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Original Article

Prevalence, co-infection and antibiotic resistance of *Escherichia Coli* from blood and urine samples at a hospital in Jamaica

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Abstract

Introduction: *Escherichia coli (E. coli)* is a very common uro-pathogen and pathogen of bloodstream infections (BSI) in Jamaica. The aim of this study was to examine this organism's prevalence, determine co-infection rates and assess antibiotic resistance patterns.

Methodology: In the absence of automated systems, data on all *E. coli* isolates identified at the University Hospital of the West Indies in Kingston, Jamaica during the first six months of 2008 and 2012 was collected and sorted. Data were analyzed using IBM SPSS Statistics version 20 for Windows.

Results: A total of 1188 isolates (1072 from urine and 116 from blood) was analyzed. Patients with *E. coli* BSI were older than those with *E. coli* urinary tract infections (UTI) (55.3 years *vs* 42.4 years, $p < 0.05$) and both had a female predominance. Sensitivity profiles in 2012 for *E. coli* in blood and urine were highest for the carbapenems, Amikacin and Nitrofurantoin and lowest for the fluoroquinolones and Trimethoprim-sulfamethoxazole. Based on antimicrobial susceptibility patterns, Nitrofurantoin was identified as an appropriate choice for empiric therapy for UTI. Ten antibiotics were noted in this study to have developed statistically significant antibiotic resistance. Patients with *E. coli* BSI had a co-infection *E. coli* UTI rate of 39%.

Conclusions: Resistance patterns change drastically in a few years making frequent antimicrobial susceptibility profiling necessary. Further studies would be beneficial in guiding management of these patients.

Key words: *Escherichia coli*; urine; blood.

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Introduction

Escherichia coli (E. coli) has been recognized as a common pathogen implicated in urinary tract infections (UTI) and bloodstream infections (BSI). Internationally, *E. coli* has been shown to be the most common pathogen causing UTI in various populations in countries in North America, Latin America, Europe, and Asia [1-3]. In Jamaica, previous studies have also found *E. coli* to be the most common pathogen in urinary tract infections [4-5]. The contribution of *E. coli* in BSI is not as distinct as its role in UTI but *E. coli* has been found as a top pathogen in BSI. It is the most common gram negative bacilli causing BSI in North America and Latin America [6-7]. A previous study found *E. coli* to be the second most common gram negative bacteria in neonatal sepsis in Jamaica [8]. Over a decade ago, *E. coli* placed 5th alongside *Salmonella sp.* among the top pathogens causing bacteremia in Jamaica [9].

Because of the paramount role of *E. coli* in causing extra-intestinal infection, we carried out this study to determine the prevalence of (i) *E. coli* UTI, (ii) *E. coli* BSI, and (iii) *E. coli* blood and urine co-infection and to assess their respective trends and antibiotic resistance patterns over time.

Methodology

This was a cross-sectional study that compared data collected at the Department of Microbiology, University Hospital of the West Indies, Kingston, Jamaica from 2008 and 2012. Approval was granted by the UHWI/UWI/FMS Ethics Committee. Data was collected for the first 6 months of the respective years. *E. coli* isolates were identified by manual sorting of all blood and urine culture carbon copies of results issued by the department for those time periods. Demographic data, as well as the antibiotic susceptibility profile, were collected from these carbon copies. The intradepartmental log was also reviewed to ensure no isolates were missed.

The total number of *E. coli* isolated from blood and urine specimens from January 1, 2008, to December 31, 2012, was 6372 isolates. During the data collection period, urine specimens were noted to be missing for

January and part of February 2008. Despite this, our study period had 1274 *E. coli* isolates which approximately represented 20% of all *E. coli* isolated for the 5-years period of which 86 were identified as duplicates as illustrated in Figure 1. Duplicates were defined as, *E. coli* isolated from the same patient and specimen type within the respective 6-months period with identical antibiotic susceptibility profiles. In total there were 1188 samples included in the study. There were no other exclusion criteria.

Co-infection was defined as having a positive blood and urine culture in the same patient. Accident and emergency, casualty and clinics were considered acute care settings.

Data were analyzed using IBM SPSS Statistics version 20 for Windows. A p value of < 0.05 was deemed to represent statistical significance.

Results

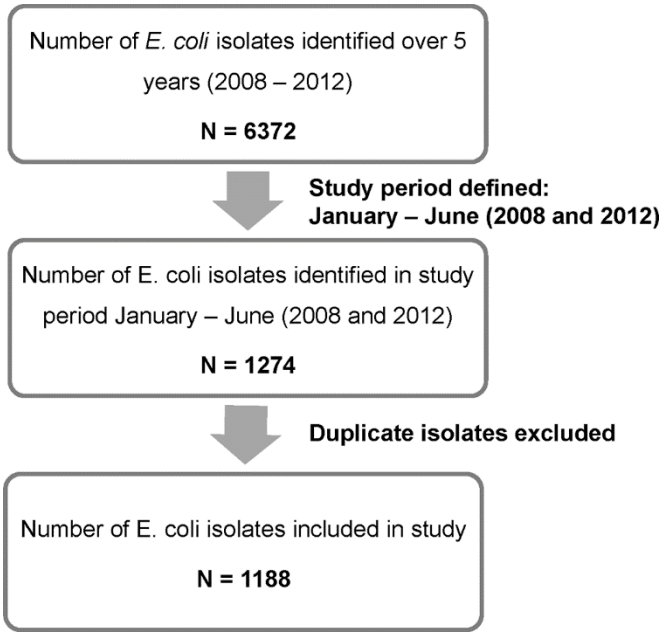
After removing duplicates from the 1274 *E. coli* isolates, there were 1188 isolates remaining. Of 1188 *E. coli* isolates in this study, 90% (1072) were from urine specimens and the remaining 10% (116) were from blood specimens. Isolates were evenly distributed between the years. Of *E. coli* urine specimens 57% were identified in 2012 and the remaining 43% were identified in 2008. Of *E. coli* blood specimens 55% were identified in 2008 and the remaining 45% were identified in 2012.

Prevalence of E. coli UTI and BSI

Patients with *E. coli* UTI were predominantly female (75.6%, n = 790). Obstetric patients accounted for 13% of *E. coli* UTI. The average age of a patient with *E. coli* UTI in 2008 was 42 years (range 21 days - 98 years) whereas in 2012 it was 43 years (range 2 days - 97 years). Children (< 12 years) accounted for 11% of isolates (2008 n = 49, 2012 n = 62). As seen in Figure 2, over two-thirds of *E. coli* isolated in urine was from specimens sent from an acute care setting.

Gender was more evenly distributed among patients with *E. coli* BSI (female 56.5%, n = 65). The average age of a patient with *E. coli* BSI was 50 years in 2008 compared to 60 years in 2012 (2008 range: 3 months-95 years, 2012 range: 4 months-93 years of age). An independent-samples t-test showed a significant difference in the average age of patients in 2008 (M= 50.16, SD = 26.31) and 2012 (M = 60.13, SD = 22.48); $t(99) = -2.03$, $p = 0.045$. Patients with *E. coli* BSI were older in 2012. Children accounted for < 10% of *E. coli* BSI (n = 7).

Figure 1. *E. coli* UTI and BSI isolate selection process.



An independent-samples t-test showed a significant difference in the average ages of patients with *E. coli* UTI (M = 42.40, SD = 25.69) and *E. coli* BSI (M = 55.34, SD = 24.52); $t(1014) = -4.80$, $p < 0.05$. Patients with *E. coli* BSI were older than patients with *E. coli* UTI.

E. coli isolated in blood was predominantly sent from specimens from an acute care setting as depicted in Figure 2.

Prevalence of E. coli blood and urine co-infection

Of the patients with *E. coli* BSI in 2008, 36% had a concurrent *E. coli* UTI whereas, in 2012, 42% of *E. coli* BSI had a concurrent *E. coli* UTI. Combined, 39% of patients with *E. coli* BSI had a concurrent *E. coli* UTI (n = 45). Conversely, of the 1072 urine samples with *E. coli* isolated only 4% had a concurrent *E. coli* BSI.

Females made up 70.3% of patients with co-infections. The average age was 62 with a range of 19-95 years of age. There were no children identified with co-infections. The majority of samples for co-infections were sent from the accident and emergency department. All co-infections identified in the clinic setting were from the Sickle Cell Unit (11%). No co-infections were identified from the critical care units. See Figure 2.

80% of these samples were received either on the same day or a day apart. 60% shared the same antibiotic susceptibility while 29% had a difference in susceptibility to one antibiotic. Of those that did not share the exact same susceptibility, 61% of them were from samples sent a day or more apart.

Antimicrobial Resistance

Antibiotic susceptibilities were similar for *E. coli* isolates causing UTI and *E. coli* isolates causing BSI. Overall, resistance was noted for ampicillin, trimethoprim-sulfamethoxazole, nalidixic acid, and the fluoroquinolones. Statistically significant resistance developed for *E. coli* isolates causing UTI to piperacillin-tazobactam, ceftazidime, cefuroxime, and tobramycin (> 10% decrease in susceptibility). Resistance also developed to nitrofurantoin and amikacin but the level of susceptibilities continued to remain high (89.6% and 95.1% respectively).

On the other hand, isolates became more susceptible to amoxicillin-clavulanate, cefazolin, and cefepime became more susceptible with time (22%, 34% and 56% increase respectively, p-value < 0.05). This increase in susceptibility to cefepime was noted for *E. coli* isolates causing UTI.

Obstetric patients are a unique population group as antibiotic choices are limited because of fetotoxic effects. Children as well have limitations to antibiotic options. The antibiotic susceptibility profiles for these subgroups groups were further analyzed and, in general, their resistance patterns correlated with that of the general population. See Table 1.

Figure 2. The specimen location of *E. Coli* UTI in (A) 2008 and (B) 2012, BSI in (C) 2008 and (D) 2012 and co-infection in (E) 2008 and 2012 at the University Hospital of the West Indies, Jamaica.

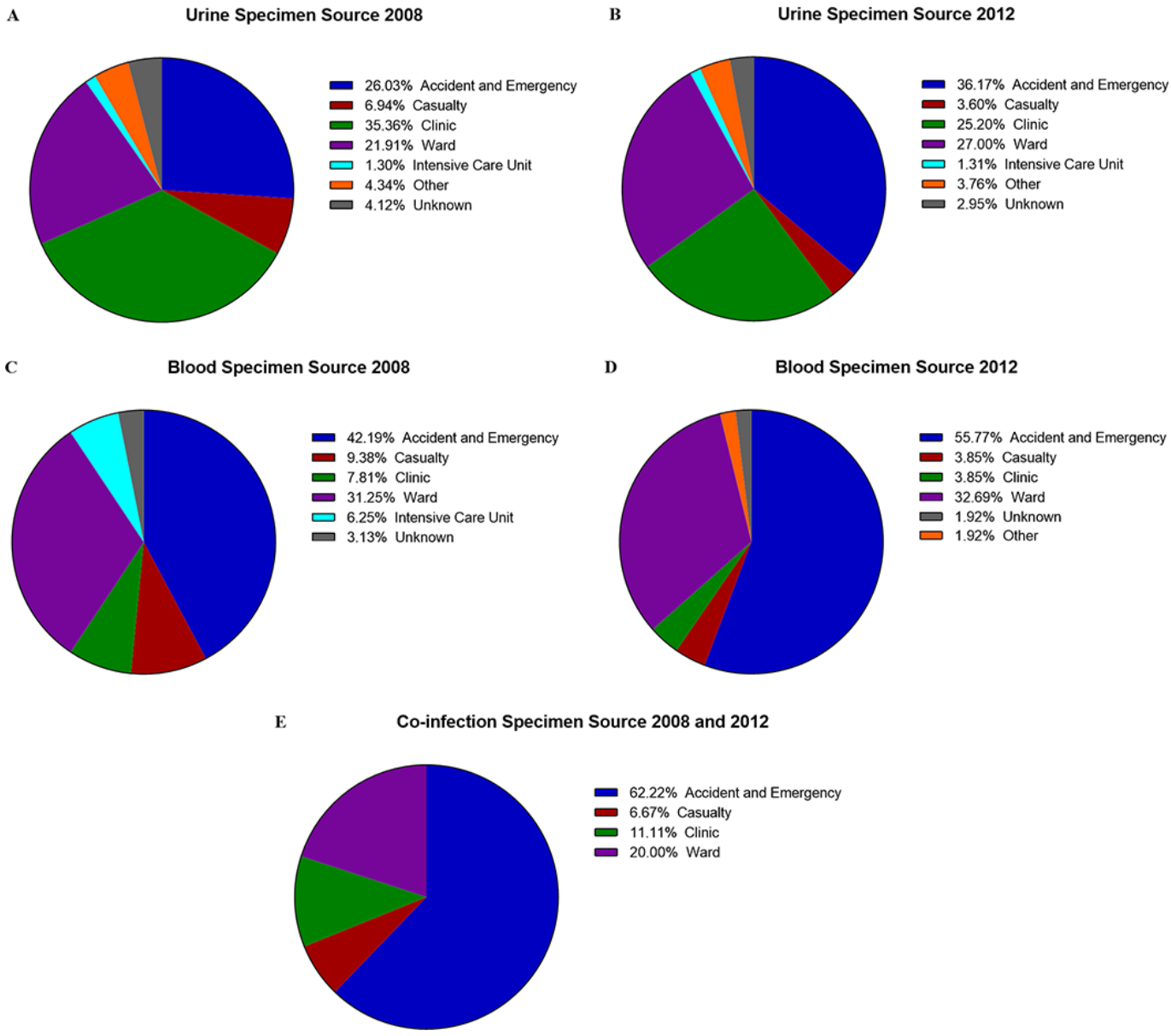


Table 1. Sensitivity profile of *E. coli* isolated from blood and urine samples collected from January to June of the years 2008 and 2012 at the University Hospital of the West Indies Jamaica.

	OVERALL SENSITIVITIES			CHILDREN			CRITICAL CARE UNIT			OBSTETRIC PATIENTS		
	2008	2012	p-value	2008	2012	p-value	2008	2012	p-value	2008	2012	p-value
Ak (Amikacin)												
Blood	100%	97.90%	> 0.05	100%	100%		100%	-				
Urine	99.40%	95.10%	< 0.05	100%	100%		100%	100%		100%	98.10%	> 0.05
AMC (Amoxicillin-clavulanate)												
Blood	57.10%	84.20%	< 0.05	50%	100%	> 0.05	60%	-				
Urine	65%	81.50%	< 0.05	61%	70%	> 0.05	66.70%	76.90%	> 0.05	68.50%	92.20%	< 0.05
AMP (Ampicillin)												
Blood	35.90%	42.90%	> 0.05	40%	0%	> 0.05	0	-				
Urine	43.50%	42.10%	> 0.05	31%	34%	> 0.05	25%	25%	> 0.05	49.20%	54.20%	> 0.05
AZT (Aztreonam)												
Blood	-	87.50%		-	-		-	-				
Urine	-	82.40%		90%	90%		-	83.30%		-	95.70%	
CAZ (Ceftazidime)												
Blood	100%	91.90%	> 0.05	100%	100%		100%	-				
Urine	89%	65.50%	< 0.05	95%	86%	> 0.05	100%	100%		96.60%	75%	> 0.05
CEFA (Cefazolin)												
Blood	54.20%	90%	< 0.05	100%	100%		-	-				
Urine	47%	78.60%	< 0.05	36%	90%	< 0.05	25%	66.70%	> 0.05	64.30%	93.60%	< 0.05
CEFE (Cefepime)												
Blood	72%	94.70%	> 0.05	100%	100%		-	-				
Urine	33.30%	89.30%	< 0.05	94%	94%		-	83.30%		-	100%	
CEFO (Cefoxitin)												
Blood	-	100%		-	-		-	-				
Urine	-	100%		-	-		-	100%		-	-	
CIP (Ciprofloxacin)												
Blood	71.90%	65.10%	> 0.05	100%	50%	> 0.05	80%	-				
Urine	68.70%	63.10%	> 0.05	92%	76%	> 0.05	100%	28.60%	< 0.05	89.20%	87.80%	> 0.05
CN (Gentamicin)												
Blood	85.90%	76.50%	> 0.05	80%	50%	> 0.05	80%	-				
Urine	84.80%	81%	> 0.05	91%	81%	> 0.05	87.50%	78.60%	> 0.05	98.40%	88%	< 0.05
CRO (Ceftriaxone)												
Blood	84.50%	87%	> 0.05	100%	100%		75%	-				
Urine	85.80%	79.70%	< 0.05	87%	93%	> 0.05	83.30%	75%	> 0.05	95.30%	96%	> 0.05
CXM (Cefuroxime)												
Blood	75.80%	65.50%	> 0.05	80%	0%	> 0.05	80%	-				
Urine	78.50%	59.60%	< 0.05	88%	83%	> 0.05	83.30%	50%*	> 0.05	82.20%	100%	> 0.05
ERT(Ertapenem)												
Blood	-	100%		-	-		-	-				
Urine	-	99.40%		-	97%		-	100%		-	100%	
F (Nitrofurantoin)												
Blood	100%	90.50%	> 0.05	100%	100%		-	-				
Urine	96.30%	89.60%	< 0.05	98%	92%	> 0.05	87.50%	92.30%	> 0.05	95.10%	94.70%	> 0.05
IMI (Imipenem)												
Blood	100%	100%		100%	100%		-	-				
Urine	100%	99.40%	> 0.05	-	97%		-	100%		-	100%	
LEV (Levofloxacin)												
Blood	68%	76.20%	> 0.05	100%	0%	> 0.05	-	-				
Urine	65.70%	64%	> 0.05	91%	78%	> 0.05	75%	33.30%	> 0.05	86.20%	87.80%	> 0.05
LZD (Linezolid)												
Blood	-	-		-	-		-	-				
Urine	-	100%		-	100%		-	100%		-	100%	

Table 1 (continued). Sensitivity profile of *E. coli* isolated from blood and urine samples collected from January to June of the years 2008 and 2012 at the University Hospital of the West Indies Jamaica.

	OVERALL SENSITIVITIES			CHILDREN			CRITICAL CARE UNIT			OBSTETRIC PATIENTS		
	2008	2012	p-value	2008	2012	p-value	2008	2012	p-value	2008	2012	p-value
MEM (Meropenem)												
Blood	100%	100%		100%	100%		100%	-				
Urine	100%	98.90%	> 0.05	100%	95%	> 0.05	100%	100%		100%	100%	
MH (Minocycline)												
Blood	-	-		-	-		-	-				
Urine	61.40%	100%	> 0.05	73%	100%	> 0.05	66.70%	-		-	-	
NA (Nalidixic Acid)												
Blood	-	-		-	-		-	-				
Urine	62.40%	50%	> 0.05	81%	-		75%	-		85.50%	0%	< 0.05
NOR (Norfloxacin)												
Blood	-	-		-	-		-	-				
Urine	68.70%	67.50%	> 0.05	88%	77%	> 0.05	87.50%	66.70%	> 0.05	90%	83.30%	> 0.05
POLY B (Polymixin B)												
Blood	-	-		-	-		-	-				
Urine	80%	100%	> 0.05	80%	-		80%	100%		-	-	
SXT (Trimethoprim/sulfamethoxazole)												
Blood	54.70%	66%	> 0.05	80%	50%	> 0.05	80%	-				
Urine	60.50%	62.30%	> 0.05	51%	70%	< 0.05	37.50%	64.30%	> 0.05	80.30%	65.90%	< 0.05
TE (Tetracycline)												
Blood	-	75%		-	-		-	-				
Urine	-	51.30%		-	69%		16.70%	16.70%		-	-	
TOB (Tobramycin)												
Blood	76%	75%	> 0.05	100%	0%	> 0.05	-	-				
Urine	89.60%	33.30%	< 0.05	91%	-		100%	-		89.30%	0%	< 0.05
TZP (Piperacillin/Tazobactam)												
Blood	83.10%	93.30%	> 0.05	100%	50%	> 0.05	75%	-				
Urine	94.70%	83%	< 0.05	90%	83%	> 0.05	100%	100%		100%	75%	< 0.05

Values reported represent the proportion of isolates sensitive to the various antibiotics.

E. coli isolates causing co-infections were similarly resistant to the fluoroquinolones, the aminoglycosides (with an exception), the tetracyclines, and ampicillin. They were however highly susceptible to the carbapenems, amikacin, and piperacillin-tazobactam. See Table 2.

Discussion

One of the main objectives of this study was to assess the prevalence of *E. coli* UTI and *E. coli* BSI. This study showed that a patient with *E. coli* UTI was more likely female in her 40s whereas a patient with *E. coli* BSI was much more likely to be significantly older. The female predominance found in this study matched that of findings found in other studies [10-12]. The mean age of patients with *E. coli* BSI in 2012 was 60 years which was in keeping with means found in other studies [11-13]. However, it is interesting to note that from this study, patients with *E. coli* BSI were younger in 2008 and did not match the average age of other studies until 2012. Though more patients in 2008 had missing age data, it is noticeable that far more patients that year were in the 13-30 age group. The reason behind this is beyond the scope of this study. Further studies could assess if improvements in health care practice, particularly among Jamaica's at risk large sickle cell population, may have accounted for this change.

This study found an overall *E. coli* blood and urine co-infection rate of 39%. Three other studies were identified in the literature review that isolated *E. coli* in urine cultures among patients with *E. coli* BSI [11,12,14]. Co-infection rates of 45-63.5% were found in these studies [11,12,14]. This study found a lower co-infection rate which may be because of differences in the time period of study, population age and location. Despite the lower co-infection rate in our study, over a third of patients with *E. coli* BSI will have a concurrent *E. coli* UTI. Whether these cases represented *E. coli* UTI that progressed to *E. coli* bacteremia could not be determined with the data collected from this study. The patient at risk of co-infection was likely to be an elderly

female in her 60s. Additional studies assessing other risk factors and virulence factors of the *E. coli* resulting in co-infection may be able to identify patients whose UTI should be treated more aggressively to prevent bacteremia. There may be little benefit in culturing the urine of a patient already being treated for an *E. coli* BSI as this study showed antibiotic susceptibility profiles will be identical 80% of the time. Based on the 2012 susceptibility profile, amikacin, piperacillin-tazobactam or a carbapenem are good choices for empiric treatment of suspected urosepsis.

Sensitivity profiles in 2012 for *E. coli* in blood and urine were highest for the carbapenems, amikacin, and nitrofurantoin and lowest for the fluoroquinolones and trimethoprim-sulfamethoxazole. Nitrofurantoin would be an appropriate choice for empiric antibiotic treatment of a UTI. Amoxicillin-clavulanate, surprisingly, would be a good alternative as, contrary to what would be expected [10], resistance to this antibiotic decreased with time. The concern for resistance weighs heavily in clinical practice and physicians may have a tendency to lean towards what is perceived as a more potent antibiotic. Similar to "older" antibiotics being reintroduced to treat multidrug resistant organisms [15], this "shelving"/decreased use of amoxicillin-clavulanate could explain its re-emergence as a contender in treating UTI in Jamaica. Ten antibiotics were noted in this study to have statistically significant reductions in susceptibility levels. It is clear that antibiotic resistance patterns can change drastically in a few years and a more rapid way of identifying the most current susceptibility antibiotic profile is needed locally. This further underscores the important role of antibiotic stewardship.

Table 2. Sensitivity Profile of *E. coli* isolates causing blood and urine co-infections collected from January to June of 2008 and 2012 at the University Hospital of the West Indies Jamaica.

Antibiotic	2008	2012	p-value
AMP	28.90%	42.10%	0.05
AMC	51.40%	78.40%	< 0.05
CAZ	95.50%	78.90%	> 0.05
CRO	81.40%	73%	> 0.05
CXM	73.80%	50%	> 0.05
CEFA	35%	86.40%	< 0.05
CEFE	63.60%	85.70%	> 0.05
CEFO	-	100%	
TZP	81.80%	93.80%	> 0.05
ERT	-	100%	
IMI	100%	100%	
MEM	100%	100%	
AZT	-	82.40%	
SXT	40%	51.10%	> 0.05
NA	40.90%	-	
F	100%	84.80%	< 0.05
Ak	100%	93.90%	> 0.05
CN	77.80%	66.70%	> 0.05
TOB	68.20%	66.7%*	> 0.05
TE	-	64.70%	
MH	44.40%	-	
CIP	55.90%	51.50%	> 0.05
LEV	45.50%	60.90%	> 0.05
NOR	50%	42.90%	> 0.05

Values reported represent proportion of isolates sensitive to the various antibiotics. Antibiotic abbreviations used Ampicillin (AMP), Amoxicillin-clavulanate (AMC), Ceftazidime (CAZ), Ceftriaxone (CRO), Cefuroxime (CXM), Cefazolin (CEFA), Cefepime (CEFE), Cefoxitin (CEFO), Piperacillin/tazobactam (TZP), Ertapenem (ERT), Imipenem (IMI), Meronem (MEM), Aztreonam (AZT), Trimethoprim/sulfamethoxazole (SXT), Nalidixic Acid (NA), Nitrofurantoin (F), Amikacin (AK), Gentamicin (CN), Tobramycin (TOB), Tetracycline (TE), Minocycline (MH), Ciprofloxacin (CIP), Levofloxacin (LEV), Norfloxacin (NOR).

Because of the labor intensive restrictions in data collection in this study, the first six months of the respective years studied were arbitrarily chosen. Human errors are more likely to occur with data collection in this manner. In an attempt to counter this, the intradepartmental log was utilized. Though a 20% representation was obtained, missing data of over a month's period may have affected results. Data was not available for all parameters studied as requisition forms sent by physicians for cultures were not always completely filled. Antibiotics may not have had susceptibility testing done on some *E. coli* isolates which may affect reported susceptibility percentages. Once *E. coli* was identified in urine, this study made the assumption that the patient had a UTI, colonization was not taken into account. Because of *E. coli*'s previously established role as a top pathogen in UTI and BSI, assumptions are made that its susceptibility profile can be used to identify empiric antibiotic choices; however this study did not specifically look at its current rank in causing infection locally and does not take into account differing susceptibility profiles of other top pathogens.

Conclusion

The prevalence of *E. coli* infection in Jamaica matched that of other international studies. There is a female predominance with patients with BSI being older. Nitrofurantoin was identified as an appropriate choice for empiric therapy for UTI, but resistance patterns change drastically in 5 years making frequent antimicrobial susceptibility profiling necessary. Emerging antibiotic resistance was identified among ten antibiotics. This was the first study of its type in the Jamaican setting, to look specifically at *E. coli* UTI among patients with *E. coli* BSI in Jamaica which yielded a co-infection rate of 39%. Further studies on

this disease process would be beneficial in guiding management of these patients.

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