

Review Article





# Urinary tract infection: an overview of the infection and the associated risk factors

#### **Abstract**

Urinary tract infection (UTI) is a common bacterial infection known to affect the different parts of the urinary tract and the occurrence is found in both males and females. Despite the fact, that both the genders are susceptible to the infection, women are mostly vulnerable due to their anatomy and reproductive physiology. The infection is usually caused as a consequence of bacterial invasion of the urinary tract including the lower and the upper urinary tract. Among the bacterial species Escherichia coli account to 80% to 85% of the infection followed by Staphylococcus species that constitutes to 10% to 15%. In addition, bacterial species Klebsiella, Pseudomonas, Proteus and Enterococcus species plays a minor role in conferring the infection. A variety of parameters are related to UTI which include age, parity, gravidity, pregnancy and association of diseases augment the condition of the infection. The current review attempts to highlight the various factors associated with UTI, prime perpetrators responsible for the infection, the emergence of growing resistance and possible remedy to overcome the infection. The review specially focuses on UTI among women during pregnancy.

**Keywords:** cystitism, phylonephritis, UTI during pregnancy, asymptomatic and symptomatic bacteriuria and diabetes associated UTI, UTI antimicrobial resistance and susceptibility pattern

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#### Introduction

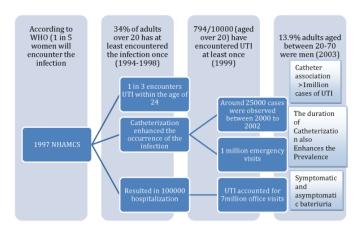
Urinary tract infection is a common contagion among men and women but the incidence is quite high among women due to their physiology. In simple terms, it can be referred as a condition which women will certainly encounter during the span of their life time and the prevalence is higher among women during pregnancy. As the name indicates, the infected parts involve the urinary tract comprising of the upper and lower urinary tract. The infection is named after the part that gets infected and is referred to as cystitis (bladder infection) and phylonephritis (kidney infection). The symptoms associated with the bladder and kidney infections are contrasting which includes painful and frequent urination in case of cystitis as a result of bladder infection whereas conditions like high fever and flank pain are commonly experienced in case of kidney contagion which is referred to as phylonephritis. This prevalence of the infection among children and elderly people is not clearly understood and is currently under study. Bacteria are the prime perpetrator responsible for conferring the infection among humans but the role of certain fungi and viruses cannot be over looked. However, the incidence of UTI as a result of viral or fungal infection is considered to be rare phenomena. Though the infection seems to be harmless in the initial stages, the patient shows a variety of symptoms as the stage progresses and can lead to death in severe circumstances. Research studies have defined urinary tract infection as the most common form of bacterial infection.<sup>1,2</sup> Urinary tract infection can be a consequence of poor diagnosis and is regarded as the common hospital acquired infection.<sup>3,4</sup> The infection encompasses a diverse group of clinical syndromes and diseases that differ in epidemiology, etiology, location severity of the condition.<sup>5</sup> In addition to the above factors, it also vary in expressed local symptoms, frequency of recurrence, extent of damage caused, presence of complicating factors and the risk from their reiterate incidence.<sup>6</sup> The occurrence of bladder infection is usually followed by kidney infection and results in blood borne infection and in severe circumstances can lead to dire consequences including death. Therefore, UTI is capable of claiming lives under severe circumstances and proper treatment results in quick recovery from the contagion. The onset of the infection is in the 6th week of pregnancy through 24th week. Although the prevalence of bacteriuria during pregnancy is similar to that in non pregnant women, pregnancy enhances the possibility of infection among women.<sup>8,9</sup> The occurrence of the infection is at its peak during pregnancy which in turn relies on several other factors. Though the higher incidence of UTI during pregnancy cannot be accepted as a universal fact as the concept is under the verge of research and several researchers are attempting to figure out the significance of pregnancy in relation to urinary tract infection. The concept of the predominance of UTI among women during pregnancy is a complex aspect and is yet to be understood and validated. Many researchers have made several attempts in the past and the quest is still going on to derive suitable facts to correlate the prevalence of UTI during pregnancy but nevertheless, pregnancy is considered to be a crucial time and requires various precautionary measures to safeguard the women and unborn child. 10 In addition to pregnancy; sexual intercourse and family history also has a central role in conferring UTI.11 The invasion of lower urinary tract by the bacteria which usually comprises the bladder causes cystitis which is trailed by the upper urinary tract infection referred to as phylonephritis. This could be a consequence of blood borne infection. Despite the fact, that 80% of the infection is caused by Escherichia coli, the involvement of other pathogens cannot be denied and one of the perpetrators responsible for conferring UTI are Gram positive cocci. Gram positive cocci are gaining worldwide importance and Staphylococcus species are one of the major pathogens belonging to the cocci group. Pathogens associated with UTI are known to exhibit a



property called as bio film formation which is responsible for causing the infection.

Researchers all around the globe are making efforts to elucidate the significance of bio film as a prime source of infection. It is a widely accepted fact that pregnancy is one of the crucial periods and lack of essential care can lead to adverse outcomes. There are several infections that can lead to pregnancy related complications and one of those is the urinary tract infection which invades the lower and the upper urinary tracts. Despite the fact that *E. coli* is responsible for causing the urinary tract infection, a new perpetrator is gaining significance due to its complex genetic makeup responsible for its pathogenecity and toxicity. The pathogen is none other than *S. aureus* and sufficient research evidences are available to substantiate their role in causing the infection.

# Overview of UTI



Prevalence of UTI among different groups of people over the last fewyears.

#### Biology of urinary tract

Biology of urinary tract Urinary tract infection affects the parts of the urinary tract which includes the upper and lower urinary tract and the occurrence is high in females due to their reproductive anatomy.<sup>12</sup> The whole urinary system comprising of the parts of the urinary tract is at risk as the infection can affect any part of the urinary tract.

Figure 1 depicts the urinary system comprising of the various parts of the urinary tract including the renal artery and vein, kidneys, bladder, ureter, urethra and provision for urine exit. Kidneys are the organs of utmost significance and are known to perform crucial regulatory functions. These acts as innate filters and play a vital role in removing the unwanted water soluble waste from the blood and also enables the re-absorption of essential ingredients like water, glucose and amino acids. Kidneys are known for the production of urine which is diverted to the urinary bladder by means of thin tubular structure known as ureter. The urinary bladder is a muscular flexible organ which accumulates the urine collected from the kidneys before they are disposed. The collected water soluble waste in the form of urine is then flushed out from the genitals by means of urethra which connects the urinary bladder and genitals. This process of production of urine and its disposal is systematic and urinary tract infection greatly influences this process and may result in a variety of symptoms which the patient experiences during the process of contagion. In

simple terms urinary tract infection is a consequence of invasion of the urinary tract by infectious organisms resulting in bladder infection and untreated condition leads to renal defects damaging the kidneys. The organized operation of the urinary system relies on the lower and upper tracts which are known to perform diverse regulatory tasks ranging from the production of the urine till their disposal. Entry of an infectious pathogen in the urinary tract causes the infection which usually occurs through the urethra. This is one of the prime reasons for higher incidence among women than men due to the shorter length of urethra in women which makes them vulnerable to such infections.

Since the urethra is shorter in women (about 1.5 to 2 inches) when compared to men (8 inches), they are more prone to infections associated with the urinary tract. The shorter length of the urethra in women enhances the scope for the pathogen to invade the bladder resulting in bladder infection.

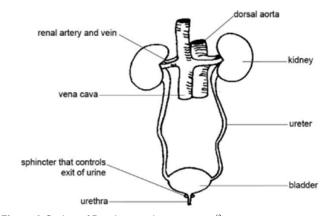


Figure I Outline of Female reproductive system. 12

#### Classification of UTI

It is understood that the infection targets the different parts of the urinary tract and as a consequence results in the contagion of the lower and the upper urinary tracts. The infection is named based on the site of infection. The infection of urethra and ureter are referred to as urethritis and ureteritis respectively where as cystitis and phylonephritis corresponds to bladder and kidney infections. <sup>13</sup> Cystitis is a common type of infection where as the infection associated with the renal damage is an issue of serious concern. Therefore the infection of bladder and urethra are referred as the infection of the lower urinary tract whereas the kidney and ureter infection is an indication of upper tract infection. Generally UTIs are classified based on the factors that trigger the infection and the nature of occurrence.

Taking these aspects in to consideration, UTIs can be classified as follows:

- i. Uncomplicated or complicated (based on the factor that triggers the infection)
- ii. Primary or recurrent (depending on the nature of occurrence)

**Uncomplicated and complicated urinary tract infection:** This is a consequence of bacterial infection and the prevalence is higher in women than men. This includes the common form of the infection like the cystitis and phylonephritis which affects the lower and the upper tracts leading to bladder and kidney infections. In contrast, complicated urinary tract infection occurs in men and women at any point of their life and has the tendency to produce severe outcomes

resulting in death under serious circumstances. These infections are highly intricate and are difficult to treat and they are persistent. These complicated urinary tract infections can lead to outcomes like structural anomalies that blights that capability of the urinary tract to flush out the urine and this in turn provides better scope for the growth of bacteria as urine is considered to be a suitable growth medium and leads to dire consequences. Patients with urinary tract infection are often subjected to medical devices and one such device commonly employed among the patients are the urinary catheters which serve as a common means of infection. In addition, bladder and kidney malfunction and kidney transplants are the other factors for complicated urinary tract infection. The first three months after kidney transplant is very crucial and the patient is vulnerable to develop such complications.

Recurrent urinary tract infection: This is a common phenomenon that is observed among women who have experienced uncomplicated UTIs and they are classified as re-infection and relapse. Major cases of UTIs are referred to as re-infections and the condition is encountered by the patient after several weeks of antibiotic treatment. The less frequent type of recurrent UTI is known as relapse which is an outcome of treatment failure and the patient encounters the condition within two weeks of the previous infection. Relapse UTIs are usually associated with phylonephritis which results in renal failures, kidney impediments through kidney stones and anatomical abnormalities in men and women. In addition, the classification of UTIs is also based on the extent of symptoms exhibited by the patients which groups the UTIs in to symptomatic and asymptomatic UTIs.

The bacterial count is an important parameter to signify the presence of symptomatic and asymptomatic UTIs. The most common pathogen known for conferring the infection is *E. coli* which constitutes up to 80 to 85% followed by the other pathogens that reside in the urinary tract like *Pseudomonas*, *Klebsiella*, *Staphylococcus*, *Enterococcus* etc. In addition, to bacteria other microbes like fungi and viruses are known to cause UTIs but bacterial mean of infection predominates.

## **Symptoms of UTI**

UTI can be manifested as asymptomatic or symptomatic infection based on the presence and absence of the symptoms. Hence symptoms enhance the diagnosis process among young healthy women. The infection is less common in children.

### Symptoms of urinary tract infection

- A) Cystitis: This is commonly called as lower urinary tract infection or bladder infection and affects the bladder. It causes the following symptoms
  - i. Pressure in lower pelvis pain
  - ii. Dysuria (painful urination)
  - iii. Polyuria (frequent urination)
  - iv. Urinary urgency
  - v. Nocturia (urination during night)
  - vi. Haematuria (urine with traces of blood)

Cystitis is further classified based on the etiology and therapeutic approach and traumatic cystitis considered as the common form of cystitis among females causing the bruising of the bladder. This is often followed by bacterial cystitis. The coliform bacteria are transferred to the bladder from the bowel through the urethra.

B) Phylonephritis: This is commonly referred to as upper urinary tract infection and affects the kidneys. It is also known as "pyelitis". Severe incidence causes the accumulation of pus around kidneys and is known as "pyonephrosis". Symptoms of phylonephritis include fever and flank pain in addition to symptoms seen in lower urinary tract infection. Among young children, high fever is the only symptom of urinary tract infection and the symptoms are difficult to detect in elderly people. Hence it is recommended to carry out an analysis of the urine culture.

#### Causative agent

Urine is generally considered to be sterile and is believed to be germ free. Any source of possible infection occurs through urethra which initiates the incidence of the infection. The predominant pathogen responsible for UTI is *E. coli* which constitutes up to 80-85% and is followed by *Staphylococcus saprophyticus* which accounts to 5-10%. The occurrence of the infection due to viral or fungal agents is a rare phenomenon. In addition to the above mentioned bacterial species, *Klebsiella*, *Proteus*, *Pseudomonas* and *Enterobacter* are associated with UTI. The bacteria enter the bladder through urethra and the infection can also occur through blood and lymph. The microbial etiology of UTIs is deemed to be well established and frequent.

Pathogens like E. coli and S. saprophyticus are associated with population acquired acute uncomplicated infection where as Klebsiella, Enterococcus, Proteus Species, Enterobacter are known to confer uncomplicated cystitis and phylonephritis that are sporadic. Mainstream pathogens associated with UTIs are known for their resilience and exhibit the property of antimicrobial tolerance. In addition, they are also known for their phenotypic and genotypic features that make them prime contenders in conferring the infection. Host factors have to be considered as they are equally responsible for the cause of the infection and make the individual vulnerable. These include age, diabetes, long term hospitalized patients and the kind of medical devices among the patients like the catheters.<sup>15</sup> The bacteria are transmitted to the bladder from the bowel. The attachment of the bacteria is followed by the formation of the bio-film which resists the immune response and is the main cause of the infection. Incidence of UTI due to S. aureus is usually considered as a secondary infection next to blood borne infections. In addition urinary catheters elevate the risk of UTI. Depending on the presence or absence of the symptoms, it is known as symptomatic and asymptomatic UTI. As the name indicates, symptomatic is the condition in which the symptoms are seen in the patient and in case of asymptomatic the symptoms are not found. In both the conditions, the urine will have a considerable count of bacteria. A count of >10<sup>5</sup> to 10<sup>6</sup> is considered to confirm the presence of symptomatic or asymptomatic bacteriuria during pregnancy.<sup>16</sup> According to researchers, count exceeding 100,000 bacteria/ml in two consecutive clean catch urine samples or same count in a single mid stream urine sample can be considered as true bacteriuria.17

#### Asymptomatic and symptomatic UTI

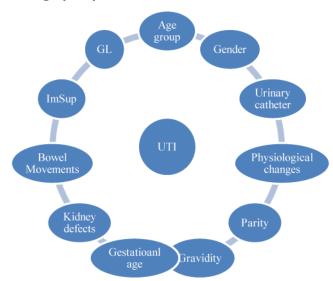
Researchers have extensively investigated the infection among people of different age groups belonging to different races and have produced reliable output. Asymptomatic bacteriuria is defined as a condition where the symptoms are not observed in the patient. Studies have substantiated an enumeration of 10<sup>3</sup> CFU/ml of sample to be appropriate for the diagnosis of group *B streptococcus* (GBS) urinary tract infection.<sup>18</sup> The researchers also feel that the diagnosis of UTI among asymptomatic patients should be supported by positive

cultures for uropathogens to confirm the presence of the infection.<sup>19</sup> Attempts have been made to demonstrate the occurrence of asymptomatic and symptomatic UTI as a consequence of bacteriuria which is the presence of bacteria in urine.20 Despite the fact, that symptomatic bacteriuria is common among the pregnant women and leads to various complications, asymptomatic bacteriuria could also lead to assorted complications. Studies in the past have carried out a convoluted analysis to explore the incidence of asymptomatic bacteriuria among pregnant women at Komfo Anokye Teaching Hospital (KATH), Ghana. 21 They have defined urinary tract infection as microbial colonization of urine and tissue invasion of any structure of the urinary tract. The incidence of UTI among pregnant women across the world varies widely and has been demonstrated by the scientific studies carried out by the researchers. In Canada the prevalence rate varies from 4-7% and 7% of incidence has been recorded in Ethiopia. Experimental studies have revealed the incidence of the infection up to 23.9%.<sup>22</sup> Reports have also suggested a higher rate of prevalence up to 86.6% in the Southern part of Nigeria.<sup>23</sup> It is understood from the above findings that the rate of occurrence of UTI in Nigeria has drastically increased over a period of 8years. Additional reports have illustrated the occurrence of asymptomatic bacteriuria among pregnant and non-pregnant women ranging from 5 to 9%. Lack of proper treatment can lead to consequences like acute cystitis and phylonephritis cropping up at a rate of 15 to 45% and pregnant women are prone to higher risk compared to non-pregnant women. The rate of occurrence is 4times higher during pregnancy compared to nonpregnant women.

Attempts have been made to prove the role of asymptomatic bacteriuria in causing symptomatic bacteriuria and research studies have confirmed the occurrence of symptomatic bacteriuria due to untreated asymptomatic bacteriuria.<sup>24</sup> Thus asymptomatic bacteriuria accounts to about 70% of cases of symptomatic UTI among unscreened pregnant women. Asymptomatic bacteriuria is generally defined as a true bacteriuria in absence of specific symptoms during acute UTI. The criteria for diagnosing is the presence of >10<sup>5</sup> bacteria/ml in a single sample of mid stream urine or presence of same amount of bacteria in two consecutive clean catch urine samples. The occurrence of asymptomatic bacteriuria during pregnancy ranges between 2 to 10%. Certain experimental analysis has claimed the prevalence of symptomatic UTI as a consequence of physiological changes during pregnancy.<sup>25</sup> In addition, glycosuria, proteinuria and aminoaciduria also facilitate the bacterial growth. Hence it is understood that 20-40% of patients during their pregnancy diagnosed with asymptomatic bacteriuria are vulnerable to develop symptomatic bacteriuria in due course if untreated. This in turn leads to phylonephritis which in later stages causes kidney failure. Usage of antibiotics is necessary to alleviate the prevalence of phylonephritis. A similar kind of study was carried out to investigate the prevalence of asymptomatic bacteriuria and the associated risk factors among pregnant women during the first pre-natal visit.26 They have stressed on the significance of physiological factors leading to UTI. Research studies have explored the role of S. aureus in association with urinary tract infection and subsequent bacteremia.<sup>27</sup> According to their study, the presence of S. aureus was apparent in the urine samples of the long term care patients. In spite of its association with UTI, the significance of Staphylococcal bacteriuria is tentative. Their study has proposed S. aureus as a urinary pathogen and its colonization of the urinary tract can lead to future complications. Urinary tract instrumentation and presence of indwelling catheters elevates the risk of S. aureus carriage in the

urinary tract.<sup>28,29</sup> Hence it is understood that asymptomatic UTI is a consequence of bacterial infection in the absence of symptoms and can transform in to symptomatic UTI under severe circumstances and one of the prime reasons for this to occur is the lack of adequate medical facilities and health care centers. However, the fact of occurrence of the infection as a consequence of long term hospitalized conditions cannot be contracdicted. Several research studies have confirmed the presence of the infection based on a specific enumeration which ranges from 103 to 105 CFU/ml and the presence of symptoms is a vital indication for the onset of the symptomatic UTI. However, the count varies as certain studies have considered a count less than 105 cfu/ml to signify the infection. But majority of the research studies in relation to UTI usually consider a count of 100000cfu/ml. The prime reason for taking the enumeration in to consideration is due to the fact that urine is considered to be sterile and the presence of bacteria in the urine is a consequence of bacterial colonization due to infection.

#### **Demographic parameters**



Demographic parameters associated with UTI ImSup, immuno suppressants GL, geographical location

#### **UTI** during pregnancy

The prevalence of symptomatic and asymptomatic bacteriuria among women during pregnancy is very common and the previous history of the infection is a major risk factor. The effect of asymptomatic UTI can be subsided by employing suitable treatment which in turn prevents the adverse consequences of its progress. Urinary tract infection is a consequence of poor diagnosis during pregnancy and this in turn enhances the scope of infection and pregnant women under such circumstances are susceptible to serious complication. Their study has revealed the occurrence of the infection to be 56% among women during pregnancy and the incidence was up to 50% during the second trimester among the pregnant women. Women within the age group of 15-32 were prone to the infection and pregnancy has in turn enhanced the susceptibility rate among women. UTI is considered as the most common hospital acquired infection constituting up to 35% of nosocomial infection and is regarded as a vital factor for the outbreak of bacteremia among hospitalized patients. Despite the fact, that E. coli is considered as the prime perpetrator, studies have validated the significance of S. aureus in conferring the

infection.<sup>30</sup> Enhanced risk of phylonephritis can be a consequence of untreated UTI and can lead to serious outcomes like ephemeral kidney failure, acute respiratory disorders and hematological abnormalities.<sup>31</sup> It is a widely accepted fact that pregnancy is associated with variety anatomical changes in women followed by hormonal and physical changes which increases the possibility of urinary stasis which in turn causes the backward flow of urine from bladder to ureter. This as a consequence of physical aberrations enhances the occurrence of UTI among women during pregnancy.<sup>32</sup> Many researchers have regarded UTI as the most common bacterial infection encountered by human beings and have attempted to investigate the antimicrobial pattern exhibited by these pathogens responsible for the infection.

They have investigated the significance of associated risk factors and its role in affecting thousands of people annually due to the infection of Gram negative pathogen leading to bacteremia. The significance of risk factors like anaemia, low income level, past history of UTI and sexual activity in causing UTI among women during pregnancy has been explored and validated by several researchers.<sup>33</sup> Presence of 100000 organisms per ml of urine sample in addition to the presence of an exceeding number of white blood cells can signify the occurrence of UTI. The count of >5 white blood cells in a symptomatic patient is considered to be significant. However, recent demonstrative studies have considered this number of colony count to be inappropriate and have reduced the count to 10<sup>3</sup>CFU/ml to confirm the presence of the infection. Though E. coli is regarded as the prime pathogen in conferring the infection, different studies carried out by researchers have validated the presence of Proteus Species. An increase in the number of Proteus species ranging from 5.8% to 12.4% have been demonstrated by several researchers.  $^{34,35}$  In addition to factors like shorter urethra which enhances the scope of pathogenic invasion of the urinary tract, sexual activity also facilitates the entry of pathogens which as a consequence results in UTI.<sup>36</sup> The prevalence of asymptomatic UTI among women varies from 2% to 15% compared symptomatic UTI during pregnancy.<sup>37</sup> This in turn is a consequence of microbial colonization of the urinary tract. The occurrence of the infection among the hospitalized patients belonging to different groups varies considerably Ipe et al.20 The patients can be grouped as healthy adults, elderly patients, pregnant women and immune compromised and the extent of prevalence of UTI among these groups significantly varies.<sup>38</sup> Evaluation of bacteriuria among infected individuals symbolizes a diagnostic challenge due to the involvement of variety of microorganisms and requires a careful assessment to evaluate the etiologies as a consequence of bacteriuria among the different groups of patients. Treatment during pregnancy is very crucial and the employment of empirical treatment or misuse of the antimicrobial agents due to lack of proper assessment of the condition has resulted in a widespread resistance among the pathogens conferring UTI.<sup>39</sup> The prevalence of the infection among women during pregnancy was 14% and this was comparable to the findings of the preceding studies which revealed a prevalence of UTI to be about 16% among women during pregnancy. 40,41

*E. coli* is considered to be the most dominant pathogen associated with the infection and many studies in the past and present have validated the significance of the pathogen and its role in conferring the infection. Studies have revealed the predominance of *E. coli* to be over 40% when compared to other pathogens associated with the infection.<sup>42</sup> The demonstrative endeavor of researchers have supported the outcomes of several other researchers by regarding UTI as the most common bacterial infection and untreated condition can

lead to obstetric complications. 43 They have attempted to investigate the occurrence of asymptomatic bacteriuria among women during their antenatal visit to identify the perpetrators associated with asymptomatic bacteriuria among women during pregnancy. Their study has shown the predominance presence of E. coli accounting to over 60% and this coincides with the findings of many scientific investigators. 24,44-46 The prevalence of the infection due to Klebsiella species accounted to 16%.47 Scientific analysts have also defined UTI as the most common non-intestinal infection. S,49 and have cited the lack of access to necessary health care centers can be a cause for the outbreak of the infection. They have attempted to exemplify the prevalence of the infection among women of reproductive age and have confirmed the occurrence of hematuria, pyuria and the infection of the upper urinary tract resulting in phylonephritis. Their study has also validated the persistence of the symptoms among women in their reproductive age which lasts for a time duration ranging from several days toyears. The microbes responsible for causing the infection are considered to be highly consistent and involve the microbial colonization of the perineum as a consequence of coliform bacteria which accounts to 80% of the infection where as S. saprophyticus constitutes to 5% to 10% followed by the other Gram negative rods which are sporadic in conferring the infection.<sup>50</sup> However researchers consider that UTI is not significantly associated with morbidity as well as mortality but the condition could be deteriorated due to lack of adequate medical treatment leading to life claiming consequences. Despite the fact, the symptoms include painful and frequent urination; untreated UTI can be detrimental to the upper urinary tract leading to renal failure. Pregnant women diagnosed with asymptomatic bacteriuria are liable to encounter phylonephritis which could bring about dire consequences and this condition was found in 50% of women during pregnancy.

Despite the fact, that the prevalence of bacteriuria among pregnant and non pregnant is similar the occurrence of acute phylonephritis is higher among the pregnant women. Pregnancy is associated with many anatomical and physiological changes of the urinary tract and enhances the possibility of phylonephritis. The dilation of the renal pelvis and the ureter occurs by the eight week of pregnancy and also results in the displacement of the bladder.<sup>51</sup> Symptomatic bacteriuria is classified as acute cystitis and acute phylonephritis and the former and latter are associated with bladder and kidney infections respectively.<sup>52</sup> Many research studies have reported higher prevalence of phylonephritis during the second half of the pregnancy and the enlargement of the uterus during the course of pregnancy is one of the vital factors to encounter phylonephritis. As the uterus widens, it compresses the bladder and this prevent the complete emptying of the bladder and urine retention in the bladder facilitate the growth of the pathogens resulting in the infection. The clinical symptoms of phylonephritis are similar in pregnant and non pregnant women which includes fever, flank pain and vomiting. The hormonal changes during pregnancy are an important parameter associated with the infection. The precedent studies carried out by the researchers have thoroughly investigated the rate of prevalence and the outcome of asymptomatic bacteriuria during pregnancy. A count of ≥100,000 colony forming units is considered as an important criterion to confirm the presence of asymptomatic bacteriuria.53,54 The prevalence of UTI was ranging between 2.5-15% and the value has gone down to 11.6% in 2012.<sup>39</sup> The variation in the incidence of UTI can be elucidated by the population characters and screening methods.

In females, the urinary tract has a significant affiliation with the

47

reproductive organs due to its propinquity. The position of the uterus plays a vital role in conferring the infection. The uterus lies above the bladder in the non-pregnant state and the enlargement of the uterus during pregnancy negatively influences the tissues of the urinary tract.<sup>55</sup> The infection can be diagnosed by isolating the urinary pathogen from the patient. Researchers have reported that the occurrence of the infection during pregnancy may be related to the socio economic status of the patient as the indigent group was more prone to the infection.<sup>56</sup> The occurrence of bacteriuria among the non- indigent was found to be 2% compared to 6.5% in indigent population.<sup>57</sup> Factors like history of the previous infection, diabetes and physiological aberrations of the urinary tract also signify the infection.<sup>58</sup> The pathogens responsible for conferring the infection are similar among the pregnant and non pregnant women. 59,60 E. coli accounts to 80% of the infection and the presence of pili allows the pathogen to attach to the uroepithelial cells and results in tissue invasion. 61 Untreated infection during pregnancy can lead to premature labor which can be fatal to the new born infant. 62 Babies are considered to be premature if they are born before the 37th week of the pregnancy and this enhances the scope of infection in the new born babies. In severe cases preterm delivery can also result in abortion leading to infant's death.

#### Physiological changes during pregnancy

The physiological changes associated with pregnancy makes the healthy pregnant women prone to serious complications of the urinary tract. Researchers have validated the significance of physiological changes as one of the vital factors for the occurrence of UTI during pregnancy. Factors like hormonal, mechanical and physiological changes during pregnancy ads up to the vital changes in the urinary tract. 63 This in turn has an intense impact on the acquirement of the infection

The physiological changes include the expansion of the uterus, reduced flow of urine through the ureter (phenomenon referred to as urinary peristalsis) and reduced bladder tone. These changes also elevate the plasma volume and researchers have made various attempts to correlate its role in facilitating the bacterial growth. The widening of the ureter begins at the eight week of pregnancy resulting in the bladder displacement. The enlargement of uterus results in mechanical compression and as a consequence leads to hydroureter and hydronephrosis. The progesterone produced during pregnancy allows the relaxation of the smooth muscles which leads to decreased peristalsis of the ureters which in turn increase the bladed capacity and urinary stasis. These changes may facilitate the bacterial growth.<sup>64</sup> The elevated plasma volume during pregnancy reduces the urine concentration and promotes the urinary progestins and estrogens. This in turn declines the capability of the lower urinary tract to defend against the invading pathogen. Various factors like ureteral dilation, increased bladder volume and decreased bladder tone leads to increased urinary stasis and ureterovescical reflux and this in turn enhances the scope of urine to remain in the bladder resulting in infection as urine serves as the best growth medium for the pathogens to augment. The count of bacteria and white blood cells in the urine sample decides the severity of the infection. However, there are cases where pregnant women with positive urinary tests have no symptoms of the infection. Research studies in the past have validated the involvement of wide variety clinical entities associated with UTI which include urethritis, cystitis, severe and persistent phylonephritis. Presence of microorganisms in urine is a vital sign of indication stating the commencement of the infection. Asymptomatic

and symptomatic conditions may be confined to colonization of urine without any inciting response.

Existence of pus cells in urine without any vital symptoms indicates the condition of asymptomatic bacteriuria and the presence of pus cells in urine is known as pyuria. Individuals with asymptomatic bacteriuria are prone and vulnerable to encounter symptomatic bacteriuria which can result in severe consequences depending on the stage of infection and condition of the patient. The entry of the microorganisms through the anal outlet initially results in the invasion of the urinary tract and this in turn makes the respective parts vulnerable and enhances the scope of risk due to infection. During the process, in addition to lower and upper tract adjacent parts like perinephric fascia, prostate and epididymis are at risk. Therefore presence of microorganisms in the urine and inflammatory symptoms are considered to be characteristic features of the infection as urine is usually considered to be germ free.

#### Route of infection

Reproductive physiology of females makes them more vulnerable to the infection and can occur through congenital sites like the urethra, vaginal opening, perineum, anus which are known to dwell their own microbial flora. The fact that most women do not encounter the infection despite of sexual practices, menstrual cycle and personal hygiene cannot be denied, the incursion of periurethral zone by enteric and other gut microorganisms' results in the initiation o the infection. The bowel movements are the primary sources of these microbes to invade the urinary system and colonize and later on confer the infection. Existence of microbial population in varying numbers in the urinary tract has been proved by the preceding studies and their recovery from rectum, urethra and cervix of women is obvious. These sites can serve as major route of infection. Nevertheless, the population of S. saprophyticus which is considered to be one of the perpetrators of the infection is yet to be established, recovery of these microbes from the different parts of the urinary tract has been validated.

The major ingredient that favors the growth of the microbes is the urine as it comprises of the essential factors to allow the augmentation of microbes and is considered as the best natural medium for the growth and establishment of the microorganisms. Urinary instrumentation such as catheters serves as one of the routes of the infection and in the absence of medical devices the microbes invades the urinary tract through the urinary stream. The microorganisms adhere to the urothelial cells and infiltrate in to the urothelial linings resulting in the infection. In addition to bowel movements and urine stream which allows the pathogens to invade the urinary system, there are certain bacteria that are motile due to the presence of flagella which allows them to invade the different parts of the urinary tract. The pathogens generally follow an ascending patter of invading the different parts of the urinary tract as the common route of the infection commences from the lower urinary tract from urethra which invades the bladder and later on ascends to the parts of the upper urinary tract like ureter and kidney.

# Hospitalized conditions enhances the prevalence of the infection

The nosocomial urinary tract infections accounts to about 40% of the hospital acquired infections and are associated with elevated morbidity and mortality rates. Long term hospitalized patients with indwelling urinary catheters and patients undergoing urological treatment are prone to nosocomial infections. The pathogens accountable for the infection instigate from the individual's endogenous flora and the moist environment of the hospital aggravates the condition. Despite the fact, that women are more vulnerable to the infection the research studies in the past and present have validated the increased incidence of the infection in males who have been hospitalized on a long term basis. Many demonstrative studies carried out at the hospitals have highlighted the fact of occurrence of the infection among the older men undergoing long term treatment. The issue of concern associated with these hospital acquired infections is the extent of resilience exhibited by the pathogens responsible for the infection. These pathogens are known to exhibit the property of antibiotic resistance which makes them to oppose the employed antibiotic. According to medical reports and data available at the Henry Ford Hospital in Detroit, older men with severe renal defects are highly vulnerable to UTIs. Therefore, UTI is also referred to as hospital acquired infection as hospitalized conditions favor the commencement of the infection. Researchers at the Henry Ford Urology Institute have revealed an alarming fact which has become an issue of serious concern. Their research studies have revealed a tenfold increase in the incidence of the hospital acquired infection when compared to the previous data over a period of a decade. During the period of their study, they have focused on 10.8million patients for the primary diagnosis of bladder infection (cystitis) and renal damage (phylonephritis) of which 1.8million patients were hospitalized for further treatment. Their study has shown that the number of patients for primary diagnosis was less than a million in 1997 and the number of emergency cases was about 100,000 and the current scenario is about 2.7million visits with over 450,000 admissions. The outpatient visits for UTI accounted to 8.6million in 2007 constituting 23% of emergency cases of which 84% of them were women. Though the incidence was high among the elderly people, women between the age group of 15 to 25 were mostly vulnerable. Nevertheless, women are highly prone to the infection men are more likely to be admitted in the hospitals.

#### **Diabetes and UTI**

Diabetes is a metabolic disease associated with blood sugar levels and high sugar level than required results in dire consequences. Demonstrative research studies have substantiated the significance of diabetes in relation to UTI and sufficient evidence in the form of data has been provided to imply the role of diabetes in UTI.65 Women with diabetes are more vulnerable to UTI than women without diabetes. It is a known fact that the initiation of the infection begins as asymptomatic bacteriuria which develops in to symptomatic bacteriuria as the infection progresses. Studies have highlighted the consequences of asymptomatic bacteriuria and its role in causing renal defect under untreated condition is substantiated. Occurrence of type I and type II diabetes enhances the factors associated with UTI.66,67 Presence of bacteria in urine in the absence of any clinical symptoms can be termed as asymptomatic bacteriuria and a population of  $\geq 10^5$  cfu/ml from the mid stream urine sample signifies the condition.<sup>68</sup> The occurrence of asymptomatic bacteriuria among healthy women range from 2% to 5% and the incidence is three to four folds higher among women with diabetes.<sup>69</sup> Symptomatic bacteriuria is clinically significant and treatment can reduce the consequences of the condition and in turn lessens renal defects that could arise as a consequence of phylonephritis and preterm delivery. 17,70 However, investigators found that the treatment among women hospitalized for diabetes has not reduced the pervasiveness of asymptomatic bacteriuria.<sup>71</sup> Research studies also substantiated the relation between asymptomatic bacteriuria, diabetes and impaired kidney function. 72,73

Many other researchers have attempted to unveil the association between asymptomatic bacteriuria and diabetes and have successfully revealed the alliance of asymptomatic bacteriuria and the host factors among women with diabetes. 74–77 Various case control studies signifies that the occurrence of bacteriuria and UTI is common among women and presence of debilitating diseases worsens the condition.

Patients diagnosed with diabetes often encounter the dire consequences of UTI which includes emphysematous cystitis and pyelonephritis, fungal infections. Candida is the common fungal species known to confer the disease. The urinary tract anomalies in relation to anatomical and functional aspects are associated with diabetes. Such aberration increases the employment of medical devices like the urinary catheter which in turn enhances the scope of the infection. Apart from these, a patient diagnosed with diabetes or other diseases that can likely affect the urinary tract is at higher risk because of the kind of treatment the patient undertakes. One of the major reasons for the development of the multidrug resistant pathogens is due to the employment of empirical treatment which offers the power of resistance to the pathogen. Hence it is necessary that the treatment should be based on the Gram stain and urine culture as it reveals the pathogen and the condition of the infection. An instance is the employment of fluoroquinolones among diabetic patients is an empiric choice. However, the prime motive of appropriate treatment among diabetic patients with asymptomatic UTIs is to avoid the severe consequences that could arise as a result of symptomatic UTIs. The outlook of UTIs among diabetic patients relies on several factors and vulnerability increases with protracted duration and greater severity of the disease.78 Higher content of glucose in urine and compromised immune system aspects incline towards the infection. High blood sugar levels negatively influences the functioning of the neutrophils resulting in their malfunction which in turn amplifies the intracellular calcium levels and as a consequence leads to phagocytosis. Periodic infections are also a consequence of vaginal candidiasis and vascular disease.

Medical conditions as a consequence of diabetes among UTI patients: Patients with diabetes are also susceptible to conditions like cystopathy, nephropathy, and renal papillary necrosis, complications that incline them towards UTI. Diabetic cystopathy as a consequence causes vesicourethral reflux which causes the backward flow of the urine from the bladder to ureter and kidney and this result in periodic infections. Around 30% of women diagnosed with diabetes are prone to medical conditions like cystocele, cystourethrocele, or rectocele which may in turn cause persistent UTIs among diabetic females.<sup>79</sup> Medical condition like renal and perirenal abscess, emphysematous pyelonephritis and emphysematous cystitis is often encountered among diabetic women with complicated UTI. In addition, fungal infections, xanthogranulomatous pyelonephritis, and papillary necrosis are persistent among diabetic females. Obstruction of the urinary tract as a result of diabetes can cause emphysematous UTIs which leads to necrosis and hemorrhagic infarction.80 The emphysematous UTIs of the upper urinary tract are responsible for pyelonephritis, pyelitis and Emphysematous cystitis. The prime perpetrators accountable for this condition are E. coli, Klebsiella, pneumoniae, and Candida.<sup>81</sup>

# Other factors associated with risk of UTI

The previous sections have highlighted the significance of UTI among men and women including its classification, prevalence and symptoms. Demonstrative research studies in the past and present have attempted to explore the consequences of UTI among patients

and long term hospitalized conditions and diabetic individuals are highly susceptible to the disease. In addition, it is a universal fact that the prevalence of UTI is more among women when compared to men due to their reproductive physiology and pregnancy enhances the occurrence of the infection. When pregnancy is taken in to consideration there are a variety of aspects that can bring about the disease. It is a well known fact that the infection commences at the 6th week of pregnancy and attains peaks by the 20th week of pregnancy. During the course of pregnancy factors like parity and gravidity play a vital role in conferring the infection. Gravidity is defined as the number of pregnancies and parity is the number of healthy deliveries. Scientific studies have cited multiple pregnancies as a problematic indication but this remains arguable.82 Factors like age, parity and gestational age are associated with the risk of UTI.83,84 In addition, factors like employment of immunosuppressant, financial condition of the individual as well as geographical location also have a prominent in conferring the infection. Immuno suppressants are the substances that the given to a patient after a transplantation surgery in order to avoid the rejection of the transplanted organ. Immune suppressants are known to suppress the immune system of an individual and a compromised immune system is susceptible to the attack of pathogenic microbes. Financial situation may not be considered as a prime factor but a prevalence of 17% of UTI was recorded among women during pregnancy in nations like Tanzania. 85,86 Therefore, the incidence of UTI is common among males and females and females are more prone due to their anatomy. Despite the fact, that UTI is considered as a consequence of bacterial infection there are several other factors which signifies the infection. Pregnancy is considered as a crucial period and enhances the occurrence of the infection due to hormonal effects and physiological changes. Patients with diabetes are equally prone to the infection. Parity and gravidity are equally associated with the medical condition and reports and available data have validated the significance of these parameters in conferring the infection.87

# Emergence of resistance among UTI pathogens

Studies to validate the fact of growing resistance among UTI causing pathogens have been going on for the last three decades and the available data and reports confirm that the increase in resistance to commonly employed antibiotics is a consequence of inappropriate use of the antimicrobial agent. Surfacing of resistance among the pathogens responsible for UTI is an issue of serious concern and requires an immediate attention in order to derive suitable remedy to overcome the problem. Despite the fact, that the extent and nature of treatment does not remain the same for all group of people and varies among women in their reproductive age as well as pregnancy and the kind of treatment employed among the elderly people and patients hospitalized on a long term basis would be contrasting in comparison with the former group. The existence of Gram negative bacteria exhibiting multidrug resistance among the pregnant women and the extent of antimicrobial resilience among these pathogens has become an issue of concern. Treatment of asymptomatic bacteriuria among elderly and non pregnant women does not seem to be beneficial but they insist on a prior screening process of the condition before the employment of the antimicrobial agents.88 However, the extent of antimicrobial resistance shown by the pathogens towards the commonly employed drugs is an issue of global concern and this antimicrobial pattern exhibited by the pathogens varies according to

the factors like the site of their isolation, environmental conditions as well as the stage of the infection. Many health centers and hospitals in developing countries rely on the strip urinalysis method for assessing urine sample in pregnant women and this does not provide the true sign of the infection. This could in turn result in inappropriate use of antimicrobial agents as well as empirical practices. This is one prime reason for the development of resistance for different antibiotics among UTI causing pathogens. Research studies have shown the existence of resistance among the Gram negative pathogens to commonly employed beta lactum antibiotics like ampicillin and amoxicillin and have revealed the presence of pathogens exhibiting multidrug resistance. Research studies in the past have confirmed the altered antimicrobial pattern among the UTI causing pathogens. The antimicrobial susceptibility pattern among pregnant women during their first pre natal visit was studied and revealed the existence of pathogens exhibiting multidrug resistance. 89,90 Pathogens like E. coli, P. aureginosa, Klebsiella Species and Proteus species were highly resistant to antibiotics like ampicillin and cotrimoxazole.

In addition, antibiotics like cefotaxime and ciprofloxacin weren't effective against P. aureginosa which is considered to be a sporadic pathogen when compared to etiological agents like E. coli and Staphylococcus species. This is an indication of the development of surfacing resistance among major pathogens conferring UTI and has made them resilient towards the commonly employed antimicrobial agents. Despite the fact of its affectivity, Proteus species and Enterobacter species are resistant to nitrofurantoin. Prior scientific studies have investigated the antimicrobial pattern exhibited by the UTI pathogens by analyzing the mid stream urine samples. Their study has revealed a varying percentage of resistance ranging from 40% to 80% to various antibiotics and they have demonstrated the presence of multidrug resistant pathogens. Though trimethoprim is commonly used against Gram negative bacteria, their study has demonstrated the least activity of trimethoprim against E. coli and has substantiated the use of trimethoprim in empirical treatment. Even though the occurrence of UTI is a consequence of E. coli infection which accounts to 80%, the involvement of other pathogens cannot be denied. The pathogen that is gaining significance in its association with UTI is S. aureus and the development of resistance of the pathogens towards the antimicrobial agents is a global issue. Many investigators have studied the antimicrobial pattern of S. aureus among pregnant women during their antenatal visit.<sup>91</sup> Their studies have confirmed the role of the pathogen in colonizing the intestines and vagina. Studies have also implicated the role of S. aureus in asymptomatic UTI as well as uncomplicated skin infections. The occurrence of UTI up to 6.9% and 7.7% in pregnant and non pregnant women as a consequence of Staphylococcal infection was revealed and has shown the presence of multidrug resistant S. aureus. Over 30 species of Staphylococcus have been recognized of which the pathogenecity of S. aureus have been established since a long time and is regarded as the most virulent strain of the genus.

The role of *S. aureus* in causing the infection was demonstrated by several researchers and the capability of the pathogen in causing the health care and community associated infection was demonstrated. <sup>92,93</sup> The extent of variation in the antimicrobial susceptibility pattern exhibited by *S. aureus* differed from one site to the other and the antimicrobial resistance shown by the pathogens isolated from the reproductive tract differed from the resistance pattern of the pathogen isolated form a different site. <sup>94,95</sup> Several studies signify *S. aureus* as a prime competitor of *E. coli* during the course of infection and

have shown a predominant population *S. aureus* ahead of *E. coli* and *Klebsiella*. Research studies have provided sufficient amount of evidences to support the colonization of *S. aureus* among pregnant women and its influence on the neonate and neonates born to mother with *S. aureus* colonization and vulnerable to infection. Demographic parameters like maternal, gestational age, gravidity, parity, socioeconomic condition and previous history of the infection can be vital and signifies the infection. However some research studies feel that other pathogens of Staphylococcal genus are mistaken to be *S. aureus* but the other species of the genus are capable of causing the infection. Aureus colonization among women during pregnancy enhances the rate of morbidity and mortality. The resistance of *S. aureus* against fluoroquinolones such as ciprofloxacin, ofloxacin and norfloxacin is a consequence of empirical treatment.

#### **Treatment of UTI**

Studies over the past few decades have endeavored to counteract the infection and the pervasiveness of anti infective use during pregnancy was 24.5%. Generally the commencement of the treatment process starts after the diagnosis of the infection but these initial attempts of treating the disease can lead to problematic consequences as the treatment has to be made after the confirmation of the etiological agent. The initial treatment efforts involve the employment a variety of antimicrobial agents and this could in turn make the pathogen resistant to commonly employed drugs. Such kind of treatment is referred to as empirical treatment. Therefore, a sporadic assessment of the causative pathogens against the antimicrobial agents is necessary. The significance of the bacterial resistance towards to the commonly employed antibiotics during pregnancy has gained the interest of my scientific analysts and researchers. 104 The administration of the anti infective drugs during pregnancy should be carefully monitored to ensure the safety of the fetus as majority of the anti infective drugs are capable of crossing the placental barrier. 105 Synthetic antimicrobial agents belonging to the family of quinolones are generally not recommended in animals due to associated risk factors related to pregnancy but the adverse effect has not been illustrated in humans. 83,106 Research studies have confirmed the safety of beta lactum antibiotics like penicillin and cephalosporin during pregnancy. 107,108 However, these antibiotics are deemed to be safe due to the absence of teratogenic affects that can bring about any physiological defects in the new born fetus but is sometimes associated with allergic reactions.

Studies have also provided sufficient evidences to confirm the property of antibiotic resistance exhibited by certain pathogens against amoxicillin and ampicillin which in turn has limited their usage. 109 Though studies demonstrate the efficacy of nitrofurantoin, it is ineffective against *Proteus* species. 110-112 Employment of trimehoprim during the first trimester of pregnancy has resulted in cardiovascular defects in newborns. 113 Demonstrative studies have revealed the harmful effects of suphonamides during the last two trimesters of pregnancy. Therefore, women diagnosed with asymptomatic bacteriuria are prone to experience repeated infection and continuous antibiotic treatment is recommended in such cases. However, employment of antimicrobial agents interferes with the normal gastrointestinal flora. The occurrence of bacteriuria among elderly people is a characteristic feature of genetic inconsistencies, factor of ageing and allied co-morbidities.

#### **Discussion**

The current review makes an attempt to put forth the various factors that are responsible for the occurrence of the urinary tract

infection and endeavors to confirm the significance of other factors like physiological changes during pregnancy, patients with the history of diabetes, age and medical instrumentation in conferring the infection. Urinary tract infection is a common both the genders but the incidence is quite high among women due to their anatomy. 114 Females are vulnerable to encounter the infection at any point of their life time and the infection is also seen among young children and elderly people. The prevalence of UTI among pregnant women during the second trimester accounted up to 50% and has defined UTI as a consequence of lack of adequate and appropriate treatment during pregnancy.3 UTI is considered as the most common hospital acquired infection constituting up to 35% of nosocomial infection and is regarded as a vital factor for the outbreak of bacteremia among hospitalized patients.4 The percentage of women encountering any form of UTI during pregnancy is estimated to be 2% to 8%.106 E. coli is considered to be the predominant pathogen associated with the infection and many studies in the past and present have confirmed the role of the pathogen in conferring the infection.<sup>24,42,44–46</sup> Bacterial infections are considered as the main source of the disease and E. coli is considered to be the predominating pathogen followed by Staphylococcus saprophyticus and other pathogens like Proteus species, Klebsiella species and Enterococcus species have a minor role in conferring the disease.

However, in contrast to the previous studies which account E. coli to be a major etiological agent, the significance of S. aureus in colonizing the perineum of the women during pregnancy cannot be denied and is highly resistant to commonly employed antimicrobial agents. 50 The role of S. aureus in causing the infection is supported by the several research and demonstrative studies and the capability of the pathogen in causing hospitalized and community associated infection has been validated.93 A count of 100000 organisms per ml of urine sample in addition to the presence of an exceeding number of white blood cells signifies the occurrence of the infection. 19,107 The count of >5 white blood cells in a symptomatic patient is considered to be significant. However, certain studies have considered this count of 10<sup>5</sup> CFU/ml to be inappropriate and have reduced the count to 10<sup>3</sup> CFU/ml to confirm the presence of the infection as a consequence of Streptococcus spcies. 18 The significance of risk factors like anaemia, low income level, past history of UTI and sexual activity and its association with UTI among women during pregnancy have been confirmed.<sup>33,114</sup> Despite the fact, that the infection seems to be harmless in the initial stages, advancement of the contagion leads to variety of symptoms. Scientists have regarded UTI as a contagion comprising of a variety clinical syndromes and factors like epidemiology, etiology, location severity of the condition signifies the infection.<sup>5</sup> Factors like periodic recurrence is a matter of concern and the significance of risk factors as a consequence of reiterate incidence was validated.6 Pregnancy is considered to be one of the decisive periods for the epidemic and preceding research studies have substantially validated the significance of pregnancy is relation to the infection. The onset of the infection is in the 6th week of pregnancy through 24th week.7 Development of increase in resistance towards many antibiotics has become a serious issue and the existence of Gram negative bacteria exhibiting multidrug resistance among the pregnant women have been demonstrated.39,89

*E. coli*, P. aureginosa, *Klebsiella* Species and *Proteus* species were highly resistant to antibiotics like ampicillin and cotrimoxazole.<sup>43</sup> Despite the fact, that nitrofurantoin is effective against many UTI causing pathogens; it is ineffective against *Enterobacter* and *Proteus* species.<sup>90</sup> It is very obvious that the extent of antibiotic resistance

51

shown by S. aureus significantly vary from the site of isolation as the resistance pattern of the isolates from the reproductive parts differed from the isolates from a different site. 94,95 Colonization of S. aureus among pregnant women and its influence on the neonate and neonates born to mother with S. aureus colonization have been supported through the studies. 115 Occurrence of UTI among children has become a global problem and requires suitable measures to be addressed. Studies have demonstrated the extent of resistance exhibited the UTI pathogens among children. 116 Antibiotics like trimethoprim-sulfamethoxazole, cefalotine, and cephalexin were not affective against E. coli. In addition, Enterobacter species was highly resistant to antimicrobial agents like Nitrofurantoin, ceftazidime, and cefalotine. Regular usage of these antibiotics among children has become a prime reason for the development of resistance among the pathogens towards the commonly employed antimicrobial agents. UTI among children has also increased the rate of morbidity and mortality.<sup>117</sup> Factors like geographical location and socioeconomic status directly reflects up on the extent of resistance exhibited by the pathogens among children diagnosed with UTI. Occurrence of UTI among women during pregnancy is high when compared to non pregnant women.<sup>7,9</sup> Nevertheless, the concept of increased prevalence of UTI during pregnancy is complicated and under debate, the significance of pregnancy as one of the key factors in relation to UTI cannot be contradicted. 118 Though demonstrative studies in the past have attempted to validate this point and have emerged with suitable conclusions, the efforts are still going on to explore the novel hidden facts to enlighten the mankind.

The incidence of the infection is higher among sexually active women and the possibilities of encountering the infection after a sexual intercourse is higher. 11,55 The infection usually affects the various parts of the urinary tract and the infection generally initiates from the lower urinary tract which comprises of the bladder and urethra and the infection is referred to as cystitis. The advancement of the condition results in the spreading of the infection to the upper tract leading to renal failure and the condition is referred to as phylonephritis. Based on the severity of the infection they are classified as acute cystitis and phylonephritis. Improper treatment increases the rate of occurrence of the acute cystitis and phylonephritis from 15% to 45% and lack of proper treatment during pregnancy worsen the condition. Demonstrative investigations carried out by renowned researchers have endeavored to reveal the rate of occurrence of the disease among people of different race and locality. They have defined the infection as the bacterial colonization of the urine and can be asymptomatic or symptomatic. Uncomplicated UTI is considered as the infection interfering with the normal flow of urine in the absence of any structural or functional irregularities.<sup>119</sup> Though the occurrence of phylonephritis among women during pregnancy is considered to be low, women diagnosed with asymptomatic bacteriuria are liable to encounter phylonephritis ranging from 20% to 40%. 120 Research studies have substantiated the occurrence of acute phylonephritis up to 30% in women at child bearing age. The crucial period for the incidence of infection is pregnancy<sup>121</sup> and the recurrence of the infection throughout pregnancy is a common phenomenon. 122 In addition to urethral colonization, employment of spermicides also favors the outbreak of the infection. 123 Factors like ureter dilation by the eighth week of gestation and the displaced bladder facilitates bacterial colonization.124

Apart from these, diabetic patients are highly vulnerable to encounter the infection when compared to non diabetic individuals. Genetic factors of an individual also make him liable to encounter the infection and the condition is generally found in elderly patients subjected to long term hospitalized conditions. Appropriate measures to manage the co-morbid illnesses and nutritional status are enviable among the elderly population. However there are no experimental evidences to substantiate their role in preventing bacteriuria.

#### **Conclusion**

Urinary tract infection is a common contagion among both genders with higher prevalence among women due to their physiology and pregnancy enhances the occurrence of the infection due to a variety of physiological changes during the course of pregnancy. In addition, age is an important factor where elderly people with urinary devices like catheters are prone to the infection. Patients undergoing long term treatment are also vulnerable to the infection due to moist hospitalized conditions. In addition, diabetes enhances the incidence due to elevated blood sugar levels and other factors like parity, gravidity, hormonal imbalance, immunosuppressant and geographical location also has a significant role in the incidence of the infection. Though antibiotic usage has proven to be beneficial in counteracting the infection, plant source like cranberry juice is equally effective in fighting the infection and can be used as an alternative to counteract the pathogen causing UTI.

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#### **Conflict of interest**

Author declares that there is no conflict of interest.

#### References

- 1. Demilie T, Beyene G, Melaku S, et al. Urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in north west ethiopia. *Ethiop J Health Sci.* 2012;22(2):121–128.
- Parveen K, Momen A, Begum AA, et al. Prevalence of urinary tract infection during pregnancy. J Dhaka National Med Coll Hos. 2011;17(2):8–12.
- 3. Koffuor GA, Boye A, Siakwa PM, et al. Asymptomatic urinary tract infections in pregnant women attending antenatal clinic in Cape Coast, Ghana. *E3 Journal of Medical Research*. 2012;1(6):74–83.
- Kolawole AS, Kolawole OM, Kandaki-Olukemi YT, et al. Prevalence of urinary tract infections (UTI) among patients attending Dalhatu Araf Specialist Hospital, Lafia, Nasarawa State, Nigeria. *International Journal of Medicine and Medical Sciences*. 2009;1(5):163–167.
- Lucas MJ, Cunningham FG. Urinary tract infections in pregnancy. Clin Obstet Gynecol. 1993;36(4):855–868.
- Gupta K, Stamm WE. Pathogenesis and management of recurrent urinary tract infections in women. World J Urol. 1990;17(6):415–420.
- Rahimkhani M, Khaveri-Daneshvar H, Sharifian R. Asymptomatic bacteriuria and pyuria in pregnancy. *Acta Medica Iranica*. 2008;46(5):409–412.
- 8. Whalley P. Bacteriuria of pregnancy. Am J Obstet Gynecol. 1967;97(5):723–738.
- Dafnis E, Sabatini S. The effect of pregnancy on renal function: physiology and pathophysiology. Am J Med Sci. 1992;303(3):184–205.

52

- 10. http://health.india.com/diseases-conditions/urinary-tract-infections-oruti-causes-symptoms-diagnosis-and-treatment-p314/?gclid=CJummfyl5 70CFcF8vQodc1gA2w
- 11. Fatima N, Ishrat S. Frequency and risk factors of asymptomatic bacteriuria during pregnancy. J Coll Physicians Surg Pak. 2006;16(4):273-275.
- 12. http://www.medicalnewstoday.com/articles/189953.php
- 13. http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/ Urinary tract infections
- 14. http://www.nhs.uk/conditions/urinary-tract-infection-adults/pages/ introduction.aspx
- 15. http://www.infectioncontroltoday.com/news/2013/10/women-mostoften-suffer-utis-but-men-more-likely-to-be-hospitalized.aspx
- 16. Harding GK, Zhanel GG, Nicolle LE, et al. Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. N Engl J Med. 2002;347(20):1576-1583.
- 17. Smaill F, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev. 2007;(2):CD000490.
- 18. Tan CK, Ulett KB, Steele M, et al. Prognostic value of semi-quantitative bacteriuria counts in the diagnosis of group B streptococcus urinary tract infection: a 4year retrospective study in adult patients. BMC Infect Dis.
- 19. Emilie KJ, Edward DK. FACS. UTIs in pregnancy. Int J Antimicrobial Agents. 2011:85-90.
- 20. Ipe DS, Sundac L, Benjamin WH Jr, et al. Asymptomatic bacteriuria: prevalence rates of causal microorganisms, etiology of infection in different patient populations, and recent advances in molecular detection. FEMS Microbiol Lett. 2013;346(1):1-10.
- 21. Turpin C, Minkah B, Danso K, et al. Asymptomatic bacteriuria in pregnant women attending antenatal clinic at komfo anokye teaching hospital, kumasi, ghana. Ghana Med J. 2007;41(1):26-28.
- 22. Olusanya O, Ogunledun A, Fakoya TA. Asymptomatic significant bacteriuria among pregnant and non-pregnant women in Sagamu, Nigeria. West Afr J Med. 1993;12(1):27-33.
- 23. Akerele J, Abhulimen P, Okonofua F. Prevalence of asymptomatic bacteriuria among pregnant women in Benin City, Nigeria. J Obstet Gynaecol. 2001;21(2):141-144.
- 24. Sibiani SAA. Asymptomatic Bacteriuria in Pregnant Women in Jeddah, Western Region of Saudi Arabia: Call for Assessment. JKAU Med Sci. 2010;17(1):29-42.
- 25. Jones LA, Woodman PJ, Ruiz HE. Urinary tract infection during pregnancy. E medicine. 2009:9.
- 26. Sescon NIC, Garingalao-Molina FD, Ycasiano CEJ, et al. Prevalence of asymptomatic bacteriuria and associated risks factors in pregnant women. Phil J Microbiol Infect Dis. 2003;32(2):63-69.
- 27. Muder RR, Brennen C, Rihs JD, et al. Isolation of Staphylococcus aureus from the urinary tract: association of isolation with symptomatic urinary tract infection and subsequent staphylococcal bacteremia. Clin Infec Dis. 2006;42(1):46-50.
- 28. Demuth PJ, Gerding DN, Crossley K. Staphylococcus aureus Bacteriuria. Arch Intern Med. 1979;139(1):78-80.
- 29. Pratt RJ, Pellowe C, Loveday HP, et al. The epic project: developing national evidence-based guidelines for preventing healthcare associated infections. Phase I: Guidelines for preventing hospitalacquired infections. Department of Health (England). J Hosp Infect. 2001;47Suppl:S3-S82.

- 30. Ugbogu O, Ogbonnaya R, Nworie O. Asymptomatic bacteriuria among pregnant women in Aba. Nigeria Journal of Microbiology. 2010;24:2024-2027.
- 31. Obirikorang C, Quaye L, Bio FY, et al. Asymptomatic bacteriuria among pregnant women attending antenatal clinic at the University Hospital, Kumasi, Ghana. J Med Biomed Sci. 2012;1(1):38-44.
- 32. http://emedicine.medscape.com/article/452604-overview
- 33. Emiru T, Beyene G, Tsegaye W, et al. Associated risk factors of urinary tract infection among pregnant women at Felege Hiwot Referral Hospital, Bahir Dar, North West Ethiopia. BMC Res Notes. 2013;6:292.
- 34. Kashef N, Djavid GE, Shahbazi S. Antimicrobial susceptibility patterns of community-acquired uropathogens in Tehran, Iran. J Infect Dev Ctries. 2010;4(4):202-206.
- 35. Chakupurakal R, Ahmed M, Sobithadevi DN, et al. Urinary tract pathogens and resistance pattern. J Clin Pathol. 2010;63(7):652-654.
- 36. Feitosa DC, da Silva MG, de Lima Parada CM. Accuracy of simple urine tests for diagnosis of urinary tract infections in low-risk pregnant women. Rev Lat Am Enfermagem. 2009;17(4):507-513.
- 37. http://www.ncbi.nlm.nih.gov/pubmed/23808987
- 38. http://www.webmd.com/a-to-z-guides/urinary-tract-infections-in-teensand-adults-topic-overview
- 39. Alemu A, Moges F, Shiferaw Y, et al. Bacterial profile and drug susceptibility pattern of urinary tract infection in pregnant women at University of Gondar Teaching Hospital, Northwest Ethiopia. BMC Research Notes. 2012;5:197.
- 40. Hamdan HZ, Ziad AH, Ali SK, et al. Epidemiology of urinary tract infections and antibiotics sensitivity among pregnant women at Khartoum North Hospital. Ann Clin Microbiol Antimicrob. 2011;10:2.
- 41. Moyo SJ, Aboud S, Kasubi M, et al. Bacterial isolates and drug susceptibility patterns of urinary tract infection among pregnant women at Muhimbili National Hospital in Tanzania. Tanzan J Health Res. 2010:12(4):236-240.
- 42. Okonko IO, Ijandipe LA, Ilusanya AO, et al. Detection of Urinary Tract Infection (UTI) among pregnant women in Oluyoro Catholic Hospital, Ibadan, South-Western Nigeria. Malaysian Journal of Microbiology. 2010;6(1):16-24.
- 43. Tamalli M, Sangar B, Alghazal MA. Urinary tract infection during pregnancy at Al-Khoms, Libya. International Journal of Medicine and Medical Sciences. 2013;3(5):455-459.
- 44. Al-Jiffri O, El-Sayed ZMF, Al-Sharif FM. Urinary tract infection with Esherichia coli and antibacterial activity of some plants extracts. Int J Microbiol Res. 2011;2(1):1-7.
- 45. Parveen SS, Reddy SV, Rama Rao MV, et al. Uropathogens and their Drug susceptibility patterns among pregnant women in a teaching hospital. Ann Biol Res. 2011;2(5):516-521.
- 46. El-Sokkary M. Prevalence of Asymptomatic Bacteriuria in Antenatal Women with Preterm Labor at an Egyptian Tertiary Center. J Am Sci. 2011;7(4):605-610.
- 47. Taneja N, Chatterjee SS, Singh M, et al. Urinary tract infection in a tertiary, care centre from north India. Indian J Med Res. 2010;131:101-105.
- 48. August SL, De Rosa MJ. Evaluation of the prevalence of urinary tract infection in rural panamanian women. PLoS One. 2012;7(10):e47752.
- 49. Dielubanza EJ, Schaeffer AJ. Urinary tract infections in women. Med Clin North Am. 2011;95(1):27-41.

- Zalmanovici Trestioreanu A, Green H, Paul M, et al. Antimicrobial agents for treating uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2010;(10):CD007182.
- Fried AM. Hydronephrosis of pregnancy: ultrasonographic study and classification of asymptomatic women. Am J Obstet Gynecol. 1979;135(8):1066–1070.
- 52. Connolly A, Thorp JM Jr. Urinary tract infections in pregnancy. *Urol Clin North Am.* 1999;26(4):779–787.
- Kiningham RB. Asymptomatic bacteriuria in pregnancy. Am Fam Physician. 1993;47(5):1232–1238.
- 54. Zhanel GG, Nicolle LE, Harding GK. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus: the Manitoba Diabetic Urinary Infection Study Group. *Clin Infect Dis*. 1995;21(2):316–322.
- Mittal P, Wing DA. Urinary tract infections in pregnancy. Clin Perinatol. 2005;32(3):749–764.
- 56. http://emedicine.medscape.com/article/452604-overview
- 57. Turck M, Goffe BS, Petersdorf RG. Bacteriuria of pregnancy. Relation to socioeconomic factors. *N Engl J Med.* 1962;266:857–860.
- Golan A, Wexler S, Amit A, et al. Asymptomatic bacteriuria in normal and high-risk pregnancy. Eur J Obstet Gynecol Reprod Biol. 1989;33(2):101–108.
- Hill JB, Sheffield JS, McIntire DD, et al. Acute pyelonephritis in pregnancy. Obstet Gynecol. 2005;105(1):18–23.
- Sharma P, Thapa L. Acute pyelonephritis in pregnancy: a retrospective study. Aust N Z J Obstet Gynaecol. 2007;47(4):313–315.
- Eisenstein BI, Jones GW. The spectrum of infections and pathogenic mechanisms of *Escherichia coli*. Adv Intern Med. 1988;33:231–252.
- 62. http://www.webmd.boots.com/pregnancy/guide/preterm-labour-premature-birth
- Patterson TF, Andriole VT. Bacteriuria in pregnancy. Infect Dis Clin North Am. 1987;1(4):807–822.
- 64. Jeyabalan A, Lain KY. Anatomic and functional changes of the upper urinary tract during pregnancy. *Urol Clin North Am.* 2007;34(1):1–6.
- 65. http://emedicine.medscape.com/article/2040207-overview
- Wild S, Roglic G, Green A, et al. Global prevalence of diabetes: estimates for the year 2000 and projections for the year 2030. *Diabetes Care*. 2004;27(5):1047–1053.
- Harjutsalo V, Sjoberg L, Tuomilehto J. Time trends in the incidence of type I diabetes in Finnish children: a cohort study. *Lancet*. 2008;371(9626):1777–1782.
- Raz R. Asymptomatic bacteriruia: Clinical significance and management. Int J Antimicrob Agents. 2003;22(Suppl 2):45–47.
- Balasoiu D, Van Kessel KC, Van Kats-Renaud HJ, et al. Granulocyte function in women with diabetes and asymptomatic bacteriuria. *Diabetes Care*. 1997;20(3):392–395.
- Lin K, Fajardo K, U.S. Preventive Services Task Force. Screening for asymptomatic bacteriuria in adults: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med.* 2008;149(1):W20–W24.
- 71. Karunajeewa H, McGechie D, Stuccio G, et al. Asymptomatic bacteriuria as a predictor of subsequent hospitalisation with urinary tract infection in diabetic adults: The Fremantle Diabetes Study. *Diabetologia*. 2005;48(7):1288–1291.

- Bonadio M, Boldrini E, Forotti G, et al. Asymptomatic bacteriuria in women with diabetes: influence of metabolic control. *Clin Infect Dis*. 2004;38(6):e41–e45.
- Meiland R, Geerlings SE, Stolk RP, et al. Asymptomatic bacteriuria in women with diabetes mellitus: effect on renal function after 6years of follow-up. *Arch Intern Med.* 2006;166(20):2222–2227.
- Geerlings SE, Stolk RP, Camps MJ, et al. Consequences of asymptomatic bacteriuria in women with diabetes mellitus. *Arch Intern Med.* 2001;161(11):1421–1427.
- Rozsai B, Lanyi E, Soltesz G. Asymptomatic bacteriuria and leukocyturia in type 1 diabetic children and young adults. *Diabetes Care*. 2003;26(7):2209–2210.
- 76. Sotiropoulos A, Skourtis S, Merkouris P, et al. Incidence and outcome of asymptomatic bacteriuria in females with type 2 diabetes mellitus over a 1-year follow-up period and association with risk factors. *Diabet Med.* 2005;22(11):1625–1626.
- Geerlings SE, Stolk RP, Camps MJ, et al. Asymptomatic bacteriuria may be considered a complication in women with diabetes: Diabetes Mellitus Women Asymptomatic Bacteriuria Utrecht Study Group. *Diabetes Care*. 2000;23(6):744–749.
- Chen SL, Jackson SL, Boyko EJ. Diabetes mellitus and urinary tract infection: epidemiology, pathogenesis and proposed studies in animal models. *J Urol*. 2009;182(6 Suppl):S51–S56.
- 79. http://www.sciencedirect.com/science/article/pii/S0002934302010628
- Wan YL, Lee TY, Bullard MJ, et al. Acute gas-producing bacterial renal infection: correlation between imaging findings and clinical outcome. *Radiology*. 1996;198(2):433–438.
- Huang JJ, Tseng CC. Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis. *Arch Intern Med.* 2000;160(6):797–805.
- 82. Creinin MD, Simhan HN. Can we communicate gravidity and parity better? *Obstet Gynecol*. 2009;113(3):709–711.
- 83. Gilstrap LC 3rd, Ramin SM. Urinary tract infections during pregnancy. *Obstetric Gynaecol Clin North Am.* 2001;28(3):581–591.
- 84. Dimetry SR, El-Tokhy HM, Abdo NM, et al. Urinary tract infection and adverse outcome of pregnancy. *J Egypt Public Health* Assoc. 2007;82(3–4):203–218.
- Masinde A, Gumodoka B, Kilonzol A, et al. Prevalence of urinary tract infection among pregnant women at Bugando Medical Centre, Mwanza, Tanzania. *Tanzania Journal of Health Research*. 2009;11(3):154–161.
- Olsen BE, Hinderaker SG, Lie RT, et al. The diagnosis of urinary tract infections among pregnant women in rural Tanzania; prevalences and correspondence between different diagnostic methods. *Acta Obstet Gynecol Scand*. 2000;79(9):729–736.
- 87. http://www.patient.co.uk/doctor/gravidity-and-parity-definitions-and-their-implications-in-risk-assessment
- Lentz GM. Urinary Tract Infections in Obstetrics and Gynecology. *In Global Library of Women's medicine*. University of Washington, Washington, USA; 2009.
- 89. Tadesse E, Teshome M, Merid Y, et al. Asymptomatic urinary tract infection among pregnant women attending the antenatal clinic of Hawassa Referral Hospital, Southern Ethiopia. *BMC Res Notes*. 2014;7:155.
- 90. Manikandan S, Ganesapandian S, Singh M, et al. Emergence of multidrug resistance human pathogens from urinary tract infections. *Current research in Bacteriology*. 2011;4(1):9–15.

- 91. Stanley CN, Ugboma HAA, Ibezim EC, et al. Prevalence and Antibiotic Susceptibility of Staphylococcus aureus and Other Staphylococcal Infections in Pregnant Women Attending Antenatal Clinic in a Tertiary Hospital in Port Harcourt, Nigeria. J Infect Dis Ther. 2013;1:125.
- Otto M. Looking toward basic science for potential drug discovery targets against community-associated MRSA. Med Res Rev. 2010;30(1):1–22.
- David MZ, Daum RS. Community-associated methicilin-resistant Staphylococcus aereus: epidemiology and clinical consequences of an emerging epidemic. *Clin Microbiol Rev.* 2010;23(3):616–687.
- 94. Imade PE, Izekor PE, Eghafona NO, et al. Asymptomatic bacteriuria among pregnant women. N Am J Med Sci. 2010;2(6):263–266.
- 95. Ilusanya OAF, Adesetan TO, Egberongbe HO, et al. Asymptomatic bacteriuria in ante-natal patients attending state hospital, Ado Ekiti, Nigeria. *Current Research Journal of Biological Sciences*. 2012;4(3):261–264.
- 96. Top KA, Buet A, Whittier S, et al. Predictors of Staphylococcus aureus rectovaginal colonization in pregnant women and risk for maternal and neonatal infections. *J Pediatric Infect Dis Soc.* 2012;1(1):7–15.
- Jimenez-Truque N, Tedeschi S, Saye EJ, et al. Relationship between maternal and neonatal Staphylococcus aureus colonization. *Pediatrics*. 2012;129(5):e1252–e1259.
- Kurewa NE, Mapingure MP, Munjoma MW, et al. The burden and risk factors of Sexually Transmitted Infections and Reproductive Tract Infections among pregnant women in Zimbabwe. BMC Infect Dis. 2010:10:127.
- Shittu AO, Okon K, Adesida S, et al. Antibiotic resistance and molecular epidemiology of Staphylococcus aureus in Nigeria. *BMC Microbiol*. 2011:11:92.
- Watkins RR, David MZ, Salata RA. Current concepts on the virulence mechanisms of meticillin-resistant Staphylococcus aureus. J Med Microbiol. 2012;61(Pt 9):1179–1193.
- Cheung GY, Otto M. Understanding the significance of Staphylococcus epidermidis bacteremia in babies and children. Curr Opin Infect Dis. 2010;23(3):208–216.
- 102. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275859/
- Santos F, Oraichi D, Berard A. Prevalence and predictors of antiinfective use during pregnancy. *Pharmacoepidemiol Drug Saf.* 2010;19(4):418–427.
- 104. Duarte G, Marcolin AC, Quintana SM, et al. Urinary tract infection in pregnancy. *Rev Bras Ginecol Obstet*. 2008;30(2):93–100.
- Macejko AM, Schaeffer AJ. Asymptomatic bacteriuria and symptomatic urinary tract infections during pregnancy. *Urol Clin North* Am. 2007;34(1):35–42.
- Lee M, Bozzo P, Einarson A, et al. Urinary tract infections in pregnancy. Can Fam Physician. 2008;54(6):853–854.
- Schnarr J, Smaill F. Asymptomatic bacteriuria and symptomatic urinary tract infections in pregnancy. *Eur J Clin Invest*. 2008;38(Suppl 2):50–57.

- Guinto VT, De Guia B, Festin MR, et al. Different antibiotic regimens for treating symptomatic bacteriuria in pregnancy. *Cochrane Database* Syst Rev. 2010;(9):CD007855.
- Dashe JS, Gilstrap LC 3<sup>rd</sup>. Antibiotic use in pregnancy. Obstet Gynecol Clin North Am. 1997;24(3):617–629.
- Ben David S, Einarson T, Ben David Y, et al. The safety of nitrofurantoin during the first trimester of pregnancy: meta-analysis. Fundam Clin Pharmacol. 1995;9(5):503–507.
- Christensen B. Which antibiotics are appropriate for treating bacteriuria in pregnancy? *J Antimicrob Chemother*. 2000;46(Suppl 1):29–34.
- 112. Sahm DF, Thornsberry C, Mayfield DC, et al. Multidrug-resistant urinary tract isolates of *Escherichia coli*: prevalence and patient demographics in the United States in 2000. *Antimicrob Agents Chemother*. 2001;45(5):1402–1406.
- Milo G, Katchman EA, Paul M, et al. Duration of antibacterial treatment for uncomplicated urinary tract infection in women. *Cochrane Database Syst Rev.* 2005;(2):CD004682.
- 114. http://www.jstor.org/over/10.2307/4457547?uid=3738256&uid=2&uid=4&sid=2110<sup>3</sup>681000971
- Jimenez-Truque N, Tedeschi S, Saye EJ, et al. Relationship between maternal and neonatal *Staphylococcus aureus* colonization. *Pediatrics*. 2012;129(5):e1252–e1259.
- Afsharpaiman S, Bairaghdar F, Torkaman M, et al. Bacterial pathogens and resistance patterns in children with community-acquired urinary tract infection: a cross sectional study. J Compr Ped. 2012;3(1):16–20.
- Al-Mardeni RI, Batarseh A, Omaish L, et al. Empirical treatment for pediatric urinary tract infection and resistance patterns of uropathogens, in Queen Alia hospital and prince A'Isha military center-Jordan. Saudi J Kidney Dis Transpl. 2009;20(1):135–139.
- 118. http://www.babycenter.com/0\_urinary-tract-infections-during-pregnancy\_9403.bc#articlesection2
- DiPiro JT, Talbert RL, Yee GC, et al. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. Columbus, Ohio: McGraw-Hill Medical; 2011.
- Jolley JA, Wing DA. Pyelonephritis in pregnancy: an update on treatment options for optimal outcomes. *Drugs*. 2010;70(13):1643–1655.
- 121. Nowicki B. Urinary tract infection in pregnant women: old dogmas and current concepts regarding pathogenesis. *Curr Infect Dis Rep.* 2002;4(6):529–535.
- 122. Foxman B, Brown P. Epidemiology of urinary tract infections: transmission and risk factors, incidence, and costs. *Infect Dis Clin North Am.* 2003;17(2):227–241.
- 123. Fihn SD. Clinical practice. Acute uncomplicated urinary tract infection in women. *N Engl J Med*. 2003;349(3):259–266.
- 124. http://www.biomedcentral.com/1756-0500/6/292