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The Rates Incidence of Urinary Tract Infection in the Community and Development Uropathogens Resistance to Antibiotics

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A B S T R A C T

Urinary tract infections (UTIs) are common bacterial infections, it considers the second diseases that are frequent in the general population. This study aimed to resolve data of bacterial isolates among 3687 UTI patients at Sabratha Teaching Hospital during the years 1999, 2014 and 2015. Including results of urine culture test, biochemical test and antimicrobial susceptibility test. Results reveal that 398 (15.4%) uropathogens were isolated in 1999, 187(22.6%) in 2014 and 61(22.4%) in 2015. There was an increase in rates of isolation of uropathogens in 2014 and 2015 compared to 1999. *Escherichia coli* was the most common isolated uropathogen represented 69.6%, 18.7% and 19.7% of organisms isolated in 1999, 2014 and 2015 respectively. Other gram-negative represented 25.6%, 65.8% and 52.4%, in 1999, 2014 and 2015 respectively. Gram-positive cocci represented 4.8%, 15.5% and 21.3%, in 1999, 2014 and 2015 respectively. Rates of infections in females were higher (58%, 67% and 65%) compared to males (42%, 33% and 35%) in the three years. In this study high resistance was found of *E. coli* and other gram-negative rods (47%, 44.1%) to ceftriaxone in 1999 year compared to 2014 and 2015 years (19.1%, 28.4%). Also found high resistance of *E. coli* and other gram-negative rods (29.8%, 28.4%) to nalidixic acid in 2014 and 2015 years compared to 1999 year (11.5%, 15.6%). Urinary tract infections UTIs are the most common infections in the community. Also, showed increased uropathogens resistance to most antibiotics. So, this leads to a significant financial burden on the health system.

1 Introduction

Urinary tract infections (UTIs) are highly common infections that can affect any region of the urinary system and are typically caused by bacteria (Motse *et al*., 2019). Urinary tract infections (UTIs) can be classified as urethritis (limited to the urethra), cystitis (infection of the bladder), pyelonephritis (infection of the kidneys), and vaginitis (infection of the vagina). (Bissong *et al*., 2017; Fosso *et al*., 2017).

UTIs may be classified as uncomplicated or complicated (Flores-Mireles *et al*., 2015).

Uncomplicated UTIs, which are often community-onset cystitis, are more common in outpatient settings (Nimri *et al*., 2017). and affect otherwise healthy people without anatomical or neurologic abnormalities of the urinary tract. Uncomplicated UTIs are more common in women of all ages, although they can also affect some groups of men, such as older men and infant boys. (O'Brien *et al*., 2017; Tambyah and Maki, 2000) On the other hand, complicated UTIs are associated with patient-level factors that compromise urodynamics or host defenses, such as indwelling or intermittent urinary catheterization, urinary obstruction (e.g., by stones) or retention,

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immunosuppression, renal failure, renal transplantation, and pregnancy. (Levison and Kaye, 2013; Lichtenberger and Hooton, 2008)

UTIs are a major public health concern today and cause more than 150 million cases of disease annually throughout the world. (Motse *et al*., 2019). UTIs are more likely to occur in women than men over all age groups (Abou Heidar *et al*., 2019) and up to 50% of women report having had at least one urinary tract infection in their lifetime (Agarwal *et al*., 2020). Rates of UTIs are higher in women compared with men. Because the anatomy of women differs from that of men, their urethra is shorter and there is relative proximity between the urethra and the anus (Walsh and Collyns, 2020). The rates of UTIs among sexually active young women have been reported to vary from 0.5 to 0.7 per person-year, while this incidence rate among young men was only 0.01 (Rowe and Juthani-Mehta, 2013). However, the prevalence of UTIs reduces during middle age but increases in older adults. In addition, several other factors such as sexual intercourse and the use of spermicides have also been shown to increase the risk of UTI in women (Walsh and Collyns, 2020).

80%–90% of UTIs are caused by uropathogenic *Escherichia coli* (UPEC) (Abraham and Miao, 2015; Ejrnaes *et al*., 2011), while 5%–10% are due to *Staphylococcus saprophyticus* (Nickel, 2008). These infections are rarely viral or fungal but can involve a much wider range of pathogens, especially *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Acinetobacter baumannii*, *Streptococcus*, and *Enterococcus faecalis* (Amdekar *et al*., 2011; Flores-Mireles *et al*., 2015; Mann *et al*., 2017; Saka and Okunuga, 2017; Salvatore *et al*., 2011)

Nowadays, the rise in uropathogens (UPs) antibiotics resistance leads to significant challenges in the treatment of urinary tract infections (UTIs). (Sweileh *et al*., 2018; Shaji *et al*.,2021; Silva *et al*.,2022). Indeed, many studies are conducted annually to assess the antibiotics resistance of UPs isolated from UTI patients, and the results almost always show an increase in antibiotic resistance over time. (Magyar *et al*., 2017; Sultan *et al*., 2015; Sweileh *et al*., 2018; Shaji *et al*.,2021; Silva *et al*.,2022).

This study aims to find out the rates of urinary tract infections in community, as well as their incidence in females compared to males. In addition to knowing the types of bacteria that cause urinary tract infections and their resistance to antibiotics.

2 Materials and Methods

This study collected data of bacterial isolates among 3687 patients with urinary tract infections in the microbiology department of Sabratha Teaching Hospital during the years 1999, 2014 and 2015. Including results of urine culture test, biochemical test and antimicrobial susceptibility test. Unfortunately, there is not enough information in recent years (after 2015) to be studied due to the lack of capabilities in the hospital in recent years.

In this study, the statistical analysis was done using the Chi-squares test by the program Epi 2000 Centers for Disease Control and Prevention [CDC], Georgia, Atlanta to analyze the results.

3 Results

This study included 3687 patients with urinary tract infections who were enrolled in the microbiology department`s records of Sabratha Teaching Hospital during the years 1999, 2014 and 2015

Uropathogens isolated from patients with urinary tract infections in 2014 (22.6%) were more than uropathogens isolated from patients with urinary tract infections in 1999 (15.4%), with significant differences statistically (P<0.000002, Odds ratio: 1.60). Also, uropathogens isolated from patients with urinary tract infections in 2015 (22.4%) were more than from uropathogens isolated from patients with urinary tract infections in 1999 (15.4%), with significant differences statistically (P<0.003, Odds ratio: 1.58). On the other hand, there were no significant differences statistically in uropathogens isolated in 2014 compared to the 2015 year (P>0.05). Table (1).

Found an increase in rates of isolation of uropathogens, the rates of isolated uropathogens were higher in 2014 and 2015 compared to 1999.

Table (1): The ratio of isolated uropathogens in patients with UTIs in 1999, 2014 and 2015 years

years	Number of samples	Number of uropathogens	%
1999	2579	398	15.4
2014	827	187	22.6
2015	272	*61	22.4
Total number	3678	646	17.6

* The results include four candida species

Rates of infections in females were higher than in males in the three years represented 58%, 67% and 65% of organisms isolated from females in 1999, 2014 and 2015 respectively, while ratios of organisms isolated from males were 42%, 33% and 35% in 1999, 2014 and 2015 respectively. (Table 2).

Table (2): The ratio of patients with UTIs according to gender in 1999, 2014 and 2015 years

years	Number of samples	males		females	
		Number of samples	%	Number of samples	%
1999	2579	1082	42	1497	58
2014	827	272	33	555	67
2015	272	94	35	178	65

Escherichia coli represented (11%) in 1999 year followed by *Klebsiella spp*. (3%). While the other uropathogens represented lower percentages. Table (3).

Table (3): Isolation rate of uropathogens in patients with UTIs in 1999 year

Type of bacteria	Number of samples =2579	
	Isolated number	%
Escherichia coli	277	11
Klebsiella spp.	81	3
Enterobacter spp.	3	0.1
Proteus spp.	4	0.1
Pseudomonas spp.	14	0.5
Staphylococcus aureus	9	0.3
Enterococcus spp.	10	0.4
total	398	15.4

In the 1999 year, rates of infections in females (17.3%) were higher than in males (12.8%) with significant differences statistically (P <0.002, odds ratio=1.4.2). As well as, *E. coli* isolated from females (12.3%) was more than from males (8.5%) with significant differences statistically (P <0.002, odds ratio=1.52).

In addition, *Klebsiella spp*., *Staphylococcus aureus*, and *Enterococcus spp*. isolated from females (3.5%, 0.5%, 0.5%) were higher compared to males (2.6%, 0.2%, 0.3%) without significant differences statistically (P>0.05). Table (4)

Table (4): Isolation rate of uropathogens in patients with UTIs according to gender in the1999 year

Type of bacteria	Males Number of samples=1082		Females Number of samples=1497	
	Isolated number	**%**	Isolated number	%
Escherichia coli	92	8.5	185	12.3
Klebsiella spp.	29	2.6	52	3.5
Enterobacter spp.	3	0.3	0	0.0
Proteus spp.	2	0.2	2	0.1
Pseudomonas spp.	8	0.7	6	0.4
Staphylococcus aureus	2	0.2	7	0.5
Enterococcus spp.	3	0.3	7	0.5
Total	139	12.8	259	17.3

In the 2014 year, *Escherichia coli* represented (4.2%) of uropathogens isolated from patients with UTIs while ratios of gram-negative rods, *Streptococcus* spp. and *Staphylococcus* spp. were 14.9%, 3%, 0.5% respectively. Table (5).

Table (5): Isolation rate of uropathogens in patients with UTIs in 2014 year

Type of bacteria	Number of samples = 827	
	Isolated number	%
Escherichia coli	35	4.2
Gram-negative rods	123	14.9
Streptococcus spp.	25	3.0
Staphylococcus spp.	4	0.5
Total	187	22.6

Rates of infections in females (25.4%) were higher than in males (17%) with significant differences statistically (P<0.007, odds ratio=1.67) in the 2014 year. Also, *Streptococcus* spp. isolated from females (4.2%) was more than from males (0.7%) with significant differences statistically (P<0.008, odds ration=5.84).

The isolation rate of *Escherichia coli*, Gram-negative rods and *Staphylococcus* spp. from females (5%, 15.7%, 0.5%) were greater than from males (2.7%, 13.2%, 0.4%) without significant differences statistically (P>0.05). Table (6).

Table (6): Isolation rate of uropathogens in patients with UTIs according to gender in the 2014 year

Type of bacteria	Males Number of samples= 272		Females Number of samples= 555	
	Isolated number	%	Isolated number	%
Escherichia coli	7	2.7	28	5.0
Gram-negative rods	36	13.2	87	15.7
Streptococcus spp.	2	0.7	23	4.2
Staphylococcus spp.	1	0.4	3	0.5
total	46	17	141	25.4

Escherichia coli isolated from patients with UTIs was (4.4%) among isolated uropathogens in the 2015 year. While Gram-negative rods, *Streptococcus* spp., *Staphylococcus* spp. and *Candida* spp. represent 11.7%, 4.4%, 0.4%, 1.5% respectively. Table (7)

Table (7): Isolation rate of uropathogens in patients with UTIs in 2015 year

Type of bacteria or fungi	Number of samples= 272	
	Isolated number	%
Escherichia coli	12	4.4
Gram negative rods	32	11.7
Streptococcus spp.	12	4.4
Staphylococcus spp.	1	0.4
Candida spp.	4	1.5
total	61	22.4

The rates of isolated uropathogenes from females (28%) were higher compared to males (11.7%) in 2015 year with significant differences statistically (P<0.003, odds ratio=2.95). In addition, *Escherichia coli* was isolated from females (6.7%) and not from males (0.0%) and the difference in the isolation rates between females and males was statistically significant (P<0.02, odds ratio=undefined).

Also found the isolation rate of Gram-negative rods, *Streptococcus* spp. and *Candida* spp. higher in females (13.5%, 5.6%, 2.2%) compared to males (8.5%, 2.1%, 0.0%) without significant differences statistically (P>0.05). Table (8).

Table (8): Isolation rate of uropathogens in patients with UTIs according to gender in the 2015 year

Type of bacteria or fungi	Males Number of samples= 94		Females Number of samples= 178	
	Isolated number	%	Isolated number	%
Escherichia coli	0	0.0	12	6.7
Gram negative rods	8	8.5	24	13.5
Streptococcus spp.	2	2.1	10	5.6
Staphylococcus spp.	1	1.1	0	0.0
Candida spp.	0	0.0	4	2.2
total	11	11.7	50	28

This study found high resistance with significant differences statistically (P<0.0004, Odds ratio=3.73) of *E. coli* (47%) to ceftriaxone in the 1999 year compared to 2014 and 2015 years (19.1%). On the other hand, found high resistance with significant differences statistically (P<0.001, Odds ratio=3.25) of *E. coli* (29.8%) to nalidixic acid in 2014 and 2015 years compared to 1999 year (11.5%).

Regarding isolated gram-negative rods were more resistant (44.1%) to ceftriaxone in the 1999 year compared to 2014 and 2015 years (28.4%) with significant differences statistically (P<0.01, odds ratio=1.99). Also found high resistance with significant differences statistically (P<0.02, odds ratio=2.13) of Gram-negative rods (28.4%) to nalidixic acid in 2014 and 2015 years compared to 1999 year (15.6%). While there were no statistically significant differences in the antibiotic Augmentin. Table (9).

Table (9): Resistance of *E. coli* and Gram-negative rods in patients with UTIs to Augmentin, Ceftriaxone and Nalidixic acid in1999, 2014 and 2015 years.

Antibiotics	years							
	1999				2014&2015			
	Escherichia coli		Gram-negative rods		*Escherichia coli*		Gram-negative rods	
	The number 277 =	%	The number= 102	%	The number= 47	%	The number= 155	%
Augmentin	74	26.7	34	33.3	8	17	52	33.5
Ceftriaxone	130	47	45	44.1	9	19.1	44	28.4
Nalidixic acid	32	11.5	16	15.6	14	29.8	44	28.4

In three years found high resistance of *E. coli* and other gram-negative rods to most antibiotics used. Table (10, 11).

Table (10): Resistance of *E. coli* and Gram-negative rods in patients with UTIs to Ampicillin, Chloramphenicol, Co-trimethoxazole and Nitrofurantion in1999 year.

Antibiotics	*Escherichia coli*		Gram-negative rods	
	The number= 277	%	The number = 102	%
Ampicillin	149	53.7	52	51
Chloramphenicol	86	31	38	37.2
Co- trimethoxazole	110	39.7	35	34.3
Nitrofurantion	38	13.7	46	45

Table (11): Resistance of *E. coli* and Gram-negative rods in patients with UTIs to Ceftazidime, Cefuroxime, Ciprofloxacin and Gentamicin in 2014 and 2015.

Antibiotics	*Escherichia coli*		Gram-negative rods	
	The number= 47	%	The number= 155	%
Ceftazidime	3	6.4	26	16.8
Cefuroxime	11	23.4	45	29
Ciprofloxacin	10	21.3	30	19.4
Gentamicin	9	19	20	13

4 Discussion

Many studies conducted in the past showed that urinary tract infections were among the most common bacterial infections. Due to the high prevalence of urinary infections, it is projected that their identification and treatment will have a significant economic impact, resulting in substantial yearly healthcare costs. (Islam *et al*., 2022; Motse *et al*., 2019; Foxman, 2010; Zeng *et al*., 2022; Sammon *et al*., 2014; Stamm and Norrby., 2001; Flores-Mireles *et al*., 2015; Pezeshki Najafabadi *et al*., 2018; Medina and Castillo-Pino., 2019).

UTIs are more likely to occur in women than men over all age groups (Abou Heidar *et al*., 2019; Foxman, 2014; Geerlings, 2016) and up to 50% of women report having had at least one urinary tract infection in their lifetime (Agarwal *et al*., 2020)

In this study isolation rate of uropathogens in patients with urinary tract infections in 2014 (22.6%) and 2015 (22.4%) was more than from isolation rate of uropathogens in patients with urinary tract infections in 1999 (15.4%), with significant differences statistically. On the other hand, there were no significant differences statistically in uropathogens isolated in 2014 compared with the 2015 year. This indicates an increased incidence of urinary tract infections in the community, Although the number of patients who visited the hospital was lower in 2014 and 2015 years compared to 1999 year. This is due to the lack of facilities in government hospitals and the tendency of patients to private hospitals. The prevalence of urinary tract infections varies according to geographic and health conditions, as the deterioration of health and economic conditions has caused a high rate of infection and the spread of many diseases.

Zeng *et al* (2022) conducted a study in China, on UTIs burden in 204 countries and territories from 1990 to 2019. Data were obtained from the Global Health Data Exchange GBD Results Tool. The study showed an increase in the global number of individuals with UTIs from approximately 252.2 million to more than 404.6 million, an increase of approximately 152.4 million cases. the number of incident cases was significantly higher in females than males in all years from 1990 to 2019. Also, the number of deaths increased from approximately 99 000 to 237 000-an increase of approximately 130 000 deaths. The study results suggest a globally rising trend of UTI burden between 1990 and 2019.

The present study *Escherichia coli* was the most commonly isolated uropathogens in all years followed by gram negative rods and Gram-positive cocci.

Similar results were also reported in previous studies, a study conducted from June 2015 to January 2016 at Siddhi Memorial Hospital, Bhaktapur, Nepal, showed that *E. coli* was the most common pathogen (58.7%), followed by *Klebsiella pneumoniae* (22.5%). (Ganesh *et al*., 2019)

Another study was conducted in The Department of Pediatrics, Harran University Medical Faculty Hospital, Sanliurfa, Turkey from May 2015 to May 2017. *Escherichia coli* was detected in (58.9%) of the patients, *Klebsiella* (17.9%) and *Proteus* (15.8%). (Demir and Kazanasmaz., 2020)

Islam *et al* (2022) conducted a study in Dhaka, Bangladesh during 2016–2018. *E. coli* (51.6%) was the predominant causative pathogen followed by *Streptococcus spp*. (15.7%), *Klebsiella spp*. (12.1%),

Enterococcus spp. (6.4%), *Pseudomonas* spp. (4.4%), coagulase negative *Staphylococcus spp*. (2.0%), and other pathogens (7.8%).

A recent study was conducted at the Cumilla Medical College Hospital's Medicine Department in three phases (2011, 2016, 2021), In Bangladesh. *Escherichia coli* (62% in 2021, 86% in 2016 and 76% in 2011) and *Klebsiella* species (11% in 2021, 10% in 2016 and 11% in 2011) were the most frequently isolated bacteria over the study period. (Majumder *et al*., 2022).

The pathogenicity of uropathogens (UPs) is associated with the expression of several virulence factors (VFs), such as adhesion elements, toxins, capsules, flagella, serum resistance factors, and iron uptake systems (Rodriguez-Siek *et al*., 2005).

The prevalence of urinary tract infections in females is higher than in males. (Abou Heidar *et al*., 2019; Walsh and Collyns, 2020). Several predisposing factors might contribute to the higher prevalence of UTIs among women. (August and de Rosa, 2012). It is well recognized that UTI is more prevalent in female than in male, and the present study corroborates this generalization and correspond with many previous studies. Deshpande *et al*., 2011; Sharifan *et al*., 2006; Majumder *et al*., 2022; Ahmed *et al*, 2019; Islam *et al*., 2022).

The current study showed that urinary tract infections occurred in women more than men in the three years. higher incidence of UTI in women compared with men is explained by the anatomy of women because, compared to men, their urethra is shorter and there is relative proximity between the urethra and the anus. In addition, several other factors such as sexual intercourse and the use of spermicides have also been shown to increase the risk of UTI in women. Spermicides affect the vaginal microbial flora, which leads to a reduction in lactobacilli and allows the proliferation of potentially pathogenic bacteria in the genital tract (Walsh and Collyns, 2020). Furthermore, menopause can also significantly increase the risks of recurrent UTIs. Indeed, the reduction in estrogen levels can promote vaginal atrophy and lead to vaginal dryness and an increase in pH, which alters the vaginal flora and also reduces the level of lactobacilli. (Bleibel and Nguyen, 2022; Kasap *et al*, 2019).

Regarding resistance of uropathgens to antibiotics, this study found high resistance of *E. coli* and other gram-negative rods to most antibiotics used in three years. Furthermore, high resistance with significant differences statistically of *E. coli* (47%) and other gram-negative rods (44.1%) to ceftriaxone in 1999 year compared with 2014 and 2015 years (19.1% *E. coli*, 28.4% gram-negative rods). Also, found high resistance with significant differences statistically of *E. coli* (29.8%) and other gram-negative rods (28.4%) to nalidixic acid in 2014 and 2015 years compared to the 1999 year (11.5% *E. coli*, 15.6% gram-negative rods).

The reason for decrease in the resistance to ceftriaxone in the 2014 and 2015 years compared to the 1999 year and increased the resistance to nalidixic acid in 2014 and 2015 years compared to the 1999 year perhaps is deteriorating economic conditions and high prices, especially drugs. And because the price of ceftriaxone antibiotic is more expensive than nalidixic acid antibiotic. So, the tendency was to use nalidixic acid antibiotic in the treatment of urinary tract infections. This confirms the higher use of antibiotics leads to increased resistance of bacteria to antibiotics.

The result in the study similar to a study conducted in Bangladesh from June 2011 to June 2021 revealed the highest resistance (>70%) was observed against *E. coli Klebsiella spp*., and *Proteus spp*. to almost all the tested antibiotics except carbapenem. (Majumder *et al*., 2022).

Another study found drug resistance in 92% (n = 82/89) of samples, with most (80%) being resistant to at least two drugs. (Ahmed *et al*., 2019)

The incidence of UTIs caused by multidrug-resistant uropathogens has been increasing at an alarming rate worldwide. Such common infections can turn into life-threatening illnesses, especially in developing countries. (Mazzariol *et al*, 2017; Gupta *et al*, 2012).

Several studies have revealed that there is a correlation between virulence factors (VFs) and antibiotic resistance (Karam *et al*., 2018; Momtaz *et al*., 2013; Paniagua-Contreras *et al*., 2017; Shah *et al*., 2019; Tabasi *et al*., 2015). In general, in bacteria, whether they are UPs or not, several mechanisms such as changes in cell permeability and multiple efflux pumps, mutations of the antibiotic target, and horizontal transfer of resistance genes are responsible for the development of the antibiotic resistance (Mukherjee, 2019; Palma *et al*., 2020).

Effective treatment of patients with bacterial urinary tract infections is often dependent on pathogen

identification and antibiotic selection based on ongoing surveillance of the antimicrobial susceptibility pattern of urinary tract pathogens in specific regions. (Grigoryan *et al*., 2014)

5 Conclusions

Urinary tract infections are the most common infections in the community. Due to the high prevalence of infection in the community and hospital setting, urinary tract infections have imposed a significant financial burden on the health system. If UTIs are not treated can turn into life-threatening illnesses. prevalence of UTIs in females is higher than in males. And showed increased uropathogens resistance to most antibiotics used for the treatment of UTIs. This causes problems in future to treat UTIs.

Each center's identification of its uropathogens and antibiotics susceptibilities at specific intervals is important in terms of increased treatment success, prevention of unnecessary antibiotics use and prevention of antibiotics resistance. Also, should be reduce common use of antibiotics to avoiding development resistance of bacteria to antibiotics.

Conflict of Interest: The authors declare that there are no conflicts of interest.

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