May 10, 2016

Dear Editor,

Enclosed please find our revised manuscript in Word format (file name: 24769-Revised Manuscript).

Title: Hepatitis E in Israel: A nation-wide retrospective study

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Name of Journal: World Journal of Gastroenterology ESPS

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Thank you very much for your kind reply, which gave us the chance to revise our manuscript. We have tried to amend the paper according to the reviewers' comments. The point by point responses to the comments suggested by the reviewer are attached below. All text that has been altered is highlighted red in the revised manuscript.

We hope that the revised version will fulfill the requirements for publication in the ***World Journal of gastroenterology***.

Sincerely,

Ortal Erez-Granat,

Eli Schwartz

On behalf all authors

Reply to Editorial comments:

1. ***Comment:*** *The sensitivity and specificity of serologic techniques which have been used are reported in base to the data directly obtained from reagents providers. The authors must provide this data from the comparison of these DS-EIA-anti-HEV-G, DS-EIA-anti-HEV-M, DSI S.R.L. Serronno (VA) with other available methodology such as Wantai and Microgen.*

   Response:

   A pan-genotypic evaluation by CDC of 6 serologic assays for IgM anti-HEV identified the assay manufactured by Diagnostic Systems, which was used in our study, as having the best performance characteristics. Its diagnostic sensitivity and specificity were 98% and 95.2%, respectively. For comparison, the assay manufactured by Mikrogen was found to have a sensitivity of 92% and a specificity of 95.6% (Drobeniuc J et al, *CID* 2010; 51:e24-7. Reference was added to the article as Ref 23).

   We used an assay for the detection of IgG anti-HEV from the same manufacturer, with a specificity of 97.5%, sensitivity of 100% (Ditah I et al, *Hepatology* 2014; 60:815-22. Reference was added to the article as Ref 24).

2. ***Comment:*** *Indicate the sensitivity of detection of HEV RNA.*

   Response:

   Sensitivity of the PCR test (detection of HEV-RNA) is usually dependent on time since onset of disease. In our series, the vast majority of patients were diagnosed based on PCR testing (50/68, 73.5%), however 10 cases (10/68, 14.7%) were diagnosed based on positive anti-HEV-IgM test while PCR test was negative. Unfortunately we do not know the exact interval from blood sampling and the disease onset, therefore we cannot discuss sensitivity of the PCR test.

3. ***Comment:*** *the authors should provide more information about the subsequent evolution of the pregnant patients and their children.*

   Response:

   Information about the outcome of pregnant women with HEV in industrialized countries is scarce. Therefore we summarized our data of 9 pregnant women together with other previously reported cases from Western countries in a larger case-series, which was published last year (Lachish et al, *J Clin Virol* 2015; **73**:20-4. Reference was added to the article as Ref 26).

4. *Comment: A copy of the full approved grant application form(s), consisting of the information section and body section, should be provided to the BPG in PDF format.*

   Response:

   The Portoricco-Gendal Endowment is supporting the Hadassah Liver Unit through an annual payment forwarded by the Hadassah Medical Organiztion, New-York, USA. The approved grant application form is now provided.

5. *Comment:* Please revise the language of your manuscript. For manuscripts submitted by Non-Native Speakers of English, the authors are required to provide a language editing certificate, which will serve to verify that the language of the manuscript has reached Grade A.

   Response:

   All manuscripts were reviewed by native English speakers at the Institute of Tropical Medicine, Sheba Medical Center.