**O-010 - GENETIC DIAGNOSIS AND GENOTYPE-PHENOTYPE ASSOCIATION IN 113 BRAZILIAN INDIVIDUALS WITH REDUCED BIOTINIDASE ACTIVITY**

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***INTRODUCTION:*** Neonatal screening for biotinidase deficiency (BD) is mandatory in Brazil since 2012. Our group has been studying the mutational profile of BTD gene in Brazilian individuals detected by neonatal screening since then, and has already published the results for 72 patients (Borsatto et al. 2014 and 2017). OBJECTIVES: To provide an update of the genetic diagnosis of BD in Brazil, including the results by Borsatto et al. 2014 and 2017. ***METHODS:*** One hundred and thirteen individuals were included (male=57; parental consanguinity=5), from different regions of Brazil (southeast=17, northeast=28 and south=68). Enzyme activity was available in plasma for 98/113 individuals (current normal=7, heterozygous=52, partial BD=23, borderline heterozygous/partial BD=9, profound BD=4, and borderline heterozygous/normal=3.) Genomic DNA was extracted from blood samples in EDTA or buccal epithelial cells using commercial kits followed by PCR, purification and sequencing of exons 2, 3 and 4 of the BTD gene. The reference sequence NG 00819.1 was employed to identify the variants. The software Polyphen2, SIFT and Mutation Taster were used to predict their pathogenicity. ***RESULTS:*** Considering the whole sample, 27 pathogenic variants were identified. The most frequent were c.1330G>C (p.Asp444His), c.755A>G (p.Asp252Gly) and c.1368A>C (p.Gln456His), with allele frequency of 42%, 4% and 3%, respectively. In addition to the five novel variants published in our previous study, three novel variants were found: c.1321G>A (p.Gly441Arg), c.855G>T (p.Gln285His) and c.269T>A (p.Leu90His); all predicted to be pathogenic in silico. The BD classification according to the genotype was: heterozygous=41; partial BD=26; normal=23; profound BD=4; and undetermined=19. The classification based on genotype matched the biochemical phenotype in 69% cases. ***CONCLUSION:*** Currently, neonatal screening for BD in Brazil mainly detects heterozygous individuals. Profound BD is rare. Although the association between genotype and phenotype is not always consistent, genetic analysis helps in the classification of borderline cases and consecutive discordant enzymatic results.