April 2, 2013

Dear Editor,

Please find enclosed the edited manuscript (revised WJG-2293) in PDF format

Title: Adipokines and C-reactive protein in relation to bone mineralization in pediatric nonalcoholic fatty liver disease

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The manuscript has been improved according to the suggestions of reviewers:

1. The manuscript has been edited in PDF format

2. Revision has been made according to the suggestions of the reviewer:
   (1) As suggested by the reviewer, we have rewritten the sentence regarding the aims of the study to read: "To investigate bone mineral density (BMD) in obese children with and without nonalcoholic fatty liver disease (NAFLD); and the association between BMD and serum adipokines, and high-sensitivity CRP (HSCRP)"(Abstract); and "The aims of this study were to evaluate: 1) BMD in obese children with and without NAFLD; and 2) the association between BMD and the serum adipokines, leptin and adiponectin, and a circulating marker of systemic inflammation, high-sensitivity CRP (HSCRP), using multiple regression" (Introduction);
   (2) We have deleted from the revised Abstract and text the sentence "…. and was expected to be confirmed by liver biopsy with ≥ 5% of hepatocytes containing macrovesicular fat";
   (3) We have clarified why only 35/44 patients underwent liver biopsy: "Liver biopsy was obtained in 35 of the 44 children with MRI-diagnosed NAFLD, with parental refusal in 9 cases. The 35 children did not differ from those having only liver MRI with respect to age, gender, body composition, metabolic parameters, and bone measures";
   (4) We have deleted previous references #1,#2, and included new specific references (quoted as #1,#2) reporting epidemiological studies of NAFLD in children ;
   (5) In the section "Methods", we have clarified the conditions potentially affecting BMI: "Finally, children were excluded for conditions that could have adversely influenced BMD including glucocorticoid therapy, hypothyroidism, Cushing's disease; history of long bone fractures; indwelling hardware; and abnormality of the skeleton or spine";
   (6) HFF of both patients and controls as well as P values between patients and controls are shown in the revised Table 1;
   (7) As suggested by the reviewer, we have incorporated into the revised text the clinical features of patients with and without NASH (including HFF) among children with biopsy-proven NAFLD: "Among patients with biopsy-proven NAFLD, 20 (57%) had definite NASH, while 15 (43%) no NASH. No statistically significant differences in body composition as well as in laboratory parameters such as glucose, insulin, leptin, adiponectin levels, and HOMA-

IR values were found between children with NASH and those with simple steatosis. AST [mean, 41 (95% CI, 34-48) vs 26 (22-29) U/L; P < 0.001)], ALT [mean, 58 (95% CI, 41-75) vs 30 (20-45) U/L; P < 0.001)] as well as HFF [mean, 24.8 (95% CI, 19.5-30.2) vs 15.7 (5.6-28.8) %; P < 0.001)] were significantly higher in patients with NASH compared to children without NASH. HSCRP was also higher [mean, 4055 (95% CI, 2690-5419) vs 2870 (1794-3936) μg/L; P = 0.07], although did not reach statistically significance";
(8) We have included the results of multivariate analysis in which NAFLD (rather than NASH) was considered (new Tables 2A and 2B);
(9) As suggested by the reviewer, the conclusions have been modified to read "This study reveals that NAFLD is associated with low BMD in obese children, and that systemic, low-grade inflammation may accelerate loss of bone mass in patients with NAFLD"

3. References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology.*

Sincerely yours,

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