Reviewer's report

Title: Phenotypic and Genetic Characterization of a Cohort of Pediatric Wilson Disease Patients

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Reviewer: michael L schilsky

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The very interesting finding of early onset disease in this Egyptian cohort is reminiscent of the early onset disease in another pediatric cohort in India (see point one below) but the excellent characterization of the group and the longitudinal follow-up make this work important. The presence of the higher percent of males with ALF versus adult cohorts where females predominate may indeed be due to pre-adolescent disease onset, but confirms the prior finding of Dhawan et al in a similarly young patient group. The scoring system of Dhawan et al for severe liver disease and Wilson disease predicted outcome for most but not all patients in this cohort as well. Treatment options of penicillamine, zinc or a combination were effective in most but were accompanied by a significant percent with non-adherence that influenced outcome and survival. This occurred despite frequent monitoring of patients. The genetic variants of ATP7B responsible for the disease in this cohort were identified, and consanguinity was common for parents of affected individuals. Despite this, genotype-phenotype correlations were not clearly identified.

1. Minor essential revision: The authors should cite the work by Kalra V, Khurana D, Mittal R. Indian Pediatr. 2000 Jun;37(6):595-601 - Wilson's disease--early onset and lessons from a pediatric cohort in India. This cohort also had very early onset disease and a high percentage of young patients with KF rings.

2. Discretionary point: For such early onset and frequency of KF rings, the authors should potentially stress environmental exposure as an exacerbating factor.

3. Minor essential revision: With such a high incidence of non adherence to treatment yet such a regular routine monitoring schedule, did the authors note elevations in liver tests preceding worsening disease as previously reported by Arnon et al? Could the patients that suffered from the non adherence been recognized earlier?

4. Major point: The authors treated some patients with once daily zinc along with penicillamine. There is no basis for recommending only once daily zinc sulfate for treatment, even with a chelating agent. Data from Brewer has previously shown that at least twice daily treatment is needed. The authors should state why they chose this once daily treatment option and present evidence of its utility or state that it is uncertain in discussion.
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'