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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:** 4665

**Title:** The Approach to the Patient with HIV and Nodular Regenerative Hyperplasia

**Reviewer code:** 00013180

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-07-15 11:36

**Date reviewed:** 2013-07-17 02:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The review article "The Approach to the Patient with HIV and NRH" is a concise, well written and well referenced article. As most patients with HIV/AIDS throughout the world have less exposure to DDI. it is likely that the occurrence of NRH will diminish in the future. A major omission in the article is the absence of a histopathology figure. NRH is a hisopathological diagnosis and the value of the article will be enhanced by the addition of a figure of NRH. Minor comments: 1. Page 6, first paragraph, 2nd to 4th sentence, In one series....liver dysfunction noted by normal INR". This requires reference which likely was missed by oversight. 2. Table 1. Adding reference number after authors name in the first column will aid in easily identifying the article. 3. Table 1. Under Mallet et al. The figure 16 patients is incorrect. It is 13. 4. Figure 1. Also under Mallet et al. under clinical presentation, "unknown" is incorrect and should be replaced by portal hypertension. 5. Under references: Reference 27, the tile is placed within parenthesis. Does it need to be deleted? 6. Reference 53. After Saito K "&" needs to be deleted.



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## ESPS Peer-review Report

**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 4665

**Title:** The Approach to the Patient with HIV and Nodular Regenerative Hyperplasia

**Reviewer code:** 00038981

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-07-15 11:36

**Date reviewed:** 2013-08-05 21:38

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This manuscript reviews this manuscript reviews the available epidemiological and clinical management data regarding nodular regenerative hyperplasia (NRH) in HIV positive patients; since NRH is an emerging cause of liver disease in this population, and since HIV positive patients are expected to largely increase in the next decades the topic is of interest for hepatologists. The following concerns should be addressed: 1-English grammar needs improvement across the text and in particular in the abstract. E.g. "The appropriate management of HIV-infected persons with suspected NRH is yet to be outlined, however it is an important concept as it can be a clinically subtle condition that is difficult to diagnose". This sentence should be changed, for example, as follows: "The appropriate management of HIV-infected persons with suspected NRH is yet to be outlined. However, NRH is a clinically subtle condition that is difficult to diagnose, and it is important to be able to manage it according to the best available evidence". In addition, some part of the text are too long and could be shortened. Please, revise with the help of a medical writer. 2- references for the pathophysiological mechanisms suggested in the introduction should be given. Similarly, references for the sentence "On ultrasound, findings may include widespread nodularity of the liver can mimic cirrhosis" should be given. 3- a paragraph focusing on causes of NCPH other than NRH in HIV patients should be added; I am referring in particular to idiopathic portal hypertension, since this has been also linked to antiretroviral therapy sharing the same pathophysiological mechanisms as NRH, and it has been hypothesised that IPH can lead both to NRH and portal vein thrombosis in this population (see Chang PE et al. Am J Gastroenterol 2009 and the references in this paper).

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Hepatology

**ESPS Manuscript NO:** 4665

**Title:** The Approach to the Patient with HIV and Nodular Regenerative Hyperplasia

**Reviewer code:** 00045831

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-07-15 11:36

**Date reviewed:** 2013-08-10 21:45

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

Authors: General Comments: 1. Importance of the research and the significance of research contents: Considering the longevity of HIV patients with effect HAART and complexities associated with investigating liver involvement in HIV be it portal hypertension or hepatic dysfunction this review is appropriate. 2. Novelty and innovation of the research: Only review, not applicable. 3. Presentation and readability: Language needs improvement. 4. Ethics of research: Not applicable; data review only

Specific comments: Title: Existing "The approach to the patient with HIV and nodular regenerative hyperplasia" Suggested: HIV and Nodular regenerative hyperplasia of liver - a systematic review.

Abstract: The abstract emphasizes the need for information in this field but doesn't summarize the concept and some guidelines to follow. Material and Methods: In view of complexities and variability nomenclature of NRH the material methods needs to mention the exact inclusion and exclusion that were applied in the final analysis. A flow diagram would have been appropriate mentioning total hits, sequence of exclusion and final number. Merits: It is appropriate that only biopsy proven cases were included. Comments: Since the entire applicability of this review depends on biopsy proof, has any pathologist experienced in liver pathology has been involved in the analysis of reports before inclusion? Results: The authors mention that "Liver associated test abnormalities were most often consistent with a cholestatic picture, with findings of some combinations of elevated bilirubin, alkaline phosphate or gamma glutamyl transpeltidase(GGT)" Page 5 Para 3 lines 2,3 and 4. Comment: Cholestatic picture is unusual with pure non HIV related NRH. How what are the histopathological findings in such cases? A reference to this aspect is necessary. Are these cases of some kind of overlap clinical entities with NRH. Discussion: Needs revision in discussion, the flow of contents and order. 1. Some discussion on pathogenesis in terms



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of differences between HIV specific and HIV non specific NRH, especially occurrence of Ascites (32%), hepatocellular dysfunction and the need for liver transplantation on the basis of dysfunction rather than uncontrolled portal hypertension. Could be thought provoking. 2. Discussion of liver biopsy (Page 11, para 4) is non specific and inappropriate to the topic under consideration. The discussion should evolve around complexities in diagnosing NRH in patient with HIV rather than too well know facts of liver biopsy in any situation. 3. Page 12 para 3, Could be summarized in further in three or four sentences. 4. Suggested flow: Relative rarity of the entity; discussion on pathogenesis relevant to HIV; high index of suspicion in patient of HIV presenting with portal hypertension or incidental finding in imaging; ruling out other causes of similar clinical picture; the need and specific difficulties in biopsy assessment; and suggested management. Reference: Some references are of general nature not particularly relevant to the topic under consideration; like those on liver biopsy; could be deleted for want of being specific. Supporting reference to cholestatic presentation and reference to HIV cholangiopathy can be incorporated.