*Reviewer #1:*

*Scientific Quality: Grade B (Very good)*

*Language Quality: Grade A (Priority publishing)*

*Conclusion: Accept (General priority)*

*Specific Comments to Authors: This topic provides a new message in liver diseases. It is well worded. Some suggestions: 1. These 2 parts 'Human Glutathione-S-transferase' and 'Nonalcoholic fatty liver disease' are too lengthy. Please make them more concise. 2. The author should discuss the relationship between GSTM1-GSTT1 and HCC in HBV / HCV infected subjects. 3. In page 6, the authors discussed that GSTs contribute to the host resistance against various microorganism, but this should be more clearly stated. In some studies published in 2020, this issue was explained more clearly.*

First of all, we would like cordially thank Reviewer 1 for the time spent under the reviewing of our article and critical comments addressing to the improvement of the article. Here I send a reply to the comments which have been done.

*1. These 2 parts 'Human Glutathione-S-transferase' and 'Nonalcoholic fatty liver disease' are too lengthy. Please make them more concise.*

Have done. We have shortened two parts of the article as it was recommended.

*2. The author should discuss the relationship between GSTM1-GSTT1 and HCC in HBV / HCV infected subjects.*

Have done. GSTT1 null genotype was associated with more than 2-fold increased risk for HCC development in patients with hepatitis associated with hepatitis C virus (HCV) as compared to the control group. However, GSTM1 null genotype was found to have a protective effect when hepatitis patients were considered in Indian population[101]. Meanwhile, in older study it was found that the GSTT1-null genotype alone did not affect risk of HCC development in hepatitis B virus (HBV), but the GSTM1-null genotype was associated with a decreased risk for early-onset HCC[102].

*3. In page 6, the authors discussed that GSTs contribute to the host resistance against various microorganism, but this should be more clearly stated. In some studies published in 2020, this issue was explained more clearly.*

Have done. Several functional studies of individual GSTs showed that they can positively contribute to host resistance against various microorganisms, whereas some physiologic mechanisms undergo further studying. Notwithstanding, the elevated total GST enzyme activities and notable accumulation of multiple GST transcripts and proteins was often observed in numerous host-pathogen interactions[23,37]. GSH is the most important non-protein thiol compound in several organisms and plays an important role in signaling and host defense reactions in infection. GSTs' participation in antioxidative react together with the crucial cellular antioxidant GSH in order to eliminate lipid hydroperoxides that accumulate in infected tissues, is clearly their distinguishable function[38,39,40].

*Reviewer #2:*

*Scientific Quality: Grade B (Very good)*

*Language Quality: Grade B (Minor language polishing)*

*Conclusion: Accept (General priority)*

*Specific Comments to Authors: Aim And objectives, methodology and study design not clearly defined*

We would like to thank Reviewer 2 for the time spent on the reviewing of our article and valuable suggestions. We have determined the abovementioned categories

The aim of the current review was to overview up-to-date data and sum up results of own investigations regarding the distribution of GST genes polymorphisms, possible mechanisms of their involvement in the processes of desintoxication, drugs metabolism and cancerogenesis, and their role in the natural course of various liver diseases.

*(1) Science editor: 1 Scientific quality: The manuscript describes a Review of the predictors of hepatic dysfunction. The topic is within the scope of the WJH. (1) Classification: Grade B and Grade B; (2) Summary of the Peer-Review Report: The author should discuss the relationship between GSTM1-GSTT1 and HCC in HBV / HCV infected subjects. Aim And objectives, methodology and study design not clearly defined The questions raised by the reviewers should be answered; (3) Format: There is no table or figure; (4) References: A total of 110 references are cited, including 6 references published in the last 3 years; (5) Self-cited references: There are 7 self-cited references; and (6) References recommendations (kindly remind): The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade A and Grade B. A language editing certificate issued by FELIVIC was provided. 3 Academic norms and rules: No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJH. 5 Issues raised: The "Author Contributions" section is missing. Please provide the author contributions. 6 Recommendation: Conditional acceptance.*

We would like to thank Scientific Editor for such a detailed analysis of our article and would like to assure that now our article includes Author contributions

Vasyl Prysyazhnyuk – conception and design; analysis and interpretation of the clinical data, critical revision of the manuscript; final approval of the article;

Larysa Sydorchuk - analysis and interpretation of the pathophysiological data, critical revision of the manuscript; final approval of the article;

Ryslan Sydorchuk - analysis and interpretation of the pathophysiological data, critical revision of the manuscript; final approval of the article;

Iryna Prysiazhniuk - acquisition of data, drafting of the article, critical revision of the manuscript; final approval of the article;

Kateryna Bobkovych - acquisition of data, critical revision of the manuscript; final approval of the article;

Inna Buzdugan - acquisition of data, critical revision of the manuscript; final approval of the article;

Valentina Dzhuryak - acquisition of data, critical revision of the manuscript; final approval of the article;

Petro Prysyazhnyuk – acquisition of data, critical revision of the manuscript; final approval of the article

*(3) Company editor-in-chief: I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World*

*Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, the author(s) must add a table/figure to the manuscript.*

We express our words of thank to Company Editor-in-Chief for the revision of our article, and would like to inform that we have included a table regarding the polymorphism distribution frequency of allelic variations in the GSTP1 A313G in NAFLD patients and healthy individuals. This was statistically significant difference in distribution of GST genes in NAFLD and chronic hepatitis patients and healthy people in Ukrainian population. That is why we have chosen this data to be defined as a table in current review Table 1

**Distribution of polymorphic variants of the A313G polymorphism of the GSTP1 gene in patients with nonalcoholic fatty liver disease and healthy individuals**

| Genotypes of the gene *GSTP1* | Patients with NAFLD, n = 104 | | Healthy individuals, n = 45 | |
|---|---|---|---|---|
| | Absolute number, n | % | Absolute number, n | % |
| AA | 47 | 45,2% | 28 | 62,2% |
| AG | 42 | 40,4% | 16 | 35,6% |
| GG | 15 | 14,4% | 1 | 2,2% |
| A-allele | 136 | 65,4% | 72 | 80,0% |
| G-allele | 72 | 34,6% | 18 | 20,0% |