ABSTRACT

Introduction: Mitochondrial diseases are multifaceted in nature, progressing over time and in the vast majority of cases, difficult to treat. Due to their low incidence, their diagnostics is difficult, and it is not uncommon for it to be completed only in the phase of irreversible damage to the organism.

Objective: The aim of this study was to investigate the natural course of selected mitochondrial diseases, characterize the development of individual symptoms, and subsequently individualize outpatient care with the goal of preventing further deterioration of the clinical condition. The next task was to document the potential of registries in caring for patients with rare diseases so that the collected data would lead to the optimization of clinical and laboratory monitoring of patients and the optimal adjustment of appropriate treatment.

Material: The study included 50 diagnosed Czech patients with a prevalent mutation in the *MT-TL1* gene causing MELAS syndrome, an international cohort of 48 patients with a deficiency in transmembrane protein 70, a group of five patients presenting psychiatric symptoms due to mitochondrial diseases, and a patient with a rare biochemical manifestation of hyperammonemia in mitochondrial disease. The section focusing on the role of international registries in the study of rare metabolic disorders included 38 patients from the Czech Republic with diseases from the group of organic acidurias and urea cycle disorders.

Conclusion: This study enabled a detailed clinical and biochemical-genetic investigation of over 140 individuals with a rare disease. The obtained data led to new genotype-phenotype correlations and expanded differentially diagnostic considerations. Although the diseases are difficult to treat, our data support the importance of early diagnosis and ensuring adequate therapy. The initiation of treatment before the clinical manifestation of the disease and the options for prenatal genetic diagnostics are currently the only ways to prevent irreversible damage to the body in the vast majority of rare diseases.

Keywords: rare diseases, mitochondrial diseases, MELAS syndrome, TMEM70 deficiency, hyperammonemia, organic acidurias, urea cycle disorders