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Medium-chain acyl-CoA dehydrogenase deficiency in North Macedonia – ten years experience

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Abstract

Objectives

Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) is an autosomal recessive disorder of fatty acid oxidation, with potentialy fatal outcome. Early diagnosis of MCADD by acylcarnitine analysis on newborn screening using tandem mass spectrometry can potentially reduce morbidity and mortality. In this study, we evaluate the prevalence and genetic background of MCADD in North Macedonia.

Methods

Medium chain length acylcarnitines, were measured on newborn screening blood spot cards by tandem mass spectrometry. The molecular diagnosis was performed by whole exome sequencing of the *ACADM* gene, and detected mutations were confirmed with Sanger sequencing in all neonates with positive MCAD screening markers, and their parents as well.

Results

A total of 52,942 newborns were covered by metabolic screening during the period May 2014–May 2024. 11 unrelated Macedonian neonates were detected with positive MCADD screening markers, and prevalence of 1/4,813 live births was estimated. Molecular analysis of the *ACADM* gene showed that c.985A>G was the most prevalent mutation occurred on 77.27 % of the alleles, while 18.18 % alleles carried c.244dupT pathogenic variant. Seven

patients were homozygous for c.985A>G (63.6 %) while one was homozygous for c.244dupT (9.1 %) variant. Two patients were compound heterozygotes with c.985A>G/c.244dupT genotype (18.2 %), and one patient had c.985A>G allele without detection of the second *ACADM* mutant allele.

Conclusions

The NBS estimated prevalence of MCADD in Macedonian population was more frequent than in the other European population and worldwide incidence in general. This is the first report of the genetic background of MCADD in North Macedonia.

Keywords: ACADM mutations; fatty acid oxidation disorder; medium-chain acyl-CoA dehydrogenase deficiency; neonatal screening

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Research ethics: This study was approved by the Ethics Committee of the University Clinic for Pediatrics in Skopje.
Informed consent: Informed consent for molecular analysis was obtained from all individuals included in this study.
Author contributions: VA carried out the screening for inborn errors of metabolism in the country, performed the retrospective evaluation of the data, the designing, writing, and editing of the manuscript. MK and NZ were instrumental in the editing of the manuscript, they treated, and followed babies and children with MCAD. TT, MD, and JK performed the molecular analysis of *ACADM* gene, and interpretation of the NGS results as well as contributed in the editing of the manuscript. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
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Keywords for this article
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