Retrospective Analysis of Bacterial Urinary Tract Infections Documented in the Health Record System (2013-2017) of Entoto Number One Health Center, Addis Ababa

By
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Abstract

Urinary tract infection (UTI) is caused by an array of pathogens. But, UTI of bacterial origin is by far the most common one affecting millions of people worldwide. The present retrospective study was conducted to assess the status of UTI in Entoto Number One Health Center (ENOHC), Addis Ababa. The objective of this study was to assess yearly trend, and the distribution of UTI based on gender and age among patients who visited ENOHC from 2013 to 2017. Data collected from the health center's record office from 1 February to 31 May 2018, processed and analyzed using SPSS version 20.Chi-squared test was used to test age, gender-based variations, and yearly differences at p-value ≤0.05,Totally 1805 (6.0%) were examined by urinalysis and microscopy and were positive for bacterial UTI. The study shows that yearly UTI prevalence in the study area increased successively for the last five years. It was 3.7, 6.0, 7.5, 8.0 and 8.3% in 2013, 2014, 2015, 2016, 2017. From a total positive 1293(71.6%; 95% CI: 69.4-73.7%) were females and 512(28.4%, 95% CI: 26.3-30.6%) males with female to male ratio of 2.5:1.The mean age was 34.33 (95% CI: 33.72-35.26) and standard deviation 16.189. The prevalence of UTI based on age group, the highest proportion (26.3%) was noted in the age group 15-24 years, and the lowest (0.4%) among 0-4 age grouped. From the highest age distribution of 15-24, 19.2% were females and 7.1% males. The proportion of UTI-positive patients among females was significantly higher. Females, especially women of child bearing age were highly affected. Overall, the findings demonstrate that UTI remains a growing challenge in the health center. Regular monitoring and devising appropriate intervention mechanisms is required.

Keywords: *prevalence, retrospective, urinary tract infection*

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Acronyms

ASB	Asymptomatic Bacteria
BA	Blood Agar
CAUTIs	Catheter Associated Urinary Tract Infections
CFU	Colony Forming Units
CL	Confidence Level
CLED	Cysteine Lactose Electrolytes Deficient
CLSI	Clinical and Laboratory Standard Institute
CNS	Coagulase Negative Staphylococci
CT	Computed Tomography
DM	Diabetes Mellitus
EAU	European Association of Urology
EPI	Expanded program in Immunization
ENOHC	Entoto Number One Health Center
ESIU	European Section of Infection in Urology
EXPEC	Extraintestinal Pathogenic *Escherichia coli*
HPA	Health Protection Agency
IBM	International Business Machines
MAC	MacConkey
MGS	Metagenomic Sequencing
MRI	Magnetic Resonance Imaging
MSU	Mid-Stream Urine
NHANES-III	National Health and Nutrition Examination Survey III
ORENUC	No Risk Factor Recurrent Extraurogenital Nephropathy Urologic Catheter
RPM	Rotation per Minute
RUTI	Recurrent Urinary Tract Infection
SMX	Sulfamethoxazole
TMP	Trimethoprim
SPSS	Statistical Package for the Social Sciences
UPEC	Uropathogenic *Escherichia coli*

UN	United Nations
UT	Urinary Tract
UTI	Urinary Tract Infection
VUR	Vesico Ureteral reflux
WBC	White Blood Cell
WHO	World Health Organization

1. Introduction

Urinary tract infection (UTI) is an infection caused by the presence and growth of pathogens anywhere in the urinary tract (UT) including the kidney, ureter, bladder, and urethra and produce inflammation (Dielubanza and Schaeffer, 2011; Getachew Kabew *et al*., 2013; Kekuda *et al*., 2014; Tan and Chlebicki, 2016).The causative agents of UTIs are bacteria, viruses (especially adenoviruses), protozoa (*Trichomonas vaginalis)*, fungi, particularly *Candida spp*, and to a lesser extent *Aspergillus spp* and *Cryptococcus neoforman*, and helminths like *Schistosoma haematobium* (Zorc *et al*., 2005; Abdurehman *et al*., 2013; Grabe *et al*., 2015).

Even though these diversified group of pathogens can cause UTI, almost 95% of the cases are attributed to bacteria, the non-bacterial are less common and tend to occur more often in immunosuppressed individuals (Bonadio *et al*., 2001; Zorc *et al*., 2005; Mittal *et al*., 2017). Nearly 85% of UTIs are caused by the Gram-negative bacillus *Escherichia coli* and the rest by other Gram-negative bacteria like *Proteus mirabilis, Klebsiella pneumoniae*, *Pseudomonas aeruginosa, Acinetobacter* spp. and *Serratia* spp. In contrast, Gram-positive bacteria that are commonly implicated in UTI are *Enterococcus faecalis, Staphylococcus saprophyticus* especially coagulase-negative cause 15% and *Streptococcus agalactiae* (Zorc *et al*., 2005; Vasudevan, 2014; Flores-Mireles *et al*., 2015; Awoke Derbie, *et al*., 2017).

The uropathogenic bacteria can invade the UT through ascending, haematogenous or descending and lymphatic route. However, almost all urobacterial infections commonly originated from rectal flora multiply at the opening of the urethra and travel up to the bladder through ascending route . Much less often, bacteria spread to the kidney from the bloodstream. In general, UTIs are commonly seen in the lower UT (urethra and bladder) and if not properly treated may ascend to the upper parts, ureters and kidneys, causing severe damaged to these organs (Grabe *et al*., 2015; John *et al*., 2016).

UTI is among common diseases affecting a large number of people ranking next to respiratory tract infections flu and common cold (Vasudevan, 2014; Moue *et al*,. 2015; Ogbukagu *et al*., 2016; Tan and Chlebicki, 2016; Mittal *et al*., 2017; Ranjan *et al*., 2017). The problem is wide spread both in the community and healthcare settings. UTI affects all age groups from neonate to geriatric, and both male and female. However, women are more vulnerable than men due to some anatomical and physiological factors (Shaikh *et al*., 2008; Kekuda *et al*., 2014; Vasudevan, 2014; Ogbukagu *et al*., 2016). Anatomically, the urethra in females is short, straight, wider, drier urethral meatus and close association with anus. As a result, it is easily and highly contaminated by fecal flora of digestive tract or vagina cling to the opening of the urethra and begins to multiply. The other factor is reproductive physiology the absence of prostatic secretion, pregnancy and menopause are associated with increased likelihood of having UTIs (Krishnan, 2005; Turay *et al*., 2014; Dhungana and Shakya, 2015; John *et al*., 2016; Subhashini *et al*., 2016; Ranjan *et al*., 2017).

Diagnosis of UTIs in low-income countries is mainly based on signs and symptoms. Clinical symptoms of UTI are characterized by urinary frequency, dysuria, abdominal pain, back pain, fever, suprapubic discomfort, inability to empty the bladder completely. In addition to symptom the signs of UTI are indication of blood in urine, unpleasant odor and cloudy color of urine. Especially during Pregnancy rate of UTI is very high due to hormonal, mechanical and physiological change in UT and cause the following complications can develop pyelonephritis, hypertensive disease of pregnancy, anaemia, chronic renal failure, low birth weight premature delivery and higher fetal mortality rate (Foxman ,2002; Moya *et al*., 2010; Dhungana and Shakya, 2015; John *et al*., 2016; Ranjan *et al*., 2017). Laboratory diagnosis of bacterial UTI is routinely done by collection of midstream urine specimens for urinalysis, microscopic examination and culture

2. Problem Statement

Numerous surveys showed that UTI is among the major health problem in Ethiopia (Abdurehman Eshete *et al*., 2013; Getachew Kabew *et al*., 2013; Asrat Agalu *et al*.,2014; Fatuma Ahmed *et al*., 2016; Tigist Gezmu *et al*.,2016; Awoke Derbie, *et al*.,2017; Matifan Dereje *et al*., 2017). The studies indicate the prevalence and antimicrobial resistance patterns of bacterial UTIs in the general and specific group of populations at the hospital level. Asrat Agalu *et al*., 2014 and Awoke Derbie *et al*., 2017 reported from north Ethiopia in Dessie and Bahirdar, Fatuma Ahmed *et al.*, 2016 and Tigist Gezmu *et al*., 2016 from Borena and Arba Minch in the south respectively. The problem is believed to be enhanced by a number of contributing factors like large population size, lower coverage of healthcare system and shortage of health professions.

Residents of Addis Ababa have the advantage of obtaining a better healthcare services compared to the peripheral areas. However studies indicate similarly high prevalence of UTI particularly among females. Adane Bitew *et al*., 2017 and Matifan Dereje *et al*., 2017 reported 81.3% and 58.1% from Arsho Advanced Medical Laboratory and Hamlin Fistula Hospital respectively. Apart from these reports information about UTIs in Addis Ababa is limited. Many of studies conducted in the UTI shows that Women shoulder carries the greatest burden. Therefore assessing the magnitude of UTIs is very important to reduce the burden of morbidity and related complications. There are no enough data describing the problem of UTI in primary care especially at the health center level in Addis Ababa. This study was, thus, aimed at assessing retrospective UTI cases in the last five years (2013-2017) as reported by ENOHC in Addis Ababa.

3. Objectives

3.1 General objective

The general objective of this study was to estimate the prevalence of UTIs among patients admitted to ENOHC in the last 5 years.

3.2 Specific objectives

The study had the following specific objectives.

3.2.1 To assess yearly trend of UTI cases

3.2.2 To assess gender, age and yearly distribution of UTI among the study population

4. Literature Review

4.1 Global burden

UTI is a widespread infectious disease next to respiratory infection prevailing in both low- and high-income nations (Rahimkhani *et al*., 2008; Moya *et al*., 2010; August *et al*., 2014). Studies show that UTI remains one of the most common infections occurring in the community, in hospitals and other healthcare institutions (Mittal *et al*., 2009; Najar *et al*., 2009; Asrat Agalu *et al*., 2014; Kekuda *et al*., 2014 ; Moue *et al*., 2015). Global estimation of annual UTIs reaches as many as 8.3 million visits to outpatient clinic (Naber *et al*., 2008). In low-income countries annual incidence of UTI is about 250 million (Ranald *et al*., 2001). It accounts for nearly 7 million office visits and 1 million emergency department visits, resulting in 100,000 hospitalizations each year even in technologically advanced countries like the US with annual healthcare cost of an estimated 1.6 billion US dollars and rising (Grude *et al*., 2001; Grabe *et al*., 2015; Smelov *et al*., 2016).Thus, the economic loss related to this infection particularly for antibacterial drugs is substantial.

Particularly, UTI highly affects women, at least one third of women developing a UTI before the age of 24 years (Subhashini *et al*., 2016). Women carry the greatest burden of UTI, with a greater predilection for infection after the first year of life. According to the National Health and Nutrition Examination Survey III data (NHANES-III), the lifetime prevalence of UTI is 53,067 cases per 100,000 women, compared with 13,689 cases per 100,000 men (Griebling, 2005). The widest gender gap occurs in young adulthood between ages 16 and 35 years (Dielubanza and Schaeffer, 2011). UTI during pregnancy may cause complications such as pyelonephritis, hypertensive disease of pregnancy, anemia, chronic renal failure, premature delivery and fetal mortality (Moyo *et al*., 2010; Minardi *et al*., 2011).

4.2 Etiology

UTIs are caused by bacteria, viruses, protozoa, fungi and helminthes. However, the predominant causes are bacteria and fungi as occasional agents especially in diabetic patients (Selamu Kebamo *et al*., 2017).The most widely identified bacterial species associated with UTI are *E. coli K. pneumoniae*, *P. mirabilis, P. aeruginsa, E faecalis* and *S. saprophyticus,* a Gram-positive coagulase negative *Staphylococcus*. *E. coli* remains the most common causative agent of UTI accounting to 80-85% of the cases and *Staphylococcus* species constitutes to 10-15% (Vasudevan, 2014; Awoke Agalu *et al*., 2017). *Klebsiella, Pseudomonas, Proteusa* and *Enterococcus* species play a minor role in conferring the infection (Vasudevan, 2014). However, *S aureus* was isolated in 15.5% of patients which may have developed UTI due to increased frequency of hospital acquired infection (Dhangana and Shakya, 2014).

4.3 Classification

Classification of UTI is very important for clinical decisions, research, quality measurement and teaching (Johansen *et al*., 2011).Traditionally, UTIs can be classified based on clinical symptoms, laboratory data and presence of bacteria in urine and practically categorized uncomplicated and complicated. Therefore for effective management of UTI appropriate classification is very important and the simplified guideline prepared by the European Association of Urology (EAU) and European Section of Infection in Urology (ESIU) is used as a working instrument for daily patient assessment and clinical research purpose. The guideline is based on clinical presentation, host risk factors, and severity scale, and known as ORENUC. In adults, uncomplicated UTIs fall under categories O, R and partially E, while complicated UTIs are mainly in categories N, U and C ESIU (Grabe *et al*., 2015; Smelov *et al*., 2016; Tan and Chlebicki, 2016).

Recurrent UTIs are symptomatic cases mainly caused by reinfection of UT by the same pathogen following eradication of previous infection as confirmed by negative urine culture. Such infections are usually common in young women which have anatomically and physiologically normal UT system. By convention, the term recurrent UTI is reserved for a pattern of two or

more infections within 1 year (Al-Badr and Al-Shaikh, 2013; Dielubanza and Schaeffer, 2011; Tan and Chlebicki, 2016).

UTIs are characterized as being either upper or lower based primarily on the anatomical location of the infection. While the lower UT encompasses the bladder and urethra, the kidneys and the ureters form the upper (John *et al*., 2016). Upper UTIs result in pyleonephritises infection of kidney of different nature like acute, chronic and interstitial. For example, acute pyelonephritis is an inflammation of one or both kidneys and sometimes include lower tract and characterized by fever, chills, and flank pain. Patients may also experience nausea and vomiting. The infection caused by *E. coli* of the renal parenchyma that spreads up the UT or from an obstruction in the UT. Obstruction means backflow urine into the ureters and kidneys (Dielubanza and Schaeffer, 2011; Roberts, 1991).Chronic pyelonephritis is a particular type of pathology of the kidney caused by UTI, vesicoureteral reflux or anatomical abnormality (Pulipati *et al*., 2017).

Lower UTIs include cystitis and urethritis. Cystitis is a bacterial infection in the bladder that often moves up from the urethra and urethritis is to an inflammation or infection of the urethra. Both upper and lower UTI can be further divided into complicated and uncomplicated. The uncomplicated UTI is infection in normal UT, both structurally and physiologically, whereas the complicated one is associated with structural or functional abnormality. During complicated UTI cystitis of long duration or hemorrhagic cystitis occurs. UTIs usually develop first in lower and if untreated, they may progress to the upper part resulting in complications (Park, 2012; Pulipati *et al*., 2017).

4.4 Pathogenesis

Microorganisms can reach and cause infections in the UT through the routes of ascending, haematogenous or descending route and lymphatic path way (Grabe *et al*., 2015). But commonly uropathogens originate from rectal flora external (genital and perineal) and enter the UT via the urethra into the bladder. The enhancement of this route is exacerbated in patients with soiling around the perineum, with urinary catheters and in females that use chemical contraceptive such as spermicidal agents (Foxman, 2002). The causes of infections are by urinary catheterization,

circumcision status in males, periurethral flora, micturation disorders, bowel disorders, and hygienic measures are important factors involve in the pathogenesis of UTI (Mustafa *et al*., 2012; John *et al*., 2016).

Haematogenous infection of the UT is restricted to a few relatively uncommon microorganisms, such as *S. aureus*, *Candida* sp., *Salmonella* sp. and *Mycobacterium tuberculosis*, which cause primary infections elsewhere in the body (Grabe *et al*., 2015).

Pathogenic mechanisms are also complicated and influenced by biological and behavioral features of the host as well as adhesions from the invading uropathogen. Adherence is a key event initiating each step in UTI and depends on three major features; bacteria's own adhesive mechanism, the receptive features of the urothelium organism and finally the fluid that is present between both surfaces. Adhesins found on the surface of the bacterial membrane are responsible for initial attachment on to UT tissues forming a biofilm (John *et al*., 2016).

The pathogenesis of UTI is the results of interaction between specific infecting bacteria and UT epithelium nature. Studies revealed that most uropathogens colonize the colon, the perianal region, and in females the periurethral region forming a biofilm that usually resists the body's immune response (John *et al*., 2016). The largest proportion of UTI was caused by *E. coli* and this is due to its possession of virulence factors that not only aid in mucosal adherence and climb, but also evasions of host immune response (Dielubanza and Schaeffer, 2011). Adhesions can be fimbrial or nonfimbrial, and mediate attachment to epithelial receptors. Mannose-sensitive, type-1 pili are expressed widely across *E. coli* subtypes and appear to be among the most important adhesions for establishing colonization and infection (Dielubanza and Schaeffer, 2011).

Catheter-associated UTIs (CAUTIs) put an unnecessary burden on patients and healthcare systems. A single insertion of a catheter into the urinary bladder in ambulatory patients results in urinary infection in 1-2% of cases and indwelling catheters with open-drainage systems result in bacteriuria in almost 100% of cases within 3-4 days (Grabe *et al*., 2015).

4.5 Predisposing factors

The urinary system is biologically structured help to prevent infections. The flow of urine from the bladder is designed to wash bacterial out of the body. The ureters and bladder are made to prevent urine from backing up towards the kidneys. Despite all these, infections still occurs due to several risk factors and abnormalities of UTI that interfere with its natural resistance to infections (Subhashini *et al*., 2016).The predisposing factors are alterations of the host's natural defense mechanisms, anatomical, physiological and behavioral risk factor, sex ,age and urinary stasis. Additionally disease condition aggravate UTI such as Obstruction, hospitalization, catheterization, diabetes mellitus, sickle cell disease, kidney stones and spinal cord injury (Valiquette, 2001; Al-Badr and Al-Shaikh, 2013; Grabe *et al*., 2015; Pulipati *et al*., 2017). Especially, in women a number of factors that aggravate vulnerability of UTI. For instance, when, we see Anatomy and physiology. The anatomy of urethra in female is short (average 4.0 cm) comparing to that of male which is about 15cm (Hickling *et al*., 2015).On the other hand, when we see physiological factor estrogen is the most important age-specific risk determinant for UTI. Estrogen maintains acidic vaginal pH and lactobacillus proliferation, which are the greatest host defenses against pathogenic colonization. Withdrawal of estrogen at the time of menopause leads to conversion of the predominant vaginal flora from lactobacillus to *E. coli* and other Enterobacteriaceae, thus increasing the incidence of infection (Patterson and Andriole, 1987; Dielubanza and Schaeffer, 2011).

In Addition, host behavioral risk factors include voiding dysfunction, high intercourse frequency, and oral contraceptive and spermicide use (John *et al*., 2016). Additional predisposing factors are low socioeconomic status and previous treatment for UTI. Patients with asymptomatic UT bacteriuria, 25%, will develop symptomatic UTI (cystitis, pyelonephritis) than those without (Ronald, 2003; Nabbugodi *et al*., 2015).

Especially acute pyelonephritis in children may lead to renal scarring with the risk of later hypertension, preeclampsia during pregnancy, proteinuria, and renal insufficiency (Park, 2012). Patients with UTIs are primarily young, sexually active women, who experience dysuria, frequency, and urgency but yield fewer than 10^5 (e.g. over 100,000) colony forming units (CFU)

per ml on culture. The more severe types of urinary tract infection are less common but usually require hospital admission for patient management. Different from the above listed factors circumcision have a role in reduction of UTI but uncircumcised boys have a tendency to harbor organism in the foreskin likely due to the warm moist mucosal environment (Mulugeta Erifo, 2012; Mustefa *et al*., 2012).

4.6 Diagnosis

UTIs are very common infectious disease and account for the majority of the workload in the clinical microbiology laboratory (Oyaerta *et al*., 2018). They are challenging, not only the large number of infections that occur each year, but also diagnosis is not easy task (Kolawole *et al*., 2009).Therefore diagnosis of UTI could be based on a focused patient's history, description of symptoms and individual risk factors (Hummers-Pradier and Kochen, 2002).

The symptoms of a UTI depend on age, gender, the presence of a catheter, and part of the UT that has been infected (Pulipati *et al*., 2017). In general, the symptoms are characterized by urinary frequency, urgency, fever, dysuria, abdominal pain, suprapubic discomfort, and inability to empty the bladder completely and haematuria. The urine affected individuals may have unpleasant odor and appear cloudy systemic symptoms are usually slight or absent (Ranjan *et al*., 2017). The physicians must distinguish UTI from other diseases that have a similar clinical presentation, some UTIs are asymptomatic or present with strange signs and symptoms, for example, the diagnosis of UTIs in neutropenic patients (who do not typically have pyuria) may require different diagnostic criteria than those used for the general patient (Wilson and Gaido, 2004).

Laboratory diagnosis consists of urinary white blood cell (WBC) count, dipstick analysis and urine culture. Microscopy is a valuable diagnostic tool for patients with urinary symptoms. The urine samples were thoroughly mixed and aliquots centrifuged at 5000 rpm for 5 min. The sediments were investigated using microscope with a magnification of 10x and 40x objective lens. Urine which consists of 9 WBCs or less was considered as normal while those with ≥10 were regarded as pyuria .Microscopic test has limitations in detecting bacteriuria and pyuria because of lack of standardization for the microscope itself (including magnification) and the

volume of urine that can be observed, stained or unstained. However, if microscopy is performed, the absence of pyuria should cause a physician to reconsider UTI as a diagnosis (Nickel, 2005).

Urinanalys is made with regard to typical complaints and the presence of WBC and nitrites in the urine (Hummers-Pradier and Kochen, 2002). Leukocyte esterase and nitrite are the most commonly indices from the urine dipstick screening assay. The presence of leukocyte esterase suggests pyuria, indicative of host inflammatory response. Nitrite is the product of bacterial reduction of urine nitrate, and suggests the presence of gram-negative bacteria. Although they are less sensitive than microscopic examination of the urine, they provide additional confirmation of a UTI when contemplating empiric therapy and while culture results are not available (Nickel, 2005; Dielubanza and Schaeffer, 2011).

Urine culture is a standard criterion for the diagnosis of UTI. Properly collected urine (midstream or catheterized specimen) and cultured quickly or refrigerated (McCartney *et al*., 1989). All culture media are incubated at 35-37°C for at least 18 hours for optimal growth. Culture provides information regarding the number of CFU/ mL and it delivers isolated colonies that can be used for identification and susceptibility testing. But cysteine lactose electrolytes deficient (CLED) agar medium incubated at 37°C for 24 hours and growth of one type of organism of $>10^5$ CFU was considered as significant bacteriuria. Identification of isolates was done by observing colonial morphology on CLED medium. Colonies were further identified using standard biochemical (McCartney *et al*., 1989).

Clinical findings currently based on, dipstick or microscopy and culture tests, remain the standard methods for diagnosing UTIs (Smelov *et al*., 2016). Especially, urine culture is performed to isolate a single bacterim specious of the infecting pathogens and for antimicrobial susceptibility testing. However culture have certain limitation because applied for only culturable aerobic bacteria and does not comprise fastidious and anaerobic bacteria (Wilson and Gaido, 2004).Today, the advancement of technologies develop a novel diagnostic approach, metagenomic sequencing (MGS), will further explore the interactions between the host and microorganisms in the urogenital tract does not require isolation of bacteria. It provides more information than the standard urine culture about the spectrum of organisms that are present in

the urinary microbiota. MGS permits extremely high throughput at relatively low cost per base pair and generates millions of sequence reads per sample for multiple samples in a single sequencing run (Brubaker and Wolfe, 2015).

Furthermore, many patients with recurrent UTIs do not respond to appropriate antimicrobial therapy after 5 to 6 days of treatment hematuria, radiologic investigations and cystoscopy are required. Currently renal ultrasonography is the preferred UT imaging technique because it is noninvasive, easy-to-perform and relatively inexpensive. Computed tomography (CT) and magnetic resonance imaging (MRI) offer the best anatomical detail, but because of cost they may not always be the most appropriate screening procedures (Nickel *et al*., 1992).

4.7 Treatment

Management based on dipstick testing and empirical use of first-line antibiotics is still appropriate for patients with uncomplicated UTI (Hummers-Pradier and Kochen , 2002). UTI is one of the most common infections disease and account a large proportion of antibacterial drug consumption (Grude *et al*., 2001). Antimicrobial therapy is the core treatment for UTIs, with the main objective being the eradication of bacteria growth in the UT through an efficacious, safe and cost-effective antimicrobial agent. First-line antibiotic is trimethoprim -sulfamethoxazole in communities with resistance rates for *E. coli* <20%. This antibiotic should be avoided in women who have been treated within six months, as they are more likely to have resistant organisms. Second-line antibiotic or first-line in resistant communities is fluroquinolones - ciprofloxacin, levofloxacin, norfloxacin, ofloxacin (Pulipati *et al*., 2017).

Alternative method to maintain the health of the urinary system is usage of natural products that have diuretics and antimicrobial effects. Natural products have many advantages comparing to synthetic and semisynthetic drug products to treat UTI .The advantages are less side effects and have low cost. Some of the examples were listed by Pulpati *et al*.(2017), pineapple (*Ananas comosus*). This fruit possesses an enzyme bromelian that have anti-inflammatory property which reduces UTI symptoms. Daily intake of one cup of pine apple juice helps to cure UTI. It is recommended to take prescribed antibiotics along with pine apple juice.

Clove *(Syzygium aromaticum*) oil is a well-known essential oil used to treat microbial infections. It possesses antibacterial, antifungal, antiviral, analgesic and immune boosting properties. promotes quick healing and reduces inflammation caused by the infection (Pulipati *et al*., 2017).

Lemongrass (*Cymbopogan citratus*) is another natural product of relevance for UTI treatment. The essential oil of lemongrass is an effective fighter of many different types of bacteria (Pulipati *et al*., 2017). including *E. coli*. Lemongrass oil effective to destroy harmful pathogens such as *S. aureus, B. cereus, B. subtilis, E. coli* and *K. pneumonia* from the urinary bladder (Pulipati *et al*., 2017).

5. Materials and Methods

5.1 Study area

The retrospective study was conducted in ENOHC which is located in Yeka sub-city, wereda 3, Addis Ababa near Italian Embassy. It was established in 1984 and provides various health services for residents. The service includes child delivery, ante-natal and postnatal care, In addition, provides anti-retroviral therapy, family planning, male circumcision, expanded program on immunization (EPI), laboratory and Tuberculosis/HIV collaborative care services and other routine medical cares for outpatient and inpatient attendants.

5.2 Study design

The study was a retrospective patient health record examination. Past five-year (2013-2017) patient records containing at least sex and age data were included in the study. Data recorded with recurrent UTI information were excluded.

5.3 Sample size determination

The required sample size (n) was calculated using a formula for a single population proportion (Daniel and Cross 2013). The assumption of 50% P=0.5 expected prevalence of UTI. Taking critical value at 95% confidence level (CL) Z = 1.96 and precision (in proportion of one; if 5%, d = 0.05). With this assumption a total of 1805 records were selected out of 29,872. Due to large number of patient medical records between 2013 and 2017 the formula indicated below was used, n=$\frac{Z^2p(1-p)}{d^2}$ n=$\frac{1.96^2 \times 0.5(1-0.5)}{0.05^2}$, 384; $\frac{384}{10{,}483} = 0.036$ should less than 5%, if $\frac{n}{N} \geq 5\% = \frac{384}{6015} = 0.063$ the following formula was used $\frac{Nz^2p(1-p)}{d^2(N-1)+z^2p(1-p)}$, $\frac{6{,}015 \times 1.96^2 0.5(1-0.5)}{0.05^2(6{,}015-1)+1.96^2 \times 0.5(1-0.5)}$ = 361 in 2014.

In ENOHC, The total population (N) each year was 10,483; 6,015; 4,712; 4,397; 4,256 in 2013, 2014, 2015, 2016 and 2017 respectively. UTI-positive cards were selected from the above total for each year until the calculated number (proportion) was obtained. Accordingly n was, 384, 361, 355, 353 and 352 UTI-positive cards were obtained from collections in 2013, 2014, 2015, 2016 and 2017.

5.4 Retrospective data extraction

Data was collected between 1February2018 and 31May 2018 from the health center's patient medical record. The collected data consisted of UTI patients approved by laboratory test and prescribed antibiotic drug by health personnel. Whereas UTI prevalence is the single dependent variable, age, sex and year are independent variables.

5.5 Data quality control

The collected data was checked for its completeness, accuracy, clarity and consistency before being entered into Microsoft excel. When any ambiguity or incompleteness was encountered, the problem was assessed and corrected immediately before proceeding to the next step.

5.6 Data analysis

Data was analyzed using SPSS version 20 statistical packages International Business Machines (IBM SPSS, NewYork, USA). In this regard, frequency, percentages and tables were used to present the results. The chi-squared test was used to test the differences between yearly UTI cases, and with respect to sex and age. P-value of ≤ 0.05 was considered statistically significant difference.

6. Results

6.1 Patients examined for UTI and positive cases.

Between 2013 and 2017, totally 1805 patients were diagnosed with bacterial UTI out of 29872 examined with prevalence of 6.0%. The number and proportion of total patients examined has shown a significant declining trend ($p<0.0001$) in the consecutive years (Table 1). Thismight be due to the opening of a new health center at district level near the residential area of the population that were previously seeking healthcare in ENOHC. In the contrary, the prevalence of UTI positive patients showed slight increment from year to year. The proportion of positives in 2013, 2014, 2015, 2016 and 2017 were 3.7, 6.0, 7.5, 8.0 and 8.3% respectively. The proportion of patients treated in the health center for UTI in 2017 (8.3%) was more than twice that was in 2013 (3.7%) with statistically significant difference ($p<0.0001$).

Table 1 Number and proportion of patients examined for UTI and positive cases between 2013 and 2017 in ENOHC, Addis Ababa, Ethiopia

	Year						
	2013 no(%)	2014 no(%)	2015 no(%)	2016 no(%)	2017 no(%)	Total no(%)	p-value
Examined	10483(35.1)	6015(20.1)	4721(15.8)	4397(14.7)	4256(14.2)	29872(100)	<0.0001
Positive	384(3.7)	361(6.0)	355(7.5)	353(8.0)	352(8.3)	1805(6.0)	<0.0001

6.2 Gender-based number and proportion UTI positive patients

The distribution of UTI was influenced by gender; the result of this study also shows that the female UTI positive patients were higher than male. Out of the total of 1805 UTI positive patients the majority 1293(71.6%; 95% CI: 69.4-73.7%) were females and 512 (28.4%; 95% CI: 26.3-30.6%) males with a female to male ratio of 2.5:1. The data showed that the female proportion of positive cases was twice that of males (Table 2).

Table 2 Gender-based number and proportion of UTI positive patients between 2013 and 2017 in ENOHC, Addis Ababa, Ethiopia

Gender	Year					
	2013, no(%)	**2014, no(%)**	**2015, no(%)**	**2016, no(%)**	**2017, no(%)**	**Total**
Female	276(71.9)	254(70.4)	261(73.5)	242(68.6)	260(73.9)	1293(71.6)
Male	108(28.1)	107(29.6)	94(26.5)	111(21.7)	92(26.1)	512(28.4)
Total	384(21.3)	361(20.0)	355(19.7)	353(19.6)	352(19.5)	1805(100)

6.3 Age, sex and annual distribution of UTI

The population of UTI patients in ENOCH were grouped into eight age groups as per the WHO age classification (UN 1982). The age range of UTI patients was between 2 and 92years and the mean age was 34.3 (95% CI: 33.7-35.3) and standard deviation (SD) 16.189.Accordingly, the number(proportion) of patients positive for UTI in each category was 8(0.4%), 99(5.5%), 475(26.3%), 452(25.0%), 311(17.2%), 209(11.6%), 144(8.0%) and 107(5.9%) in 0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64 and ≥65 respectively.

As the data shows, the highest age specific UTI prevalence (26.3%) was seen in age group 15-24 and the lowest (0.4%) in the age group 0-4. Comparing the age of the total positive patients with mean age which is 34.46, 1034(57.3%) of the patients were found less or equal to mean and 771(42.7%) were greater than the mean age of the study population (Table 3). The results show

that from the age 2-34 years, the proportion of UTI positives increased while from 35 onwards it decreased annually. When comparing the proportion of UTI positive among 15-34 years each year, the results were 384(53.9%), 361(44.0%), 355(50.1%), 353(53.0%), 352(55.7%) in 2013, 2014, 2015, 2016 and 2017 respectively with the highest in 2017 and the lowest in 2014. Almost half of the population is found in this age range. The proportion of female and male cases increased up to mean age of 34. Then after, it declined in both sexes. The mean age of female was 33.8 and the male 35.7. That is, the number of males was greater than females by 1.87 approximately by 2 years comparing the mean of the total 34.3. The average female age was less than by 0.5 whereas the male was greater than by 1.3.

Table 3 Age, sex and annual distribution of UTI among patients attending ENOHC between 2013 and 2017

Age	Year					
	2013 no(%)	**2014 no(%)**	**2015 no(%)**	**2016 no(%)**	**2017 no(%)**	**Total no(%)**
0-4						
Female	3(0.8)	2(0.6)	0(0.0)	0(0.0)	2(0.6)	7(0.4)
Male	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(0.3)	1(0.1)
Total	3(0.8)	2(0.6)	0(0.0)	0(0.0)	3(0.9)	8(0.4)
5-14						
Female	17(4.4)	16(4.4)	15(4.2)	12(3.4)	11(3.1)	71(3.9)
Male	6(1.6)	5(1.4)	3(0.8)	9(2.5)	5(1.4)	28(1.6)
Total	23(6.0)	21(5.8)	18(5.1)	21(5.9)	16(4.5)	99(5.5)
15-24						
Female	72(18.8)	43(11.9)	70(19.7)	67(19.0)	94(26.7)	346(19.2)
Male	32(8.3)	19(5.3)	18(5.1)	25(7.1)	35(9.9)	129(7.1)
Total	104(27.1)	62(17.2)	88(24.8)	92(26.1)	129(36.6)	475(26.3)
25-34						
Female	74(19.3)	71 (19.7)	58 (16.3)	68(19.3)	51(14.5)	322(17.8)
Male	29(7.6)	26(7.2)	32(9.0)	27(7.6)	16(4.5)	130(7.2)
Total	103(26.8)	97(26.9)	90(25.4)	95(26.9)	67(19.0)	452(25.0)
35-44						
Female	48(12.5)	54(15.0)	35(9.9)	43(12.2)	54(15.3)	234(13.0)
Male	14(3.6)	16(4.4)	12(3.4)	16(4.5)	19(5.4)	77(4.3)
Total	62(16.1)	70(19.4)	47(13.2)	59(16.7)	73(20.7)	311(17.2)
45-54						
Female	28(7.3)	37(10.2)	38(10.7)	19(5.4)	27(7.7)	149(8.3)
Male	11(2.9)	19(5.3)	9(2.5)	16(4.5)	5(1.4)	60(3.3)
Total	39(10.2)	56(15.5)	47(13.2)	35(9.9)	32(9.1)	209(11.6)
55-64						
Female	19(4.9)	19(5.3)	30(8.5)	18(5.1)	13(3.7)	99(5.5)
Male	6(1.6)	11(3.0)	14(3.9)	8(2.3)	6(1.7)	45(2.5)
Total	25(6.5)	30(8.3)	44(12.4)	26(7.4)	19(5.4)	144(8.0)
≥65						
Female	15(3.9)	12(3.3)	15(4.2)	15(4.2)	8(2.3)	65(3.6)
Male	10(2.6)	11(3.0)	6(1.7)	10(2.8)	5(1.4)	42(2.3)
Total	25(6.5)	23(6.4)	21(5.9)	25(7.1)	13(3.7)	107(5.9)
Overall	384(1.3)	361(1.2)	355(1.2)	353(1.2)	352(1.2)	1805(6.0)

7. Discussion

From the present study it was found that overall prevalence rate of UTI was (6%) during the study period of five years. The prevalence was a little bit comparable with study 9.6%, in Malaysia (Mustefa *et al*., 2012).On the other hand, there were much higher reports in Ethiopia. For instance, 23.32, 22.7 and 30.5% prevalence were recorded by Getachew Kabew *et al*., (2013), Mulugeta Kibret *et al*., (2014), Awoke Derbie *et al*., (2017) respectively. Similarly, very large numbers prevalence 79.5% reported by Moue *et al*., (2015) in Bangladesh.

The reason for this relatively lower rate of prevalence may happen due to some factors such as, sample size and sample source, methodological differences as well large site coverage. Inaddition to these the level of healthy institution obtaining the data highly organized and established facility and laboratory diagnosis data sources.

Even if small sample size and proportion UTIs cases showed slight increment from year to year ranging from 3.7% in 2013 to 8.3% in 2017 indicating that the problem remains as an important public health problem in the study area. The prevalence of UTI in relation to gender in this study showed that the number and proportion of females was higher than that of male. From a total of 1805 UTI positive patients 71.6% were females. Previous reports in Ethiopia reported similarly higher burden of UTI on women. The proportion of patients treated for UTI in different health settings was invariably high. Getachew Kabew *et al*., (2013), Asrat Agalu *et al*., (2014), Tigist Gezmue *et al*., (2016), Adane Bitew *et al*.,(2017), Awoke Derbie *et al*., (2017) found female participants of UTIs 57.4, 77.6, 68.8. 88.1. 78.8, % Comparable reports are noted from different countries. A study from Nepal (Dhungana and Shakya, 2015) reported that 68.7% of the patients were females. While the proportion of female patients was 79.0% in Bangladesh (Moue *et al*., 2015) it was 52% in Nigeria (Ogbukagu *et al*., 2016).

Even though the study was done with a lower level health facility and restricted type of diagnostic service, it seems that bacterial UTI is a great health problem in women's life. Globally, UTI mentioned to be the second most common infectious disease affecting women after gastrointestinal disorders (August *et al*., 2012; Moue *et al*., 2015).

Even though the current study documented UTI in all age groups, it shows a significant variation between age groups. The highest (26.3%) age specific prevalence of UTI was seen in age group 15-24 years and the lowest (0.4%) was among those belonging to the age group 0-4. But, almost half of the UTI positive (51.4%) patients were 15-34 years old with the mean age of 34.46.In already stated previous studies people 21-30 years old constituted 27.2% of the infected population (Getachew Kabew *et al*., 2013). The slightly higher prevalence from previous similar study might have been due to the width of age range difference. In general, the result showed that the prevalence of UTI is greatly influenced by sex as well as age.

With increasing age the elderly of both sexes are at increased risk of UTIs. Old men have high probability of developing prostate problems due to loss of prostatic fluid which has a protective role. As a result, such men may become more vulnerable to UTIs and associated symptoms. The other factor that may make males prone to developing UTIs is circumcision.

Uncircumcised boys with prepuce have tendency to harbor organism in the foreskin likely due to the warm moist mucosal environment (Mustafa *et al*., 2012). Similarly, in women of menopause age withdrawal of estrogen leads to conversion of the predominant vaginal microbiome from lactobacillus to *E. coli* and other Enterobacteriaceae thus increasing the incidence of UTI with older age (Dielubanza and Schaeffer, 2011).

Limitation of the study

In this study there is no information on the pathogenic bacterial species. Only urine of suspected UTI patients was tested by urinanalysis and microscopic method. Bacterial culture could not be performed at the health center level. This is a major setback as to identifying the causative agents.Any antibiotic resistance which is an increasing problem nowadays could not be assessed from the data.

This study had some challenges. The prevalence obtained in the study is lower probably due to lower sample size. This is related to very poor patient records system which is very much cumbersome, disorganized and scattered. There was no pattern of whatsoever in filing. As a result it took long time to extract just five-year data. The study did not include pregnant women, recurrent UTI and related disease like diabetes and hypertension because of incomplete record system of age and arrangement of documentation system made the study complicated. All relevant information is not available in the patient history card and was difficult to extract data. The annual report system of the health center, age classification of the patient is not convenient for retrospective study. Number of examined in terms of age and sex was not properly documented.

Accurate diagnosis and treatment of UTI is essential to ensure optimal management and prevent complications. However, the health center lacks vital laboratory facilities like urine culture and UTI diagnosis is not straightforward and reliable. Apart from that, health professionals usually do not strictly follow guidelines or recommendations.

8. Conclusions and Recommendations

8.1 Conclusions

The findings show that bacterial UTI is a common health problem in ENOHC. The problem successively increased annually for the last five years. Although infected cases were found in both females and males aged 2-92 years, females were more vulnerable possibly due to physiological, anatomical and behavioral factors. In the reproductive age (15-34 years), UTI prevalence among females was twice that of males. Overall, the prevalence of UTI in ENOHC in the last five years was comparable with results of other studies in both low and high-level healthcare facilities including hospitals.

8.2 Recommendations

It is recommended that UTI must be clearly distinguished from other diseases that have a similar clinical presentation in the health center. It is required that appropriate history of patients be recorded, accurate diagnosis made and causative organisms identified, and results recorded in an easy-to-track manner. Furthermore, it is necessary to recognize the burden of UTI among residents served in ENOHC and design a strategic plan for better prevention and management.

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Declaration

I, the undersigned, declare that this Thesis is my original work and all source materials are duly acknowledged.

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Statement of the supervisor(s)

This Thesis is approved for submission to the Department of Zoological Sciences for public defense.

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