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ESPS Peer-review Report
Name of Journal: World Journal of Respirology
ESPS Manuscript NO: 7299
Title: Obstructive Sleep Apnea and Non Alcoholic Fatty Liver Disease: the growing link and management issues
Reviewer code: 02461842
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-28 14:06
Date reviewed: 2013-12-02 02:09

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] 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	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
This is a potentially interesting review. the authors should include some more information about 1- the PNPLA3 and GCKR in the NAFLD 2- the role of the INS VNTR gene variant as a risk factor for the OSA. 3- more information regarding the pediatric population should be included. IN particular the studies from David Gozal would useful to the authors 4- a table reassuming the risk factors for OSA would enrich the paper. 5- the animal models showing the effect of intermittent hypoxia on the metabolism should be discussed in details.

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ESPS Peer-review Report
Name of Journal: World Journal of Respirology
ESPS Manuscript NO: 7299
Title: Obstructive Sleep Apnea and Non Alcoholic Fatty Liver Disease: the growing link and management issues
Reviewer code: 00053727
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-28 14:06
Date reviewed: 2013-12-02 14:56

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] 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	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
The review article on Obstructive Sleep Apnea interlink on Non Alcoholic Fatty Liver Disease is interesting and various reports having OSA predicted the severity of NAFLD . However I need the manuscript to revise considering the following points as i feel the manuscript is too lengthy The details of previous observation on NAFLD with AST and ALT, Liver biopsy studies should be more in Tabular form for easy catch. The Mechanistic of action can be demonstrated in flow chart or Figures The animal's models for OSA with NAFLD/NASH can be discussed. Basic details of NAFLD and OSA can be shortened. The details on TGY,CHO and ALP should be discussed

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ESPS Peer-review Report
Name of Journal: World Journal of Respirology
ESPS Manuscript NO: 7299
Title: Obstructive Sleep Apnea and Non Alcoholic Fatty Liver Disease: the growing link and management issues
Reviewer code: 00504802
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-28 14:06
Date reviewed: 2013-12-09 12:17

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] 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	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

General Comments: The paper is generally reasonably well written, the thought process of the Authors easy to follow, aside from occasional clustering of relatively less informative part. The English is generally well polished, occasional suggestions in the minor comments sections below. The paper pulls attention to the emergence of both sleep apnea and non-alcoholic fatty liver disease, with particular attention to the nocturnal hypoxic link between them, in urbanizing populations of the Indian subcontinent. Such problem is indeed rapidly exploding in the rest of the Westernized Word, including in the US being particularly severely affected. Indeed, large, representative studies of urbanized African-Americans in Southeast US (they are particularly impacted by the obesity epidemics) found even higher then formerly reported burden of potential OSA symptoms, then reported in the past (Fulop T, Hickson DM et al. Sleep-disordered breathing symptoms among African-Americans in the Jackson Heart Study. Sleep Medicine 2012, 13 (8); 1039–1049). In the paper most of the concerns are relatively minor and easy to rectify. Major comments: Abstract/Title page: -consider adding additional Key Words: Obstructive Sleep Apnea; Sleep-Disordered Breathing; Hypoxia; Fatty Liver Disease [whichever the Authors think would be the best] Genetics of NAFLD and OSA Interesting data has emerged on recent GWAS with regard to OSA and OSA symptoms. Would suggest incorporating a very recent paper into the discussion (Patel SR et al. Association of Genetic Loci with Sleep Apnea in European Americans and African-Americans: The Candidate Gene Association Resource (CARe), Plos One, November 14, 2012), detailing some of the recent development on the subject from the CARe consortium. In particular, all the described genes from this large cohort are tentatively associated with inflammation or inflammatory pathways. In section

"OSA, NAFLD and Inflammation": 3rd sentence after this section started -" In mice with diet-induced…" - sentence corrupted and does not make sense; please, revise In section "Oxidative Stress" - last sentence of first para (" in particular, importance in vasculature…") does not make sense - please, revise References: extensive and applicable to the subjects. Some additional dereferences above, and would suggest incorporating also into the Bibliography Minor comments: -irregular capitation in the title ((growing lin and…etc, to be started with upper case letter) -corresponding author's institution: "sleep disorders" - to start with upper case letter, too -On page 3, end of the first paragraph: replace the word "A person" with "Subjects" … in the same sentence: replace "more than 100 waking episodes" with "more than 100 arousals" -on page 3, 1st sentence of 2nd para: sentence "Prevalence of OSA in habitual snorers is 35-64% (25% of men and 20% of women in the normal adult white population)" -s internally inconsistent - consider revising -page 4, 4th line form the bottom" change "various country" to "several countries" and "developed counties" to "developed countries" -page 5, 3rd paragraph (1st under section "OSA and NAFLD"), 4th line of the paragraph: explain "patients with AST" - do you mean elevated/abnormal AST? Also, sell out AST first (before abbreviating) -page 10, 2nd row form top: explain "ROS" abbreviation first; 4th row: explain "RNS" first [before abbreviating] -page 3, 6th row from the bottom: "is more prevalent in, but no confirmed" - change to …prevalent, but not limited…"

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ESPS Peer-review Report
Name of Journal: World Journal of Respirology
ESPS Manuscript NO: 7299
Title: Obstructive Sleep Apnea and Non Alcoholic Fatty Liver Disease: the growing link and management issues
Reviewer code: 00503703
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-28 14:06
Date reviewed: 2013-12-15 07:06

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
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

Title: Given that within the entire manuscript emphasis is put on asian Indian populations, it would be pertinent to mirror this issue on the manuscript' s title Manuscript Introduction section: on page 3, the definition of OSA should be revised. Additionally, the definition of "habitual snorers" should be clearly stated. It is unclear at what part of the manuscript the introduction ends. Genetics of NAFLD It is unclear whether OSA and NAFLD share common pathogenetic pathways. Are there any genetic data in Asian Indians or in other populations that predispose to the development of both NAFLD and OSA? Are there any experimental models available of concomitant OSA and NAFLD? On page 7 the authors state that "Also serum TNFα levels were significantly higher in obese subjects with OSA, when compared with obese subjects without OSA" What is the respective relationship with NAFLD? The association between TNF-a and OSA is well known Additionally, on page 7 the authors state that "….hypoxia also decreases expression of genes that regulate mitochondrial β oxidation [e.g. PPAR-αand carnitine palmitoyltransferase-1 (CPT-1)". What is the relationship of hypoxia with NAFLD? On page 10 the authors state that "Several groups have studied markers of oxidative stress in liver samples as well as plasma samples from subjects with NAFLD and NASH". Please provide the respective references. Page 13: it should be clearly stated that neither anti-diabetic treatment is indicated for treatment of OSA, nor CPAP for the treatment of NAFLD. On page 13, in the Conclusion, the authors state that: "OSA might induce NAFLD in the absence of obesity and metabolic syndrome, and the link with hypoxia might be instrumental in precipitating fatty liver" What evidence is presented in the manuscript? Please provide the necessary references in support of this argument. On page 14, the authors report

that “individuals with OSA require a full evaluation of their CVD risk”. A more refined and clear statement on what a full evaluation of CVD risk represents should definitively be included in this part of the manuscript.

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ESPS Peer-review Report
Name of Journal: World Journal of Respirology
ESPS Manuscript NO: 7299
Title: Obstructive Sleep Apnea and Non Alcoholic Fatty Liver Disease: the growing link and management issues
Reviewer code: 02446694
Science editor: Gou, Su-Xin
Date sent for review: 2013-11-28 14:06
Date reviewed: 2013-12-16 05:56

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

COMMENTS TO AUTHORS
The authors reviewed the relationship between obstructive sleep apnea (OSA) and non alcoholic fattly liver disease (NAFLD). They showed the mechanisms and treatments of OSA-related NAFLD closely. This review is well-written and very educatitive. Regarding the contents of manuscript, I have no questions and requests. In Page 4, NAFLD was firstly used before spelling it out.