



OPEN Burden of multi-drug resistant bacterial isolates and its associated risk factors among UTI-confirmed geriatrics in Gondar town

Getachew Bitew¹✉, Mulat Dagne¹, Mahliet Dereje², Abebe Birhanu¹, Yalewayker Gashaw³, Aklilu Ambachew¹ & Belay Tessema^{1,4}

Multi-drug resistant (MDR) bacterial urinary tract infection (UTI) is a significant health threat in the geriatric population, with limited data in this study area. Therefore, this study aimed to assess the burden of MDR bacterial isolates and associated risk factors among UTI-confirmed geriatrics in Gondar, providing essential information for geriatric patients, healthcare workers, scientists, and policymakers to guide antibiotic stewardship interventions. A prospective cross-sectional study was conducted among 204 UTI-confirmed geriatrics. Socio-demographic data were collected via a structured questionnaire, and bacterial identification and drug resistance testing followed standard microbiological techniques. Data were entered using Epi Data version 4.0.0 and analyzed by Stata/IC version 14.0, with bivariate and multivariate logistic regressions to identify risk factors. A P -value < 0.05 was considered statistically significant. The overall prevalence of MDR UTI-confirmed geriatrics and MDR bacterial isolates were 115 (56.4%) and 126 (49.6%), respectively. The MDR Gram-negative isolates accounted for 105 (83.3%), and Gram-positive isolates 21 (16.7%). The predominant MDR bacterium was *E. coli* 60 (47.6%), followed by *K. pneumoniae* 24 (19.1%), *S. aureus* 13 (10.3%), *P. mirabilis* and *S. saprophyticus* 8 (6.4%), *Pseudomonas* spp. 6 (4.8%), *P. vulgaris* 4 (3.2%) and *K. rhinos* 3 (2.4%). Extensive (XDR) and pan-drug resistant (PDR) isolates were 63 (24.8%) and 6 (4.8%), respectively. Risk factors such as recurrent UTI, hospitalization (≥ 4 days), antibiotic and urinary catheter use were statistically significant. This study found a high prevalence of MDR bacterial isolates in UTI-confirmed geriatrics, with most isolates resistant to tetracycline, beta-lactams, and quinolones. *Escherichia coli* was the most common MDR and XDR bacteria, while *Pseudomonas* was the only PDR isolate. Independent risk factors included recurrent UTI, hospitalization (≥ 4 days), antibiotic and urinary catheter use. Therefore, efforts should focus on reducing hospital stays, promoting rational drug use, and further research.

Keywords Multi-drug resistant, Geriatrics, Bacterial urinary tract infection

Abbreviations

ASP	Antibiotic Stewardship Program
CFU	Colony Forming Unit
CI	Confidence Interval
CLED	Cysteine-Lactose-Electrolyte-Deficient
CLSI	Clinical and Laboratory Standards Institute
ESKAPE	(Enterococci faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas and Enterobacter species)
GNB	Gram-Negative Bacteria
GPB	Gram-Positive Bacteria

¹Department of Medical Microbiology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia. ²Microbiology Laboratory, University of Gondar Comprehensive Specialized Hospital, Gondar, Ethiopia. ³Department of Medical Microbiology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, Woldia University, Woldia, Ethiopia. ⁴Institute of Clinical Immunology, Faculty of Medicine, University of Leipzig, 04103 Leipzig, Germany. ✉email: gtwbtw4550@gmail.com

MDR	Multi-Drug Resistant
MHA	Muller-Hinton Agar
MRSA	Methicillin Resistant Staphylococcus aureus
MSA	Mannitol Salt Agar
PDR	Pan-Drug Resistant
UTI	Urinary Tract Infection
WHO	World Health Organization
XDR	Extensive-Drug Resistant

Urinary tract infections (UTIs) are infections caused by the presence, growth and spread of microorganisms in the urinary tract associated with significant morbidity, mortality and health care costs¹. It is frequently caused by bacterial pathogens originated from the gastrointestinal tract². Worldwide, about 150 million people are diagnosed with UTI each year, costing the global economy in excess of 6 billion dollars^{3,4}. In developing countries, including Ethiopia, the facilities for urine culture and antimicrobial susceptibility testing are still not sufficiently available, leading to improper diagnosis and irrational antibiotic treatment of UTI, which accelerates the emergence of multi-drug resistant (MDR) strains.

The emergence of MDR bacterial uropathogens are now a major concern in many parts of the world⁵. The expansion of global trade and tourism leads to increased potential of MDR bacterial uropathogens to spread all over the world and decrease in export and import of various products affecting the economy of developing countries⁶. Regarding public health attention, MDR bacterial isolates are described as superbugs having very limited treatment options⁷.

Both Gram-negative and Gram-positive bacterial isolates can infect the urinary tract of geriatrics. However, by far the most common and resistant agents are the Gram-negative bacilli⁸. Geriatrics UTIs are caused by wider etiology of MDR bacterial isolates and the infection is characteristically polymicrobial, usually with two to five isolates. Resistant isolates include common uropathogens, such as *E. coli*, *K. pneumoniae*, *P. mirabilis*, *Staphylococci*, *Enterococci*, isolates with higher levels of intrinsic resistance, such as *P. aeruginosa* or *P. stuartii*, and other bacterial species⁹.

Urinary bacterial isolates develop resistance to antibiotics in three ways via intrinsic, acquired and adaptive mechanisms, although acquired resistance in common uropathogens may be more frequent in geriatrics¹⁰. In urinary tract infected geriatrics several different bacteria like *P. mirabilis*, *P. aeruginosa*, and *P. stuartii* may form biofilm and camouflage with it. Bacteria within the biofilm survive in a relatively protected environment¹¹. Antibiotics in the urine may not kill bacteria because of its poor diffusion into the biofilms or a reduced metabolic rate of the bacteria resulted in persist bacterial cells¹². Persistent bacterial colonization of the geriatric's urinary tract together with antibiotics exposure without effective killing promotes the emergence of multi-drug resistance¹³.

Risk factors that increase exposure to MDR bacterial uropathogens in geriatrics includes previous and recurrent UTIs, frequent and prolonged hospitalization, catheterization, antibiotic exposure, immune senescence, co-morbidity, and an increase in the number of geriatric patients due to a rise in life expectancy^{14,15}. Urinary tract infected geriatrics living in long-term-care facilities are an important reservoir of MDR bacterial uropathogens, which can be transmitted to acute care hospitals through inter-hospital transfer¹³.

Not all UTIs require antibiotic treatment. In cases where microbial isolation is found in catheterized urine samples, simply replacing the catheter may suffice. Antibiotic treatment should only be considered if the patient exhibits UTI symptoms (such as dysuria, fever, or loin pain) and if the same organism is confirmed in blood cultures^{13,15}.

General principles for the management of MDR UTI in geriatrics are ensuring that there is an indication for antimicrobial therapy, obtaining a urine specimen for microbiological documentation of the infecting organism and resistance testing before initiation of antimicrobial therapy, limiting the use of empirical therapy, if possible, by awaiting culture results before instituting therapy, and reassessing empirical therapy once culture results are available^{16,17}. Additional considerations include the local or institutional prevalence of resistant uropathogens and the experience of the individual patient with prior antimicrobial therapy. When empirical therapy is used in a setting where there is an increased likelihood of resistant bacteria, a broader spectrum antimicrobial is usually selected. But it will also contribute to the larger problem of promoting multi-drug resistance⁴.

Multi-drug resistance is a silent tsunami, so antibiotic stewardship (ASPs) from geriatric patients, health care workers, scientists, industries, and policy makers are needed¹⁸. Geriatrics who have UTI should avoid self-medication, misuse, overuse, frequent use, leftover drugs, and sharing. They should complete the treatment course even if they feel better¹³. Scientists and industries need to promote the development of novel drugs and new diagnostic techniques, like bacteriophage therapy¹⁹. Health care workers should diagnose empirically if the patients are in emergency situation. However, definitive diagnosis with culture and antibiotic resistant test for acute patients and review for critical patients. Policymakers must organize awareness programs and pass laws to restrict the sale of un-prescribed drugs^{18,20}.

Antimicrobial resistance was ranked fifth among the top ten threats to global health by the WHO report in 2019²¹. It is a serious public health issue that puts the huge population at risk of cross resistance even though they have not been exposed. The global spread of MDR bacteria has resulted in an increase in difficult-to-treat geriatric UTIs. Misuse and overuse of broad-spectrum antibiotics in urinary tract infected geriatrics creates selective pressure that facilitate the emergence of resistant bacterial isolates to the most routinely used antibiotics^{20,22}. The spread of emerging strains can be minimized by raising awareness and reporting findings regularly. Therefore, this study was performed to determine the burden of multi-drug resistant bacterial isolates and their associated risk factors among UTI-confirmed geriatrics in Gondar town.

Materials and methods

Study design, period, study area, and population

A prospective cross-sectional study was conducted from May 1 to July 14, 2022 at the University of Gondar Comprehensive Specialized Hospital, and Kallen Bnakaf and Menna Geriatrics Support Centers Clinics. Both the hospital and geriatrics support centers are 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 more than 5 million inhabitants in Northwest Ethiopia. Kallen Bnakaf and Menna Geriatrics Support Centers Clinics provides care and support for more than 110 versus 200 geriatrics permanently within the centers and for more than 100 versus 160 geriatrics outside the center, respectively. All geriatric patients who attended at the University of Gondar Comprehensive Specialized Hospital and lived in Kallen Bnakaf and Menna Geriatrics Support Centers were used as the source population while all UTI-confirmed geriatrics admitted at the University of Gondar Comprehensive Specialized Hospital and attended in Kallen Bnakaf and Menna Geriatrics Support Centers Clinics were used as the study population.

Inclusion criteria: Geriatric patients admitted to the University of Gondar Comprehensive Specialized Hospital and attending the Kallen Bnakaf and Menna Geriatrics Support Centers Clinics, who presented with urinary symptoms, were diagnosed with a UTI, and provided informed consent, were included in the study.

Exclusion criteria: Geriatric patients with cognitive impairments and those who had used antibiotics in the two weeks prior to or during the data collection period were excluded.

Study variables: The dependent variable was prevalence of multi-drug resistant bacterial isolates whereas the independent variables were previous history of UTI, recurrent UTI, catheterization, antibiotic use without prescriptions, diabetes Miletus, and frequent hospitalization of UTI-confirmed geriatrics.

Operational definitions

Geriatric was defined as age group equal and above 65 years²³. **UTI-confirmed geriatrics** were defined as those geriatrics having significant bacteriuria from microbiological analysis of urine in the hospital adult wards (C and D) and geriatric support center clinics. **Significant bacteriuria** was defined as when a properly collected midstream urine specimen shown to contain $>10^5$ CFU per ml²⁴. **Symptomatic UTI** was associated with the patients complaining of dysuria, fever, urgent and frequent urination, flank pain, along with malodorous and/or cloudy urine and the number of bacteria on the urine is greater than 10^5 CFU/ml of midstream urine¹⁰. **Mid-stream urine** was defined as a specimen obtained from the middle part of urine flow that is free of contamination, the pre-urethral area is cleansed and the patient is requested to discard the initial flow of urine before collecting the specimen in a sterile container. **Multi-drug resistance** was defined as non-susceptibility to at least one agent in three or more antimicrobial classes²⁵. **Extensive-drug resistance** was defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories tested for a particular microorganism. (i.e., bacterial susceptibility to one or two antimicrobial classes) in this study²². **Pan-drug resistance** was defined as non-susceptibility all to agents in all antimicrobial classes for each bacterium in this study²⁶.

Sample size determination and sampling technique

The sample size was determined by using a single population proportion formula. The proportion was taken at 50%, with 95% of confidence intervals (CI) and 5% of margin error.

$$n = \frac{(Z\alpha/2)^2 P(1-p)}{(d)^2}$$

$$n = \frac{(1.96)^2 * 0.5(1-0.5)}{(0.05)^2} = 384$$

Using reduction formula as the total UTI-confirmed geriatric population based on the same period of the last year's record, estimated population was 440.

$$n_f = \frac{n * N}{n + N}$$

$$n_f = \frac{384 * 440}{384 + 440} = 205$$

By considering a 10% non-response rate: $205 \times 0.1 = 20.5 \sim 21$,
 $n_f = 205 + 21 = 226$

Therefore, the final calculated sample size was equal to 226.

Where N is the total population, n_f = the final sample size, $Z\alpha/2$ = the standard normal deviation, at 95% confidence level = 1.96, the prevalence (p) = 0.5; $1-p = 0.5$ and the desired degree of accuracy (d) = 0.05.

A total of 226 study participants having UTI were recruited in the study using systematic sampling technique.

Data collection and laboratory methods

The important socio-demographic and clinical history of the study participants such as age, gender, education level, income status, residence, occupation, history of UTI and antibiotic use, hospitalization, catheterization and presence of comorbidities like history of diabetes were collected by trained nurses using a structured

questionnaire via face-to-face interviews with geriatrics. Clean catch mid-stream urine was collected in a sterile screw-capped, wide-mouthed urine cup with prior adequate instruction of the participants.

Culture and bacterial 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 sub-cultured on MacConkey agar and mannitol salt agar (MSA) for isolation of a single species and further characterization by lactose fermentation on MacConkey agar and mannitol fermentation on MSA. Identification of bacteria was done using colony characteristic, Gram staining, biochemical tests such as triple sugar iron, motility, indole, citrate, urease, lysine decarboxylase tests, and novobiocin antibiotic test.

Antimicrobial susceptibility testing

The antimicrobial susceptibility test of all identified bacterial isolates were performed in vitro according to the criteria of clinical and laboratory standards institute (CLSI) using the Kirby-Bauer disk diffusion method on Muller-Hinton agar (MHA). A loop full of bacteria (3–5 identical colonies) were taken from a pure culture colony and transferred to a tube containing 5 ml of normal saline and mixed gently until it forms a homogeneous suspension. The turbidity of the suspension then adjusted to the turbidity of McFarland 0.5 in order to standardize the inoculum size and swabbed on MHA using a sterile cotton swab. The following antimicrobials were used with their respective concentration: ampicillin (10 µg), amoxicillin-clavulanate (20/10 µg), tobramycin (10 µg), tetracycline (30 µg), ciprofloxacin (5 µg), ceftazidime (30 µg), ceftazolin (30 µg), cefotaxime (30 µg), meropenem (10 µg), nitrofurantoin (300 µg) and nalidixic acid (30 µg) for Enterobacteriaceae. For *Pseudomonas* species the antimicrobial disks were gentamycin (10 µg), tobramycin (10 µg), norfloxacin (10 µg), meropenem (10 µg). Whereas, vancomycin (30 µg), norfloxacin (10 µg), penicillin (10 units), ceftazidime (30 µg), trimethoprim-sulfamethoxazole (1.25/23.75 µg), gentamycin (10 µg) and doxycycline (30 µg) were for pathogenic Gram-positive cocci. The criteria used to select the antimicrobial agents were based on both their availability for the management of UTIs and the 2022 CLSI guideline²⁷. The plates then incubated at 37 °C for 18–24 h. Diameters of the zone of inhibition around the discs were measured to the nearest millimeter using a ruler and the isolates classified as susceptible and resistant. Isolates intermediate between susceptible and resistant were considered as resistant²⁸.

Methicillin resistant *Staphylococcus aureus* detection

A lawn culture of *S. aureus* was made on the MHA plate and ceftazidime (30 µg) disc applied and incubated at (35–37 °C) for 24 h in ambient air. According to CLSI criteria <10 , 11–12 mm, and >13 mm were categorized as methicillin resistant, intermediate and susceptible, respectively.

Quality control

The questionnaire was checked for its completeness and validity. It was also assured for its consistency by develop first in English, translated to the local language (Amharic), and then re-translated back to English. The culture media were checked for sterility prior to inoculation by incubating 5% of the newly prepared media at (35–37 °C) overnight. Gram's staining reagents, culture media, and antimicrobial discs were also assured for their expiry date. Turbidity of the suspension was standardized against 0.5 McFarland standards. All antimicrobial discs and culture plates were stored at recommended refrigeration temperature (2–8 °C). Reference strains of *E. coli* (ATCC-25922), *P. aeruginosa* (ATCC-27853), and *S. aureus* (ATCC-25923) were used to check the performance of the media and antimicrobials.

Statistical analysis

Data was coded, entered into Epi Data version 4.6.0.0 and its completeness and clearance was checked to ensure the validity of all recorded data. Then it was exported to Stata/IC version 14.0 software for analysis. The study population was described by using summary statistics. Texts, tables, and figures were used to present the data. Logistic regression model was used to see the association between each independent and the outcome variable. All variable with P -value <0.05 in the bivariate analysis were included in the final model of multivariate analysis in order to identify associated factors for the prevalence of MDR UTI. The direction and strength of the statistical association were measured using an odds ratio with a 95% confidence interval. An adjusted odds ratio along with a 95% CI was estimated, and a P -value <0.05 was considered statistically significant.

Results

Socio-demographic and clinical characteristics of the study participants

In this study, out of the expected 226 study participants, only 204 were eligible and included as study subjects with a response rate of 90.3%. Of which, the highest number 187 (91.7%) of study participants were females and their age was ranged from 65 to 88 years with mean age of (70.6 ± 6.83) SD years. The majority of the participants 129 (63.2%) were in the age group of 65–75 and 158 (77.5%) of them had not get the chance of formal education. Due to their age and health problem, most of this study participants 138 (67.7%) had no a job and 89 (43.6%) of them had no any monthly income. According to their residence, the majority 121 (59.3%) of participants were urban dwellers. The most common symptoms reported in large number of UTI-confirmed geriatrics were dysuria 117 (57.4%), urgency of urine 155 (76%), fever 159 (77.9%), frequency of urination 164 (80.4%), and loin pain 175 (85.8%) in ascending order. However, relatively lower number of UTI-confirmed geriatrics manifested abdominal pain and vomiting each symptoms accounted 100 (49%), and 67 (32.8%), respectively (Table 1).

Variables		Status of UTI		Total
		Single growth	Mixed growth	
Age (years)	65–75	103 (63.2%)	26 (63.2%)	129 (63.2%)
	76–85	43 (63.2%)	19 (63.2%)	62 (30.4%)
	≥ 86	8 (63.2%)	5 (63.2%)	13 (6.37%)
Gender	Male	14 (63.2%)	3 (63.2%)	17 (8.3%)
	Female	140 (63.2%)	47 (63.2%)	187 (91.7%)
Education level	No formal education	118 (63.2%)	40 (63.2%)	158 (77.5%)
	Primary level	24 (63.2%)	6 (63.2%)	30 (14.7%)
	Secondary level and above	12 (63.2%)	4 (63.2%)	16 (7.8%)
Income status (ETB)	No monthly income	89 (63.2%)	0 (63.2%)	89 (43.6%)
	1000–2000	22 (63.2%)	18 (63.2%)	40 (19.6%)
	2001–3000	15 (63.2%)	18 (63.2%)	33 (16.2%)
	3001–4000	19 (63.2%)	8 (63.2%)	27 (13.2%)
	≥ 4001	9 (63.2%)	6 (63.2%)	15 (7.35%)
Residence	Urban	106 (63.2%)	15 (63.2%)	121 (59.3%)
	Rural	48 (63.2%)	35 (63.2%)	83 (40.7%)
Occupation	Private employee	5 (63.2%)	4 (63.2%)	9 (4.4%)
	House wife	22 (63.2%)	11 (63.2%)	33 (16.2%)
	Merchant	8 (63.2%)	3 (63.2%)	11 (5.4%)
	No job	108 (63.2%)	30 (63.2%)	138 (67.7%)
	Others	11 (63.2%)	2 (63.2%)	13 (6.4%)
Fever	Yes	115 (72.3%)	44 (27.7%)	159 (77.9%)
	No	39 (86.7%)	6 (13.3%)	45 (22.1%)
Dysuria	Yes	88 (75.2%)	29 (24.8%)	117 (57.4%)
	No	66 (75.9%)	21 (24.1%)	87 (42.6%)
Urgent urination	Yes	111 (71.6%)	44 (28.4%)	155 (76%)
	No	43 (87.8%)	6 (12.2%)	49 (24%)
Frequent urination	Yes	117 (71.3%)	47 (28.7%)	164 (80.4%)
	No	37 (92.5%)	3 (7.5%)	40 (19.6%)
Vomiting	Yes	50 (74.6%)	17 (25.4%)	67 (32.8%)
	No	104 (75.9%)	33 (24.1%)	137 (67.2%)
Loin pain	Yes	133 (76%)	42 (24%)	175 (85.8%)
	No	21 (72.4%)	8 (27.6%)	29 (14.2%)
Abdominal pain	Yes	75 (75%)	25 (25%)	100 (49%)
	No	79 (76%)	25 (24%)	104 (51%)

Table 1. Socio-demographic and clinical characteristics of UTI-confirmed geriatrics. *ETB* Ethiopian Birr, others types of job farmer, cultural drink (tela, tej and areki) workers and food handler, *UTI* urinary tract infection.

Prevalence of MDR and MRSA bacterial isolates of the study participants

The overall prevalence of MDR UTI-confirmed geriatrics in this study was 115 (56.4%) (95% CI: 49.79–58.90). The prevalence of MDR bacterial isolates was 126 (49.6%) (95% CI: 41.79–55.90) and the highest prevalence rate was obtained in both 65 to 75 and 76 to 86 years-old age groups equally of 48 (41.7%) (Fig. 1).

Multi-drug resistant bacterial isolates in females 108 (93.9%) was relatively higher than that of males 7 (6.1%) (Fig. 2). Of the total 204 urine specimens with significant growth, 154 (75.5%) being single growth and 50 (24.5%) being mixed growth with two organisms (Fig. 3). Fifty of two hundred four (24.5%) samples with two bacteria each were isolated, making the number of bacteria isolated to be 254. Out of 23 *S. aureus* isolates 18 (78.3%) were resistant to cefoxitin (surrogate marker for methicillin resistance).

From a total of 254 different isolated bacterial uropathogens, 206 (81.1%) were Gram-negative bacilli, and 48 (18.9%) were Gram-positive cocci. Out of the total MDR bacteria isolated, the prevalence of Gram-negative bacteria (GNB) was significantly higher (105 (83.3%) than that of Gram-positive bacteria (GPB), 21 (16.7%). The most frequently isolated MDR bacteria was *E. coli* 60 (47.6%), followed by *K. pneumoniae* 24 (19.1%). Other urinary tract pathogens that cause a significant MDR UTI burden includes *S. aureus* 13 (10.3%), *P. mirabilis* and *S. saprophyticus* 8 (6.4%), *Pseudomonas spp.* 6 (4.8%), *P. vulgaris* 4 (3.2%) and *K. rhinos* 3 (2.4%). Out of the total 254 isolates the magnitude of MDR isolates were almost half 126 (49.6%) (Table 2).

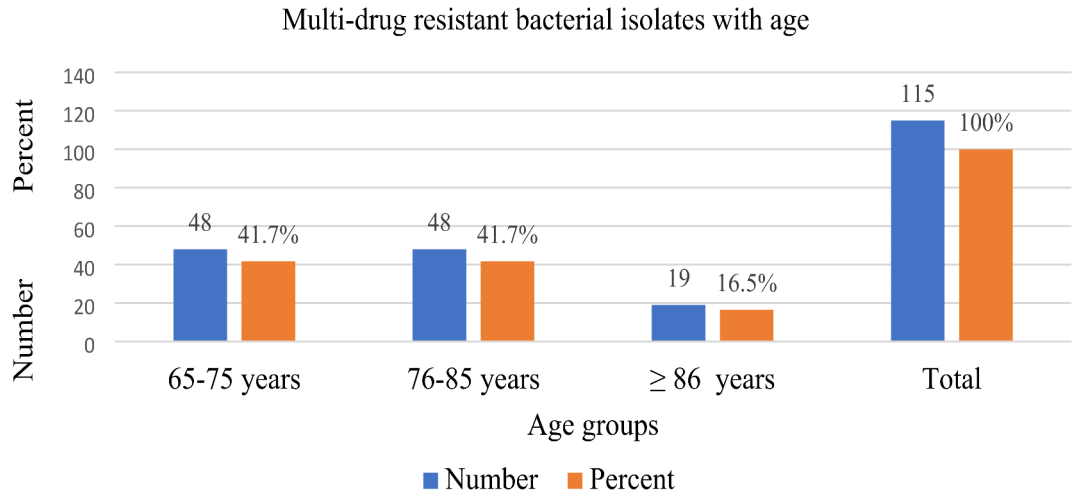


Fig. 1. Prevalence of MDR bacterial isolates across various age groups in geriatric patients with confirmed UTIs.

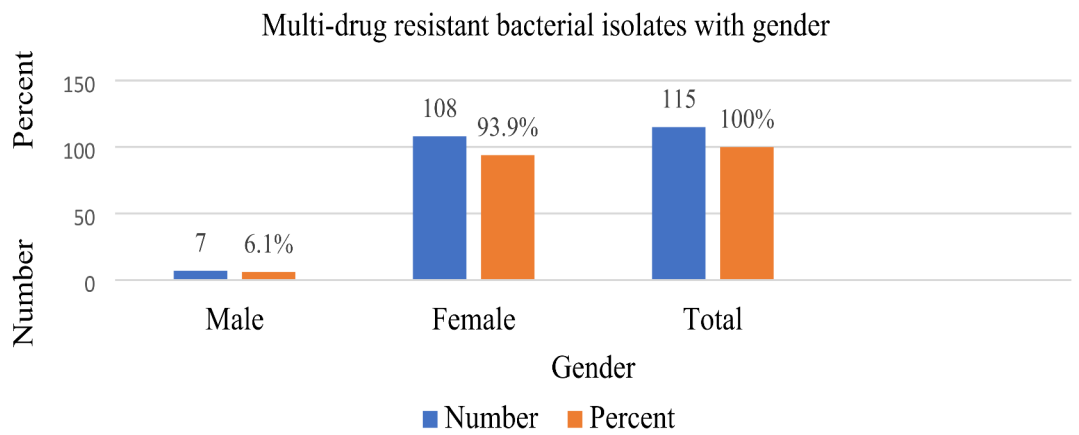


Fig. 2. Comparative prevalence of MDR bacterial isolates in male and female geriatric patients with confirmed UTIs.

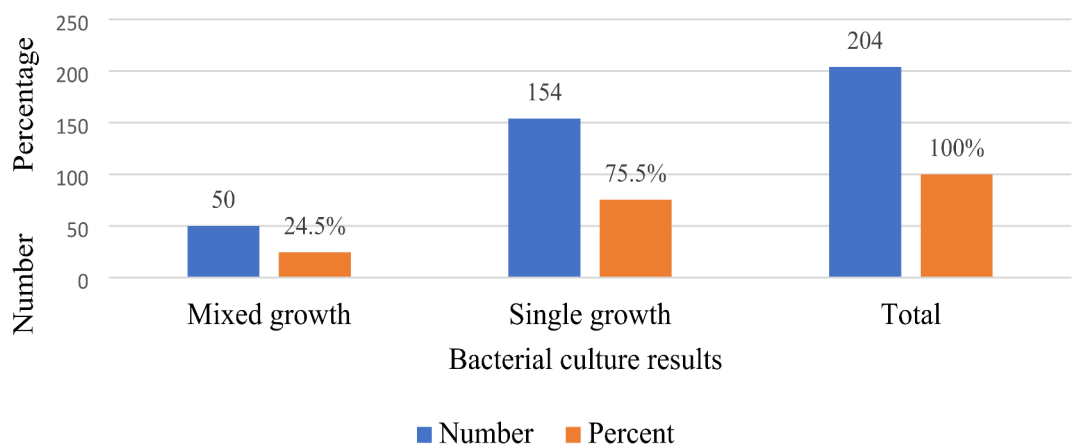


Fig. 3. Results of bacterial growth in culture media.

Bacterial isolates	Number of isolates <i>n</i> (%)		Total
	MDR isolates <i>n</i> (%)	Non-MDR isolates <i>n</i> (%)	
Gram-negative	105 (83.3%)	101 (78.9%)	206 (81.1%)
<i>Escherichia coli</i>	60 (47.6%)	49 (38.3%)	109 (42.9%)
<i>K. pneumoniae</i>	24 (19.1%)	22 (17.2%)	46 (18.1%)
<i>K. rhinos</i>	3 (2.4%)	7 (5.5%)	10 (3.9%)
<i>P. mirabilis</i>	8 (6.4%)	7 (5.5%)	15 (5.9%)
<i>P. vulgaris</i>	4 (3.2%)	3 (2.3%)	7 (2.8%)
<i>Citrobacter</i> spp.	0 (0%)	7 (5.5%)	7 (2.8%)
<i>Pseudomonas</i> spp.	6 (4.8%)	6 (4.7%)	12 (100%)
Gram-positive	21 (16.7%)	27 (21.1%)	48 (18.9%)
<i>S. aureus</i>	13 (10.3%)	10 (7.8%)	23 (9.1%)
<i>S. saprophyticus</i>	8 (6.4%)	17 (13.3%)	25 (9.8%)
Total	126 (49.6%)	128 (50.4%)	254 (100%)

Table 2. Distribution of MDR bacterial isolates in UTI-confirmed geriatrics. MDR multi-drug resistant, UTI urinary tract infection.

Variables		MDR UTI					
		MDR <i>n</i> (%)	Total <i>N</i> (%)	COR	P-Value	AOR (95% CI)	P-value
Previous UTI (204)	Yes	91 (79.1%)	150 (73.5%)	1.93	0.041	3.20 (0.99–10.40)	0.053
	No	24 (20.9%)	54 (26.5%)	1	-	-	-
Recurrent UTI (204)	No recurrence	51 (44.3%)	122 (59.8%)	1	-	-	-
	≥ 2 per 6 months	22 (19.1%)	31 (15.2%)	3.40	0.005	5.02 (1.15–21.85)	0.032
	≥ 3 per 12 months	42 (36.5%)	51 (25%)	6.50	<0.001	6.61 (1.98–22.02)	0.002
Catheterization (204)	Yes	57 (49.6%)	77 (37.8%)	3.39	<0.001	2.83 (1.98–22.02)	0.038
	No	58 (50.4%)	127 (62.3%)	1	-	-	-
Antibiotic use without prescription (204)	Yes	87 (75.7%)	127 (62.3%)	3.81	<0.001	3.36 (1.17–9.68)	0.025
	No	28 (24.3%)	77 (37.8%)	1	-	-	-
Diabetes Miletus (204)	Yes	45 (39.1%)	67 (32.8%)	1.96	0.031	1.74 (0.58–5.23)	0.325
	No	70 (60.9%)	137 (67.1%)	1	-	-	-
Hospitalization (204)	Yes	71 (61.7%)	115 (56.4%)	1.65	0.080	-	-
	No	44 (38.3%)	89 (43.6%)	1	-	-	-
Hospital stays (days) (<i>n</i> = 115)	2 days	5 (7%)	20 (17.4%)	1	-	-	-
	3 days	12 (16.6%)	19 (16.5%)	5.14	0.020	3.06 (0.55–17.15)	0.203
	4 days	15 (21.1%)	22 (19.1%)	6.43	0.007	5.46 (1.01–29.59)	0.049
	≥ 5 days	39 (54.9%)	54 (47%)	7.8	0.001	5.61 (1.27–24.83)	0.023

Table 3. Bivariate and multivariate analysis of risk factors associated with multi-drug resistance. AOR adjusted odds ratio, CI confidence interval, COR crude odds ratio, 1 reference category.

Risk factors of the study participants

In bivariate analysis of UTI-confirmed study participants, risk factors for MDR UTI included history of previous UTI, history of recurrent UTI, use of a urinary catheter, history of antibiotic use without prescription, diabetes Miletus, and hospitalization of ≥ 3 days. Among the variables analyzed in bivariate logistic regression, those with a *P*-value < 0.05 were eligible and entered into multivariate analysis (Table 3).

Multivariate logistic regression modeling revealed four independent risk factors associated with UTI by MDR bacterial isolates: history of recurrent UTI (≥ 2 per 6 months) (AOR=5.02; CI, 1.15–21.85, *P*=0.032) and (≥ 3 per 12 months) (AOR=6.61; CI, 1.98–22.02, *P*=0.002), use of a urinary catheter (AOR=2.83; CI, 1.98–22.02, *P*=0.038), history of antibiotic use without prescription (AOR=3.36; CI, 1.17–9.68, *P*=0.025), and hospitalization of 4 days (AOR=5.46; CI, 1.01–29.59, *P*=0.049) and ≥ 5 days (AOR=5.61; CI, 1.27–24.83, *P*=0.023) (Table 3).

MDR, XDR, and PDR isolates and antibiogram

The antibiotic resistance profile of 254 bacterial isolates were studied. Among the tested bacterial isolates, 126 (49.6%) were MDR, 63 (24.8%) were XDR, and 6 (4.8%) were PDR. Among tested GNB isolates, 105 (51%) were MDR, 63 (30.6%) were XDR, and 6 (2.9%) were PDR respectively. The results of MDR within species showed that the species of *P. vulgaris* 4 (57.1%), followed by *E. coli* 60 (55.1%), *P. mirabilis* 8 (53.3%), *K. pneumoniae* 24 (52.2%), *Pseudomonas* spp. 6 (50%), and *K. rhinos* 3 (30%). Likewise, 6 (40%) of *P. mirabilis*, 6 (50%) of

Pseudomonas spp., 37 (34%) of *E. coli*, 2 (28.6%) of *P. vulgaris*, 11 (23.9%) of *K. pneumoniae*, and 1 (10%) of *K. rhinos* were XDR isolates. However, there was no MDR, XDR and PDR isolates detected in *Citrobacter spp.* The only PDR bacterial isolate was attributed to *Pseudomonas spp.* 6 (50%) (Table 4).

Among GPB isolated, MDR isolates accounted for 21 (43.8%). Within the tested isolates 13 (56.5%) and 8 (32%) of *S. aureus* and *S. saprophyticus* were found to be MDR, respectively. However, there was no XDR and PDR isolates detected in the *S. aureus* and *S. saprophyticus* bacterial species (Table 4).

Discussion

Resistance to multiple antibiotics is a major concern across the globe, which leads to frequent treatment failure and complications^{29,30}. Therefore, strengthen knowledge of antimicrobial resistance through surveillance and research is necessary and now applied by World Health Organization (WHO)²⁰. Age or chronic diseases related immune alteration, the high prevalence of UTI and fear of its complication in geriatric patients encourages the irrational use of antibiotics^{22,31}, especially in the developing world where empirical treatment is common. Knowing the prevalence of drug-resistant bacterial uropathogens among geriatric patients could help the clinicians to improve the wise prescription of antibiotics.

In this study, the overall prevalence of MDR UTI was 115 (56.4%). The prevalence of MDR bacterial isolates was 126 (49.6%). This prevalence was comparable with studies in Saudi Arabia 111 (46.3%)³², Turkey 129 (53.8%)³³, and Ethiopia-Gondar 473 (44.1%)²⁰. In contrast, this study reported a lower prevalence than studies in Ghana 25 (80.1%)³⁴, and Hawassa-Ethiopia 102 (80.3%)³⁵. On the other hand, the result of this study was higher than studies done in Nepal 90 (41.1%)³⁶, and German 147 (41.4%)²² and 3 (5.5%)⁸. The variation in prevalence of MDR bacteria could be due to increase in trend of MDR bacteria with time, and difference in study period, target population, MDR definition and the antibiotics tested.

In the present study, among MDR isolates the magnitude of GNB were 105 (83.3%) which was higher than the study documented in Iraq 96 (76.2%)³⁷, and Arba Minch-Ethiopia 66 (50.4%)³⁰. In this study, 63 (30.6%) and 6 (2.9%) of the Gram-negative isolates were XDR and PDR, respectively, which were higher than the study conducted in Indian women patients XDR 11 (12%)²⁶, and in Iraq XDR 5 (4%) vs. PDR 1 (0.8%)³⁷. The reason for this higher resistance might be due to self-medication, non-compliance with medication and sales of the substandard drugs may account for the rise in antibiotic resistance observed in this study. In this study area; there is also high tourist flow, and many of residents have relatives from abroad, which may have an impact on the emergence of MDR GNB in this locality, particularly³⁸.

In the current study, among MDR isolates the prevalence of GPB was 21 (16.7%). Among the isolated MDR GPB, *S. aureus* represents a high drug resistance 13 (61.9%). This result was higher than previous study documented in Ethiopia-Gondar 31 (6.6%)²⁰. Methicillin resistant *S. aureus* (MRSA) isolates were also found at a higher rate 18 (78.3%) in this study. The high rate of resistance might be due to easy access, self-medication, weak adherence of patients to prescribed antimicrobial agents, and wider availability of empirical treatment in the setting.

Comparatively, this study showed that MDR-GNB 105 (83.3%) were more common than MDR-GPB 21 (16.7%). This pattern was similar with studies reported in Ethiopia-Dessie MDR-GNB and MDR-GPB (42 (73.7%) vs. 15 (26.3%))², German (140 (95.2%) vs. 7 (4.7%))²², and Turkey (129 (100%) vs. 0 (0%))³³. According to this study, XDR-GNB and PDR-GNB (63 (24.8%) vs. 6 (2.4%)) were also frequently reported than XDR-

Isolates	R0	R1	R2	R3	R4	R5	R6	MDR	XDR	PDR
<i>Escherichia coli</i> (109)	10	7	32	23	23	10	4	60 (55.1%)	37 (34%)	0 (0%)
<i>K. pneumoniae</i> (46)	6	3	13	13	5	4	2	24 (56.5%)	11 (23.9%)	0 (0%)
<i>K. rhinos</i> (10)	2	1	4	2	0	1	0	3 (30%)	1 (10%)	0 (0%)
<i>P. mirabilis</i> (15)	2	1	4	2	3	3	0	8 (53.3%)	6 (40%)	0 (0%)
<i>P. vulgaris</i> (7)	1	0	2	2	2	0	0	4 (57.1%)	2 (28.6%)	0 (0%)
<i>Citrobacter spp.</i> (7)	1	3	3	0	0	0	0	0 (0%)	0 (0%)	0 (0%)
<i>Pseudomonas spp.</i> (12)	2	1	3	6	0	0	0	6 (50%)	6 (50%)	6 (50%)
Total (206)	24	16	61	48	33	18	6	105 (51%)	63 (30.6%)	6 (2.9%)
<i>S. aureus</i> (23)	3	2	5	13	0	0	0	13 (56.5%)	0 (0%)	0 (0%)
<i>S. saprophyticus</i> (25)	7	5	5	8	0	0	0	8 (32%)	0 (0%)	0 (0%)
Total (48)	10	7	10	21	0	0	0	21 (43.8%)	0 (0%)	0 (0%)
Grand total (254)	34	13	71	69	33	18	6	126 (49.6%)	63 (24.8%)	6 (2.4%)

Table 4. Bacterial resistance levels in urine samples. MDR multi-drug resistant, PDR pan-drug resistant, R0 sensitive for all classes of antibiotics, R1 resistant for one class of antibiotics, R2 resistant for two classes of antibiotics, R3 resistant for three classes of antibiotics etc., XDR extensive-drug resistant. The Gram-negative bacterial isolates were highly resistant to gentamycin 12 (100%), nalidixic acid 167 (91.8%), ampicillin 144 (79.1%), tetracycline 139 (76.4%), norfloxacin 9 (75%), cefazolin 114 (62.6%), and ceftazidime 108 (59.3%) for the tested isolates but demonstrated low level of resistance to meropenem 27 (13.9%), ciprofloxacin 52 (28.6%), nitrofurantoin 60 (33.0%), tobramycin 72 (37.1%), Amoxicillin-clavulanate 70 (38.5%), and cefotaxime 87 (47.8%). The overall resistance rate was 1061 (48.6%), which means almost half of isolates were resistant to antibiotics tested (table 5).

Antimicrobial tested		Number of isolates (n = 206)												Total R (%)		
		<i>E. coli</i> (n = 109)		<i>K. pneumoniae</i> (n = 46)		<i>K. rhinos</i> (n = 10)		<i>P. mirabilis</i> (n = 15)		<i>P. vulgaris</i> (n = 7)		<i>Pseudomonas</i> spp. (n = 12)			<i>Citrobacterspp.</i> (n = 7)	
Classes	Antibiotics	T	R	T	R	T	R	T	R	T	R	T	R	T	R	
Nitrofurans	NIT	109	28 (25.7%)	46	11 (23.9%)	10	4 (40%)	15	12 (80%)	7	2 (28.6%)	-	-	7	3 (42.9%)	60 (33.0%)
	GEN	-	-	-	-	-	-	-	-	-	-	12 (100%)	-	-	-	12 (100%)
Aminoglycosides	TOB	109	29 (26.6%)	46	18 (39.1%)	10	5 (50%)	15	4 (26.7%)	7	1 (14.3%)	12 (100%)	7	3 (42.9%)	72 (37.1%)	
	CPR	109	24 (22%)	46	8 (17.4%)	10	9 (90%)	15	5 (33.3%)	7	4 (57.1%)	-	-	7	2 (28.6%)	52 (28.6%)
Fluoroquinolones	NOR	-	-	-	-	-	-	-	-	-	-	12 (75%)	-	-	-	9 (75%)
	AMP	109	72 (66.1%)	46	41 (89.1%)	10	8 (80%)	15	13 (86.7%)	7	7 (100%)	-	-	7	3 (38.6%)	144 (79.1%)
Beta-Lactams	AMC	109	34 (38.6%)	46	13 (38.6%)	10	7 (38.6%)	15	8 (38.6%)	7	5 (38.6%)	-	-	7	3 (42.9%)	70 (38.5%)
	CAZ	109	56 (51.4%)	46	32 (69.6%)	10	1 (10%)	15	7 (46.7%)	7	5 (71.4%)	-	-	7	7 (100%)	108 (59.3%)
	CZN	109	69 (63.3%)	46	26 (56.5%)	10	4 (40%)	15	8 (53.3%)	7	4 (57.1%)	-	-	7	3 (42.9%)	114 (62.6%)
	CTX	109	43 (39.5%)	46	23 (50%)	10	4 (40%)	15	9 (60%)	7	3 (42.9%)	-	-	7	5 (71.4%)	87 (47.8%)
	MRP	109	14 (12.8%)	46	4 (8.7%)	10	0 (0%)	15	0 (0%)	7	3 (42.9%)	12 (6 (50%))	-	7	0 (0%)	27 (13.9%)
Tetracycline	TET	109	87 (79.8%)	46	27 (58.7%)	10	5 (50%)	15	14 (93.3%)	7	4 (57.1%)	-	-	7	2 (28.6%)	139 (76.4%)
Quinolone	NAL	109	97 (89%)	46	39 (84.8%)	10	5 (50%)	15	13 (86.7%)	7	7 (100%)	-	-	7	6 (85.7%)	167 (91.8%)
Overall AMR for a bacterium		1199	553 (49.1%)	506	242 (47.8%)	110	52 (42.3%)	165	93 (56.4%)	77	45 (58.4%)	48	39 (81.3%)	77	37 (48.1%)	
Overall AMR for tested isolates		Total tested isolates 2182, resistant isolates 1061 (48.6%)														

Table 5. Resistance profile of Gram-negative bacteria identified from UTI-confirmed geriatrics. AMC amoxicillin-clavulanate, AMP ampicillin, AMR antimicrobial resistance, CAZ ceftazidime, CPR ciprofloxacin, CTX cefotaxime, CZN ceftazoline, GEN gentamicin, MRP meropenem, NAL nalidixic acid, NIT nitrofurantoin, NOR norfloxacin, R resistance isolates in %, T total number of tested isolates, TET tetracycline, TOB tobramycin. The Gram-positive bacterial isolates were highly resistant to penicillin 30 (62.5%). However, low level of resistance to gentamicin 5 (22.9%), trimethoprim-sulfamethoxazole 15 (31.3%), doxycycline 11 (33.0%), norfloxacin 16 (33.3%), Vancomycin 18 (37.5%), and ceftoxitin 21 (43.8%). Among tested Gram-positive isolates, the drug resistance rate of *S. Aureus* was higher 65 (40.4%) than *S. Saprophyticus* 51 (29.1%). The total resistance rate of Gram-positive bacterial isolates was 116 (34.5%) (table 6).

Antimicrobial tested		Number of Isolates (n = 48)				
Classes	Antibiotics	<i>S. aureus</i> (n = 23)		<i>S. saprophyticus</i> (n = 25)		Total (n = 48)
		T	R (%)	T	R (%)	R (%)
Glycopeptide	VAN	23	9 (39.1%)	25	9 (36%)	18 (37.5%)
Aminoglycosides	GEN	23	2 (8.7%)	25	3 (12%)	5 (22.9%)
Tetracyclines	DOX	23	7 (30.4%)	25	4 (14.3%)	11 (33.0%)
Beta-Lactams	PEN	23	18 (78.3%)	25	12 (48%)	30 (62.5%)
	FOX	23	14 (60.9%)	25	7 (28%)	21 (43.8%)
Sulfonamides	SXT	23	8 (34.8%)	25	7 (28%)	15 (31.3%)
Fluoroquinolones	NOR	23	7 (30.4%)	25	9 (36%)	16 (33.3%)
Overall AMR for a bacterium		161	65 (40.4%)	175	51 (29.1%)	(34.5%)
Overall AMR for isolates		Total tested isolates 336, Resistant isolates 116 (34.5%)				

Table 6. Resistance profile of Gram-positive bacteria identified from UTI patients. AMR antimicrobial resistance, DOX doxycycline, FOX cefoxitin, GEN gentamycin, NOR norfloxacin, PEN penicillin, R resistant isolates in percentage, SXT trimethoprim-sulfamethoxazole, T total number of tested isolates, VAN Vancomycin.

GPB and PDR-GPB (0 (0%) for each), respectively. This might be due to the resistant GNB originated from the patient's gastro-intestine, which is the frontline exposed to different antibiotics and the constant source of infection, poor hand-hygiene practices after a toilet and before a meal in geriatric patients, and the number of antibiotic choices for GPB is relatively fewer with last resorts.

The predominant MDR bacteria was *E. coli* isolated from UTI-confirmed geriatric patients indicate high levels of resistance 60 (47.6%) to the commonly used antibiotics. This pattern was similar with studies in India 46 (66.7%)²⁶, and Ethiopia-Gondar 104 (65%)³⁸. The main possible reason might be due to plasmid-mediated transfer of multi-drug resistance among MDR *E. coli* isolates. Other MDR bacteria isolated were *K. pneumoniae* 24 (19.1%), *S. aureus* 13 (10.3%), *P. mirabilis* and *S. saprophyticus* (8 (6.4%) for each), *Pseudomonas spp.* 6 (4.8%), *P. vulgaris* 4 (3.2%), and *K. rhinos* 3 (2.4%).

Escherichia coli was also the frequent XDR bacteria isolated at a rate of 37 (58.7%), followed by *K. pneumoniae* 11 (17.5%), *P. mirabilis* and *Pseudomonas spp.* (6 (9.5%) for each), *P. vulgaris* 2 (3.2%), and *K. rhinos* 1 (1.6%). However, there was no any *Citrobacter spp.*, *S. aureus* and *S. saprophyticus* XDR bacterial isolate reported. The possible reasons may be due to the increasing irrational use of antibiotics, the transmission of resistance genes between people and people or/and animals to people, and consumption of animal products that were treated with antibiotics.

Pseudomonas spp. were the only bacterial species that obey the definition of MDR, XDR, and PDR (6 (100%) for each). And were also the lonely bacterial species detected as PDR in this study. Besides, this bacterium is frequently difficult to treat, most probably due to their intrinsic, acquired and adaptive resistance ability to multiple groups of antibiotics.

The current prioritized lists of bacterial pathogens by WHO, categorized *E. coli*, *K. pneumoniae*, *Pseudomonas* and *Proteus spp.* identified in our study, as critical or most life-threatening Gram-negative pathogens under surveillance due to their high antibiotic resistance. In particular, *S. aureus*, *K. pneumoniae* and *Pseudomonas spp.* have further been described by the Infectious Diseases Society of America as ESKAPE (*E. faecium*, *S. aureus*, *K. pneumoniae*, *A. baumannii*, *Pseudomonas spp.* and *Enterobacter spp.*) pathogens, frequently associated with MDR^{39,40}. These three ESKAPE pathogens were reported 43 (34.1%) of MDR bacterial isolates therefore, posing a major threat to public healthcare in Ethiopia.

In our study, history of recurrent UTIs (≥ 2 per 6 months) and (≥ 3 per 12 months) were significantly associated ($P=0.032$) and ($P=0.002$) with the prevalence of MDR bacteria, respectively. This result had a similar pattern with a study in Turkey (≥ 2 per 6 months) ($P=0.001$)³³. The possible reasons for this finding might be due to prolonged hospitalization, catheterization, lack of new novel antibiotics and the frequent use of antibiotics associated with relapse and reinfection.

In this study, the use of a urinary catheter was one of the independent risk factors for MDR bacteria to emerge. This finding is similar with the studies recorded in Serbia⁴¹ and by a recollective study in Bulgaria, Greece, Hungary, Israel, Italy, Romania, Spain and Turkey UTI geriatric patients⁵. From the total of 77 (37.8%) previously catheterized geriatrics, 57 (49.6%) of them were infected by MDR bacteria. This finding reflected that the catheter introduces extraneous more resistant types of bacteria from the environment and/or the patient's own flora. The possible reasons might be due to previous inappropriate technique of catheter insertion, poor hand hygiene and prolonged catheterization.

History of antibiotic use without prescriptions was one of the most important variables significantly associated ($P=0.025$) with the presence of MDR bacterial uropathogens. Out of 127 (62.3%) previous antibiotic users, 87 (75.7%) of them were infected with MDR bacterial uropathogens. Our study reflected that the prior and continuous use of antibiotics correlates with an increase in the prevalence of multi-drug resistance. This might be due to the use of broad-spectrum antibiotics, empirical treatment of geriatric patients before culture and drug resistance test has been done, misuse and overuse of antibiotics which creates selective pressure where

antibiotics kill susceptible strains and leave the resistant one to multiply. This finding correlated with the study conducted in Turkey³³, and Ethiopia-Gondar³⁸.

The statistically significant association between the presence of MDR bacterial uropathogens and hospitalization of 4 days ($P=0.049$) and ≥ 5 days ($P=0.023$) could be due to long duration of hospitalization, vulnerability of patients to the hospital environments, and the presence of highly resistant bacteria available in an environment. This finding was in agreement with the study reports in Greece⁴², and German²².

Limitation of the study

The study did not include obligate anaerobic bacteria, and some bacterial isolates could not be identified at the species level due to limited resources. Additionally, antimicrobial susceptibility testing was conducted solely using the disk diffusion method rather than the more precise microdilution technique.

Conclusion and recommendations

The study reveals a high burden of multidrug-resistant (MDR) bacterial isolates, with *Escherichia coli* being the most common MDR and XDR pathogen, and *Pseudomonas* spp. as the only pan-drug-resistant (PDR) isolate. Most MDR isolates showed heightened resistance to tetracyclines, beta-lactams, and quinolones. Independent risk factors included recurrent UTIs, urinary catheterization, antibiotic use, and hospital stays of ≥ 4 days. These findings stress the need for routine diagnostics and antimicrobial susceptibility testing over empiric treatment.

The misuse of broad-spectrum antibiotics without prescriptions exacerbates resistance, reducing treatment efficacy and fostering resistant strains in the population. Healthcare policies should promote accurate diagnoses, prudent antibiotic use, and mitigate risks such as recurrent UTIs, improper catheterization, and prolonged hospitalizations (≥ 4 days). In geriatric patients, MDR prevalence necessitates careful UTI management, with treatment for catheterized patients only when identical organisms are confirmed in urine and blood cultures. Antimicrobial stewardship programs are essential to control MDR spread. Future research should prioritize identifying effective strategies to reduce the risk factors associated with multidrug-resistant (MDR) bacterial uropathogens. Additionally, molecular studies should be conducted to better characterize the diverse MDR bacterial isolates.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

G.B. participated in the design of the study, performed the statistical analysis, drafted and reviewed the manuscript. M.D., B.T. and A.A. participated in the design and coordination, performed the initial analyses, and reviewed the manuscript. A.B., M.D. and Y.G. participated in the acquisition of data. All authors read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

The study was conducted after getting institutional ethical clearance from the Research and Ethical Review Committee of School of Biomedical and Laboratory Science, College of Medicine and Health Sciences, University of Gondar. Permission was also obtained from the University of Gondar Comprehensive Specialized Hospital Clinical Director, Kallen Bnakaf and Menna Geriatric Support Centers Administration Office. The study participants were informed about the process, its purpose, and their right to refuse the study. A written informed consent was signed by geriatric study subjects. Codes were used to represent the study participants so that only authorized personnel could access the data. Geriatrics who had positive MDR bacteriological results were linked to health professionals for the required care. The study has been performed in accordance with the Declaration of Helsinki.

Additional information

Correspondence and requests for materials should be addressed to G.B.

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