

ASSOCIATION BETWEEN CYTOKINE GENE POLYMORPHISMS AND RECURRENT URINARY TRACT INFECTIONS IN PEDIATRIC PATIENTS

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Abstract

Recurrent urinary tract infections (rUTIs) are among the most frequent bacterial infections in childhood and remain a significant cause of renal morbidity worldwide. Although bacterial virulence contributes to disease development, host genetic factors have emerged as important determinants of infection susceptibility and recurrence. Cytokine gene polymorphisms, particularly within interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α) genes, influence inflammatory responses and may alter disease severity. This review summarizes current evidence regarding the association between cytokine gene polymorphisms and recurrent urinary tract infections in children, emphasizing their potential role as prognostic biomarkers and targets for personalized medical approaches.

Keywords: recurrent urinary tract infection, cytokines, IL-6, TNF- α , polymorphism, pediatrics, biomarkers.

Introduction

Urinary tract infections affect approximately 8–10% of children during the first years of life and remain one of the leading causes of pediatric hospitalization due to bacterial infections. Despite advances in antimicrobial therapy, nearly one-third of affected children experience recurrent infections, increasing the risk of renal scarring, hypertension, and chronic kidney disease. These observations suggest that host immune response plays a crucial role in determining disease outcome.

Inflammatory cytokines represent essential mediators of innate and adaptive immunity. Genetic variations affecting cytokine production may influence bacterial elimination, tissue inflammation, and recovery following infection. Therefore, cytokine gene polymorphisms have become an important research focus in pediatric infectious diseases

Main Discussion

Interleukin-6 (IL-6) is a multifunctional cytokine produced by macrophages, epithelial cells, and lymphocytes following bacterial invasion. It regulates acute inflammatory responses, stimulates neutrophil activation, and promotes adaptive immune responses. Variations within the IL-6 promoter region, particularly functional single nucleotide polymorphisms (SNPs), may significantly alter cytokine expression levels.

Individuals carrying high-expression IL-6 variants may develop excessive inflammatory reactions that contribute to renal tissue injury, whereas low-expression variants may impair bacterial clearance and increase susceptibility to recurrent infections. Consequently, IL-6 polymorphisms have attracted considerable attention as potential biomarkers for predicting recurrent urinary tract infections.

Tumor necrosis factor-alpha (TNF- α) is another key mediator involved in bacterial defense. Produced primarily by activated macrophages, TNF- α initiates inflammatory cascades, increases vascular permeability, and promotes leukocyte recruitment. Functional polymorphisms in the TNF- α promoter gene, especially the -308G/A variant, have been associated with altered cytokine production and different clinical outcomes in infectious diseases.

Recent molecular studies suggest that simultaneous evaluation of IL-6 and TNF- α polymorphisms provides greater predictive accuracy than assessment of individual genetic markers alone. Combined cytokine profiling may improve identification of children at high risk for recurrent urinary tract infections and long-term renal complications.

The integration of cytokine genetic analysis with conventional clinical parameters—including urine culture, inflammatory biomarkers, renal ultrasonography, and patient history—may substantially enhance personalized management strategies. Furthermore, advances in genomic medicine and next-generation sequencing technologies have facilitated rapid identification of immune-related genetic variants suitable for routine clinical practice.

Current evidence also indicates that population-specific genetic diversity influences the distribution of cytokine polymorphisms. Therefore, molecular epidemiological studies involving Central Asian pediatric populations are essential for developing region-specific diagnostic algorithms and individualized preventive strategies.

Conclusion

Cytokine gene polymorphisms, particularly within IL-6 and TNF- α , represent important genetic determinants influencing susceptibility to recurrent urinary tract infections in children. Identification of these polymorphisms may improve early risk assessment, facilitate personalized therapeutic decisions, and reduce long-term renal

complications. Future multicenter studies involving larger pediatric cohorts are necessary to validate cytokine-based prognostic models and incorporate them into routine pediatric nephrology practice.

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