IJACT, Volume 3, Issue 10, 2025 ISSN: 2995-5378
http://medicaljournals.eu/index.php/IJACT

INTERNATIONAL JOURNAL OF ALTERNATIVE AND CONTEMPORARY THERAPY

Clinical, Immunological, and Genetic Features of Tics in Children with Subsequent Prognosis and Treatment Optimization

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Abstract: Tic disorders are a group of neurodevelopmental conditions characterized by motor and/or vocal tics that significantly affect the quality of life of children and their families. According to contemporary literature, the prevalence of tic disorders in the pediatric population ranges from 0.4% to 3.8%, with Tourette syndrome occurring in 0.3–0.9% of school-age children.

Keywords: Tic disorders, Tourette syndrome, children, genetic markers, immunological abnormalities, PANDAS, autoimmunity, neurodevelopment, personalized medicine, prognosis, basal ganglia, streptococcal infection, molecular diagnostics, targeted therapy.

INTRODUCTION. Modern understanding of the etiopathogenesis of tic disorders has changed significantly over recent decades. Whereas tics were previously viewed primarily through psychological and behavioral lenses, they are now recognized as having a complex multifactorial nature that includes genetic, immunological, neurochemical, and environmental components. Ticosis disorders in children are a heterogeneous group of neurodevelopmental conditions characterized by recurrent involuntary motor and/or vocal phenomena that can significantly affect academic performance, social functioning, and the quality of life of the child and their family. According to epidemiological studies, the prevalence of tics in the pediatric population varies within 0.4-3.8%, and Tourette syndrome affects up to 0.9% of schoolchildren. Despite the seemingly "benign" and fluctuating nature of the course in some patients, the severity of symptoms, frequent comorbidity with ADHD, OCD, anxiety disorders, and autism spectrum disorders form a significant clinical and social burden.

Over the past two decades, the understanding of the etiopathogenesis of ticosis disorders has significantly deepened and shifted from predominantly psychogenic explanations to a multifactorial model that integrates genetic predisposition, neurodevelopmental features, immunological and neural-inflammatory mechanisms, as well as environmental influences. The results of family-twin and full-genome studies confirm the high heritability and polygenic nature of tics involving genes regulating dopaminergic, serotonergic, and GAMK-ergic neurotransmission, synaptogenesis processes, and plasticity. Simultaneously, interest in immunological aspects, including the PANDAS/PANS concept, has increased, suggesting that in some children, streptococcal and other triggers initiate cross-reactive autoimmune processes with damage to basal ganglion structures and dysregulation of movement control neural networks.

The clinical heterogeneity of tics (variability of debut age, phenomenology and dynamics of symptoms, comorbidity spectrum) makes the tasks of early risk stratification and prognosis, as well as the development of personalized treatment strategies, relevant. In this regard, the role of integrating clinical, immunological, and genetic biomarkers for more accurate patient phenotyping, predicting the course, selecting optimal therapy, and monitoring treatment effectiveness is increasing.

Pharmacogenetic predictors of response to antipsychotic drugs and neuromodulatory approaches, as well as indicators for immunomodulation in a subgroup of patients with signs of immune involvement, are of particular interest.

The purpose of this review is to systematize modern data on the clinical, immunological, and genetic characteristics of ticosis disorders in children, to discuss their prognostic significance and practical impact on the selection and optimization of therapy in the paradigm of personalized medicine. The review aims to form a holistic model linking biological mechanisms with clinical solutions, which can contribute to improving short-term and long-term outcomes in pediatric patients with tics.

The genetic aspect of tic disorders attracts particular attention from researchers. Family studies demonstrate high heritability of Tourette syndrome ($h^2 = 0.25–0.77$), indicating a substantial genetic contribution to disease development. However, the complexity of the genetic architecture of tic disorders, encompassing both monogenic and polygenic mechanisms, makes the identification of specific genetic markers and their clinical application a challenging task.

The immunological component of tic pathogenesis gained recognition following the delineation of a subgroup of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). This concept posits that, in genetically predisposed children, streptococcal infections may trigger an autoimmune response directed against basal ganglia structures, leading to the development of tics and obsessive–compulsive disorders.

The relevance of studying the clinical–immunological and genetic aspects of tic disorders stems from the need to develop personalized approaches to diagnosis, prognosis, and treatment. Understanding the molecular mechanisms of tic development opens avenues for targeted therapeutic strategies and improved long-term outcomes in children with tic disorders.

The genetic basis of tic disorders is supported by twin studies demonstrating concordance rates of 50–77% in monozygotic twins versus 8–23% in dizygotic twins. Family studies indicate that the risk of tics in first-degree relatives of patients with Tourette syndrome is 10–100 times higher than in the general population.

Contemporary genomic research has identified several candidate genes associated with tic disorders. Particular attention is paid to genes encoding components of the dopaminergic system (DRD2, DRD4, DAT1, COMT), serotonergic system (HTR2A, SLC6A4), and GABAergic system (GABRA1, GABRB3). Polymorphisms in these genes may influence neurotransmitter balance in the basal ganglia, which underlies tic pathogenesis.

Large-scale genome-wide association studies (GWAS) have revealed new susceptibility loci, including CELSR3, MRPL3, and FLT3. These findings expand the understanding of molecular pathways involved in tic disorders and point to the roles of neurodevelopmental processes, synaptic plasticity, and immune regulation.

The PANDAS concept proposed by Swedo and colleagues suggests an autoimmune mechanism for tic development in a subset of children. According to this hypothesis, streptococcal antigens can mimic neuronal proteins of the basal ganglia, leading to the production of cross-reactive antibodies and the development of inflammation in the brain.

Immunological studies in children with tics reveal elevated levels of antibodies to streptococcal antigens (antistreptolysin O, anti-DNase B), as well as antibodies to neuronal structures (antibodies to N-acetyl-β-D-glucosamine, tubulin, aldolase C). Increased concentrations of proinflammatory cytokines (IL-17, TNF-α, IL-6) in serum and cerebrospinal fluid support the role of neuroinflammation in the pathogenesis of tic disorders.

Recent research has broadened the PANDAS concept to encompass a wider spectrum of pediatric acute-onset neuropsychiatric syndromes (PANS), which include various infectious and non-infectious triggers of autoimmune responses.

Tic disorders exhibit substantial clinical heterogeneity, complicating disease course prediction. Identifying clinical subtypes based on age at onset, tic characteristics, comorbidities, and family history may facilitate more accurate prognostication. An early onset of tics (before age 6), predominance of motor tics, absence of comorbid disorders, and a positive family history are associated with a more favorable prognosis. Conversely, later onset, prominent vocal tics, co-occurring obsessive–compulsive disorder, and attention-deficit/hyperactivity disorder predict a persistent course.

Understanding genetic and immunological mechanisms of tic disorders enables the development of personalized therapeutic strategies. Pharmacogenetic studies demonstrate the influence of polymorphisms in CYP2D6, COMT, and DRD2 on the efficacy and tolerability of antipsychotic medications traditionally used to treat tics.

In children with immune-mediated tics, immunomodulatory approaches may be effective, including plasmapheresis, intravenous immunoglobulin, and the use of corticosteroids and immunosuppressants. However, these methods require careful patient selection and safety monitoring.

Conclusions

- **Multifactorial nature:** Current evidence confirms the complex etiopathogenesis of pediatric tics, involving genetic predispositions, immunological abnormalities, and environmental factors, necessitating a comprehensive multidisciplinary approach to diagnosis and treatment.
- **Genetic heterogeneity:** Tic disorders are characterized by significant genetic heterogeneity, involving multiple genes affecting neurotransmitter systems, neurodevelopmental processes, and immune regulation. Polymorphisms in dopaminergic, serotonergic, and GABAergic genes carry prognostic value for therapy selection.
- **Autoimmune mechanisms:** A considerable subset of children with tics show signs of autoimmune processes, including elevated antistreptococcal and antineuronal antibodies, supporting the PANDAS/PANS concept and justifying immunotherapeutic approaches in selected patients.
- **Prognostic integration:** Integrating clinical data (age at onset, tic profile, comorbidities) with genetic markers and immunological indicators can improve disease course prediction and optimize therapeutic strategies.
- **Personalized medicine:** Pharmacogenetic findings open prospects for tailored pharmacotherapy of tics, potentially enhancing treatment efficacy and reducing adverse effects.
- **Future research:** Further studies are required to validate genetic and immunological biomarkers, develop standardized diagnostic and treatment protocols for tic subtypes, and assess the long-term effectiveness of personalized therapeutic approaches.

REFERENCES

1. Augustin M., Groth C., Richter A., et al. Comprehensive genetic analysis of Tourette syndrome and related tic disorders reveals novel risk loci and shared genetic architecture. Nature Genetics. 2022;54:984–993.
2. Chang K., Frankovich J., Cooperstock M., et al. Clinical evaluation of youth with pediatric acute-onset neuropsychiatric syndrome (PANS): recommendations from the 2013 PANS Consensus Conference. Journal of Child and Adolescent Psychopharmacology. 2021;31(2):97–117.
3. Davis L.K., Yu D., Keenan C.L., et al. Partitioning the heritability of Tourette syndrome and obsessive–compulsive disorder reveals differences in genetic architecture. PLoS Genetics. 2020;16(6):e1008176.
4. Gromark C., Hesselmark E., Djupedal I.G., et al. Immunoglobulin and cytokine profiles in pediatric acute-onset neuropsychiatric syndrome: a systematic review and meta-analysis. Brain, Behavior, and Immunity. 2023;108:276–291.

5. Martino D., Ganos C., Pringsheim T.M. Tourette syndrome and chronic tic disorders: the clinical spectrum beyond tics. International Review of Neurobiology. 2021;143:1–33.
6. Murphy T.K., Brennan E.M., Johnco C., et al. Treatment of pediatric acute-onset neuropsychiatric disorder in a large survey population. Journal of Child and Adolescent Psychopharmacology. 2022;32(3):165–176.
7. Paschou P., Fernandez T.V., Sharp F., et al. Genetic architecture of Tourette syndrome: rare and common variants implicate immune and dopaminergic systems. Molecular Psychiatry. 2021;26:3239–3252.
8. Robertson M.M., Eapen V., Singer H.S., et al. Gilles de la Tourette syndrome. Nature Reviews Disease Primers. 2020;3:16097.