if the preterm/term infant survived the neonatal period or 2) unsuccessful if there was a miscarriage/fetal demise/perinatal death. Drug regimen during pregnancy were 1) penicillamine (DPA), 2) zinc (Zn) or 3) DPA/Zn if the patient had switched therapy for any reason. Statistical analysis was carried out using Fisher's test, with significance level at $p<0.05$.

Results and Discussion: Of the 49 pregnancies analyzed, 2 (4.1%) ended in maternal death and 17/49 (34.7%) in miscarriage/fetal or neonatal death. The Table below presents the results. The analysis of medication and pregnancy outcomes combined deteriorating and stable cases. There was a correlation between successful births and asymptomatic patients who had given birth before the onset of WD ($p<0.001$). In stable patients, successful births were slightly above significance ($p=0.062$). There was no significant difference among the outcomes in relation to the medication taken.

Conclusions: Pregnancy in symptomatic WD is potentially harmful to mother and conceptus. Successful births were significantly associated with pregnancies before the onset of WD symptoms, but were also possible with stable disease under treatment. Anti-copper drug regimen was not associated with pregnancy outcome.

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OP-16 FREQUENCY OF ATP7B GENE MUTATIONS IN A BRAZILIAN COHORT OF PATIENTS WITH WILSON'S DISEASE

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Conflict of interest: No

Introduction and Objectives: Wilson's disease (WD) is a rare genetic disease presenting more than 900 mutations in the ATP7B gene. The knowledge of the regional distribution of these mutations can improve the diagnosis of WD. We aimed to evaluate the frequency of ATP7B mutations in a WD Brazilian cohort and the association with disease phenotypes.

Patients / Materials and Methods: We performed molecular analysis by NGS of the 21 exons of ATP7B (Mendelics Genomic Analysis Laboratory) in patients with diagnosis of WD and in first-degree relatives undergoing WD investigation, followed in a single hepatology center. Demographic data and predominant type of WD presentation were assessed.

Results and Discussion: 28 patients were included (60% female; mean age 25 $\pm$ 13 years): 25 had an established diagnosis of WD and 3 were heterozygous relatives without disease. The phenotypes of WD were as follows: 15/25 (60%) with exclusively hepatic manifestation, 8/25 (32%) combination of hepatic and neurological, 1/25 (4.0%) isolated neurological manifestations and 1/25 (4.0%) were pre-symptomatic. We identified 17 ATP7B gene distinct mutations. The pathogenic variants c.3402delC, c.2123T>C and c.3818C>T presented the highest allele frequency, respectively, 25.5%, 15.7% and 15.7%. The majority (80.0%) presented the mutation in compound heterozygosity, 12.0% in homozygosity and 8.0% in simple heterozygosity. The c.2145C>T, c.1552T>C and c.3188C>T variants were considered of undetermined significance; c.2072G>T and c.3071_3072delTG variants were considered probably pathogenic. Regarding the disease phenotype, patients with mutations c.3402delC CG>C and c.2123T>C presented equal distribution of isolated hepatic or hepatic plus neurological phenotype, while c.3818C>T mutation was associated with predominantly hepatic phenotype. Presence of exon 2 deletion was associated with severe neurological manifestations.

Conclusions: The mutations c.3402delC, c.2123T>C and c.3818C>T were the most prevalent. The c.2145C>T and c.3188C>T variants, considered of undetermined significance, were found in confirmed cases of WD. An important heterogeneity of the ATP7B genotype associated with variation in phenotypic presentation was observed.

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P- 1 DEVELOPMENT OF LENTIVIRAL VECTORS FOR INHIBITION OF HEPATITIS B VIRUS, VIA SMALL INTERFERING RNA

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Conflict of interest: No

Introduction and Objectives: INTRODUCTION: Chronic hepatitis B represents a significant global health challenge. Current treatments often fail due to the persistence of HBV DNA as covalently closed circular DNA or integrated into the host genome, leading to viral reactivation. RNA interference (RNAi) emerges as a promising approach for treating chronic hepatitis through post-transcriptional gene silencing. OBJECTIVE: To design and evaluate the efficacy of RNAi lentiviral vectors targeting key HBV proteins (HBsAg, HBcAg, HBeAg) and pregenomic RNA (pgRNA) for silencing.

Patients / Materials and Methods: Silencing vectors were designed to target overlapping open reading frames, allowing simultaneous silencing of multiple viral proteins and pgRNA with a single RNAi construct. Three vector candidates (siHBV-1 to 3) underwent rigorous in silico testing to minimize off-target effects, evaluating stability and secondary structures. Lentiviral vector production was assessed using flow cytometry to detect green fluorescent protein expression in cell culture. Huh7 cells were transfected with 1 μg of purified HBV genotype A circular monomers, followed by infection