Antimicrobial Resistance and Infection Control

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Temporal trends in antimicrobial resistance of medically important pathogens on Curaçao

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Abstract

Background The Caribbean lacks recent comprehensive antimicrobial resistance data to inform clinicians and decision-makers. This study aims to provide a snapshot of susceptibility trends for pathogens on Curaçao, an island in the southern Caribbean.

Methods We analyzed susceptibility data of bacterial pathogens isolated from samples submitted from patients attending general practitioners, outpatient clinics and those who were hospitalized between January 2018 and December 2023. Samples originating from blood, urine, genital tract, soft tissue, and lungs were included. Susceptibility testing was performed by VITEK2 according using the European Committee on Antimicrobial Susceptibility Testing criteria.

Results In total, 13,528 patients contributed to 22,876 first isolates. Of all infections in adults with *Staphylococcus aureus*, 14% (95% confidence interval 10–18%) were methicillin-resistant *S. aureus* (MRSA) in blood, and up to 27% (20–35%) in soft-tissue cultures. For *Escherichia coli* and *Klebsiella pneumoniae*, resistance levels were up to 27% (95% CI 22–32%) for cefuroxime and up to 18% (95% CI 18–28%) for third-generation cephalosporins. The addition of gentamicin to empirical therapy with cefuroxime increased coverage only moderately, especially in *K. pneumoniae* (16%, 95% CI 12–20%). Resistance to amoxicillin-clavulanic acid was up to 47% (95% CI 43–50%), to ciprofloxacin 34% (95% CI 31–37%) and to cotrimoxazole 37% (95% CI 34–39) in urine cultures from outpatients. In contrast, low levels of carbapenem resistant Enterobacterales and *Pseudomonas aeruginosa* were observed.

Conclusions Antimicrobial resistance is high and widespread across several important antibiotic classes. The widespread occurrence of MRSA and resistance to third-generation cephalosporins highlights the importance of identifying risk factors, enabling more effective guidance for antimicrobial stewardship.

Introduction

The World Health Organization (WHO) has recently identified antimicrobial resistance (AMR) as a significant global health threat [1]. According to a recent study, an estimated 5 million individuals experienced an infection, resulting in death, caused by bacterial AMR in 2019 [2]. Out of these cases, 1.27 million deaths were directly attributed to AMR.

Curaçao is a small Caribbean island covering about 444 square kilometers. It has approximately 160,000 residents and attracts roughly half a million tourists annually. The ethnic composition includes 70–80% Afro-Caribbean, 15–20% mixed-race, 5–10% of Dutch and European descent, and a small but growing percentage of Latin Americans (around 5%, primarily Venezuelans and Colombians). Approximately 90% of the population lives in urban areas, primarily concentrated in the capital city, Willemstad. Healthcare is accessible, with approximately

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90 general practitioners, one teaching hospital and a smaller hospital. Patients in need of more complex interventions are sent abroad (mainly Colombia). A basic healthcare package is funded through a mandatory health insurance system and covers a wide range of medical services. As part of the Kingdom of the Netherlands, Curaçao's healthcare system shares similarities with the Dutch system; for example, many medical specialists are trained in the Netherlands.

There is a limited availability of local data concerning AMR on Curaçao. A 2015 analysis examining resistance trends noted significant rises in methicillin-resistant *Staphylococcus aureus* (MRSA) and *Klebsiella pneumoniae* carbapenemase cases [3], but since then no other data were generated.

The objective of this study is to present susceptibility trends over the past six years for bacterial pathogens in Curaçao, addressing the existing gap in antimicrobial resistance data, and comparing it with data from the Netherlands, since most local antibiotic treatment guidelines are based on Dutch practice.

Methods

The study was approved by the Institutional Review Board of the Curaçao Medical Centre (CMC) with a waiver of consent (METC20240621-01). Data was sourced from the laboratory information system of the Analytical Diagnostic Centre (ADC) spanning from January 1, 2018 to December 31, 2023. The ADC, serving as the national laboratory of Curaçao, is exclusive to the CMC, a 300-bed teaching hospital (up to 2019 the hospital was at a nearby location and named SEHOS). The majority of nationwide cultures from outpatient clinics and hospitalized patients were included. Additionally, the ADC offers its services to a representative sample of general practitioners (GP). The island has three microbiological laboratories that serve roughly equal numbers of GPs. Susceptibility testing was performed using the VITEK2 antimicrobial susceptibility testing, with a minority performed by e-test or disk diffusion. Breakpoints were set using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria [4]. The first isolate per patient per year was included to mitigate bias from repeated sampling. Relevant diagnostic isolates were included, originating from blood, urine, genital tract (vaginal and cervical cultures), tissue or pus (including wounds but no superficial skin cultures), or pulmonary tract; screening cultures (e.g. for multi-resistance) were excluded. Standardized protocols were used for culturing.

We focused on bacteria mentioned in the WHO priority list e.g. third-generation cephalosporins and meropenem resistant Enterobacterales, carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii,* ampicillin-resistant *Haemophilus influenzae,* third-generation cephalosporin and/or fluoroquinolone-resistant *Neisseria gonorrhoeae,* methicillin-resistant *Staphylococcus aureus,* macrolide-resistant *Streptococcus pneumoniae* and group A streptococci, penicillin-resistant group B streptococci and vancomycin-resistant *Enterococcus faecium* [5]. We only included other species if more than 30 isolates were available to enhance robustness.

The Dutch NethMap, an annual report on antibiotic usage and trends in AMR issued by the Dutch Centre for Disease Control (RIVM) was used to compare resistance levels [6]. In these reports, AMR trends are tracked through the national surveillance system (ISIS-AR), utilizing routine antibiotic susceptibility testing data from microbiology laboratories across the Netherlands [7].

Data were analyzed using the R-package AMR [8]. We quantified the effects of age, insurance (as a proxy for residency), gender, and the submitting health care specialty on the resistance of *E. coli* in urine cultures for each tested antibiotic separately, and on the occurrence of MRSA in blood and soft tissue cultures in univariable analyses. We excluded insurance status from the multivariable logistic regression models since it was not significantly associated with resistance in the univariable analyses ($p > 0.2$).

Results

In total, 13,528 patients contributed to 22,876 first isolates, of which 4021 isolates were from materials collected by the GP, 3257 from outpatients, and 15,598 from hospitalized patients. Table 1 shows the distribution of isolates stratified by source of infection and age and Table 2 gives the numbers of pathogens by source of infection.

Tables 3 and 4 show the resistance levels of gram-negative and gram-positive bacteria for commonly used antibiotics. For *E. coli*, resistance to cefuroxime in adult blood isolates was 18% (95% confidence interval 15–22%) and to third-generation cephalosporines (mainly extended spectrum beta-lactamases, ESBL) was 13% (95% CI 10–15%). For *E. coli* urinary tract infections, resistance to cefuroxime ranged from 11% (95% CI 10–13%) to 17% (95% CI 15–19%) in isolates from GPs and admitted patients, respectively. Resistance to third-generation cephalosporines in urine isolates ranged from 6% (95% CI 5–7%) to 11% (95% CI 9–12%), to amoxicillin-clavulanic acid 40% (95% CI 37–43%) to 47% (95% CI 44–50%), to ciprofloxacin 25% (95% CI 23–28%) to 35% (95% CI 32–38%), to cotrimoxazole 27% (95% CI 25–30%) to 37% (95% CI 34–41%), and to all of the oral options amoxicillin-clavulanic acid, ciprofloxacin and cotrimoxazole 8% (95% CI 8–10%) to 16% (95% CI

Table 1 Number of isolates stratified by source of infection, patient category and age

Source	Blood	Genital tract	Respiratory tract	Soft tissue	Urine	Total
Adults						
General practioner	29	535	24	472	2670	3730
Outpatients	47	250	34	1123	1650	3104
Admitted	3273	687	1388	4588	4509	14,445
Total	3349	1472	1446	6183	8829	21,279
Children						
General practioner	0	29	43	87	132	291
Outpatients	2	8	3	76	64	153
Admitted	396	15	72	254	416	1153
Total	398	52	118	417	612	1597

Table 2 Overview of bacterial species stratified by source of infection

	Blood	Genital tract	Respiratory tract	Soft tissue	Urine	Total
E.coli	611	84	92	612	4115	5514
K.pneumoniae	340	24	216	383	1421	2384
P.mirabilis	72	8	38	472	552	1142
Other Enterobacterales	354	17	269	1183	978	2801
P.aeruginosa	126	7	243	961	414	1751
A.baumannii	36	2	39	64	73	214
Other gram negatives	81	18	144	189	49	481
S.aureus	365	209	233	1284	128	2219
S.pneumoniae	75	0	26	19	2	122
S.pyogenes	24	17	11	65	7	124
S.agalactiae	72	892	17	323	440	1744
E.faecium	12	0	0	21	19	52
Other gram positives	1509	55	40	709	854	3167
Other microorganisms	70	191	196	315	389	1161
Total	3747	1524	1564	6600	9441	22,876

14–19%) with the highest levels of resistance in cultures from outpatients. Urinary tract infections with *E. coli* had low levels of resistance to nitrofurantoin and fosfomycin, with resistance levels below 4%. *K. pneumoniae* was more resistant to cefuroxime and ceftriaxone than *E. coli* in blood cultures: 27% (95% CI 22–32%) and 18% (95% CI 18–28%), respectively. Resistance to oral medication was lower than in E. coli with levels up to 28% (95% CI 25–31%), 23 (95% CI 20–26%) and 26% (95% CI 23–29%) for amoxicillin-clavulanic acid, ciprofloxacin, and cotrimoxazole, respectively.

Empirical combination therapy of gentamicin with cefuroxime in blood isolates with *E. coli* and *K. pneumoniae* was less effective compared to the Netherlands: resistance to this combination was 16% (95% CI 12–20%), compared to ~ 3% in the Netherlands. This moderate effect of gentamicin might be caused by the fact that the resistance of gentamicin alone was 18% (95% CI 12–22%) which is markedly higher than in the Netherlands (typically less than 5%).

Overall, Enterobacterales in blood cultures were resistant to cefuroxime, ceftriaxone, cefuroxime-gentamicin, or meropenem in 34% (95% CI 32–37%), 17% (95% CI 15–19%), 13% (95% CI 11–14%), and 1% (95% CI 0–1%) of cases, respectively. Resistances to oral medications were 48% (95% CI 45–51%), 21 (95% CI 19–23%) and 24% (95% CI 22–27%) for amoxicillin-clavulanic acid, ciprofloxacin, and cotrimoxazole, respectively.

Figure 1 show the trends in resistance for *E. coli* and *K. pneumoniae* in samples collected by the GP, outpatients, hospitalized patients and blood isolates from 2018–2023. For most bug-drug combinations, the resistance was higher on Curaçao compared to the Netherlands for all years. In the Netherlands, a tentative trend to decreased

Table 3 Resistance in selected Enterobacterales and non-fermenters

	Number of isolate (n)	Amoxicillin	Amoxicillin/ clavulanic acid	Piperacillin/ tazobactam	Cefuroxime	Ceftriaxone	Ceftazidime	Meropenem	Gentamicin	Ciprofloxacin	Trimethoprim/ sulfamethoxazole	Nitrofurantoin	Amoxicillin/ clavulanic acid plus gentamicin	Cefuroxime plus gentamicin	MDOT*
Adults															
C. freundii	88	100	100	30	100	33	31	0	15	24	24	–	15	14	13
C. koseri	311	100	8	7	20	3	2	0	2	1	3	–	1	1	0
E. cloacae	616	100	99	33	100	29	28	1	7	11	12	–	7	7	6
E. coli	5144	52	43	7	16	10	9	0	12	27	31	2	11	5	10
K. aerogenes	158	100	100	36	100	32	31	1	5	4	4	–	5	5	3
K. oxytoca	61	100	15	11	11	10	8	3	5	7	8	–	3	3	3
K. pneumoniae	2238	100	27	15	22	18	18	0	14	21	22	–	13	12	14
K. varicola	39	100	10	5	13	10	10	0	8	10	10	–	8	8	8
M. morganii	493	100	100	21	100	28	19	0	9	18	19	–	9	9	10
P. hauseri	61	98	46	0	97	33	2	0	2	2	8	–	2	0	0
P. mirabilis	1083	25	13	3	7	5	3	0	9	7	13	–	4	3	4
P. rettgeri	62	100	100	20	100	5	0	0	0	3	8	–	0	0	2
P. stuartii	175	100	100	7	100	2	1	0	74	3	7	–	74	41	2
S. marcescens	251	100	100	29	100	16	7	2	6	9	4	–	6	6	4
Salmonella spp	44	41	36	0	–	0	0	0	–	–	0	–	36	–	0
A. baumannii	195	–	–	9	–	–	2	0	3	11	9	–	–	–	–
P. aeruginosa	1668	–	–	9	–	–	4	3	7	7	–	–	–	–	–
Children															
E. cloacae	36	100	100	14	100	11	11	0	3	0	0	–	3	3	0
E. coli	370	51	44	8	9	6	6	0	11	14	32	1	10	2	4
K. pneumoniae	146	100	11	3	1	1	1	0	1	2	8	–	1	0	0
P. mirabilis	59	14	7	0	5	3	2	0	5	5	7	–	3	2	0
P. aeruginosa	83	–	–	1	–	–	0	0	4	0	–	–	–	–	–

Average resistance levels in all sources of infection over 2018–2023. Species with more than 30 isolates were included. No value means that there were no European Committee on Antimicrobial Sensitivity Testing (EUCAST) breakpoints available for this bug-drug combination or that the antibiotic was not measured for other reasons (e.g. too few measurements)

MDOT, multidrug resistance to oral therapy; defined as resistance to all of the following oral agents: amoxicillin-clavulanic acid (according to breakpoint for indications other than uncomplicated urinary tract infection), ciprofloxacin, and co-trimoxazole

Table 4 Resistance in selected gram-positive bacteria

	Isolates (n)	Amoxicillin	Flucloxacillin	Gentamicin	Ciprofloxacin	Erytromycine	Clindamycin	Trimethoprim/ sulfamethoxazole	Tetracycline
Adults									
S. pyogenes	93	0	–	–	–	14	12	0	32
S. agalactiae	1684	0	–	–	–	15	14	0	79
S. aureus	2025	–	15	2	7	21	11	1	7
S. aureus (methicillin resistant)	294	–	100	5	17	52	17	3	31
S. pneumoniae	103	1	–	–	–	21	12	11	23
Children									
S. pyogenes	31	0	–	–	–	3	3	–	–
S. agalactiae	60	0	–	–	–	11	9	0	88
S. aureus	194	–	16	1	1	23	11	1	5
S. aureus (methicillin resistant)	31		100	5	15	17	13	3	27

Average resistance levels over 2018–2023. Micro-organisms with more than 30 isolates were included. No value means that there were no European Committee on Antimicrobial Sensitivity Testing (EUCAST) breakpoints available for this bug-drug combination or that the antibiotic was not measured for other reasons (e.g. too few measurements)

resistance is seen for some antibiotics (for instance cotrimoxazole and ciprofloxacin), however, no clear (clinically significant) trends were present on Curaçao during this time-frame.

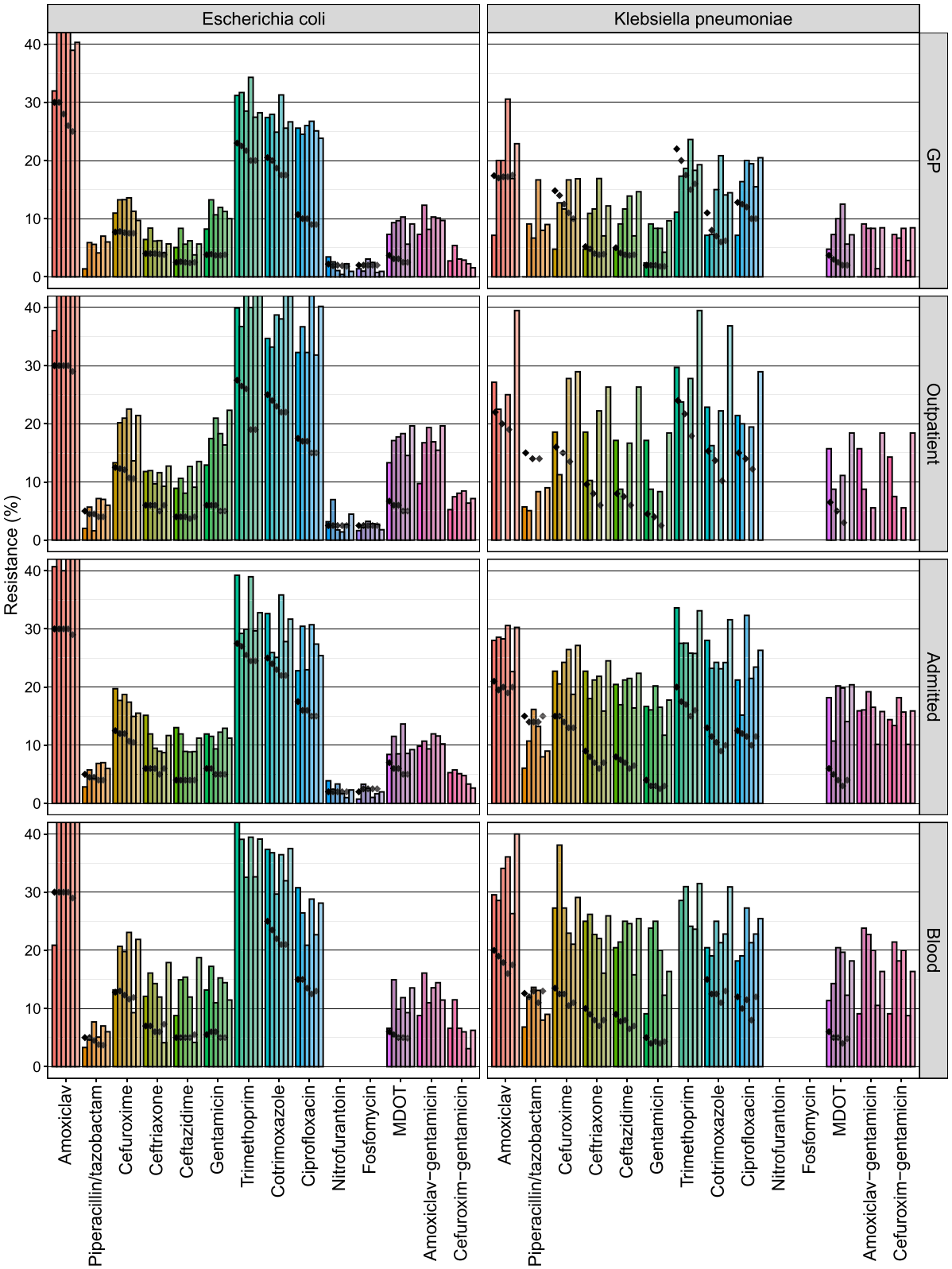
Figure 2 shows the effect of age and Fig. 3 of gender on *E.coli* resistance in urine cultures. Age was significantly associated with resistance for most antibiotics (e.g. ciprofloxacin ranged from 12% (95% CI 9–15%) in patients up to 30 years to 32% (95% CI 30–34%) in patients over 60 years; OR 1.01 per year increase, 95% CI 1.00–1.02, Table 5). Male gender was associated with higher resistance rates for almost all antibiotics, especially for ciprofloxacin (male: 38%, 95% CI 35–40%, female: 22%, 95% CI 20–23%). Urine cultures from admitted patients and, especially, outpatients were significantly more resistant to several antibiotics compared to cultures from GP patients.

For *P. aeruginosa*, resistance to meropenem in blood isolates was 4% (95% CI 1–9%) which is similar to the Netherlands. Resistance to piperacillin-tazobactam (13%, 95% CI 7–20%) was higher compared to the Netherlands (up to 6%). Ceftazidime resistance was moderately higher at 8% (95% CI 4–15%) compared to up to 4% in the Netherlands, and ciprofloxacin was in a similar range at 4% (1–9%, Netherlands 8%). No meropenem-resistant *A. baumannii* was cultured (0 of 195 isolates). Ampicillin resistance occurred in 5 of 22 (23%) and amoxicillin-clavulanic acid resistance in 2 of 19 (11%) of *H. influenzae* isolates. *N. gonorrhoeae* was not measured resistant to third-generation cephalosporin (28 isolates) but in 5 of 27 (19%) cases for fluoroquinolones.

The proportion of MRSA among infections with *S. aureus* was 14% (95% CI 10–18%) in blood cultures and up to 27% (20–35%) in tissue cultures sent in by the GPs (Fig. 4). This is significantly higher than MRSA levels in the Netherlands which are less than 2%. Table 4 shows the co-resistance levels of *S. aureus* isolates to several other antibiotics, stratified by flucloxacillin sensitive and

(See figure on next page.)

Fig. 1 Trends in antibiotic resistance for *E. coli* and *K. pneumoniae* in blood and urine cultures. Trends in antibiotic resistance (from left to right 2018 to 2023) among blood and urine isolates of *Escherichia coli* and *K. pneumoniae* stratified by adult general practitioners' patients, outpatients, and admitted patients. The black dots indicate the Dutch average (data available until 2022). For *Klebsiella pneumoniae* data for some years is not presented since the number of isolates for those years were < 30. MDOT, resistance to all of the following oral agents: amoxicillin-clavulanic acid (according to breakpoint for indications other than uncomplicated urinary tract infection), ciprofloxacin, and co-trimoxazole



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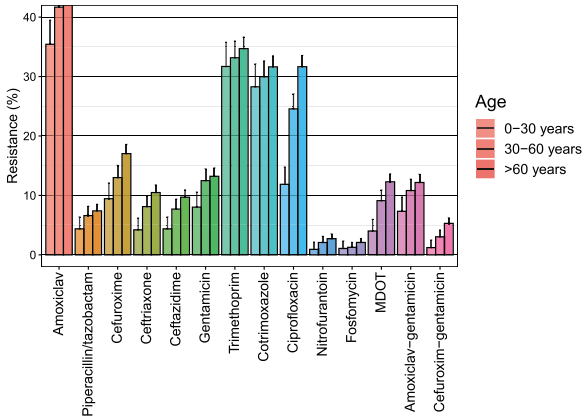

Fig. 2 Effect of age on *E.coli* resistance in urine cultures. Antibiotic resistance levels in urine isolates of *Escherichia coli* stratified by 3 age groups. MDOT, resistance to all of the following oral agents: amoxicillin-clavulanic acid (according to breakpoint for indications other than uncomplicated urinary tract infection), ciprofloxacin, and co-trimoxazole

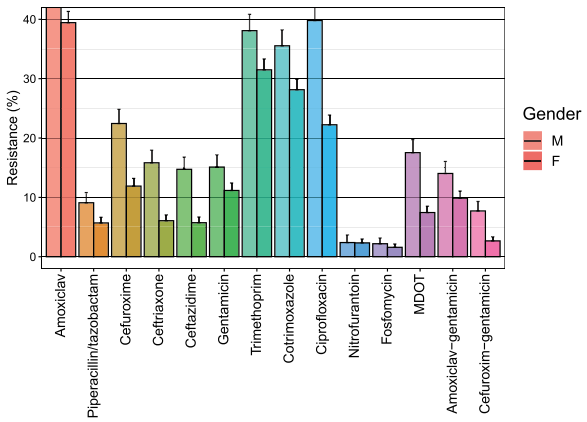

Fig. 3 Effect of gender on *E.coli* resistance in urine cultures. Antibiotic resistance levels in urine isolates of *Escherichia coli* stratified by gender. MDOT, resistance to all of the following oral agents: amoxicillin-clavulanic acid (according to breakpoint for indications other than uncomplicated urinary tract infection), ciprofloxacin, and co-trimoxazole

resistant isolates. Age had an inverse effect on the probability of having a blood culture positive for MRSA, with 25%, 16%, and 11% of MRSA in cultures of patients aged 0–30, 30–60, and > 60 years, respectively (OR 0.99, 95% CI 0.97–0.99, p = 0.035, Table 5). There was no effect of age or gender on culturing MRSA in soft tissue but a significant association with the submitting specialty (OR 1.67, 95% CI 1.12–2.44 for cultures from GP patients versus admitted patients).

We found 14% (95% CI 8–23%) of isolates of group A streptococci resistant to the macrolide erythromycin, no penicillin resistant group B streptococci (0 of 1684 isolates), 21% (95% CI 13–30%) of isolates of *S. pneumoniae* resistant to erythromycin, and no cases of vancomycin resistant *E. faecium* (0 of 53 isolates).

Discussion

Antimicrobial resistance was higher and more widespread across several important antibiotic classes as compared to the Netherlands. Notably, the prevalences of MRSA and ESBL were significantly higher. This poses a potential challenge, given that predominantly Dutch treatment guidelines are employed, and they may not necessarily align with the local situation, possibly leading to suboptimal treatment strategies.

Fourteen percent of *S. aureus* infections in blood was MRSA and up to 27% in tissue cultures, which is significantly higher than the approximately 2% prevalence observed in the Netherlands. Additionally, the resistance patterns of Enterobacterales against various antibiotic classes were elevated. In blood isolates of *E. coli* and *K. pneumoniae*, resistance to third-generation cephalosporins, gentamicin, ciprofloxacin, and cotrimoxazole were markedly higher compared to corresponding rates in the Netherlands. The island of Aruba, with demographic and healthcare similarities to Curaçao, recently published AMR data in the CarMap [9]. Aruba also reported elevated prevalences of MRSA at 17%, but only moderately high ESBL levels in *E. coli* (7%) and *K. pneumoniae* (7%), along with low prevalences of CPE and VRE. Age and male gender were significantly associated to resistance for most antibiotics in *E. coli* urine cultures. One potential reason for this could be the increasing use of these antibiotics in males and older patients, though we lack specific data to support this. The higher resistance of *E.coli* in urine cultures from hospitalized patients and particularly outpatients compared to GPs might also reflect the increasing antibiotic use in these patient categories. Conversely, age showed an inverse association with MRSA in blood cultures; the reasons for this remains elusive. In soft tissue cultures age was not significantly associated to resistance, but cultures from GPs were more likely to be positive for MRSA than from hospitalized patients, which might indicate a source of MRSA in the community or a conservative diagnostic stewardship of GPs.

The efficacy of several hypothetical empirical therapies for septic patients were investigated. As expected, the addition of an aminoglycoside to cephalosporins increased empirical coverage, although not to the same extend as in the Netherlands, because of a higher baseline resistance to gentamicin. However, the EUCAST advises to use aminoglycosides only in combination with other active therapy [10], which is most likely not the case with empirical therapy. Unfortunately, data on patient

Table 5 Risk factors for resistance of *E. coli* in urine and MRSA in blood or soft tissue

Model	Age	Female gender	Hospitalized versus GP	Outpatient versus GP
Amoxicillin/clavulanic acid	1.004 (1.002–1.007)**	0.720 (0.630–0.823)***	1.072 (0.932–1.233)	1.289 (1.086–1.529)**
Piperacillin/tazobactam	1.005 (1.000–1.011)	0.688 (0.536–0.887)**	1.366 (1.036–1.810)*	0.988 (0.686–1.410)
Cefuroxime	1.008 (1.004–1.012)***	0.544 (0.455–0.649)***	1.355 (1.107–1.662)**	1.437 (1.129–1.827)**
Ceftriaxone	1.008 (1.003–1.013)**	0.418 (0.335–0.522)***	1.648 (1.266–2.159)***	1.768 (1.299–2.407)***
Ceftazidime	1.007 (1.001–1.012)*	0.424 (0.338–0.531)***	1.676 (1.281–2.210)***	1.673 (1.216–2.302)**
Gentamicin	1.005 (1.001–1.010)*	0.774 (0.637–0.942)*	1.022 (0.822–1.273)	1.593 (1.247–2.032)***
Trimethoprim	1.000 (0.997–1.003)	0.761 (0.661–0.876)***	1.154 (0.994–1.341)	1.507 (1.260–1.802)***
Cotrimoxazole	1.000 (0.997–1.003)	0.737 (0.640–0.849)***	1.126 (0.967–1.312)	1.504 (1.256–1.801)***
Ciprofloxacin	1.013 (1.010–1.017)***	0.513 (0.444–0.594)***	0.921 (0.783–1.084)	1.539 (1.276–1.857)***
Nitrofurantoin	1.015 (1.005–1.027)**	1.213 (0.737–2.082)	1.343 (0.794–2.316)	2.408 (1.361–4.287)**
Fosfomycin	1.011 (1.000–1.023)	0.867 (0.533–1.432)	1.166 (0.675–2.050)	1.411 (0.740–2.655)
MDOT	1.011 (1.006–1.017)***	0.436 (0.354–0.536)***	1.014 (0.793–1.300)	1.893 (1.453–2.469)***
Amoxicillin/clav. acid gentamicin	1.014 (1.006–1.023)***	0.407 (0.295–0.559)***	1.299 (0.882–1.937)	2.196 (1.452–3.348)***
Cefuroxime + gentamicin	1.006 (1.001–1.010)*	0.737 (0.602–0.904)**	1.041 (0.829–1.310)	1.556 (1.204–2.009)***
MRSA blood	0.986 (0.972–0.999)*	0.930 (0.502–1.695)	NA	NA
MRSA soft tissue	0.997 (0.990–1.003)	0.952 (0.713–1.269)	0.600 (0.409–0.890)**	0.762 (0.497–1.176)

Each row shows a separate multivariable logistic regression model showing risk factors for resistance in *E. coli* in urine for the indicated antibiotic (unless otherwise indicated). Odds ratios with 95% CI intervals are shown

GP, general practitioner; MDOT, multidrug resistance to oral therapy; defined as resistance to all of the following oral agents: amoxicillin-clavulanic acid (according to breakpoint for indications other than uncomplicated urinary tract infection), ciprofloxacin, and co-trimoxazole. MRSA = methicillin resistant *Staphylococcus aureus*

P-values are shown as follows: ***: *p*-value < 0.001, **: *p*-value < 0.01, *: *p*-value < 0.05

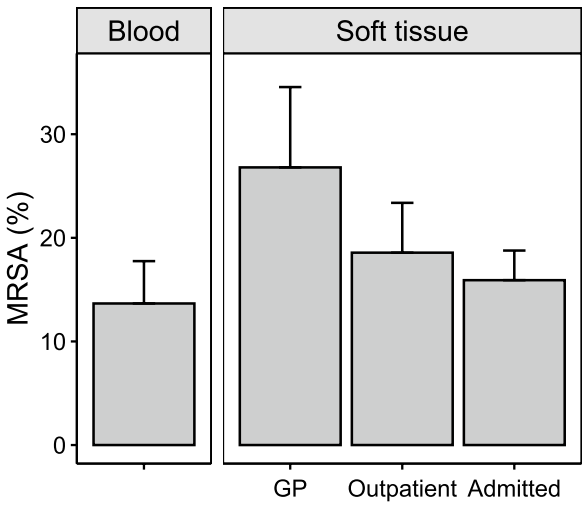

Fig. 4 Probability of methicillin resistant *S. aureus* (MRSA) in blood and soft tissue cultures. Incidence of MRSA among blood and soft tissue isolates of *S. aureus* stratified by general practitioners' (GP) patients, outpatients, and admitted patients

outcome was unavailable, but it is generally accepted that correct empirical therapy improves outcomes.

The causes behind these heightened resistance levels remain unidentified at present. Potential contributing factors could include variations in first-line antibiotic prescriptions, differences in culturing logistics, diverse demographic characteristics, or increased antibiotic utilization in agricultural settings. The majority of individuals with MRSA had not been hospitalized within the year preceding the positive culture, nor had they visited the hospital on an outpatient basis. Therefore, it is reasonable to hypothesize that the primary source of these infections lies within the community. Actually, the highest percentages of MRSA was found in soft tissue cultures of the GPs, which possibly reflects a conservative diagnostic stewardship. Subsequent investigations are warranted to explore these potential risk factors, with the aim of identifying high-risk groups and enhancing our understanding of the underlying dynamics, which is crucial for guiding optimal empiric antibiotic therapy.

Implementing an antimicrobial and diagnostic stewardship and infection prevention approach is crucial in combating AMR. A robust antimicrobial stewardship program both in collaboration with the local health authorities, the laboratory and the hospital will enhance prescribing practices based on accurate diagnostics, thereby reducing unnecessary antibiotic exposure. Concurrently, robust infection prevention protocols, such as hand hygiene, lower infection rates, diminishing the reliance on antimicrobials. Regional approaches within the Caribbean should enhance laboratory capacity for AMR detection and antimicrobial susceptibility testing, establish laboratory standards, and strengthen quality

assurance. A robust regional platform can facilitate the sharing of expertise, insights, and knowledge.

This study has certain limitations. Firstly, the data is derived from a single center, limiting its generalizability. Nevertheless, it encompasses all information of admitted patients from the largest hospital on the island, most outpatients and a representative sample of GP cultures. In addition, many Caribbean islands, particularly those that are part of the Kingdom of the Netherlands, share similar demographics and healthcare systems. Consequently, our findings may be applicable to other Caribbean islands. Secondly, inherent biases may exist in these types of studies due to selective culturing. This is particularly relevant for GP isolates, as samples are typically sent for culture and susceptibility testing in cases of antimicrobial therapy failure or more complicated or severe infections. Consequently, the presented resistance levels are likely to be higher than those in the general population. Such bias is less likely to occur for outpatient and hospital isolates. Thirdly, some patients might have been included twice because identification numbers might have been different for samples from the GP or hospital, although this will not have impacted the results in stratified analyses.

In conclusion, the widespread occurrence of MRSA and resistance to third-generation cephalosporins underscores the need for robust antimicrobial stewardship programs and infection control strategies, both in the community in collaboration with the local health authorities and in the hospital setting.

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Author contributions
PK: conception and design, data acquisition, analysis, interpretation, drafting the manuscript. CO: analysis, interpretation, drafting the manuscript. DW: data acquisition, interpretation, drafting the manuscript. LP: data acquisition, interpretation, drafting the manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Institutional Review Board of the Curaçao Medical Centre (CMC) with a waiver of consent (METC20240621-01).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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