Ann Hum Genet. 2013 Jul;77(4):299-307. doi: 10.1111/ahg.12024. Epub 2013 Apr 2.

Wilson disease mutation pattern with genotype-phenotype correlations from Western India: confirmation of p.C271* as a common Indian mutation and identification of 14 novel mutations.

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Abstract

Wilson disease (WD) is an autosomal recessive disorder resulting from mutations in the ATP7B gene, with over 600 mutations described. Identification of mutations has made genetic diagnosis of WD feasible in many countries. The heterogeneity of ATP7B mutants is, however, yet to be identified in the Indian population. We analyzed the mutational pattern of WD in a large region of Western India. We studied patients (n = 52) for ATP7B gene mutations in a cohort of families with WD and also in first-degree relatives (n = 126). All 21 exon-intron boundaries of the WD gene were amplified and directly sequenced. We identified 36 different disease-causing mutations (31 exonic and five intronic splice site variants). Fourteen novel mutations were identified. Exons 2, 8, 13, 14, and 18 accounted for the majority of mutations (86.4%). A previously recognized mutation, p.C271*, and the novel mutation p.E122fs, were the most common mutations with allelic frequencies of 20.2% and 10.6%, respectively. Frequent homozygous mutations (58.9%) and disease severity assessments allowed analysis of genotype-phenotype correlations. Our study significantly adds to the emerging data from other parts of India suggesting that p.C271* may be the most frequent mutation across India, and may harbor a moderate to severely disabling phenotype with limited variability.

KEYWORDS: ATP7B; GAS for WD; India; Wilson disease; genotype; phenotype

PMID: 23551039 DOI: 10.1111/ahg.12024

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