P-220 - MAPLE SYRUP URINE DISEASE IN COSTA RICA: MOLECULAR CHARACTERIZATION OF 30 CHILDREN IDENTIFIED BY NEWBORN SCREENING IN 1990-2018.

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INTRODUCTION: Maple syrup urine disease (MSUD) is an autosomal recessive inborn error of metabolism caused by an altered function of branched-chain α-ketoacid dehydrogenase (BCKD) complex. Mutations in subunits E1α (BCKDHA), E1β (BCKDHB) and E2 (DBT) cause the disease. Newborn screening (NBS) for MSUD has been done in Costa Rica for 28 years. OBJECTIVE: The aim of this work is to describe the genotype and estimate the frequency of the mutations encountered among our MSUD patients after 28 years of NBS implementation in Costa Rica. METHODS: Bacterial inhibition test (Guthrie) was used for NBS from 1990 to 2005. From 2006 onwards amino acids quantification is done by tandem mass spectrometry (MSMS). Molecular analysis of BCKDHA, BCKDHB and DBT genes was performed by Sanger sequencing, using specific primers for coding exons and its intronic flanking regions. RESULTS: To 2018, 1,828,312 babies have been screened, where 43 affected individuals have been identified, 21 by Guthrie test and 22 by MSMS. The estimated prevalence is 2 affected individuals per 100,000 live births (1: 42519). Here we describe 30 out of 43 detected patients, since 13 of them died before sequencing analysis implementation. All cases were confirmed by molecular analysis, and the variants detected were in BCKDHA (6 patients) and BCKDHB (24 patients) genes. In BCKDHA (NM_000709.3) the most frequent genotype was: c.117delC;[117delC] (4 patients) and the rest were: c.484+1G>A;[484+1G>A] and c.661_664delTACG;[1234G>A]. The c.117delC variant was the most frequent (67%), whereas c.484+1G>A is a novel variant, according to our literature review. Furthermore, 17 patients were homozygous for a BCKDHB (NM_183050.3), c.853C>T;[853C>T] (1 patient) and c.853C>T;[853C>T] (16 patients, including 2 brothers). Seven patients were compound heterozygous where c.564T>A;[853C>T] genotype was the most frequent (4 patients, including 2 brothers), the others carry c.853C>T variant in trans configuration with c.564T>A, c.633+1G>A and c.832G>A. As observed, the most frequent variant found in BCKDHB was c.853C>T (82%). CONCLUSIONS: In Costa Rica MSUD prevalence is 2: 100,000 live births and is caused by mutations that affect function mainly of E1β subunit, followed by E1α. In our sample, the most frequent genotype was NM_183050.3(BCKDHB): c.853C>T;[853C>T]. Furthermore, NM_000709.3(BCKDHA): c.484+1G>A variant is likely pathogenic.