

Letter to the Editor

Comments on "High serum vitamin D levels reduce the risk for nonalcoholic fatty liver disease in healthy men independent of metabolic syndrome"

Dear Sir;

We have read with a great interest an article by Rhee EJ *et al.* [1] published recently in this journal. In the past decades, increasing prevalence and co-existence of obesity, metabolic syndrome (MS), non-alcoholic fatty liver disease (NAFLD) and hypovitaminosis D elicited a public health concern [2, 3]. However, new data including this publication [1] considerably changed hierarchy of MS components, shifting the focus from obesity toward fatty liver, at first and now toward vitamin D deficiency [4]. Apart from the interest and curiosity, we are feeling certain fear that we might be misled due to the fact that we are dealing with a still imprecisely defined terms.

Firstly, it seems that there is still a place in contemporary literature for all three international definitions of MS - World Health Organization (WHO), Adult Treatment Panel III (ATP III), or International Diabetes Federation (IDF).

Secondly, performing biopsies for the assessment of hepatic steatosis in the large-scale epidemiologic studies seems inappropriate, impractical and impossible. It is important to remember that most subjects with NAFLD (79%) had normal levels of serum alanine aminotransferase [5]. Also, non-invasive imaging modalities

(such as ultrasonography, computed tomography and magnetic resonance imaging) can detect NAFLD, but only if there are more than 33% of hepatocytes affected by fatty infiltration [3, 5]. That is why the prevalence of hepatic steatosis estimated by liver ultrasonography was between 14-16.7%. If quantitative method of proton nuclear magnetic resonance spectroscopy-¹H-MRS was used, the frequency of hepatic steatosis was estimated to be around 31%, but depended significantly on ethnicity and gender [5]. In this context, it is interesting to realize that NAFLD is found by liver ultrasonography in 43.6% of healthy Korean men [1].

Finally, in available literature definition of vitamin D deficiency also varies. Usually, for adults aged 20 years or older a 25-hydroxy-vitamin D {25(OH)D} threshold of either 27.5 nmol/L or 50 nmol/L is used [2]. According to this most of the subjects included in investigation of Rhee EJ *et al.* seem vitamin D deficient (39.4±9.2 nmol/L) and there is no place for the discussion about "high serum vitamin D levels." On the contrary, vitamin D deficiency could be one of the reasons for rather high prevalence of NAFLD in this population.

It was also quite new cognisance that the correlation between age and serum vitamin D levels depends significantly on ethnicity, being positive among Koreans in contrast to most of the other regions around the world. As proportion of participants with NAFLD significantly increased with decreasing serum vitamin D levels, finding that the older age was one of significant determinants for NAFLD in this population came as surprise. Considering the remarkably large number of subjects included in final study population ($n=6,567$), it would be nice to know the prevalence of NAFLD through the same 10-year age categories [1].

Further studies are needed to determine the role of vitamin D in pathogenesis of NAFLD and answer the question whether vitamin D therapy would prove useful in these patients.

Svetlana Jelic^{1), 3)} and Iva Perovic-Blagojevic²⁾

¹⁾ Department of Endocrinology, Clinic for Internal Medicine, University Medical Centre Bezanjska kosa, Belgrade, Serbia

²⁾ Department of Biochemistry, University Medical Centre "Dr Dragisa Misovic," Belgrade, Serbia

³⁾ School of Medicine, University of Belgrade, Belgrade, Serbia

Submitted: Feb. 27, 2013; Accepted Mar. 1, 2013 as EJ13-0078

Released online in J-STAGE as advance publication Mar. 16, 2013

Correspondence to: Svetlana Jelic, Department of Endocrinology, Clinic for Internal Medicine, University Medical Center Bezanjska kosa, Bezanjska kosa bb, 11080 Belgrade, Serbia.

E-mail: svetlana.jelic011@gmail.com

References

1. Rhee EJ, Kim MK, Park SE, Park CY, Beak KH, et al. (2013) High serum vitamin D levels reduce the risk for nonalcoholic fatty liver disease in healthy men independent of metabolic syndrome. *Endocr J* 60: 743-752.
2. Stratton-Loeffler MJ, Lo JC, Hui RL, Coates A, Minkoff JR, et al. (2012) Treatment of vitamin D deficiency within a large integrated health care delivery system. *J Manag Care Pharm* 18: 497-505.

3. Barchetta I, Angelico F, Del Ben M, Baroni MG, Pozzili P, et al. (2011) Strong association between non alcoholic fatty liver disease (NAFLD) and low 25 (OH) vitamin D levels in an adult population with normal serum liver enzymes. *BMC Med* 9: 85.
4. Foss YJ (2009) Vitamin D deficiency is the cause of common obesity. *Med Hypotheses* 72: 314-321.
5. Browning JD, Szczepaniak LS, Dobbins R, Nuremberg P, Horton JD, et al. (2004) Prevalence of hepatic steatosis in an urban population in the United States: Impact of ethnicity. *Hepatology* 40: 1387-1395.