

Gram negative bacteria related urinary tract infections: spectrum of antimicrobial resistance over 9 years in a University tertiary referral Hospital

Nedbal Carlotta^{ID}, Mahobia Nitin, Browning Dave and Somani Bhaskar Kumar^{ID}

Abstract

Objective: Overuse of antibiotics has led to an increase in antimicrobial resistance (AMR) worldwide, with a negative impact on the healthcare system and the patients. In this context, our study aims to assess the current AMR patterns of urinary tract infections (UTIs) associated to Gram-negative bacteria. Thus, we provide useful information for doctors dealing with prophylactic and therapeutic empiric therapies.

Materials and methods: We retrospectively analysed more than 650,000 urine cultures collected in the Microbiology Department of a referral University Hospital of Southern England from January 2014 to December 2022.

Results: AMR spectra for 164,059 Gram-negative associated (UTIs) were analysed. The lowest percentage of resistance was found for Amikacin (2.30%), Gentamicin (5.89%) and Co-Amoxiclav (10.49%). Over a 9-year time, there was no significant change in resistance to Amikacin (2.04% in 2014 compared to 2.18% in 2022; $p=0.602$) and to Fosfomycin (11.50% in 2014 *versus* 16.65% in 2022; $p=0.577$). Overall, the trend of AMR significantly rose for Cefalexin (17.96–18.42%; $p < 0.0001$), Co-amoxiclav (9.46–12.69%; $p < 0.0001$), Nitrofurantoin (10.20–14.18%; $p < 0.0001$) and Piperacillin/Tazobactam (14.52–18.96%; $p < 0.0001$). Gram-negative resistance spectrum towards Ciprofloxacin (11.83–9.01%; $p < 0.0001$), Gentamicin (6.29–5.26%; $p < 0.0001$), Pivmecillinam (26.88–11.02%; $p < 0.0001$), Trimethoprim (36.72–29.23%; $p < 0.0001$) and Ampicillin/Amoxicillin (65.20–57.99%; $p < 0.0001$) significantly decreased.

Conclusion: Despite the application of national and international guidelines for prophylaxis and treatment of UTIs, the spectrum of resistance for the most common antibiotics is still changing. Clinicians in primary and secondary care must keep that in mind when prescribing antibiotics for suspected UTI and sepsis associated with Gram-negative infections. Up-to-date therapeutic strategies can help implement treatment of UTI, reducing selection of multi-resistant pathogens and providing more accurate care for patients. Future studies will be required to help clinicians and keep the guidelines updated.

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Plain language summary

Gram negative bacteria related urinary tract infections: spectrum of antimicrobial resistance over 9 years in a University tertiary referral Hospital

Despite the application of national and international guidelines for prophylaxis and treatment of urinary tract infections, the spectrum of resistance for the most common antibiotics

is still changing. Clinicians in primary and secondary care must keep that in mind when prescribing antibiotics for suspected urinary tract infections and sepsis associated with gram-negative bacteria. Up-to-date therapeutic strategies can help implement treatment of urinary tract infection, reducing selection of multi-resistant pathogens and providing more accurate care for patients. Future studies will be required to help clinicians and keep the guidelines updated.

Keywords: Gram negative bacteria; urinary tract infections; antimicrobial resistance; antimicrobial sensitivity; antibiotic stewardship

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Introduction

Antimicrobial resistance (AMR) is an increasing global health problem, leading to difficulties in treating complex urinary tract infection (UTI) due to poor sensitivity for the most common antibiotics.^{1,2} The development of antibiotic resistance among common pathogens has been associated to overuse of antibiotics worldwide, with increasing difficulties in empirically treating complex UTIs. The burden of AMR appears particularly heavy when treating UTIs caused by gram-negative bacteria (GNB), microorganisms that have significant clinical importance in hospitals because they can potentially put patients in the intensive care unit, and lead to high morbidity and mortality.³ Especially common in young women, GNB have a range of mechanisms that make them resistant to the action of several antimicrobials routinely used in primary and secondary care. Among those mechanisms, the presence of efflux pumps degradation enzymes, the ability to modify the drug binding site and membrane permeability, and the conformational change of the drug culminating in its inactivation are of note.⁴

Antibiotic guidelines have been developed to facilitate antibiotic stewardship by encouraging the prescription of narrow-spectrum antibiotics, reducing microbial selection and preventing the development of multi-resistant infections related to broad-spectrum antibiotic use.⁵

Antimicrobial stewardship can be described as the strategic selection, dosing, and timing of antimicrobial therapy to achieve the most favourable clinical outcomes in infection treatment or

prevention, whereas minimizing harm to the patient and the development of antibiotic resistance. These programmes play a crucial role in encouraging the judicious utilization of antibiotics, thereby decreasing their consumption and alleviating the associated financial burdens.⁶ To ensure continued efficacy and appropriate antibiotic choice, empirical antimicrobial guidelines require ongoing review of antibiotic susceptibility trends in local high-volume centres. The risk of choosing an inefficient antibiotic and increasing the resistance of pathogens represent a real burden with harmful consequences for patients.⁷ AMR makes it difficult to properly treat complex urinary infections, with the need of longer and more aggressive therapy that can have a negative impact on both the patient and healthcare systems.⁸ Moreover, with an increasing number and frequency of multi-resistant microbial species found in urine cultures, the most common types of antibiotics may not be able to act promptly and prevent the onset of sepsis, especially in the high-risk population.⁹

In the context of a growing interest towards antibiotic stewardship, alongside a larger impact of multi-resistant pathogens on our healthcare system, the importance of updated reports on antibiotic sensitivity and resistance is undeniable. However, these AMR patterns have not been thoroughly reported recently, leaving a gap in clinical guidance that needs to be filled. To this aim, we performed a retrospective analysis of the resistance patterns of GNB towards the most commonly used antibiotics in a high-volume tertiary referral university hospital over the last 9 years. Our study stands in the-objective of

updating on the AMR trends, assessing the current efficacy of antibiotics for empirical treatment and prophylaxis of gram-negative related UTIs.

Materials and methods

Urine culture analysed in the microbiology department at University Hospital Southampton (UHS) from January 2014 to December 2022 were retrospectively collected. Geographically located in southern England, UHS Foundation Trust provides services to some 1.9 million people living in Southampton and south Hampshire as well as nearly 4 million people in central southern England and the Channel Islands. With a high turnover, UHS is one of the largest trusts of the United Kingdom.

A continuous collection of specimens sent for culture to the hospital was performed during the timeline. For each specimen, the origin (primary or secondary care), kind of specimen (mid-stream urine, catheter bag), patient's characteristics (age, sex) and date of collection were recorded. To avoid over-analysis of similar specimens in patients with recurrent UTIs, urine samples from the same patient in a period shorter than 3 months were excluded from the study, including only the first sample. Urine samples were tested for pathogens growth. GNB included in our analysis were (alphabetic order): *Acinetobacter*, *Escherichia coli*, *Haemophilus*, *Klebsiella*, *Morganella*, *Neisseria*, *Salmonella*, *Serratia marcescens*, *Pseudomonas* and *Proteus*.¹⁰ The term Enterobacteriaceae was used to label the growth of multiple pathogens belonging to the family of bacteria.

Given the frequent necessity to treat UTIs with suspected origin from GNB, in accordance with the European Association of Urology (EAU) and The National Institute for Health and Care Excellence (NICE) guidelines, eleven antibiotics were selected for our study. Sensitivity and resistance spectrum towards GNB was reviewed and reported for (alphabetic order): Amikacin, Ampicillin/Amoxicillin, Cefalexin, Ciprofloxacin, Co-Amoxiclav, Fosfomicin, Gentamicin, Nitrofurantoin, Pivmecillinam, Piperacillin/Tazobactam and Trimethoprim.

Urine samples were analysed for pathogen growth primarily with semi-automated Microbiological Antibiotic Sensitivity Testing (MAST) urine culture, European Committee on antimicrobial

susceptibility testing (EUCAST) disc sensitivity was then applied to further test resistant organisms. Our microbiology laboratory is accredited by the United Kingdom Accreditation Service (UKAS), the leading accreditation body in the United Kingdom. The laboratory maintained full accreditation with UKAS during the study period. Most European microbiology laboratories follow EUCAST, including the Microbiology laboratory at UHS. The antibiotic breakpoint tables are updated yearly, starting from EUCAST breakpoint table Version 1.0 in 2010 to EUCAST breakpoint table Version 13.0 for the year 2023. During the study, the most up-to-date version of the EUCAST breakpoint table for the year of antibiotic sensitivity was used for susceptibility testing.

All samples analysed over the 9-years were collected in an excel database (Excel 2021, Microsoft Office Professional Plus 2021, Microsoft Corporation, Inc.) and classified according to positivity and pathogen characteristics. For gram negative bacteria we recorded the antibiotic sensitivity and data were further analysed through XLSTAT (XLSTAT statistical software for Microsoft Excel, Lumivero). For each antibiotic, trend in resistance was calculated using the Cochran-Armitage test for trend carried out at the 5% level to determine any significant change in resistance patterns. Significant positive or negative trends were then discussed during the multi-disciplinary-team meeting to establish protocols and stratify the role of antibiotic management inside our hospital and to formulate regional guidelines.

Our study was registered as an internal audit at UHS (audit registration: UHS7670). It was descriptive and retrospective in nature, and did not influence the clinical management of patients included. Data were strictly anonymised, by assignment of unrecognizable random codes for each specimen.

Results

Over 9 years of analysis, the Microbiology Department collected over 650,000 urine samples. Of them, 164,059 cultures were found positive for GNB growth. According to the origin of the sample, 46,029 were recorded from secondary care, 118,023 from primary care and the rest of the sample were not labelled according to the source. The female:male ratio was 129,347:34,712.

Table 1. Demographic characteristics and source of origin for urine samples provided to the microbiology department during the timeline.

Demographic Characteristics	Female	Male	Total
Type of urine sample			
Catheter urine	6266 (47.31%)	6981 (52.69%)	13,247 (8.07%)
Midstream urine	123,081 (81.61%)	27,731 (18.39%)	150,812 (91.93%)
Source of the sample			
Primary care	97,213 (82.37%)	20,810 (17.63%)	118,023 (71.94%)
Secondary care	32,128 (69.80%)	13,901 (30.20%)	46,029 (28.06%)
Accident and emergency	6517	2881	9398
Day patient	8719	2314	11,033
In-patient	16,779	8662	25,441
Other hospital	113	44	157
Unknown source	6	1	7 (<0.01%)
Total	129,347	34,712	164,059

The collected samples were obtained more frequently from midstream urine (150,812) than from catheters (13,247). Table 1 summarizes demographics and sources of the samples.

For each sample, the spectrum of antimicrobial susceptibility was analysed and reported according to the standard EUCAST Breakpoints-based methods. As the standard antimicrobial susceptibility pattern of analysis changed during the period of inclusion, some antibiotics were tested less frequently than others. The percentage of antimicrobial-resistant bacteria for each subgroup was then calculated according to the total of tested samples for each antibiotic (Figure 1).

Looking at data from 2022, Amikacin ($R=2.18\%$), Gentamycin ($R=5.26\%$) and Ciprofloxacin ($R=9.01\%$) were the antibiotics with the lowest level of resistance patterns from GNB. Pivmecillinam ($R=11.02\%$), Co-Amoxiclav ($R=12.69\%$), Fosfomycin ($R=13.65\%$), Nitrofurantoin ($R=14.18\%$), Cefalexin ($R=18.42\%$) and Piperacillin/Tazobactam ($R=18.96\%$) had an overall percentage of resistance of <20% in 2022, with good clinical applicability. On the contrary, the higher level of AMR in 2022 was

reported for Ampicillin/Amoxicillin ($R=57.99\%$) and Trimethoprim ($R=29.23\%$). Of note, Amikacin, that obtained the lowest resistance spectrum was tested very infrequently, in less than 1% of the samples.

During the 9-year timeline, the trend of resistance did not change significantly for Amikacin (increase: +6.42%; $p=0.602$) and Fosfomycin (decrease: -13.55%; $p=0.577$). A positive trend, with a significant decrease in the percentage of AMR was found towards Pivmecillinam (decrease: -142.92%; $p<0.001$), Ciprofloxacin (decrease: -31.30%; $p<0.001$), Trimethoprim (decrease: -25.62%; $p<0.001$), Gentamycin (decrease: -19.58%; $p<0.001$), Ampicillin/Amoxicillin (decrease: -12.43%; $p<0.001$). With a negative correlation, Nitrofurantoin (increase: +28.07%; $p<0.001$), Co-Amoxiclav (increase: +25.45%; $p<0.001$), Piperacillin/Tazobactam (increase: +23.42%; $p<0.001$) and Cefalexin (increase: +2.50%; $p<0.001$) had an increasing resistance comparing data collected from 2014 and 2022.

According to our results, the ‘golden antibiotics’ with a decreasing trend of resistance and an

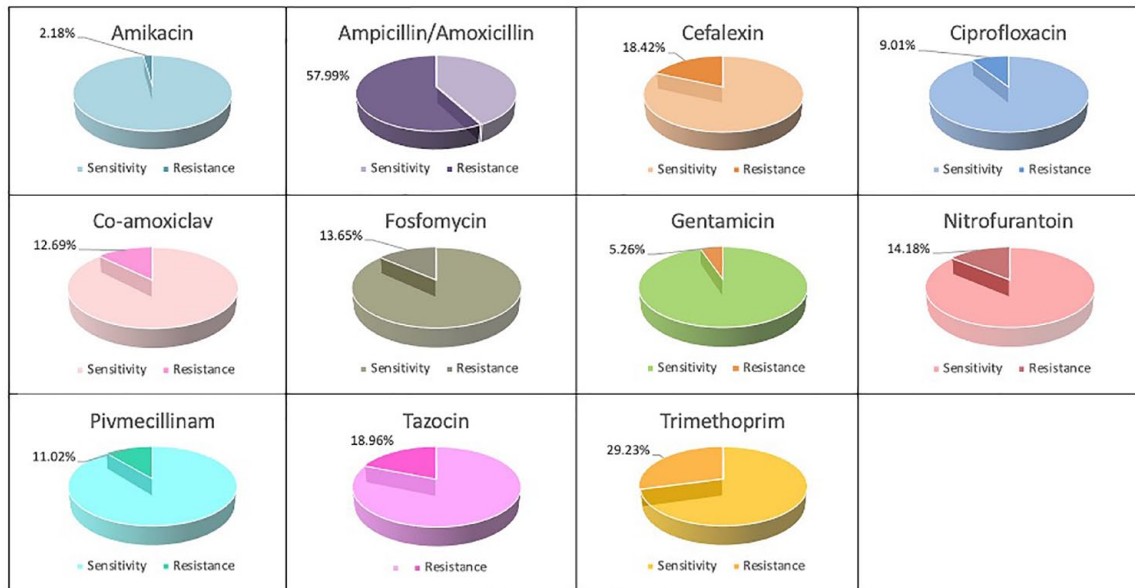


Figure 1. Microbial resistance patterns towards the eleven antibiotics considered in the study is highlighted and marked with the corresponding percentage.

adequate overall percentage of efficacy towards GNB are Ciprofloxacin, Fosfomycin, Gentamicin and Pivmecillinam. Table 2 summarizes the AMR results.

An observational analysis of the different species of GNB found in positive urine cultures was performed. As shown in Table 3, *Escherichia coli* was by far the most common GNB isolated, representing for more than 89% of the total positive samples. *Proteus*, *Pseudomonas* and *Klebsiella* accounted for slightly less than 10%, and the rest of the GNB species were found only occasionally.

Discussion

The increasing trend of AMR is a global healthcare problem, with large impact on primary and secondary care. The excessive and sometimes incorrect utilization of antibiotics as treatment or prophylaxis for UTIs, make up to 20%–50% of all prescribed antibiotics in acute care,¹¹ has led to increasing pattern of resistance towards the most commonly used antibiotics. Hence, the important role of National and International guidelines that would indicate the most appropriate first-line treatments cannot be stressed enough. United Kingdom, United States of America, South Africa, Colombia and Australia have incorporated Antimicrobial Stewardship

programmes in their healthcare systems,¹² involving both infection specialists and other health professionals, including nurses, community health workers and pharmacists, to meet the needs of the global population.

GNB represent an important percentage of bacteria responsible for AMR, due to their ability to escape treatment.¹³ In the United Kingdom, healthcare-associated risk factors for GNB-related UTIs can be addressed as the presence of foreign bodies (i.e. urinary catheters, urinary tracts drainages as stents and nephrostomies, indwelling vascular access devices), history of recent invasive procedures (i.e. endoscopic procedures, prostate biopsy, surgery especially of the gastrointestinal tract), neutropenia, history of hospital admission or antimicrobial therapy in the previous 28 days.¹⁴ When empirically treating UTI in presence of these risk factors, it is important to remind of the possible resistance spectrum of GNB.

The EAU guidelines recommend Ciprofloxacin as the first-line of treatment (parenteral and oral) for pyelonephritis.¹⁵ Our results show that in 2022 the overall percentage of AMR towards Ciprofloxacin is still low at 9%. To add value to the role of this antibiotic, its trend in resistance is decreasing, and that can possibly be related to the

Table 2. Analysis of AMR towards the 11 antibiotics selected, year by year. Significant *p* values for changes in trend.

Year	2014	2015	2016	2017	2018	2019	2020	2021	2022	Total	Trend analysis
Gram-negative (Number/yr)	18,052	18,811	19,114	18,614	18,522	19,655	15,689	17,472	18,130	164,059	
Amikacin resistance	17 (837)	14 (917)	28 (846)	24 (912)	25 (1223)	27 (1502)	28 (1039)	30 (1050)	27 (1238)	220 (9561)	<i>p</i> =0.602
(%)	2.04	1.53%	3.31%	2.63%	2.04%	1.80%	2.69%	2.86%	2.18%	2.30%	+6.42%
Ampicillin/amoxicillin resistance	11,525 (17,676)	12,140 (18,521)	12,496 (18,862)	11,979 (18,406)	11,526 (18,370)	11,375 (19,428)	10,154 (15,594)	11,511 (17,435)	10,494 (18,095)	103,200 (162,387)	<i>p</i> <0.001
(%)	65.20%	65.55%	66.25%	65.08%	62.74%	58.55%	65.11%	66.02%	57.99%	63.55%	-12.43%
Cefalexin resistance	3173 (17,666)	3269 (18,505)	3229 (18,854)	3147 (18,402)	3007 (18,365)	3284 (19,276)	3284 (15,593)	3589 (17,433)	3326 (18,056)	29,308 (16,2153)	<i>p</i> <0.001
(%)	17.96%	17.66%	17.13%	17.10%	16.37%	17.04%	21.06%	20.59%	18.42%	18.07%	+2.50%
Ciprofloxacin resistance	2091 (17,675)	2171 (18,521)	2234 (18,862)	2100 (18,507)	2072 (18,371)	2359 (19,436)	1710 (15,589)	1547 (17,421)	1630 (18,094)	17,914 (162,376)	<i>p</i> <0.001
(%)	11.83%	11.72%	11.84%	11.41%	11.28%	12.14%	10.97%	8.88%	9.01%	11.03%	-31.30%
Co-amoxiclav resistance	1670 (17,662)	1521 (18,430)	1810 (18,705)	1915 (18,273)	1802 (19,356)	2237 (19,356)	1814 (15,483)	1887 (17,369)	2253 (17,755)	16,909 (161,201)	<i>p</i> <0.001
(%)	9.46%	8.25%	9.68%	10.48%	9.92%	11.56%	11.72%	10.86%	12.69%	10.49%	+25.45%
Fosfomycin resistance	86 (555)	94 (640)	48 (333)	62 (819)	71 (821)	92 (1097)	108 (861)	98 (632)	217 (1590)	876 (7357)	<i>p</i> =0.577
(%)	15.50%	14.48%	14.41%	7.57%	8.65%	8.39%	12.54%	15.51%	13.65%	11.91%	-13.55%
Gentamycin resistance	1112 (17,673)	1106 (18,518)	1118 (18,862)	1029 (18,405)	1135 (18,372)	1336 (19,435)	955 (15,597)	821 (17,443)	953 (18,107)	9565 (162,412)	<i>p</i> <0.001
(%)	6.29%	5.97%	5.93%	5.59%	6.18%	6.87%	6.12%	4.71%	5.26%	5.89%	-19.58%
Nitrofurantoin resistance	1803 (17,672)	2043 (18,509)	2106 (18,856)	2066 (18,498)	1995 (18,354)	2166 (19,432)	2218 (15,593)	2505 (17,435)	2564 (18,088)	19,466 (162,337)	<i>p</i> <0.001
(%)	10.20%	11.04%	11.17%	11.23%	10.87%	11.15%	14.22%	14.37%	14.18%	11.99%	+28.07%
Pivmecillinam resistance	175 (651)	95 (652)	134 (685)	131 (763)	135 (810)	147 (1091)	101 (824)	102 (605)	173 (1570)	1193 (7651)	<i>p</i> <0.001
(%)	26.88%	14.57%	19.56%	17.17%	16.67%	13.47%	12.26%	16.86%	11.02%	15.59%	-143.92%
Piperacillin/tazobactam resistance	198 (1364)	127 (1292)	129 (1444)	117 (1375)	206 (1340)	251 (1486)	136 (1011)	167 (958)	225 (1187)	1556 (11,557)	<i>p</i> <0.001
(%)	14.52%	9.12%	8.93%	8.51%	15.37%	16.89%	13.45%	17.43%	18.96%	13.46%	+23.42%
Trimethoprim resistance	6490 (17,672)	6823 (18,513)	6822 (18,856)	6524 (18,401)	6129 (18,364)	6359 (19,425)	5107 (15,590)	5301 (17,435)	5288 (18,090)	54,843 (162,346)	<i>p</i> <0.001
(%)	36.72%	36.86%	36.18%	35.45%	33.38%	32.74%	32.76%	30.40%	29.23%	33.78%	-25.62%

lower usage of Quinolones as first-line treatment of uncomplicated UTIs.¹⁶ Trimethoprim is categorized as another possible option in the oral treatment of uncomplicated pyelonephritis,¹⁷ but

still high percentage of microbial resistance. Being indicated as first-line treatment of UTI in the male population, further analysis would be useful to better assess Trimethoprim efficacy.

Table 3. Prevalence of the different gram-negative species, with the respective increase from 2014 to 2022.

Year	<i>Acinetobacter</i>	<i>Enterobacteriaceae</i>	<i>Escherichia coli</i>	<i>Haemophilus</i>	<i>Klebsiella</i>	<i>Morganella</i>	<i>Neisseria</i>	<i>Salmonella</i>	<i>Serratia marcescens</i>	<i>Pseudomonas</i>	<i>Proteus</i>
2014	33	66	16,280	0	173	14	0	0	6	671	809
2015	21	64	17,081	2	94	18	1	0	7	698	825
2016	28	49	17,336	0	108	13	1	0	11	620	948
2017	24	68	16,758	0	137	9	0	0	12	751	855
2018	13	84	16,752	0	216	15	0	1	16	607	818
2019	15	101	17,506	0	366	38	0	0	21	703	905
2020	23	76	13,655	0	281	39	0	0	36	728	851
2021	20	91	15,493	0	264	51	0	1	34	762	756
2022	18	135	16,006	0	282	55	1	0	36	849	748
Total	195	734	146,867	2	1921	252	3	2	179	6389	7515
Percent of total GNB	-83.33%	51.11%	-1.71%	0%	38.65%	74.55%	100.00%	0%	83.33%	20.97%	-8.16%
Increase from 2014 to 2022	0.119%	0.447%	89.521%	0.001%	1.171%	0.154%	0.002%	0.001%	0.109%	3.894%	4.581%

Piperacillin/Tazobactam and Gentamycin are considered as a second-line parenteral treatment of pyelonephritis and as a first option for the management of urosepsis¹⁸ and they both show a very good sensitivity pattern in our analysis. Piperacillin/Tazobactam shows an increasing trend of resistance, with a high mean level of GNB-related resistance. In the next years, it will be of importance to continue monitoring its trend and the overall percentage of resistance. Gentamycin is still showing a good pattern of resistance with a decreasing trend, characteristics that underscore the reliability of this antibiotic for the treatment of hospitalized patients.

Fosfomycin and Nitrofurantoin both represents good options for treating uncomplicated cystitis in women, with a low level of overall resistance.^{19,20} The rising trend of microbial resistance showed towards Nitrofurantoin might be related to the increasing number of prescriptions in the past few years.²¹ Being an efficient and low-risk antibiotic, its application has been understandably broad, but it may at the same time lead to a wider resistance pattern from GNB.²²

According to EAU guidelines, Co-amoxiclav is usually limited as association therapy (combination of two or more different antibiotics)

or non-empirical treatment according to urine culture sensitivity pattern.¹⁷ In the NICE guidelines instead, Co-amoxiclav represents the first-line antibiotic for parenteral treatment of pyelonephritis in non-pregnant women and men aged 16 years and over.²³ Our study shows that its resistance spectrum is still low, with a slow increasing trend that is expected to keep Co-amoxiclav in a good-efficiency range for at least a few more years. This pattern reflects the know efficacy of Co-amoxiclav in the United Kingdom population.

Our study reports on the trend of the population of Hampshire, covering the Southern Regions of the United Kingdom. Analysing the massive amount of urine cultures collected by our university hospital, we were able to provide a high-volume study with hundreds of thousands of GNB-positive samples, reflecting the current situation in clinical practice. The role of antibiotic stewardship should be fully embraced and incorporated in primary and secondary care.²⁴ The first choice of treatment, often provided by general practitioners, or physicians in care home and community care, is at the front line for providing the most adequate type of antibiotic in the suspect of a clinically relevant infection of the urinary tract.²⁵ Overtreatment of asymptomatic

bacteriuria could be harmful for patient without risk factors and moreover in patients with recurrent UTIs, leading to higher rates of AMR.^{26,27} When treating a clinically significant infection, it is important to consider common resistance patterns of the most frequently responsible bacteria among the specific population, for example patients with risk factors as the presence of indwelling catheters, ureteric stents, recent surgical intervention or antibiotic therapy.

Although our study provides new and updated information on changes and trends in AMR, analysing a very large number of urine cultures from a wide cohort of patients, there are some limitations that needs to be addressed. Firstly, the retrospective nature of the study, with the consequent missing data on patient's characteristics that could have been useful. Some additional information, such as the presence of risks factors that might influence the growth of resistant GNB have not been retrieved for all patients, and therefore not included in our analysis. Further studies on our cohort may be able to fill the gaps and provide insight on resistance patterns in specific population. Moreover, we are aware of the possible bias given by the fact that a large number of patients with uncomplicated UTI can be successfully treated with empiric therapy in the community. Cases not requiring urine culture to identify the pathogen and provide a sensitivity spectrum have not been included in our analysis. This represents a limitation of the study, as the exact prevalence of GBN-related UTIs might be slightly different in the whole population. Nevertheless, given the large cohort and amount of resistance spectra included in the analysis, we believe it to be reflective of the current situation in southern England.

With this fist analysis on our 9-year data collection, we aim to provide the widest picture of the current situation of AMR patterns for GNB-related UTIs. Further analysis for different subgroups will be helpful, pointing out the differences related to epidemiologic characteristics and clinical settings. We also aim to keep updating on the changing trend of AMRs, in order to provide scientific evidence that could corroborate local guidelines of treatment.

Conclusion

Despite the application of national and international guidelines for prophylaxis and treatment of UTIs, the spectrum of resistance for most

common antibiotics is still changing. Clinicians in primary and secondary care must keep that in mind when prescribing antibiotics for suspected UTI and sepsis associated with Gram-negative infections. Up-to-date therapeutic strategies can help implement treatment of UTI, reducing prevalence of multi-resistant pathogens and providing more accurate care for patients. As the trend in sensitivity for each commonly used antibiotic is continuously changing, our study provides an up-to-date review of the current situation, helping clinicians choosing the most appropriate class of antibiotics in view of the frequent resistance patterns. Future studies will be required to maintain national and international guidelines, and clinicians updated.

Declarations

Ethics approval and consent to participate

Not applicable. Our study is an internal audit and only anonymised data were used (audit registration number UHS7670).

Consent for publication

Not applicable.

Author contributions

Nedbal Carlotta: Conceptualization; Data curation; Formal analysis; Project administration; Resources; Writing – original draft.

Mahobia Nitin: Conceptualization; Data curation; Methodology; Resources; Supervision; Writing – review & editing.

Browning Dave: Conceptualization; Data curation; Formal analysis; Methodology; Software; Validation; Writing – review & editing.

Somani Bhaskar Kumar: Conceptualization; Data curation; Project administration; Resources; Supervision; Validation; Visualization; Writing – review & editing.

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Competing interests


The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets generated and analyzed in the current study are available from the corresponding author at reasonable request.

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References

1. ECDC. Antimicrobial resistance in the EU/EEA (EARS-Net) AER for 2021 [Internet], <https://atlas.ecdc.europa.eu/>
2. Warren JW, Abrutyn E, Hebel JR, *et al.* GUIDELINES FROM THE INFECTIOUS DISEASES SOCIETY OF AMERICA Guidelines for Antimicrobial Treatment of Uncomplicated Acute Bacterial Cystitis and Acute Pyelonephritis in Women [Internet], Clinical Infectious Diseases, Vol. 29, <http://www.idsociety.org> (1999)
3. Ak O, Batirel A, Ozer S, *et al.* Nosocomial infections and risk factors in the intensive care unit of a teaching and research hospital: a prospective cohort study. *Med Sci Monit* 2011; 17: PH29–PH34.
4. Breijyeh Z, Jubeh B and Karaman R. Resistance of gram-negative bacteria to current antibacterial agents and approaches to resolve it. *Molecules* 2020; 25: 1340.
5. Cefai C, Lewis T, Charani E, *et al.* *Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use.* NICE Guidelines, England: Public Health England. 2015.
6. Zirpe K, Kapse US, Gurav SK, *et al.* Impact of an antimicrobial stewardship program on broad spectrum antibiotics consumption in the intensive care setting. *Ind J Crit Care Med* 2023; 27: 737–742.
7. Bell BG, Schellevis F, Stobberingh E, *et al.* A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance [Internet], <http://www.biomedcentral.com/1471-2334/14/13> (2014).
8. Ong A, Mahobia N, Browning D, *et al.* Trends in antibiotic resistance for over 700,000 *Escherichia coli* positive urinary tract infections over six years (2014–2019) from a university teaching hospital. *Cent Eur J Urol* 2021; 74: 249–254.
9. Teoh P, Basarab A, Pickering R, *et al.* Changing trends in antibiotic resistance for urinary *E. coli* infections over five years in a university hospital. *J Clin Urol* 2014; 7: 116–120.
10. Oliveira J and Reygaert W. Gram-Negative Bacteria, StatPearls Publishing, <https://www.ncbi.nlm.nih.gov/books/NBK538213/> (2022, cited 13 July 2023.)
11. Hulscher M, Grol R and van der Meer J. Antibiotic prescribing in hospitals: a social and behavioural scientific approach. *Lancet Infect Dis* 2010; 10: 167–175.
12. Goff DA, Kullar R, Goldstein EJC, *et al.* A global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail. *Lancet Infect Dis* 2017; 17: e56–e63.
13. Carter C, Hutchison A, Rudder S, *et al.* Uropathogenic *Escherichia coli* population structure and antimicrobial susceptibility in Norfolk, UK. *J Antimicrob Chem* 2023; 78: 2028–2036.
14. Mitchell E, Pearce MS and Roberts A. Gram-negative bloodstream infections and sepsis: risk factors, screening tools and surveillance. *Brit Med Bull* 2019; 132: 5–15.
15. Catrall JWS, Robinson AV and Kirby A. A systematic review of randomised clinical trials for oral antibiotic treatment of acute pyelonephritis. *Eur J Clin Microbiol Infect Dis* 2018; 37: 2285–2291.
16. Hooton TM. Uncomplicated urinary tract infection. *New Engl J Med* 2012; 366: 1028–1037.
17. Gupta K, Hooton TM, Naber KG, *et al.* International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011; 52: e103–e120.
18. Dellinger RP, Levy MM, Rhodes A, *et al.* Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 2013; 39: 165–228.
19. Lecomte F and Allaert FA. Le traitement monodose de la cystite par fosfomycine trométamol (Monuril®) : analyse de 15 essais comparatifs portant sur 2048 malades. *Med Mal Infect* 1996; 26: 338–343.
20. Ibrahim Z, Behiry A, Attia O, *et al.* Evaluation of in vitro effect of Fosfomycin on resistant Gram-negative pathogens in urinary tract infection. *Microbes Infect Dis* 2022; 3: 339–347.

21. Gupta K, Hooton T, Roberts P, *et al.* Short-course nitrofurantoin for the treatment of acute uncomplicated cystitis in women. *Arch Intern Med* 2007; 167: 2207.
22. Price JR, Guran LA, Gregory WT, *et al.* Nitrofurantoin vs other prophylactic agents in reducing recurrent urinary tract infections in adult women: a systematic review and meta-analysis. *Am J Obstetr Gynecol* 2016; 215: 548–560.
23. NICE guideline. *Pyelonephritis (acute): antimicrobial prescribing*. NICE guidelines, England: Public Health England. 2018, pp. 17–24.
24. Satlin MJ, van Duin D, Tamma PD, *et al.* Priorities and progress in gram-negative bacterial infection research by the antibacterial resistance leadership group. *Clin Infect Dis* 2023; 77(Supplement_4): S305–S313.
25. Ahmed H, Davies F, Francis N, *et al.* Long-term antibiotics for prevention of recurrent urinary tract infection in older adults: systematic review and meta-analysis of randomised trials. *BMJ Open* 2017; 7: e015233.
26. Köves B, Cai T, Veeratterapillay R, *et al.* Benefits and harms of treatment of asymptomatic bacteriuria: a systematic review and meta-analysis by the European Association of Urology Urological Infection Guidelines Panel. *Eur Urol* 2017; 72: 865–868.
27. Cotton E, Geraghty R, Umranikar S, *et al.* Prevalence of asymptomatic bacteriuria among pregnant women and changes in antibiotic resistance: a 6-year retrospective study. *J Clin Urol* 2024; 17: 9–15.

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