O-005 - NATURAL HISTORY OF TYPE IX GLYCOGEN STORAGE DISEASE: A BRAZILIAN MULTICENTRIC STUDY

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INTRODUCTION: Type IX glycogen storage diseases (GSD-IX) are caused by mutations in genes encoding for phosphorylase kinase subunits, resulting in subtypes IX-a, b, and c. Its diagnosis has been challenging due to wide variability of phenotypes and inheritance patterns. They can cause ketotic hypoglycemia, short stature, hepatomegaly, cirrhosis and hepatocellular carcinoma or even present as oligosymptomatic phenotypes. GSD-IX natural history is not fully known. Treatment involves avoiding hypoglycemia through use of cornstarch, frequent feeding and high protein intake. ***OBJECTIVE:*** To describe the natural history of a cohort of Brazilian patients with GSD-IX. ***METHODS:*** Retrospective observational multicentric study. Informed consent was obtained from all participants. To be included, patients needed to have a genetic diagnosis of GSD-IX. ***RESULTS:*** Seventeen individuals (GSD-IXa: 12; GSD-IXb: 2; GSD-IXc: 3), from eleven families, were included (male: 14; 82.3%). The mean age at inclusion was 13.8 years (range: 3-55 years). Hepatomegaly triggered the initial investigation in 10 cases (58.8%). First manifestations were observed during neonatal (n=3); infant (n=10); and children (n=4) ages. The specific GSD subtype was diagnosed on average at 11.3 years; and 76.4% of subjects had received a clinical diagnosis of another type of GSD before genetic confirmation. Hepatic biopsy was performed in seven individuals (41.1%), showing fibrosis in three cases. Other findings included alteration of transaminases (14/17); increase of muscular enzymes (14/17); hypoglycemia (13/17); hypertriglyceridemia (13/17); hypercholesterolemia (10/17); and hyperlactacidemia (8/17). Muscular signs and symptoms were identified only in subtypes IXa and IXb. Three individuals required use of gastrostomy to maintain adequate intake and prevent decompensation. Regarding genetic analysis, four pathogenic known variants were identified in the X-linked form. In autosomal recessive forms, five variants were identified, including four novel mutations (PHKB: c.1972-2A>G, c.2181delT, c.572_576delAGATT; PHKG2: c.454C>T). ***DISCUSSION AND CONCLUSION:*** This is the largest GSD-IX case series already described worldwide and extends the current limited knowledge about clinical variability in patients with type IX GSD. Wide clinical heterogeneity was identified. Laboratory data demonstrate high prevalence of hepatomuscular manifestations. It is observed that many individuals went through investigational invasive procedures, however these were minimally informative in diagnostic process. Long-term studies involving follow-up of these patients until adulthood are necessary.