Wilson's disease

Wilson Disease Epidemiology

O. Bandmann
Sheffield Institute for Translational Neuroscience (SITraN), University of Sheffield, UK

There is ongoing uncertainty about the incidence and prevalence of Wilson disease (WD). Scheinberg and Sternlieb first estimated the prevalence of 5 WD to be 5 per million. Subsequently, a prevalence figure of 30 per million with a heterozygote carrier frequency of 1 in 90 was frequently quoted. However, considerably higher incidence and prevalence figures have been reported for population isolates, the highest being 885 per million from within the mountainous region of Rucar in Romania. Different strategies including both biochemical and genetic screening have been used to establish the frequency of WD in the general population. A large number of different ATP7B mutations can cause WD, but studies can be further confunded by the uncertain relevance of some sequence variants with unproven pathogenicity. We undertook the largest genetic prevalence study on WD in the UK. The entire ATP7B coding region was sequenced in 1000 control samples from a perinatal blood spot screen. In addition, three mutation hot spots (exon 8, 14 and 18) were sequenced in 5000 controls. Using very strict criteria to assess the pathogenicity of the detected sequence variants, we calculated a revised figure of 0.040 or 1:25 of heterozygote mutation carriers in the UK. The resulting predicted frequency of individuals carrying two pathogenic ATP7B mutations was 142 per million, more than four times the often quoted prevalence figure of 30 per million. Future studies need to determine whether this apparent high genetic prevalence can be validated in other cohorts.