

ABSTRACT

Hemolytic uremic syndrome (HUS) induced by Shiga toxin-producing *E. coli* (STEC) is the most common causes of acute kidney injury in children. The therapy of the disease is symptomatic and the main factors leading to the development of severe course of a STEC-HUS are still unknown. In our study, we dealt with factors leading to development of a severe course of STEC-HUS in pediatric patients on both the host and pathogen side. Using retrospective analysis of the courses in children in the Czech Republic, we found that the most common cause of STEC-HUS was serotype O26 and HUS most often affected children under 3 years of age. 63,8 % required dialysis and mortality was 8.62 %. On the host side we focused on the relationship between the activation of the alternative complement pathway and the severity of the course of HUS. We found a significant difference in the level of the C3 part of complement in patients who required dialysis and patients for whom dialysis was not necessary. We also a cut-off value for the C3 part of complement and its reduction below 0.825 g / l was associated with the need for dialysis treatment and a higher incidence of extrarenal complications. Based not only on our results, it can be assumed that the therapeutic effect of complement could affect the severity of the disease. Further aim of our work was to understand STEC O26. The main method was whole genome sequencing (WGS) of 32 strains and genomic analysis of a total of 159 strains. The analysis allowed us to monitor the evolution and geographical spread of the new European clone STEC O26 (nEC), which was divided into two clones - Early (EnEC) and newly identified Late New Clone (LnEC). In 4 strains LnEC we discover yet undescribed mutation in the A subunit of Stx2a. The PCR method proposed in our study targeting a mutation in the *sen/ent* gene, which is characteristic of Late nEC, represents a fast and simple method for distinguishing Early and Late nEC in clinical microbiological laboratories. We believe that our results have contributed to the understanding of pathogenesis of the STEC-HUS and its message will be applied in the clinical care of children with this disease.

Keywords: *Hemolytic-uremic syndrome (HUS), Shiga toxin-producing E. coli (STEC), STEC-HUS, shiga toxin (Stx), enterohemorrhagic E.coli O26 (EHEC), alternative complement pathway, eculizumab*