Multiple Carboxylase Deficiency

Alternative Name
HLCS Deficiency
Multiple Carboxylase Deficiency, Neonatal Form
Multiple Carboxylase Deficiency, Early Onset

Record Category
Disease phenotype

WHO-ICD
Endocrine, nutritional and metabolic diseases
Metabolic disorders

Incidence per 100,000 Live Births
NA

OMIM Number
253270

Mode of Inheritance
Autosomal recessive

Gene Map Locus
21q22.13

Description
Multiple carboxylase deficiency is biotin-responsive disorder. Affected patients present with metabolic acidosis, hypotonia, lethargy, skin rash, alopecia and seizure. The symptoms can manifest soon after birth or late in the infantile period. The prevalence is unknown. However, it is considered a rare disorder. It is inherited in an autosomal recessive pattern. Treatment includes a supplementation of biotin 5-40mg/day. An early institution of biotin ensures a better outcome.

Molecular Genetics
Multiple carboxylase deficiency results from mutations in the HLCS gene, which is located on the long arm of chromosome 21. The HLCS gene encodes the enzyme that catalyzes the binding of biotin to carboxylase and histones. This encoded protein plays important roles in several biological processes such as fatty acid synthesis, gluconeogenesis and catabolism of branched chain amino acids. Various types of HLCS mutations were noted to be associated with multiple carboxylase deficiency including; missense and indel ones.

Epidemiology in the Arab World
Saudi Arabia
Moammar et al., (2010) reviewed all patients diagnosed with inborn errors of metabolism (IEM) from 1983 to 2008 at Saudi Aramco medical facilities in the Eastern province of Saudi Arabia. During the study period, 165530 Saudi infants were born, of whom a total of 248 newborns were diagnosed with 55 IEM. Affected patients were evaluated based on clinical manifestations or family history of similar illness and/or unexplained neonatal deaths. Almost all patients were born to consanguineous parents. Organic acidopathies (OA) were diagnosed in 48 out of 248 cases (19%), which constituted the second largest group of IEM found in this cohort after lysosomal storage disease. Among the group with OA, two cases from three families were diagnosed to have multiple carboxylase deficiency. The estimated incidence of multiple carboxylase deficiency in this cohort was 1 in 100,000 live births. The authors concluded that data obtained from this study underestimate the true figures of various IEM in the region. Therefore, there is an urgent need for centralized newborn screening program that utilizes tandem mass spectrometry, and offers genetic counseling for these families.

References
Moammar H, Cheriyan G, Mathew R, Al-Sannaa N. Incidence and patterns of inborn errors of metabolism in the Eastern Province of Saudi Arabia, 1983-2008. Ann Saudi Med. 2010 Jul-Aug;30(4):271-7. PMID:20622343

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