

**We thank the reviewers and editors for their valuable comments. Please find the point to point responses below and the relevant changes in the R1 document highlighted in yellow.**

**Response to reviewer's comments:**

**Reviewer 1:**

**Comment 1: To write uppercase.**

**Answer:** We have now written in uppercase.

**Comment 2: To write the full form of TGN.**

**Answer:** The full form of TGN is trans-Golgi network. This information has now been added.

**Comment 3: better to have an illustrated diagram done by authors show the pathogenesis.**

**Answer:** We agree with the reviewer. We have now added an illustrated diagram (Figure 1) to show the pathogenesis of Wilson's disease.

**Comment 4: They should mention why some children may manifest by early hepatic and others come from the start by neurological manifestations.**

**Answer:** We agree with the reviewer. We have added the explanation in the manuscript.

**Reviewer 2:**

**Comment 1: Better to have an illustrated diagram done by authors show the pathogenesis.**

**Answer:** We agree with the reviewer. We have now added an illustrated diagram (Figure 1) to show the pathogenesis of Wilson's disease.

**Comment 2: Extrapyrarnidal symptoms and psychiatric manifestations- how it is presented clinically**

**Answer:** Neurological presentation of Wilson's disease with extrapyramidal are tremors, dystonia, dysarthria, gait disturbances, behavioral abnormalities and psychiatric manifestations are bipolar affective disorder and psychosis with cognitive decline. This information has now been added to the manuscript.

**Comment 3: Osseo-muscular involvement -how it is presented clinically?**

**Answer:** Osseo-muscular manifestations of Wilson's disease include pathological fractures, arthralgia, and proximal muscle weakness. We have now added this information to the manuscript.

**Comment 4: Section 2.4: copper not understood?**

**Answer:** It was a typing error. Language has been changed to the following.

“Holoceruloplasmin contains 3.15 µg of copper per mg of ceruloplasmin , hence, ceruloplasmin-bound copper may be calculated as serum ceruloplasmin x 3.15 (in µg/dL).”

**Comment 5: I think we should tabulate the investigations and write diagnostic values as there are many numbers and values.**

**Answer:** We agree with the reviewer. We have now tabulated the investigations with their diagnostic values (Table 1).

**Comment 6: Are there any other investigation predict extra hepatic involvement?**

**Answer:** Exchangeable copper(CuEx) is an upcoming biomarker that is being explored. In extra-hepatic patients, CuEx was the only biological marker to be positively correlated with the neurologic disease burden (assessed by Unified Wilson Disease Rating Score). CuEx determination is, in consequence, useful when diagnosing WD with a value >2.08 µmol/L, and is indicative of the severity of the extra-hepatic involvement. There is not enough data yet to support role of CuEx in liver damage. We have added this information in the manuscript.

**Comment 7: It is better to put in table investigations to confirm diagnosis and investigations for asymptomatic sibs.**

**Answer:** We agree with the reviewer. We have added a table regarding the investigations to diagnose Wilson disease in suspected patients and asymptomatic siblings (Table 2).

**Comment 8: mention screening tests for family screening.**

**Answer:** Family members should be screened by clinical examination, liver function test, slit -lamp examination, serum ceruloplasmin, 24-hour urine copper estimation and genetic testing, especially if mutation is known in the proband. We have now added this information to the manuscript.

**Comment 9: I think renal manifestation with Wilson should be written in a way more focused And classified Due to the original diseases and due to treatment .**

**Answer:** We agree with the reviewer. We have now re-classified renal manifestation of wilson disease as 1) due to original disease and 2) due to treatment. We have also re-written the paragraph in a more focused way. We have added a table (Table 3), summarizing the differentiating features between these two conditions.

**Comment 10: Paragraph no 4.1.1 is a big paragraph needs to be reformulated in a simple to the point .**

**Answer:** We agree with the reviewer. We have now rewritten the paragraph in a focused way and shortened it. We have changed the paragraph numbering to 3.1.1

**Comment 11: Write in a table the risk factors which may lead to side effects of drug therapy.**

**Answer:** We have added a table (Table 4) enlisting the risk factors which may lead to the side effects of drug therapy.

**Comment 12: Kindly put medications in a table as regard mechanism of action when to start side effects dose .**

**Answer:** We have added a table (Table 5), summarizing all the drugs used in the treatment of Wilson's disease, their mechanism of action, dose, storage and important side effects.