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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Diabetes
ESPS manuscript NO: 13384
Title: Nonalcoholic steatohepatitis and insulin resistance in children
Reviewer code: 00519698
Science editor: Xue-Mei Gong
Date sent for review: 2014-08-21 11:32
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] 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:	[ ] Minor revision
[ ] Grade E: Poor		[ ] Existing	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

N.A.

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ESPS PEER REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

In the present submission by Arata et al. (Nonalcoholic steatohepatitis and insulin resistance in children), the authors review in short, non-alcoholic steatohepatitis and insulin resistance in children. In the world, the increase in the prevalence of obesity is a serious problem. Associated with this increment, there is a reduction of life expectancy of up to 7 years (Petersen et al., Ann Intern Med 2003; 138:1138-45.). When considering children, it is estimated that 170 million of them (under 18) globally are overweight or obese, affecting more than 20% of all children in many countries (Swinbum et al., Lancet 2011; 378:804-14). In consequence studies focuses in children are always welcome, especially considering the development of strategies to prevent or delay the pathology. However in my opinion, several points are not clearly explained. a) In general is not easy to distinguish when the authors are explaining the situation in children and when in adults. b) The authors claim that "In children, non-alcoholic fatty liver disease (NAFLD)/NASH is accompanied by insulin resistance". "Significant correlations between insulin resistance and NAFLD activity score (NAS)….were found in 177 children with NAFLD/NASH". Is this privative or unique of NAFLD/NASH in children? I do not think so. Adipose tissue insulin resistance is present in the majority of patients with NAFLD, whether patients are obese or not (Buglianesi et al., Diabetologia 2005; 48:634-42). This insulin resistance at the adipose tissue level is critical since there is a close relationship between adipose tissue and liver metabolism in humans because adipocytes supply more than two-third of fatty acids used for hepatic triglyceride synthesis. Fatty acids derived from

adipose tissue account for the majority (60%) of hepatic triglyceride accumulation in NAFLD (Donnelly et al., J Clin Invest 2005; 115:1343-51). This is not a unique feature of NAFLD in children. As the authors suggest, "insulin resistance if often accompanied by NAFLD/NASH". c) In my opinion, the Interpretation of the relationship between insulin resistance and fibrosis is obscure. The authors mention that "insulin resistance was found to correlate with changes in fat levels; however, it did not correlate with fibrosis or NASH scores". This assertion refers to adult, to children or both of them? On the other hand, as a "representative" photograph of liver sections of NAFLD/NASH patients the authors show a pediatric type with severe fibrosis. If insulin resistance did not correlate with fibrosis and severe fibrosis is "representative" of pediatric type that means that insulin resistance is not "representative" of NAFLD/NASH in children. d) Recent metabolic studies in patients with NAFLD suggest that liver fibrosis correlates closely with severe adipose tissue insulin resistance (Lomonaco et al., Hepatology 2012; 55(5):1389-97).