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ORIGINAL ARTICLE

Lessons from an 11-year retrospective cohort study of *Escherichi coli* causing UTI in Imam Hospital Ardabil, Iran

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ABSTRACT

Background and Objectives: The global problem of urinary tract infections (UTIs) caused by antibiotic-resistant bacteria is due to limited treatment options. This study aimed to examine the prevalence, etiology, and management implications of *Escherichi coli* causing UTI at Imam Hospital Ardabil, Iran.
Materials and Methods: 2340 samples of retrospective data on *E. coli* causing UTIs were collected at Imam Hospital in Ardabil, Iran, spanning from 2012 to 2022. The samples were cultured and isolated, and their antibiotic susceptibility was determined using standard laboratory methods and data were then organized and systematically categorized using Python.
Results: It was found that the lowest level of resistance was related to nitrofurantoin, followed by imipenem. In 2018, the number of *E. coli* patients resistant to trimethoprim was the highest. Cephalexin and ciprofloxacin trends indicate the reduction of the line during this retrospective period. There was a significant correlation between wards and some antibiotics like Cefepime, Cefotaxime, Ceftazidime, and Trimethoprim (P-Value <0.05).
Conclusion: Significant correlations were identified between specific hospital wards and resistance to antibiotics. These findings underscore the need for continuous surveillance and tailored antibiotic stewardship programs to combat the rising trend of antibiotic resistance.

Keywords: Urinary tract infection (UTI); Multidrug-resistance (MDR); *Escherichia coli (E. coli)*; Iran; Retrospective studies; Cohort studies

INTRODUCTION

Urinary tract infections (UTIs) are a common infectious disease, particularly among women. Several Gram-negative and Gram-positive bacterial agents are involved in the occurrence of UTIs, Gram-negative such as *Escherichia coli (E. coli)*, *Proteus* spp., *Pseudomonas aeruginosa*, *Acinetobacter* spp., *Kleb-*

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siella spp., *Enterobacter* spp., and *Citrobacter* spp., and Gram-positive such as *Enterococcus* spp. and Coagulase-negative *Staphylococcus* spp. (1-3). The most common pathogen among these bacteria is *E. coli* (4). The microbial pathogens that cause urinary tract infections (UTIs) vary in different parts of the world, according to studies. Bacteria that cause UTI primarily possess virulence factors that facilitate their attachment to the host cell, colonization, and invasion (5-7).

The treatment of UTIs frequently involves the use of broad-spectrum antibiotics (8). In certain instances, antibiotic consumption methods that are both experimental and arbitrary are employed for treatment. Antibiotic resistance in bacteria worldwide has been developed due to the inappropriate and irrational use of antibiotics, resulting in the emergence of multi-resistant strains of pathogens (9). About 25,000 deaths in Europeans are caused by MDR bacterial strains every year, usually due to UTI complications (10). Therefore, it is necessary to avoid the unreasonable use of antibiotics that lead to the development of antimicrobial resistance, and the most appropriate antibiotics should be selected for the empiric treatment of UTI as the first choice. Therefore, UTIs caused by antibiotic-resistant bacteria are becoming a growing concern due to limited treatment options (11, 12). This study presents a comprehensive analysis of *E. coli*-induced UTIs over 11 years at Imam Hospital in Ardabil, Iran. By examining data from a large cohort of patients, this retrospective study aims to uncover trends in antibiotic resistance. The findings from this extensive dataset provide valuable insights into the epidemiology of *E. coli* UTIs and offer guidance for improving treatment strategies and infection control measures in similar healthcare settings.

MATERIALS AND METHODS

Study design. This retrospective cohort study covers an extensive 11-year period from 2012 to 2022, aiming to analyze *E. coli* causing UTI within the clinical setting of Imam Hospital, Ardabil, Iran. The study design provides the opportunity to examine temporal trends and patterns in infection rates. The initial data collected were organized and systematically categorized using the Python programming language. This study included a total of 78,013 samples.

Sample collection and tests. Standard guidelines were followed by conducting Bacterial cultures, antibiogram tests, and additional diagnostic procedures. Within one hour of collecting the samples, they were transported to the laboratory and cultured. Standard laboratory tests, such as gram staining, pigment production, colony morphology, catalase, oxidase, and IMViC tests, were used for differential diagnosis of strains. The disc diffusion method (Padtan Teb, Iran) was employed to assess the susceptibility of antibiotics on Muller-Hinton agar. The zones of inhibition were evaluated by measuring and comparing them to reference standards and the manufacturer's guidelines to determine resistance.

Ethics statement. Our research was approved by the Research Ethics Committee of Ardabil University of Medical Sciences and with the code of ethics IR.ARUMS.REC.1402.240.

The study adheres to ethical guidelines, ensuring patient confidentiality and data protection. The Institutional Review Board has approved, and the appropriate steps have been taken to address informed consent issues for retrospective analyses.

Data collection. Retrospective data collection involves extracting relevant information from medical records, including patient demographics and infection-related data. The comprehensive dataset will enable a thorough analysis of the factors that affect UTIs.

Inclusion and exclusion criterias. We included patient data from individuals diagnosed with infections caused by *E. coli*, who were treated at our facility from 2012 to 2022. Exclusion criteria included patients with incomplete medical records, those who received antibiotic treatment outside our facility, and cases where the bacterial isolates were not confirmed by our laboratory.

Variables examined. Key variables under scrutiny include the incidence and prevalence of UTI infections, inpatient ward, patient demographics, and outcomes. A nuanced analysis can be achieved by categorizing according to the severity of the UTI and the cause of the infection.

Statistical analysis. We used descriptive statistics to summarize the data for continuous variables, and frequencies and percentages for categorical variables. To analyze antibiotic resistance trends, we employed chi-square tests for categorical data and logistic regression models to identify potential predictors of resistance. All statistical analyses were performed using SPSS version 25.0.

RESULTS

Demographic data. The results revealed that 2340 *E. coli* strains had been isolated. Among these, 1561 strains were isolated from females, while 779 *E. coli* strains were isolated from males. Table 1 displays information about departments, years of separation, gender, and number of months.

The trend of resistance in most used antibiotics. Figs. 1 and 2 show the pattern of susceptibility and resistance for most antibiotics used to treat UTIs. Based on the results, we see the highest resistance to trimethoprim and cephalexin in 2017 the trend of resistance to trimethoprim increased compared to last year, but resistance to cephalexin decreased compared to the previous year. In the past 11 years, nitrofurantoin has shown the most frequent sensitivity of *E. coli.* Cephalexin and ciprofloxacin trends indicate the reducing line during this retrospective period.

Distribution of drug resistance and susceptibility in different wards. The distribution of drug resistance and susceptibility in different wards is shown in Table 2. This table presents the antibiotic sensitivity profile derived from the antibiogram analysis. It includes key antibiotic classes, specific agents, and their corresponding sensitivity rates against *E. coli* causing UTI infections. As shown in Table 2, antibiotic resistance and sensitivity only to ceftazidime and cefotaxime have significant differences in different wards of the hospital, so the level of resistance to these two antibiotics is high in various departments. There was significant correlation between wards and some antibiotics like Cefepime, Cefotaxime, Ceftazidime, and Trimethoprim (P-Value <0.05).

Table 1. Distribution of *E. coli* strains based on demographic and extracted data during 11 years in Emam Hospital, Ardabil

		Number	Frequency	Valid Percent	Cumulative Percent
Wards	Cardiology	82	3.5	3.5	3.5
	CCU	45	1.9	1.9	5.4
	Emergency	808	34.5	34.5	40.0
	ICU	48	2.1	2.1	42.0
	Infectious	119	5.1	5.1	47.1
	Internal	503	21.5	21.5	68.6
	Surgery	10	.4	.4	69.0
	Outpatients	725	31.0	31.0	100.0
	Total	2340	100.0	100.0	
Gender	Male	779	33.3	33.3	33.3
	Female	1561	66.7	66.7	100.0
	Total	2340	100.0	100.0	
Year	2012	31	1.3	1.3	1.3
	2013	152	6.5	6.5	7.8
	2014	209	8.9	8.9	16.8
	2015	209	8.9	8.9	25.7
	2016	152	6.5	6.5	32.2
	2017	255	10.9	10.9	43.1
	2018	378	16.2	16.2	59.2
	2019	317	13.5	13.5	72.8
	2020	196	8.4	8.4	81.2
	2021	102	4.4	4.4	85.5
	2022	339	14.5	14.5	100.0
Months	1	263	247	10.6	11.0
	2	329	252	10.8	22.2
	3	345	185	7.9	30.4
	4	329	227	9.7	40.5
	5	305	198	8.5	49.3
	6	319	215	9.2	58.8
	7	367	200	8.5	67.7
	8	332	196	8.4	76.4
	9	285	211	9.0	85.8
	10	289	115	4.9	90.9
	11	273	113	4.8	95.9
	12	245	92	3.9	100.0

DISCUSSION

This 11-year retrospective cohort study investigates the role of *E. coli* in causing urinary tract infections (UTIs) and their antibiotic resistance patterns at Imam Ardabil Hospital, Iran. According to the information obtained from the present research, correct antibiotic management can be designed to reduce the treatment costs of patients in a timely manner.

Given that UTIs are common across all age groups and *E. coli* is a primary causative agent, but antibiotic resistance is a significant issue in Iran, we conducted

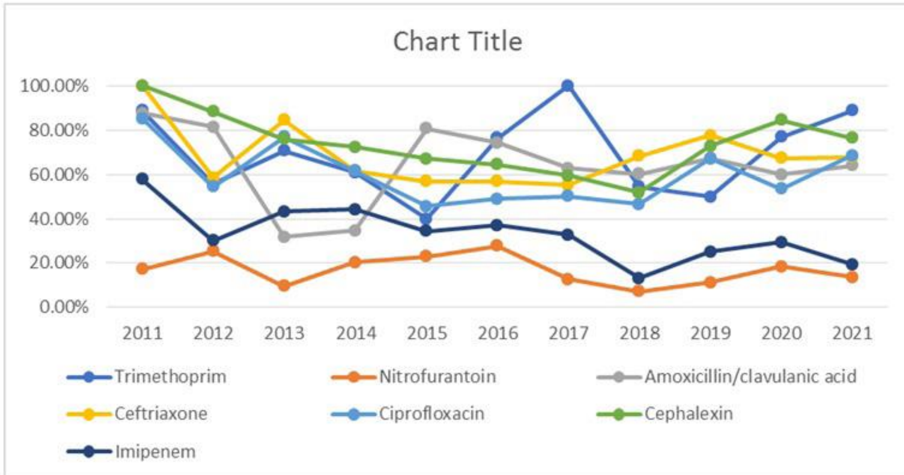

Fig. 1. The trend of resistance of *E. coli* against antibiotics most frequently used for the treatment of UTI in 11 years in Ardabil

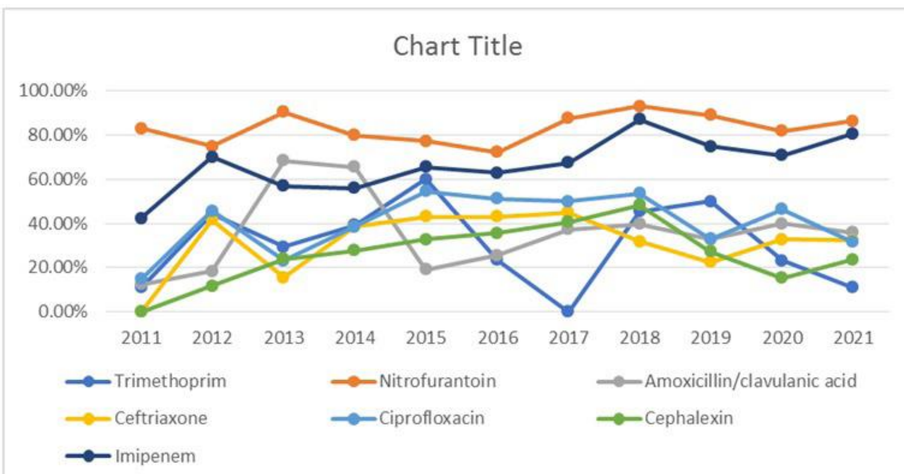

Fig. 2. The trend of *E. coli* susceptibility against antibiotic most frequently used for the treatment of UTI in 11 years in Ardabil

this study over 11 years. Antibiotic resistance among pathogenic bacteria is a global concern, posing a major challenge to the effective treatment of infectious diseases and increasing treatment costs. Resistance rates to antimicrobial agents have risen over the years and vary by region. This study highlights the importance of monitoring antibiotic resistance patterns of *E. coli* causing UTIs in different geographic areas over time. Most isolates in this study were obtained from emergency departments and outpatient laboratory referrals, indicating a predominance of outpatient cases. Over the 11 years, infection rates fluctuated, with the lowest in 2012 and the highest in 2018. However, there has been a significant overall increase in infection rates. The study found that nitrofurantoin and imipenem had the lowest resistance rates, while trimethoprim showed the highest resistance in 2018. High resistance rates to trimethoprim and cephalosporins suggest these drugs are commonly used for UTI treatment in Iran, contributing to increased resistance. The high resistance to trimethoprim may reduce its effectiveness in the region. Nitrofurantoin, followed by imipenem, was the most effective drug with the lowest resistance rates. Due to the rising antibiotic consumption and subsequent resistance, controlling drug resistance emergence is crucial. Indiscriminate and incorrect antibiotic use is a key factor in resistance development, and proper usage is essential to prevent further resistance. Nitrofurantoin is recommended only for uncomplicated UTIs due to its limited ability to achieve adequate blood levels, and not for complicat-

Table 2. Distribution of drug resistance and susceptibility in different wards of Imam Hospital in Ardabil during 11 years

		Wards								
Antibiotics		**Cardiology**	**CCU**	**Emergency**	**ICU**	**Infectious**	**Internal**	**Surgery**	**Outpatients**	**P -Value**
Amikacin	N*	43	27	437	27	66	280	7	393	
	S (%)*	93.02	85.19	85.81	77.78	86.36	84.64	85.71	83.72	0.692
	R (%)*	6.98	14.81	14.19	22.22	13.64	15.36	14.29	16.28	
Amoxicillin/	N	18	12	256	12	27	138	4	220	
clavulanic acid	S (%)	55.56	33.33	39.45	25.00	33.33	29.71	75.00	35.45	0.186
	R (%)	44.44	66.67	60.55	75.00	66.67	70.29	25.00	64.55	
Ampicillin-	N	22	19	207	14	31	129	2	219	
Sulbactam	S (%)	36.36	47.37	38.65	14.29	41.94	31.78	100.00	44.29	0.076
	R (%)	63.64	52.63	61.35	85.71	58.06	68.22	0.00	55.71	
Azithromycin	N	2	1	17	3	2	6	0	18	
	S (%)	50.00	0.00	5.88	66.67	16.67	27.78	0	50.00	0.163
	R (%)	50.00	100.00	94.12	33.33	83.33	72.22	0	50.00	
Carbenicillin	N	1	3	36	1	1	2	0	26	
	S (%)	0.00	33.33	30.56	0.00	0.00	23.53	0	7.69	0.404
	R (%)	100.00	66.67	69.44	100.00	100.00	76.47	0	92.31	
Cefazolin	N	27	21	266	14	38	163	2	202	
	S (%)	29.63	33.33	23.31	7.14	23.68	22.70	50.00	29.21	0.437
	R (%)	70.37	66.67	76.69	92.86	76.32	77.30	50.00	70.79	
Cefepime	N	25	14	293	22	34	195	5	258	
	S (%)	72.00	42.86	42.32	54.55	50.00	53.33	40.00	46.51	0.080
	R (%)	28.00	57.14	57.68	45.45	50.00	46.67	60.00	53.49	
Cefixime	N	20	7	151	8	24	84	2	155	
	S (%)	55.00	14.29	32.45	50.00	33.33	36.90	0.00	32.90	0.371
	R (%)	45.00	85.71	67.55	50.00	66.67	63.10	100.00	67.10	
Cefotaxime	N	47	24	468	34	62	265	8	375	
	S (%)	44.68	12.50	29.06	35.29	25.81	29.06	25.00	36.80	0.025
	R (%)	55.32	87.50	70.94	64.71	74.19	70.94	75.00	63.20	
Cefoxitin	N	12	7	90	4	16	34	0	46	
	S (%)	58.33	57.14	55.56	25.00	50.00	52.94	0.0	45.65	0.849
	R (%)	41.67	42.86	44.44	75.00	50.00	47.06	0.0	54.35	
Ceftazidime	N	50	24	487	33	72	320	7	428	
	S (%)	52.00%	20.83%	36.76%	36.36%	26.39%	38.13%	57.14%	42.29%	0.027
	R (%)	48.00%	79.17%	63.24%	63.64%	73.61%	61.88%	42.86%	57.71%	
Ceftizoxime	N	13	4	93	9	25	68	2	110	
	S (%)	84.62	25.00	60.22	77.78	48.00	51.47	50.00	54.55	0.211
	R (%)	15.38	75.00	39.78	22.22	52.00	48.53	50.00	45.45	
Ceftriaxone	N	45	17	346	22	55	238	3	310	
	S (%)	42.22	17.65	34.68	18.18	32.73	31.51	33.33	35.81	0.423
	R (%)	57.78	82.35	65.32	81.82	67.27	68.49	66.67	64.19	
Cefuroxime	N	2	3	64	3	4	45	1	72	
	S (%)	0.00	33.33	26.56	0.00	50.00	28.89	0.00%	16.67	0.478
	R (%)	100.00	66.67	73.44	100.00	50.00	71.11	100.00	83.33	
Cephalexin	N	28	18	264	13	34	160	4	206	
	S (%)	35.71	22.22	33.33	23.08	32.35	33.13	50.00	27.67	0.776
	R (%)	64.29	77.78	66.67	76.92	67.65	66.88	50.00	72.33	
Cephalothin	N	4	2	92	3	10	55	2	90	
	S (%)	25.00	50.00	10.87	33.33	40.00	23.64	50.00	21.11	0.155

Table 2. Continuing...

	R (%)	75.00	50.00	89.13	66.67	60.00	76.36	50.00	78.89	
Ciprofloxacin	N	64	37	637	36	99	393	10	568	
	S (%)	54.69	37.84	40.19	50.00	34.34	43.77	50.00	44.01	0.180
	R (%)	45.31	62.16	59.81	50.00	65.66	56.23	50.00	55.99	
Clindamycin	N	8	10	161	6	15	61	1	121	
	S (%)	37.50	30.00	27.33	0.00	53.33	18.03	0.00	20.66	0.074
	R (%)	62.50	70.00	72.67	100.00	46.67	81.97	100.00	79.34	
Co-trimoxazole	N	56	32	533	29	69	324	7	523	
	S (%)	39.29	18.75	32.27	37.93	33.33	30.25	14.29	32.12	0.544
	R (%)	60.71	81.25	67.73	62.07	66.67	69.75	85.71	67.88	
Doxycycline	N	6	1	2	2	2	6	0	2	
	S (%)	83.33	0.00	100.00	50.00	50.00	83.33	0	0.00	0.355
	R (%)	16.67	100.00	0.00	50.00	50.00	16.67	0	100.00	
Erythromycin	N	5	10	137	4	15	55	1	91	
	S (%)	40.00	30.00	18.98	0.00	20.00	20.00	0.00	16.48	0.799
	R (%)	60.00	70.00	81.02	100.00	80.00	80.00	100.00	83.52	
Gentamycin	N	47	24	405	21	71	251	4	400	
	S (%)	78.72	62.50	62.96	61.90	60.56	57.37	75.00	64.00	0.260
	R (%)	21.28	37.50	37.04	38.10	39.44	42.63	25.00	36.00	
Imipenem	N	40	24	475	29	245	3	388	1264	
	S (%)	80.00	70.83	72.42	68.97	71.67	70.20	33.33	71.65	0.775
	R (%)	20.00	29.17	27.58	31.03	28.33	29.80	66.67	28.35	
Meropenem	N	27	12	223	10	39	142	6	221	
	S (%)	88.89	75.00	80.72	70.00	84.62	76.76	100.00	75.57	0.449
	R (%)	11.11	25.00	19.28	30.00	15.38	23.24	0.00	24.43	
Nalidixic-acid	N	44	14	361	30	54	231	7	302	
	S (%)	29.55	21.43	18.56	23.33	18.52	26.84	28.57	24.83	0.302
	R (%)	70.45	78.57	81.44	76.67	81.48	73.16	71.43	75.17	
Nitrofurantoin	N	76	38	714	47	101	438	10	642	
	S (%)	86.84	94.74	85.71	72.34	81.19	82.42	90.00	83.80	0.108
	R (%)	13.16	5.26	14.29	27.66	18.81	17.58	10.00	16.20	
Ofloxacin	N	3	1	24	2	4	19	0	27	
	S (%)	66.67	100.00	50.00	100.00	50.00	52.63	0	29.63	0.280
	R (%)	33.33	0.00	50.00	0.00	50.00	47.37	0	70.37	
Tetracycline	N	1	2	51	0	8	35	0	51	
	S (%)	100.00	50.00	45.10	0	62.50	31.43	0	41.18	0.462
	R (%)	0.00	50.00	54.90	0	37.50	68.57	0	58.82	
Ticarcillin	N	2	2	20	1	1	11	0	26	
	S (%)	0.00	0.00	20.00	0.00	0.00	8.33	0	7.14	0.810
	R (%)	100.00	100.00	80.00	100.00	100.00	91.67	0	92.86	
Trimethoprim	N	5	56	4	19	43	1	58	186	
	S (%)	40.00	19.64	25.00	21.05	37.21	100.00	48.28	40.00	0.027
	R (%)	60.00	80.36	75.00	78.95	62.79	0.00	51.72	60.00	

*N: number, S: Sensitive, R: Resistance

ed UTIs or systemic infections (13). But also the side effects of these drugs should be taken into account, especially in the case of imipenem, which has limited use due to side effects (14).

As limitations of the study may be considered, from the evaluable clinical data it could not be well differentiated whether the underlying UTI was uncomplicated or more complicated, which is also important for the selection of an antibiotic for treatment as has been mentioned before. Patients only listed in the emergency department and the laboratory data were considered as outpatients.

In a retrospective study by Alanazi et al in Saudi Arabia evaluating *E. coli* in urinary tract infections in the emergency department at KAMC in Riyadh, Saudi Arabia, *E. coli* was the most common pathogen isolated from urine cultures of children, adults, and the elderly. A high level of resistance to ampicillin and cotrimoxazole was reported among *E. coli*. In addition, it was found that nitrofurantoin was the most effective antibiotic, which was consistent with our results (15). The high sensitivity to nitrofurantoin in the present study was consistent with the results of the study by Kader et al., (16) the study by Al-Tawfiq et al. (17) in Saudi Arabia, and the study by Sahm et al. in the USA (18). Also, the findings of this study confirm the results of other studies in different parts of the world, including Iran and Mexico City (14, 19).

There was a significant increase in resistance to ampicillin and trimethoprim in *E. coli* isolates in the UK (20). Also, A study conducted in the USA showed that MDR *E. coli* showed resistance to ampicillin, trimethoprim-sulfamethoxazole, and ciprofloxacin (21). These results are consistent with the results of our study, which showed a high level of efficacy compared to trimethoprim. In the study of Nemati et al., by examining the pattern of antimicrobial resistance in *E. coli* isolated from hospitalized patients in Kashan, Iran, it was found that high resistance was respectively against ampicillin (81.3%), nalidixic acid (71.3%), and cotrimoxazole (64.7%). and ciprofloxacin (61.3%) were observed. Also, the highest sensitivity to imipenem (96.7), cefoxitin (80), and nitrofurantoin (76.6) were reported (14).

In the study by Klingeberg et al., aimed to investigate antibiotic-resistant *E. coli* in uncomplicated community-acquired UTIs in Germany from May 2015 to February 2016. Among 1245 participants from 58 medical offices, 74.5% had *E. coli* infections. The prevalence of *E. coli* resistant to TMP and TMP/SMX was 15.2% and 13.0%, respectively. Accordingly, TMP should still be considered as an option for the treatment of uncomplicated UTIs (22).

The comparison of the results of our study with other regions has differences that this difference is caused by the difference in the pattern of antibiotic consumption and as a result the difference in the prevalence of antibiotic resistance compared to different antibiotic families, in addition to comparing the amount of antibiotic resistance in one region in the interval Different times are also different, so it is necessary to expand research in different times and different geographical areas to present the trend of antibiotic resistance and improve the treatment solutions.

Taking into account the variability of antibiotic resistance in different years, it is recommended to continuously conduct studies in different regions of the country to detect the sensitivity and antibiotic resistance of *E. coli*, the cause of UTI, and the relatively high resistance of *E. coli* to common antibiotics. Antibiotics should not be prescribed without culture and tests to determine the microbial sensitivity pattern.

Bacteria detection and antibiotic resistance pattern evaluation in a specific region are evaluated, which limits the generalizability of the results to the whole country. Therefore, more research based on the whole country's population is needed to better understand *E. coli* causing UTI.

CONCLUSION

This 11-year retrospective cohort study at Imam Hospital in Ardabil, Iran, highlights the increasing prevalence of UTIs caused by *E. coli* and the growing challenge of antibiotic resistance. The data reveals a significant rise in UTI cases over the years, with the highest incidence recorded in 2021. Notably, *E. coli* showed the lowest resistance to nitrofurantoin and imipenem, while resistance to trimethoprim peaked in 2018. The results indicated a significant increase in resistance to ciprofloxacin ($p < 0.01$) and ceftriaxone ($p < 0.05$) over the study period, while resistance to nitrofurantoin remained relatively stable ($p > 0.05$). These findings underscore the need for continuous monitoring of antibiotic resistance patterns and the development of effective treatment strategies to manage UTIs. The study provides valuable insights into the local epidemiology of *E. coli* UTIs, which can inform healthcare policies and antibiotic stewardship programs in the region.

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