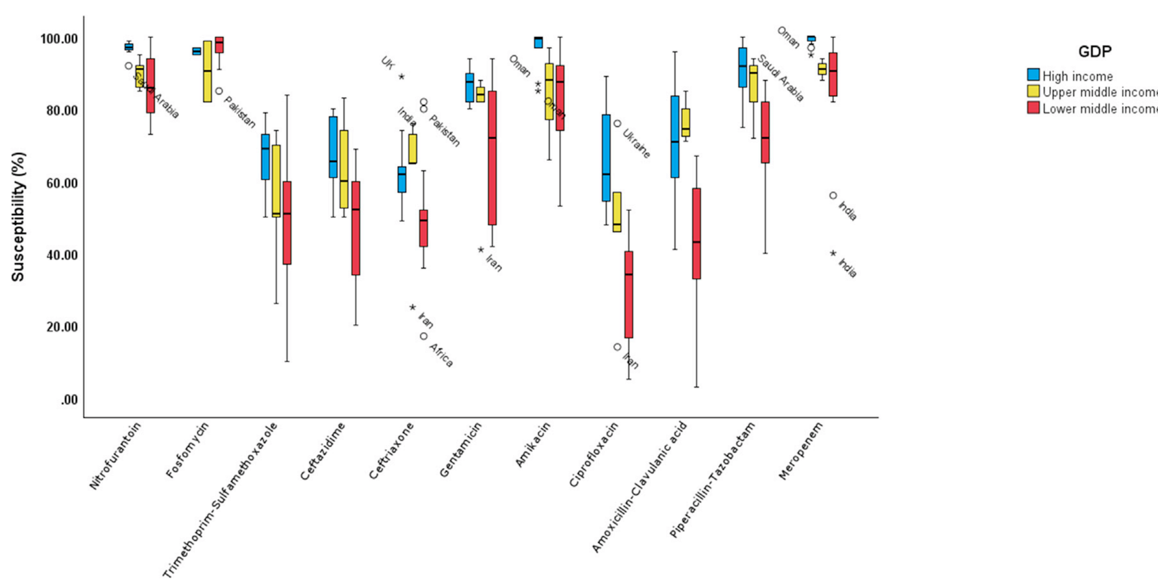

Figure 3. Association of GDP and *Escherichia coli* susceptibility in simple urine tract infections.
GDP, gross domestic product.

Third- and fourth-generation cephalosporins

The highest susceptibility to ceftazidime was observed in London, 89%, the Maldives, 83% and Al Wakra, 80%, and the lowest in Benin, 20%. In Oman, India, and Dnipro, susceptibility rates ranged from 61–65%, while in Buraydah, Iran, Cairo, and Dhaka, they ranged from 55% to 36% respectively. Cefepime susceptibility was highest in Qatar 83%, and lowest in Iran, 54%, ranging from 33–84% in the ME and 84%–53% in the IS. Buraydah reported 57%, and Cairo 50%. In the IS, cefepime susceptibility varied widely: Maldives 75%, India and Pakistan 64%, Bangladesh 58%. Extended-spectrum β-lactamase (ESBL) prevalence in countries with multiple sites was as follows: 35% in Oman, 43% in India, 45% in Iran, and 53% in Pakistan.. Among the single-site countries, London had 13%, Dnipro and Male 35%, Al Wakra 36%, Cairo 55%, Dhaka 58%, and Benin 83% ESBL prevalence.

Beta-lactam-beta-lactamase inhibitors

In MENA, piperacillin-tazobactam rates varied from 93% (92–100%) in Oman, 92% in Al Wakra, 85% (72–94%) in Iran, to 75% in Buraydah and 67% in Cairo. In the IS, the susceptibility was 90% in the Maldives, 72% (40–87%) in India, 77% in Bangladesh, and 64% in Pakistan (41–88%). In

Table 2
Effect of temperature, humidity, population density, gross domestic product and antimicrobial type on susceptibility rates of *Escherichia coli*.

Source	Sum of squares	Degree of freedom	Mean square	F-statistic	*P*-value	Effect size
Low temperature	1.228	1	1.228	0.007	0.934	0.000
High temperature	87.654	1	87.654	0.494	0.483	0.002
Humidity	1727.026	1	1727.026	9.735	0.002	0.033
Population density	58.206	1	58.206	0.328	0.567	0.001
GDP[a]	14,801.473	2	7400.736	41.717	<0.001	0.224
Antimicrobial	60,687.621	10	6068.762	34.209	<0.001	0.542
GDP * antimicrobial	6626.632	20	331.332	1.868	0.015	0.114

[a] GDP; Gross domestic product.

Table 3
Association of gross domestic product with mean (minimum, maximum) antimicrobial susceptibility of *E. coli*.

Drug	High income	Upper middle income	Lower middle income	*P*-value[a] (within drug)
Nitrofurantoin	96.93 (92.0, 99.0)	89.80 (85.0, 95.0)	86.07 (73.0, 100.0)	0.001
Fosfomycin	96.00 (95.0, 97.0)	90.50 (82.0, 99.0)	96.75 (85.0, 100.0)	**0.432**
Trimethoprim-Sulfamethoxazole	66.34 (50.0, 79.0)	54.20 (26.0, 74.0)	47.50 (10.0 84.0)	0.009
Ceftazidime	66.50 (50.0, 80.0)	63.25 (50.0, 83.0)	47.00 (20.0, 69.0)	0.046
Ceftriaxone	63.78 (49.0, 89.0)	60.80 (25.0, 76.0)	50.16 (17.0, 82.0)	**0.081**
Gentamicin	86.50 (80.0, 94.0)	76.20 (41.0, 88.0)	68.71 (42.0, 94.0)	0.010
Amikacin	97.29 (85.0, 100.0)	83.67 (66.0, 97.0)	82.50 (53.0, 100.0)	0.002
Ciprofloxacin	**64.20 (48.0, 89.0)**	**48.20 (14.0, 76.0)**	30.13 (5.0, 52.0)	0.001
Amoxicillin-Clavulanic acid	71.42 (41.0, 96.0)	76.25 (71.0, 85.0)	41.54 (3.0, 67.0)	0.001
Piperacillin-Tazobactam	90.92 (75.0, 100.0)	86.00 (72.0, 94.0)	70.39 (40.0, 88.0)	0.001
Meropenem	**99.14 (95.0, 100.0)**	**91.00 (88.0, 94.0)**	84.34 (40.0, 100.0)	0.001
P-value[a] (within gross domestic product)	**0.001**	**0.002**	0.001	

[a] Kruskal Wallis test.

the higher latitudes, Dnipro had 85%, and London, 86%. The median susceptibility to amoxicillin-clavulanic acid was 73% (53–96%) in Oman; 53% (10–66%) in India, 42% (33–67%) in Pakistan, 42% in Dhaka, and 74.5% (74–75%) in Iran. In Al Wakra, it was 75%, and 60% in Buraydah. Cairo and Benin had similar susceptibility, 35% and 37%, respectively. London reported 62%, while Dnipro was higher at 71%.

Carbapenems

In Oman and London, susceptibility was 99%, 98.5% in Al Wakra, 97% in Buraydah, and 91% in Iran. Cairo reported 86%. In the IS, 100% susceptibility was observed in Bangladesh and 94% in the Maldives, followed by Pakistan, 91% (85–96%); 88% in Dnipro, 91% in Benin. In India, it was 78% (56–95%). After removing the outlier in Bhopal (56%), the Indian rate was 89%.

Fluoroquinolones

The ciprofloxacin susceptibility rate in Oman was 62% (48–83%), 51% in Buraydah, and 52% Al Wakra. Cairo reported 45%, Pakistan 24% (15–47%), India 15% (5–52%), Iran 26% (14–48%), Bangladesh 41%, and 57% in the Maldives. It was 34% in Benin and higher in temperate Dnipro, 76%. It was excellent in London 86% and Toronto, 86%.

Aminoglycosides

Gentamicin susceptibility rates were 86% (80–94%) in Oman, 85% in Al Wakra, 80% in Buraydah, 60% in Pakistan (43–80%), 66% (42–94%) in India, 85% in Bangladesh, 86% in Maldives, 62% (41–84%) in Iran, 79% in Cairo and 47% in Benin. In colder countries, Dnipro reported 88%, and London 93%. Amikacin susceptibility was much higher. It was 95% in Oman (82–100%), 99% in Al Wakra, 97% in Buraydah, 74% in Pakistan (53–87%), 80% in India (55–100%), 92% in Bangladesh, 97% in Maldives, 80% in Iran, 94% in Cairo. It was 100% in London and 88% in Dnipro.

Influence of climate and GDP on E. coli susceptibility

The influence of temperature, humidity, GDP, and population density on antimicrobial susceptibility is shown in Table 2. There was a notable correlation between the susceptibility of *E. coli* and GDP, with higher susceptibilities observed in high-income countries ($P < 0.001$), as well as with humidity ($P = 0.002$). No significant association was found with population density or temperature.

Discussion

This multi-country study underscores the critical role of local antimicrobial susceptibility surveillance in shaping empiric treatment strategies for community-acquired *E. coli* UTIs. Our findings reveal substantial geographical variability in antimicrobial susceptibility, not only between HICs and LMICs, but also within individual regions and countries, reinforcing the need for local antibiograms to guide effective antimicrobial stewardship. Knowledge of regional antibiograms, at the very least, can support appropriate antimicrobial prescribing in traveling patients once their travel history is elicited.

Susceptibility to all classes of antimicrobials was significantly higher in HICs compared to LMICs ($P < 0.001$), suggesting a strong link between GDP and rational antimicrobial use. Higher GDPs correlate with improved sanitation, healthcare access, diagnostic stewardship, and stricter regulation of antimicrobial dispensing, which collectively reduce resistance selection pressure. Notably, Maldives despite being an LMIC, demonstrated high susceptibility rates, suggesting that governance and public health infrastructure can play a pivotal role. Good governance and public health infrastructure translate to higher literacy, good WASH (Water, Sanitation, and Hygiene) facilities, access to adequate healthcare, and high vaccine coverage, leading to lower incidence of infection and reduced pressure on antimicrobials.

Our study reveals that humidity ($P = 0.002$) had a significant impact on *E. coli* susceptibility rates, while temperature and population density per km^2 did not. This observation warrants further prospective ecological investigation. A prior study by this group on *K. pneumoniae* cystitis in different regions of India revealed a relationship between log GDP, humidity, and temperature and susceptibility rates [4]. Etaka et al. [8] reported that higher humidity 80% accelerated the die-off of *E. coli* under various storage conditions. The accelerated die-off would potentially reduce horizontal transmission of resistance, which may explain the higher susceptibility to antimicrobials. Contrary to our findings, Mouanga-Ndzime et al. [9] reported that humidity may play a role in worsening AMR. These contrasting findings suggest the role of multiple ecological factors in bacterial survival and AMR escalation, which warrant prospective ecological investigations and highlight the importance of developing a holistic approach to contain AMR, including assessment of climatic and ecological factors. A 30-year longitudinal study in the USA revealed a temporal relationship between the rise in minimum temperature and population density [10]. However, our study across different climatic and demographic regions did not find a correlation between regional increases in AMR and temperature or population density.

Nitrofurantoin and fosfomycin were consistently the most effective oral agents across all regions. The results are similar to our pan-India study and highlight the value of nitrofurantoin and fosfomycin in the management of UTI due to uropathogenic *E. coli* across both HIC and LMICs [1]. Their activity, even against ESBL-producing *E. coli*, affirms their role as first-line empiric agents for uncomplicated cystitis. A regional policy of promoting nitrofurantoin and fosfomycin and discouraging cephalosporins and fluoroquinolones should become a standard of care. However, significant intra-country variation (e.g., within India and Pakistan) highlights the importance of subnational antibiograms for precise prescribing.

In HICs, susceptibility rates to nitrofurantoin and fosfomycin were ≥95%, aminoglycosides and carbapenems were ≥85% and piperacillin-tazobactam ≥79%. The ≤60% susceptibilities to co-trimoxazole, cephalosporins, and fluoroquinolones in the majority of Asian and African centers suggest they should not be prescribed empirically. These observation merits repetition and reinforcement, especially in LMICs where fluoroquinolones and third-generation cephalosporins are used as workhorse antimicrobials in all kinds of infections, including cystitis, contributing to their gross misuse and overuse. Two temperate centers retained ≥85% susceptibility to fluoroquinolones, and all three retained ≥70% susceptibility to co-trimoxazole.

Nitrofurantoin was identified as a reliable oral antimicrobial across all regions. In HICs (ME and temperate), nitrofurantoin susceptibility was 97% and 98.5% respectively. Similar findings have emanated from Europe (100%), Toronto (97.5%), and Oman (97%) [11–13]. LMICs were characterized by 10–15% lower rates than HIC (90% in Iran, 88% in India, 86% in Bangladesh, 85% in Ukraine, 78% in Pakistan, 75% in Egypt), which aligns well with other studies [14,15]. Significant regional variations were observed in India and Pakistan, which were corroborated by other studies [16,17]. N. and E. India had high susceptibilities (94–98%), as did Karachi 97% in Pakistan, while several centers had ≤80% susceptibilities.

Fosfomycin emerged as the most active antimicrobial in all the countries that tested and used it, which makes us believe that it should be introduced in the ME. As a single oral dose (3 grams), it is an excellent choice for uncomplicated cystitis. Multiple doses of fosfomycin may be advised in complicated UTIs [18]. Susceptibilities were above 90% in most of the centers, with 100% in some centers in India and Pakistan. This was consistent with other reports [19,20]. Declining fosfomycin susceptibilities in *E. coli* causing uncomplicated UTI have been reported from Pakistan and Egypt, while Dnipro, at 82% was lower than previous reports 98% [21–23].

Across both HICs and LMICs, nitrofurantoin and fosfomycin susceptibility rates were the highest, far exceeding trimethoprim-sulfamethoxazole, oral cephalosporins, amoxicillin-clavulanic acid, and ciprofloxacin susceptibility. Their excellent activity against extended-spectrum beta-lactamases, AmpC, and in some cases, CRE is well documented [24]. Higher clinical and microbiologic cure rates are associated with 5-day nitrofurantoin than single-dose fosfomycin [25].

Significant variations in co-trimoxazole susceptibility were observed between HIC and LMICs (79% in Toronto to 10% in Benin), rates which were corroborated by Marchand-Austin et al. [12] and Assouma et al. [26]. Among the HICs, the susceptibility was ≥70% in the temperate ones and ≤60% in Qatar and Saudi Arabia. The Maldives 70% had rates comparable to HICs. Oman 66% and India 61% were also comparable, while Pakistan was low 35%. Others have reported similar rates [20,27]. It should be prescribed only if confirmed by culture and sensitivity.

Overuse and misuse of third-generation cephalosporins are reflected in the low susceptibility profiles at sites in the ME, Egypt, Benin, and IS. India, Pakistan, and Iran had low averages for third-generation cephalosporins (47–57%). In the Maldives, empirical management needs to be guided by local antibiograms, as susceptibility was much higher than in other IS countries. With ESBL rates soaring, empiric cephalosporin use should be actively discouraged, more so in the IS (53% to 58%) [28]. The lowest ESBL rates were observed in London 13%, followed by Oman, Ukraine, Maldives, and Qatar (35–36%), and the highest were in Benin, 83% (1,13). The low susceptibility of ceftriaxone (65–45%) suggests high circulation of CTX-M enzymes in Qatar, Oman, India, the Maldives, and Iran. High ceftazidime rates were reported from London 89% and the lowest 20% from Benin; findings corroborated by others [26,29]. Others have reported variable rates from respective countries [14,23,27].

Amoxicillin-clavulanate has little empiric value in most LMICs due to low susceptibility rates, 32–37% in Pakistan, Bangladesh, Egypt and Benin and 62% in India 62%, although Ehsan et al. [30] reported higher susceptibility 83%, which appears to be an outlier. Qatar and Iran both reported 75% despite marked economic disparities, suggesting that income alone does not predict resistance trends. Susceptibility in London was moderate 65%, while Dnipro was higher at 82%. Interestingly, Oman and Ukraine >80% outperformed both London and Al Buraydah 60–62%, indicating that climatic or ecological factors may play a role alongside antibiotic use practices [31].

Ciprofloxacin susceptibility was alarmingly low across most study sites, with the exception of England and Canada, where high rates were observed (86–89%). In contrast, ME HICs reported markedly lower susceptibility (51–60%). These findings are in line with previous reports from Toronto 83% and the ME, while higher rates have been reported from England [12,29]. Among LMICs, wide variability was evident: the Maldives, Cairo, and Bangladesh reported moderate susceptibility (40–60%), more than double the rates in Iran, India, and Pakistan (15–26%). These trends are consistent with earlier studies [32]. Despite this, fluoroquinolones remain in widespread empirical use, with nearly 50% of cystitis cases reportedly treated with them, highlighting a disconnect between prescribing practices and resistance data [33]. Vignette-based educational interventions that reference current local antibiograms may help drive evidence-based prescribing and improve behavioral change.

Ciprofloxacin susceptibility mirrored that of co-trimoxazole in several sites: Oman, Qatar, and KSA (61% vs 64%), Doha (52% vs 57%), and Buraydah (51% vs 50%). Comparable patterns were noted in Iran (26% vs 38%) and Dhaka (41% vs 52%). However, striking divergences were observed in India (21% vs 55%), Pakistan (24% vs 34%), and the Maldives (57% vs 70%), consistent with published data [16]. In contrast, ciprofloxacin outperformed co-trimoxazole in London (86% vs 70%) and Toronto (89% vs 79%) [12,34].

Amoxicillin-clavulanate showed better efficacy than ciprofloxacin in Oman (71% vs 61%), India (29% vs 21%), and Iran (74% vs 26%), though opposite trends were noted in London, Dhaka, and Cairo—consistent with the findings of Carter et al. [34] and Tarek et al. [35].

Piperacillin-tazobactam >90% retained excellent activity in the HIC and is recommended in difficult-to-treat UTIs. Al Buraydah, at 75% was consistent with Ahmed et al. [36]'s findings. Interestingly, the Maldives 90% paralleled HIC rates, pointing to lower antimicrobial pressure there. Iran, India, and Bangladesh exhibited comparable susceptibility near 80%, while Pakistan and Cairo showed lower rates 65% aligning with Malik et. al.'s [37] report, 72.6%, from Pakistan. Dnipro 84% and London 86%, despite being temperate countries, displayed lower susceptibility than Oman and Qatar,>90%. Low population (500 persons/km^2) in Oman and Qatar, compared to the significantly higher densities in London and Dnipro, may be instrumental. While not statistically significant, ecological factors merit exploration.

Gentamicin susceptibility exceeded 80% in the ME HICs (Oman, 86%, Qatar, 85%, 80% KSA) and temperate Western centers, (London, 93% Dnipro, 88%), consistent with international reports. Despite LMIC status Maldives 86% and Bangladesh 85% had high rates. Local antimicrobial pressures and variations in prescribing practices are reflected in the variable rates in the other LMICs (41–94%), which align with other studies [16,38,39].

With excellent susceptibilities in all regions, Oman 100%, Qatar 97%, KSA 97%, London 99%, Maldives 97%, and Dnipro 88%, amikacin is recommended as a carbapenem-sparing drug in difficult-to-treat UTIs. Lower rates in India 79%, Cairo 70%, Pakistan 68% and Iran 66% reflect injudicious antimicrobial use and access without prescription controls. Prior reports confirm the geographic variability [39–42], further reinforcing the need for local and regional surveillance.

Carbapenems demonstrated excellent activity >90% across nearly all sites, including LMICs, confirming their role as last-resort agents for UTI. While India 89%, Dnipro 88% and Cairo 86% fell slightly below this threshold, they compared favorably to other reports from Iran 76%, Pakistan (84.8–87.4%), and Bangladesh (92.5–95%) [14,21,29,36,38,40].

Our findings underscore the value of vignette-based education rooted in real-world scenarios to improve adherence to guidelines. Integrating local antibiogram discussions into such sessions fosters informed prescribing and enhances clinician engagement, both essential for effective antimicrobial stewardship.

Conclusion

The problem of AMR demands a multifaceted solution that overarches not only the one health platform but also socio-economic, environmental, and political systems. A paradigm shift in understanding the role of the multiple determinants in the containment of AMR is essential to promote public health and economic stability.

The findings of this study have direct implications for empirical prescribing policies, travel medicine, and global AMR containment. As international travel and antimicrobial misuse increase, importing and exporting resistant uropathogens becomes a growing threat. This study contributes to global AMR mapping in UTI, helping countries adapt empirical therapy based on shared regional patterns.

We advocate for (a) routine surveillance of community-acquired pathogens using standardized methods, (b) regional and local efforts to (i) promote nitrofurantoin and fosfomycin, (ii) discourage fluoroquinolones and cephalosporins, (iii) curtail piperacillin-tazobactam and meropenem in simple cystitis, c) wider access to low-resistance agents like fosfomycin in the ME and Africa and d) vignette-based antimicrobial stewardship training, integrating local antibiograms into prescribing decisions [25].

Furthermore, the conjunction of these economic and environmental factors serves to intensify the burden of antibiotic-resistant infections, not only on healthcare systems but also on the socio-economic fabric of affected populations. Consequently, the issue of antibiotic resistance must be addressed from a multifaceted perspective, taking into account not only the medical implications but also the economic, social, and environmental consequences. In the absence of a comprehensive approach, the growing threat of AMR will persist in undermining both public health and economic stability, particularly in vulnerable regions where environmental conditions, such as humidity, play a significant role.

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Ethical approval

Ethical approval for the study was obtained by the centers.

Author contributions

Meher Rizvi contributed to the conceptualization of the study, analysis, and drafting and editing of the manuscript; Maria Khan, Amina Al-Jardani, Seif Salem Al-Abri, Ujjala Ghoshal, Zaaima Al Jabri, Mohammad Ahanjan, Azza Al Mamari, Nawal Al Shizawi, Hiba Sami, Abdullah Balkhair, Adila Shaukat, Alwarith Nasser Salem Alkharusi, Abdulrahman Almahrouqi, Afreenish Hassan, Ajay Kumar, Amal Malehi, Amina Gul, Ashima Singh, Asma Said Hamed AL Shidhani, Areena Hoda Siddiqui, Aruna Poojary, Azza Al Rashdi, Bradley Langford, Dmytro Stepanskyi, Abbas Dolatabadi, Amal Al Maani, Aisha Al Mufraji, Elham Said Ahmed AlRisi, Garima Kapoor, Isabella Princess, Hawra J. Al Lawati, Hatim Ali Eltahir, Hilal Al Sidairi, Katia Iskandar, Ken Masters, Ibrahim Khalaf Hamdan Al-Busaidi, Laila Al Yazidi, Mahfuza Nasrin, Mahmood Salim AL Subhi, Mallika Sengupta, Manisha Khandait, Nada Khalfan Al Tamtami, Nada Khafan Al Siyabi, Nawal Al Kindi, Nazla Musthafa Luthfee, Neha Shreshtha, Nihal Mohamed Amur Al Riyami, Noora Hilal Ali Al Busaidi, Nupur Goel, Oksana Ishchenko, Omnia Mohamed Elnabawy Ahmed Taher, Pragnya Paramita Jena, Rajni Ekadashi, Razan Zadjali, Reba Kanungo, Sara Abolghasemi, Salima Al Maqbali, Sayantan Banerjee, Shadma Yaqoob, Shahnaz Sali, Shafqat Husnain Khan, Shalini Malhotra, Stephen Hughes, Sundas Shaukat, Syed Mohammed Atif, Vrushali Vishwas Patwardhan, Victorien Dougnon, Wahid Khan, Walid Wali, Zakariya Al Muharrmi, Zeeshana Basit, Jasashree Choudhury, Rachita Pravalina, Keith H. St John, Sanjeev Singh, Sarman Singh, Neelam Taneja, Raman Sardana, Abdul Ghafur, Pawan Kapoor, Rajeev Soman, Rashid Al Abri participated in the study and shared the data.

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman (MREC#2678 dated 23rd Feb 2022).

Declaration of competing interest

The authors have no competing interests to declare.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2025.100706.

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