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UTI prevalence among population with chronic conditions

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Abstract
UTIs are a severe public health problem and are caused by a range of pathogens, but most commonly by *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus faecalis* and *Staphylococcus saprophyticus*. High recurrence rates and increasing antimicrobial resistance among uro-pathogens threaten to greatly increase the economic burden of these infections. UTIs typically occur when bacteria enter the urinary tract through the urethra and begin to multiply in the bladder. Although the urinary system is designed to keep out such microscopic invaders, these defenses sometimes fail. If left untreated, a urinary tract infection can have serious consequences. Adult women are 30 times more likely than men to develop a UTI, with almost half of them experiencing at least one episode of UTI during their lifetime. Uncomplicated lower UTI remains one of the most commonly treated infections in primary care. A complicated UTI is an infection associated with a condition, such as a structural or functional abnormality of the genitourinary tract, or the presence of an underlying disease. Diagnosis of a UTI is based on a focused history, with appropriate investigations depending on individual risk factors. The paper reviews several chronic conditions that are risk factors for UTIs in human being.

Keywords: complicated and uncomplicated UTIs; asymptomatic bacteriuria; UTIs among obese and heart patients; UTIs among renal and hepatic insufficiency; pregnancy induced complications; urinary infections among HIV and other STD

Introduction

UTI is one of the most prevalent diseases with diverse etiological agents annually affecting 250 million and causes death of 150 million people worldwide. The disease can be developed in 40% - 50% of women and 5% of men. Financial burden of UTIs exceeds $3.5 billion in US alone, while over half of the anti-infection agents prescribed for a suspected UTI in older adults being considered unnecessary [1]. Interestingly, nosocomial UTIs account for nearly 40% of all hospital acquired infections and around half of UTI in children are missed. UTI prevention is necessary as renal scarring, low birth weight, fetal growth restrictions, neonatal UTIs, premature labor, miscarriage, hypertension, preeclampsia, septic shock, malformation, anorectal malformation and increased incidence of death in the womb are reported in several studies [2]. The most common bacterial species that are implicated in UTIs are *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas aeruginosa* and *Proteus mirabilis* [3]. The association of UTI in diabetic females is more common than males because of their anatomical structure such as shorter urethra, the absence of prostatic secretion, and perineal contamination of the urinary tract with fecal flora [4]. Complicated UTIs occur most commonly in patients with abnormal genitourinary tract [5]. About 150 million people suffer from UTIs each year globally which results in greater than 6 billion dollars in direct health care [6]. UTIs are also common among many other chronic conditions like patients with diabetes, stroke, arthritis, obesity, alcohol use disorder, hypertension, HIV, liver cirrhosis, Hepatitis C, long-term care residents, immunocompromised, or pregnancy, history of/current catheterization, spinal cord dysfunction and a few cancers.

Table 1: Key classifications of UTIs [7]

Classification	Definition
Uncomplicated UTI	A UTI where there are no relevant functional or anatomical abnormalities in the urinary tract, no relevant kidney function impairment, and no relevant concomitant diseases promoting the UTI or risk of developing serious complications
Acute uncomplicated cystitis	A lower UTI in which the acute symptoms involve only the lower urinary tract, for example, urgency, painful voiding (dysuria), pollakiuria, and pain above the symphysis
Acute uncomplicated pyelonephritis	An upper UTI with persistent symptoms including flank pain, flank tenderness, or fever (>38°C)
Asymptomatic bacteriuria	A positive urine culture (>10^5 colony-forming units/ml) in the absence of urinary symptoms
Recurrent uncomplicated UTIs	A recurrent UTI refers to the occurrence of ⩾2 symptomatic episodes within 6 months or ⩾3 symptomatic episodes within 12 months

Diabetes Mellitus

The International Diabetes Federation (IDF) estimated that, worldwide, approximately 425 million people had diabetes in 2017, projected to be 629 million by 2045. And surprisingly, 80% of people with this so called “Rich Man's Disease” live in LMICs. According to a recent study of American Medical Association, China and India collectively are home of nearly 110 million diabetic patients [8, 9]. Significant bacteriuria had an association with the consumption of alcohol, gender and glucose level [10]. Asymptomatic bacteriuria (ASB) is common in neonates, Preschool children, pregnant women, elderly, diabetics, catheterized patients, and patients with abnormal urinary tracts or renal diseases. Diabetic patients have more than twice the tendency of developing genitourinary tract infections [11]. Bharti et.al, 2019 estimated that ASB was common among diabetics, as evident by a prevalence of 21% [12]. In patients with diabetes mellitus, infections caused by *Klebsiella*, *Enterobacter*, and *Candida* are more common [7]. According to Zubair et.al 2019, *E. coli* was the most frequent pathogen, followed by Staphylococcus aureus [13]. Urine cultures are not needed in uncomplicated UTI. Urine should be cultured in all men and patients with diabetes mellitus, who are immunosuppressed, and women who are pregnant [14]. The increased risk of infection in diabetics can be partially explained by a decreased T-cell-mediated immune response and impaired neutrophil function among diabetics. Other factors such as local complications related to neuropathy such as impaired bladder emptying and higher glucose concentrations in urine may also play a role in increased incidences of UTI in diabetics [15,16]. Non-drug-related mechanisms include autonomic neuropathy, glucose-dependent ICAM-1 expression, and immune system competence. Concerning drug-related mechanisms, there are currently over 40 different drugs in 12 distinct classes approved in the United States to treat patients with T2DM. Except for SGLT-2i, among the new drugs for the treatment of DM, no risk of UTIs or genital infections has been found [17].

Stroke

Stroke is a leading cause for disability and morbidity associated with increased economic burden due to treatment and post-stroke care, which was found $4850 per month in USA, $883 in UK, $752 in Australia and $192 in Malaysia [18]. Stroke-related annual national spending was estimated to be $34 billion in US, $3.6 billion in Canada and 6$ billion in China [19,20]. Stroke is the second largest cause of death in Australia and the total burden of disease cost for stroke in 2012 was AUD 49.3 billion [21]. Approximately one-third of all stroke patients have diabetes [22]. HbA1c ≥ 7.2% (>55 mmol/mol) is an independent risk predictor for 1-year all-cause mortality after acute first-ever ischemic stroke [23]. The incidence of ischemic stroke is up to 2-fold higher in people with diabetes. The relative risk of stroke increases by 1.15 with each 1% increase in glycated hemoglobin (HbA1c) level [24]. Of interest, UTIs account for a majority of the infections, and are independently associated with 30-day readmission in stroke patients [25]. Unlike other infections such as pneumonia or invasive line infections, UTI are often present on admission, which complicates efforts at eradication [26]. Providers may reflexively prescribe antibiotics, without considering other reasons for a clinical change. This may delay appropriate interventions and lead to patient harm [27]. The incidence of infections varies, but previous studies have quoted the rate for UTI as ranging from 3% to up to 44% [26], [28]. Patients with stroke have different risks for, consequences of, and barriers to reducing UTI than other hospitalized patients [29]. The role of infection in ischemic stroke is likely to be complex and multifactorial. Infection may play a causal role in the immunological triggering of stroke, and a stroke itself may have untoward effects on the immune system. The concepts of CNS injury-induced immunodepression or stroke-induced Immunodepression have even been used to describe the findings of secondary immunodeficiency after stroke. Also, stroke patients usually have comorbidities, which seem to make them more susceptible to infections [28]. Urinary catheterization is common after acute stroke and a well-known risk factor of UTI [30].

Hypertension

Hypertension has been reported as one of the long-term complications of UTI with renal parenchymal damage [16]. Children with UTIs are at risk of renal scarring which may lead to impaired renal function and hypertension [31]. Long-term follow-up of these children has to be done for the identification of complications such as renal function deterioration and hypertension [32]. Again, UTI prevention is necessary to prevent spread to the kidneys or developing pyelonephritis, which can cause the destruction of the delicate structures in the nephrons and lead to hypertension [4]. Following a UTI there is concern with recurrences which can contribute to scarring which may lead to hypertension, pregnancy-induced hypertension and even renal failure in later years [33]. Each year 10 million women worldwide develop preeclampsia (PE) and approximately 76,000 die due to PE and related hypertension disorders, 2–13% or more are responsible for nearly 40% of premature birth delivered before 35th weeks of gestation [34]. A number of studies suggest that UTI during the course of gestation is associated with elevated risk for preeclampsia (along with premature birth and low birth weight), while others have failed to prove such an association [35-37]. However, Rasouli et.al, 2019 revealed that presence of UTI in the third trimester, is strongly associated with preeclampsia [38].

Arthritis

Recurrent UTI is significantly more common in women with RA and secondary Sjögren's syndrome [39]. RA is most probably caused or initiated by an upper UTIs with Proteus bacteria. Elevated levels of antibodies to *P. mirabilis* have been detected in patients with RA among many populations from 14 different countries including UK, USA, France, and Netherlands [40]. A positive correlation was found between high anti-Proteus antibody levels in sera of RA patients and the number of colony-forming units obtained from urine specimens of these patients [41]. Patients infected with Proteus microbes will produce not only antibodies against this microbe but also against the self-tissue molecules carrying the cross-reactive antigens [41,42]. These antibodies will bind to and be cytopathic to the joint tissues which carry *Proteus* cross-reactive antigens and this immune reaction will lead to the release of more self-tissue antigens with a consequent production of further autoantibodies, propagation of the pathological process and the development of classical RA, in the same way that *Streptococcus* causes rheumatic fever and valvular lesions in the heart [42]. Reactive arthritis following *Escherichia coli* UTI is very rare (and has a significant morbidity), with most presentations caused by *Staphylococcus aureus* [44-46]. However, Braga et.al, 2016 showed that highly diverse *E. coli* strains can be recovered from osteomyelitis and arthritis in broilers, even in the same flock. Most of these strains are multidrug resistant, with increasing rates of ceftiofur resistance, which is a public and animal health concern [47].

Obesity

By 2025, the global obesity prevalence will reach 18% in men and exceed 21% in women [48]. It is now well-established that obesity (depending on the degree, duration, and distribution of the excess weight/adipose tissue) can progressively cause and/or exacerbate a wide spectrum of co-morbidities, including T2DM, hypertension, dyslipidemia, CVDs, NAFLD, reproductive dysfunction, respiratory abnormalities and psychiatric conditions [49]. Obesity-associated DNA damage can promote cancer growth by favoring cancer cell proliferation and migration, and resistance to apoptosis [50]. The aggregate national cost of overweight and obesity combined was $113.9 billion in 2008 in US [51] and the global economic impact of obesity was estimated to be US $2.0 trillion or 2.8% of the global GDP in 2014 [52]. Interestingly, chronic use of antibiotics during adulthood may have long-lasting impacts on BMI and weight gain in several populations [53]. Again, obesity may increase the risk of infection, but the association between obesity and febrile urinary tract infection (fUTI) is controversial [54]. However, elevated BMI appears to be associated with an increased risk for UTI and pyelonephritis [55, 56]. Semins *et al*. revealed a frequency of UTI 2.5 times higher in obese subjects than in non-obese children older than five years [55]. Also, obesity affects a greater proportion of women than men [57] and was found to be associated with RUTIs in premenopausal women [58]. Several studies have demonstrated that white adipose tissue is a crucial site of the formation of proinflammatory adipokines such as leptin, adiponectin, and resistin and classical cytokines such as IL- 6 and TNF-α [59]. Altered leptin, adiponectin, resistin and ghrelin secretion may represent an intrinsic polycystic ovary syndrome abnormality [60]. Inflammation often accompanies UTIs and is associated with renal scarring and disease severity. TNF-α, IL−1β, IL-6, and IL-8, are involved in the inflammation that accompanies UTIs [61]. Kennelly et.al, 2019 speculated that obese subjects (BMI > 50) have difficulty with bowel hygiene and as such are at increased risk of vulvovaginal symptoms and UTI [62]. Many health risks of obesity, including nephrolithiasis, will add more burden on urologists and nephrologists [63].

Chronic Liver Diseases

a. **Non-alcoholic Fatty Liver Disease:** NAFLD is a leading cause of chronic liver disease and cirrhosis and is associated with metabolic syndrome, T2DM, CVDs, and 2-fold all-cause mortality among diabetics [64]. NAFLD prevails in 25% Americans, involves $103 billion from direct medical care costs alone and another $188 billion in societal costs annually [64,65]. It is more prevalent in male gender, and with increasing age, obesity, and insulin resistance [66]. It is associated with bacterial infections. Nseir et.al, 2019 concluded that NAFLD is associated with RUTI in premenopausal women, independent of metabolic syndrome [67]. No significant associations were found between NAFLD and LUTS in middle-aged men [68]. SGLT2 inhibitors reduce hepatic steatosis, steatohepatitis, and fibrosis in patients with NAFLD [66]. Pioglitazone (SGLT-2 inhibitor) is the only drug recommended in diabetes patients with biopsy proven non-alcoholic steatohepatitis, improves the serum level of liver enzymes, decrease liver fat, and fibrosis with additional beneficial effects on various metabolic parameters in type 2 diabetes patients with NAFLD [69]. The most common adverse effects of SGLT-2 inhibitors are genitourinary tract infections [69-72]. Although, Lega et.al, 2019 revealed that SGLT2 inhibitors among elderly is associated with increased risk of genital mycotic infections within 30 days but there is no associated increased risk of UTI [73].

b. **Liver Cirrhosis**: The worldwide prevalence rate for CLD is 4.5% to 9%, causing over 6.3 million cases of liver cirrhosis per year [74]. Liver cirrhosis (LC) is the end stage of multiple processes that lead to hepatic failure and is the 10th most common cause of death in the Western world. It represents the main indication for liver transplantation in both United States and Europe. Common primary etiologies for liver cirrhosis were chronic hepatitis B cirrhosis (37.3%), ALD cirrhosis (24.1%), chronic hepatitis C cirrhosis (22.3%) and NAFLD cirrhosis (16.4%) [75]. Bacterial infections increase mortality four-fold in patients with decompensated cirrhosis. The presence of UTI indicates an increased risk of 90-day mortality in patients with advanced cirrhosis. Renal dysfunction and comorbidities are predictors of death in these patients [76]. UTIs found in 20% of cirrhotic patients [77]. UTI in this population does not correlate with the severity of liver disease but is associated with sex (females have a higher risk) and DM [78]. UTIs are also more frequent in patients with Primary Biliary Cirrhosis (PBC) [79]. The prevalence of increased aminotransferase levels in UTI patients without pre-existing liver disease was approximately 20%. In most cases, this change is mild and self-limiting in children [80].

c. **Chronic Hepatitis C**: It is a major cause of CLD worldwide with an estimated 71 million people infected and a 20-year risk for developing cirrhosis of up to 30% leading to 400,000 deaths annually from hepatocellular carcinoma and end-stage liver disease [81]. From 2010 until 2019, HCV cause the loss of 1.83 million years of life in people younger than 65 with cost of $21.3 and $54.2 billion, respectively [82]. First diagnosed in 1989, HCV is a major public health problem affecting 185 million people worldwide [83]. An estimated 80 million people live with active HCV infection worldwide, with approximately 1.75 million new infections and 400,000 related deaths annually [84]. Most children are infected by hepatitis C at birth. The most common infections among these patients are spontaneous bacterial peritonitis, pneumonia, skin infections and UTIs [85].

Alcohol Use Disorder

The WHO estimated that there are 2 billion alcohol users in the world and prevalence of alcohol use disorder is highest in Europe (7.5%) [86]. Alcohol causes over 3 million deaths worldwide each year and contributes to more than 5% of the global burden of disease. In the US, alcohol use is the fourth leading cause of preventable death with approximately 88,000 people dying each year due to alcohol-related causes [87]. In 2010, alcohol misuse cost the US $350 billion [88]. An enhanced frequency and morbidity of UTIs have been observed in association with alcoholism and liver disease [89]. Alcohol increases the acidity of urine and can irritate the lining of the bladder [90]. Alcohol consumption is known to increase the urine output, which could interfere with normal hydration [91]. A person who drinks alcohol can become dehydrated, increasing the risk of a UTI [92]. Women with alcohol use disorders undergoing cesarean delivery have increased risk of hospital-acquired infections including UTIs [93].

A separate study shows that alcohol induced immune suppression increases risks of UTIs [94].

Renal Insufficiency & Compromised Immunity

In patients with chronic renal failure, UTIs occur most frequently after kidney transplantation when graft pyelonephritis is a life-threatening complication, with a reported rate of 45-72% [95,96]. CKD affects more than 10% of US adults. It is the 18th leading cause of death globally, an 82% increase in absolute number of deaths in two decades. Medicare expenditures with recognized CKD is $45.5 billion and $34.3 billion with ESRD, according to Ozieh et.al, 2017 [97]. CKD affects 12.5% of adults in Canada [98], around 15% in US [99], 10–16% of the adult in Australia [100] and 13.4% around the world [101]. Around 20% of adults aged ≥65 present to primary care at least once with a UTI, and around 20% have renal impairment [102]. Females and elderly patients with CKD are more prone to have more bacteriuria and upper UTIs than males [103]. Again, women with diabetes are more prone to severe cystitis, ascending pyelonephritis, and severe forms of pyelonephritis (e.g., perinephric abscess, papillary necrosis) [104]. Repeat UTIs may cause kidney disease and structural kidney disease may be identified through investigation of repeat UTIs [105]. In more severe renal impairment, uremic toxins impair the function of T-lymphocyte and antigen-presenting cells, which play important roles in cellular and humoral immunity [102]. These patients have a higher risk of urinary infection, but the signs of infection may be different to those in the general population [96].

Urogenital Conditions

a. **Catheterization:** Healthcare-associated UTIs are the fourth most common type of healthcare-associated infection and approximately 80% of healthcare-associated UTIs are related to the use of indwelling urinary catheters [2]. CA-UTIs can lead to more serious complications such as sepsis and endocarditis, and it is estimated that over 13,000 deaths each year are associated with healthcare-associated UTIs [106]. Incidence of bacteriuria and UTIs are a function of the duration of catheterization. After 3 days, 100% of patients with an open-drain system will have ASB, and 3−6% of patients will develop ASB per day of closed-drain catheterization [107]. The use of chlorhexidine solution for meatal cleaning before catheter insertion decreased the incidence of catheter-associated asymptomatic bacteriuria and UTI and has the potential to improve patient safety [108].
b. **Neurogenic Bladder Dysfunction:** Lesions to the nervous system commonly cause bladder dysfunction. UTIs remain one of the most prevalent and frustrating morbidities for neurogenic bladder patients, and death attributed to urosepsis in the spinal cord injury patient is higher when compared to the general population. Risk factors include urinary stasis, high bladder pressures, bladder stones, and catheter use [109]. The management of neurogenic dysfunction through urethral catheter, suprapubic catheter, or nephrostomy also increase the risk of colonization and UTIs [107].
c. **Stress Urinary Incontinence:** Stress urinary incontinence (SUI) is the involuntary leakage of urine during periods of increased intra-abdominal pressure, including exertion such as laughing, coughing, sneezing, coughing, and jumping. Coexistence of UTIs and SUI is very common and UTIs resolved in 82% of patients with previous RUTIs after surgical correction of SUI with transobturator suburethral tape (TOT) [110]. Synthetic mid-urethral slings are the most common procedures currently performed for stress urinary incontinence in women and preoperative antibiotic prophylaxis may not be needed for UTI prevention [111].
d. **Genital Prolapse:** Approximately 40% of patients with prolapse have voiding issues, resulting in increased risk of UTI. The USA alone performs approximately 200,000 pelvic prolapse surgical procedures per year. [112]. Studies have shown that the presence of residual urine reflects a high risk of UTIs in women with urinary incontinence. Interestingly, data indicate that residual urine volumes as low as 30 ml can increase the risk for UTIs [107].

Long-Term Care Residents

Dehydration has been highlighted as a common cause of admission to hospital in nursing home residents, and there is evidence that many older residents living in care homes do not receive enough fluids. Inadequate staffing, including high turnover and understaffed care homes, increases the risk of dehydration in residents [92]. The prevalence of asymptomatic bacteriuria in long-term care residents is high: it is estimated that 15%–30% of men and 25%–50% of women have the condition [113]. The major reasons for this high prevalence are chronic comorbid illnesses with neurogenic bladder and interventions to manage incontinence. Chronic degenerative neurological diseases, such Alzheimer's disease and Parkinson's disease, and cerebrovascular accidents are associated with a neurogenic bladder. These conditions cause impaired bladder emptying and ureteric reflux, which contribute to the high frequency of bacteriuria. Interventions to manage incontinence may also promote infection [114]. 30% to 50% of antibiotics prescribed in long-term care are for urinary indications [115]. The Infectious Diseases Society of America and the Association of Medical Microbiology and Infectious Disease Canada both discourage this practice. Also, Urinary catheters are still frequently used in nursing homes, with catheter prevalence ranging from 5% to 22% of all residents [116], 30% of long-stay residents were suggested a bi-modal pattern in urinary catheter use according to another study of the same author [117].

HIV and Other STDs

UTI prevalence is fueled by HIV infection. The frequency of UTI is gradually increasing amongst HIV-infected patients as an opportunistic infection. This is due to the unique pathogenesis of the virus, which decreases the CD4+ cells, and as such, the individual's immune system can no longer fight against invading commensal organisms. *E. coli*, *Proteus* spp., *Klebsiella* spp., *Pseudomonas aeruginosa*, *Enterococcus* spp., and *S. aureus* are the most causative agent of UTI in people living with HIV [118]. Of approximately 20 million new STDs each year in the US, half of cases occur among adolescents age 15–24 years. It is estimated that 1 out of 4 sexually active adolescent females have an STD, most commonly *Chlamydia trachomatis* infection and human papillomavirus infection [119]. *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis* can cause adverse birth outcomes and infertility. Syphilis (*Treponema pallidum*) can cause neurological, cardiovascular and dermatological disease in adults, and stillbirth, neonatal death, premature delivery or severe disability in infants. All four infections are implicated in increasing the risk of HIV acquisition and transmission [120]. Atypical UTIs are commonly caused by *C. trachomatis* and *N. gonorrhoeae* [107]. The clinical presentations for STDs and UTIs may overlap, and symptoms of dysuria and urinary frequency/urgency occur with both STDs and UTIs [121]. Complications in urinary tract nervous routes due to *Herpes simplex* virus type 2 and Varicella-zoster virus (unique members of the Herpesviridae family) are well known. Acute urinary retention and chronic neuropathic pain are not rare when sacral dermatomes are involved by these viruses [122]. When acute urinary retention occurs several neurological and gynecological disorders must be considered. Unusually, benign inflammatory nervous diseases also cause acute urinary retention that can be divided into CNS disorders such as the meningitis-retention syndrome, a combination of aseptic meningitis and acute urinary retention, and PNS dis-orders such as sacral herpes [123].

Pregnancy

During pregnancy, urinary tract changes predispose women to infection. The prevalence of UTI among pregnant women was estimated to be 12.5% [124]. If asymptomatic bacteriuria is untreated in pregnancy, the rate of subsequent UTI is approximately 25% [125]. Pregnancy UTI is classified into two categories of symptomatic and asymptomatic: a) The involvement of the lower urinary tract, leading to asymptomatic bacteriuria is the most common cause of UTI during pregnancy b) The involvement of the upper urinary tract can lead to symptomatic bacteriuria and is characterized by acute Pyelonephritis. Based on performed researches, the prevalence of symptomatic urinary tract infection in pregnant women has been 18% and asymptomatic form in 13%. If asymptomatic infection is not treated, it leads to some clinical manifestations in mother and newborn [126]. Women face dual risks when they experience UTIs; the risk from the infection and the risk from antibiotic treatment. Pre-natal attachment to the fetus is highlighted in the decision-making process. The focus is on the shorter-term risk from UTIs while undermining the longer-term risks from antibiotic use, especially the risk of AMR. Although AMR is a global public health threat to everyone, in pregnancy it can be particularly concerning due to the risk of resistant bacteria passing on to the neonate during birth which can be a vulnerable stage of life with regards to contracting infections. In addition to this, antibiotic use in pregnancy may also carry the risk of potentially teratogenic effects including spontaneous abortion [127].

Cancer

In immunocompromised cancer patients, UTI is one of the major causes of fever and morbidity. *E. coli* was the most common organism isolated in cancer patients with UTI. There is trend of increasing resistance to aminoglycosides, cephalosporins and fluoroquinolones among Gram negative bacilli [128]. UTI is significantly related to GUC and may serve as an early sign of genitourinary cancers (GUC), especially in the male genital organs, prostate, kidney, and urinary bladder. The symptoms of overactive bladder (OAB) have overlap with other common conditions, most notably UTI, BPH, and bladder cancer/carcinoma in situ [129]. An elevated prostate-specific antigen (PSA) level is well known in the diagnosis of prostate cancer, but it also might have a potential protective role in recurrent UTI [130]. In UTI treatment, especially when multiple pathogenic factors are entailed, antibiotics must be used cautiously, and the time and dose of antibiotics should be minimized. Because UTI may increase the incidence of genital organ, bladder, kidney, male colorectal, prostate, and female liver cancer, knowledge about preventing UTI such as proper drinking water, exercise, and toilet habits should be enhanced in educating the general public [131].

Pre- and Post- Menopausal Women

Risk factors in premenopausal women include sexual intercourse, changes in bacterial flora, history of UTIs during childhood or family history of UTIs, and blood group [132]. Specific risk factors related to sexual intercourse include frequency (four or more times per week), the use of spermicides that may alter vaginal pH and thus affect its flora (particularly the *Lactobacilli* component), and engagement with a new sexual partner within the last year [133]. Lack of postcoital urination, vaginal douches, use of hot tubs, restrictive underwear, and the hygiene and circumcision status of male partners have been proposed as risk factors, but lack an evidence base [2]. For postmenopausal women, the most significant risk factor is estrogen deficiency. Sexual intercourse and estrogen deficiency in postmenopausal women might have the strongest association with recurrent UTI. Lack of estrogen could cause thinning of the vaginal epithelium and decreased amounts of glycogen, predisposing women to introital colonization with *E. coli* [134]. The main vaginal flora usually changes from *Lactobacilli* to uropathogen such as *E. coli* after estrogen loss at menopause, leading to UTI recurrence [130], [135]. Urobiome research for bladder health and disease is a young field of investigation with significant potential to improve care for postmenopausal women affected by rUTI through novel, evidence-based prevention and treatment strategies [136].

Conclusion

UTIs cause both anxiety and depression in significant number of patients, with a significant improvement in the QoL after proper treatment and prophylaxis. Treating UTI might not be difficult, but preventing UTI recurrence sometimes might be very troublesome for both patients and physicians. Treatment of asymptomatic bacteriuria in the general population is highly discouraged due to the risk of increased AMR. Diagnosing and managing upper and lower UTI have always been a challenge to physicians, given its high prevalence, risk of recurrence and improper treatment, and the fact of worldwide increase in antibiotic resistance, necessitating implementation of a proper antibiotic stewardship. Effective UTI management should provide established guidance for the RUTI evaluation and management to prevent inappropriate use of antibiotics, decrease the risk of antibiotic resistance, reduce adverse effects of antibiotic use, provide guidance on antibiotic and non-antibiotic strategies for prevention, and improve clinical outcomes and quality of life by reducing recurrence of UTI events.

Abbreviations

International Diabetes Federation (IDF); Low-and Middle-Income Countries (LMICs); Asymptomatic bacteriuria (ASB); Intercellular Adhesion Molecule-1 (ICAM-1); Sodium-glucose co-transporter-2 inhibitors (SGLT-2i); Type 2 Diabetes Mellitus

(T2DM); Hemoglobin A1C (HbA1c); Preeclampsia (PE); Non-Alcoholic Fatty Liver Disease (NAFLD); Gross Domestic Product (GDP); febrile Urinary Tract Infection (fUTI); Tumor Necrosis Factor Alpha (TNF-α); Interleukin-1 β (IL−1β); Body Mass Index (BMI); Alcoholic Liver Disease (ALD); Chronic Liver Disease (CLD); Primary Biliary Cirrhosis (PBC); Hepatitis C Virus (HCV); End Stage Renal Disease (ESRD); Chronic Kidney Disease (CKD); Stress Urinary Incontinence (SUI); Transobturator Suburethral Tape (TOT); Recurrent UTIs (rUTIs); Sexually Transmitted Diseases (STDs); Central Nervous System (CNS); Peripheral Nervous System (PNS); Antimicrobial Resistance (AMR)

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Reference

1. Mohiuddin AK. Lifestyle Issues and Prevention of Recurrent UTIs. Biomedical Journal of Scientific & Technical Research. 2019; 21(3). doi:10.26717/bjstr.2019.21.003618.
2. Mohiuddin AK. Lifestyle Issues and Prevention of Recurrent UTIs. International Research in Medical and Health Science. April 2019. Doi: https://doi.org/10.36437/irmhs.2019.2.4.S.
3. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015; 13(5):269-84. doi: 10.1038/nrmicro3432.
4. Mohiuddin AK. Alternative Management of Uncomplicated UTIs in Women. Journal of Gynecology and Womens Health. 2019; 16(1):1-5. doi:10.19080/jgwh.2019.14.555930.
5. Woldemariam HK, Geleta DA, Tulu KD, Aber NA, Legese MH, Fenta GM. *et al*. Common uropathogens and their antibiotic susceptibility pattern among diabetic patients. BMC Infect Dis. 2019; 19(1):43. doi: 10.1186/s12879-018-3669-5.
6. Odoki M, Almustapha Aliero A, Tibyangye J, *et al*. Prevalence of Bacterial Urinary Tract Infections and Associated Factors among Patients Attending Hospitals in Bushenyi District, Uganda. Int J Microbiol, 2019; 2019:4246780. Published 2019 Feb 17. doi:10.1155/2019/4246780
7. Medina M, Castillo-Pino E. An introduction to the epidemiology and burden of urinary tract infections. Ther Adv Urol, 2019; 11:1756287219832172. Published 2019 May 2. doi:10.1177/1756287219832172
8. Mohiuddin AK. TRACK Implementation among Bangladeshi Population. Int J Diabetol Vasc Dis Res. 2019; 7(4):254-260. doi: dx.doi.org/10.19070/2328-353X-1900048
9. Mohiuddin AK. Diabetes Fact: Bangladesh Perspective. International Journal of Diabetes Research. 2019; 2(1):14-20. Doi: 10.17554/j.issn.2414-2409.2019.02.12
10. Mama M, Manilal A, Gezmu T, Kidanewold A, Gosa F, Gebresilasie A. *et al*. Prevalence and associated factors of urinary tract infections among diabetic patients in Arba Minch Hospital, Arba Minch province, South Ethiopia. Turk J Urol. 2018; 45(1):56-62. Published 2018 Nov 21. doi:10.5152/tud.2018.32855
11. Kumar R, Kumar R, Perswani P, Taimur M, Shah A, Shaukat F. *et al*. Clinical and Microbiological Profile of Urinary Tract Infections in Diabetic versus Non-Diabetic Individuals. Cureus. 2019; 11(8):e5464. Published 2019 Aug 22. doi:10.7759/cureus.5464
12. Bharti A, Chawla SPS, Kumar S. Asymptomatic bacteriuria among the patients of type 2 diabetes mellitus. J Family Med Prim Care. 2019; 8(2):539-543. doi:10.4103/jfmpc.jfmpc_403_18
13. Zubair KU, Shah AH, Fawwad A, Sabir R, Butt A. Frequency of urinary tract infection and antibiotic sensitivity of uropathogens in patients with diabetes. Pak J Med Sci. 2019; 35(6):1664-1668. doi:10.12669/pjms.35.6.115
14. Matuszkiewicz-Rowińska J, Małyszko J, Wieliczko M. Urinary tract infections in pregnancy: old and new unresolved diagnostic and therapeutic problems. Arch Med Sci. 2015; 11(1):67-77. doi:10.5114/aoms.2013.39202
15. Shih WY, Chang CC, Tsou MT, Chan HL, Chen YJ, Hwang LC. *et al*. Incidence and Risk Factors for Urinary Tract Infection in an Elder Home Care Population in Taiwan: A Retrospective Cohort Study. Int J Environ Res Public Health. 2019; 16(4):566. Published 2019 Feb 16. doi:10.3390/ijerph16040566
16. Al-Rubeaan KA, Moharram O, Al-Naqeb D, Hassan A, Rafiullah MR. Prevalence of urinary tract infection and risk factors among Saudi patients with diabetes. World J Urol. 2013; 31(3):573-8. doi: 10.1007/s00345-012-0934-x.
17. La Vignera S, Condorelli RA, Cannarella R. Urogenital infections in patients with diabetes mellitus: Beyond the conventional aspects. Int J Immunopathol Pharmacol. 2019; 33:2058738419866582. Published, 2019. doi:10.1177/2058738419866582
18. Rajsic S, Gothe H, Borba HH, Sroczynski G, Vujicic J, Toell T. *et al*. Economic burden of stroke: a systematic review on post-stroke care. Eur J Health Econ. 2019; 20(1):107-134. doi: 10.1007/s10198-018-0984-0.
19. Zhang H, Yin Y, Zhang C, Zhang D. Costs of hospitalization for stroke from two urban health insurance claims data in Guangzhou City, southern China. BMC Health Serv Res. 2019; 19(1):671. Published 2019 Sep 18. doi:10.1186/s12913-019-4530-2
20. Lapchak PA, Zhang JH. The High Cost of Stroke and Stroke Cytoprotection Research. Transl Stroke Res. 2017; 8(4):307-317. doi:10.1007/s12975-016-0518-y
21. Ramanathan S, Reeves P, Deeming S. Implementing a protocol for a research impact assessment of the Centre for Research Excellence in Stroke Rehabilitation and Brain Recovery. Health Res Policy Syst. 2018; 16(1):71. Published 2018 Aug 1. doi:10.1186/s12961-018-0349-2

22. Lau LH, Lew J, Borschmann K, Thijs V, Ekinci EI. Prevalence of diabetes and its effects on stroke outcomes: A meta-analysis and literature review. J Diabetes Investig. 2019; 10(3):780-792. doi:10.1111/jdi.12932
23. Wu S, Wang C, Jia Q, Liu G, Hoff K, Wang X. *et al*. HbA1c is associated with increased all-cause mortality in the first year after acute ischemic stroke. Neurol Res. 2014; 36(5):444-52. doi: 10.1179/1743132814Y.0000000355
24. Lim S, Oh TJ, Dawson J, Sattar N. Diabetes drugs and stroke risk: Intensive versus conventional glucose-lowering strategies, and implications of recent cardiovascular outcome trials. Diabetes Obes Metab. 2020; 22(1):6-15. doi: 10.1111/dom.13850.
25. Boehme AK, Kulick ER, Canning M. Infections Increase the Risk of 30-Day Readmissions among Stroke Survivors. Stroke. 2018; 49(12):2999-3005. doi:10.1161/STROKEAHA.118.022837
26. Bogason E, Morrison K, Zalatimo O. Urinary Tract Infections in Hospitalized Ischemic Stroke Patients: Source and Impact on Outcome. Cureus. 2017; 9(2):e1014. Published 2017 Feb 6. doi:10.7759/cureus.1014
27. Cortes-Penfield NW, Trautner BW, Jump RLP. Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. Infect Dis Clin North Am. 2017; 31(4):673-688. doi:10.1016/j.idc.2017.07.002
28. Donkor ES, Akumwena A, Amoo PK, Owolabi MO, Aspelund T, Gudnason V. *et al*. Post-stroke bacteriuria among stroke patients attending a physiotherapy clinic in Ghana: a cross-sectional study. Ther Clin Risk Manag. 2016; 12:457-462. Published 2016 Mar 17. doi:10.2147/TCRM.S90474
29. Poisson SN, Johnston SC, Josephson SA. Urinary tract infections complicating stroke: mechanisms, consequences, and possible solutions. Stroke. 2010; 41(4):e180-4. doi: 10.1161/STROKEAHA.109.576413.
30. Net P, Karnycheff F, Vasse M, Bourdain F, Bonan B, Lapergue B. *et al*. Urinary tract infection after acute stroke: Impact of indwelling urinary catheterization and assessment of catheter-use practices in French stroke centers. Rev Neurol (Paris). 2018; 174(3):145-149. doi: 10.1016/j.neurol.2017.06.029.
31. Tewary K, Narchi H. Recurrent urinary tract infections in children: Preventive interventions other than prophylactic antibiotics. World J Methodol. 2015; 5(2):13-19. Published 2015 Jun 26. doi:10.5662/wjm.v5.i2.13.
32. Bandari B, Sindgikar SP, Kumar SS, Vijaya MS, Shankar R. Renal scarring following urinary tract infections in children. Sudan J Paediatr. 2019; 19(1):25-30. doi:10.24911/SJP.106-1554791193
33. Vachvanichsanong P. Urinary tract infection: one lingering effect of childhood kidney diseases--review of the literature. J Nephrol. 2007; 20(1):21-8.
34. Schindler AE. New data about preeclampsia: some possibilities of prevention. Gynecol Endocrinol. 2018; 34(8):636-637. doi: 10.1080/09513590.2018.1441401.
35. Karmon A, Sheiner E. The relationship between urinary tract infection during pregnancy and preeclampsia: causal, confounded or spurious? Arch Gynecol Obstet. 2008; 277(6):479-81. doi: 10.1007/s00404-008-0643-2.
36. Yan L, Jin Y, Hang H, Yan B. The association between urinary tract infection during pregnancy and preeclampsia: A meta-analysis. Medicine (Baltimore). 2018; 97(36):e12192. doi:10.1097/MD.0000000000012192
37. Urinary Tract Infections. Available From: https://www.womenshealth.gov/files/documents/fact-sheet-urinary-tract-infections.pdf
38. Rasouli M, Pourheidari M, Hamzeh Gardesh Z. Effect of Self-care Before and During Pregnancy to Prevention and Control Preeclampsia in High-risk Women. Int J Prev Med, 2019, 10:21. Published 2019 Feb 12. doi:10.4103/ijpvm.IJPVM_300_17
39. Tishler M, Caspi D, Almog Y, Segal R, Yaron M. Increased incidence of urinary tract infection in patients with rheumatoid arthritis and secondary Sjögren's syndrome. Ann Rheum Dis. 1992; 51(5):604-606. doi:10.1136/ard.51.5.604
40. Ebringer A, Rashid T, Wilson C. Rheumatoid arthritis, Proteus, anti-CCP antibodies and Karl Popper. Autoimmun Rev. 2010; 9(4):216-23. doi: 10.1016/j.autrev.2009. 10.006.
41. Newkirk MM, Goldbach-Mansky R, Senior BW, Klippel J, Schumacher HR Jr, El-Gabalawy HS. *et al*. Elevated levels of IgM and IgA antibodies to Proteus mirabilis and IgM antibodies to Escherichia coli are associated with early rheumatoid factor (RF)-positive rheumatoid arthritis. Rheumatology (Oxford). 2005; 44(11):1433-41.
42. Pretorius E, Akeredolu OO, Soma P, Kell DB. Major involvement of bacterial components in rheumatoid arthritis and its accompanying oxidative stress, systemic inflammation and hypercoagulability. Exp Biol Med (Maywood). 2017; 242(4):355-373. doi:10.1177/15353702 16681549
43. Rashid T, Ebringer A. Rheumatoid Arthritis is caused by Asymptomatic Proteus Urinary Tract Infections. Clinical Management of Complicated Urinary Tract Infection. September, 2011, 171-180. doi:10.5772/24417.
44. Renou F, Wartel G, Raffray L, Kuli B, Fayeulle S, Yvin JL. *et al*. [Reactive arthritis due to Escherichia coli urinary tract infection]. Rev Med Interne. 2011; 32(1):e4-5. doi: 10.1016/j.revmed.2010.02.011.
45. Lee A, Coleman P. Escherichia coli - Marauding masquerading microbe. J Clin Orthop Trauma. 2013; 4(4):194-198. doi:10.1016/j.jcot.2013.10.001
46. Youssef D, Bhargava A. Escherichia coli bacteremia with secondary seeding in the sternoclavicular joint: A case report and literature review. Germs. 2019; 9(1):43-46. Published 2019 Mar 1. doi:10.18683/germs.2019.1156
47. Braga JFV, Chanteloup NK, Trotereau A. Diversity of Escherichia coli strains involved in vertebral osteomyelitis and arthritis in broilers in Brazil. BMC Vet Res. 2016; 12(1):140. Published 2016 Jul 14. doi:10.1186/s12917-016-0762-0
48. NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016; 387(10026):1377-1396. doi: 10.1016/S0140-6736(16)30054-X.
49. Fruh SM. Obesity: Risk factors, complications, and strategies for sustainable long-term weight management. J

Am Assoc Nurse Pract. 2017; 29(S1):S3-S14. doi:10.1002/2327-6924.12510

50. Włodarczyk M, Nowicka G. Obesity, DNA Damage, and Development of Obesity-Related Diseases. Int J Mol Sci. 2019; 20(5):1146. Published 2019 Mar 6. doi:10.3390/ijms20051146
51. Tsai AG, Williamson DF, Glick HA. Direct medical cost of overweight and obesity in the USA: a quantitative systematic review. Obes Rev. 2011; 12(1):50-61. doi:10.1111/j.1467-789X.2009.00708.x
52. Tremmel M, Gerdtham UG, Nilsson PM, Saha S. Economic Burden of Obesity: A Systematic Literature Review. Int J Environ Res Public Health. 2017; 14(4):435. Published 2017 Apr 19. doi:10.3390/ijerph14040435
53. Furlong M, Deming-Halverson S, Sandler DP. Chronic antibiotic use during adulthood and weight change in the Sister Study. PLoS One. 2019; 14(5):e0216959. Published 2019 May 16. doi:10.1371/journal.pone.0216959
54. Hsu PC, Chen SJ. Obesity and risk of urinary tract infection in young children presenting with fever. Medicine (Baltimore). 2018; 97(49):e13006. doi:10.1097/MD.0000000000013006
55. Semins MJ, Shore AD, Makary MA, Weiner J, Matlaga BR. The impact of obesity on urinary tract infection risk. Urology. 2012; 79(2):266-9. doi: 10.1016/j.urology.2011.09.040.
56. Gaither TW, Cooper CS, Kornberg Z, Baskin LS, Copp HL. Predictors of becoming overweight among pediatric patients at risk for urinary tract infections. J Pediatr Urol. 2019; 15(1):61.e1-61.e6. doi: 10.1016/j.jpurol.2018.09.002.
57. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. Metabolism. 2019; 92:6-10. doi: 10.1016/j.metabol.2018.09.005.
58. Nseir W, Farah R, Mahamid M, Sayed-Ahmad H, Mograbi J, Taha M. *et al*. Obesity and recurrent urinary tract infections in premenopausal women: a retrospective study. Int J Infect Dis. 2015; 41:32-5. doi: 10.1016/j.ijid.2015.10.014.
59. Rodríguez-Cerdeira C, Cordeiro-Rodríguez M, Carnero-Gregorio M. Biomarkers of Inflammation in Obesity-Psoriatic Patients. Mediators Inflamm. 2019; 2019:7353420. Published 2019 May 28. doi:10.1155/2019/7353420
60. Jung JH, Hong HJ, Gharderpour A. Differential interleukin-1β induction by uropathogenic Escherichia coli correlates with its phylotype and serum C-reactive protein levels in Korean infants. Scientific Reports, 2019, 9(1). doi:10.1038/s41598-019-52070-3.
61. Baldani DP, Skrgatic L, Kasum M, Zlopasa G, Kralik Oguic S, Herman M. *et al*. Altered leptin, adiponectin, resistin and ghrelin secretion may represent an intrinsic polycystic ovary syndrome abnormality. Gynecol Endocrinol. 2019; 35(5):401-405. doi: 10.1080/09513590.2018.1534096.
62. Kennelly M, Thiruchelvam N, Averbeck MA. Adult Neurogenic Lower Urinary Tract Dysfunction and Intermittent Catheterisation in a Community Setting: Risk Factors Model for Urinary Tract Infections. Adv Urol, 2019, 2019:2757862. Published 2019 Apr 2. doi:10.1155/2019/2757862
63. Carbone A, Al Salhi Y, Tasca A, Palleschi G, Fuschi A, De Nunzio C. *et al*. Obesity and kidney stone disease: a systematic review. Minerva Urol Nefrol. 2018; 70(4):393-400. doi: 10.23736/S0393-2249.18.03113-2.
64. Shetty A, Syn WK. Health and Economic Burden of Nonalcoholic Fatty Liver Disease in the United States and Its Impact on Veterans. Fed Pract. 2019; 36(1):14-19.
65. Younossi ZM, Blissett D, Blissett R, Henry L, Stepanova M, Younossi Y. *et al*. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology. 2016; 64(5):1577-1586. doi: 10.1002/hep.28785.
66. Dokmak A, Almeqdadi M, Trivedi H, Krishnan S. Rise of sodium-glucose cotransporter 2 inhibitors in the management of nonalcoholic fatty liver disease. World J Hepatol. 2019; 11(7):562-573. doi:10.4254/wjh.v11.i7.562
67. Nseir W, Amara A, Farah R, Ahmad HS, Mograbi J, Mahamid M. *et al*. Non-alcoholic Fatty Liver Disease is Associated with Recurrent Urinary Tract Infection in Premenopausal Women Independent of Metabolic Syndrome. Isr Med Assoc J. 2019; 21(6):386-389.
68. Song YA, Kwon SS, Doo SW, Kim JH, Yang WJ, Song YS. *et al*. Is There Any Relation Between the Degree of Fatty Liver Disease and Severity of Lower Urinary Tract Symptoms? Urology, 2016; 89:90-5. doi: 10.1016/j.urology.2015.11.030.
69. Kim KS, Lee BW, Kim YJ, Lee DH, Cha BS, Park CY. *et al*. Nonalcoholic Fatty Liver Disease and Diabetes: Part II: Treatment. Diabetes Metab J. 2019; 43(2):127-143. doi:10.4093/dmj.2019.0034
70. Raj H, Durgia H, Palui R. SGLT-2 inhibitors in non-alcoholic fatty liver disease patients with type 2 diabetes mellitus: A systematic review. World J Diabetes. 2019; 10(2):114-132. doi:10.4239/wjd.v10.i2.114
71. Tentolouris A, Vlachakis P, Tzeravini E, Eleftheriadou I, Tentolouris N. SGLT2 Inhibitors: A Review of Their Antidiabetic and Cardioprotective Effects. Int J Environ Res Public Health. 2019; 16(16):2965. Published 2019 Aug 17. doi:10.3390/ijerph16162965
72. Nagahisa T, Saisho Y. Cardiorenal Protection: Potential of SGLT2 Inhibitors and GLP-1 Receptor Agonists in the Treatment of Type 2 Diabetes. Diabetes Ther. 2019; 10(5):1733-1752. doi:10.1007/s13300-019-00680-5
73. Lega IC, Bronskill SE, Campitelli MA, Guan J, Stall NM, Lam K. *et al*. Sodium glucose cotransporter 2 inhibitors and risk of genital mycotic and urinary tract infection: A population-based study of older women and men with diabetes. Diabetes Obes Metab. 2019; 21(11):2394-2404. doi: 10.1111/dom.13820.
74. Méndez-Sánchez N, Zamarripa-Dorsey F, Panduro A. Current trends of liver cirrhosis in Mexico: Similitudes and differences with other world regions. World J Clin Cases. 2018; 6(15):922-930. doi:10.12998/wjcc.v6.i15.922
75. Stasi C, Silvestri C, Voller F, Cipriani F. Epidemiology of Liver Cirrhosis. J Clin Exp Hepatol. 2015; 5(3):272. doi:10.1016/j.jceh.2015.06.002
76. Reuken PA, Stallmach A, Bruns T. Mortality after urinary tract infections in patients with advanced cirrhosis - Relevance of acute kidney injury and comorbidities. Liver Int. 2013; 33(2):220-30. doi: 10.1111/liv.12029.
77. Lameirão Gomes C, Violante Silva R, Carrola P, Presa J. Bacterial Infections in Patients with Liver Cirrhosis in an

Internal Medicine Department. GE Port J Gastroenterol. 2019; 26(5):324-332. doi:10.1159/000494568

78. Milovanovic T, Dumic I, Veličkovic J, Lalosevic MS, Nikolic V, Palibrk I. *et al*. Epidemiology and risk factors for multi-drug resistant hospital-acquired urinary tract infection in patients with liver cirrhosis: single center experience in Serbia. BMC Infect Dis. 2019; 19(1):141. Published 2019 Feb 12. doi:10.1186/s12879-019-3761-5
79. Varyani FK, West J, Card TR. Primary biliary cirrhosis does not increase the risk of UTIs following diagnosis compared to other chronic liver diseases? Liver Int. 2013; 33(3):384-8. doi: 10.1111/liv.12107.
80. Park JY, Ko KO, Lim JW, Cheon EJ, Yoon JM. Increase in Aminotransferase Levels during Urinary Tract Infections in Children. Pediatr Gastroenterol Hepatol Nutr. 2013; 16(2):89-94. doi:10.5223/pghn.2013.16.2.89
81. Søholm J, Holm DK, Mössner B, *et al*. Incidence, prevalence and risk factors for hepatitis C in Danish prisons. PLoS One. 2019; 14(7):e0220297. Published 2019 Jul 26. doi:10.1371/journal.pone.0220297
82. Mohammadzadeh M, Derafshi H, Ghari T. The Estimation of Economic Burden of Hepatitis C Virus Infection in Iran. Iran J Public Health. 2018; 47(10):1575-1582.
83. Basit H, Tyagi I, Koirala J. Hepatitis C. [Updated 2019 May 15]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430897/
84. Edmunds BL, Miller ER, Tsourtos G. The distribution and socioeconomic burden of Hepatitis C virus in South Australia: a cross-sectional study 2010-2016. BMC Public Health. 2019; 19(1):527. Published 2019 May 8. doi:10.1186/s12889-019-6847-5
85. Cruz Rde C, Tanajura D, Almeida D, Cruz M, Paraná R. Urinary tract infection in non-hospitalized patients with cirrhosis and no symptoms of urinary tract infection: a case series study. Braz J Infect Dis. 2006; 10(6):380-3.
86. Mohiuddin AK. Drug Addiction in Bangladesh: “A Consequence of Social Demoralization Rather Than Individual Flaws.” International Journal of Addiction Research and Therapy, 2019. doi:10.28933/ijart-2019-11-1005.
87. Witkiewitz K, Vowles KE. Alcohol and Opioid Use, Co-Use, and Chronic Pain in the Context of the Opioid Epidemic: A Critical Review. Alcohol Clin Exp Res. 2018; 42(3):478-488. doi:10.1111/acer.13594
88. Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer RD. 2010 National and State Costs of Excessive Alcohol Consumption. Am J Prev Med. 2015; 49(5):e73-e79. doi: 10.1016/j.amepre.2015.05.031.
89. Pitts TO, Van Thiel DH. Urinary tract infections and renal papillary necrosis in alcoholism. Recent Dev Alcohol. 1986; 4:341-55.
90. Villines Z. What to know about kidney pain after drinking alcohol? (Medically reviewed by Carissa Stephens, R.N., CCRN, CPN). Medical News Today, 2019.
91. Polhuis KCMM, Wijnen AHC, Sierksma A, Calame W, Tieland M. The Diuretic Action of Weak and Strong Alcoholic Beverages in Elderly Men: A Randomized Diet-Controlled Crossover Trial. Nutrients. 2017; 9(7):660. Published 2017 Jun 28. doi:10.3390/nu9070660
92. Lean K, Nawaz RF, Jawad S, Vincent C. Reducing urinary tract infections in care homes by improving hydration. BMJ Open Qual. 2019; 8(3):e000563. Published 2019 Jul 10. doi:10.1136/bmjoq-2018-000563
93. Wit MD, Goldberg A, Chelmow D. Alcohol Use Disorders and Hospital-Acquired Infections in Women Undergoing Cesarean Delivery. Obstetrics & Gynecology. 2013; 122(1):72-78. doi:10.1097/aog.0b013e318297be8d.
94. Sander M, Neumann T, Dossow VV, Schönfeld H, Lau A, Eggers V. *et al*. Alkoholabusus. Der Internist. 2006; 47(4):332-341. doi:10.1007/s00108-006-1588-9.
95. Sobotová D. Urinary tract infections and chronic renal failure. Vnitr Lek. 2011; 57:626-30.
96. Tandogdu Z, Cai T, Koves B, Wagenlehner F, Bjerklund-Johansen TE. Urinary Tract Infections in Immunocompromised Patients with Diabetes, Chronic Kidney Disease, and Kidney Transplant. European Urology Focus. 2016; 2(4):394-399. doi:10.1016/j.euf.2016.08.006.
97. Ozieh MN, Bishu KG, Dismuke CE, Egede LE. Trends in healthcare expenditure in United States adults with chronic kidney disease: 2002-2011. BMC Health Serv Res. 2017; 17(1):368. Published 2017 May 22. doi:10.1186/s12913-017-2303-3
98. Manns B, Hemmelgarn B, Tonelli M. The Cost of Care for People with Chronic Kidney Disease. Can J Kidney Health Dis, 2019; 6:2054358119835521. Published 2019 Apr 4. doi:10.1177/2054358119835521
99. Saran R, Robinson B, Abbott KC. US Renal Data System 2018 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2019; 73(3S1):A7-A8. doi:10.1053/j.ajkd.2019.01.001
100. Jayasinghe K, Quinlan C, Stark Z. Renal genetics in Australia: Kidney medicine in the genomic age. Nephrology (Carlton). 2019;24(3):279–286. doi:10.1111/nep.13494
101. Lv JC, Zhang LX. Prevalence and Disease Burden of Chronic Kidney Disease. Adv Exp Med Biol. 2019; 1165:3-15. doi: 10.1007/978-981-13-8871-2_1.
102. Ahmed H, Farewell D, Francis NA, Paranjothy S, Butler CC. Risk of adverse outcomes following urinary tract infection in older people with renal impairment: Retrospective cohort study using linked health record data. PLoS Med. 2018; 15(9):e1002652. Published 2018 Sep 10. doi:10.1371/journal.pmed.1002652
103. Hsiao CY, Lin HL, Lin YK, Chen CW, Cheng YC, Lee WC. *et al*. Urinary tract infection in patients with chronic kidney disease. Turk J Med Sci. 2014; 44(1):145-9.
104. Gilbert DN. Urinary tract infections in patients with chronic renal insufficiency. Clin J Am Soc Nephrol. 2006; 1(2):327-31.
105. McDonald HI, Thomas SL, Nitsch D. Chronic kidney disease as a risk factor for acute community-acquired infections in high-income countries: a systematic review. BMJ Open. 2014; 4(4):e004100. Published 2014 Apr 17. doi:10.1136/bmjopen-2013-004100
106. Letica-Kriegel AS, Salmasian H, Vawdrey DK. Identifying the risk factors for catheter-associated urinary tract infections: a large cross-sectional study of six hospitals. BMJ Open. 2019; 9(2):e022137. Published 2019 Feb 21. doi:10.1136/bmjopen-2018-022137

107. Storme O, Tirán Saucedo J, Garcia-Mora A, Dehesa-Dávila M, Naber KG. Risk factors and predisposing conditions for urinary tract infection. Ther Adv Urol. 2019; 11:1756287218814382. Published 2019 May 2. doi:10.1177/1756287218814382
108. Fasugba O, Cheng AC, Gregory V. Chlorhexidine for meatal cleaning in reducing catheter-associated urinary tract infections: a multicentre stepped-wedge randomised controlled trial. The Lancet Infectious Diseases. 2019; 19(6):611-619. doi:10.1016/s1473-3099(18)30736-9.
109. Jahromi MS, Mure A, Gomez CS. UTIs in patients with neurogenic bladder. Curr Urol Rep. 2014; 15(9):433. doi: 10.1007/s11934-014-0433-2.
110. Lorenzo Gómez MF, Collazos Robles RE, Virseda Rodríguez ÁJ, García Cenador MB, Mirón Canelo JA, Padilla Fernández B. *et al*. Urinary tract infections in women with stress urinary incontinence treated with transobturator suburethral tape and benefit gained from the sublingual polibacterial vaccine. Ther Adv Urol. 2015; 7(4):180-185. doi:10.1177/1756287215576648
111. Sanaee MS, Hutcheon JA, Larouche M, Brown HL, Lee T, Geoffrion R. *et al*. Urinary tract infection prevention after midurethral slings in pelvic floor reconstructive surgery: A systematic review and meta-analysis. Acta Obstetricia et Gynecologica Scandinavica. 2019; 98(12):1514-1522. doi:10.1111/aogs.13661.
112. Hamid R, Losco G. Pelvic Organ Prolapse-Associated Cystitis. Curr Bladder Dysfunct Rep. 2014; 9(3):175-180. doi:10.1007/s11884-014-0249-4
113. Brown KA, Chambers A, MacFarlane S. Reducing unnecessary urine culturing and antibiotic overprescribing in long-term care: a before-and-after analysis. CMAJ Open. 2019; 7(1):E174-E181. Published 2019 Mar 29. doi:10.9778/cmajo.20180064
114. Nicolle LE, Yoshikawa TT. Urinary Tract Infection in Long-Term-Care Facility Residents. Clinical Infectious Diseases. 2000; 31(3):757-761. doi:10.1086/313996.
115. Genao L, Buhr GT. Urinary Tract Infections in Older Adults Residing in Long-Term Care Facilities. Ann Longterm Care. 2012; 20(4):33-38.
116. Mody L, Meddings J, Edson BS. Enhancing Resident Safety by Preventing Healthcare-Associated Infection: A National Initiative to Reduce Catheter-Associated Urinary Tract Infections in Nursing Homes. Clin Infect Dis. 2015; 61(1):86-94. doi:10.1093/cid/civ236
117. Mody L, Krein SL, Saint S, Min LC, Montoya A, Lansing B. *et al*. A targeted infection prevention intervention in nursing home residents with indwelling devices: a randomized clinical trial. JAMA Intern Med. 2015; 175(5):714-23. doi: 10.1001/jamainternmed.2015.132.
118. Marami D, Balakrishnan S, Seyoum B. Prevalence, Antimicrobial Susceptibility Pattern of Bacterial Isolates, and Associated Factors of Urinary Tract Infections among HIV-Positive Patients at Hiwot Fana Specialized University Hospital, Eastern Ethiopia. Can J Infect Dis Med Microbiol. 2019; 2019:6780354. Published 2019 Feb 6. doi:10.1155/2019/6780354
119. Shannon CL, Klausner JD. The growing epidemic of sexually transmitted infections in adolescents: a neglected population. Curr Opin Pediatr. 2018; 30(1):137-143. doi:10.1097/MOP.0000000000000578
120. Rowley J, Vander Hoorn S, Korenromp E Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull World Health Organ. 2019; 97(8):548-562P. doi:10.2471/BLT.18.228486
121. Shipman SB, Risinger CR, Evans CM, Gilbertson CD, Hogan DE. High Prevalence of Sterile Pyuria in the Setting of Sexually Transmitted Infection in Women Presenting to an Emergency Department. West J Emerg Med. 2018; 19(2):282-286. doi:10.5811/westjem.2017.12.35605
122. Mancino P, Dalessandro M, Falasca K, Ucciferri C, Pizzigallo E, Vecchiet J. *et al*. Acute urinary retention due to HSV-1: a case report. Infez Med. 2009; 17(1):38-40.
123. Yamanishi T, Yasuda K, Sakakibara R. Urinary retention due to herpes virus infections. Neurourology and Urodynamics. 1998; 17(6):613-619. https://doi.org/10.1002/(SICI)1520-6777(1998)17:6<613::AID-NAU5>3.0.CO;2-2
124. Azami M, Jaafari Z, Masoumi M. The etiology and prevalence of urinary tract infection and asymptomatic bacteriuria in pregnant women in Iran: a systematic review and Meta-analysis. BMC Urol. 2019; 19(1):43. Published 2019 May 30. doi:10.1186/s12894-019-0454-8
125. Gilstrap LC 3rd, Ramin SM. Urinary tract infections during pregnancy. Obstet Gynecol Clin North Am. 2001; 28(3):581-91.
126. Amiri M, Lavasani Z, Norouzirad R. Prevalence of Urinary Tract Infection Among Pregnant Women and its Complications in Their Newborns During the Birth in the Hospitals of Dezful City, Iran, 2012 - 2013. Iran Red Crescent Med J. 2015; 17(8):e26946. Published 2015 Aug 24. doi:10.5812/ircmj.26946
127. Ghouri F, Hollywood A, Ryan K. Urinary tract infections and antibiotic use in pregnancy - qualitative analysis of online forum content. BMC Pregnancy Childbirth. 2019; 19(1):289. Published, 2019. doi:10.1186/s12884-019-2451-z
128. Parikh P, Bhat V. Urinary tract infection in cancer patients in a tertiary cancer setting in India: microbial spectrum and antibiotic susceptibility pattern. Antimicrob Resist Infect Control. 2015; 4(Suppl 1):P221. Published 2015 Jun 16. doi:10.1186/2047-2994-4-S1-P221
129. Nik-Ahd F, Lenore Ackerman A, Anger J. Recurrent Urinary Tract Infections in Females and the Overlap with Overactive Bladder. Curr Urol Rep. 2018; 19(11):94. doi: 10.1007/s11934-018-0839-3.
130. Jhang JF, Kuo HC. Recent advances in recurrent urinary tract infection from pathogenesis and biomarkers to prevention. Ci Ji Yi Xue Za Zhi. 2017; 29(3):131-137. doi:10.4103/tcmj.tcmj_53_17
131. Huang CH, Chou YH, Yeh HW, Huang JY, Yang SF, Yeh CB. *et al*. Risk of Cancer after Lower Urinary Tract Infection: A Population-Based Cohort Study. Int J Environ Res Public Health. 2019; 16(3):390. Published 2019 Jan 30. doi:10.3390/ijerph16030390

132. Glover M, Moreira CG, Sperandio V, Zimmern P. Recurrent urinary tract infections in healthy and nonpregnant women. Urol Sci. 2014; 25(1):1-8. doi:10.1016/j.urols.2013.11.007
133. Al-Badr A, Al-Shaikh G. Recurrent Urinary Tract Infections Management in Women: A review. Sultan Qaboos Univ Med J. 2013; 13(3):359-367. doi:10.12816/0003256
134. Alvisi S, Gava G, Orsili I. Vaginal Health in Menopausal Women. Medicina (Kaunas). 2019; 55(10):615. Published 2019 Sep 20. doi:10.3390/medicina55100615
135. Abou Heidar NF, Degheili JA, Yacoubian AA, Khauli RB. Management of urinary tract infection in women: A practical approach for everyday practice. Urol Ann. 2019; 11(4):339-346. doi:10.4103/UA.UA_104_19
136. Jung C, Brubaker L. The etiology and management of recurrent urinary tract infections in postmenopausal women. Climacteric. 2019; 22(3):242-249. doi: 10.1080/13697137.2018.1551871.