

Dear Dr Yuan Qi  
Science Editor, Editorial Office  
**Baishideng Publishing Group Inc**  
E-mail: [y.qi@wjgnet.com](mailto:y.qi@wjgnet.com)

**Subject : Manuscript NO.: 34405**

Dear Sir,

I would like to thank the Editorial office and reviewers for their comments and suggestions. I have carefully revised the manuscript as per reviewers' comments. I am resubmitting a revised manuscript taking into consideration all queries as listed below. Highlighted in yellow are changes in the resubmitted revised version

**1. Title:** There was a minor change in the title. The word Arab was removed because Turkey and Iran are non Arab countries but are referred to as regional Non-European countries. In addition homozygosity was added to emphasize that majority of our patients were homozygous for disease causing mutations.

**Old Title :** Wilson Disease in Lebanon and Regional Arab Countries: Predominance of Hepatic Phenotype

**New Title :** Wilson Disease in Lebanon and Regional Countries: Homozygosity and Hepatic Phenotype Predominance.

**Authors:** Kassem Barada, Aline El Haddad, Meghri Katerji, Mustapha Jomaa, and Julnar Usta.

**In addition as suggested Tables 1A and 1B in the old version are now labeled as Table 1 and Table 2.**

**Table 2 in the old version is now table 3 and**

**Table 3 in the old version is now Table 4**

**Correspondence to:** Julnar Usta, Professor, Department of Biochemistry and Molecular Genetics, American University of Beirut. Riad el Solh, 110236 Beirut, Lebanon  
[j.usta@aub.edu.lb](mailto:j.usta@aub.edu.lb)

**Reviewer code:** 03647931, and 02860849

**Step 1. Please revise your manuscript according to each of the reviewers' comments.**

Response to reviewers comments are attached

**Step 2. Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Basic Study.**

Revised manuscript has been uploaded taking into consideration all the comments

**Step 3. Please provide the Scientific Research Process write-up.**

- 1 What did this study explore?
- 2 How did the authors perform all experiments?
- 3 How did the authors process all experimental data?
- 4 How did the authors deal with the pre-study hypothesis?
- 5 What are the novel findings of this study?

All questions 1-5 have been answered and uploaded as file named Format for scientific research process

**Step 4. Please provide an Audio Core Tip.**

Uploaded

**Step 5. Please subject the final title of your manuscript to a Google Scholar search, and store screenshot images of the results.**

Uploaded and as indicated in our letter to editor first submission

Under screen shot the first result entitled: genotypic-phenotypic profile of Wilson Disease patients in Lebanon comparison with regional Arab countries by Haddad et al is the **Abstract proceedings of the poster presentation** submitted to *International Liver congress , European Association for the study of the Liver-EASL, Amsterdam – The Netherlands 19-23 April 2017 meeting on Genetic and pediatric liver diseases.*

**Step 6. Please provide all files related to the Academic Rules and Norms.**

Uploaded file scan present one of the IRB letters that I received showing dates of IRB letters renewing the protocol between years 2004 -2014. If you need actual 10 letters I can scan and send as well.

**Step 7. Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s).**

The work was supported by Medical Practice plan fund (MPP) and University Research board. Uploaded under file scan please find 2 representative letters of the funds granted on yearly basis

**Step 8. Please revise the language of your manuscript.**

We have revised the language and composition of sentences. The authors would like to clarify that American University of Beirut is an English speaking organization in which all communications, teaching are in English. Proficiency in English language is a must and a requirement for appointment.

**Step 9. Please sign the Copyright Assignment form.**

Signed and uploaded

**Step 10. Submit the revised manuscript and all related documents.**

Uploaded with changes highlighted

**We hope the revised manuscript have addressed successfully all your queries and concerns. Do not hesitate to request should you need further elaboration or information on any issue.**

**Thank you for your guidance and kind cooperation**

Warm regards



Julnar Usta

## 1. RESPONSES TO REVIEWERS

*We sincerely thank the reviewers and editor for their criticisms and comments. We hereby respond to their queries and present below point by point response to their concerns.*

**Reviewer Code: 03647931; Egypt**

**This study is well designed, methodology and data collection are competent, the paper is well written in a clear language.**

*We thank the reviewer for his/her positive and constructive comment.*

**I have the following comments:**

- i) **The number of patients on whom genetic analysis was performed is small (36 only) and the authors compared their findings to similar studies in neighboring countries (total more than 500 subjects) so the authors can extend their genotyping work on more patients in Lebanon to reach solid conclusions.**

*We thank the reviewer for this comment. We agree with the reviewer that a larger number of patients is desirable. However, Wilson Disease is rare and the worldwide frequency is 1 in 40000. Hence 36 patients out of 5.8 million Lebanese is quite comparable to 198 patients out of 91.5 million Egyptians or 152 patients out of 31.5 million Saudi Arabians. Regardless of the number in our extensive study, our conclusions were similar to those reported from regional Arab and Non-European countries.*

- ii) **This good study would be suitable for publication at a genetics journal particularly regional ones.**

*Again we thank the reviewer for this recommendation; however we are not aware of any reputable regional genetics journal with good impact. Furthermore, we think our findings are interesting and have impact on Wilson disease management and understanding and that they deserve to be seen and read by international readers. Several population studies from different European countries, the USA, China, Taiwan, and Egypt were published in international journals.*

- iii) **The clinical impact of this study on WD management is limited, therefore many clinicians would not be so interested in this study.**

*We respectfully disagree with the reviewer. Our study has relevance to disease prevention and early detection. Thus, screening of family members of index patients, as well as screening patients with unexplained liver disease might lead to the early detection of WD, and hence early treatment and better outcome. Also, premarital and post-marital education and counseling of people on consanguineous marriage in carriers of WD mutations is of obvious importance.*

**Reviewer Code: 02860849; Russia**

**Comments: Thank you for your investigation**

*We thank as well the reviewer for the positive response*