1. Introduction

Urinary tract infection is a collective term that describes any infection that involve any part of the urinary tract: upper urinary tract (kidneys and ureters) or lower urinary tract (bladder and urethra) [1].

According to Magdalena E. Sobieszczyk (Columbia University), lower urinary tract infections include cystitis, urethritis and prostatitis, and upper urinary tract infections include pyelonephritis, intra-renal abscess and perinephric abscess.

Clinically, urinary tract infections are categorized as uncomplicated or complicated urinary tract infections.

A urinary tract infection is classified as uncomplicated if there are no functional or anatomical anomalies in the urinary tract, no renal functional impairment, and no concomitant disease that would promote the urinary tract infection [2].

Uncomplicated urinary tract infections are among the most frequently encountered infections in the outpatient setting [3]. Uncomplicated urinary tract infections include acute uncomplicated cystitis and acute uncomplicated pyelonephritis [3].

A complicated urinary tract infection is a urinary infection occurring in a patient with a structural or functional abnormality of the genitourinary tract (ex. indwelling catheters and renal calculi) [4].

Urinary tract infections are some of the most common bacterial infections, affecting 150 million people each year worldwide [5], are one of the most common diseases, occurring from the neonate up to the geriatric age group [6].
Urinary tract infection is a significant cause of morbidity in infant boys, older men and females of all ages [7].

2. Causes and Risk Factors

2.1. Common causes and risk factors

- **Age** - In the first few months of life, infants are at a higher risk for urinary tract infections. This susceptibility has been attributed to an incompletely developed immune system [8]. Table 1 summarizes the risk factors for urinary-tract infections by age group.

- **Gender** - Because of anatomical factors, women face a much higher risk of urinary tract infections, compared to men.

- **Pregnancy** - Because of the changes in the urinary tract, urinary tract infections are more common during pregnancy (especially from week six through week 24).

- **Menopause** - Because of the hormonal changes that might affect the beneficial bacteria responsible for fighting off harmful microorganisms in the urinary tract, women who have gone through menopause may also have a greater risk of urinary tract infections.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Risk factors for urinary tract infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>Anatomic or functional urologic abnormalities</td>
</tr>
<tr>
<td>1-5</td>
<td>Congenital abnormalities; Vesicoureteral reflux.</td>
</tr>
<tr>
<td>16 - 35</td>
<td>Congenital abnormalities; Uncircumcised penis.</td>
</tr>
<tr>
<td>36-65</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td></td>
<td>Gynecologic surgery; Bladder prolapse; Previous urinary tract infection.</td>
</tr>
<tr>
<td></td>
<td>Prostate hypertrophy; Obstruction; Catherization; Surgery.</td>
</tr>
<tr>
<td>&gt;65</td>
<td>Estrogen deficiency; Loss of vaginal lactobacilli.</td>
</tr>
<tr>
<td></td>
<td>Prostate hypertrophy; Obstruction; Surgery; Incontinence, Long-term catherization; Condom catheters.</td>
</tr>
</tbody>
</table>

According to Magdalena E. Sobieszczyk, Columbia University
• **Health and Medical conditions:**
  
  ✓ Anatomic anomalies of urinary tract

  ➢ **Lower Urinary Tract Anomalies:**

    • Urachal Reminant,
    • Posterior Urethral Valves,
    • Ureterocele,
    • Vesicoureteral Reflux,
    • Agenesis of the ureter,
    • Ectopic Ureter,
    • Megaureter,
    • Duplication of the ureter,
    • Hydronephrosis,
    • Prune Belly Syndrome.

  ➢ **Upper Urinary Tract Anomalies:**

    • Renal agenesis,
    • Renal dysplasia kidney: renal aplasia or multicystic and cystic dysplastic kidneys,
    • Renal hypoplasia: oligomeganephronia,
    • Duplex kidney,
    • Horseshoe kidney,
    • Ureteropelvic junction obstruction,
    • Duplicated Collecting System (with/without ureterocele).

  ✓ Vesicoureteral reflux

  ✓ Enlarged prostate, kidney stones - that blocks the normal flow of urine and encourages bacterial growth
✓ Systemic disorders:
  • Diabetes,
  • HIV/AIDS,
  • Solid organ transplant recipients,
  • Sickle cell anemia.

✓ Alzheimer’s disease (because of the personal hygiene)

✓ Spinal cord injuries or nerve damage around the bladder can prohibit complete emptying of the bladder.

✓ Urinary catheter - The primary risk of short-term catheterization is a urinary tract infection.

✓ Immunosuppressant medications.

2.2. Risk factors for pediatric urinary tract infections

  • Neonate/infant
  • Gender Foreskin
  • Fecal and perineal colonization
  • Urinary tract anomalies
  • Functional abnormalities
  • Immunocompromised states
  • Sexual activity [9].

2.3. Lifestyle risk factors

  • Sexual activity - Sexual intercourse may transport bacteria from the genitals and anus into the urethra and, in turn, lead to infection. For men, unprotected sexual activity involving women with a vaginal infection may increase risk of urinary tract infections.

  • Birth Control - Use of diaphragms or spermicidal foam may also raise urinary tract infections risk in women.
• Personal Hygiene habits:
  ✔ use of douches, soaps, cleansers and feminine hygiene sprays or powders in the vaginal area (can produce local allergies)
  ✔ wiping from back to front after urinating, especially for women
  ✔ retaining urine for an abnormally prolonged period (waiting too long to pass urine)
  ✔ extended periods of immobility (during recovery from an injury or illness).

3. Genetics

Urinary tract infections represent a classical example of multifactorial disease combining gene environment and probably gene-gene interactions [10].

3.1. Genetic susceptibility

The first evidence that susceptibility to urinary tract infections (acute pyelonephritis and asymptomatic bacteriuria) could be genetic inherited came only a few years ago [11, 12].

As in other common diseases, numerous genes seem to contribute to the urinary tract infection -prone phenotype and, therefore, coordinated multicenter studies in strictly defined patient populations are needed to define shared genetic parameters suitable for risk assessment [13].

The identification of a genetic component of urinary tract infection recurrences will make it possible to diagnose at-risk adults and to predict genetic recurrences in their offspring.

Urinary tract infection susceptibility is influenced by the genetic makeup of the host, especially by genes that regulate the innate immune response to infection [13].

3.2. Human genes

The human genes HSPA1B, CXCR 1 and CXCR 2, TLR1, TLR 2, TLR 4, TLR 5, SIGIRR, TRIF, TRAM, MyD88, TIRAP, VEGF, and TGF- β1 may be associated with susceptibility to recurrent urinary tract infection in humans, and in particular, the HSPA1B, CXCR1 & 2, TLR2, TLR4 and TGF-β1 genes [14].

Functionally relevant genes are regulatory, suggesting that control of gene expression is essential [13]. Table 2 summarizes the 14 genes investigated in humans, associated with susceptibility to recurrent urinary tract infections [14].
Table 2: Human genes and urological malformations included

<table>
<thead>
<tr>
<th>No.</th>
<th>Genes</th>
<th>Gene expression</th>
<th>Urological malformations included</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HSPA1B</td>
<td>-</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>2</td>
<td>CXCR1</td>
<td>+</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>3</td>
<td>CXCR2</td>
<td>+</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>4</td>
<td>TLR1</td>
<td>-</td>
<td>Urinary tract malformation</td>
</tr>
<tr>
<td>5</td>
<td>TLR2</td>
<td>-</td>
<td>Urinary tract malformation</td>
</tr>
<tr>
<td>6</td>
<td>TLR4</td>
<td>-</td>
<td>Urinary tract malformation</td>
</tr>
<tr>
<td>7</td>
<td>TLR5</td>
<td>-</td>
<td>Urinary tract malformation</td>
</tr>
<tr>
<td>8</td>
<td>SIGIRR</td>
<td>+</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>9</td>
<td>TRIF</td>
<td>+</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>10</td>
<td>TRAM</td>
<td>+</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>11</td>
<td>MyD88</td>
<td>+</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>12</td>
<td>TIRAP</td>
<td>-</td>
<td>Urinary tract malformation</td>
</tr>
<tr>
<td>13</td>
<td>VEGF</td>
<td>-</td>
<td>Vesicoureteral reflux</td>
</tr>
<tr>
<td>14</td>
<td>TGF-β1</td>
<td>-</td>
<td>Vesicoureteral reflux</td>
</tr>
</tbody>
</table>

3.3. Genetic predisposition

The large intraindividual differences in the frequency and severity of urinary tract infection are consistent with a genetic predisposition among disease-prone individuals, but inherited defects in the defense against urinary tract infection have not been identified [15].

4. Special Groups

The following special groups may be at increased risk of urinary tract infection:

- Very young infants
- Young children
- Children of all ages
- Hospitalized patients or nursing home residents: Many of these individuals are catheterized for long periods and are thus vulnerable to infection of the urinary tract.

4.1. Pediatric urinary tract infections

In the pediatric population, infections of the urinary tract are a frequent cause of morbidity and affect up to 10% of children [14].

The true incidence of pediatric urinary tract infection is difficult to determine because
there are varying presentations that range from an absence of specific urinary complaints to fulminant urosepsis [16]. Data from the Urologic Disease in America project, suggest that pediatric urinary tract infections constitutes a significant health care burden on the American public. The study revealed that Urinary tract infections affect 2.4% to 2.8% of children every year, and in-patient hospital costs for children with pyelonephritis total more than $180 million per year in the United States [17].

The recurrence rate of urinary tract infection in the pediatric population is estimated at 30% to 40%. [18]. If not treated promptly and appropriately, pediatric infections of the urinary tract may lead to significant acute morbidity and irreversible renal damage.

5. Congenital Abnormalities of Kidney and Urinary Tract

Congenital abnormalities of kidney and urinary tract are a group of congenital anomalies affecting the kidneys or other structures of the urinary tract, and represent a important causes of a pediatric urinary tract infections.

Congenital abnormalities of kidney and urinary tract occur in 1 in 100 to 500 newborns.

5.1. Causes and risk factors

The causes are complex and the familial inheritance of congenital abnormalities of kidney and urinary tract and not completely understood. A combination of genetic and environmental factors contributes to the formation of kidney and urinary tract abnormalities.

5.2. Human genes

Two human genes PAX2 and HNF1B, are most commonly associated with congenital abnormalities of kidney and urinary tract. During embryonic development, PAX2 and HNF1B genes are involved in the formation of the kidneys, urinary tract, and other tissues.

5.3. Genetic inheritance

According to Stefanie Weber, the majority of patients manifesting with congenital abnormalities of kidney and urinary tract are sporadic cases (the condition is not inherited or the inheritance pattern is unknown), but also familiar forms have been described suggesting that the pathogenesis is influenced by genetic factors.

Genetic inheritance of congenital abnormalities of kidney and urinary tract, most commonly, follows an autosomal dominant pattern. Less commonly, congenital abnormalities of kidney and urinary tract follow an autosomal recessive pattern.
6. Genetic Counseling

In families with hereditary congenital abnormalities of kidney and urinary tract, genetic counseling is very important.

Prenatal ultrasound and genetic diagnosis of the hereditary congenital abnormalities of kidney and urinary tract is very useful in the management, prognosis and detection of a fetus with a congenital grave disease.

The prenatal diagnosis is necessary for the detection of fetal abnormalities to all pregnancies and especially for the risk categories [19].

7. References

   
   
   
   
   
   
   
   
   
   
   
   


