Multiple drug resistance bacterial isolates and associated factors among urinary stone patients at the University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia

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Abstract

Background: The urinary stone and urinary tract infection (UTI) are invariably associated and are frequent causes of morbidity. Data on burden of UTI among urinary stone patients is lacking in Ethiopia. This study was aimed to assess bacterial profile, antimicrobial susceptibility and associated factors among urinary stone patients at the University of Gondar Comprehensive Specialized Hospital.

Methods: An institution based cross sectional study was conducted. Basic sociodemographic data were collected using a structured questionnaire. Bacterial identification of uropathogens and drug susceptibility testing were done following standard microbiological techniques. The data were entered and analyzed using SPSS version-23. Bivariate and multivariate logistic regressions were used to identify possible associated risk factors. Results with P value < 0.05 was considered statistically significant.

Result: A total of 300 urinary stone patients were enrolled. Of these, 153 (51%) were male and 261 (87%) were urban residents. The overall prevalence of urinary tract infection was 49 (16.3%) (95% CI 12–21%). A high level of resistance was observed to ampicillin, penicillin and trimethoprim-sulfamethoxazole while majority of isolates were most sensitive to nitrofurantoin and ciprofloxacin. Multi-drug resistant isolates were 16/49 (32.7%), 75% of them being Enterobacteriaceae isolates. More than one-third 9/26 (34.6%) of Gram-negative isolates were Extended Spectrum Beta-Lactamase (ESBL) producing E. coli and K. pneumoniae. Being female, history of urinary tract infection and history of drug use were the independent risk factors.

Conclusion: Most of the bacterial isolates from urinary stone patients were resistant to ampicillin, penicillin and trimethoprim-sulfamethoxazole. E. coli and K. pneumoniae were the most common extended spectrum beta-lactamase producing isolates. Sex, history of urinary tract infection and previous drug use were found to be risk factors. Routine diagnosis of urinary stone patients for urinary tract infection should be promoted and further researches are encouraged.

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**Background**

Urinary stone and urinary tract infections (UTI) are constantly associated complaints of the urinary system [1]. Urinary stones also known as urolithiasis [2] are hard masses produced in the urinary tract and cause infection, pain, bleeding or obstruction. Multiple types of stones such as oxalate, uric acid, cysteine, or struvite stone can be produced in the urinary tract [3]. Infection stones include magnesium ammonium phosphate or struvite (which accounts to 10–15% of urinary stone), carbonate apatite and ammonium urate. Urease producing bacteria such as *Proteus* are responsible for production of urease enzyme which alkalinizes urine and produce these stones [4, 5]. Moreover, ammonia and oxalate stones damage the urothelial layer facilitating microbial invasion [6].

*E. coli*, a urease negative bacterium is the most common cause of UTI and dominant isolate in urinary stones and urine cultures. Its existence in stone indicates either urease negative bacteria have a role in stone formation or urease producing bacteria transiently infect and lost after stone formation [7]. Uреase producing bacteria include *Proteus, Morganella, Pseudomonas, Providencia, Klebsiella* and *S. aureus* and are common causes of UTI [8]. *P. mirabilis* is the prominent urease producing species and cause of struvite calculi [9]. Bacteria incrusted in or attached on the surface of stone forming biofilm and cause recurrent and multidrug resistant (MDR) UTI [10].

The rate of UTI among urolithiasis patients ranges from 7 to 60% [11] with the coincidence of these comorbidities results in complications such as renal failure and death [12].

Urinary stone disease is one of the worldwide threats which has been increasing particularly in the last 15 years [13, 14]. Factors such as sex, previous history of UTI, condom use, vaginal infection, extremes of age, anatomical abnormalities like congenital urinary tract malformations, urinary obstruction, catheterization, recent sexual activity, comorbidities like urinary stone, diabetes and obesity [8, 15, 16], hospitalization, antibiotic use are risks factors to UTI [17]. Information about the burden of UTI among patients with urinary calculi is lacking in Ethiopia. This study is aimed to investigate bacterial uropathogens, antimicrobial resistance and associated factors among urinary stone patients at the University of Gondar Comprehensive Specialized Hospital, Gondar Ethiopia.

**Materials and methods**

**Study area, design, and period**

A prospective cross-sectional study was conducted from January to April, 2019, at the University of Gondar Comprehensive Specialized Hospital. The hospital is located in Gondar town, Amhara regional state, Northwest Ethiopia, situated at 742 km from the capital city of Ethiopia, Addis Ababa. The hospital is a tertiary level teaching and referral hospital catering more than 500 beds for inpatients and rendering referral health services for over 5 million inhabitants in Northwest Ethiopia.

**Population** All patients who have visited the hospital during the study period and clinically suspected of urinary stone disease were the source population while patients with ultrasound confirmed urinary stone were study population. All the study participants were enrolled from the outpatient department.

**Exclusion criteria** Patients with history of antibiotic use in the last 2 weeks prior to diagnosis and during the data collection period were excluded or denied from the study because those who have been taking antibiotics may have culture negative due to their resent drug use. All patients who had urinary system complains, were confirmed to have urinary stone with ultrasound and not on antibiotics treatment in the last 2 weeks as well as during the study period and willing to be included were eligible to this study.

**Sample size and sampling methods**

The sample size was calculated by a single population proportion formula taking 50% prevalence since previous study involving urinary stone patients was not available.

\[
 n = \frac{z^2_{\alpha/2}p(1-p)}{d^2} = \frac{1.96^2 \times 0.5(1-0.5)}{(0.05)^2} = 384
\]

Using reduction formula as the total population based on the same period of the last year’s record, estimated population was 1350, the final sample size was

\[
 n_f = \frac{n \times N}{n + N} = \frac{384 \times 1350}{384 + 1350} = 299
\]
where \( N \) is the total population, \( n \)—the final sample size, \( Z_{n/2} \)—the standard normal deviation, at 95% confidence level = 1.96, \( p \)—The prevalence = 0.5; \( 1 - p = 0.5 \) and \( d \)—The desired degree of accuracy = 0.05.

**Data collection and laboratory methods**

A total of 300 study participants with urinary stone were enrolled in the study using convenient sampling technique. Sociodemographic and clinical features of study participants such as age, gender, residence, history of UTI and drug use, stone size and its position, presence of stone on multiple sites, condom use, catheterization and presence of comorbidities like history of diabetes, HIV were collected using structured questionnaire. Clean catch mid-stream urine was collected in a sterile wide mouthed urine cup with prior adequate instruction of the participant (Additional file 1).

**Culture and microbiological identification**

Early morning mid-stream urine sample was collected and transported to medical bacteriology laboratory; inoculated in Cysteine lactose electrolyte deficient (CLED) agar (BIOMARKR Laboratories, India) within two hours and incubated for 18–24 h at 35–37 °C. A 0.001 mL inoculating loop was used to inoculate the urine specimen. Colonies with significant bacteriuria (≥10^5 CFU/mL) were subcultured on blood agar plate (BAP) and MacConkey agar for isolation of a single species and further characterization by hemolysis on BAP, lactose fermentation on MacConkey agar. Gram staining and biochemical tests such as TSI, motility test, indole test, citrate test, urease test, Lysine decarboxylase, catalase, coagulase tests, novobiocin sensitivity, and Bile Esculin (BIOMARKR Laboratories, India) hydrolysis test were used for species identification [18].

**Antimicrobial susceptibility testing**

Antimicrobial susceptibility testing (AST) was performed using Kirby-Bauer disc diffusion method on Muller-Hinton agar (BIOMARKR Laboratories, India). Selected antimicrobial agents such as Ampicillin (10 µg), Amoxicillin-clavulanate (20/10 µg), Ciprofloxacin (5 µg), Tobramycin (10 µg), Gentamicin (10 µg), Cefixime (5 µg), Cefotaxin (30 µg), Cefuroxime (30 µg), Nitrofurantoin (300 µg), Rifampin (5 µg), Tetracycline (30 µg), Penicillin 10 units, Norfloxacin (10 µg), Vancomycin (30 µg), Trimethoprim-sulphamethoxazole (1.25/23.75 µg) (Abtek Biologicals Ltd, United Kingdom) and Cefotaxime (30 µg), Ceftazidine (30 µg), Cefotaxime-Clavulanate (30/10 µg), Ceftazidine-Clavulanate (30/10 µg) (HiMedia Laboratories Pvt Ltd India) were used for antimicrobial susceptibility test [19]. Zones of inhibition were measured after 16–18 h of incubation at 37 °C and classified as susceptible or resistant. Isolates intermediate between susceptible and resistant were considered as resistant [20]. Isolates resistant to three or more classes of antibiotics were considered as MDR [21].

**Extended spectrum beta lactamase detection**

First screening for ESBL production was done for Ceftazidine and Ceftazidime 30 µg each. Isolates with zone of inhibition ≤27 mm for cefotaxime and ≤22 mm for ceftazidime were phenotypically confirmed for ESBL production by using Ceftazidine-clavulanic acid (30 µg/10 µg), Cefotaxime-clavulanic acid (30 µg/10 µg) with their respective single disks using combined disk test. The suspension of screened isolates was prepared and inoculated on MHA. The target antibiotics were then placed at least 25 mm apart from each other followed by 16–18 h of incubation at 35 °C±2 °C and zone of inhibition was measured. At least 5 mm difference to either of the combined drugs and their respective single disks was considered as ESBL producing species [19].

**Quality control**

The questionnaire was pretested for standardization and clarity. The culture media were checked for sterility and performance prior to inoculation by incubating 5% of the newly prepared media overnight. The reagents for Gram’s stain were also assured for their expiry date and staining. The control strains E. coli ATCC25922 and S. aureus ATCC25923 were used to control performance of media and antibiotic disks. Furthermore, K. pneumoniae ATCC 700603 and E. coli ATCC25922 were used as a positive and negative control for ESBL production respectively. The suspension was standardized against 0.5 McFarland standards [19].

**Data processing and analysis**

Data were entered and analyzed using SPSS version 23 software. Descriptive statistics such as frequency and percentage were determined. The binary logistic regression model was used. The assumption Hosmer-Lemeshow goodness of fit as well as cox and snell and Nagelkerke R square values were checked and the model was fit. Bivariate and multivariate logistic regression analysis were carried out with enter method to determine statistically significant association and odds ratio at 95% confidence interval was computed. Variables with a \( P \) value < 0.2 in bivariate logistic regression analysis were entered to multivariate logistic regression analysis [22, 23]. Variables with \( P \) value < 0.05 in multivariate logistic regression analysis were considered as statistically significant.
Table 1 Sociodemographic characteristics of urinary stone patients at the University of Gondar Comprehensive Specialized Hospital, January to April 2019

| Variables                      | Frequency (%) |
|--------------------------------|---------------|
| Sex                            |               |
| Male                           | 153(51)       |
| Female                         | 147(49)       |
| Age                            |               |
| < 20 years                     | 23(7.7)       |
| 20–29                          | 123(41)       |
| 30–39                          | 97(32.3)      |
| 40–49                          | 32(10.7)      |
| ≥ 50                           | 25(8.3)       |
| Residence                      |               |
| Urban                          | 261(87)       |
| Rural                          | 39(13)        |
| Educational level              |               |
| Cannot read and write          | 35(11.7)      |
| Elementary                     | 71(23.7)      |
| High school and preparatory    | 60(20)        |
| College and above              | 134(44.7)     |
| Family monthly income (ETB)    |               |
| < 1000                         | 54(18)        |
| 1001–2000                      | 70(23.3)      |
| > 2000                         | 176(58.7)     |
| Sexual activity                |               |
| Within 2 days                  | 43(14.3)      |
| Within 7 days                  | 84(28)        |
| Pregnancy (for females)        |               |
| Yes                            | 6(2)          |
| No                             | 141(47)       |
| Use of birth control mechanisms|               |
| Condom                         | 6(2)          |
| No                             | 141(46.3)     |
| Body mass index                |               |
| < 18.5                         | 40(13.3)      |
| 18.5–24.5                      | 211(70.3)     |
| > 24.5                         | 49(16.3)      |

Table 2 Clinical characteristics of urinary stone patients at the University of Gondar Comprehensive Specialized Hospital, January to April 2019

| Variable                          | Frequency (%) |
|-----------------------------------|---------------|
| History of UTI                    |               |
| Yes                               | 33(11)        |
| No                                | 267(89)       |
| Urinary blockage                  |               |
| Yes                               | 9(3)          |
| No                                | 291(97)       |
| History of catheterization        |               |
| Yes                               | 4(1.3)        |
| No                                | 296(98.7)     |
| Stone size                        |               |
| < 5 mm                            | 275(91.7)     |
| ≥ 5 mm                            | 25(8.3)       |
| Stones at multiple locations      |               |
| Yes                               | 75(25)        |
| No                                | 225(75)       |
| Location of stone                 |               |
| Renal                             | 282(94)       |
| Renal and/or extra renal          | 18(6)         |
| History of chronic disease        |               |
| Yes                               | 21(7)         |
| No                                | 279(93)       |
| History of drug use               |               |
| Yes                               | 172(57.3)     |
| No                                | 128(42.7)     |
| Drug type used                    |               |
| Antibiotics                       | 166(55.3)     |
| Antibiotics, steroids and HAART   | 7(2.3)        |
| Antibiotic use                    |               |
| Within the past one month         | 70(23.3)      |
| Within the past 3 months          | 41(13.7)      |
| History of hospitalization        |               |
| Yes                               | 17(5.7)       |
| No                                | 283(94.3)     |

Extra renal-(Kidney and ureter, Kidney and bladder, or Kidney and urethra)

Result

Sociodemographic and clinical characteristics of patients with urinary stone

Of the 300 urinary stone patients enrolled in the present study, 153(51%) were male, 123(41%) were in age group 20–29 years, 261(87%) were urban dwellers and 134(44.7%) were patients with educational level of college and above (Table 1). Thirty-three (11%) of study participants had history of UTI, 25(8.3%) of them had stone size of 5 mm and above. Nine (3%) of the participants had history of urinary blockage and 166(55.3%) of them had history of antibiotic use while 17(5.7%) were hospitalized previously (Table 2).

The prevalence of bacterial uropathogens among patients with urinary stone

Forty-nine 49/300(16.3%) (95% CI 12–21%) of the urinary stone patients had UTI. The most common cause of UTI was E. coli 14/49(28.6%) followed by S. saprophyticus and Enterococcus species 8/49(16.3%) each, K. pneumoniae and S. aureus 7/49(14.3%) each (Fig. 1).
Majority of Gram-negative isolates were resistant to ampicillin 25/26 (96.2%), amoxicillin-clavulanate 18/26 (69.2%) while 46/49 (94%) and 44/49 (90%) of the Gram-negative isolates were susceptible to nitrofurantoin and ciprofloxacin respectively. All S. saprophyticus 8(100%) and 6/7 (85.7%) of S. aureus were susceptible to gentamycin. Two 2/8 (25%) S. saprophyticus and 1/7 (14.3%) of S. aureus isolates were resistant to cefoxitin (surrogate marker for methicillin resistance), and one vancomycin resistant Enterococcus was isolated (Table 3).

Of the total uropathogens, 16/49 (32.7%) were MDR and 75% of which were Enterobacteriaceae. The most common MDR species were E. coli 7/49 (14.3%), followed by K. pneumoniae 3/49 (6.12%). Furthermore, from a total of 26 Enterobacteriaceae 9/26 (34.6%) isolates were confirmed ESBL producing species. These confirmed ESBL producing isolates were E. coli 6/26 (23.1%) and K. pneumoniae 3/26 (11.5%) (Table 4).

Among the variables, sex, age, education, monthly income, history of UTI, blockage of urinary system, stone size, stone location in the urinary system, history of chronic disease and drug use, sexual activity, history of hospitalization, and body mass index had P value < 0.2 in bivariate analysis and were computed by multivariate logistic regression analysis to check statistically significant association by controlling possible confounders. The result of multivariate logistic regression showed that being female, history of UTI, drug use had a P value of < 0.05; which indicates statistically significant association with patients having urinary stone diseases (Table 5).

The overall prevalence of UTI among patients with urinary stone was 49/300 (16.3%) (95% CI 12–21%). This result is similar to reports by Gutierrez et al. 16.2%
Table 3  Antimicrobial Susceptibility Pattern of Bacterial Isolates from Urinary stone Patients at the UOGCSH, January to April 2019

| Antibiotic used | Species of isolate with their antibiotic susceptibility |
|-----------------|--------------------------------------------------------|
|                 | E. coli N (%) | K. pneumoniae N(%) | C. diversus N (%) | E. cloacae N (%) | P. mirabilis N (%) | Enterococci N (%) | S. saprophyticus N (%) | S. aureus N (%) |
| AMP             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 1(14.3)      |                   |                   |                 |                    |                   |                          |                |
| R               | 14(100)      | 6(85.7)           | 2(100)            | 2(100%)         | 1(100)             |                   | 6(75)                    |                |
| AMC             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 2(14.3)      | 4(57.1)           |                   |                 |                    |                   |                          |                |
| R               | 12(85.7)     | 3(42.9)           | 2(100)            | 1(50)           |                    |                   |                          |                |
| CTX             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 7(50)        | 6(85.7)           | 1(50)             | 2(100)          | 1(100)             |                   |                          |                |
| R               | 7(50)        | 1(14.3)           | 1(50)             |                 |                    |                   |                          |                |
| CAZ             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 14(100)      | 6(85.7)           | 1(50)             | 2(100%)         | 1(100)             |                   |                          |                |
| R               | 1(14.3)      | 1(50)             |                 |                 |                    |                   |                          |                |
| FOX             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 13(92.9)     | 6(85.7)           | 2(100)            | 2(100%)         | 1(100)             | 5(62.5)           | 6(85.7)                  |                |
| R               | 1(7.1)       | 1(14.3)           |                 |                 |                    | 3(37.3)           | 1(14.3)                  |                |
| CFM             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 12(85.7)     | 4(57.1)           | 1(50)             | 2(100)          | 1(100)             |                   |                          |                |
| R               | 2(14.3)      | 3(42.9)           | 1(50)             |                 |                    |                   |                          |                |
| CRX             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 13(92.9)     | 6(85.7)           | 1(50)             | 2(100)          | 1(100)             |                   |                          |                |
| R               | 1(7.1)       | 1(14.3)           | 1(50)             |                 |                    |                   |                          |                |
| CPR             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 12(85.7)     | 6(85.7)           | 1(50)             | 2(100)          | 1(100)             | 8(100)            | 7(87.5)                  | 7(100)         |
| R               | 2(14.3)      | 1(14.3)           | 1(50)             |                 |                    | 1(12.5)           |                          |                |
| GEN             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 13(92.9)     | 7(100)            | 1(50)             | 2(100)          | 1(100)             | 8(100)            | 6(85.7)                  | 1(14.3)        |
| R               | 1(7.1)       | 1(50)             |                 |                 |                    |                   |                          |                |
| TOB             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 10(71.4)     | 7(100)            | 1(50)             | 2(100)          | 1(100)             |                   |                          |                |
| R               | 4(28.6)      | 1(50)             |                 |                 |                    |                   |                          |                |
| TET             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 7(50)        | 4(57.1)           | 2(100)            |                 |                    | 3(37.5)           | 3(37.5)                  | 5(71.4)        |
| R               | 7(50)        | 3(42.9)           | 1(100)            | 5(62.5)         | 5(62.5)            | 2(28.3)           |                          |                |
| SXT             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 6(42.9)      | 4(57.1)           | 2(100%)           | 1(100)          | 6(75)              | 5(71.4)           |                          |                |
| R               | 8(57.1)      | 3(42.9)           | 2(100)            |                 | 2(25)              | 2(28.6)           |                          |                |
| NIT             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 14(100)      | 6(85.7)           | 2(100)            | 2(100%)         | 1(100)             | 8(100)            | 6(75)                    | 7(100)         |
| R               | 1(14.3)      | 1(50)             |                 |                 |                    | 2(25)             |                          |                |
| NOR             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 11(78.6)     | 6(85.7)           | 1(50)             | 2(100%)         | 1(100)             | 5(62.5)           | 7(87.5)                  | 6(85.7)        |
| R               | 3(21.4)      | 1(14.3)           | 1(50)             |                 |                    | 3(37.5)           | 1(12.5)                  | 1(14.3)        |
| PEN             |              |                   |                   |                 |                    |                   |                          |                |
| S               | 3(37.5)      | 2(25)             |                 |                 |                    | 4(57.1)           |                          |                |
| R               | 5(62.5)      | 6(75)             | 3(42.9)           |                 |                    |                    |                          |                |
[24] and lower than a study done in China 22.0% [25], Iran 35.5% [26], Romania 25.8% [27] and India 45% [11] among urinary stone patients. However, this result was higher than 7.8% prevalence of UTI reported from Los Angeles, United States [28]. The variation might be because of the socioeconomic, geographical and population difference. The predominant species isolated in this study were E. coli, 14/49 (28.6%) followed by S. saprophyticus and Enterococcus species 8/49 (16.3%) each. The result was comparable to other reports 33% E.coli and 18.5% Enterococci isolated from patients with urinary stone [29]. On the other hand the result was higher than 6.5% prevalence of E.coli reported by Gutierrez et al. [24].

The resistance to antibiotics such as ampicillin, amoxicillin-clavulanate and Trimethoprim-sulphamethoxazole in this study was 31/33 (94%), 18/26 (69.23%) and 17 (41.5%) respectively which was slightly lower than a report in India ampicillin 96% and amoxicillin-clavulanic acid 87% [30]. The result of this study was higher than resistance to Ampicillin 70%, and Amoxicillin-clavulanic acid 30% reported in Romania [27]. The high rate of resistance might be due to easy access and

### Table 3 (continued)

| Antibiotic used | Species of isolate with their antibiotic susceptibility |
|-----------------|--------------------------------------------------------|
|                 | E. coli N (%) K. pneumoniae N(%) C. diversus N (%) E. cloacae N (%) P. mirabilis N (%) Enterococci N (%) S. saprophyticus N (%) S. aureus N (%) |
| RIF             | S 6(75) R 2(25) |
| VAN             | S 7(87.5) R 1(12.5) |

AMP Amoxicillin, AMC Amoxicillin-clavulanate, FOX Cefoxitin, CFM Cefoxime, CRX Cefuroxime, CPR Ciprofloxacin, GEN Gentamycin, CAZ Ceftazidime, CTX Cefotaxime, RIF Rifampin, NOR Norfloxacin, NIT Nitrofurantoin, PEN Penicillin, RIF Rifampin, SXT Trimethoprim-Sulfamethoxazole, TET Tetracycline, TOB Tobramycin, VAN Vancomycin

### Table 4

The prevalence of MDR isolates from urinary stone patients at the University of Gondar Comprehensive Specialized Hospital, January to April 2019

| Antibiotics | Species of bacteria | Total |
|-------------|---------------------|-------|
|             | E. coli | K. pneumoniae | C. diversus | Enterococci | S. saprophyticus | |
| AMP, TET, NOR | 2      | 2             | |
| AMP, TET, SXT | 1      | 1             | |
| AMP, AMC, TOB, SXT | 1  | 1             | |
| AMP, TET, TOB, SXT | 1  | 1             | |
| AMP, AMC, TET, SXT | 1  | 1             | |
| AMP, AMC, CTX, SXT | 1  | 1             | |
| CXT, TET, SXT, PEN | 1  | 1             | |
| CXT, TET, NOR, PEN | 1      | 1             | |
| AMP, AMC, CTX, SXT, TET | 1  | 1             | |
| AMP, AMC, CTX, CFM, SXT | 1  | 1             | |
| AMP, FOX, CFM, CPR, NIT | 1  | 1             | |
| AMP, AMC, CRX, TET, SXT | 1  | 1             | |
| AMP, AMC, SXT, GEN, NOR, TET, TOB | 1  | 1             | |
| AMP, AMC, CTX, CFM, GEN, TET, CPR, SXT, NIT | 1  | 1             | |
| AMP, AMC, CTX, FOX, CFM, CRX, CPR, TET, TET, NOR | 1  | 1             | |
| Total | 7      | 3             | 2  | 2  | 2  | 16 |
| ESBL positive | 6      | 3             | |

AMP Amoxicillin, AMC Amoxicillin-clavulanate, CTX cefotaxime, FOX Cefoxitin, TET Tetracycline, CPR Ciprofloxacin, CTX Cefotaxime, PEN Penicillin, TOB Tobramycin, SXT Trimethoprim-Sulfamethoxazole, CRX Cefuroxime, GEN Gentamycin, NOR Norfloxacin
| Variable                      | Significant bacteriuria | COR 95% CI | P value | AOR 95% CI | P value |
|-------------------------------|-------------------------|------------|---------|------------|---------|
|                              | Yes (%) | No (%) |                                |          |
| Sex                           |         |        |                                |          |
| Male                          | 13(26.5) | 140(55.8) | 1 |          |
| Female                        | 36(73.5) | 111(44.2) | 3.5(1.77–6.90) | 0.00 | 5.76(2.23–13.32) | 0.00 |
| Age                           |         |        |                                |          |
| < 20 years                    | 3(6) | 20(8) | 1 |          |
| 20–29                         | 21(42.9) | 102(40.6) | 1.37(0.37–5.04) | 0.63 | 2.00(0.43–9.26) | 0.38 |
| 30–39                         | 12(24.5) | 85(33.9) | 0.94(0.24–3.65) | 0.93 | 1.05(0.25–6.57) | 0.77 |
| 40–49                         | 9(18.4) | 23(9.16) | 2.60(0.62–10.98) | 0.19 | 2.04(0.38–14.92) | 0.36 |
| ≥ 50 years                    | 4(8.2) | 21(8.4) | 1.27(0.25–6.40) | 0.77 | 1.25(0.16–12.16) | 0.77 |
| Residence                     |         |        |                                |          |
| Urban                         | 42(85.7) | 219(87.3) | 1 |          |
| Rural                         | 7(14.3) | 32(12.7) | 1.14(0.47–2.76) | 0.77 | 1 |          |
| Education                     |         |        |                                |          |
| Cannot read and write         | 10(20.4) | 25(10) | 2.15(0.90–5.13) | 0.08 | 1.80(0.54–5.95) | 0.34 |
| Elementary                    | 13(28.3) | 58(23.1) | 1.21(0.56–2.58) | 0.63 | 1.42(0.50–4.07) | 0.51 |
| High school                   | 5(10.2) | 55(23.1) | 0.49(0.18–1.37) | 0.17 | 0.31(0.09–1.02) | 0.05 |
| College and above             | 21(42.9) | 113(45) | 1 |          |
| Family monthly income (ETB)   |         |        |                                |          |
| ≤ 1000                        | 16(32.7) | 38(15.1) | 2.95(1.413–6.15) | 0.004 | 2.40(0.84–6.88) | 0.104 |
| 1001–2000                     | 11(22.4) | 59(23.5) | 1.31(0.596–2.857) | 0.50 | 1.60(0.61–4.20) | 0.34 |
| > 2000                        | 22(44.9) | 154(61.4) | 1 |          |
| History of UTI                |         |        |                                |          |
| Yes                           | 15(30.6) | 18(7.2) | 5.71(2.63–12.38) | 0.00 | 4.66(1.76–12.30) | 0.002 |
| No                            | 34(69.4) | 233(92.8) | 1 |          |
| Urinary blockage              |         |        |                                |          |
| Yes                           | 3(6.1) | 6(2.4) | 2.66(0.64–11.03) | 0.18 | 0.26(0.03–2.20) | 0.22 |
| No                            | 46(93.9) | 245(97.6) | 1 |          |
| Stone size                    |         |        |                                |          |
| < 5 mm                        | 43(87.8) | 232(92.4) | 1 |          |
| ≥ 5                           | 6(12.2) | 19(7.6) | 1.7(0.64–4.5) | 0.28 |          |
| Stone location                |         |        |                                |          |
| Renal                         | 46(93.9) | 236(94) | 1 |          |
| Renal and/or extra renal      | 3(6) | 15(6) | 1.03(0.29–3.7) | 0.97 |          |
| Chronic disease               |         |        |                                |          |
| Yes                           | 6(12.2) | 15(6) | 2.20(0.81–5.97) | 0.12 | 1.17(0.24–5.65) | 0.85 |
| No                            | 43(87.8) | 236(94) | 1 |          |
| Drug use                      |         |        |                                |          |
| Yes                           | 36(73.5) | 136(54.2) | 1 |          |
| No                            | 36(26.5) | 115(45.8) | 0.43(0.22–0.84) | 0.014 | 0.33(0.14–0.77) | 0.01 |
| Hospitalization               |         |        |                                |          |
| Yes                           | 7(14.3) | 10(4) | 4.02(1.45–11.14) | 0.008 | 3.85(0.92–16.07) | 0.065 |
| No                            | 42(85.7) | 241(96) | 1 |          |
| Sexual activity               |         |        |                                |          |
| Within 2 days                 | 6(12.2) | 37(14.7) | 0.55(0.21–1.45) | 0.23 | 0.61(0.20–1.92) | 0.40 |
| Within 7 days                 | 11(22.4) | 73(29.1) | 0.51(0.24–1.10) | 0.09 | 0.48(0.19–1.21) | 0.12 |
| Within a month                | 5(10.2) | 49(19.5) | 0.35(0.13–0.96) | 0.041 | 0.30(0.086–1.02) | 0.054 |
| Never                         | 27(55.1) | 92(36.7) | 1 |          |
| BMI                           |         |        |                                |          |
| 18.5–24.5                     | 32(65.3) | 179(71.3) | 1 |          |
| > 24.5                        | 7(14.3) | 42(16.7) | 0.536(0.24–1.20) | 0.13 | 1.24(0.41–3.79) | 0.71 |
| ≤ 18.5                        | 10(20.4) | 30(12) | 0.5(0.17–1.46) | 0.21 | 2.89(0.98–8.50) | 0.053 |
The factors that predispose to the occurrence of the infection [15]. The treatment might not have completely removed the etiologic agent of UTI in patients. Because the bacteria can be incrusted in the stone or extracellular matrix and escape from the treatment [34].

In addition, 36/49 (73.5%) patients with significant bacteriuria had previous history of drug use and showed a statistically significant association with UTI. The risk of UTI among patients who had not history of drug use reduces by 67% compared to those who had history of drug use (AOR 0.33, 95% CI 0.14–0.77). This could be due to the fact that steroidal drugs are immunosuppressive and patients could be immunocompromised [30]. The increased antimicrobial resistance in drug users and the recurrence or persistence of drug resistant UTI might also contribute.

As a limitation only urine specimen was taken for culture and stone culture was not performed to which could help to know the agreement of stone and urine culture strain characterization was not performed due to lack of resources.

**Conclusion**

The commonest bacterial species isolated from patients with urinary stone disease was *E. coli*. The most common MDR and ESBL producing isolates were *E. coli* and *K. pneumoniae*. Being female, previous history of UTI and drug use were the independent risk factors. Isolated uropathogens were most susceptible to nitrofurantoin, ciprofloxacin and gentamycin. However, most of the isolates were resistant to ampicillin, penicillin and trimethoprim-Sulfamethoxazole. Routine diagnosis of urinary stone patients for urinary tract infection should be promoted. Antimicrobial stewardship program should be implemented to reduce drug resistance.

**Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12894-021-00794-8.

**Abbreviations**

AST: Antimicrobial susceptibility test; ATCC: American Type Culture Collection; BAP: Blood agar plate; CLSI: Clinical Laboratory Standards Institute; CLED: Cysteine lactose electrolyte deficient agar; ESBL: Extended spectrum beta lactamase; HAART: Highly active antiretroviral therapy; MAC: MacConkey
aggar, MDR: Multidrug resistance, TSI: Triple sugar iron agar, USD: Urinary stone disease, UTI: Urinary tract infection.

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Authors' contributions
DK: Conception of the research idea, study design, data collection, data analysis, interpretation, write up of the research. ZT, FM and SE: supervision and review of the manuscript. AD: Data collection and review of the manuscript. All authors read and approved the final manuscript.

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

Ethical approval and consent to participate
Ethical approval was obtained from an Ethical review committee of the School of Biomedical and Laboratory Sciences, college of Medicine and health sciences, University of Gondar (SBMLS/2923/11). The study was conducted in accordance with the ethical principles of the declaration of Helsinki on human subjects. The purpose of the study, the possible benefits and risks on participants were explained to the study participants and participation was fully voluntary. Written informed consent was obtained from the study participants and assent was sought from families or legal guardians of under 18 years children. All the ethical standards were followed. Positive cases were connected to physicians for management.

Consent for publication
Not applicable.

Competing interests
Authors declare that there is no competing interest.

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