P-218 - GALACTOSEMIA IN COSTA RICA: MOLECULAR CHARACTERIZATION OF 22 CHILDREN IDENTIFIED BY NEWBORN SCREENING IN 2001-2018.

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INTRODUCTION: Galactosemia is an autosomal recessive inborn error of metabolism of carbohydrates. This pathology is caused by the deficiency of any of the following enzymes of galactose metabolism: galactokinase 1 (GALK1), galactose-1-phosphate uridylyltransferase (GALT) and UDP-galactose-4-epimerase (GALE). Newborn screening (NBS) for galactosemia has been done in Costa Rica for 18 years (2001-2018). OBJECTIVE: This study presents data about GAL mutations, and describe the genotype and estimate the frequency of the mutations encountered among our galactosemic patients confirmed, after 18 years of NBS implementation in Costa Rica. MATERIALS AND METHODS: Total galactose (TGal) concentration was determined by fluorescent galactose oxidase method (2001-2013: Victor 1420-TM, and 2014-2018: GSP), with Neonatal Total Galactose kit, PerkinElmer, Inc. The cut off value was 12.8 mg/dL (trust interval of 99.2%). Confirmatory tests included: thin layer chromatography and molecular analysis of GALK1, GALT and GALE genes, by Sanger sequencing. RESULTS: Throughout 18 years of NBS, 1 118 625 babies have been screened, where 32 of them had positive confirmatory test for galactosemia. Molecular analysis confirmed the diagnosis of 19 patients, in 3 cases a single variant was identified and finally in 10 cases no variants were detected. Among patients in whom some variant was identified, 9 were in GALT and 13 in GALK1. In GALT (NM_000152.3) 2 patients were homozygous (p.Q188R) (c.[563A>G];c.[563A>G]). Five patients were compound heterozygous, where c.[-119_-116delGTCA;940A>G] (Duarte variant);[563A>G] genotype was the most frequent (3 patients), the other 2 patients were c.[-119_16delGTCA;940A>G];[c.584T>C] (p.L195P). Finally, in 2 cases just a single variant was detected, these patients carried c.[-119_-116delGTCA;940A>G] and c.512T>C variant (p.F171S). Furthermore, 9 patients were homozygous for a GALK1 (NM_000154.1), c.[1144C>T];[1144C>T] (p.Q382*).Three cases were compound heterozygous c.[766C>T] (p.R256W);[1144C>T], and one patient carried a single variant , c.1144C>T. CONCLUSIONS: The variants found most frequently in GALT and GALK1 were c.[-119_-116delGTCA;940A>G] and c.1144C>T, respectively. Further analysis are required in order to confirm or rule out the diagnosis in heterozygous patients, and in those where no variants were detected. In those patients, where no variants were detected, closer follow-up should be recommended in order to identify which clinical factors produce increases in TGal determination.