

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 31931

**Title:** Refractory hepatic encephalopathy in a patient with hypothyroidism: another element in the ammonia metabolism

**Reviewer's code:** 02861225

**Reviewer's country:** Austria

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-12-17 20:27

**Date reviewed:** 2016-12-19 01:17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

In the paper of Diaz-Fontenla et al an interesting case of a patients with refractory hepatic encephalopathy and hypothyroidism is described. This paper might benefit by implementing the following suggestions. MINOR: #1 Please shorten the paper by approximately 20-30%. #2 Tables 1+2, and figure 1 are of importance, however figure 2 might be omitted. #3 Please mention also Hashimoto's encephalopathy in your discussion as it might present with high TSH, low fT4, elevated liver enzymes and severe neurological symptoms. #4 Please check your manuscript for grammatical and language errors. Some passages are difficult to read and there are some typos. e.g.: - Then, she recognized a history of alcohol abuse for years, other causes of liver disease were rule[d] out and a diagnosis of alcoholic cirrhosis Child-Pugh B7 was stablished. - She had no ascites neither hepatocellular carcinoma and primary prophylaxis with propranolol because of [O]esophageal oesophageal varices grade II-III/IV was started. - The question[,] whether the neurological impairment was cause[d] by the hypothyroidism or [it] was attributable to the large portosystemic shunt[,] was very important [in order] to make [further] therapeutic decisions.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 31931

**Title:** Refractory hepatic encephalopathy in a patient with hypothyroidism: another element in the ammonia metabolism

**Reviewer's code:** 00038007

**Reviewer's country:** United States

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-12-17 20:27

**Date reviewed:** 2016-12-29 12:22

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is an excellent case report describing an incidence whereby hypothyroidism was a precipitating factor that contributed to a recurrence of hepatic encephalopathy in a patient with liver cirrhosis. Overall, the report was very well written, with a clear description of the time line of events followed by a thorough discussion of the literature and known interactions between hypothyroidism and hepatic encephalopathy. There are only very minor corrections: Page 6, line 2: "stablished" should be "established"? Page 6, line 2: sentence "She had no ascites neither hepatocellular carcinoma and primary prophylaxis with propranolol because of Oesophageal varices grade II-III/IV was started" doesn't make sense. Should it be "She had no ascites nor hepatocellular carcinoma and primary prophylaxis with propranolol because of Oesophageal varices grade II-III/IV was started" Page 7: 3rd paragraph, spelling "hyperammoniemia" (also found on page 9 2nd paragraph, and other places throughout) and "Encephalopatya" Table 1: Spelling error "amonia"

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 31931

**Title:** Refractory hepatic encephalopathy in a patient with hypothyroidism: another element in the ammonia metabolism

**Reviewer's code:** 02485745

**Reviewer's country:** Denmark

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-12-17 20:27

**Date reviewed:** 2016-12-30 16:03

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

The case is interesting and provide some interesting observations on the association of hypothyroidism and refractory HE. The authors propose that hypothyroidism may result in decreased hepatic ammonia clearance which again could enhance brain exposition to ammonia. However, other precipitating factors could also contribute and these need to be commented on in more detail: 1) the patient had macrocytosis at admission, this could be due to hypothyroidism but an alternative explanation could be reintroduction of excessive alcohol intake - do you have any data to support that the patient was actually abstaining from alcohol at admission? 2) the patient was constipated at admission which could be secondary to hypothyroidism, did the patient normalize defaecation during lactulose treatment? 3) It is difficult to understand that decreased hepatic ammonia clearance induced by hypothyroidism is the principal cause of HE in this patient where a large shunt is demonstrated - much of the blood from the GI tract will likely never reach the liver but shunt directly into the systemic circulation and reach the brain - this needs commenting and alternative mechanisms should be discussed - direct toxic effect on the brain secondary to hypothyroidism?



## BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

<http://www.wjgnet.com>

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Decreased cerebral ammonia metabolism? Overall the case should be shortened to improve readability and major language revision is needed. The case needs language polishing and should be shortened as there is a lot of redundancy in the discussion.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 31931

**Title:** Refractory hepatic encephalopathy in a patient with hypothyroidism: another element in the ammonia metabolism

**Reviewer's code:** 02540266

**Reviewer's country:** Iran

**Science editor:** Ze-Mao Gong

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**Date reviewed:** 2017-01-08 05:10

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is an interesting case report addressing the possible pathophysiological relation between hypothyroidism and hepatic encephalopathy. However, the manuscript needs English edition as there are many mistakes in text and tables. The discussion part needs to be shortened and omitting unnecessary repeated phrases. Table 1 needs major revision. Correct abbreviations should be used and all abbreviations should be defined properly.