Magnitude and associated factors of bacterial urinary tract infections among paediatric patients in Arba Minch, southern Ethiopia

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Abstract

Bacterial urinary tract infections (UTI) commonly occur in children; if left untreated, they may result in severe consequences such as urosepsis and renal damage. This study aimed to determine the bacterial profile, antimicrobial susceptibility patterns and associated factors among paediatric patients suspected of urinary tract infections in Arba Minch General Hospital (AMGH). An institution-based cross-sectional study was conducted from 01 October 2020 to 31 January 2021. A convenient sampling technique was used to recruit the participants; data were collected using a pre-tested questionnaire. To quantify the bacteria (as per the Kass count, >10^{5}CFU/ml), midstream urine samples were streaked onto bacteriological media. Isolates were identified by following standard procedures. The antibiotic susceptibility test was performed as per the Kirby−Bauer disc diffusion technique. Data were analyzed using SPSS software. Out of the 246 children included, 38 (15.4%) were found to be positive for significant bacteriuria. Isolates of *Escherichia coli*, 9/38 (23.7%), and *Staphylococcus aureus*, 9/38 (23.7%), were the most predominant. The majority of Gram-negative bacterial (GNB) isolates showed resistance towards amoxicillin-clavulanate (89.5%), ampicillin (84.6%), and ceftazidime (81%). Likewise, 76.9 and 76.5% of Gram-positive bacteria (GPB), respectively, had shown resistance towards co-trimoxazole and tetracycline. Multi-drug and extensively drug resistance were detected respectively in the case of 68.4 and 15.8% of the total isolates; ESBL production was found in 57.1% of GNB, whereas 55.6% of *S. aureus* were methicillin-resistant *S. aureus* (MRSA). The process of un-circumcision was significantly associated with UTI [(adjusted odds ratio= 3.578; 95% confidence interval: 1.263 − 10.13; *p*=0.016)].
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1. Introduction

Urinary tract infections (UTI) are the second most commonly occurring bacterial infections in children, the first being those involving the respiratory tract [1]. Globally, UTI are a common cause of morbidity and complications among children, showing a varying rate of prevalence among children [2].

Etiologies of UTI are diverse (bacteria, viruses, fungi and parasites); most infections are due to bacteria. Bacterial virulence is a multifactorial phenomenon that facilitates their persistence in the urinary tract, including adhesins, capsules, aerobactin, cytotoxic necrotizing factors, hemolysins, and siderophore receptors [3]. Among the uropathogenic bacteria, Gram-negatives, particularly those of enteric origin, for instance, *E. coli* (uropathogenic serotypes O1, O2, O4, O6, O7 and O75) is the single most common causative agent of UTI, accounting for 70−75% of all cases. An array of virulence factors help this uropathogen to colonize and survive in the hostile environment of the urinary tract. Bacteria typically adhere to the uro-epithelial cells via fimbrial appendage (e.g. P fimbriae), for instance, those specific strains causing lower UTI. Another example is the strains with capsular K antigen creating upper UTI [3]. Besides, they also carry a set of virulence factors

facilitating the invasion of the host, interfering with the defence system (e.g. siderophore, capsule, hemolytic, cytotoxic necrotizing factor one and secreted auto-transporter toxin) [4]. Other members of the Enterobacteriaceae such as *Klebsiella* spp., *Proteus* spp., *Enterobacter* spp., *Citrobacter* spp., and *Serratia* spp., as well as *Pseudomonas aeruginosa,* are also associated with UTI. Among Gram-positives, *Staphylococcus* spp., *Enterococcus* spp. and group B *Streptococci* are well-known etiologies of UTI in children [2]. Earlier studies reported that of late, there is an upsurge in the prevalence of *S. aureus* in UTI [5].

There are several predisposing factors in the case of children that either directly or indirectly subject them to acquiring UTI. These include age, gender, weaker immune system, catheterization, frequent use of antibiotics, un-circumcision in boys, constipation and history of UTI [6,7]. According to the findings of a recent review, having a previous history of UTI enhances the risk for a recurring infection to the extent of three-fold, whereas those who are frequently treated by antibiotics are four times more affected than their counterparts [8]. Another systematic review revealed that malnourished children have two and a half times augmented risk of acquiring UTI than those who are healthy [9].

Evidence from another study indicated that up to 30% of infants and children experience recurrent infections during the first six to twelve months after the onset of UTI [10]. Findings from an extensive systematic review showed that 57% of children with UTI develop acute pyelonephritis, and 15 % develop renal scarring [11]. Data obtained through long-term studies suggest that about 5% of children with UTI develop permanent renal damage and may require dialysis and transplant, which in resource-limiting countries are not affordable [12]. Therefore an early diagnosis and appropriate management are very much essential. However, signs and symptoms of UTI in children, particularly in the younger age group, are non-specific and may resemble childhood viral illness and thus can be easily missed [13]. On the other hand, the presence of symptoms in older children is not a reliable indicator of UTI [7].

Moreover, collecting reliable urine samples for culture is also challenging unless an invasive procedure such as catheterization is performed [14]. All these conditions put together to make the diagnosis and the management quite challenging and enforce physicians to initiate an empirical antibiotic therapy [15]. Children receive a lot of primary healthcare and a disproportionately higher number and amount of antibiotics compared to the middle-aged group. Most of the antibiotic regimens practiced are empirical and are based on national guidelines [16].

Several emerging bacterial pathogens are extremely resistant to existing treatment regimens due to their physiology or growth characteristics, and uropathogens are of no exception [17,18]. Recently, bacterial uropathogens in the paediatric patient group became highly resistant to commonly used antibiotics such as ampicillin, co-trimoxazole, fluoroquinolones and the third generation cephalosporins, and these drugs became unsuitable for empirical use [19]. This situation enhanced the frequency and number of hospitalizations and limited the availability of suitable treatment options, making the scenario more intricate, which can even lead to several deaths [19]. A recent multinational systematic review dealing with UTI in children revealed that one out of seven (14%) cases are caused by ESBL-producing Enterobacteriaceae [8]. Moreover, in developing countries, more than 80% of bacterial strains causing UTI in children are now resistant to co-trimoxazole, an antibiotic commonly prescribed for the treatment of uncomplicated UTI [20]. Findings from previous studies on childhood UTI in other parts of Ethiopia indicated that multi-drug resistant (MDR) bacterial uropathogens are rising, and geographical variations of common bacterial etiologies of UTI exist in the country [21,22].

Currently, most children having UTI attending Arba Minch General Hospital (AMGH) are treated with empirical regimens, and the frequently prescribed antibiotic is cotrimoxazole (personal communication with paediatric care providers of AMGH). This is not even supported by urine culture due to a lack of facility in the study setup. In this regard, data on local prevalence and antimicrobial susceptibility patterns of uropathogens may aid physicians significantly. To the best of our knowledge, there is only a single study [14] done in the southern part of Ethiopia in this context; however, data on the prevalence, antimicrobial susceptibility patterns and associated factors of bacterial uropathogens among children in the study area, Arba Minch are not available, and hence the present study.

2. Materials and methods

2.1. Study area, design and period

The study was conducted at AMGH, Arba Minch town, Gamo Gofa Zone from 01 October 2020 to 31 January 2021. This hospital provides health care services to more than one and a half million in and around Arba Minch town. The services provided by the hospital include preventive, curative and rehabilitative care. Currently, it has separate outpatient and paediatric emergency departments and also a paediatric ward (with 42 beds). Annually, about 25,000 children (under the age of 14) receive different healthcare services from this hospital. On the basis of clinical investigations, urinalysis and dipstick tests, about 600 children have been diagnosed with UTI annually (record from Health Management and Information System).

2.2. Study design, study population, and eligibility criteria

An institution-based cross-sectional study was conducted, and the study population comprised all paediatrics aged from 2 to 14 years with clinically suspected symptoms of UTI and those who were sent to the emergency and outpatient paediatric departments (OPD) of AMGH during the study period for urinalysis and dipstick tests. The inclusion criteria is: 1. all pediatrics aged from 2 to 14 year with clinically suspected UTI, 2. Who were sent to the laboratory for a urinalysis and/or the dipstick test. The exclusion criteria include 1. Paediatric patients who took antibiotics in the preceding seven days of being presented to the hospital, 2. Those who have known urologic abnormalities such as urinary obstruction, 3. Those who were put under antibiotics and or in follow-up and also were critically ill.

2.3. Sample size determination and sampling technique

The sample size was calculated using a single population proportion formula ($N = (Z\alpha/2)^2 P (1-P)/D^2$) [23]. To determine the required sample size, a prevalence of 16.7% was taken from a previous study conducted in the northwestern part of Ethiopia [22]. After considering a confidence interval of 95% ($z = 1.96$) and 5% of marginal error ($d = 0.05$), the initial sample size was computed as 214, and by including a 15% non-response rate, the final sample size was consolidated as 246 (n). A convenient sampling technique was used to recruit the participants consecutively until the final sample size was achieved.

2.4. Data collection tool and method

A well-designed and pre-tested structured questionnaire was used to collect the socio-demographic (age, sex and residence) and clinical factors (previous history of UTI, hospitalization, history of catheterization and status of circumcision in males). These data were collected from the medical records of participants by a senior nurse and through interviews with parents (which were performed at the emergency and OPD rooms).

2.5. Collection, transportation, handling and processing of urine samples

After receiving the written parental/guardian consent or assent from older children, wide-mouthed sterile urine cups were provided, and 5 to 10 ml of midstream urine samples were collected with the help of parents and trained laboratory technicians [24]. Samples were then transported in an ice bag to the Microbiology and Parasitology Laboratory, Department of Medical Laboratory Science, College of Medicine and Health Sciences within one hour.

2.6. Culturing of urine samples

Urine samples were well mixed and inoculated onto CLED and MacConkey agars by using a sterile disposable calibrated plastic loop (1μL). Inoculated plates were incubated aerobically at 37°C at an inverted position and, after 24 hours, checked for growth. Negative cultures were further incubated for an additional 24 hours. In this study, only the count of $\geq 10^5$ colony forming unit/ml (Kass count) of urine samples was considered significant, thus confirming the infection [25].

2.7. Bacterial isolation and phenotypic identification

Isolates were identified phenotypically by examining the colony characteristics (shape, edge, elevation, consistency, density and colour), Gram staining (Hi Media), motility and a series of standard biochemical tests [26]. Briefly mentioning, Gram-positive isolates were identified using catalase and coagulase (*Staphylococcus* sp.); heat tolerance and bile esculin hydrolysis tests (*Enterococcus* sp.) [27]. In addition, the novobiocin disk was used to distinguish between *S. epidermidis* and *S. saprophyticus* [27]. Isolates of members of the Enterobacteriaceae family (tribe I (*E. coli*), tribe V (*K. pneumoniae*, *K. oxytoca* and *Enterobacter* sp.) and tribe VI (*P. vulgaris* and *M. morganii*)) were identified by means of a series of tests: catalase, indole, citrate, urease, triple-sugar iron, H_2S production, methyl red, and Voges−Proskauer. Non−lactose fermenting Gram-negative bacteria (*P. aeruginosa*) were identified by indole, citrate, triple-sugar iron, urease, oxidase, and catalase tests [27]. Media and reagents used in the biochemical tests were procured from Hi Media, Mumbai, India.

2.8. Antimicrobial susceptibility testing

An antimicrobial susceptibility test was carried out by Kirby-Bauer disk diffusion technique on Mueller Hinton agar (Hi Media, Mumbai, India) according to the criteria set by the Clinical Laboratory Standard Institute (CLSI) [28]. Two to five colonies of fresh inoculum were taken and suspended into normal physiological saline (pH = 7), and the turbidity was adjusted to 0.5 McFarland standard, after which it was uniformly swabbed onto the Mueller Hinton agar. Respective disks were dispensed into inoculated plates using sterile forceps and incubated at 37°C for 18−24 hours; diameters of zones of inhibition around the disks were measured. Results were interpreted as susceptible, intermediate and resistant according to the CLSI guideline [26], and commercially available antibiotic disks (Oxoid, Basingstoke, and Hampshire, UK) were used. For GNB, the drugs used were penicillin (ampicillin (AMP, 10μg)), penicillin plus beta-lactamase inhibitor (amoxicillin-clavulanate (AMC, 30μg), anti-pseudomonal penicillin (piperacillin (PIP, 100μg)) second, third and fourth generation cephalosporin

(cefoxitin (CXT, 30μg), cefuroxime (CRX, 30μg), cefixime (CXM, 30μg), ceftriaxone (CTR, 30μg), ceftazidime (CAZ, 30μg), cefotaxime (CTX, 30μg) and cefepime (CFP, 30μg))), aminoglycosides (gentamicin (GEN, 10μg) and amikacin (AMK, 10μg)), anti-30 S ribosomal subunit inhibitor-tetracycline (tetracycline (TC, 30μg)), fluoroquinolones (ciprofloxacin (CIP, 5μg)), folate pathway inhibitors (co-trimoxazole (COT, 25μg)), and DNA synthesis inhibitor-nitrofuran (nitrofurantoin (NIT 300μg)). For GPB; anti-50 S ribosomal subunit inhibitor-chloramphenicol (chloramphenicol (C, 30μg)), anti-30 S ribosomal subunit inhibitor (tetracycline (TET, 30μg)), anti-50 S ribosomal subunit inhibitor-macrolide (erythromycin (ERY, 15μg)), aminoglycosides (gentamicin (GEN, 10μg)), fluoroquinolones (ciprofloxacin (CIP, 5μg)), second-generation cephalosporin (cefoxitin (CXT, 30μg)), penicillin (penicillin (PEN, 10μg), amino-penicillin (ampicillin (AMP, 10μg)), glycolpeptides (vancomycin (VAN, 30μg)), folate pathway inhibitors (co-trimoxazole (COT, 25μg)), anti-50 S ribosomal subunit inhibitor-lincosamides (clindamycin (CLN, 300 μg)) and DNA synthesis inhibitor-nitrofuran (nitrofurantoin (NIT, 300 μg)) were used. These were selected based on CLSI guideline and also by considering the national antibiotic policy. Bacterial isolates that showed acquired non-susceptibility to at least one agent from a minimum of three antimicrobial categories were considered as MDR, and extensively drug resistance (XDR) corresponds to at least one agent in all but two or fewer antimicrobial categories [29].

2.9. Detection of methicillin resistant *S. aureus*
Isolates of *S. aureus* were further subjected to a cefoxitin disk (surrogate test for oxacillin), and those isolates that showed zones of inhibition <21 mm were considered methicillin-resistant *S. aureus* according to the CLSI guideline [28].

2.10. Detection of extended-spectrum beta-lactamase (ESBL) producing GNB
2.10.1. Screening test. The susceptibility of Gram-negative bacterial isolates of UTI was tested against the third generation of cephalosporin such as ceftriaxone, cefotaxime and ceftazidime by using the routine Kirby-Bauer disk diffusion method on Mueller-Hinton agar. Isolates that showed zones of inhibition <23 mm for ceftriaxone (30μg), <27 mm for cefotaxime (30μg) and/or <22 mm for ceftazidime (30μg) were considered as positive for ESBL production [29].

2.11. Confirmatory test
A disk of amoxicillin-clavulanate (30μg) with the third generation cephalosporin such as ceftriaxone (30μg), cefotaxime (30μg) and ceftazidime (30μg) was used for the confirmation. Amoxicillin-clavulanate (30μg) disk was placed at the center of

the inoculum on Mueller-Hinton agar media, and disks of ceftriaxone (30μg), cefotaxime (30μg) and ceftazidime (30μg) each were placed 15 mm apart from amoxicillin-clavulanate (30μg). An enhanced zone of inhibition produced towards amoxicillin-clavulanate (30μg) corresponds to a potential ESBL producer [28].

2.12. Quality control
The structured questionnaire was subjected to a pre-test of 5% carried out on 5% of the sample size at the Torra Primary Hospital, Silte Zone, Southern Nations, Nationalities and Peoples Region of Ethiopia. Prior to the collection of actual data and urine samples, adequate training sessions were provided to the data collectors and laboratory technicians (who assisted in the sample collection). Data were checked daily for accuracy, clarity, and completeness and any incompleteness and errors found were immediately rectified. Standard operating procedures (in-house SOP manual) were followed during collection (aseptic technique), transportation, and processing to maintain quality. All laboratory reagents, culture media and antibiotic discs were checked for shelf life and physical deterioration and kept safely (2-8°C). Sterility of the prepared culture media was assured (until the actual sample processing) by incubating the prepared un-inoculated media at 37°C overnight; its performance was checked by overnight incubation using a known control strain; reference strains of *S. aureus* (ATCC 25923) and *E. coli* (ATCC 25922) were used as controls.

2.13. Data analysis
Data were entered, coded, cleaned, and checked for its completeness and analyzed by using Statistical Package for Social Sciences (SPSS) version 25 (IBM Corporation, Armonk, NY, USA). First, socio-demographic and clinical factors were described using descriptive statistics like frequency and percentage. Then, inferential statistics such as bivariable and multivariable binary logistic regression analyses were done to determine the strength of association among independent and outcome variables. Initially, the data were subjected to a series of bivariable analyses and those with a cut-off point of p-value less than 0.25 were processed further by multivariable analysis. The Hosmer-Lemeshow goodness fit test checked the fitness of the model. Adjusted odds ratio (AOR) and 95% confidence interval (CI) were used to determine the strength of association; p-values <0.05 in multivariable analysis were considered as statistically significant.

2.14. Ethical considerations
Ethical clearance was obtained from the Institutional Review Board, College of Medicine and Health Science, Arba Minch University (Ref. IRB/467/13/17/03/2020). In addition, written

Variables	Categories	Frequency (n)	Percentage (%)
Sex	Male	137	55.7
	Female	109	44.3
Age (years)	2-5	129	52.4
	6-9	65	26.4
	10-14	52	21.2
Residence	Urban	169	68.7
	Rural	77	31.3

parental consent or assent from older children was sought before the commencement of the actual collection of data and samples. Results of the urine culture of those children who had confirmed UTI were communicated to their physicians and recorded on the medical cards of the respective patient.

3. Results

3.1. Socio-demographic and clinical characteristics

A total of two hundred forty-six (*n* = 246) paediatrics were clinically suspected of urinary tract infections and sent to the laboratory for urinalysis and dipstick test. Of them, 137 (55.7%) were males, and the age of participants varied from 2 to 14 years, with a mean of 6.12 ± 3.5. More than half of the participants, i.e., 52.4% (*n* = 129), were in the age group of 2-5 years. The majority of the study participants, i.e., 68.7% (*n* = 169), were urban residents (Table 1), and among male patients, 29.2% (*n* = 40) were found to be uncircumcised. It was also found that 27.2% (*n* = 67) of the study participants had a history of frequent exposure to antibiotics, whereas only a tiny fraction, 1.2% (*n* = 3) of them, had a history of catheterization. Of the different signs and symptoms of UTI, fever was the most common, i.e., in 68.7% (*n* = 169) followed by vomiting in 52.4% (*n* = 129) (Table 2).

3.2. Prevalence of UTI

Out of the total 246 paediatrics involved in this study, 38 were positive with significant bacteriuria, making an overall prevalence of 15.4% (95% CI: 11.0-20.3).

3.3. Phenotypic characterization of bacterial isolates

From the total 246 cultured urine samples, thirty-eight (*n* = 38) bacterial uropathogens were isolated and identified based on phenotypic results following Bergey's manual of bacteriological classification and sorted into eight genera such as *Escherichia*, *Klebsiella*, *Pseudomonas*, *Morganella*, *Proteus*, *Enterobacter*,

Variables	Categories	Frequency (n)	Percentage (%)
Clinical factors			
Circumcision in boys	Yes	97	70.8
	No	40	29.2
Frequent exposure to antibiotics	Yes	67	27.2
	No	179	72.8
History of UTI	Yes	28	11.4
	No	218	88.6
History of hospitalization	Yes	24	9.8
	No	222	90.2
Constipation	Yes	12	4.9
	No	234	95.1
Malnutrition	Yes	8	3.3
	No	238	96.7
History of catheterization	Yes	3	1.2
	No	233	98.8
Clinical presentations			
Fever	Yes	169	68.7
	No	77	31.3
Vomiting	Yes	129	52.4
	No	117	47.6
Urinary frequency	Yes	54	22.0
	No	192	78.0
Lower abdominal pain	Yes	53	21.5
	No	193	78.5
Dysuria	Yes	29	11.8
	No	217	88.2

Staphylococcus and *Enterococcus*. Of the eight genera of bacterial isolates recovered, six were Gram-negative bacilli, while the rest were Gram-positive cocci.

More than half (55.3%, *n* = 21) of the isolates were Gram-negative, while their Gram-positive counterparts corresponded to 44.7% (*n* = 17). Both *E. coli* (23.7%, *n* = 9) and *S. aureus* (23.7%, n = 9) were the most predominantly isolated uropathogens followed by *K. pneumoniae* (10.5%, *n* = 4), *Enterococcus* spp. (10.5%, *n* = 4), *S. epidermidis* (7.9%, *n* = 3), *K. oxytoca* (5.3%, *n* = 2), *M. morganii* (5.3%, n = 2), *P. aeruginosa* (5.3%, *n* = 2), *S. saprophyticus*, *P. vulgaris* and *Enterobacter* spp. (2.6%, for each of the last three, *n* = 1).

3.4. Antimicrobial susceptibility patterns

3.4.1. Antimicrobial susceptibility patterns of GNB isolates. The susceptibility patterns of GNB (n = 21) against 16 antibiotics isolated from the urine samples of children with UTI are presented in Table 3 as susceptible and resistant, while the intermediates were also considered resistant for the purpose of statistical analysis. In the present study, isolates of Gram-negative bacterial uropathogens showed a wider range of variations in terms of their susceptibility (10.5 to 90.5%) as well as resistance (9.5 to 89.5%) patterns. These isolates showed higher resistance to ampicillin (84.6%), amoxicillin-clavulanate (89.5%), ceftazidime (81%), cefuroxime (78.9%), tetracycline (73.7%) and co-trimoxazole (68.4%); however only much lower

TABLE 3. Antimicrobial susceptibility patterns of Gram-negative bacterial isolates of UTI in children attending AMGH, January, 2021

Tested antibiotics	Gram-negative bacterial isolates													
	E. coli (n = 9)		*Klebsiella* spp. (n = 6)		*P. aeruginosa* (n = 2)		*M. morganii* (n = 2)		*P. vulgaris* (n = 1)		*Enterobacter* spp. (n = 1)		Total (n = 21)	
	Antimicrobial susceptibility patterns n (%)													
	R	S	R	S	R	S	R	S	R	S	R	S	TR (%)	TS (%)
AMP	7 (77.8)	2 (22.2)	NT	NT	NT	NT	2 (100)	0	1 (100)	0	1 (100)	0	11 (84.6)	2 (15.4%)
AUG	7 (77.8)	2 (22.2)	6 (100)	0 (0)	NT	NT	2 (100)	0	1 (100)	0	1 (100)	0	17 (89.5)	2 (10.5)
CFP	4 (44.4)	5 (55.6)	4 (66.7)	2 (33.3)	1 (50)	1 (50)	0	2 (100)	1 (100)	0	0	1 (100)	9 (47.6)	10 (52.4)
CTX	5 (55.6)	4 (44.4)	5 (83.3)	1 (16.7)	NT	NT	1 (50)	1 (50)	1 (100)	0	0	1 (100)	12 (63.2)	7 (36.8)
CTR	5 (55.6)	4 (44.4)	5 (83.3)	1 (16.7)	NT	NT	2 (100)	0	0	1 (100)	0	1 (100)	12 (63.2)	7 (36.8)
CXT	2 (22.2)	7 (77.8)	2 (33.3)	4 (66.7)	NT	NT	1 (50)	1 (50)	1 (100)	0	0	1 (100)	6 (31.6)	13 (68.4)
CRX	6 (66.7)	3 (33.3)	5 (83.3)	1 (16.7)	NT	NT	2 (100)	0	1 (100)	0	1 (100)	0	15 (78.9)	4 (21.1)
CAZ	7 (77.8)	2 (22.2)	5 (83.3)	1 (16.7)	2 (100)	0	2 (100)	0	1 (100)	0	0	1 (100)	17 (81)	4 (19)
CXM	4 (44.4)	5 (55.6)	4 (66.7)	2 (33.3)	NT	NT	2 (100)	0	1 (100)	0	0	1 (100)	11 (57.9)	8 (42.1)
GEN	5 (55.6)	4 (44.4)	4 (66.7)	2 (33.3)	1 (50)	1 (50)	2 (100)	0	0	1 (100)	0	1 (100)	12 (63.2)	9 (42.8)
AMK	1 (11.1)	8 (88.9)	2 (33.3)	4 (66.7)	0	2 (100)	2 (100)	0	0	1 (100)	0	1 (100)	5 (23.8)	16 (76.2)
TET	7 (77.8)	2 (22.2)	4 (66.7)	2 (33.3)	NT	NT	2 (100)	0	1 (100)	0	0	1 (100)	14 (73.7)	5 (26.3)
CIP	0	9 (100)	2 (33.3)	4 (66.7)	0	2 (100)	0	2 (100)	0	1 (100)	0	1 (100)	2 (9.5)	19 (90.5)
NIT	1 (11.1)	8 (88.9)	0	6 (100)	NT	NT	0	2 (100)	1 (100)	0	0	1 (100)	2 (10.5)	17 (89.5)
COT	6 (66.7)	3 (33.3)	4 (66.7)	2 (33.3)	NT	NT	2 (100)	0	1 (100)	0	0	1 (100)	13 (68.4)	6 (31.6)
PIP	NT	NT	NT	NT	1 (50)	1 (50)	NT	NT	NT	NT	NT	NT	1 (50)	1 (50)

AMP: ampicillin, AUG: amoxicillin-clavulanate, CFP: cefepime, CTX: cefotaxime, CTR: ceftriaxone, CXT: cefoxitin, CRX: cefuroxime, CAZ: ceftazidime, CXM: cefixime, GEN: gentamicin, AMK: amikacin, TET: tetracycline, CIP: ciprofloxacin, NIT: nitrofurantoin, COT: cotrimoxazole, PIP: piperacillin, NT: not tested, R%: percent of resistance, S%: percent of susceptible, TR%: total percent of resistance, TS%: total percent of susceptible.

resistance were observed towards amikacin (23.8%), nitrofurantoin (10.5%) and ciprofloxacin (9.5%).

All six isolates of *Klebsiella* spp. Showed resistance towards amoxicillin-clavulanate, and 83.3% (5/6) of them were resistant to the third-generation cephalosporin (ceftazidime, cefotaxime and ceftriaxone), and 66.7% (4/6) were resistant against co-trimoxazole. However, 100% of these isolates were susceptible to nitrofurantoin, and only one-third of them (i.e., 33.3% (2/6)) showed resistance to ciprofloxacin. Isolates of *E. coli* showed 77.8% (7/9) resistance to three antibiotics such as ampicillin, amoxicillin-clavulanate and ceftazidime, and 66.7% (6/9) were resistant to co-trimoxazole. However, all (9/9) of the isolates were susceptible to ciprofloxacin; likewise, 88.9% (8/9) of these isolates were susceptible to both nitrofurantoin and amikacin. Both isolates of *M. morganii* were resistant to seven antibiotics (co-trimoxazole, tetracycline, ampicillin, amoxicillin-

TABLE 4. Antimicrobial susceptibility patterns of Gram-positive bacterial isolates of UTI in children attending AMGH; January 2021

Tested antibiotics	Gram-positive bacterial isolates									
	S. aureus (n = 9)		*S. epidermidis* (n = 3)		*S. saprophyticus* (n = 1)		*Enterococcus* spp. (n = 4)		Total (n = 17)	
	Antimicrobial susceptibility patterns n (%)									
	R	S	R	S	R	S	R	S	TR (%)	TS (%)
AMP	NT	NT	NT	NT	NT	NT	2 (50)	2 (50)	(50)	(50)
CIP	1 (11.1)	8 (88.9)	0	3 (100)	1 (100)	0	2 (50)	2 (50)	23.5%	76.5%
C	4 (44.4)	5 (55.6)	3 (100)	0	0	1 (100)	NT	NT	61.5%	38.5%
COT	6 (66.7)	3 (33.3)	3 (100)	0	1 (100)	0	NT	NT	76.9	23.1
CLN	0	9 (100)	0	3 (100)	0	1 (100)	NT	NT	0	100
CXT	5 (55.6)	4 (44.4)	2 (66.7)	1 (33.3%)	1 (100)	0	NT	NT	61.5	38.5
ERY	5 (55.6)	4 (44.4)	2 (66.7)	1 (33.3)	1 (100)	0	3 (75)	1 (25)	64.7%	35.3
GEN	0	9 (100)	0	3 (100)	0	1 (100)	NT	NT	0	100
NIT	0	9 (100)	1 (33.3)	2 (66.7)	0	1 (100)	0	4 (100)	5.9	94.1
PEN	8 (88.9)	1 (11.1)	2 (66.7)	1 (33.3)	1 (100)	0	1 (25)	3 (75)	70.6	23.5
TET	6 (66.7)	3 (33.3)	2 (66.7)	1 (33.3)	1 (100)	0	4 (100)	0	76.5	23.5
VAN	NT	NT	NT	NT	NT	NT	1 (25)	3 (75)	25	75

AMP: ampicillin, CIP: ciprofloxacin, C: chloramphenicol, COT: cotrimoxazole, CLN: clindamycin, CXT: cefoxitin, ERY: erythromycin, GEN: gentamicin, NIT: nitrofurantoin, PEN: penicillin, TET: tetracycline, VAN: vancomycin, R %: percent of resistance, S %: percent of susceptible, TR%: total percent of resistance, TS %: total percent of susceptible, NT: not tested.

TABLE 5. Multiple drug resistance and extensively drug resistance patterns of bacterial isolates of UTI in children at AMGH

Bacterial isolates (n)	Level of resistance (%)							
	R_3	R_4	R_5	R_6	R_7	R_8	MDR	XDR
E .coli (9)	0 (0)	2 (22.2)	5 (55.6)	0 (0)	1 (11.1)	0 (0)	8 (88.9)	0 (0)
Klebsiella spp. (6)	1 (16.7)	0 (0)	0 (0)	0 (0)	1 (16.7)	3 (50)	5 (83.3)	4 (66.7)
M. morganii (2)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	2 (100)	0 (0)
P. vulgaris (1)	0 (0)	0 (0	0 (0	0 (0	0 (0	1 (100)	1 (100)	1 (100)
S. aureus (9)	1 (11.1)	2 (22.2)	2 (22.2)	1 (11.1)	0 (0)	0 (0)	6 (66.7)	0 (0)
S. epidermidis (3)	0 (0)	0 (0)	0	2 (50)	0 (0)	0 (0)	2 (66.7%)	0 (0)
S. saprophyticus (1)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)
Enterococcus spp. (4)	0 (0)	0 (0)	1 (25)	0 (0)	0 (0)	0 (0)	1 (25)	1 (25)
Total (*n* = 38)	2 (7.7)	4 (15.4)	9 (34.6)	4 (15.4)	3 (11.5)	4 (15.4)	26 (68.4)	6 (15.8)

R_3 (resistant to 3 antibiotics), R_4 (resistant to 4 antibiotics), R_5 (resistant to 5 antibiotics), R_6 (resistant to 6 antibiotics), R_7 (resistant to 7 antibiotics), R_8 (resistant to 8 antibiotics).
Note: Isolates of *E. coli, P. vulgaris, M. morganii* and *Enterobacter,* were tested against 10 categories of antimicrobials; *Klebsiella* species were tested against 9 categories of antimicrobials, *P. aeruginosa* isolates were tested against 4 categories of antimicrobials, *Enterococcus* species were tested against 7 categories of antimicrobials, *S. aureus, S. saphrophyticus* and *S. epidermidis* were tested against 10 categories of antimicrobials.

clavulanate, amikacin, gentamicin and ceftazidime). However, none of these isolates showed resistance to ciprofloxacin, nitrofurantoin and cefepime. Isolates of non-fermenting GNB (*P. aeruginosa*) showed 100% (2/2) resistance to ceftazidime, whereas susceptibility to ciprofloxacin and amikacin was 100% (2/2).

3.5. Antimicrobial susceptibility patterns of gram-positive bacterial isolates

The susceptibility patterns of GPB (*n* = 17) against twelve antibiotics isolated from the urine sample of children with UTI are presented in Table 4 as susceptible and resistant. The intermediates were also considered resistant for the purpose of statistical analysis, as mentioned earlier.

Similar to that of Gram-negative bacterial isolates, a wider range of variations in resistance (5.9 to 76.9%) as well as susceptibility (23.1 to 100%) patterns were also observed, in this case too. Isolates of GNB showed a higher degree of resistance to co-trimoxazole (76.9%), tetracycline (75.6%) and penicillin (70.6%) and erythromycin (64.7%). However, a much lower resistance was only detected against ciprofloxacin (23.5%) and nitrofurantoin (5.9%).

Isolates of *S. aureus* also showed considerable variations in their resistance (0 to 88.9%) and susceptibility patterns (11.1 to 100%). At the same time, it exhibited a higher rate of resistance to penicillin (88.9%), co-trimoxazole and tetracycline (66.7% for each). However, none of these isolates showed resistance to nitrofurantoin, gentamicin and clindamycin, and only a much lower resistance was detected against ciprofloxacin (11.1%).

Isolates of *S. epidermidis* also exhibited large-scale variations in their resistance (0 to 100%) as well as susceptibility (0 to 100%) patterns. Invariably, all the isolates, i.e., 100% (3/3) of *S. epidermidis,* showed resistance to chloramphenicol and co-trimoxazole. Similarly, a very high rate of resistance was also detected against tetracycline and nitrofurantoin (66.7% each).

However, none of these isolates was resistant to ciprofloxacin, gentamicin, and clindamycin.

In the present study, out of the nine isolates of *S. aureus*, five (55.6%) were found to be MRSA. An enhanced rate of resistance towards cefoxitin was also observed among the isolates of *S. epidermidis*. Two out of three (66.7%) of these isolates were methicillin-resistant.

In the case of *Enterococci* spp., all the isolates 4/4 (100%) showed resistance to tetracycline, and 3/4 (75%) were resistant to erythromycin. However, none of these isolates showed resistance to nitrofurantoin; one-fourth (25%) of *Enterococci* spp. Isolates were found to be vancomycin resistant.

3.6. MDR and XDR patterns of uropathogenic bacterial isolates

In the current study, out of the 38 uropathogenic bacterial isolates, 26 were MDR, making an overall prevalence rate of 68.4% (26/38), while 6 (15.8%) were XDR. However, none of the isolates was found to be resistant to all the selected antimicrobial categories tested. This means that we have not detected any pan-drug-resistant isolates.

Of the total (*n* = 26) MDR, 61.5% (16/26) belong to the Gram-negative group. Also among them, *E. coli* 50% (8/16) was the predominant one, followed by *Klebsiella* spp., 31.3 % (5/16). In the case of Gram-positive MDR isolates, *S. aureus* 60 % (6/10) was the leading entity, followed by *S. epidermidis* 20% (2/10). It was also found that 88.9% (8/9) of *E. coli*, 83.3% (5/6) of *Klebsiella* spp., 66.7% (6/9) each of *S. aureus* and *S. epidermidis* (2/3) were MDR. Besides, 34.6% (9/26) and 7.7% (2/26) of MDR bacterial isolates were resistant to five and three antimicrobials, respectively. It is to be noted that MDR was not observed among the isolates of *P. aeruginosa* and *Enterobacter* spp. On the other hand, isolates of *Klebsiella* spp. Were the most prominent among the XDR, i.e., 4 (66.7%) (Table 5).

3.7. Prevalence of ESBL-producing GNB

In the present study, all the Gram-negative bacterial isolates of UTI (n = 21) were tested against the third-generation cephalosporin (ceftazidime, cefotaxime and ceftriaxone), and sixteen were found to be resistant or intermediate to one or more of these antibiotics, and are subsequently subjected to confirmatory tests. The results revealed that 12 were confirmed cases of ESBL producers, making an overall ESBL prevalence of 57.1% (12/21). In addition, it was also found that 55.6% (5/9) of *E. coli* and 75% (3/4) of *K. pneumoniae* were ESBL producers. The rest of the ESBL producers were *P. aeruginosa* 100% (2/2), *K. oxytoca* 50% (1/2) and *P. vulgaris* 100% (1/1).

3.8. Factors associated with urinary tract infections

Different socio-demographic and clinical factors were subjected to bivariable analysis and found that four variables such as residence (*p* = 0.055), un-circumcision in boys (*p* = 0.004), frequent use of antibiotics (*p* = 0.151) and malnutrition (*p* = 0.098) were statistically significant (*p* < 0.25). Results of the multivariable analysis revealed that of the four variables analyzed, only one, i.e., un-circumcision in boys, was found to be statistically significant (*p* = 0.016; AOR = 3.578; 95% CI = 1.263 − 10.134) (Table 6).

4. Discussions

To the best of our knowledge, this is the first report on the magnitude and drug resistance profile of uropathogens isolated from paediatric population in the study area. In the present study, the overall prevalence of culture-confirmed UTI was 15.4% (95% CI: 11.0-20.3), which is in line with the findings of previous studies conducted at Addis Ababa (15.9%) and Bahir Dar (15.8%), Ethiopia [30,31], Nigeria (13.7%) [32] and Nepal (16%) [33]. In contrast, our findings correspond to a lower prevalence rate compared to results of earlier studies reported from different regions of Ethiopia, such as Hawassa (27.5%) [14] and Gondar (26.5%) [21]. This divergence in prevalence may be due to variations in age, sex, circumcision in boys, the extent of malnutrition, the method of urine sample collection employed and the sample size.

In our study, altogether, eight pathogenic bacterial genera (*Escherichia*, *Klebsiella*, *Pseudomonas*, *Morganella*, *Proteus*, *Enterobacter*, *Staphylococcus* and *Enterococcus*) were found to be responsible for UTI, which is in line with a previous study done in Gondar, Ethiopia [21]. It was also found that all UTI cases were mono-bacterial, which is in accordance with some of the previous studies conducted in Gondar, Ethiopia [21] and Nepal [33]. Majority of UTI cases, i.e., 55.3% (21/38) in our study were caused by GNB uropathogens. Similar trends were reported by earlier studies conducted in Addis Ababa [30] and Bahir Dar, Ethiopia [31], and Nigeria [34].

In the present study, isolates of *E. coli* (23.7% (9/38)) and *S. aureus* (23.7% (9/38)) were the leading causative agents of UTI followed by *Klebsiella* spp. (15.8% (6/38)) which are in agreement with a previous study conducted in Gondar, Ethiopia [21]. Higher isolation rates of *E. coli* and *Klebsiella* spp. In UTI cases can be attributed to the presence of special virulence factors such as pili in Enterobacteriaceae, which help them to attach to the uro-epithelium of the host, eventually leading to UTI [35].

TABLE 6. Bivariable and multivariable logistic regression analysis of sociodemographic and clinical factors of UTI in children at AMGH, January 2021

Variables	Categories(f)	UTI, n (%)		Bivariable analysis		Multivariable-analysis	
		Present	Absent	*p*-value	COR (95% CI)	*p*-value	AOR (95% CI)
Residence	Urban (169)	21 (12.4)	148 (87.6)	1		1	1.442 (0.487– 4.274)
	Rural (77)	17 (22.1)	60 (77.9)	0.055*	1.997 (0.985-4.047)	0.509	
Age group (in years)	2-5 (129)	20 (15.5)	109 (84.5)	0.984	1.009 (0.414-2.461)		
	6-9 (65)	10 (15.4)	55 (84.6)	1.00	1.00 (0.364-2.747)		
	10-14 (52)	8 (15.4)	44 (84.6)	1		—	—
Sex	Male (137)	21 (15.3)	116 (84.7)	1		—	—
	Female (109)	17 (15.6)	92 (84.4)	0.954	1.021 (0.509 -2.046)		
Circumcision (in males)	Yes (97)	9 (9.3)	88 (90.7)	1		1	
	No (40)	12 (30)	28 (70)	0.004*	4.19 (1.599-10.980)	0.016**	3.578 (1.263 − 10.134)
Previous UTI	Yes (28)	6 (21.4)	22 (78.6)	0.356		—	—
	No (218)	32 (14.7)	186 (85.3)	1	1.585 (0.596-4.213)		
Frequent- antibiotics use	Yes (67)	14 (20.9)	53 (79.1)	0.151*		0.369	1.636 (0.558– 4.790)
	No (179)	24 (13.4)	155 (86.6)	1	1.706 (0.823-3.537)	1	
Hospitalization	Yes (24)	5 (20.8)	19 (79.2))	0.445		—	—
	No (222)	33 (14.9)	189 (85.1)	1	1.507 (0.526-4.317)		
Malnutrition	Yes (8)	3 (37.5)	5 (62.5)	0.098*		0.704	1.484 (0.193 − 11.384)
	No (238)	35 (14.7)	203 (85.3)	1	3.48 (0.796-15.221)	1	

Note: *(Statistically significant at *p* < 0.25), ** (statistically significant at *p* < 0.05), **COR**: Crude odds ratio, **AOR**: Adjusted odds ratio **CI**: confidence interval, **n**: number of positive or negative cases of UTI, **%**: percent, **1**: reference group, **f**: frequency, **-** (not eligible).

Among Gram-negative bacterial isolates, *E. coli* was the most predominant one (42.9%, (9/21)) followed by *Klebsiella* spp. (28.6%, 6/21), which is in line with the findings of a couple of studies conducted in Ethiopia [14,30]. In the case of GPB isolates, *S. aureus* (52.3% 9/17)) was the predominant type, followed by *Enterococcus* spp., (23.55% (4/17)) and *S. epidermidis* (17.6% (3/17)). Similarly, a study conducted in Gondar reported *S. aureus* as the most prevalent isolate [21].

Antibiotic resistance is one of the greatest and most urgent cross-border public health threats. Bacteria are becoming increasingly resistant to existing antibiotics, and pathogens associated with UTI are of no exception. Compliance and resistance are proven factors in determining the success or failure of a treatment regimen. Knowing the status of local susceptibility profile and prevalence of antibiotic resistance are important guiding principles related to the selection of a treatment regimen and are helpful in militating against uropathogens. We have found that Gram-negative bacterial isolates exhibited high rates of resistance towards amoxicillin-clavulanate (89.5%), ampicillin (84.6%), tetracycline (73.7%) and co-trimoxazole (68.4%). This is in agreement with the findings of previous studies conducted in Bahir Dar, Ethiopia [22,31], Kenya [36] and Nigeria [37]. Our results imply that these antibiotics have only the least efficacy and hence cannot be used in an empirical therapy for the management of UTI in children in the study area. The widespread availability of these antibiotics and their irrational use could be a probable cause of the rapid emergence of bacterial resistance. Surprisingly, these isolates were highly susceptible to ciprofloxacin (90.5%), nitrofurantoin (89.5%) and amikacin (76.2%), making them suitable for the management of UTI. This is also in line with the findings of some of the previous studies done in other regions of Ethiopia, such as Gondar [21] and Bahir Dar [31], and Kenya [36]. Limited availability and higher cost may be attributed as the reasons for much lower resistance linked to these antibiotics. In contrast, an enhanced rate of resistance to nitrofurantoin was detected in an earlier study conducted in Bahir Dar [31]. The emergence of bacterial uropathogens resistant to these newer and effective antibiotics may be correlated to their frequent use in the above-mentioned places/countries or the accumulation of resistant genes.

Results of our study also revealed that isolates of *E. coli* were highly resistant to ampicillin, amoxicillin-clavulanate and tetracycline 77.8% each (7/9), and co-trimoxazole 66.7% (6/9), which are comparable to the outcome of studies conducted in Bahir Dar, Ethiopia [22], and Nepal [33]. In addition, it is to be noted that 77.8% (7/9), 66.7% (6/9) and 55.% (5/9) of *E. coli* were resistant to ceftazidime, cefuroxime and ceftriaxone, respectively, which are comparable to the results of studies conducted in India [38] and Bangladesh [39].

On the contrary, the same isolates were found to be highly susceptible to ciprofloxacin 100% (9/9), amikacin and nitrofurantoin, 88.9% (8/9), for each and cefoxitin 77.8% (7/9), which are in parity with the findings of studies conducted in the capital city of Ethiopia [30], India [38] and Nepal [33].

Our results also showed that all isolates of *Klebsiella* spp., (6/6) were resistant to amoxicillin-clavulanate. A similar trend of resistance to this antibiotic was reported earlier from another city in Ethiopia [22] and India [38], and this alarming rate of resistance can be attributed to its easy availability and low cost leading to irrational use. It is also found that isolates of *Klebsiella* spp., have strong resistance, 83.3% (5/6), to each one of the second and third-generation cephalosporin such as cefuroxime, ceftazidime, cefotaxime and ceftriaxone; however a reduction in resistance can be observed in the case of co-trimoxazole, and tetracycline i.e., 66.7% (4/6) for each drug. Comparable rate of resistance were reported from previous studies conducted in India [38] and Bangladesh [39]. The occurrence of a pronounced rate of resistance to the cephalosporin group of drugs may be due to their frequent use; the production of beta-lactamase enzyme by *Klebsiella* spp., can hydrolyze the beta-lactam ring in the cephalosporin structure. It is to be specified that *K. pneumoniae* showed 100% (6/6) susceptibility to nitrofurantoin and 66.7% (4/6) each to ciprofloxacin, amikacin and cefoxitin each. A similar trend in susceptibility patterns was reported from the capital city of Ethiopia [30] as well as from Nepal [33]. Another Gram-negative bacterial isolate studied was *P. aeruginosa*, which showed 100% (2/2) resistance to ceftazidime. Similar patterns of resistance were reported by an earlier study done in Ethiopia [22]; on the contrary, it was 100% (2/2) susceptible to ciprofloxacin. An identical susceptibility pattern was reported by a previous study done elsewhere in Ethiopia [21]. The rising trend of resistance must be monitored vigilantly, especially by restricting the excessive usage of antibiotics.

Isolates of Gram-positive bacteria showed moderate to a higher degree of resistance to erythromycin (64.7%), penicillin (70.6%), and tetracycline (76.5%). A similar trend in resistance was reported by previous studies done in Hawassa, Ethiopia [14], and India [38]. At the same time, these isolates showed a higher degree of susceptibility to nitrofurantoin (94.1%) and ciprofloxacin (76.5%). A more or less identical trend in susceptibility patterns was reported from a couple of cities in Ethiopia [21,30] and Nepal [33]. It is also found that isolates of *S. aureus*, exhibited an enhanced degree of resistance to penicillin 88.9% (8/9); tetracycline and co-trimoxazole each, 66.7% (6/9). A comparable extent of resistance was reported by previous studies conducted in Ethiopia [31] and Nepal [33]. However, 100% (9/9) of these isolates were susceptible to gentamicin and nitrofurantoin, and 88.9% (8/9) yielded to

ciprofloxacin. Similar patterns of susceptibility were reported from Ethiopia (Gondar and Bahir Dar) [21,31]. The enhance rates of susceptibility to these antibiotics may due to their less frequent use in the title hospital.

Our present findings also revealed that 55.6% (5/4) of isolates of *S. aureus* were MRSA. This trend was by and large similar to a recent study conducted among HIV patients in the study area, Arba Minch [40]. However, it is on the higher side in comparison to the outcome of previous studies conducted in Bahir Dar [22] and Arba Minch [41], Ethiopia where the resistance observed was only 33.3 and 42.5% respectively. These differences observed in the extent of resistance in a series of studies may be attributed to the extensive, irrational and non-uniform usage of the above-mentioned drugs or related cephalosporin group of antibiotics, which would have resulted in a cross-resistance.

According to the current study, 100% (4/4) of *Enterococcus* spp. Were resistant to tetracycline, which is also in agreement with the outcome of earlier work done in southern part of Ethiopia [14], and Nepal [33]. Three fourth (75%) of the isolates of *Enterococcus* spp. In our study were found to be susceptible to penicillin, which resembles the findings of a previous study done in Addis Ababa [30]. We also found that the isolates of *Enterococcus* spp. Were invariably 100% (4/4) susceptible to nitrofurantoin. A similar trend of susceptibility was reported from several previous studies done in the same city [30] and in Nepal [33]. It has been found that 25% (1/4) of *Enterococcus* spp. Was vancomycin-resistant, which is similar to the findings of an earlier study done in Ethiopia [21].

Multiple drug resistance exhibited by bacterial pathogens, is a growing global public health threat culminating in frequent and prolonged hospitalizations, loss of manpower, greater morbidity and mortality, and enhanced healthcare costs [42]. Indiscriminate and extensive consumption of several antibiotics can catalyze bacterial mutation creating resistance, and the resistant strains propagate exponentially under the selective pressure of antibiotics. A rising trend in the multi-drug resistance of uropathogens makes their management more challenging [42]. Strategies to prevent drug resistance include the judicious selection of antimicrobials, inspection of susceptibility patterns, as well as effective screening tests for checking the emergence of MDR strains. A more alarming finding of our study is that 68.4% (26/38) of bacterial isolates were MDR. This is in line with the outcome of a couple of studies done in Ethiopia itself, such as Bahir Dar and Addis Ababa [22,30]. In contrast, an enhanced rate of MDR isolates was reported in an earlier study done in Ethiopia [31]. The reason for the augmented multi-drug resistance in the latter study could be correlated to the criteria fixed, which consider the bacterial isolates resistant to two antibiotics also as MDR. Nevertheless,

only a lower extent of MDR was reported from northern part of Ethiopia [21], and Nepal [33]. The present study also revealed that a higher prevalence (76.2%) of MDR was shown by GNB, which is in line with the results of a couple of studies done in Ethiopia (Bahir Dar and Arba Minch) [22,40]. In contrast, a higher prevalence of MDR among Gram-positive strains was reported by a couple of previous studies done in Ethiopia [30,31]. On the other hand, a lower prevalence of MDR was reported in an earlier study conducted in Gondar, Ethiopia [21]. Among the Gram-positive bacteria, 58.8% of isolates were MDR, which is comparable to a study done in Gondar [21]. In this study, the overall percentage of XDR isolates was 15.8, which is comparatively lower than that reported in an earlier study in the country [18]. Results of the present study indicated that 57.1% (12/21) of Gram-negative bacilli were ESBL-positive. This is comparable to the findings of a study done in Addis Ababa (although the study participants were not similar to ours) [43] as well as in Turkey [44]. In contrast, lower prevalence of ESBL were reported in some of the previous studies conducted in Arba Minch [40], Bahir Dar [22], Nepal [33] and India [38]. Also, it has been found that *K. pneumoniae* 66.7% (4/6) is the most predominant ESBL producer, followed by *E. coli* 55.6% (5/9). In contrast, findings of an earlier study in Arba Minch itself revealed that *E. coli* is the most prominent ESBL producer, followed by *K. pneumoniae* [40].

The higher prevalence of ESBL in our study can be due to the extensive and irrational use of third-generation cephalosporin and related antibiotics in the title hospital. In developing countries like Ethiopia, most often, at the beginning of therapy for UTI, the causative agents and their susceptibility patterns are not much known. Hence, the therapy usually follows established clinical guidelines to the extent allowable for choosing an initial antimicrobial regimen. In fact, in the case of non-response, therapy should be changed according to culture and susceptibility results.

The mechanism of drug resistance observed among uropathogens in our study may be due to the mutations in chromosomal genes (intrinsic resistance) or the acquisition of plasmid-mediated resistance determinants (extrinsic resistance). The intrinsic resistance primarily occurs due to selection pressure (include the abuse, overuse, and misuse of antimicrobials in therapy), whereas extrinsic genes are acquired through horizontal transfer [45]. In fact the intrinsic mechanisms confer only lower level of antibiotic resistance in the original host, on the other hand, extrinsic mechanisms pose a greater risk due to a shift, in the context of the resistance determinant from chromosomal to plasmid-mediated, which leads to their enhanced expression and dissemination [46].

However, further genome-wide analysis of the resistome is required to arrive at a conclusion.

Among the different socio-demographic and clinical factors analyzed for determining the associations with UTI, only un-circumcision in boys was found to be statistically significant ([(AOR = 3.578; 95% CI: 1.263 − 10.134; p = 0.016)]), which is in agreement with the results of a series of previous studies conducted in a couple of cities in Ethiopia [14,22]. The probable reason for this may be linked to the fact that the uncircumcised prepuce may readily be colonized by uropathogenic bacteria causing frequent infestation [46].

Since the present work is a single cross-sectional and non-randomized hospital-based study, a meaningful generalization based on it may not be possible and hence cannot be extrapolated to the entire community of children in Arba Minch. However, our results may provide valuable and current inputs linked to the patterns of antimicrobial resistance and distribution of predominant bacterial uropathogens in the study area.

4.1. Limitations

Scarcity of urine bags (because of which children less than two years of age were excluded), application of non-randomized sampling technique, shorter duration of the study and smaller sample size taken, paucity of antibiotics for testing the minimum inhibitory/bactericidal concentrations, lack of ESBL positive control strains which are required for enhancing the reliability of findings, non-availability of some antibiotics belonging to the group of carbapenems, lack of some of the reagents for identifying bacterial species in the genus such as *Enterococcus* and absence of serological identification of uropathogenic *E. coli*. Molecular detection of virulence and analysis of antimicrobial-resistant genes of major isolates were not performed due to limited infrastructure or other facilities (*E. coli* and *S. aureus*).

5. Conclusions

Results of the current study indicate that the prevalence of UTI among children in the study area, Arba Minch is on the rise. Isolates of *E. coli* and *S. aureus* are the most predominant causative agents of UTI. Significant bacteriuria had an association with un-circumcision. Resistance to the commonly prescribed antibiotics such as co-trimoxazole, ampicillin, tetracycline, amoxicillin-clavulanic acid, ceftriaxone, and ceftazidime was on the sharp rise and posed significant therapeutic challenges. However, ciprofloxacin and nitrofurantoin are still the reserve antibiotics for the treatment of both Gram-negative and positive bacterial uropathogens.

Similarly, amikacin is effective against Gram-negative, while gentamicin works well in the case of Gram-positive bacterial

isolates. An alarming finding is that the uropathogenic isolates involve VRE, MRSA and ESBL-producing strains listed as top-priority pathogens by WHO. Therefore, laboratory-based effective and constant surveillance is imperative in the study area to know the local antibiogram patterns, which can guide clinicians in providing better empirical therapy. The results of such studies will become a springboard for establishing antimicrobial stewardship. Finally, a further in-depth research is warranted to assess the influence of other risk factors and molecular surveillance connected to the emergence and evolution of resistant strains.

Credit author statement

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Declaration of conflict of interest

The authors declare that they have no competing interests.

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