Investigating the appropriateness of antibiotic usage and misuse for uncomplicated urinary tract infections (UTIs) in the clinics at King Abdul-Aziz Hospital (KAH) in Makkah, Kingdom of Saudi Arabia

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General Note

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ABSTRACT

Inflammation or infection of the urinary tract is considered to be a critical and common condition that can affect vast numbers of patients yearly. Inappropriate antibiotic prescriptions lead to an increased risk to patients whom can face bacterial resistance. The main aim was to investigate the frequency of this infection and the antibiotic-treatment schemes and errors. A retrospective study was done in three months' time period during 2019 in the out-patient and in-patient clinics at King Abdulaziz Hospital in Makkah (KAH) in the Kingdom of Saudi Arabia. In general, (1,556) subjects have been diagnosed with this infection, consisted of children (13.7%), grown-ups (77.5%), and seniors (8.9%) subjects. 88.7% was the total frequency of these subjects attended clinics. Wide-spectrum of empirical antibiotics was endorsed for 80% of the subjects. The total wide-spread of antibiotic endorsement with at least one type of error was 45.2 (children 52%, grown-ups 45%, and seniors 46%). The most common mistakes were found in dose (38%), length of the treatment (9%), repetition (5%), and the choice of the antibiotic (3.5%). Mistakes in the dosage were significantly higher in children. However, misfolds in the treatment duration were greater in the seniors. Urine cultures of positive results were found in 31.50 % of patients, with Escherichia coli at high rates (77%). In conclusion the findings showed a large degree of misuse use of antibiotics in the care of UTIs at King Abdulaziz Hospital in Makkah, Saudi Arabia.

Keywords: Urinary tract infection, antibiotics, Errors.

1. BACKGROUND

Urinary tract disease (UTI) is viewed as one of the well-known outpatient grumblings in human clinical services settings (Nawar et al., 2005). It additionally puts a noteworthy weight on the patient and on society (Nawar et al., 2005). UTI definition is based on the appearance of any antibacterial infection in the urinary tract system. The infection can be divided anatomically into the upper tract infection (kidneys and ureters) and is called pyelonephritis and lower tract infection (bladder and urethra) that is called cystitis (Shapiro et al., 2014).

Indeed, Inflammation or infection of the urinary tract is considered to be critical and common condition that can affect vast numbers of patients yearly (Caterino et al., 2005; Kallen et al., 2006). The vast misuse of antibiotics is a major causes of antibiotics resistance (May et al., 2006). The World Health Organization has clarified that around 80% of anti-infection agents has been utilized a ton in the network, and that around 20%–half of these drugs are abused (May et al., 2006). Antibiotic resistance is a very complex harm towards health in the public patients worldwide. It can affect the therapeutic process of the patient and their outcomes, resulting in an accelerated health care costs increase as well as high rates of morbidity and mortality (Taur and Smith, 2007).

The solution to this problem is the appropriate antibiotic use to control this resistance. Antibiotics are the major line of therapy for UTIs, thus to select the appropriate antibiotic it should be effective, safe, and cost-effective. A study was done in Riyadh, Saudi Arabia, provided that the prevalence of community acquired UTIs as 25% of all infections commonly admitted in the department of emergency (Dalhoff, 2012). Likewise, another examination was done in Riyadh, Saudi Arabia oftentimes saw a generous level of lacking utilization of anti-microbials under the watchful eye of UTIs in the crisis office (Sanchez et al., 2000). In this manner, our fundamental point was to decide the rate pace of UTIs in KAH in Makkah, Saudi Arabia; also, to assess the kinds of anti-infection remedy among those patients.

2. METHODOLOGY

Our study was taken place in the out-patient and in-patient clinics at King Abdulaziz Hospital in Makkah in Saudi Arabia (KAH). KAH is a 500-bed tertiary care center in Makkah, Saudi Arabia. The design of the study was in the concept of observational retrospective type and was established by examining data from the files of patients in the out-patient and in-patient clinics complaining of UTIs in three months period of the year 2019.

In the inclusion criteria of the study we included patients in both the out-patient and in-patient clinics complaining of UTIs in three months period of the year 2019. Those patients who are from six months to eighty years old with the diagnosis of UTI were included. At that point we gathered them as children, grown- ups and seniors. Patients matured a half year to 15 years has been classified as children, those aged 15–64 years has been classified as grown-ups, while those of 65 years or more has been classified as senior subjects. These definitions were taken as it had been considered before in comparative investigates (Gupta et al., 2010).

Exclusion criteria were incomplete antibiotic endorsements and infants weighing five or less kilograms have been barred from the start of the study. Any subjects determined to have complicated UTI for instance sepsis or bacteremia associated with UTI, or any permanent damages to the kidney. Moreover, any subjects suffering from chronic disorders such as cancer were likewise barred.

The data on this study was collected on the basis of subject's characteristics such as the age, gender, number of attending the out-patients and in-patients' clinics within 3 months, and reappearance of the disease were also investigated. Reappearance is defined as 2 or more occurrence of the disease or the same condition for the whole length of the study.

Characteristics of the antibiotic's endorsements were the name, dose, frequency, duration, were all examined for each endorsement.

Data collection also consisted of urine cultures that were ordered and taken during clinic visits within the study duration, with both definite and invalidated results and the type of the pathogen has been examined.

Our main study outcome was measuring the inadequate use of antibiotic therapy. Four key ways in which antibiotic therapy may be inadequate have been identified: errors in choosing the drug, error in the dose, errors in the frequency, and errors in the duration. Every antibiotic endorsement has been examined for adequacy according to the guidelines form USA guidelines (WHO, 2007).
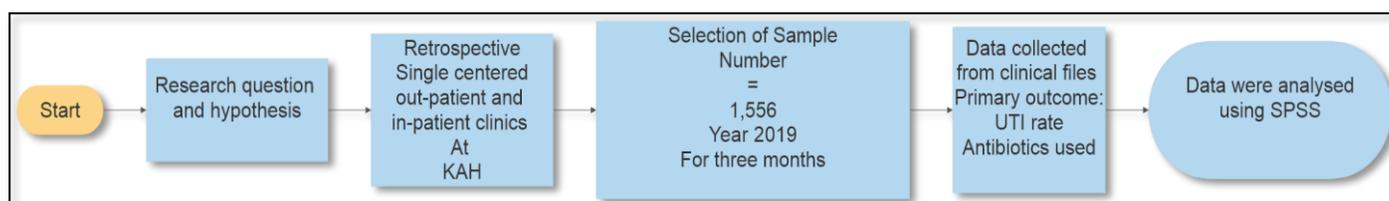

Figure 1: Methodology flow chart

Data management and analysis

SPSS factual programming (var 23; IBM, USA) was utilized for information passage and examination. Bivariate examination utilizing Pearson's χ2 test was utilized for straight out information, for example, age-gathering, sex, and anti-microbial class. Predominance of unseemly anti-microbial medicines was resolved as the quantity of doctor orders with at least one kinds of blunder isolated by the all-out number of medicines and increased by 100. The commonness of errors (choice, portion, recurrence, and length) was first determined as fundamentally unrelated predominance by isolating the quantity of mistakes over the quantity of anti-infection remedies increased by 100. For every factual test, P<0.05 was considered measurably significant.

Ethics statement

The present study protocol was reviewed and approved by the Institutional Review Board of Umm Al-Qura University (approval number: HAOP-02-K-012-2020-06-401). There was no need for informed consent of the patient to review their medical history and there was no contact with the subjects directly. Investigators have ensured patient privacy and the confidentiality of the data.

3. RESULTS

Overall, over the course of the study a total of 1,556 subjects were diagnosed with uncomplicated UTIs. These included subjects who were children (13.7 percent), grown-ups (77.5 percent), and seniors (8.9 percent). Most of the diagnosed subjects were female (87.5 per cent). The male-to- female ratio was 1 to 2.7, and 80.29% of all grown-ups, 57.83% of children and 33.49% of seniors were also female. The rate of the recurrent infection was 30%. The re-infection was increased more in females, especially in grown-ups', but to a lesser extent in children and senior females (80.29%, 75.84%, and 33.48%, respectively). These differences were significant statistically for females in all the classified groups (Table 1).

The general predominance of the infection was 88.7% of the complete clinic's attendance to the facilities. However, the attending rate in the grown-ups and older folks was ~20.6% and ~13% for children.

The physicians ordered urine culture for 22 per cent of the subjects. Of the 350 urine cultures in total, 199 with positive results and 151were invalidated. There were major differences between all the groups in the sum of the culture outcomes. E. coli was the main pathogen detected for the uncomplicated UTIs. Moreover, this pathogen has been seen to be very sensitive to nitrofurantoin (94%), ciprofloxacin was next (77.7%), and cefazolin (70.4%). On the other hand, E. coli has been seen to decrease its sensitivity to co-trimoxazole (45.5%) and ampicillin (22.3%).

Expansive range anti-microbials have been endorsed for 80.0% of patients. Three fundamental anti-infection agents were recommended: fluoroquinolone (88%), nitrofurantoin (15%), and trimethoprim/sulfamethoxazole (6%) with noteworthy contrasts among the three age-gatherings (Table 1). The anti-infection agents frequently recommended in children subjects were amoxicillin–clavulanic acid (46.27%), then cefprozil (22%), cefuroxime (15.13%) and amoxicillin (10.5 %).

Table 1 Analysis of characteristics and antibiotic endorsements in all the study groups subjects

	Sample, n (%) (total 1,556)	Children, n (%) (total 211 [13.6])	Grown-ups, n (%) (total 1,205 [77.5])	Seniors, n (%), (total 138 [8.9])	X^2, P-value
Gender					70.755, 0.05
Male	195 (12.5)	11 (16.4)	184 (66.5)	8 (25.8)	
Female	1,361(87.5)	200 (57.83)	1,031 (80.29)	130 (33.49)	
Infection frequency in 3 months					70.377, 0.001
Once	1,290 (81.9)	145 (88.5)	1,022 (85.3)	123 (67.4)	
Reappearance	266 (30.1)	76 (11.5)	183 (14.7)	33 (32.6)	
Urine culture request at clinic					1.023, 0.234
Yes	350 (35)	15 (2.8)	310 (87.9)	25 (28.8)	
no	1,206 (73)	196 (67.2)	895 (82.1)	113 (11.3)	
Culture Result					7.803, 0.05
+ve	199 (56.8)	10 (26.1)	170 (39.4)	19 (31.2)	
-ve	151 (43.1)	5 (3.9)	140 (80.6)	6 (6.8)	
Antibiotics treatment in 3 months, n					71.917, 0.001
One type	1,167 (84.9)	208 (84.5)	832 (85.3)	117 (67.4)	
Two types	203 (14)	28 (10.4)	103 (10.4)	72 (22.4)	
Three or more	59 (4.1)	3 (1.1)	23 (2.7)	33 (10.2)	
Name of antibiotic group					175.462, 0.001
Norfloxacin	567 (39.1)	117 (43.5)	322 (45.6)	128 (39.8)	
Cefuroxime	39 (2.7)	8 (15.3)	19 (35.4)	120 (35.2)	
Penicillin	379 (26.3)	119 (44.2)	226 (26.3)	134 (47.7)	
Tetracycline	3 (0.2)	0	2 (0.2)	1 (0.3)	
Miscellaneous	70 (4.8)	3 (1.1)	61 (7.1)	6 (1.9)	
Fluoroquinolone	327 (22.6)	7 (2.6)	190 (22.1)	130 (40.4)	
Sulfonamide	64 (4.4)	15 (5.6)	38 (4.4)	11 (3.4)	
Antibiotic spectrum					36.101, 0.001
Narrow	213 (14.2)	46 (24.5)	224 (24.5)	26 (5)	
Wide	1,443 (85.8)	213 (75.5)	834 (85.5)	206 (95)	

In grown-ups, the most usually recommended anti-infection agents were norfloxacin (45.6%), cefuroxime (35.4%), amoxicillin–clavulanic acid (23.6%), nitrofurantoin (6.9%), and ciprofloxacin (4.1%), and the least regularly endorsed in grown-ups was azithromycin (1.0%). In the seniors, the most generally recommended anti-infection agents were cefuroxime (47.7%), norfloxacin (35.2%), and amoxicillin (14.5%), and the least regularly endorsed was ciprofloxacin. There were measurably significant contrasts between the groups in the sorts of anti-toxins utilized (Table 1). Most of patients (78.9%) got one course of anti-infection agents for the treatment of UTI during the examination time frame, however, in any event 7 percent of patients got at least three courses of anti-microbials for intermittent UTIs during a similar time (Table 1).

Table 2 Incidence of antibiotic endorsements inadequacies and mistakes types in prescribing of error by all the groups of the study

Characteristics	Children, n (%) (total 211 [13.6])	Grown-ups, n (%) (total 1,205 [77.5])	Seniors, n (%), (total 138 [8.9])	Total, n (%)	x^2, P-value
Antibiotic inadequacy	137 (52.4)	495 (45)	132 (47.2)	768 (57.3)	5.677, 0.21
Type of mistakes					

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Dose	111 (34.2)	304 (35.5)	130 (37.3)	544 (38.3)	3.409, 0.05
High	71 (22.6)	242 (34.5)	110 (36)	489 (33.7)	
Low	11 (4.1)	9 (1)	4 (1.2)	24 (1.7)	
Others	31 (11.5)			41 (11.5)	
Mistake in the frequency	16 (5.9)	58 (6.8)	15 (4.7)	39 (5)	1.516, 0.343
High	4 (1.5)	17 (1.9)	7 (2.2)	17 (1.9)	
Low	12 (4.5)	42 (4.9)	8 (2.5)	72 (4.3)	
Mistake in the length of treatment	17 (6.3)	95 (11.4)	44 (13.7)	139 (9)	8.527, 0.14
Long	4 (1.5)	22 (2.8)	9 (2.8)	36 (2.6)	
Short	12 (4.8)	72 (8.6)	35 (10.9)	132 (8.4)	
Mistake in choosing the antibiotics	9 (3.3)	14 (1.2)	6 (2.2)	33 (3.4)	1.2213, 0.245

The commonness of mistaken anti-infection solutions with in any event at least one types of errors was 57.3 percent and was higher in children subjects (54.2 percent) in comparison with grown-ups (36 percent) and older patients (37.2 percent; Table 2). The fundamentally unrelated recurrence of various types of mistake demonstrated that portion errors were generally common (47.5 percent). Followed by span errors (21 percent), recurrence mistakes (7.1 percent) and, at last, unseemly decision of anti-microbial class (1.4 percent). Children subjects were dependent upon a marginally higher pace of unnecessary anti-infection dosages (P<0.05).

Table 3 Analysis of antibiotic endorsements inadequacy by all the study groups subjects

Characteristics	Sample, n (%) (total 1,556)	Children, n (%) (total 211 [13.6])	Grown-ups, n (%) (total 1,205 [77.5])	Seniors, n (%), (total 138 [8.9])	Total, n (%)	x^2, P-value
Antibiotic inadequacy		139 (52.3%)	394 (45%)	155 (45.2%)	695 (46.3%)	2.255, 0.22
Gender						
Male	195 (12.5)	51 (51.1)	89 (30.7)	77 (57.8)	233 (55.3)	4.581, 0.112
Female	1,361(87.5)	84 (51.9)	290 (58.1)	65 (56.4)	459 (45.4)	0.555, 0.620
Urine culture request at clinic						
Yes	1,290 (81.9)	64 (59.1)	145 (44.6)	57 (45.6)	270 (47.8)	6.580, ‚0.05
no	266 (18.1)	70 (35.5)	350 (66.9)	90 (38.2)	515 (66.9)	0.247, 0.475
Culture results						
+ve	350 (35)	14 (23.3)	74 (50)	25 (69)	104 (53.8)	1.261, 0.323
-ve	1,206 (73)	119 (48.8)	331 (45.3)	129 (45.6)	579 (46.2)	1.448, 0.273
Antibiotics use in three months, n						
One type	199 (56.8)	131 (40.8)	238 (46.2)	104 (45.8)	577 (47.8)	1.993, 0.369
Two types	151 (43.1)	13 (30.7)	46 (44.7)	31 (23.1)	95 (46.3)	1.716, 0.152
Three or more		0	21 (47.8)	11(29.4)	23 (30.2)	1.561, 0.277
Incidence of the infection in three months						
Once	203 (14)	121 (50.8)	238 (46.2)	118 (49.8)	567 (47.8)	1.993, 0.169
Reappearance	59 (4.1)	12 (52.8)	27 (45.2)	44 (41.9)	118 (45)	1.621, 0.415
Name of antibiotic group						
Norfloxacin	567 (39.1)	78 (66.7)	292 (90.7)	107 (83.6)	477 (84.1)	35.104, 0.001
Cefuroxime	39 (2.7)	40 (33.6)	24 (10.6)	2 (5.9)	66 (17.4)	35.512, 0.001
Penicillin	379 (26.3)	0	29 (15.3)	27 (20.8)	56 (17.1)	3.157, 0.209
Tetracycline	3 (0.2)	6 (75)	6 (31.6)	5 (41.7)	17 (43.6)	4.333, 0.114
Miscellaneous	70 (4.8)	3 (100)	25 (41)	4 (66.7)	32 (45.7)	2.134, 0.035

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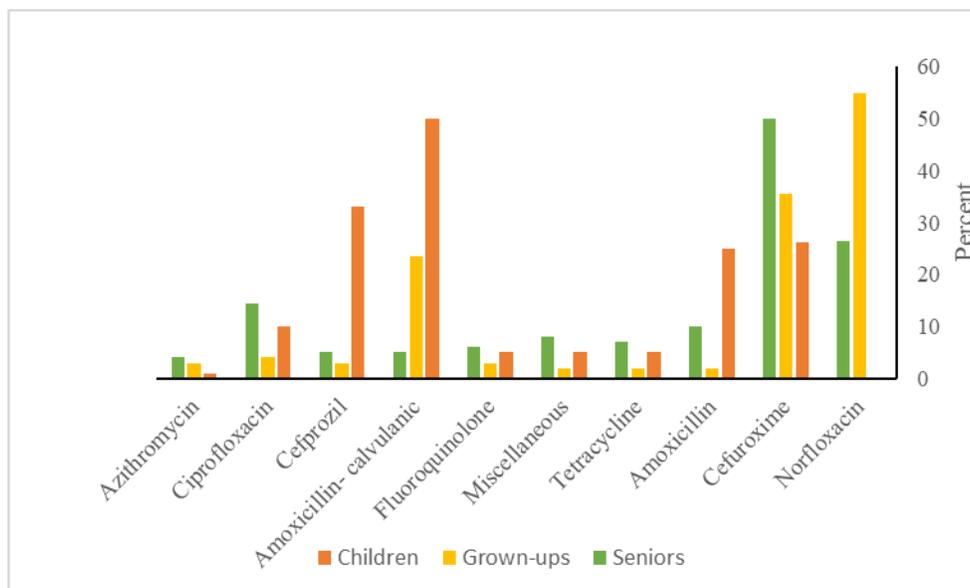| Fluoroquinolone | 327 (22.6) | 11 (73.3) | 19 (50) | 7 (63.6) | 37 (57.8) | 2.585, 0.175 |
Antibiotic spectrum						
Narrow	213 (14.2)	32 (45.5)	29 (23.4)	7 (34.8)	66 (32)	10.226, 0.05
Wide	1,443 (85.8)	111 (53.2)	336 (43.9)	145 (33.4)	619 (49.8)	1.624, 0.337

Figure 2 Distribution of antibiotics prescribed by all groups in the study.

4. DISCUSSION

Our study supplies novel data among the prevalence of UTIs in out-patients and in-patient's clinics in KAH in Makkah. It's indeed known that the prevalence of UTIs differs largely among countries, this is contributed to many criterions for example, the location, age, gender, the socioeconomic and health status (CDC, 2013; Bryce et al., 2016). In our study, UTIs was considered for almost 11.7% of clinic attending during three months period in 2019. For children attended the clinics the frequency of the infection was around 13%, similar to studies that was done before in some other countries, where the incidence ranged from 5 to 14 percent of attended clinics per year (Alanazi et al., 2015; AHFS, 2015; Lexicomp, 2020).

Also, we found in this study the frequency of the infection in the both grownups and senior subjects were almost 20.4% of all the attended clinics over the three months in 2019. The result was almost more than 22 per cent in a similar study that was done in Saudi Arabia (Shaikh et al., 2008; Freedman, 2005). Moreover, an investigation was done in America concluded that 5 percent of the elderly and 3 percent of the adults visiting the emergency department or clinics with a UTI diagnosis (Hang et al., 2002; GAFS, 2020). In contrast to this figure in Spain, the frequency of UTI in the grownups and seniors was 52% (ACOG, 2008; Garout et al., 2008).

We found also in our examination that female subjects hold a fundamentally high frequency rate of the infection in contrast with their opposite gender, which might be because of anatomical and physiological contrasts. These outcomes are corresponding to information from major epidemiological UTI considers (Albrahim et al., 2002). It is a fact that UTI is viewed as a normal continuous pathogenic disease in female subjects who may represent 1 of every 3 females with in any event one side effect of UTI and need to had anti-microbial treatment for it (Medina et al., 2003). Foxman et al, inferred that 10.8% of females matured 18 years and more can have at any rate one UTI every year (Turner et al., 2010). In this investigation, the quantity of females who visited facilities for an UTI was around 773.

Moreover, in the present study, the rate of this infection in the female subjects decreased with age, but the rate was higher in older seniors of males. There was however a study that found a similar rate of UTIs in both genders of senior subjects (Spenser et al., 2010). Another study also found that UTI frequency in male children subjects were decreased with age (François et al., 2016).

In our examination, the repetitive diseases were around 30% of all instances of UTI. In any case, the pace of repeat of UTI was higher in female than in male. Intermittent UTIs have been appeared to influence 25%-30% of solid young ladies with anatomically and physiologically typical urinary tract. This can be alluded to the hereditary and social elements of the females. Repetitive

infections in children subjects demonstrated 9 percent of all children cases in this examination. A past investigation in Saudi Arabia was similar to this result (Caterino et al., 2005).

Negative outcomes were accounted for in 151 of urine cultures. There was a comparable report done when all is said in done practice that found that around half of the diagnosed infections with invalidated results of cultures (Foxman, 2014). We found that evaluating clinical signs and indications in conjunction with the after effects of pyuria and nitrituria in the responsive strip test can help doctors make the choices before UTI is confirmed by the results of culture. In our study E. coli was considered the most widely recognized organism to UTI. In any event, in most cases it was impervious to use anti-toxins regularly. Ampicillin and co-trimoxazole is seen as the greatest resistance, and the least interference with nitrofurantoin. Such findings were similar to previous investigations (Foxman, 2014).

Fluoroquinolone, nitrofurantoin, and trimethoprim/sulfamethoxazole were the most widely recognized anti-infection agents used to treat UTIs in this investigation. This is like different investigations, as a result of the expansive antimicrobial action, clinical adequacy, and great bearableness profiles of these anti-toxins. In this investigation, norfloxacin, cefuroxime, amoxicillin–clavulanic, nitrofurantoin and ciprofloxacin (4.1%), were the anti-microbials endorsed frequently in grown-ups, while cefuroxime, norfloxacin and ciprofloxacin were regularly recommended in the old. In pediatric patients, amoxicillin–clavulanic corrosive, trailed by cefprozil and cefuroxime amoxicillin were the anti-infection agents most as often as possible recommended, like a huge scope overview of treatment for this infection in youngsters in essential and auxiliary consideration rehearses in Europe (Nawar et al., 2005; Martinez et al., 2007).

Examples of anti-infection medicine for the treatment of UTIs may fluctuate among various nations as indicated by the patient's age and sex, any hidden sicknesses, doctor inclination/nature, understanding hypersensitivities, nearby opposition designs, persistent populace, reaction profile, and cost (Foxman, 2002). The inpatient and outpatients' clinics are viewed as one of the administration units where anti-microbial treatment is usually recommended (Schappert and Rechtsteiner, 2007). That is the reason abuses and unseemly antimicrobial treatment in proposals centers are generally high. This can put patients in danger of incapable treatment and creating safe microscopic organisms, and utilizing more than the suggested routine puts them in danger of reactions .

There is an immense distinction among nations in recommending blunders for UTIs. The commonness of mistake in this examination was 57.3%, which was corresponding to like an investigation led in Turkey (Foxman et al., 2000). In any case, this rate was higher than an investigation directed in Spain by (12%), (Shapiro et al., 2014). The pervasiveness of mistakes was seen as expanded in patients with wide range anti-infection agents, as had been appeared in a past report. Wrong medication choice, for example, the utilization of macrolides for the therapy of this infection, was seen in 1.6% of the conditions. Macrolides are not viewed as dynamic against UTI pathogens, for example, E. coli (Wang et al., 2009).

Our examination had its own restrictions. To start with, it was led in just two settings, outpatients and inpatients facilities, which doesn't speak to other human services settings in Makkah, and in this way the discoveries can't be summed up. Second, this was a short review study was accomplished for multi month that did exclude all cases.

5. CONCLUSION

To summarize, in this study, UTIs were one of the most well-known contaminations that justified a visit to the facilities. The outcomes demonstrated a significant level of extreme utilization of anti-infection agents in the treatment of UTIs in both inpatient and outpatient facilities, especially among children and senior subjects. They additionally demonstrated a critical increment in the pervasiveness of protection from a few usually utilized antimicrobials. These discoveries clarify that the improvement of rules for the treatment of UTIs ought to be founded on information on the neighborhood commonness and sensitivities of bacterial living beings as opposed to on all-inclusive rules. Progressively productive anti-toxin treatment ought to improve adequacy and cost-viability. It is essential to change doctors' recommending propensities by presenting projects of clinical instruction focused on the suitable utilization of anti-infection agents. Extra research ought to be acted in the field of financially savvy treatment approaches for UTIs in Saudi Arabia. Commonness and anti-microbial weakness consider should be performed all the time, which will advance early identification of anti-microbial opposition improvement and empower proposals for worthy and cleverness treatment of UTIs to be set up .

Abbreviations
KAH- King Abdul-Aziz Hospital
UTIs - Urinary tract infections

Acknowledgement

Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards (ethical approval number: HAPO-02-K-012-2020-08-401).

Data and materials availability

All data associated with this study are present in the paper.

Peer-review

External peer-review was done through double-blind method.

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