P-221 - BIOTINIDASE DEFICIENCY: INCIDENCE AND CORRELATION BETWEEN ENZYMATIC ACTIVITY AND MOLECULAR FINDINGS IN A POPULATION OF MEXICAN NEWBORNS

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INTRODUCTION: Biotinidase deficiency (BIOT) is an inborn error of metabolism with an estimated incidence of 1 in 61,000 newborns (NB). BIOT impairs biotin recycling and diminishes its bioavailability, leading to neurocutaneous manifestations, ketolactic acidosis, as well as organic aciduria. To prevent such manifestations, newborn screening (NBS) allows timely detection and early treatment. Therapeutic decisions are currently based on enzymatic activity, as no clear genotype-phenotype correlation has been established for BIOT, due to the heterogeneity in clinical presentation described among patients. OBJECTIVES: To estimate BIOT incidence in a Mexican NB population, and to demonstrate a correlation between enzymatic activity and genetic findings in BIOT NBS referred patients. MATERIALS AND METHODS: We analyzed 249,442 NBS reports performed by Genomi-k from July 2005 to December 2018. Presumptive positives cases, previously assessed by semi-quantitative fluorometric assay, were requested for serum enzymatic activity and BTD gene sequencing. A normal enzymatic activity was considered above 5 nmol/min/ml. The biochemical phenotype under the limit was classified in: profound deficiency (<0.75), partial deficiency (0.75-2.25), and false positive (2.26-4.9) characterized by low-activity and lack of symptoms. We applied the Mann-Whitney U test to analyze the genotype-phenotype impact (i.e. variants and enzymatic activity, respectively) between group 1 (D444H/D444H; n=8) and group 2 (D444H/pathogenic variant; n=7). RESULTS: Overall, we identified 8 NB for partial BIOT, with an estimated incidence of 3.2: 100,000 NB, no NB for profound BIOT, and 21 false positive cases. Furthermore, D543E, Q456H, D444H (most frequent variant), F443Y, F403V-D444H, R211H, K176N, A171T-D444H, and C33Ffs variants were identified. The statistical analysis concluded a significant effect between enzymatic activity and genotype (mean of groups 1 and 2 was 4.2 and 11.3 respectively; U = 1.5, z = -3.067, p = 0.001, r = 0.792). DISCUSSION AND CONCLUSIONS: Our estimated incidence is comparable to the U.S. and Spain (3.9 and 3.3: 100,000 NB, respectively). Furthermore, D444H/pathogenic variant had a significant impact, causing lower enzymatic activity than D444H/D444H. Therefore, molecular findings may help in defining the biotin dose in ambiguous cases, supporting current literature. NBS is of paramount importance to detect patients for this condition and start promptly their appropriate therapeutic approach.