PYRUVATE DEHYDROGENASE E1-ALPHA DEFICIENCY; PDHAD

Alternative Names
PYRUVATE DEHYDROGENASE
COMPLEX DEFICIENCY
PYRUVATE DECARBOXYLASE DEFICIENCY
ATAXIA, INTERMITTENT, WITH
ABNORMAL PYRUVATE METABOLISM
PDH DEFICIENCY
ATAXIA, INTERMITTENT,
WITH PYRUVATE DEHYDROGENASE DEFICI
ENCY
ATAXIA WITH LACTIC ACIDOSIS I

Record Category
Disease phenotype

WHO-ICD
Disorders of pyruvate metabolism and gluconeogenesis

Incidence per 100,000 Live Births
NA

OMIM Number
312170

Mode of Inheritance
X-linked dominant

Gene Map Locus
Xp22.12

Description
Pyruvate dehydrogenase E1-alpha deficiency is the most frequent form of pyruvate dehydrogenase deficiency (PDHD). The signs and symptoms usually first appear shortly after birth and include; lactic acidosis, psychomotor retardation, hypotonia, seizure, ataxia and other signs of neurological dysfunction. The exact prevalence is unknown, however more than 200 patients have been described. It was noted that male patients are more severely affected the female patients. Some patients have structural brain lesions. Dignosis can be made by measuring the level of lactic acid and pyrovate in on to perform enzyme assay and molecular genetic testing. Clinically, check for signs of central nervous system dysfunctions. Treatments include cofactor supplementation with thiamine, carnitine, and lipoic acid in order to optimize the function of pyruvate dehydrogenase complex. The correction of lactic acidosis does not restore the damaged CNS.

Molecular Genetics
Mutations in the PDHA1 gene cause Pyruvate dehydrogenase E1-alpha deficiency. PDHA1 gene is located on the short arm of chromosome X. The E1 component of the PDH complex catalyzes the thiamine pyrophosphate (TPP)-dependent decarboxylation of pyruvate. Moreover, E1 alpha-subunit contains a conserved TPP binding motif. Several mutations have been identified in this gene.

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. Organelle disorders were identified in 18 out of 248 of diagnosed subjects. Among them, 3 cases from 2 families were found to have PDH deficiency; additionally, 4 cases from 4 families were found to have congenital lactic acididemia. The incidence is estimated at 2 per 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

Related CTGA Records

External Links
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=79243

https://ghr.nlm.nih.gov/condition/pyruvate-dehydrogenase-deficiency#genes

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