JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

INVESTIGATION OF THE OCCURRENCE AND ANTIBIOTIC RESISTANCE OF GRAM – NEGATIVE BACTERIA CAUSING URINARY TRACT INFECTIONS AMONG PREGNANT WOMEN AT PRINCESS CHRISTIAN MATERNITY HOSPITAL IN FREETOWN SIERRA LEONE

[1]Tamba Buffa, [2]Amidu Gibril Torto, [3]Zikan Koroma, [4]Abdulai Kanu, [5]Julian Sydney Olufemi Campbell

[1]Pharmacist, [2]Pharmacist, [3]Medical Doctor, [4]Pharmacist, [5]Molecular Biologist

[1]Department of Pharmaceutics/Pharmaceutical Microbiology

[1]College of Medicine and Allied Health Sciences, University Of Sierra Leone, Freetown, Sierra Leone.

ABSTRACT

Background: The urinary tract is a common site for infections, particularly among pregnant women, due to physiological changes that occur during pregnancy. These alterations predispose them to infections. This study investigated the prevalence and susceptibility pattern of Gram-negative bacteria associated with urinary tract infections among pregnant women.

Method: A cross–sectional *in vitro* experimental study conducted among pregnant women who attended antenatal clinic at the Princess Christian Maternity (PCMH) Hospital. Participant's information was captured using structured questionnaire. A total of 154 clean-catch midstream urine samples were collected and cultured at the microbiology laboratory of the same hospital. Susceptibility tests using the Vitek 2 compact automated system were used

Result: The prevalence of urinary tract infections among pregnant women was 27.9%. Infection was most prevalent among the age range of 16-20 years. *Pseudomonas aeruginosa, Klebsiella pneumonia, Acinetobacter baumanni, Proteus mirabilis and Escherichia coli* were the microorganisms identified. However, *Escherichia coli* (*E. coli*) was the predominant Gram-negative microorganism isolated in this study as it accounted for 50% of the total microbes. All the isolates were resistant to ampicillin. The most common isolate was highly susceptible to ciprofloxacin, gentamicin ceftriaxone and ceftazidine.

Conclusion: This study recorded high prevalence of urinary tract infections among pregnant women. *E. coli* was the most prevalent Gram-negative microorganism isolated and all the organisms were resistant to ampicillin.

Key Words: UTI, Pregnancy, Gram – negative bacteria, *E.coli, K. pneumonia*, resistance and susceptibility.

I. INTRODUCTION

Urinary tract infections, also referred to as UTIs are the most prevalent diseases that affect half of the world population at least once in their lifetime, and sometimes lead to major health consequences (4)**.** The common pathogens include the Gram-negative bacteria such as *Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, and Enterobacter* species (spp) (32). Depending on the anatomical location, urinary tract infections can be categorized as lower UTIs such as cystitis, urethritis, and prostatitis, and upper urinary tract infection (UTIs) such as pyelonephritis (infection of the kidney). (46). Additionally, they can also be grouped as complicated or uncomplicated urinary tract infection (UTIs) (44). Due to anatomical and physiological factors, women are eight times more likely than males to get a UTI. (34). Due to physiological, anatomical, hormonal changes and personal hygiene issues, pregnant women are more prone to UTIs (6). UTIs are a serious health issue that affect 20% of expectant mothers and frequently lead to obstetric hospitalization (10). Complications such as anaemia, pre-eclampsia, renal failure, sepsis, low birth weight, intra-uterine growth restriction, preterm labor, early birth, intrauterine fetal death, increased fetal mortality, and morbidity can occur if this condition is left untreated (29). In contrast to wealthy nations, the prevalence of UTIs is increasing in underdeveloped nations because of inadequate nutrition, low socioeconomic level, and improper antibiotic use (47). Studies conducted in Ethiopia reported 9-14% prevalence range of UTIs during pregnancy (48). Urinary pathogen antibiotic resistance is becoming more prevalent globally and is a serious public health concern, particularly in developing nations. In environments that depend on empirical therapies before laboratory confirmation of infections, it is essential to understand the distribution of urinary pathogens and their antibiotic susceptibility because antimicrobial resistance varies throughout the world (15). While sophisticated surveillance systems exist in some countries (mainly high-income), antibiotic resistance surveillance data are sparse in many countries with limited resources, particularly in sub-Saharan Africa. A six-month study conducted by Kengne *et al* in Chad in 2014, identified *Escherichia coli* as the main cause of UITs, and greater than 60% of all isolates exhibited multidrug resistance (15). A researched in which more than 1, 000 urine samples were collected and examined between 2012 and 2017, 30% of the samples confirmed positive for bacteria isolates and *E. coli* accounted for 50% of the samples that tested positive (13) and close to 90% of the isolates were, multidrug resistant (13).

In Bo, the second largest city in Sierra Leone, a study reported the presence of *Citrobacter freundii, Klebsiella pneumoniae, Enterobacter cloacae, Escherichia coli, Enterobacter sp. Leclercia sp.* and *Escherichia.*

Hermannii in urine samples and 85.7% of these isolates demonstrated multidrug resistance to extended-spectrum ß-lactamase (41). Widespread resistance was reported for sulphonamides (91.4 %), chloramphenicol (72.9 %), gentamycin (72.9 %), ampicillin with sulbactam (51.4 %) and ciprofloxacin (47.1 %) with *C. freundii* exhibiting the highest and *E. coli* the lowest prevalence of multidrug resistance (41).

A study conducted at two tertiary hospitals in Freetown, Sierra Leone reported *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus,* and *Pseudomonas spp* (13). The study further reported 55% overall multidrug resistance particularly for *E. coli* (58%), *Pseudomonas spp*. (50%), and *S. aureus* (44%). The isolates were resistant to trimethoprim-sulfamethoxazole (47%), nalidixic acid (44%), nitrofurantoin (32%) and cefotaxime (36%) (13).

II. MATERIALS AND METHOD

Materials

Materials such as MacConkey ager, Cystine Lactose Electrolyte Deficient (CLED) ager, Nutrient ager, Petri dishes, Viteck 2 compact, cotton swab, safety cabinet, hot air oven, incubator, laboratory coat, hand glove, face mask, distilled water, Hot plate, loop holder, wire loop, graphite pencil, permanent maker, plane slide, frosted end slide, cover glasses, urine strips, microscope, Coleman coolers, Ice pack, urine container were used in this study.

Study design

It was an in vitro cross–sectional experimental study designed to investigate the prevalence and susceptibility

Pattern of the prevalence and susceptibility pattern of Gram-negative bacteria isolated from the urine samples of pregnant women who visited Princess Christian Maternity Hospital (PCMH).

Hermannii in urine samples and 85.7% of these isolates demonstrated multidrug resistance to extended-spectrum ß-lactamase (41). Widespread resistance was reported for sulphonamides (91.4 %), chloramphenicol (72.9 %), gentamycin (72.9 %), ampicillin with sulbactam (51.4 %) and ciprofloxacin (47.1 %) with *C. freundii* exhibiting the highest and *E. coli* the lowest prevalence of multidrug resistance (41).

A study conducted at two tertiary hospitals in Freetown, Sierra Leone reported *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus,* and *Pseudomonas spp* (13). The study further reported 55% overall multidrug resistance particularly for *E. coli* (58%), *Pseudomonas spp*. (50%), and *S. aureus* (44%). The isolates were resistant to trimethoprim-sulfamethoxazole (47%), nalidixic acid (44%), nitrofurantoin (32%) and cefotaxime (36%) (13).

Study site

The study was conducted at the Princess Christian Maternity Hospital (PCMH) which is one of the University Teaching Hospitals in Sierra Leone purposely built for maternity cases. This facility has a 168-bed capacity and admits 850 patients each month.

Study populations

This study was conducted among pregnant women who attended antenatal clinic at the Princess Christian Maternity Hospital (PCMH).

Sample size

Due to the paucity of data on urinary tract infections among pregnant women in Sierra Leone, 50% of the population proportion was used to determine the sample size based on a single population proportion. The tolerable margin of error/precision (d) = 5%, Z score for 95% confidence level.

From the Fischer equation: $n = \frac{Z^2 \times p(1-p)}{d^2}$

Where; n =? (Required sample size), z = 95% = 1.96 (confidence level), p = 50% (prevalence rate of disease) and d = 5% (precision/margin of error).

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

$$n = 384$$

By substituting the value of $n = 384$ and $N = 258$ into Cochrane formula (Since the total pregnant women visiting the hospital are less than 10000)

$$N_F = \frac{n}{1+\frac{n}{N}} = \frac{384}{1+\frac{384}{258}} = 154.31$$

Thus, **154** pregnant women were targeted to conduct this study

Collection and coding of urine samples

A well-structured on-the-spot questionnaire was developed to capture demographic data of participants. A sterile container with air-tight screw cap was given to each participant and clear instruction on how mid-stream urine is collected was also made. Each participant collected urine to the 15ml mark of the container. Each container was coded with the patient initials, age and time of collection. The containers were taken to the Princess Christian Maternity Microbiology Laboratory for culture and microscopy.

Inoculation and incubation of sample

A calibrated wire loop (0.001ml) was used to inoculate urine samples on Cystine Lactose Electrolyte Deficient (CLED) and Blood ager plates and the plates were then incubated at 37^0C for 24 hours. Colony counts were carried out on culture plates to check significant growth, and those with a colony count of >105 Colony forming unit (CFU)/ml were considered significant. The method employed in the identification and characterization of isolated bacteria included examination of morphological features of the colonies on the agar plates and convectional biochemical tests

Urine dipstick test

This test was done immediately after the collection of each urine sample. This was done by gently pouring the urine sample over the uristrip one after another where all samples presenting with leucocytes, proteins and nitrites were counted as positive for bacteriuria and those without, as negative for absence of bacteriuria. All the urine samples that were positive for protein, nitrite and leucocytes were subjected to culture procedure.

Microscopic examination

Exactly 5 ml of each urine sample was taken in a clean sterile centrifuge tube and centrifuged at 3000 rpm for 5 minutes. The supernatant was discarded. The sediment was then examined under high power magnification for the presence of pus, red blood cells, epithelial cells, casts, crystals, and yeast cells.

Gram staining technique

Gram staining technique is a differential staining used to classify and categorize bacteria in specimens or cultures by their Gram reactions (Gram positives or Gram negatives) and morphology (rods, cocci, vibrios, spirilla and spirochaetes. The test was carried out using the procedure of Gram (1884). Smears were made from pure colonies after overnight growth on grease free slides. These were air dried and covered with crystal violet stain for one minute and rinsed with clean water, it was then covered with lugos iodine for one minute and rinsed. The smear was decolorized with acetone-alcohol for thirty seconds and then counterstained with neutral red for two minutes, rinsed and air dried. The stained smears were examined microscopically under oil immersion objective (100×) (Gram, 1884).

Pure culture for identification

Before performing biochemical and other tests each of the organisms was isolated in pure form. Gram staining of an isolated colony was done from primary culture. For gram-negative organism, a speck of single isolated colony from Cystine Lactose Electrolyte Deficient (CLED) agar was transferred into the nutrient broth and incubated at 37ºC for 4 hours. It was then sub cultured on dried nutrient agar plate and incubated at 37ºC for 18-24 hours. Thus, obtained overnight incubated culture of organism on nutrient agar was used to perform identification with Vitek 2 compact automated system.

Microbial identification

Before performing biochemical and other tests each of the organisms was isolated in pure form. Gram staining of an isolated colony was done from primary culture. For gram-negative organisms, a speck of a single isolated colony from Cystine Lactose Electrolyte Deficient (CLED) agar was transferred into the nutrient broth and incubated at 37ºC for 24 hours. It was then sub-cultured on a dried nutrient agar plate and incubated at 37ºC for 18-24 hours. Thus, overnight incubated culture of organism on nutrient agar was used to perform identification with Vitek 2 compact automated system.

Antimicrobial susceptibility

After Gram staining, appropriate cards were selected based on whether the organism is Gram-positive or Gram-negative. The cards were allowed to attained room temperature before package liners were opened. Two tubes were labeled one was used for identification and the other tube was used for antimicrobial susceptibility test. Sterile saline (3 ml) was placed in the first test tube and a pure colony was collected and transferred into the test tube and mixed to obtained bacteria suspension. The suspension was compared with 0.5 McFarland standards. Turbid suspensions beyond the standard were discarded and those that matched the 0.5 McFarland standards were used for the study. About 0.5 ml of an aliquot of the suspension was micro pipetted and transferred to first test tube that already contained 3 ml saline. This was mixed to obtain uniform suspension and was used for identification. Another 0.5 ml of the same preparation was collected and transferred to another test tube that had 3 ml saline and mixed for uniformity. This was used for antimicrobial susceptibility test. The tubes were placed in the cassette and loaded into the Vitek 2 compact automated system for identification and susceptibility test.

III. RESULTS

Sociodemographic characteristics

Participants were within the age range targeted 16-45 years with a mean age of 2.53 (± 1.21 SD) years. The highest number of the study participants 35 (22.7%) were in the age range of 16-20 years. More than half of the participants 138 (89.6%) had gravidity in the range of 1 – 3 times (table 1). History of miscarriages and urinary tract infection (UTI) were found in 34 (22.1%) and 148 (96.1%) of study participants respectively. Only small proportion of the participants 32 (20.8%) attained tertiary education

Prevalence of urinary tract infection

One hundred and fifty-four (154) urine samples were collected and analyzed during this study. Forty-three (43) showed growths which accounted for urinary tract infection's prevalence of 27.9% (figure 1).

Prevalence of bacterial isolates

More than half (56%) of the urine samples that showed growths were revealed to have Gram-negative microorganisms (figure 2). Twenty-four (24) Gram-negative isolates were identified in the samples analyzed. Escherichia coli was the most prevalent 12 (50%) Gram-negative microorganism identified among the isolates (table 2).

Table 1: Sociodemographic characteristics of study participants

Variables	Frequency	Percentage (%)
Age		
16 – 20	35	22.7
21 – 25	11	7.1
26 – 30	28	18.2
31 – 35	31	20.1
36 – 40	21	13.6
41 – 45	28	18.2

Educational status		
Illiterate	26	16.9
Primary	11	7.1
Secondary	85	55.2
Tertiary	32	20.8
Gravidity		
1 – 3	138	89.6
4 – 6	16	10.4
Miscarriages		
Yes	34	22.1
No	120	77.9
Symptoms of urinary tract infection (UTI)		
Yes	148	96.1
No	6	3.9

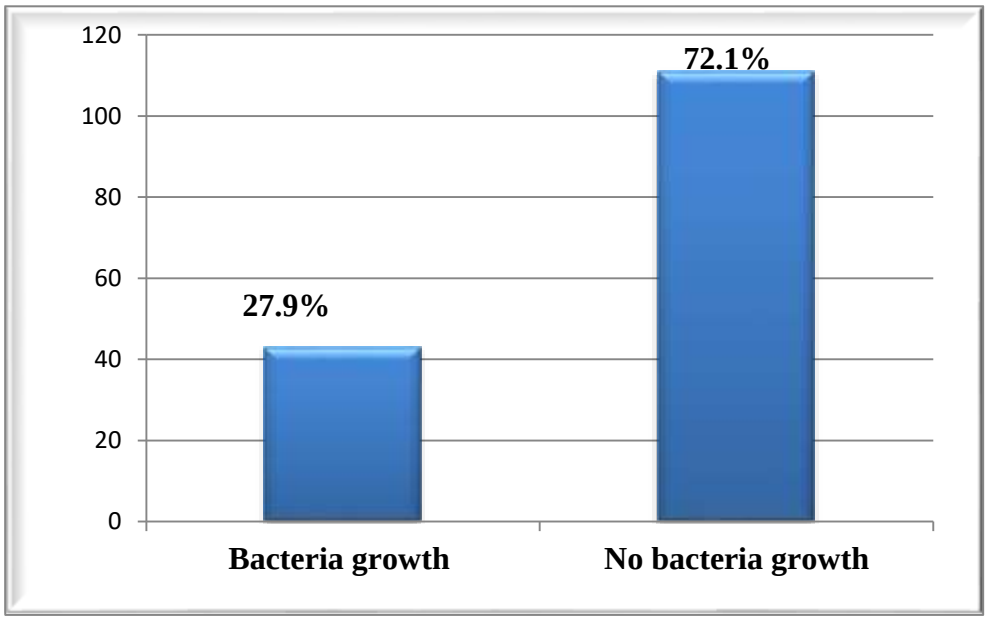

Figure 1: Samples with bacteria growth and non-growth

Table 2: Gram-negative bacteria isolated from urine samples collected from pregnant women

Gram-negative organisms isolated	Frequency	Percentage (%)
Escherichia coli	12	50

Pseudomonas aeruginosa	4	16.7
Klebsiella pneumoniae	3	12.5
Acinetobacter baumanni	3	12.5
Proteus mirabilis	2	8.33

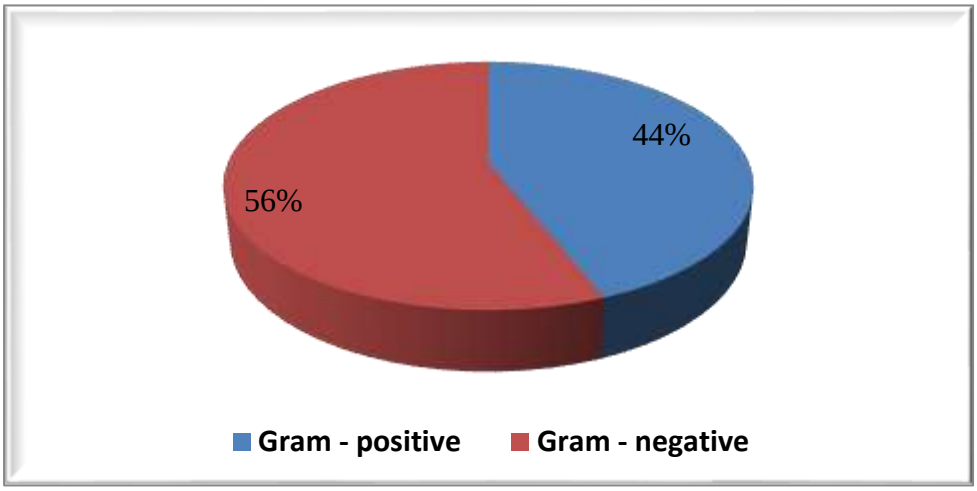

Figure 2: Category of pathogens isolated from urine samples

Bacterial isolates and their susceptibility

Among the *Escherichia coli* (*E. coli*) isolates, 91.7% were resistant to ampicillin and 66.7% were resistant to trimethoprim/sulfamethoxazole (table 3). *E. coli* was highly susceptible to gentamicin (75%) and ciprofloxacin (75%) and ceftazidine (83.3%). *Pseudomonas aeruginosa* was completely (100%) susceptible to ciprofloxacin but 75% intermediate resistant to ampicillin**.** On the other hand, 75.0% of *P. aeruginosa* were resistance to azithromycin. All (100%) of the *Proteus mirabilis* were resistant to ampicillin and augmentin. Regarding *K. pneumonia*, 66.7% resistant to Ampicillin, Ceftriaxone and Nitrofurantoin.

All (100%) of *Acinetobacter baumanni*, were susceptible to Cefotaxime, Ceftriaxone, Cefepime, Ceftazidine and Ciprofloxacin.

Table 3: Antimicrobial susceptibility patterns of the isolates

Bacterial Isolate	Total	Pattern	Antimicrobial Susceptibility Pattern										
			AMP	AUG	CTX	CAZ	CRO	CP	ATH	NI	GM	CIP	TS
			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
E. coli	12	S	0 (0)	2 (16.7)	8 (66.7	10 (83.3)	9 (75.0)	7 (58.3)	7 (58.3)	5 (41.7)	9 (75.0)	9 (75.0)	2 (16.7)
		I	1 (8.)	5 (41.7)	2 (16.7)	0 (0)	0 (0)	2 (16.7)	1 (8.3)	3 (25.0)	0 (0)	2 (16.7)	2 (16.7)
		R	11 (91.7)	5 (41.7)	2 (16.7)	2 (16.7)	3 (25.0)	3 (25.0)	4 (33.3)	4 (33.3)	3 (25.0)	1 (8.3)	8 (66.7)
P. aeruginosa	4	S	1 (25.0)	1 (25.0)	2 (50.0)	2 (50.0)	2 (50.0)	2 (50.0)	0 (0)	2 (50.0)	1 (25.0)	4 (100.0)	1 (25.0)
		I	3 (75.0)	1 (25.0)	1 (25.0)	0 (0)	0 (0)	1 (25.0)	1 (25.0)	0 (0)	1 (25.0)	0 (0)	1 (25.0)
		R	0 (0)	2 (50.0)	1 (25.0)	2 (50.0)	2 (50.0)	1 (25.0)	3 (75.0)	2 (50.0)	2 (50.0)	0 (0)	2 (50.0)
K. pneumoniae	3	S	1 (33.3)	3 (100.0)	2 (66.7)	1 (33.3)	1 (33.3)	0 (0)	0 (0)	1 (33.3)	1 (33.3)	3 (100.0)	1 (33.3)
		I	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)	1 (33.3)
		R	2 (66.7)	0 (0)	1 (33.3)	1 (33.3)	2 (66.7)	3 (100.)	3 (100.0)	2 (66.7)	1 (33.3)	0 (0)	1 (33.3)
A. baumanni	3	S	1 (33.3)	1 (33.3)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	2 (66.7)	2 (66.7)	2 (66.7)	3 (100.0)	2 (66.7)
		I	1 (33.3)	2 (66.7	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)	1 (33.3)	1 (33.3)	0 (0)	0 (0)
		R	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)
P. mirabilis	2	S	0 (0)	0 (0)	1 (50.0)	1 (50.0)	2 (100.0)	2 (100.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	0 (0)
		I	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)
		R	2 (100.0)	2 (100.0)	1 (50.)	1 (50.0)	0 (0)	0 (0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)	1 (50.0)

AMP = Ampicillin CAZ = Ceftazidine ATH = Azithromycin CIP = Ciprofloxacin

AUG = Augmentin CRO = Ceftriaxone NI = Nitrofurantoin TS = Trimethoprim/

Sulfamethoxazole CTX = Cefotaxime CP = Cefepime GM = Gentamicin

DISCUSSION

This study assessed the prevalence and susceptibility patterns of Gram-negative bacteria isolated from urine samples of pregnant women who visited Princess Christian Maternity Hospital (PCMH), Freetown, Sierra Leone. A total of 154 urine samples were collected from pregnant women aged 16-45 years. According to this study, 16.9% of respondents had no formal education. This is comparable to 15.8% proportion of non-formal education among respondents in a study that was reported in Zakho City, Kurdistan Region, and Iraq (19). In this study, the obstetric data showed that 89.6% had gravidity of 1-3 times. This finding is similar to a study conducted in Eastern Ethiopia, where 79% reported having gravidity of 1-3 times (15). This study also reported 96.1% history of urinary tract infection occurrence among study participants which is in contrast with a 27% history of UTIs reported study that was conducted in Eastern Ethiopia (15). The overall prevalence of urinary tract infection found in pregnant women in this study was 27.9%. This is higher than those the 10.4% prevalence reported in Gondar, Ethiopia, 15.8% prevalence reported in Kano, Northern Nigeria and the 14.6% prevalence reported in Mwanza, Tanzania (3) but lower than the 32% prevalence El Menoufia Governorate and the 35% prevalence reported in South-West Uganda (18, 33). In this study, highest prevalence (37.2%) of UTI was reported among 21-25 years age range. This is in contrast with a study conducted in Northern Nigeria which 31-40 years as the age range that recorded the highest (45.8%) prevalence of UTI (25).

E. coli was the most common Gram-negative isolate found in this study as it accounted for 50% of the total microorganisms found. This is higher than the 38.1% prevalence found in a study conducted in Samawah, Iraq and the 47.5% prevalence reported in Gander, Northwest Ethiopia (3, 23).

Regarding the level of resistance exhibited by specific pathogens, *E. coli* was highly resistant to ampicillin (91.7%) and trimethoprim/sulfamethoxazole (66.7%). The finding of this study is consistent with study conducted Goba and Sinana Woredas, Bale Zone, Southeast Ethiopia (37). It is also very similar to research conducted in Northwest Ethiopia in which all (100%) *E. coli* isolates were resistant to ampicillin (3). However, majority of the *E. coli* isolates exhibited very high susceptibility to gentamicin (75%), ciprofloxacin (75%) and ceftazidine (83.3%). This is similar to a study conducted in Zakho City, Kurdistan Region, and Iraq, where *E. coli* isolates from the samples were extremely sensitive to gentamicin (82.4%) (19).

All (100%) of *K. pneumoniae* isolated in this study were susceptible to Augmentin and ciprofloxacin and moderately susceptible to Cefotaxime (66.7%). This is similar to a study that was conducted in Kaduna, Nigeria in which K. pneumonia isolates (100%) were found to be highly susceptible augmentin, ciprofloxacin and 88.24% susceptible amoxicillin (2). It was moderately resistant to ampicillin (66.7%) and nitrofurantoin (66.7%).

The *Pseudomonas aeruginosa* (*P. aeruginosa*) isolates were sensitive to ciprofloxacin (100%) and ampicillin (75%). This is similar to a study reported in Kaduna in which the isolates of *P. aeruginosa* were highly sensitive to ciprofloxacin (2). High resistance was observed cefepime (75%) whilst moderate resistance (50%) was recorded for augmentin, ceftazidine, ceftriaxone, nitrofurantoin, gentamicin, and trimethoprim and sulfamethoxazole. In another study conducted in Nepal, gentamicin was observed to highly effective against *p. aeruginosa* (21).

In this study, all (100%) of the isolates of *Acinetobacter baumanni* were susceptible to ceftazidine, ciprofloxacin and ceftriaxone. This is contrary to studies conducted in Baghdad where 81% of the isolates were resistant to ciprofloxacin and Southwest Nigeria which reported 100% resistance to ciprofloxacin and ceftazidine (26. 38).

All (100%) isolates of *Proteus mirabilis* were susceptible to ceftriaxone and cefepime and completely resistant to ampicillin and augmentin. This is similar to a study conducted in south-west Uganda which reported 100% susceptibility of this isolate to ceftriaxone and 85.7% resistance to ampicillin (18).

IV. CONCLUSION

In this study, the overall prevalence of urinary tract infection among pregnant women was 27.9%. The highest prevalence was found in the age range of 16-20 years. The dominant isolate identified in this study was *E. coli*. All the isolates were resistant to ampicillin. *E. coli* exhibited high susceptibility to gentamicin and ciprofloxacin. *P. aeruginosa* had very high susceptibility to ciprofloxacin. *K. pneumoniae* also exhibited outstanding susceptibility to augmentin and ciprofloxacin.

Consent:

Written informed consent was sought for and obtained from the participants before they were included in this study.

Ethical approval:

The Institutional Review Board of the College of Medicine and Allied Health Sciences granted approval for the study to be conducted.

Source of funding:

Authors received no external funding for the research

Conflict of interest:

The authors declared that they have no conflict of interest.

REFERENCE

[1] Abraham, S.N., Shin, J. and Malaviya, R. (2001) 'Type 1 Fimbriated *Escherichia coli*– Mast Cell Interactions in Cystitis', *The Journal of Infectious Diseases*, 183(s1), pp. S51–S55. Available at: https://doi.org/10.1086/318853.

[2] Abdulfatai, A., Olonitola, O. S., Inabo, H. I., & Yakubu, S. E. (2023). Antibiotic susceptibility profile of Pseudomonas aeruginosa isolated from clinical specimens in Kaduna, Nigeria. African Journal of Clinical and Experimental Microbiology, 24(2), 145-152. DOI: 10.4314/ajcem.v24i2.5

[3] Alemu, A., Moges, F., Shiferaw, Y., Tafess, K., Kassu, A., Anagaw, B., & Agegn, A. (2012). Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women at University of Gondar Teaching Hospital, Northwest Ethiopia. BMC Research Notes, 5(1), 197. DOI: 10.1186/1756-0500-5-197

[4] Al Mijalli, S.H. (2017) 'Bacterial Uropathogens in Urinary Tract Infection and Antibiotic Susceptibility Pattern in Riyadh Hospital, Saudi Arabia', *Cellular & Molecular Medicine: Open access*, 03(01). Available at: https://doi.org/10.21767/2573-5365.100028.

[5] Ali, A.H., Reda, D.Y. and Ormago, M.D. (2021) 'Prevalence and Antimicrobial Susceptibility Pattern of Urinary Tract Infection among Pregnant Women Attending Hargeisa Group Hospital, Hargeisa, Somaliland'. Available at: https://doi.org/10.21203/rs.3.rs-957306/v1.

[6] Ali, M.A. *et al.* (2019) 'Prevalence of urinary tract infection and antibiotic resistance pattern in pregnant women, Najran region, Saudi Arabia', *African Journal of Microbiology Research*, 13(26), pp. 407–413. Available at: https://doi.org/10.5897/AJMR2019.9084.

[7] Amiri, M. *et al.* (2015) 'Prevalence of Urinary Tract Infection Among Pregnant Women and its Complications in Their Newborns During the Birth in the Hospitals of Dezful City, Iran, 2012 - 2013', *Iranian Red Crescent Medical Journal*, 17(8). Available at: https://doi.org/10.5812/ircmj.26946.

[8] Archabald, K.L. *et al.* (2009) 'Impact of trimester on morbidity of acute pyelonephritis in pregnancy', *American Journal of Obstetrics and Gynecology*, 201(4), p. 406.e1-406.e4. Available at: https://doi.org/10.1016/j.ajog.2009.06.067.

[9] Babic, M., Hujer, A. and Bonomo, R. (2006) 'What's new in antibiotic resistance? Focus on beta-lactamases', *Drug Resistance Updates*, 9(3), pp. 142–156. Available at: https://doi.org/10.1016/j.drup.2006.05.005.

[10] Bacak, S.J. *et al.* (2005) 'Pregnancy-associated hospitalizations in the United States, 1999-2000', *American Journal of Obstetrics and Gynecology*, 192(2), pp. 592–597. Available at: https://doi.org/10.1016/j.ajog.2004.10.638.

[11] Bennett, J.E., Dolin, R. and Blaser, M.J. (eds) (2015) *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. Eighth edition. Philadelphia, PA: Elsevier/Saunders.

[12] Beyene, G. and Tsegaye, W. (2011) 'Bacterial Uropathogens in Urinary Tract Infection and Antibiotic Susceptibility Pattern in Jimma University Specialized Hospital, Southwest Ethiopia', *Ethiopian Journal of Health Sciences*, 21(2), pp. 141–146. Available at: https://doi.org/10.4314/ejhs.v21i2.69055.

[13] Campbell, J.S.O. *et al.* (2022) 'Culture Requests and Multi-Drug Resistance among Suspected Urinary Tract Infections in Two Tertiary Hospitals in Freetown, Sierra Leone (2017–21): A Cross-Sectional Study', *International Journal of Environmental Research and Public Health*, 19(8), p. 4865. Available at: https://doi.org/10.3390/ijerph19084865.

[14] Cheesbrough, M. (2005) *District laboratory practice in tropical countries*. 2nd ed. Cambridge ; New York: Cambridge University Press (Tropical health technology).

[15] Ejerssa, A.W., Gadisa, D.A. and Orjino, T.A. (2021) 'Prevalence of bacterial uropathogens and their antimicrobial susceptibility patterns among pregnant women in Eastern Ethiopia: hospital-based cross-sectional study', *BMC Women's Health*, 21(1), p. 291. Available at: https://doi.org/10.1186/s12905-021-01439-6.

[16] Glaser, A.P. and Schaeffer, A.J. (2015) 'Urinary Tract Infection and Bacteriuria in Pregnancy', *Urologic Clinics of North America*, 42(4), pp. 547–560. Available at: https://doi.org/10.1016/j.ucl.2015.05.004.

[17] Hugo, W.B. (ed.) (1980) *Pharmaceutical microbiology*. 2. ed. Oxford: Blackwell.

[18] Johnson, O., Anywaine, Z., & Achan, B. (2021). High antibiotic resistance profiles of Pseudomonas aeruginosa isolates from tertiary hospitals in Southwestern Uganda. Infection and Drug Resistance, 14, 4563-4572.DOI: 10.2147/IDR.S330 490

[19] Mohammed IJ, Naqid IA, Süer HK. Prevalence, Antimicrobial Susceptibility Profile, and the Associated Risk Factors of Uropathogenic E. coli among Pregnant Women in Zakho City, Kurdistan Region, Iraq. Women. Health. Bull. 2022;9(1):34-41. doi: 10.30476/WHB.2022.93607.1154

[20] Kass, E.H. (2002) 'Asymptomatic infections of the urinary tract', *Journal of Urology*, 167(2 Part 2), pp. 1016–1020. Available at: https://doi.org/10.1016/S0022-5347(02)80328-7.

[21] Khatri, S., Pant, N. D., Bhandari, R., & Shrestha, K. L. (2012). Antimicrobial susceptibility pattern of Pseudomonas aeruginosa isolated from patients attending a tertiary care hospital in Kathmandu, Nepal. International Journal of Microbiology, Article ID 456253.DOI: 10.1155/2012/456253

[22] Livermore, D.M. (2008) 'Defining an extended-spectrum β-lactamase', *Clinical Microbiology and Infection*, 14, pp. 3–10. Available at: https://doi.org/10.1111/j.1469-0691.2007.01857.x.

[23] Nahab, W. B., Al-Mayah, Q. S., & Al-Khafaji, N. S. (2021). Antimicrobial resistance patterns of Pseudomonas aeruginosa isolated from clinical specimens in Samawah, Iraq. Journal of Global Antimicrobial Resistance, 25, 314-319. DOI: 10.1016/j.jgar.2021.03.024

[24] Matuszkiewicz-Rowińska, J., Małyszko, J. and Wieliczko, M. (2015) 'State of the art paper Urinary tract infections in pregnancy: old and new unresolved diagnostic and therapeutic problems', *Archives of Medical Science*, 1, pp. 67–77. Available at: https://doi.org/10.5114/aoms.2013.39202.

[25] Oko, O.J., Okoro, U.C. and Anyiam, P.N. (2017)Antibiotics Susceptibility Study of Uropathogens Isolated from Asymptomatic Pregnant Women Attending a Tertiary Maternity Clinic in Northern Nigeria *Journal of Chemical and Alternative Medical Research (JOCAMR)*, 2(3), pp. 1-9 32159.

[26] Oladapo, O. T., Adesanya, T. A., & Adeoye, A. O. (2014). Antimicrobial resistance pattern of Acinetobacter baumannii isolates from clinical specimens in a tertiary hospital in Southwest Nigeria. African Journal of Clinical and Experimental Microbiology, 15(3), 128-133.

[27] Paterson, D.L. and Bonomo, R.A. (2005) 'Extended-Spectrum β-Lactamases: a Clinical Update', *Clinical Microbiology Reviews*, 18(4), pp. 657–686. Available at: https://doi.org/10.1128/CMR.18.4.657-686.2005.

[28] Pitout, J.D. and Laupland, K.B. (2008) 'Extended-spectrum β-lactamase-producing Enterobacteriaceae: an emerging public-health concern', *The Lancet Infectious Diseases*, 8(3), pp. 159–166. Available at: https://doi.org/10.1016/S1473-3099(08)70041-0.

[29] Rajaratnam, A. (2014) 'Diagnosis of Asymptomatic Bacteriuria and Associated Risk Factors Among Pregnant Women in Mangalore, Karnataka, India', *Journal of Clinical and diagnostic research*. Available at: https://doi.org/10.7860/JCDR/2014/8537.4842.

[30] Ronald, A. (2002) 'The etiology of urinary tract infection: traditional and emerging pathogens', *The American Journal of Medicine*, 113(1), pp. 14–19. Available at: https://doi.org/10.1016/S0002-9343(02)01055-0.

[31] Schnarr, J. and Smaill, F. (2008) 'Asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy', *European Journal of Clinical Investigation*, 38(s2), pp. 50–57. Available at: https://doi.org/10.1111/j.1365-2362.2008.02009.x.

[32] Sester, U. and Fünfstück, R. (2011) 'Diagnostik und Therapie der unkomplizierten Harnwegsinfektionen', *Nieren- und Hochdruckkrankheiten*, 40(01), p. 1. Available at: https://doi.org/10.5414/NHP40001.

[33] Shaheen, Z., Al-Charrakh, A. H., & Al-Khafaji, J. K. (2016). Prevalence and antimicrobial resistance patterns of Pseudomonas aeruginosa isolates from clinical specimens in Al-Najaf Governorate, Iraq. Journal of Pharmaceutical Sciences and Research, *8*(7), 674-678.

[34] Shirishkumar, P., Pankajkumar, P.T., Mala, S., Javadekar, T.P. and Chaudhari, V.P. (2012) 'Urinary Tract Infections (UTI) among Patients at G.G. Hospital and Medical College, Jamnagar', National Journal of Community Medicine, 3, pp. 138-141. Available at: scirp.org.

[35] Souza, R.B., Trevisol, D.J. and Schuelter-Trevisol, F. (2015) 'Bacterial sensitivity to fosfomycin in pregnant women with urinary infection', *The Brazilian Journal of Infectious Diseases*, 19(3), pp. 319–323. Available at: https://doi.org/10.1016/j.bjid.2014.12.009.

[36] Stamm, W.E. *et al.* (1980) 'Causes of the Acute Urethral Syndrome in Women', *New England Journal of Medicine*, 303(8), pp. 409–415. Available at: https://doi.org/10.1056/NEJM198008213030801.

[37] Taye, S. *et al.* (2018) 'Bacterial profile, antibiotic susceptibility pattern and associated factors among pregnant women with Urinary Tract Infection in Goba and Sinana Woredas, Bale Zone, Southeast Ethiopia', *BMC Research Notes*, 11(1), p. 799. Available at: https://doi.org/10.1186/s13104-018-3910-8.

[38] Tektook, N. K., Al-Kadmy, I. M., & Khitir, S. M. (2016). High prevalence of multidrug-resistant Acinetobacter baumannii in Baghdad hospitals. Journal of Global Antimicrobial Resistance, *7*, 60-62. DOI: 10.1016/j.jgar.2016.07.011

[39] Teppa, R.J. and Roberts, J.M. (2005) 'The Uriscreen Test to Detect Significant A symptomatic Bacteriuria During Pregnancy', *Journal of the Society for Gynecologic Investigation*, 12(1), pp. 50–53. Available at: https://doi.org/10.1016/j.jsgi.2004.07.007.

[40] Thomas, A.A. *et al.* (2010) 'Urologic Emergencies in Pregnancy', *Urology*, 76(2), pp. 453–460. Available at: https://doi.org/10.1016/j.urology.2010.01.047.

[41] Tomasz A. Leski1*, Chris R. Taitt1 , Umaru Bangura2,4, Michael G. Stockelman1 , Rashid Ansumana2,3,4, William H. Cooper III5 , David A. Stenger1 and Gary J. Vora1. High prevalence of multidrug resistant Enterobacteriaceae isolated from outpatient urine samples but not the hospital environment in Bo, Sierra Leon. BMC Infectious Diseases (2016) 16:167 DOI 10.1186/s12879-016-14951

[42] Trunkey, D., Holcroft, J. and Carpenter, M.A. (1976) 'Monitoring resuscitation of primates from hemorrhagic and septic shock', *JACEP*, 5(4), pp. 249–252. Available at: https://doi.org/10.1016/s0361-1124(76)80002-0.

[43] Turner, P.J. (2005) 'Extended-Spectrum β-Lactamases', *Clinical Infectious Diseases*, 41(s4), pp. S273–S275. Available at: https://doi.org/10.1086/430789.

[44] Vasudevan, R. (2014) 'Urinary Tract Infection: An Overview of the Infection and the Associated Risk Factors', *Journal of Microbiology & Experimentation*, 1(2). Available at: https://doi.org/10.15406/jmen.2014.01.00008.

[45] Watts, R.E. *et al.* (2010) '*Escherichia coli* Isolates Causing Asymptomatic Bacteriuria in Catheterized and Noncatheterized Individuals Possess Similar Virulence Properties', *Journal of Clinical Microbiology*, 48(7), pp. 2449–2458. Available at: https://doi.org/10.1128/JCM.01611-Weiss, M.D. *et al.* (2006) 'Sleep Hygiene and Melatonin Treatment for Children and Adolescents With ADHD and Initial Insomnia', *Journal of the American Academy of Child & Adolescent Psychiatry*, 45(5), pp. 512–519. Available at: https://doi.org/10.1097/01.

[46] Weizer, M. (1997) 'Pharmacotherapy: A Pathophysiologic Approach, Third Edition', *American Journal of Health-System Pharmacy*, 54(14), pp. 1668–1669. Available at: https://doi.org/10.1093/ajhp/54.14.1668.

[47] Wiesmann, U.N., DiDonato, S. and Herschkowitz, N.N. (1975a) 'Effect of chloroquine on cultured fibroblasts: release of lysosomal hydrolases and inhibition of their uptake', *Biochemical and Biophysical Research Communications*, 66(4), pp. 1338–1343. Available at: https://doi.org/10.1016/0006-291x(75)90506-9.

[48] Wiesmann, U.N., DiDonato, S. and Herschkowitz, N.N. (1975b) 'Effect of chloroquine on cultured fibroblasts: release of lysosomal hydrolases and inhibition of their uptake', *Biochemical and Biophysical Research Communications*, 66(4), pp. 1338–1343. Available at: https://doi.org/10.1016/0006-291x(75)90506-9.

[49] Wing, D.A., Fassett, M.J. and Getahun, D. (2014) 'Acute pyelonephritis in pregnancy: an 18-year retrospective analysis', *American Journal of Obstetrics and Gynecology*, 210(3), p. 219.e1-219.e6. Available at: https://doi.org/10.1016/j.ajog.2013.10.006.

[50] Wolfensberger, A. *et al.* (2013) 'Change of Antibiotic Susceptibility Testing Guidelines from CLSI to EUCAST: Influence on Cumulative Hospital Antibiograms', *PLoS ONE*. Edited by V. Chaturvedi, 8(11), p. e79130. Available at: https://doi.org/10.1371/journal.pone.0079130.