Community-Acquired Urinary Tract Infections: Epidemiology, Etiology, and β-Lactam Resistance

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Abstract: Urinary tract infection is considered a serious public health problem. One hundred and fifty patients were included in the present study and suspected to have community-acquired urinary tract infections depending on crucial indicators. Out of 150 urine cultures, 69.3% were confirmed as urinary tract infection with significant growth and 30.7% was sterile pyuria. Community-acquired urinary tract infections showed high incidence in females (44.1%), followed by kids (32.3%; 19.6% girls and 12.7% boys), and males (23.5%) with differences regarding age groups. Gram staining indicated that 63.2% of total isolated uropathogens were gram-negative isolates, and 36.7% were gram-positive isolates. The identification of 106 bacterial isolates led to the presence of 16 distinct species belonging to 12 genera including Escherichia coli (40.56%), Enterococcus spp. (18.86%), Streptococcus spp. (10.37%), Klebsiella spp. (8.49%), Citrobacter koseri (6.60%), Corynebacterium urealyticum (4.71%), Proteus mirabilis (2.83%), Enterobacter intermedius (1.88%), Pseudomonas aeruginosa (1.88%), Staphylococcus saprophyticus (1.88%), Serratia fonticola (0.94%) and Bacillus cereus (0.94%). Phenotypic detection of ESBL revealed that 35.8% of total isolated gram-negative uropathogens were ESBL-producers. Escherichia coli comprised a serious threat as the most dominant ESBL-producing organism representing 66.7% of total ESBL-producing bacteria detected followed by Klebsiella pneumonia (12.5%), Citrobacter koseri (8.3%), Serratia fonticola (4.1%), Proteus mirabilis (4.1%), and Pseudomonas aeruginosa (4.1%).

Keywords: Urinary Tract Infection, CA-UTIs, β-lactam, Enterobacteriaceae, ESBL.

1. Introduction

Urinary tract infection (UTI) stands as a serious public health problem with substantial economic and medical burdens. Its global incidence exceeds 250 million cases [1]. In addition, UTI is a noteworthy cause of morbidity and mortality with a wide spectrum of severity that ranges from harmless asymptomatic bacteriuria and self-curing cystitis to severe pyelonephritis with life-threatening sepsis.

The term "UTI" is referred to an inflammatory response of the urothelium to the invasion of microorganisms, called uropathogens [2]. Although several different organisms can cause UTIs, including fungi (Candida albicans), viruses (Herpes hominis), protozoa (Trichomonas vaginalis), and helminths (Schistosoma haematobium), bacteria are the major causative agents of UTIs [3]. Escherichia coli is the most common gram-negative urinary tract infection followed by Klebsiella sp., Proteus sp., and other Enterobacteriaceae members in addition to gram-positive bacteria such as Enterococcus and Staphylococcus spp. [4-6].

Classification of UTIs can be performed according to the location and the circumstances of infection to community-acquired urinary tract infection (CA-UTI) and healthcare-associated urinary tract infection (HA-UTI) [2, 7]. CA-UTI is identified as an infection of the urinary tract that occurs in the community or within less than 48 hours of hospital admission and was not incubating at the time of hospital admission. Clinically, uncomplicated CA-UTI is considered the second most predominant diagnosed infection in the community [7] which preferably colonizes the bladder and causes cystitis. However, bacteria may ascend through the ureters to the kidneys causing more severe complications such as pyelonephritis [8].

Current treatment of UTIs usually depends on empirical therapy, without performing a urine culture and susceptibility testing [9, 10]. As in many community-acquired infections, uropathogens that cause CA-UTIs, have developed resistance to many antimicrobial agents [11]. The drug-resistant strains initially appeared in hospitals, where most antibiotics were being used. Soon after, the community became similarly encumbered with drug-resistant organisms. The frequency of antimicrobial resistance in the community has extended the resistance problem beyond the boundaries of the hospital. Resistant strains can be traced from the community to the hospital and vice versa, indicating that antimicrobial resistance is no longer localized [12].

Resistance of E. coli and other uropathogens to β-lactams, such as penicillins and cephalosporins, has continued to increase in the past decade. Availability and misuse of antibiotics via patients without medical surveillance are the major factors implied in drug resistance. As a consequence, β-lactams are no longer recommended for empirical therapy of UTI [13].

Extended spectrum β-lactamases (ESBLs) are enzymes that can pave resistance to β-lactam antibiotics, new antibiotic
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2. Materials and methods

2.1. Sampling

2.1.1. Patients

This study was conducted on patients presented to three laboratories in the Sohag government from June 2021 to December 2021 and suspected to have community-acquired urinary tract infections. All patients were asked to perform a urine analysis according to the urology specialist’s recommendations. A total of 150 patients (50 females, 50 males, and 50 kids; 25 girls and 25 boys) were included in this study. The patients had at least one of the common symptoms of UTI (dysuria, frequency, urgency, and/or suprapubic pain) as a primitive indicator of the infection.

2.1.2. Samples Collection

Fresh urine samples were collected in sterilized plastic cups. In the case of kids who were not capable of giving the samples, sterilized urine collection bags were used. Immediate processing of the samples after collection was done to avoid the contamination. Samples that were difficult to transport to the laboratory quickly, were refrigerated at 4 °C for a few hours.

2.1.3. Examination of Urine Samples

Macroscopic examination of urine was performed via a rapid dipstick (Combur 10 Test) to detect the presence of both nitrite and leukocyte esterase in the urine as primitive indicators of the infection. Microscopic examination of centrifuged urine was performed to detect the presence of pyuria by high power field (pus cells are ≥5 /HPF).

2.2. Isolation

Urine samples were streaked on cysteine lactose electrolyte-deficient agar, (C.L.E.D. agar w/bromothymol blue M792 – HiMedia laboratories, India), a differential nonselective medium, recommended for isolation and identification of urine pathogens. The C.L.E.D plates were incubated aerobically at 35 ± 2 °C for 24 hrs. Separate single colonies were picked up, streaked again on C.L.E.D agar, and incubated aerobically at 35 ± 2 °C for 24 hours to ensure having purified bacterial isolates for further investigations.

2.3. Identification of Bacterial Isolates

Examination of Colony morphology, Gram Staining, and Biochemical tests were performed on each isolate. The isolates were identified according to the classification schemes, described in Bergey’s Manual of Determinative Bacteriology [19]. Gram-negative bacteria isolated were identified via biochemical tests including glucose fermentation, triple sugar iron, H₂S production, oxidase, urease, indole, citrate utilization, methyl red, Voges Proskauer, and motility tests. Gram-positive bacterial isolates were identified via biochemical tests including mannitol fermentation, catalase, hemolysis, starch hydrolysis, and bile aesculin tests.

2.4. Antibiotic Sensitivity Testing

The Kirby-Bauer disk diffusion susceptibility test [20] was performed based on the criteria described by Clinical Laboratory Standards Institute (CLSI) published documents [21, 22]. A 24-hour bacterial growth of each bacterial isolate was adjusted to a 0.5 McFarland standard and inoculated to the Mueller-Hinton agar plate. Commercially available β-lactam antibiotic (Oxoid, UK) disks were used: ceftazidime (30 μg), cefotaxime (30 μg), ceftriaxone (30 μg), aztreonam (30 μg), amoxicillin/clavulanate (20/10 μg), cefoperazone (75 μg) and cefoperazone/sulbactam (75 μg, 2:1). The plates were incubated at 35 ± 2 °C for 18-24 hrs. Phenotypic screening of ESBL-producing isolates was detected as recommended by CLSI. The expected inhibition zones for ESBL-producing isolates are (ceftazidime zone ≤22mm), (cefotaxime zone ≤27mm), (ceftriaxone zone ≤25mm), and (aztreonam zone ≤27mm). ESBL-producing bacterial isolate would show clear extension toward the disc containing clavulanate which indicates a synergistic effect [23] and/or an increase in inhibition zone diameter of ≥5 mm for cefoperazone / sulbactam than cefoperazone alone [24].

3. Results and Discussion

3.1. Sampling

3.1.1. Patients

It was generally noticed that the number of adult females who had symptoms and were suspected to have UTI was higher than the number in the case of adult males and kids. That could be acceptable because the structure of the urogenital system in women is different. The shorter distance of the urethral opening to the vagina and rectum, both of which harbor diverse bacterial populations, makes it easier for bacteria to ascend in the urinary tract. Neupane et al. have also noticed that the number of samples from females was higher than males [25].
3.1.2. Samples Collection

To avoid contamination, all urine samples collected in sterilized plastic cups and sterilized urine collection bags were immediately prepared for further investigations. According to this procedure, the urine cultures will show no contamination later. This procedure is preferred and agreed with a randomized controlled trial performed to study the effect of contamination on urine samples and cultures and recommended a clean-catch urine sample in sterilized urine collection cups/funnels to obtain a urine culture in symptomatic adults with suspected UTI [26].

3.1.3. Examination of Urine Samples

We suggested that a combination of symptom history, and positive nitrites and leukocyte esterase may raise the possibility of UTI indication. A study reported that the sensitivity of the leukocyte esterase test and the combined leukocyte esterase with nitrite test to predict a UTI were 63.6% and 66.7%, respectively [27].

Positive leukocyte esterase on a dipstick test has already reflected the presence of pus cells in urine. The presence of pus cells ≥5/HPF was considered as pyuria (Fig.1). However, a microscopic examination of centrifuged urine was performed to ensure that UTI was likely caused by bacteria. Trying to limit our research to bacterial infections, urine samples that showed the presence of any other causal agents such as ova of parasites, were excluded from the study. Rao et al. reported that pyuria with urine culture has a positive predictive value up to 68% [28].

3.2. Isolation

Urine culture was the gold standard to identify UTI in our study. Cultures were distinguished as significant, insignificant, and no growth. C.L.E.D. agar plates which appeared in yellow confirmed lactose fermentation and those with green color confirmed non-lactose fermentation (Fig.2).

Out of 150 urine samples streaked on C.L.E.D. agar, 104 (69.3%) were confirmed as UTI with significant growth including 102 (68%) cultures referred to bacteria as the causal agent and 2 cases had a fungal infection with Candida sp. Out of those 102 urine cultures with bacterial infection, 98 cultures were observed to have significant growth of one single organism, while 4 cultures had mixed growth of two organisms. The results reflected that a combination of symptom history, positive leukocyte esterase, positive nitrite, and microscopic examination for pyuria had a bacterial-UTI predictive value of 68% which is compatible with the previous studies [25, 28]. That is also totally agreed with Hassuna et al. study in which community-acquired UTI caused by uropathogenic bacteria represented 68.6% of samples in upper Egypt [29]. Another study performed to identify UTI demonstrated that CA-UTI represented 69.3% depending on pyuria and symptoms history [30].

In our study, it was concluded that 48 (32%) cases, including 43 cases had no growth at all (sterile pyuria), 3 cases with insignificant growth (<10 CFU/ml), and 2 cases had a fungal infection with Candida sp., all of which have probably received antibiotic courses without need depending on the presence of pyuria which may affect the body’s normal microbiota.

**Figure 1:** Microscopic examination of urine indicating pyuria.

**Figure 2:** Urine cultures on C.L.E.D. agar plates; (A) lactose-fermenter, (B) non-lactose-fermenter.

The cases of sterile pyuria may refer to several elucidations such as renal tract stones, a recently treated UTI, and receiving even a single dose of antibiotics. Drug intake such as nitrofurantoin is one of the common causes of sterile pyuria. Additionally, sterile pyuria can be a sign of intra-abdominal infection unrelated to UTI [31-33].

Accordingly, it is not preferred to depend only on pyuria to start antibiotic treatment. We assert that depending on more than one indicator is crucial to confirm a UTI caused by bacteria and decrease the prescription of multiple antibiotics that participate in the rise of drug-resistant bacteria. Cheng et al. agreed that pyuria alone does not provide adequate diagnostic accuracy to predict bacteriuria supporting the current guideline recommendation against antibiotic treatment based on urine analysis alone [34].

Furthermore, a high incidence of UTI was detected in females with a percentage of 44.1%, followed by kids (32.3%, including 19.6% girls and 12.7% boys), and males (23.5%) in the present study. Zubair et al. estimated that the frequency of UTIs was 12.06% in male and 87.94% in female [35]. In another study conducted on kids depending on symptoms and urine dipsticks, female kids had a greater incidence of UTI than male kids (11.8% and 8.9%, respectively) proved by urine cultures [28].

The high incidence of UTI in females refers to anatomical, behavioral, and physiological factors that evolve over a woman’s lifetime. The difference in structure of the urogenital
system indeed predisposes women to infection but also there are other risk factors.

In our study, it was observed that UTI showed the highest dominance in reproductive-aged women, particularly in (30-40 years old) age group (Fig. 3) which may refer to specific age-regarding reasons. That is compatible with Gopalakrishnan in his study on UTI among females of reproductive age revealing that 44% of females belonged to the 15-24 years age group followed by 36% in the 35-44 years age group and 20% in the 25-34 years age group [36].

In studies regarding age groups, it was observed that sexual intercourse and related hygiene practices are the most common risk factors of CA-UTI among adult healthy women as it promotes the migration of bacteria into the bladder [37-39].

Through our study, it was noticed that CA-UTI in females has moderate incidence over 40 years old age groups supposing that the incidence of CA-UTI in postmenopausal healthy women may be combined with anatomical and functional alteration.

After menopause, there is a significant reduction in estrogen secretion by the ovary, which is often associated with vaginal atrophy. Estrogens stimulate the proliferation of Lactobacillus in the vaginal epithelium, causing a reduction of vaginal pH (3.8-5) by producing hydrogen peroxide, thereby preventing vaginal colonization by Enterobacteriaceae [40]. Kirjavainen et al. confirmed the incidence of UTI in 22 disease-free women combined with an alteration in the vaginal microbiota [41].

In the present study, adult males have a low incidence of CA-UTI in general, representing 23.5% of total cases. Male cases with UTI showed no big differences among age groups however it was observed that UTI barely happened beneath the (20 years old) age group (Fig. 3), which was noteworthy. CA-UTIs in young men are very uncommon [42]. UTI has a higher incidence in elder men than younger because its incidence is often complicated and associated with invasion of the tissue in the prostate (acute bacterial prostatitis) or the kidney (pyelonephritis) [43].

An observational study was conducted to estimate the incidence of diagnosed UTI, in which it was observed that the incidence of clinically diagnosed UTI in men per 100 person-years at risk increased (2.81-3.05) in those aged 65-74, (5.90-6.13) in those aged 75-84, and (8.08-10.54) in those aged ≥85 [44].

In our study, kids came in the second rank after women in the presence of CA-UTI. Female-kids showed a high incidence of UTI as predicted which may refer to the reasons concerning the difference in urinary tract anatomy. It was observed that UTI cases under 10 years old were little higher in girls than boys which is reasonable and compatible with Leung et al. who confirmed that after one year of age, girls are much more likely than boys to develop UTI [45]. But overall, there was an equally significant increase in cases of both girls and boys in (the 10-12 years old) age group, the preadolescent age, representing 42.4% of total kids UTI cases (Fig. 4).

Our results agree with Badhan et al. in their study concerning UTI in children, which demonstrated that the most common age group was preteens (9-12 years old) in percent 52.1% [46]. Adolescence is the period during which there is a complex interaction among biological, psychological, and social factors so adolescents should have an increased awareness of themselves and their hygiene. Adolescents in the lower socio-economic groups may be more affected [47].

In a study estimating the hygiene practices among young adolescents in low- and middle-income countries, it was observed that the prevalence of never washing hands was 7.4% before eating, 5.9% after using the toilet, and 9.0% with soap which can transmit several pathogens [48].

### 3.3. Identification of Bacterial Isolates

The identification of 106 bacterial isolates depended on the morphological appearance of colonies on C.L.E.D. agar, gram staining, and particulate biochemical tests. Microscopic examination of each isolate confirmed the cells shape, arrangement, and gram staining result and indicated 67 (63.2%) gram-negative isolates and 39 (36.79%) gram-positive isolates. That is compatible with a study conducted on CA-UTIs in Egypt which revealed that gram-negative bacteria were more common than gram-positive representing 66% and 34% respectively [49]. Zhang et al. confirmed a compatible result that gram-negative bacteria represented 69% and gram-positive bacteria represented 31% in a study conducted on UTI-suffering renal transplant recipients [50].

The identification of 106 bacterial isolates led to the presence of 16 distinct species belonging to 12 genera. Escherichia coli was identified in 43 isolates (40.56%) representing the most dominant uropathogen in CA-UTIs. A total of 20 isolates (18.86%) Enterococcus spp. represented the second dominant uropathogen including E. faecalis (17 isolates) and E. faecium (3 isolates), followed by 11 isolates (10.3%) Streptococcus spp. including S. mitis (9 isolates), S. pneumonia (1 isolate), and S. agalactia group B (1 isolate).

Klebsiella spp. Showed 9 isolates (8.49%) including K. pneumonia (8 isolates) and K. oxytoca (1 isolate), Citrobacter koseri showed 7 isolates (6.6%), and Corynebacterium urealyticum showed 5 isolates (4.71%).
Other species appeared at a little rate such as Proteus mirabilis as 3 isolates (2.83%), Enterobacter intermedius, Pseudomonas aeruginosa, and Staphylococcus saprophyticus were represented by 2 isolates (1.88%) for each species. Finally, Serratia fonticilia and Bacillus cereus were represented by only 1 isolate (0.94%) for each species.

The etiology of UTI is quite relevant to geographical location; however, Escherichia coli has been known for decades as the most prominent uropathogen implicated in both community-acquired and healthcare-associated urinary tract infections [51].

In our study, E. coli represented 40.56% of uropathogenic isolated bacteria implicated in CA-UTIs. That is compatible with other recent studies conducted in Egypt concerning UTIs. Abou-Dobara et al. reported that E. coli represented 42% of total uropathogens isolated from CA-UTI cases in Mansoura University, Egypt [52]. Hassuna et al. found that among 400 uropathogens isolated from CA-UTI cases, 134 E. coli isolates (33.5%) were identified [29]. Moreover, Ali et al. confirmed that E. coli was among the most predominant uropathogens isolated with a rate of 34.69% [30]. Another study revealed that E. coli was the most common isolated uropathogen representing 39% of samples in CA-UTI [49].

The dominance of E. coli in UTIs has a rational explanation. E. coli colonizes the gastrointestinal tract of human infants within a few hours after birth, coexisting in a beneficial symbiotic relationship [53]. It rarely causes complications except in immunocompromised hosts or where the normal gastrointestinal barriers are penetrated as in peritonitis. E. coli inhabitants the mucous layer of the mammalian colon representing a phenomenally successful competitor and the most abundant facultative anaerobe of the intestinal microbiome.

One significant hypothesis suggests that E. coli might exploit its ability to utilize gluconate in the colon more efficiently than other resident species, thereby allowing it to occupy a highly specific metabolic niche [53]. However, there are highly adapted E. coli strains that have acquired specific virulence factors such as DNA horizontal transfer of transposons, plasmids, bacteriophages, and pathogenicity islands. These virulence factors enable them to adapt to new niches, modify, and damage the host promoting an infection. UTIs are the most common extraintestinal E. coli infections that are caused by uropathogenic E. coli [54].

For perfect colonization in their main habitat, the colon, E. coli first need to survive passage through the acidic pH of the stomach, and upper intestine, and then penetrate the viscous upper mucus layer of the colon epithelium, survive other host defense mechanisms, and compete with other microbiota for acquisition and utilization of nutrients. Some E. coli cells remain or are shed into the intestinal lumen and then excreted in feces. UTIs are initiated when UPEC contaminates, colonizes the urethra and invade the bladder epithelium undergoing an intracellular infection cycle. Lower UTI could progress to the kidneys and enter the bloodstream causing potentially fatal urosepsis [55].

The second dominant uropathogen in our study was Enterococcus spp. which represented 18.86% including Enterococcus faecalis (16%) and Enterococcus faecium (2.8%). That agrees with Shrestha et al. who observed high incidence of Enterococcus spp. and considered it as the most common gram-positive uropathogen isolated from CA-UTIs [56]. The genus Enterococcus was described as an intestinal microorganism and important uropathogen as it is the most common type of enteroococcal clinical disease that occurs in the urinary tract. It has been ranked among the top five pathogens for UTIs with a significant pathogenicity via biofilm formation [57]. Majid et al. estimated Enterococcus spp. in CA-UTIs as 17.3% [58]. Unlike that, Nemr et al. noticed that Enterococcus has a low incidence (2%) in CA-UTIs [49].

Another significant gram-positive uropathogen in our study, Streptococcus spp. which represented 10.3% including Streptococcus mitis (8.5%) as the most common streptococci, Streptococcus pneumonia (0.94%) and Streptococcus agalactia group B (0.94%). Juralowicz et al. estimated the presence of S. mitis as 6.2% among UTI bacterial etiology [59]. Streptococcus pneumonia is not a common agent of UTI. Its incidence as a uropathogen does not exceed 0.1% [60]. Group B Streptococcus agalactiae (GBS), β-hemolytic streptococci, is an uncommon causative agent of UTI estimated to cause approximately 1-2% incidence [61].

Klebsiella spp. represented in our study as 8.49% including Klebsiella pneumonia (7.5%) and Klebsiella oxytoca (0.9%). These results came in agreement with a study revealed that K. pneumonia and K. oxytoca represented 7.2% and 0.5%, respectively in urine cultures [62].

Juralowicz et al. found that K. pneumonia and K. oxytoca represented 6.4% and 0.6%, respectively in UTIs [59]. It was noticed in our study that all Klebsiella isolates were hypermucoid referred to the polysaccharide capsule as the most important virulence factor allowing bacteria to evade phagocytosis. That is compatible with Russo and Marr regarding the increase of hypermucoviscous type of K. pneumonia in the last three decades, particularly in community-acquired infections [63].

**Figure 4:** Incidence of CA-UTIs in female- and male kids regarding age groups.
In the present study, *Citrobacter koseri* showed 6.6%. Nair et al. estimated the prevalence of *C. koseri* as 6.5% of total gram-negative uropathogens isolated [64]. On the other side, AL-Ethari et al. found that *C. koseri* had a lower incidence, representing 2.8% of UTI patients [65]. Another significant uropathogen is *Corynebacterium urealyticum* representing 4.71% in our study. *C. urealyticum* is an opportunistic nosocomial pathogen and not common among community-acquired infections, mainly causing acute cystitis, pyelonephritis, and alkaline-encrusted cystitis [66]. Juralowicz et al. reported a compatible result that *C. urealyticum* represented 3.7% of total isolated uropathogens [59].

*Proteus mirabilis*, an opportunistic pathogen, represented 2.83% of total isolated uropathogens in our study. Unlike the other members of *Enterobacteriaceae*, *P. mirabilis* is an uncommon uropathogen in normal hosts and frequently isolated in complicated UTIs, such as patients with chronic indwelling urinary catheters [67]. Fang et al. reported that *P. mirabilis* represented 2.2% of total uropathogens isolated from CA-UTI patients [60]. In contrast, Maione et al. estimated a higher prevalence of *P. mirabilis* at 9.0% [68].

There were some uncommon uropathogens implicated in CA-UTIs in our study such as *Enterobacter intermedius*, *Pseudomonas aeruginosa*, and *Staphylococcus saprophyticus*, each of which represented 1.88% of total isolated uropathogens. In particular, Assourama et al. demonstrated that *E. intermedius* represented 1% of total isolated uropathogens from CA-UTIs [69]. Juralowicz et al. demonstrated that *P. aeruginosa* comprised 1.5% of CA-UTIs [59]. Moreover, studies reported that *S. saprophyticus* comprised 1.0% of all CA-UTIs [59, 70].

There were rare uropathogens isolated from CA-UTIs in our study including *Serratia fonticola* and *Bacillus cereus* both of which represented 0.94% of total isolated uropathogens.

A study reported *S. fonticola* represented 0.17% of all uropathogens [62]. A case of pyelonephritis caused by *B. cereus* was reported [71].

### 3.4. Antibiotic Sensitivity Testing

β-lactam antibiotics were tested on 106 bacterial isolates. Through our results, the increasing of uropathogens resistance to β-lactam antibiotics was highly observed, even in the presence of β-lactamase inhibitor (Table 1). That is compatible with Mloka et al. considering the higher prevalence of resistance to β-lactam antibiotics among gram-negative and gram-positive bacteria [72]. However, β-lactam antibiotics are still prescribed in empiric therapy as the first-line antibiotics despite the therapeutic failure.

Moreover, in our study, All tested gram-negative bacteria (100%) exhibited inhibition zones ≤ 22 mm and ≤ 27 mm for ceftazidime (30 µg) and aztreonam (30 µg) respectively which reflects their probability of being ESBL-producing bacteria. In addition, the majority of tested isolates (95.5%) exhibited inhibition zones ≤ 27 mm for cefotaxime (30 µg), and (79.1%) exhibited inhibition zones ≤ 25 mm for ceftriaxone (30 µg) which increased the probability of being ESBL-producing bacteria.

Phenotypic detection of ESBL revealed that out of 67 gram-negative bacterial isolates, 14 isolates exhibited a synergistic effect towards amoxicillin/clavulanate (20/10 µg) disc (Fig. 5), and 17 isolates exhibited an increase in inhibition zone diameter ≥ 5 mm for Cefoperazone/Sulbactam (75 µg, 2:1) than Cefoperazone (75 µg) alone (Fig. 6).

It was revealed that 35.8% of total isolated gram-negative uropathogens were ESBL-producers. *Escherichia coli* comprised a serious threat as the most dominant ESBL-producing organism representing 66.7% of total ESBL-producing bacteria detected.
ESBL detection is limited to Enterobacteriaceae members such as Citrobacter spp. Citrobacter koseri represented 8.3% of total ESBL-producing organisms and 28.5% of total C. koseri isolates included in our study. Kanamori et al. reported a high prevalence of ESBL producers among C. koseri isolates (32.1%) [78].

Other gram-negative bacteria exhibited a low incidence of ESBL production such as Serratia fonticola, Proteus mirabilis, and Pseudomonas aeruginosa, each of which represented only one isolate (4.1%) of total ESBL-producing organisms included in our study. A case report described S. fonticola as an ESBL-producer that developed urosepsis [79]. Shrestha et al. reported that each of Pseudomonas spp. and Proteus spp. represented 7.5% and 2.5%, respectively of ESBL-producing organisms [80].

4. Conclusion

Although ESBLs emerges as a nosocomial infection, CA-UTIs due to ESBL-producing bacteria have become an important problem in daily practice. Available antibiotics that are often used without medical supervision have resulted in an increasing reservoir of these infections in the community. Detection of these resistant isolates is crucial for effective treatment and avoiding therapeutic failures. Regular surveys of bacterial resistance in the community can guide the empirical prescribing and prophylaxis regimens for urological procedures.

CRediT authorship contribution statement:

“Conceptualization, M.A. designed the study; G.A. performed the experiments and J.M. contributed to the writing. All authors have read and agreed to the published version of the manuscript.”

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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