Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00503546
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-09-25 11:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[Y] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

The objectives of this study are interesting and the results are informative. But the authors' comments/conclusions in Discussion seem to be somewhat rough-and-ready or hasty. Comments 1. Precise treatment resume should be shown because the outcome may be different by the method. Which type of IFN were used, peginterferon α, conventional IFNα, or IFNβ? And authors had better present the period of treatment for enrolled patients. 2. SVR rates and pretreatment viral loads should be shown in each genotype (1, 2, or 3) in a table. 3. How was the SVR rate in patients with Gilbert syndrome? 4. Generally, SVR rates in genotype 2/3 patients are much higher than those in genotype 1 patients. Therefore, even if the rates were almost similar in your patients, analyses of the data should be performed by genotype (genotype 1 vs. 2and 3). 5. After all, enrolled patient number is small. 6. Table 3: P value of viral load (0.115) is wrong?

Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00051373
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-09-25 15:09

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
1) This basic study is very interesting and extensive to clarify the association of inherited liver disorders with chronic hepatitis C in biogenetic characteristic and treatment response to antiviral agents. 2) Readers want to know the relationship between the genotype (76.25% genotype 1, 61/80 in this study) of the chronic C hepatitis and the inherited liver disorders especially Wilson disease (gene ATP7B in H1069Q mutation).

Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00051344
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-09-29 14:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[Y] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

Abstract: Background: too much speculation Objectives: it is not proved that monogenic (some not monogenic) liver disorders can cause mutations in chronic hepatitis C patients. Patients and Methods: Mutations in the genes ATP7B (H1069Q), HFE (C282Y, H63D), UGT1A1 ((TA)7) and SERPINA1 (PIZ) were assessed in 86 chronic hepatitis C patients and 271 healthy individuals. The numbers for each disease are small. Results: not clear-cut Conclusions: the authors can not draw conclusions from the results, is speculation Material and methods Results Why the results for HCV therapy are reported? Is it necessary? Numbers very small, some did not show statistically significant difference.

Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00013213
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-09-30 16:08

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[Y]Rejection
[ ] Grade D (Fair)	[Y] Grade D: rejected	BPG Search:	[ ] Minor revision
[Y] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

-The idea of your study is interesting,however the way you have studied and writing your manuscript makes it hardly difficult to grasp any outcome or conclusion. -It is not clear whether you aimed to study the infuence of inherited diseases on the outcome of HCV infection whether through mutations in the virus genome or through other mechanisms,or otherwise the virus itself could induce gene mutations of inborn liver diseases. -It is not clear in your study whether those patents carrying mutations of inborn liver diseases present the phenotypic features of the diseases or just the monogenic mutation was an accidental finding. your manuscript needs major language corrections.

Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00050195
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-10-01 03:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The authors describe the prevalence of several inherited liver disease in patients with chronic hepatitis C. Since HCV is a common infection with more than 150 million people infected worldwide, it is to be expected that there will be patients with both HCV infection and inherited liver diseases. The authors employ state of the art techniques in molecular diagnosis. The main problem with the paper is the small number of patients with HCV hepatitis included. Although the control group included 271 healthy individuals, the HCV group consisted of only 86 patients. Only 9 patients had inherited liver diseases and of these 8 had Gilbert's syndrome which is a totally benign entity. The authors did detect an association with the ATP 7B gene. This is an interesting finding and I think justifies the publication of this paper and the need for a repeat study in other populations with larger number of HCV patients.

Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00053634
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-10-06 18:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	
[Y] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

General comment The authors aimed at comparing the frequency of 4 inherited monogenic liver disorders in chronic hepatitis C patients vs. healthy controls. They found a higher prevalence of Wilson disease causing mutation H1069Q in patients than in controls. The paper is interesting and original. However it is unclear, confusing and not-well written. This reviewer suggests to totally rewrite the paper according to the following suggestions. Major issues 1) At page last line of subject paragraph the authors state: “There was not done clinical examination for control group”. This is a major limitation of the study that the authors should at-least acknowledge in the discussion. In fact HCV chronic infection is usually asymptomatic and therefore a proportion of “healthy” subjects could be unconsciously carriers. 2) At page 4 last 2 lines the authors state: “There was no significant difference between virus genotype and response to viral treatment ($p>0.05$)”. The punctual value of p, the rate of SVR (and confidence interval) in the different populations should be provided instead of $p>0.05$! 3) The authors should present data that were not significant! 4) The authors mention some factors that are known to influence chance of achieving SVR. However they should also mention other factors such as: - Race, gender, stage of the disease, baseline viral load, vitamin D, homocysteine, ferritin, HOMA index as reviewed by ? Ismail MH. Prediction of sustained virologic responses to combination therapy of pegylated interferon-α and ribavirin in patients with chronic hepatitis C infection. J Family Community Med. 2013 Jan;20(1):35-40. ? Mandorfer M, et al. Low vitamin D levels are associated with impaired virologic response to PEGIFN?+?RBV therapy in HIV-hepatitis C virus coinfected patients. AIDS. 2013 Jan 14;27(2):227-32. ? Borgia G, et al. Homocysteine levels and sustained virological response to pegylated-interferon alpha2b plus ribavirin therapy for chronic hepatitis C: a prospective study. Liver Int. 2009 Feb;29(2):248-52. ?

Pellicelli AM, et al. HCV genotype 1a shows a better virological response to antiviral therapy than HCV genotype 1b. BMC Gastroenterol. 2012 Nov 16;12:162. Particularly they should cite the following papers that deal with ferritin levels and SVR rate ? Distante S, et al. Raised serum ferritin predicts non-response to interferon and ribavirin treatment in patients with chronic hepatitis C infection. Liver. 2002 Jun;22(3):269-75. ? Gentile I, et al. Iron depletion before HCV antiviral therapy: a pilot, randomized, controlled trial. J Clin Apher. 2009;24(5):190-6. 5) It is unclear whether the authors performed the genetic analysis between patients with and without SVR. This analysis should be performed and clearly described in the manuscript. 6) At page 5, lines -3 to -6 of result section the authors state: " The strongest model was DOMDEV (BETA=–295.7, p=0.0087), and the significance remained after adjusting for age (BETAadjusted=–264.4, padjusted=0.0219) and for gender (BETAadjusted=–249.3, padjusted=0.0305)". This sentence is totally unclear. Did the authors refer to a model for high ferritin levels? 7) It is not true that the incidence (new cases") of hepatitis C is increasing as the authors state at the beginning of discussion 8) The sample size is small and this may explain why factors such as genotype, viral load, or ferritin levels result non-significantly associated with SVR rate. The authors should comment on this. 9) No details on liver histology or on type of interferon used are provided. This reviewer suggests to use a univariate and a logistic regression model to evaluate the effect of the studied mutation on SVR rate and that of the other factors (included genotype, liver histology, etc) . Minor issue 1. English language should be improved throughout the manuscript. For example at page 3, last line of subject paragraph the sentence: "There was not done clinical examination for co

Baishideng Publishing Group Co., Limited
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report
Name of Journal: World Journal of Hepatology
ESPS Manuscript NO: 5716
Title: Association of inherited liver disorders with chronic hepatitis C
Reviewer code: 00013065
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-24 09:07
Date reviewed: 2013-10-08 20:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[Y] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
Dr. Piekuse and colleagues presented an interesting study in which they aimed to determine the role of inherited monogenic liver disorders with host and antiviral treatment response to hepatitis C. Overall, the study is well performed and the data are concise in its content although the study population is very small. In general, there are a number of typing errors and the English spelling and grammar has to be checked carefully possibly by a native English speaker. Comments 1)The HCV genotype of the patients would be of interest. Please provide the reader with the HCV genotypes for each patient group 2)The clinical course and time of SVR was not presented. 3)The discussion is somehow confusing and should be rewritten appropriate