

PREDICTIVE VALUE OF IMMUNE GENE POLYMORPHISMS FOR RECURRENT URINARY TRACT INFECTIONS IN CHILDREN

Zukhriddin Zokirov, Iroda Sa'dullayeva

Bukhara State Medical Institute named after Abu Ali ibn Sino

ORCID: <https://orcid.org/0009-0009-7959-9872>

ORCID: <https://orcid.org/0009-0002-2487-3693>

E-mail: zuxriddinzokirov08@gmail.com

E-mail: sq.iroda1985@gmail.com

Abstract

Recurrent urinary tract infections (rUTIs) remain a major pediatric health concern due to their association with renal scarring, hypertension, and chronic kidney disease. Traditional clinical risk factors alone are often insufficient to accurately predict recurrence. Recent advances in molecular genetics have demonstrated that immune gene polymorphisms may serve as valuable biomarkers for identifying children at increased risk of recurrent urinary tract infections. This review summarizes current evidence regarding the predictive significance of polymorphisms in innate and adaptive immune response genes and discusses their integration into personalized risk assessment models.

Keywords: recurrent urinary tract infection, immune genes, polymorphism, biomarkers, risk prediction, personalized medicine, children.

Introduction

Urinary tract infections are among the most common bacterial diseases affecting children worldwide. Although appropriate antimicrobial therapy successfully treats the majority of acute infections, approximately one-third of pediatric patients develop recurrent episodes. Recurrent infections considerably increase the probability of renal scarring, impaired kidney function, and long-term nephrological complications.

Current clinical assessment is mainly based on age, sex, urinary tract abnormalities, microbiological findings, and imaging studies. However, these parameters alone do not adequately explain why some children experience repeated infections despite normal urinary tract anatomy. Therefore, increasing attention has focused on host genetic susceptibility as an important determinant of disease recurrence.

Main Discussion

The innate immune system plays a central role in protecting the urinary tract against invading microorganisms. Recognition of bacterial pathogens depends on several immune receptors and signaling molecules encoded by highly polymorphic genes.

Variations within these genes may significantly influence the intensity and effectiveness of immune responses.

Recent genomic studies have identified several immune-related genes associated with recurrent urinary tract infections, including TLR2, TLR4, IL-6, IL-8, TNF- α , CXCR1, TGF- β 1, HSPA1B, VEGFA, and VDR. Functional polymorphisms within these genes may alter cytokine production, neutrophil recruitment, epithelial defense mechanisms, and bacterial clearance.

Among these biomarkers, polymorphisms of TLR4 reduce recognition of Gram-negative bacterial lipopolysaccharides, while CXCR1 variants impair neutrophil migration toward infected tissues. Similarly, polymorphisms within IL-6 and TNF- α influence inflammatory cytokine production, thereby affecting infection severity and recurrence.

Recent systematic reviews indicate that combining multiple immune gene polymorphisms provides substantially higher predictive accuracy than evaluating individual genetic variants separately. Multigene risk models have demonstrated improved identification of children susceptible to recurrent urinary tract infections and renal complications.

The incorporation of molecular biomarkers into routine pediatric practice offers several clinical advantages. Genetic profiling may facilitate early identification of high-risk patients, individualized follow-up schedules, optimized antimicrobial strategies, and targeted preventive interventions. Furthermore, advances in next-generation sequencing technologies have significantly reduced both the cost and turnaround time of genetic testing, making precision medicine increasingly feasible in pediatric nephrology.

Artificial intelligence and machine learning algorithms further enhance predictive performance by integrating genetic information with laboratory parameters, imaging findings, demographic characteristics, and clinical history. Such comprehensive predictive models may improve decision-making and reduce unnecessary diagnostic procedures.

Despite these advances, most available evidence originates from European and Asian populations outside Central Asia. Therefore, further molecular epidemiological studies involving Uzbek children are required to validate existing biomarkers and establish region-specific genetic prediction models.

Conclusion

Immune gene polymorphisms represent promising biomarkers for predicting recurrent urinary tract infections in pediatric patients. The combined analysis of multiple genetic variants provides greater predictive value than single-gene evaluation and supports the

development of precision medicine approaches. Future large-scale studies in Central Asian populations will contribute to establishing clinically applicable genetic risk prediction models capable of improving early diagnosis, individualized prevention, and long-term renal outcomes.

References

1. Yu J, Pereira GMV, Allen-Brady K, et al. Genetic polymorphisms associated with urinary tract infection in children and adults: A systematic review and meta-analysis. *American Journal of Obstetrics and Gynecology*. 2024;230(6):600–609.e3.
2. Isali I, Wong TR, Batur AF, et al. Recurrent urinary tract infection genetic risk: A systematic review and gene network analysis. *International Urogynecology Journal*. 2024.
3. John PP, Mike L, Mysorekar IU, et al. Urinary Tract Infections in Children. *Nature Reviews Urology*. 2026.
4. Gnech M, et al. Update and Summary of the EAU/ESPU Paediatric Guidelines on Urinary Tract Infection in Children. *Journal of Pediatric Urology*. 2025.
5. Aksu B, Afonso AC, Akil I, et al. Urine Soluble TLR4 Levels May Contribute to Predict Urinary Tract Infection in Children: The UTILISE Study. *Pediatric Nephrology*. 2024.
6. Agrawal P, Paunikar VM. Urinary Tract Infection in Children: A Narrative Review. *Cureus*. 2024.
7. Gkiourtzis N, Stoimeni A, Glava A, et al. Prophylaxis Options in Children With a History of Recurrent Urinary Tract Infections: A Systematic Review. *Pediatrics*. 2024.
8. Korbel L, Howell M, Spencer JD. The Clinical Diagnosis and Management of Urinary Tract Infections in Children and Adolescents. *Journal of Pediatric Urology*. 2024.