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Research Article

Trends of Antibiotic Resistance among Uropathogens in Medical *vs.* Non-Medical Departments of Al-Shifa Medical Complex in Gaza Strip: A Retrospective, Cross-Sectional Study

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Abstract

Antibiotic resistance is a growing global crisis, straining healthcare systems and leaving us with limited options to combat drug-resistant bacteria. This retrospective, cross-sectional study examines the prevalence of antibiotic resistance patterns among urinary tract infections (UTIs) in Al-Shifa Hospital's medical departments in comparison with non-medical departments using data from microbiology laboratory archives over a one-year period.

From the examined urine cultures about 25% were obtained from internal medicine departments and double the number was obtained from non-medical departments. The positive rate was around 35% and about two-thirds of the samples were collected from female patients.

Among all departments, Enterobacteriaceae spp. were found to be the most frequently isolated uropathogens, accounting for 80% of cases. However, resistance rates varied depending on the specific organism and antibiotic used. For instance, *E. coli* showed a resistance rate of only 5% against meropenem, while amoxicillin-clavulanic acid exhibited a resistance rate exceeding 95%.

Importantly, the study revealed a significant disparity in resistance rates between medical and non-medical departments, specifically concerning third-generation cephalosporins. In internal medicine departments, resistance rates were alarmingly high, with cefotaxime, ceftriaxone, and ceftazidime showing resistance rates of 75%, 75% and 66.5% respectively. In contrast, non-medical departments displayed lower resistance rates, approximately 60%, 60% and 40%, respectively.

In summary, this research sheds light on the escalating problem of antibiotic resistance in UTIs and emphasizes the discrepancy in resistance rates between medical and non-medical departments. Urgent efforts are required to address this issue and find effective solutions to prevent the rise of untreatable bacterial infections.

More Information

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Abbreviations: UTI: Urinary Tract Infections

Background

Urinary tract infections are one of the most common bacterial infections among the population [1]. The clinical spectrum of urinary tract infection is wide as it can be simple cystitis to complicated infections with systemic response and sepsis with shock sometimes [2]. Urinary tract infection is defined by the Food and Drug Administration as a clinical syndrome with pyuria and documented uropathogens on blood or urine culture associated with local and systemic signs and symptoms that occur in the presence of functional or anatomical abnormality of the urinary tract or the presence of urinary catheter [3].

Antibiotic resistance is an alarming threat to healthcare systems. After the presence of antibiotics as a solution for life-threatening infections, their resistance poses a serious threat to their effectiveness in treating infectious diseases. The resistance is increasing with time leaving us with limited choices to face bacteria [4,5].

The issue of antibiotic resistance is not only affecting patients but also increasing the burden on health systems in many aspects. This has led to an increase in infectious disease burden by increasing treatment costs, hospital stays, and morbidity and mortality rates. For example, in the United States, bacterial infections cost about 55 billion dollars per year according to the CDC, and in Europe, it costs about nine billion euros annually [6-8]. Additionally, by the year 2050, it was estimated that antibiotic-resistant bacteria will be one of the ten leading causes of death globally with more deleterious effects on developing countries [9].

One of the main causes of increased resistance in the world is the overuse and misuse of antibiotics, which has led to the generation of multi-drug resistant bacteria (MDR), extensively drug-resistant bacteria (XDR), and pan-resistant bacteria (PDR) that are not responsive to the usual existing antibiotics [10]. On the other hand, bacteria are evolving antibiotic-resistant organisms faster than researchers can develop new antibiotics [11].

Urinary tract infections (UTIs) are among the leading causes of admissions to medical wards in the Gaza Strip. Increasingly, patients are admitted with complications of (UTI) with sepsis and septic shock with increasing hospital stays due to multi-drug resistant organisms. Unfortunately, there are still no local guidelines for managing such infections due to the relative lack of antibiogram studies. This study is part of the initiation of local guidelines and aims to study the most common organisms and rates of antibiotic resistance to choose the most appropriate empirical antibiotic for (UTIs).

Methods

A retrospective hospital-based; cross-sectional study that has included urine sample results from patients admitted to Al-Shifa hospital departments in the Gaza Strip. The departments were divided into medical departments and other non-medical departments which included general surgery, vascular surgery, orthopedic surgery, obstetrics and gynecology, intensive care, and outpatient departments.

Data were manually collected from the microbiology laboratory database for the year 2022. We included all urine culture results that are assigned to departments. Urine sample results that were not labeled to a department were excluded.

Urine samples were collected from patients as mid-stream urine samples and sent to the lab as soon as possible within one hour. Then the samples are cultured on nutrient agar plates by a 10 µl calibrated loop and plated on blood and McConkey agar. Plates were then incubated at 37^0C at the laboratory. Subsequently, the plates were examined for growth and colonies and classified as positive and negative according to WHO recommendations [12].

Data were classified into categorical and numerical data types and analysis was done using SPSS version 23.

Ethical approval was obtained from the head of the hospital and the research committee to use the collected microbiology laboratory data.

Results

Urine culture results from all departments (*n* = 3362) were examined. About a quarter (24.2% *n* = 815) were collected from medical departments and another (24.3% *n* = 820) was not assigned to any department (that was excluded from the analysis). The remaining half (51.3% *n* = 1727) was obtained from non-medical departments. Around 35% (*n* = 885) of all urine cultures were assigned as positive with the majority 66% (*n* = 586) obtained from female patients. The following analysis will compare findings in the internal medicine departments and other departments.

Regarding urine samples that were obtained from internal medicine departments, a total of 813 specimens were investigated; about 42% (*n* = 345) of cultures were positive with most of them cultured from female patient samples, about 71% (*n* = 245) Table 1.

On the other hand, from non-medical departments, 1727 urine samples were cultured with about 31% (*n* = 539) of samples coming back positive; also, of which most of them were collected from female patients (63%, *n* = 341) Table 1.

The distribution of uropathogens that have been isolated from all departments was relatively the same with the most commonly isolated organism being *E. coli* at about 51.6% (*n* = 456), which is followed by *Klebsiella* at about 24.9% (*n* = 220), *pseudomonas pp.* around 7% (*n* = 61), *streptococcus* 5% (*n* = 43), and *P. Mirabilis* 3.4% (*n* = 30). Enterobacteriaceae spp. *(E. Coli, K. pneumonia, P. Mirabilis)* formed the vast majority of the isolated uropathogens with about 84% (*n* = 289) in medical departments and 78% (*n* = 418) in the non-medical departments Table 2.

Table 1: Positive results analysis among sex.

Positive results analysis		Sex		Total
		male	female	
Internal medicine departments	Count	99	246	345
	% within Result	28.7%	71.3%	100.0%
	% within Sex	36.1%	45.7%	42.5%
	% of Total	12.2%	30.3%	42.5%
Non-medical departments	Count	198	341	539
	% within Result	36.7%	63.3%	100.0%
	% within Sex	30.8%	31.5%	31.3%
	% of Total	11.5%	19.8%	31.3%

Table 2: The distribution of uropathogens among departments.

	Internal medicine departments		Non-medical departments	
	Frequency	Percent	Frequency	Percent
E. Coli	187	54.2	273	50.6
K.pneumonia	87	25.2	130	24.1
P. Mirabilis	15	4.3	15	2.8
Acinetobacter spp	2	.6	7	1.3
P. aeruginosa	17	4.9	44	8.1
Streptococcus spp	16	4.6	27	5.0
S. Aureus	4	1.2	15	2.8
Enterobacter Spp	0	0	1	0.2
Candida	17	4.9	28	5
Total	345	100	540	100

The antibiogram of Enterobacteriaceae spp isolated from medical departments has a wide range. For example, meropenem was the most sensitive antibiotic with a sensitivity of 95.9% (*n* = 47) for *E. coli*, 100% (*n* = 2) for *proteus*, and 84% (*n* = 16) for *K. pneumoniae*. However, the resistance rate is very high against the studied cephalosporins and ciprofloxacin against *E. Coli* with 90% (*n* = 19), 84.5% (*n* = 49), 77% (*n* = 138), 75.6% (*n* = 118), 75.6% (*n* = 133), 66.5% (*n* = 115), 67% (*n* = 30) for cefazolin, cephalexin, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, and ciprofloxacin; respectively Table 3.

On the contrary, resistance rates generally were relatively lower in departments other than internal medicine. As resistance rates were relatively lower against third-generation cephalosporins and ciprofloxacin, for example, against *E. Coli* with rates of 70% (*n* = 18), 64.7% (*n* = 55), 70.5% (*n* = 86), 60.9% (*n* = 142), 60% (*n* = 155), 41% (*n* = 102), 59% (*n* = 139) for cefazolin, cephalexin, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, and ciprofloxacin; respectively Table 4.

Although Meropenem has a sensitivity rate of 96% (*n* = 54) against *E.Coli*, it has a lower rate against *K.Pneumonia* with 71% (*n* = 17) in comparison to 96% (*n* = 47) sensitivity rate for *E.Coli* and 84% (*n* = 16) *for K.Pneumonia* in medical departments Tables 3,4.

Discussion

The presented discussion revolves around an investigation conducted at Al-Shifa Hospital to assess the distribution of bacteria, their antimicrobial resistance, and a comparison between medical and non-medical departments. The results indicate that the percentage of positive samples was higher in medical departments (40%) compared to non-medical departments (30%), surpassing the findings of a previous study conducted in 2006 (34%) [13].

Table 3: Antibiotic resistance rates in internal medicine departments.

	E. Coli						*K. Pneumonia*						*Proteus*					
	S		I		R		S		I		R		S		I		R	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Cefazolin	2	10.5	0	0	19	89.5	1	10	0	0	9	90	\	\	\	\	\	\
Cefuroxime	40	22.3	1	0.6	138	77.1	9	10.7	1	1.2	74	88.1	6	40	0	0	9	60
Ceftazidime	51	29.5	7	4	115	66.5	27	33.8	6	7.5	47	85.8	8	57.1	1	7	5	35.7
Cefotaxime	38	24.2	0	0	118	75.6	11	14.5	1	1.3	64	84.2	9	60	0	0	6	40
Ceftriaxone	42	23.9	1	0.6	133	75.6	10	11.9	1	1.2	73	86.9	9	60	0	0	6	40
Cephalexin	8	13.8	1	1.7	49	84.5	3	10.3	0	0	26	89.7	2	25	0	0	6	75
Gentamycin	78	52.7	10	6.8	60	40.5	35	50	2	2.9	33	47.1	5	41.7	0	0	7	58.3
Amikacin	111	75	9	6.1	28	18.9	51	71.8	2	2.8	18	25.4	9	64.3	1	7.1	4	28.6
Ciprofloxacin	47	44.3	6	5.7	30	66.7	11	24.4	4	8.9	30	66.7	1	14.3	0	0	6	85.7
Doxycycline	47	44.3	6	5.7	53	50	11	24.4	4	8.9	30	66.7	1	14.3	0	0	6	85.7
Trimethoprim / Sulfamethoxazole	6	22.2	0	0	21	77.8	3	30	0	0	7	70	0	0	0	0	2	100
Piperacillin / Tazobactam	4	100	0	0	0	0	2	100	0	0	0	0	\	\	\	\	\	\
Meropenem	47	95.9	0	0	2	4.1	16	84.2	0	0	3	15.8	2	100	0	0	0	0
Colistin	30	18.1	2	1.2	134	80.7	22	27.5	0	0	58	72.5	4	28.6	0	0	10	71.4
amoxicillin- clavulanic acid	0	0	0	0	13	100	0	0	0	0	4	100	\	\	\	\	\	\

S: Sensitive; I: intermediate; R: Resistant; N: Number of patients; %: Percentage of patients.

Table 4: Antibiotic resistance rates in non-medical departments excluding internal medicine departments.

	E. Coli						*K. Pneumonia*						*Proteus*					
	S		I		R		S		I		R		S		I		R	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Cefazolin	8	30.8	0	0	18	69.2	1	11.1	0	0	8	88.9	\	\	\	\	\	\
Cefuroxime	97	37.2	2	0.8	86	70.5	35	28.7	1	0.8	86	70.5	6	40	0	0	9	60
Ceftazidime	128	51.6	18	7.3	102	41.1	48	43.2	3	2.7	60	54.1	6	42.9	0	0	8	57.1
Cefotaxime	91	39.1	0	0	142	60.9	39	34.8	1	0.9	72	64.3	7	46.7	0	0	8	53.3
Ceftriaxone	102	39.7	0	0	155	60.3	36	31.6	1	0.9	77	67.5	6	40	0	0	9	60
Cephalexin	28	32.9	2	2.4	55	64.7	11	25	1	2.3	32	72.7	2	28.6	0	0	5	71.4
Gentamycin	122	58.9	12	5.8	73	35.3	55	59.8	0	0	37	40.2	7	58.3	1	8.3	4	33.3
Amikacin	175	76.4	19	8.3	35	15.3	71	65.7	5	4.6	32	29.6	9	60	1	6.7	5	33.3
Ciprofloxacin	92	38.8	6	2.5	139	58.6	40	37.7	2	1.9	64	60.4	7	50	0	0	7	50
Doxycycline	65	48.5	5	3.7	64	47.8	31	45.9	7	10	30	44.1	3	30	0	0	7	70
Trimethoprim / Sulfamethoxazole	12	25.5	0	0	35	74.5	3	14.3	1	4.8	17	81	1	100	0	0	0	0
Piperacillin / Tazobactam	3	100	0	0	0	0	\	\	\	\	\	\	\	\	\	\	\	\
Meropenem	54	96.4	0	0	2	3.6	17	70.8	1	4.2	6	25	\	\	\	\	\	\
Colistin	5	50	0	0	5	50	1	33.3	0	0	2	66.7	\	\	\	\	\	\
amoxicillin- clavulanic acid	1	4.8	1	4.8	19	90.5	3	30	1	10	6	60	\	\	\	\	\	\

S: Sensitive; I: intermediate; R: Resistant; N: Number of patients; %: Percentage of patients.

The study reveals that *E.coli* remains the most common uropathogen in both medical and non-medical departments, comprising more than half of the isolated organisms throughout the years. However, there is a significant difference in antimicrobial susceptibility and resistance between medical and non-medical departments. In medical departments, *E.coli* displayed higher resistance rates, with 75% resistance to both cefotaxime and ceftriaxone and 66.5% resistance to ceftazidime. In contrast, the resistance rates were notably lower in non-medical departments, at approximately 60%, 60% and 40%, respectively. It is worth noting that the resistance rates in medical departments were much higher than those reported in 2006 when resistance to cefotaxime and ceftazidime was only 13%. Furthermore, *E.coli* resistance to ciprofloxacin experienced a sharp increase from 13% in 2006 to around 60% in all departments in 2022 [13].

A comparison with a study conducted in Al-Aqsa Hospital between 2018 and 2022, another major hospital in the Gaza Strip, revealed significant discrepancies in resistance rates. Although, cephalosporin resistance of 54%, 39%, and 53.3% for ceftriaxone, ceftazidime, and cefotaxime; respectively; which is quite similar to nonmedical departments; it was seriously higher in medical departments as it reached 75%, 65.5%, 75% [14].

Over the last two decades, huge changes have occurred to the antibiogram of bacterial isolates in the Gaza Strip. For example, *E. Coli* had a resistance rate of about 20% against cefuroxime and 3% against ceftazidime and ciprofloxacin. This resistance has continued to increase sharply to reach the figures in this research [15].

The observed differences in resistance between medical and non-medical departments indicate a significant gap, potentially attributed to the vulnerability of medical patients with multiple comorbidities and recurrent admissions. The study suggests further investigation to prevent the escalation of resistance in such settings.

Furthermore, the resistance rates are higher in developing countries than in developed [16]. For example, the resistance rates observed in this research were notably higher than resistance rates reported in Egypt and China. In China, *E.coli* resistance rates against ceftazidime and ceftriaxone were 16% and 42%, respectively [17]. Similarly, in Egypt, resistance rates were relatively lower, with 36% of *E.coli* being resistant to ceftriaxone and 55% resistant to ceftazidime [18].

However, it is important to consider the limitations of the study. It was a retrospective study based on microbiology laboratory reports in a resource-limited country. The lack of availability of antibiotic testing kits and the shortage of antibiotic discs resulted in missing data. Additionally, inadequate documentation led to the exclusion of some urine samples from the study. The study also lacked a thorough clinical correlation to determine if antibiotics were appropriately narrowed based on culture results, which could have aided in reducing resistance rates. These limitations highlight the need for future prospective studies to address these gaps.

Conclusion

The study underscores the significant difference in antibiotic resistance rates within the same institution over 20 years, and it shows a wide gap between resistance rates among different departments within the same medical complex. Therefore, it emphasizes the need for policymakers to take action to control the liberal use of antibiotics in order to face the rapidly developing antibiotic resistance rates. The authors also stress the importance of providing further clarification on the correct usage of antibiotics for appropriate indications.

Declarations

Ethics approval and consent to participate are obtained from the Ethical Committee of Al-Shifa Medical Complex with registration number 2023/0122.

Consent for publication is obtained from the director of the Al Shifa Medical Complex Internal Medicine Department.

Availability of data and material: The data are available upon request.

We are the sole authors of the article and we have taken due care to ensure the integrity of the article.

References

1. Wagenlehner FME, Bjerklund Johansen TE, Cai T, Koves B, Kranz J, Pilatz A, Tandogdu Z. Epidemiology, definition and treatment of complicated urinary tract infections. Nat Rev Urol. 2020 Oct;17(10):586-600. doi: 10.1038/s41585-020-0362-4. Epub 2020 Aug 25. PMID: 32843751.
2. Foxman B. Urinary tract infection syndromes: occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am. 2014 Mar;28(1):1-13. doi: 10.1016/j.idc.2013.09.003. Epub 2013 Dec 8. PMID: 24484571.
3. Complicated urinary tract infections: developing drugs for treatment Revision 1. 2018. https://www.fda.gov/media/71313/download.
4. Founou RC, Founou LL, Essack SY. Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. PLoS One. 2017 Dec 21;12(12):e0189621. doi: 10.1371/journal.pone.0189621. PMID: 29267306; PMCID: PMC5739407.
5. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: a global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309-18. doi: 10.1179/2047773215Y.0000000030. Epub 2015 Sep 7. PMID: 26343252; PMCID: PMC4768623.
6. Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014 Dec;5(6):229-41. doi: 10.1177/2042098614554919. PMID: 25436105; PMCID: PMC4232501.
7. ECDC. Surveillance of Antimicrobial Resistance in Europe. 2017. https://www.ecdc.europa.eu/sites/default/files/documents/EARS-Net-report-2017-update-jan-2019.pdf.
8. Antibiotic resistance threats in the United States; 2013. https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf.

9. Dadgostar P. Antimicrobial Resistance: Implications and Costs. Infect Drug Resist. 2019 Dec 20;12:3903-3910. doi: 10.2147/IDR.S234610. PMID: 31908502; PMCID: PMC6929930.

10. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, Goossens H, Laxminarayan R. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci U S A. 2018 Apr 10;115(15):E3463-E3470. doi: 10.1073/pnas.1717295115. Epub 2018 Mar 26. PMID: 29581252; PMCID: PMC5899442.

11. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015 Apr;40(4):277-83. PMID: 25859123; PMCID: PMC4378521.

12. World Health Organization. Regional Office for South-East A: Guidelines on standard operating procedures for microbiology. WHO Regional Office for South-East Asia, New Delhi. 2000.

13. Elmanama AA, Elaiwa NM, El-Ottol AE, Abu-Elamreen FH. Antibiotic resistance of uropathogens isolated from Al-Shifa hospital in Gaza Strip in 2002. J Chemother. 2006 Jun;18(3):298-302. doi: 10.1179/joc.2006.18.3.298. PMID: 17129841.

14. Elmanama AA, El-Aydi I, Al-Reefi M, Ferwana N. Antibiogram of bacterial isolates from clinical specimens during 2018-2020 at Al-Aqsa hospital, Gaza, Palestine. The International Arabic Journal of Antimicrobial Agents. 2022; 12: 10;3823/867.

15. Elmanama AA, Abu Tayyem NES, Sjölander I. Antimicrobial resistance of bacterial isolates from the clinical and hospital environment in Gaza Strip, Palestine: A review over 20-year. The International Arabic Journal of Antimicrobial Agents. 2021; 10.3823/859.

16. Kot B. Antibiotic Resistance Among Uropathogenic *Escherichia coli*. Pol J Microbiol. 2019 Dec;68(4):403-415. doi: 10.33073/pjm-2019-048. Epub 2019 Dec 5. PMID: 31880885; PMCID: PMC7260639.

17. Wang S, Zhao S, Zhou Y, Jin S, Ye T, Pan X. Antibiotic resistance spectrum of *E. coli* strains from different samples and age-grouped patients: a 10-year retrospective study. BMJ Open. 2023 Apr 12;13(4):e067490. doi: 10.1136/bmjopen-2022-067490. PMID: 37045577; PMCID: PMC10106033.

18. Abdel Gawad AM, Ashry WMO, El-Ghannam S, Hussein M, Yousef A. Antibiotic resistance profile of common uropathogens during COVID-19 pandemic: hospital based epidemiologic study. BMC Microbiol. 2023 Jan 25;23(1):28. doi: 10.1186/s12866-023-02773-5. PMID: 36694128; PMCID: PMC9873538.