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Multicentre evaluation of significant bacteriuria among pregnant women in the cascade of referral healthcare system in North-western Tanzania: Bacterial pathogens, antimicrobial resistance profiles and predictors

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ABSTRACT

Objectives: The aim of this multicentre study was to evaluate the magnitude of significant bacteriuria (SB) as well as the implicated bacterial pathogens, antimicrobial resistance (AMR) profiles and risk factors for SB among pregnant women attending different levels of healthcare facilities (HCFs) in Tanzania in order to guide antimicrobial therapy and preventive measures.
Methods: Information on sociodemographic and clinical characteristics, midstream urine culture and antimicrobial susceptibility testing was collected from 1828 pregnant women between March 2016 and May 2017. Data were analysed using STATA v.13.0 software.
Results: The prevalence of SB among pregnant women was 17.7% (323/1828; 95% CI 16.0–19.5%), with a predominance of *Escherichia coli* (164/323; 50.8%), *Klebsiella* spp. (55/323; 17.0%) and *Staphylococcus aureus* (28/323; 8.7%). Moreover, 37.5% (121/323) of bacteria were multidrug-resistant [84.3% (102/121) Gram-negative bacteria and 15.7% (19/121) in Gram-positive bacteria; $P < 0.001$]. Third-generation cephalosporin resistance in *E. coli*, *Klebsiella* spp. and other Enterobacteriaceae was 13.4%, 21.8% and 27.5%, respectively, and was higher in strains from a tertiary hospital (OR = 3.27, 95% CI 1.02–10.49; $P = 0.046$) compared with lower HCFs. Predictors of SB among pregnant women were lack of formal occupation, current hospital admission and presence of co-morbidities.
Conclusions: The prevalence of SB among pregnant women in this study was high (17.7%) and was within the same range reported 10 years ago in a single-centre baseline study. However, there is an increase in AMR in the cascade of referral healthcare system, underscoring the need for health facility level-specific antimicrobial stewardship.

1. Introduction

Urinary tract infections (UTIs) account for millions of visits to physicians and emergency departments annually worldwide, leading to significant healthcare expenditure [1,2]. Pregnant women are at increased risk of UTI because of their anatomical predisposition, hormonal changes during pregnancy, and the physical effect of the gravid uterus on the urinary bladder that often results in urinary stasis and therefore facilitates the

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proliferation of bacteria ascending from the external urethral meatus [1,3].

Escherichia coli remains the most commonly implicated bacterial pathogen causing UTIs globally, with other bacterial pathogens being *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Enterococcus* spp. and other Enterobacteriaceae [3,4]. In pregnant women, both symptomatic and asymptomatic significant bacteriuria (SB), i.e. growth of $\geq 10^5$ CFU of bacteria per millilitre of midstream urine, can result in adverse maternal–foetal outcomes, hence the need for prompt diagnosis and treatment [5–8].

Antimicrobial susceptibility testing (AST) remains a challenge in most low-income countries. In Tanzania, for example, culture and AST services are offered routinely in tertiary hospitals and a few regional hospitals [9–11]. As a result, most patients, including pregnant women, receive empirical antimicrobial therapy, a situation that facilitates the development of antimicrobial resistance (AMR) [7,12]. Previous studies in Tanzania reported the prevalence of SB among pregnant women to range from 13% to 22%, but these studies were conducted in tertiary hospitals with small sample sizes thereby limiting the generalisation of their findings [9,10]. The aim of the current study was to evaluate the prevalence of SB as well as the implicated bacterial pathogens, AMR profiles and risk factors for SB among pregnant women attending different levels of healthcare facilities (HCFs) in Tanzania in order to guide antimicrobial therapy and preventive measures.

2. Methodology

2.1. Study design and settings

This was a cross-sectional analytical study conducted from March 2016 to May 2017 in the North-western part of Tanzania. Tanzania has a total population of 44 928 923 (51.3% females; 70.4% rural residents) [13]. It has a well-structured health system divided into five levels of HCF, namely dispensaries, health centres, district hospitals, regional/referral hospitals and tertiary hospitals [14]. This study involved seven HCFs constituting a cascade of referral healthcare system (Table 1).

2.2. Study population and inclusion and exclusion criteria

The study involved pregnant women with SB (irrespective of age and symptoms) presenting to the HCFs and who voluntarily consented to participate in the study. Pregnant women with incomplete clinical information in their files as well as those known to have congenital malformation of the urinary tract were excluded. A sample size was estimated by the Kish formula [15] using a previous prevalence of 17.9% among pregnant women with SB in Mwanza, resulting in a minimum of 226 pregnant women per site [9]. Taking into account four levels of HCF and multiplying by this factor resulted in a minimum of 904 pregnant women. *Escherichia coli* (as the predominant pathogen) was used to assess AMR profiles in different levels of HCF. The assumption made from previous studies was that approximately 10% of samples would yield *E. coli* [9], giving a minimum of 133 *E. coli* strains for robust analysis. Therefore, a total of 1870 pregnant women were enrolled into this study; 42 (2.2%) were excluded because of incomplete information on the questionnaires.

2.3. Data collection and laboratory procedures

Sociodemographic and clinical characteristics were collected using structured questionnaires and patients' clinical records. Each pregnant woman was instructed by the principal investigator or a trained research assistant to collect ca. 20–30 mL of midstream urine sample in a sterile plastic container for laboratory analysis. Quantitative urine cultures were performed using a previously described method [16,17]. A standard sterile plastic loop was used to inoculate ca. 10 μL of urine sample from each pregnant woman onto blood agar and MacConkey agar plates (Oxoid Ltd., Basingstoke, UK) and the plates were incubated at 37 °C for 18–24 h. Phenotypic methods of identification of bacteria were Gram staining, colony morphology on culture media and specific biochemical identification tests [17]. AST was performed by the conventional Kirby–Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines on Muller–Hinton agar (Oxoid Ltd.). Specifically, the disks used (Oxoid Ltd.) were ampicillin (10 μg), trimethoprim/sulfamethoxazole (SXT) (1.25/23.75 μg), ciprofloxacin (5 μg), gentamicin (10 μg) [high-level gentamicin (120 μg) for *Enterococcus* spp.] and nitrofurantoin (300 μg). In addition, for Gram-positive bacteria erythromycin (15 μg) and vancomycin (30 μg) were used, whereas for Gram-negative bacteria amoxicillin/clavulanic acid (AMC) (20/10 μg), ceftriaxone (30 μg), ceftazidime (30 μg) and meropenem (10 μg) were used [18]. Piperacillin (100 μg) and piperacillin/tazobactam (TZP) (100/10 μg) instead of ampicillin and AMC, respectively, were used for *Pseudomonas aeruginosa* and *Acinetobacter* spp. only according to CLSI recommendations [18]. Phenotypic identification of extended-spectrum β-lactamase (ESBL) production and methicillin-resistant *S. aureus* (MRSA) was performed on Mueller–Hinton agar as described previously [18,19]. Multidrug-resistant (MDR) was bacteria were defined as strains resistant to at least one agent in three or more classes of antimicrobial agents [20].

2.4. Quality control

E. coli ATCC 25922 and *S. aureus* ATCC 25923 were used as reference strains for Gram-negative and Gram-positive bacteria, respectively, for quality control of culture, biochemical identification and AST.

Table 1
Demographic descriptions of health facilities (HCFs) and number of study participants involved.

Level/rank of HCF	Ideal HCF bed capacity	HCF involved	HCF catchment population	HCF bed capacity	Obstetric ward bed capacity	No. of study participants enrolled (% of total)
Tertiary hospital	550–1500	BMC	16 252 410	950	78	463 (25.3)
Regional/referral hospital	176–450	SRRH	2 772 509	375	49	366 (20.0)
District hospital	150–175	NDH (urban)	363 452	88	16	354 (19.4)
		SDDH (rural)	663 034	320	30	256 (14.0)
HCs and dispensaries[a]	4–24	HC	NI	4–10	1–4	389 (21.3)

BMC, Bugando Medical Center; SRRH, Sekou-Toure Regional Referral Hospital; NDH, Nyamagana District Hospital; SDDH, Sengerema District Designated Hospital; HC, health centres; NI, no information.

[a] Makongoro ($n = 127$) and Buzuruga ($n = 219$) in Mwanza City; and Sengerema ($n = 43$) in SDDH. Makongoro and Sengerema HCs serve only outpatients.Sources: Hospital records, Tanzania Population and Health Census (2012) and Staffing Levels for Ministry of Health Tanzania (2014–2019).

2.5. Data management

Data were entered into Microsoft Excel (Microsoft Corp., Redmond, WA) and were then exported to Stata Statistical Software: Release 13 (StataCorp LP, College Station, TX) for analysis. Continuous variables were described using the mean ± standard deviation (S.D.) or the median and interquartile range (IQR) for normally distributed and skewed data, respectively. Proportions of pregnant women with culture-confirmed SB, bacterial species and resistance to various antimicrobial agents were determined. Risk factors of SB were computed by univariate and multivariate logistic regression analysis using the odds ratio (OR) and respective 95% confidence interval (CI). Variables that were significant on univariate analysis (i.e. with a *P*-value of ≤0.05) were subjected to multivariate logistic regression analysis to ascertain the independent predictors of SB among pregnant women.

2.6. Study permission and ethical considerations

This study was approved by the joint Catholic University of Health and Allied Sciences/Bugando Medical Center (CUHAS/BMC) Research and Ethics Committee in Tanzania. Permission to conduct the study in various HCFs was sought and provided by relevant authorities in Tanzania. All patient information was kept confidential. Preliminary results of AST were reported to the attending doctors within 24 h and the final results were reported within 72 h after sample collection to guide specific management.

3. Results

3.1. Sociodemographic and clinical characteristics of enrolled pregnant women

The mean ± S.D. age of the participants was 26.4 ± 6.1 years. The majority of the women resided in urban areas (81.7%) and were married (88.0%). Approximately one-half of the enrolled women had one to three previous deliveries, with the median gestational age of the current pregnancy being 30 weeks (IQR 22–36 weeks). Moreover, 28.8% were admitted at the time of the study and 23.5% had co-morbidities (Table 2).

Table 2
Sociodemographic and clinical characteristics of pregnant women enrolled in the study.

Characteristic	*n* (%)
Residence	
Rural	335 (18.3)
Urban	1493 (81.7)
Education	
No formal education	93 (5.1)
Primary	1090 (59.6)
Secondary	502 (27.5)
College and above	143 (7.8)
Marital status	
Single	220 (12.0)
Married	1608 (88.0)
Occupation	
Peasant	388 (21.2)
No formal occupation	653 (35.7)
Petty trader	543 (29.7)
Employed	244 (13.3)
Parity	
Nulliparous	655 (35.8)
Para 1–3	896 (49.0)
Para ≥4	277 (15.2)
Gestational age	
First trimester	92 (5.0)
Second trimester	604 (33.0)
Third trimester	1132 (61.9)
Admission status	
No	1301 (71.2)
Yes	527 (28.8)
Co-morbidities[a]	
No	1398 (76.5)
Yes	430 (23.5)
Presence of urinary symptoms[b]	
No	1243 (68.0)
Yes	585 (32.0)

[a] Human immunodeficiency virus (HIV) (*n* = 299), preeclampsia (*n* = 130) or both (*n* = 1)].
[b] Fever, dysuria, pyuria, haematuria, frequency or suprapubic pain.

3.2. Prevalence of significant bacteriuria among pregnant women and antimicrobial resistance patterns of bacterial strains

The prevalence of SB among pregnant women in North-western Tanzania was 17.7% (323/1828; 95% CI 16.0–19.5%). The proportion of asymptomatic and symptomatic SB was 17.7% (220/1243) and 17.6% (103/585), respectively (*P* = 0.962). The proportions of pregnant women with SB in the cascade of referral healthcare system were 13.9% (54/389) in health centres, 15.6% (95/610) in district hospitals, 21.6% (79/366) in a regional/referral hospital and 20.5% (95/463) in a tertiary hospital. The most common bacterial species were *E. coli* (164/323; 50.8%), *Klebsiella* spp. (55/323; 17.0%) and *S. aureus* (28/323; 8.7%).

Resistance to ampicillin and SXT ranged from 85.0% to 100.0% among Gram-negative bacteria and from 50.0% to 85.7% among Gram-positive bacteria. There was variable resistance to nitrofurantoin (12.8–52.7%), and resistance to gentamicin ranged from 0.0% to 27.5% in various bacterial species. All Gram-negative bacteria were susceptible to meropenem except for one *Klebsiella pneumoniae* strain. Resistance of *P. aeruginosa and Acinetobacter* spp. to piperacillin was 100%, whereas their resistance to TZP was 0.0% and 15.4%, respectively. Third-generation cephalosporin resistance was found to be lower in *E. coli* (13.4%) compared with *Klebsiella* spp. (21.8%) and other Gram-negative Enterobacteriaceae (27.5%). *E. coli* and *Klebsiella* spp. resistant to third-generation cephalosporins were all confirmed to be ESBL-producers. The proportion of MRSA among *S. aureus* strains was 28.6%. One MRSA strain was found to be non-susceptible to vancomycin (Table 3).

3.3. Multidrug-resistant bacteria in various levels of healthcare facilities

Of the 323 bacteria, 121 (37.5%) of were MDR, with the majority of these being Gram-negative bacteria compared with Gram-positive bacteria [84.3% (102/121) vs. 15.7% (19/121); *P* < 0.001]. Overall third-generation cephalosporin resistance among members of the Enterobacteriaceae family was 16.6% (43/259). Irrespective of the bacterial species, third-generation cephalosporin resistance was significantly higher in strains from BMC tertiary hospital (OR = 3.27, 95% CI 1.02–10.49; *P* = 0.046) compared with the lower HCFs (Table 4). Of note, third-generation cephalosporin resistance among Enterobacteriaceae strains was two times higher in admitted pregnant women compared with pregnant women attending outpatient clinics [22.1% (23/104) vs. 12.9% (20/155); OR = 1.92, 95% CI 0.99–3.71; *P* = 0.053].

3.4. Antimicrobial resistance patterns of Escherichia coli in various healthcare facilities

There was high resistance among *E. coli* strains to ampicillin and SXT (>83.9%) but low resistance to nitrofurantoin, gentamicin and cephalosporins (<26.3%) in all levels of HCF. The proportions of *E. coli* producing ESBL was higher at BMC (18.4%) compared with the other HCFs [SRRH (13.9%), NDH and SDDH (10.7%) and health

Table 3
Antimicrobial resistance patterns of bacteria causing significant bacteriuria in pregnant women in North-western Tanzania.

Bacteria (*n*)	Antimicrobial resistance (%)										
	AMP	SXT	NIT	GEN	CIP	ERY	VAN	AMC	CAZ	CRO	MEM
Escherichia coli (164)	94.5	88.4	12.8	16.5	16.5	NA	NA	50.0	12.8	13.4	0.0
Klebsiella spp. (55)[a]	98.2	89.1	52.7	16.4	23.6	NA	NA	76.4	16.4	21.8	1.8
Staphylococcus aureus (28)	85.7	82.1	21.4	10.7	25.0	42.7	3.6	NA	NA	NA	NA
Acinetobacter spp. (13)	NA	100.0	NA	15.4	23.1	NA	NA	NA	38.5	NA	0.0
Pseudomonas aeruginosa (9)	NA	NA	NA	0.0	22.2	NA	NA	NA	22.2	NA	0.0
Other GNB (40)[b]	97.5	85.0	37.5	27.5	17.5	NA	NA	62.5	22.5	27.5	0.0
Other GPB (14)[c]	50.0	66.7	20.0	15.4	20.1	42.7	0.0	NA	NA	NA	NA

AMP, ampicillin; SXT, trimethoprim/sulfamethoxazole; NIT, nitrofurantoin; GEN, gentamicin; CIP, ciprofloxacin; ERY, erythromycin; VAN, vancomycin; AMC, amoxicillin/clavulanic acid; CAZ, ceftazidime; CRO, ceftriaxone; MEM, meropenem; NA, not applicable; GNB, Gram-negative bacteria; GPB, Gram-positive bacteria.
[a] Includes *Klebsiella pneumoniae* (*n* = 43) and *Klebsiella oxytoca* (*n* = 12).
[b] Other GNB includes *Enterobacter* spp. (11), *Proteus mirabilis* (7), *Citrobacter freundii* (4), *Providencia* spp. (2) and unidentified GNB (16).
[c] Other GPB includes *Streptococcus agalactiae* (6), *Staphylococcus saprophyticus* (2), *Enterococcus* spp. (1) and other *Streptococcus* spp. (5).

Table 4
Cephalosporin resistance among Enterobacteriaceae strains causing significant bacteriuria in pregnant women in North-western Tanzania.

Health facility (*n*)[a]	Cephalosporin resistance		
	n (%)	OR (95% CI)	*P*-value
Health centres (49)	4 (8.2)	1	
NDH & SDDH (74)	10 (13.5)	1.76 (0.52–5.96)	0.365
SRRH (65)	13 (20.0)	2.81 (0.86–9.24)	0.088
BMC (71)	16 (22.5)	3.27 (1.02–10.49)	0.046
Total (259)	43 (16.6)		

OR, odds ratio; CI, confidence interval.
[a] See Table 1 for description of healthcare facilities.

centres and dispensaries (11.7%)], although the difference was not statistically significant (*P* = 0.751) (Fig. 1).

3.5. Predictors of significant bacteriuria among pregnant women in North-western Tanzania

On univariate analysis, SB among pregnant women was significantly associated with women attending regional and tertiary hospitals, residing in an urban area, lack of formal occupation, hospital admission, having an intravenous (i.v.) line, indwelling urinary catheter and the presence of co-morbidities. Conversely, having either a domestic or pet animal at home was found to be associated with low SB. Subanalysis of invasive procedures among admitted pregnant women (*n* = 527) also showed an increased odds of having SB: e.g. presence of i.v. line compared with those without, 40.6% vs. 23.0% (OR = 2.29, 95% CI 1.10–4.77; *P* = 0.028); and catheterised pregnant women compared with non-catheterised women, 43.5% vs. 23.2% (OR = 2.54, 95% CI 1.09–5.95; *P* = 0.031).

On multivariate logistic regression analysis, lack of formal occupation (OR = 1.61, 95% CI 1.05–2.47; *P* = 0.030), hospital admission (OR = 2.10, 95% CI 1.30–3.39; *P* = 0.002) and presence of co-morbidities (OR = 1.63, 95% CI 1.23–2.17; *P* = 0.001) were found to be independent predictors of SB (Table 5).

4. Discussion

4.1. Magnitude of significant bacteriuria among pregnant women

The prevalence of SB in the current study (17.7%) is comparable with the prevalences of 13.0% and 17.9% reported previously at BMC [9] and is also similar to other studies in Tanzania (21%), Ethiopia (18.8%), Nigeria (15.5%) and South Africa (5% clinical diagnosis; 16.4% laboratory diagnosis) [10,21–23], but is higher than the prevalences of 1.4% and 6% reported in the USA and Canada, respectively [8,24]. The differences may be accounted for by varying epidemiology of the disease across countries. Previous

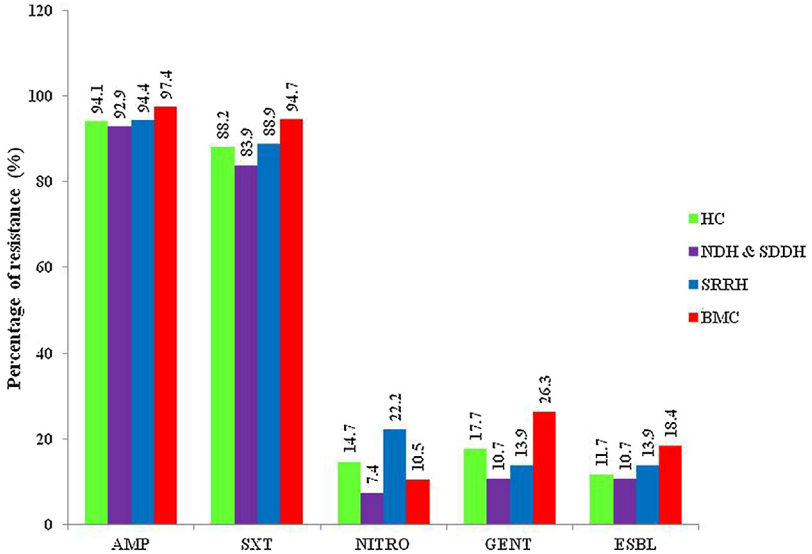

Fig. 1. Resistance patterns of *Escherichia coli* in various healthcare facilities. AMP, ampicillin; SXT, trimethoprim/sulfamethoxazole; NITRO, nitrofurantoin; GENT, gentamicin; ESBL, extended-spectrum β-lactamases-producing Enterobacteriaceae. See Table 1 for description of healthcare facilities.

Table 5
Risk factors of significant bacteriuria (SB) among pregnant women in North-western Tanzania.

Variable (*N*)	SB [*n* (%)]	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Health facility[a]					
HC (389)	54 (13.9)	1			
NDH & SDDH (610)	95 (15.6)	1.14 (0.80–1.64)	0.464	1.36 (0.93–2.00)	0.114
SRRH (366)	79 (21.6)	1.71 (1.17–2.50)	0.006	0.86 (0.46–1.59)	0.625
BMC (463)	95 (20.5)	1.60 (1.11 −2.31)	0.012	1.26 (0.81–1.94)	0.303
Residence					
Rural (335)	42 (12.5)	1			
Urban (1493)	281 (18.8)	1.62 (1.14–2.29)	0.007	1.18 (0.75–1.87)	0.475
Education					
College (143)	27 (18.9)	1			
None (93)	12 (12.9)	0.64 (0.31–1.33)	0.229		
Primary (1090)	192 (17.6)	0.92 (0.59–1.44)	0.710		
Secondary (502)	92 (18.3)	0.96 (0.60–1.55)	0.880		
Marital status					
Single (220)	47 (21.4)	1			
Married (1608)	276 (17.2)	0.76 (0.54–1.08)	0.127		
Occupation					
Employed (244)	34 (13.9)	1			
Peasant (388)	54 (13.9)	1.00 (0.63–1.59)	0.995	1.09 (0.65–1.83)	0.750
No formal occupation (653)	140 (21.4)	1.69 (1.12–2.53)	0.012	1.61 (1.05–2.47)	0.030
Petty trader (543)	95 (17.5)	1.31 (0.86–2.00)	0.213	1.20 (0.77–1.85)	0.421
Coitus (times per week)					
No (237)	36 (15.2)	1			
Once (720)	125 (17.4)	1.17 (0.78–1.76)	0.439		
Twice (686)	124 (18.1)	1.23 (0.82–1.85)	0.312		
≥Three times (185)	38 (20.5)	1.44 (0.87–2.39)	0.153		
Animal at home[b]					
No (1488)	291 (19.6)	1			
Yes (340)	32 (9.4)	0.43 (0.29–0.63)	<0.001		
Parity					
Nulliparous (655)	130 (19.8)	1			
Para 1–3 (896)	152 (17.0)	0.82 (0.64–1.07)	0.146		
Para ≥4 (277)	41 (14.8)	0.70 (0.48–1.03)	0.070		
Gestational age					
First trimester (92)	19 (20.7)	1			
Second trimester (604)	87 (14.4)	0.65 (0.37–1.12)	0.123		
Third trimester (1132)	217 (19.2)	0.91 (0.54–1.54)	0.729		
Antibiotic use in the past 3 months					
No (1372)	243 (17.7)	1			
Yes (456)	80 (17.5)	0.99 (0.75–1.31)	0.935		
Admission status					
Outpatient (1301)	196 (15.1)	1			
Inpatient (527)	127 (24.1)	1.79 (1.39–2.30)	<0.001	2.10 (1.30–3.39)	0.002
Presence of intravenous line					
No (1796)	310 (17.3)	1			
Yes (32)	13 (40.6)	3.28 (1.60–6.71)	0.001	1.60 (0.58–4.42)	0.362
Indwelling urinary catheter					
No (1805)	313 (17.3)	1			
Yes (23)	10 (43.5)	3.67 (1.59–8.44)	0.002	1.15 (0.35–3.76)	0.822
Co-morbidities[c]					
No (1398)	215 (15.4)	1			
Yes (430)	108 (25.1)	1.85 (1.42–2.40)	<0.001	1.63 (1.23–2.17)	0.001
Urinary symptoms					
No (1243)	220 (17.7)	1			
Yes (585)	103 (17.6)	0.99 (0.77–1.29)	0.962		

OR, odds ratio; CI, confidence interval.
[c]Human immunodeficiency virus (HIV) ($n = 299$), preeclampsia ($n = 130$) or both ($n = 1$)].
[a] See Table 1 for description of healthcare facilities.
[b] Presence of pet or domestic animal at home (this variable was not subjected to multivariate analysis because of collinearity with residence).

studies have also shown a lower prevalence of SB (1–10%) in non-pregnant women, connoting increased predisposition among pregnant women [4,25].

4.2. Bacterial species causing significant bacteriuria among pregnant women

The current study as well as previous studies from Tanzania, South Africa and Iran showed an overall preponderance of Gram-negative bacteria (with *E. coli* in approximately one-half of cases) compared with Gram-positive bacteria causing SB [6,9,10,23,26]. Conversely, two studies in the USA and Canada showed a predominance of *E. coli*, group B *Streptococcus* and other Gram-positive bacteria [8,24]. The differences may be accounted for by the lack of adequate hygiene and sanitation measures in resource-limited settings in the former group leading both to endogenous and exogenous infections, whereas in the later group SB is mostly from endogenous sources. This speculation is supported by another study from Iran in which poor hygiene measures increased the odds of SB among pregnant women [27]. Also, in a recent

systematic review, improved hygiene measures were shown to be associated with low SB among pregnant women compared with other measures such as use of cranberry juice, ascorbic acid, Canephron® and immunisation [28].

4.3. Antimicrobial resistance profiles of bacteria causing significant bacteriuria

In Tanzania, the recommended treatment in pregnant women is amoxicillin or AMC (first-line) for uncomplicated UTIs and ceftriaxone in complicated cases (second-line) [29]. This study and previous reports have shown high resistance to commonly used antimicrobial agents such as ampicillin and SXT in contrast to less commonly agents such as nitrofurantoin, gentamicin and ceftriaxone [2,30,31]. Resistance to nitrofurantoin among *E. coli* strains was 12.8% in all HCFs (10.5% at BMC) compared with 5.9% in a previous study, showing a gradual increase in resistance to this agent [9]. Of note, third-generation cephalosporin resistance was twice as high among inpatients compared with outpatients, indicating a preponderance in the former group. Existence of third-generation cephalosporin resistance among outpatients may be accounted for by high ESBL faecal carriage as previously reported in the same region among delivering women (14%), the general community (16.5%) and mothers of neonates (28.3%), respectively [32–34]. The proportion of MRSA among *S. aureus* strains was high (28.6%) and was comparable with 25% in Dar es Salaam, Tanzania [10]. Therefore, in light of increasing MDR strains in the cascade of referral healthcare system (notably at BMC tertiary hospital), there is an obvious need to introduce routine culture and AST in district and regional hospitals as well as strengthening of this service in the tertiary hospital. Also taking into account the predominance of *E. coli*-attributable SB among pregnant women, nitrofurantoin (first-line) and gentamicin or ceftriaxone (second-line) can be judiciously chosen as potential antimicrobial treatment options in settings where culture and AST services are not available in the North-western part of Tanzania. These findings are also critical in the context of the recently launched Tanzanian National Action Plan on AMR (2017–2022) for future monitoring of AMR trends [35].

4.4. Predictors of significant bacteriuria among pregnant women

The association of SB and lack of formal occupation among pregnant women in this study may be related to financial constraints hindering their to access health services. Despite the fact that antenatal services are free of charge in Tanzania, accessing these services require costs related to travel along with other indirect costs. The association of SB and human immunodeficiency virus (HIV) infections have been widely reported and correlates with the severity of HIV/AIDS (measured by decrease in $CD4^+$ T-lymphocyte count and/or increase in HIV viral load) [22,23]. These findings are also reiterated in the specific subanalysis involving 234 pregnant women with HIV infection in which the prevalence of SB was 21.4% and was predicted by single marital status and low $CD4^+$ count of $<200/\mu L$ [11]. Also, another subanalysis of 131 pregnant women with preeclampsia (cases) paired with 262 women without preeclampsia (controls) by age and gravidity showed that pregnant women with preeclampsia were found to have a 7.7 odds of developing SB compared with those without preeclampsia [36]. Possible reasons for the preponderance of SB among admitted patients in this study may be co-existing illnesses (as described above for HIV infections and preeclampsia) and invasive procedures while patients are admitted such as i.v. cannulation and urinary catheterisation, which were all found to be statistically significant in the univariate analysis. As a result, this calls for a comprehensive approach in managing all co-morbidities associated with pregnancy as well as the strengthening of aseptic techniques while undertaking invasive procedures.

5. Conclusions

The prevalence of SB among pregnant women in this large multicentre study was high (17.7%). The most common bacterial species were *E. coli*, *Klebsiella* spp. and *S. aureus*. Third-generation cephalosporin resistance among members of the family Enterobacteriaceae was found to be significantly higher in strains from BMC tertiary hospital compared with lower HCFs. Strengthening of routine culture and AST in antenatal clinics is recommended to ensure specific management. Pregnant women with no formal occupation, inpatients and those with co-morbidities should be specific target groups for preventive measures against SB. A prospective study will be of interest in the future to assess pregnancy outcomes.

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Competing interests

None declared.

Ethical approval

This study was approved by the joint CUHAS/BMC Research and Ethics Committee [CREC 123/2016] in Tanzania.

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