Background

Urinary tract infections (UTIs) are very common worldwide. Such an infection is usually treated with empirical antimicrobial therapy. However, there are trends of increasing rates of antibiotic resistance. The aims of this study were to determine the most common bacterial causative agents and their antibiotic sensitivity pattern in women suffering from UTI in Duhok, Kurdistan, northern Iraq.

Methods: Urine samples were collected from 371 subjects afflicted with UTI and inoculated directly on blood and MacConkey agar and then incubated at 37°C for 24 hours. Bacterial colonies were determined by standard culture and biochemical characteristics. All isolates were tested for their antibiotic susceptibility.

Results: The vast majority of the isolates were Gram-negative and only 2 (0.5%) of them were Gram-positive. The highest infection by Gram-negative bacteria belonged to Escherichia coli 276/371 (74.4%) and about 74.2% of which were resistant to amoxicillin/clavulanic acid. Additionally, around 65% of the isolated E. coli were resistant to ceftriaxone, ceftazidime, and cefepime. It was found that the Pseudomonas strains were resistant to ceftazidime (42%), ertapenem (75%), and ciprofloxacin (50%).

Conclusions: There were increasing rates of antibiotic resistance especially in E. coli. Urgent measures are needed to contain such a resistance pattern and a plan for continuous surveillance is required to monitor antibiotic sensitivity pattern.

Keywords: UTI, Antibiotic sensitivity, Multidrug resistant, Duhok, Iraq
Patients and Methods
Sample Collection
Urine samples were collected from 371 UTI afflicted subjects residing in residing in Duhok, Kurdistan, Iraq. Clean catch midstream urine was obtained from the patients to avoid contamination. The collected samples were inoculated on blood and MacConkey agars and then incubated at 37°C for 24 hours. The presence of ≥10⁵ identical colonies was considered as microbiological evidence of a UTI. Bacterial colonies were initially classified by gram staining and then determined depending upon standard culture and biochemical characteristics of isolates and identification was performed in accordance with local standards and guidelines.

Antimicrobial Susceptibility Test
Phoenix system (Becton Dickinson) was used for identification of bacteria and antimicrobial susceptibility testing. The test was performed according to the manufacturer’s instructions.

Ethics Statement
Consent was obtained from patients recruited in the report. This research and method of attaining consent were approved by the scientific committee of the department of sciences, University of Zakho, Kurdistan, Iraq.

Results
Patients Characteristics
In this study, 371 female patients were recruited; the majority of these patients were within the age range of 13-45 years. Sixty out of 371 (16.1%) and 70 out of 371 (18.9%) of the patients were older than 45 years old and within the age range of 19-30 years, respectively (Table 1).

Antibiotics Sensitivity Pattern
The vast majority of the isolates were gram negative and only 2 (0.5%) isolates were gram positive. The highest infection by gram-negative bacteria belonged to E. coli (276 isolates, 74.4%) followed by Klebsiella species (15.6%) (Table 1). Amongst 276 E. coli isolates, about 74.2 % were resistant to amoxicillin/clavulanic acid. In addition, around 65% of isolated E. coli were resistant to ceftriaxone, ceftazidime, and cefpime (Table 2). It was found that 31% and 0% of isolated Klebsiella strains were resistant to ciprofloxacin and amikacin, respectively (Table 2). Regarding the sensitivity pattern of pseudomonas, it was revealed that 42%, 75%, and 50% of the strains were resistant to ceftazidime, ertapenem, and ciprofloxacin, respectively. The sensitivity of Proteus to ciprofloxacin and ceftazidime was found to be 26% and 18.7%, respectively (Table 2).

Discussion
The UTI is considered to be one of the most widespread infections worldwide. Although every individual is susceptible to UTI, some groups are more vulnerable. Women, in general, are more susceptible to such an infection due to anatomical and physiological features.

The vast majority of national and international guidelines recommend empirical antibiotic therapy for UTI treatment. However, the effectiveness of such an empirical antibiotic treatment relies upon local antimicrobial resistance patterns. It is worth mentioning that the spectrum of microorganisms isolated from subjects suffering from UTI is almost stable and E. coli remains as the most prevalent causative agent. In a study conducted in Iran where 1513 patients participated, it was found that E. coli was the most common pathogen especially in women. In the same study, Klebsiella was observed as the second most common infection (10).

In another study carried out in Turkey involving 629 women between the age of 18 to 65 years old, E. coli was found to be the most common causative agent of UTI (11). In agreement with this, it was revealed that E. coli strains were the most common causative microorganisms of UTI in our locality. It is important to notice that significant changes in bacterial susceptibility profile have been demonstrated over the last decades (12). For example, the average resistance for ampicillin is more than 50% in some countries (12). In a study conducted in Turkey, the resistance rates of E. coli for ampicillin, amoxicillin/clavulanic acid, ceftriaxone, ciprofloxacin as well as sulfamethoxazole/trimethoprim were 55.1%, 32.7%, 15.9%, 25.2%, and 41.1%, respectively (11). In the present study, about 75% of the isolated E. coli strains were resistant to amoxicillin/clavulanic acid. Moreover, our results showed that around 65% of isolated E. coli were resistant to ceftriaxone, ceftazidime, and cefpime. Besides, it was found that 31% and 0% of isolated Klebsiella strains were resistant to ciprofloxacin and amikacin, respectively. The resistance pattern of Klebsiella to ciprofloxacin was similar to what was found in Africa. However, the sensitivity to amikacin in this study was much better that of found in Africa (0% comparing to 11%) (13). The sensitivity pattern of Pseudomonas was alarming as 42%, 75%, and 50% of the strains were resistant to ciprofloxacin and amikacin, respectively.

Table 1. Distribution of Urine Pathogens According to Age Groups

| Organism       | Age Group     | Total No.% |
|----------------|---------------|------------|
|                | <18           | 19-30      | 31-45      | >45          |
| Staphylococcus sp. | 0             | 1          | 1          | 0            | 2 (0.5)     |
| Acinetobacter sp.  | 0             | 1          | 6          | 2            | 9 (2.4)     |
| E. coli         | 14            | 46         | 171        | 45           | 276 (74.4)  |
| Klebsiella sp.  | 1             | 13         | 32         | 12           | 58 (15.6)   |
| Pseudomonas sp. | 0             | 5          | 7          | 0            | 12 (2.8)    |
| Proteus mirabilis | 3             | 4          | 6          | 3            | 16 (4.3)    |
| Total           | 18            | 70         | 223        | 60           | 371 (100)   |
Antibiogram pattern of isolates from UTI cases among women in Iraq

Table 2. Antimicrobial Resistance Patterns of Isolated Uropathogens

| Antibiotic          | E. coli | Klebsiella sp. | Acinetobacter sp. | Pseudomonas sp. | Proteus sp | Staph sp. |
|---------------------|---------|----------------|-------------------|----------------|------------|-----------|
| Amikacin            | 5 (1.7) | 0 (0)          | 2 (22.2)          | 8 (16.6)       | 4 (25)     | 0 (0)     |
| Gentamicin          | 124 (44.9) | 15 (25.8)    | 2 (22.2)          | 5 (41.6)       | 11 (68.7)  | 0 (0)     |
| Ertapenem           | 13 (4.7)  | 2 (3.4)       | 5 (55.5)          | 8 (66.6)       | 0 (0)      | 0 (0)     |
| Imipenem            | 6 (2.1)   | 3 (5.1)       | 2 (22.2)          | 3 (25)         | 0 (0)      | 0 (0)     |
| Meropenem           | 7 (2.5)   | 0 (0)         | 2 (22.2)          | 2 (16.6)       | 0 (0)      | 0 (0)     |
| Cefazolin           | 169 (61.2) | 33 (56.9)    | 4 (44.4)          | 4 (33.3)       | 8 (50)     | 1 (50)    |
| Ceftazidime         | 178 (64.4) | 30 (51.7)    | 2 (22.2)          | 5 (41.6)       | 3 (18.7)   | 1 (50)    |
| Ceftaxone           | 181 (65.3) | 28 (48.2)    | 4 (44.4)          | 7 (58.3)       | 9 (56.2)   | 1 (50)    |
| Cefepime            | 179 (64.8) | 28 (48.2)    | 2 (22.2)          | 4 (33.3)       | 7 (43.7)   | 1 (50)    |
| Aztreonam           | 183 (66.3) | 25 (43.1)    | 9 (100)           | 5 (41.6)       | 3 (18.7)   | 1 (50)    |
| Augmentin           | 205 (74.2) | 33 (56.9)    | 9 (100)           | 12 (100)       | 2 (12.4)   | 2 (100)   |
| Piperacillin-tazobactam | 31 (11.2) | 4 (6.9)       | 2 (22.2)          | 2 (16.6)       | 0 (0)      | 0 (0)     |
| Bacterem            | 176 (63.7) | 7 (12)        | 2 (22.2)          | 10 (83.3)      | 7 (43.7)   | 2 (100)   |
| Cefoxitin           | 26 (9.4)   | 11 (18.9)     | 6 (66.6)          | 4 (33.3)       | 1 (6.2)    | 1 (50)    |
| Nitrofurantoin      | 28 (10.1)  | 31 (53.4)     | 9 (100)           | 10 (83.3)      | 14 (87.5)  | 1 (50)    |
| Ciprofloxacin       | 148 (53.6) | 18 (31)       | 2 (22.2)          | 6 (50)         | 4 (25)     | 2 (100)   |
| Norfloxacin         | 149 (53.9) | 15 (25.8)     | 0 (0)             | 4 (33.3)       | 4 (25)     | 1 (50)    |

The current study makes a clear case that resistance of microorganisms causing UTI has reached alarming levels and immediate plan is required to cope with the issue. Another important finding of this study is that continuous surveillance of antibacterial resistance is required to monitor the changes taking place in the sensitivity pattern in any society. Strengthening local and global antibiotics resistance surveillance is critical since it provides essential information for global strategies, monitors the effectiveness of public health measures, and determines new trends and threats.

Conflict of Interests
None.

References
1. Stamm WE, Hooton TM. Management of urinary tract infections in adults. N Engl J Med. 1993;329(18):1328-34. doi: 10.1056/nejm199310283291808.
2. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med. 2002;113 Suppl 1A:5s-13s.
3. Magliano E, Grazioso V, Dellorio L, Leuci AL, Mattina R, Romano P, et al. Gender and age-dependent etiology of community-acquired urinary tract infections. ScientificWorldJournal. 2012;2012:349597. doi: 10.1100/2012/349597.
4. Komaroff AL. Diagnostic decision: Urinalysis and urine culture in women with dysuria. Ann Intern Med. 1986;104(2):212-8. doi: 10.7326/0003-4819-104-2-212.
5. Assafi MS, Pulse RF, Hussein NR, Haji AH, Issa AR. The prevalence of S. aureus nasal colonisation and its antibiotic sensitivity pattern amongst primary school pupils. Sci J Univ Zakho. 2017;5(1):7-10. doi: 10.25271/2017.5.1.291.
6. Hussein NR, Assafi MS, Ijaz T. Methicillin-resistant Staphylococcus aureus nasal colonisation amongst healthcare workers in Kurdistan Region, Iraq. J Glob Antimicrob Resist. 2017;9:78-81. doi: 10.1016/j.jgar.2017.01.010.
7. Assafi MS, Ibrahim NMR, Hussein NR, Taha AA, Balatay

resistant to ceftazidime, ertapenem, and ciprofloxacin, respectively. The sensitivity of Proteus to ciprofloxacin and ceftazidime was reported to be 26% and 18.7% in the current study which was less than what was found in a study in Taiwan (54% and 80%, respectively) (14).

The association of Acinetobacter species and UTIs is well established. Risk factors predisposing to infection with such bacteria include prolonged hospital and intensive care unit admission, surgical intervention, and prolong antibiotics use (15). In this study, few causes of UTI resulted from Acinetobacter species showing 100% resistance to aztreonam and amoxicillin/clavulanic were reported. Unfortunately, due to missing data, it was not possible to determine whether or not those patients were exposed to above-mentioned risk factors.

In a previous study in Iraq, it was indicated that about 50% of the bacteria causing UTI were gram positive and the vast majority of them were staph species (7). Surprisingly, in this study, 2 cases of UTI caused by staph species were found. This is difficult to explain and more study is needed in this respect.

It was previously demonstrated that the distribution of microorganisms causing UTI was age dependent (3, 16). A lower prevalence of E. coli isolates was found in patients younger than 13 years or older than 60 years. Unfortunately, such a comparison was not reliable in the present study as the majority (60%) of the patients were within the age range of 31-45 years old.

Conclusion
The current study makes a clear case that resistance of microorganisms causing UTI has reached alarming
8. Hussein NR, Alyas A, Majeed M, Assafi MS. Prevalence Rate and Prevalent Genotypes of CA-MRSA in Kurdistan Region: First Report from Iraq. Int J Pure Appl Sci Technol. 2015;27(1):44-49.

9. Habeeb A, Hussein NR, Assafi MS, Al-Dabbagh SA. Methicillin resistant Staphylococcus aureus nasal colonization among secondary school students at Duhok City-Iraq. J Microbiol Infect Dis. 2014;4(2):59-63. doi: 10.5799/ahinjs.02.2014.02.0128.

10. Mirsoleymani SR, Salimi M, Shareghi Brojeni M, Ranjbar M, Mehtapoor M. Bacterial pathogens and antimicrobial resistance patterns in pediatric urinary tract infections: a four-year surveillance study (2009-2012). Int J Pediatr. 2014;2014:126142. doi: 10.1155/2014/126142.

11. Aypak C, Altunsoy A, Duzgun N. Empiric antibiotic therapy in acute uncomplicated urinary tract infections and fluoroquinolone resistance: a prospective observational study. Ann Clin Microbiol Antimicrob. 2009;8:27. doi: 10.1186/1476-0711-8-27.

12. Kahlmeter G. An international survey of the antimicrobial susceptibility of pathogens from uncomplicated urinary tract infections: the ECO.SENS Project. J Antimicrob Chemother. 2003;51(1):69-76.

13. El Bouamri MC, Ansalane L, El Kamouni Y, Zouhair S. Antimicrobial susceptibility of urinary Klebsiella pneumoniae and the emergence of carbapenem-resistant strains: A retrospective study from a university hospital in Morocco, North Africa. Afr J Urol. 2015;21(1):36-40. doi: 10.1016/j.afju.2014.10.004.

14. Wang JT, Chen PC, Chang SC, Shiau YR, Wang HY, Lai JF, et al. Antimicrobial susceptibilities of Proteus mirabilis: a longitudinal nationwide study from the Taiwan surveillance of antimicrobial resistance (TSAR) program. BMC Infect Dis. 2014;14:486. doi: 10.1186/1471-2334-14-486.

15. Maragakis LL, Perl TM. Acinetobacter baumannii: epidemiology, antimicrobial resistance, and treatment options. Clin Infect Dis. 2008;46(8):1254-63. doi: 10.1086/529198.

16. Kiffer CR, Mendes C, Oplustil CP, Sampaio JL. Antibiotic resistance and trend of urinary pathogens in general outpatients from a major urban city. Int Braz J Urol. 2007;33(1):42-8.