# Assessment of Environmental Exposure to Tick-Borne Encephalitis in Northeastern Poland and Analysis of Disease Biomarkers in Children

The tick-borne encephalitis (TBE) virus, recently assigned to the genus *Orthoflavivirus* (previously *Flavivirus*) and re-named to *Orthoflavivirus encephalitidis,* is causing central nervous system infections in Europe and Asia. The infection may be mild or even asymptomatic, however sometimes it takes a severe course, leading to permanent neurological complications. A significant proportion of patients who recover from the illness develop post-encephalitic syndrome, regardless of the severity of the disease. The causes of the variable clinical course of the disease remain not fully understood, being a challenge for modern medicine. It is supposed that the clinical variability of TBE is associated with individual differences in the immune response. Having no effective antiviral treatment available, the key is to prevent infections through vaccinations and avoiding tick bites.

The aim of this study was to measure seroprevalence of TBE antibodies in northeastern Poland, to assess the extent of TBE virus infections. A questionnaire-based survey among respondents from this endemic was also conduced to test their attitudes toward the TBE vaccine. Another aim of the study was to evaluate the usefulness of measuring chitinase-3-like protein 1 (CHI3L1) levels in serum and cerebrospinal fluid as a biomarker for the severity of TBE in the pediatric population. The study also examined the relationships between CHI3L1 and inflammatory cytokine levels, blood-brain barrier (BBB) integrity, immune response, and the severity of infection in children and adolescents.

Anti-TBE IgG antibodies were detected in 14 out of 298 (5%) blood donors and in 4 out of 180 (2%) children, who had neither been vaccinated against TBE nor diagnosed with the disease. Based on the survey results, only 9% of respondents were vaccinated against TBE, and a similar percentage had vaccinated their children. One-third of unvaccinated respondents said they would vaccinate themselves or their children in the future. Our study showed that this intention was significantly higher among respondents who had recently been bitten by a tick or had a close relative diagnosed with a tick-borne disease. Negative attitudes toward TBE vaccination were associated with the younger age of respondents.

Cerebrospinal fluid and serum levels of CHI3L1 in did not differ between children with encephalitis and children with meningitis caused by the TBE virus. After adjusting for BBB permeability, the CHI3L1 index was 2.4 times lower in patients with encephalitis than in those with meningitis. In younger children, post-treatment, a reduction in CHI3L1, IL-6, and TNF-α concentrations in cerebrospinal fluid was observed, along with improvement of BBB permeability. However, in older children, the albumin index remained abnormal in both severity groups. Correlation analysis revealed associations between CHI3L1 levels and pro-inflammatory markers, particularly chemerin, IL-6, and TNF-α, in both clinical groups.

In conclusion, the vaccination rate and willingness to uptake the TBE vaccine in this endemic region remains alarmingly low. There was a correlation between vaccine acceptance and personal experiences with tick bites, which emphasizes the need for educational campaigns raising awareness about the risks associated with ticks. The analysis of TBE pathophysiology showed that CHI3L1 plays an important role in modulating inflammatory and immune responses during infection, making this protein a promising biomarker. A prolonged pathological processes within the BBB were also found, what may be associated with complications of TBE, which are more frequently observed in older patients. This is particularly important because this study found that undiagnosed mild or asymptomatic TBE infections are common, both in adults and children.

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