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Letter to the Editor

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Nonalcoholic Fatty Liver Disease and Abdominal Fat Accumulation According to Vitamin D Status in Patients with Type 2 Diabetes (J Obes Metab Syndr 2018;27:53-60)

Juchul Hwang[1], Joon Young Kim[2,3,*]

[1]Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA; [2]Center for Pediatric Research in Obesity and Metabolism, Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center, Pittsburgh, PA; [3]Department of Medicine, Division of Endocrinology and Metabolism, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

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*Corresponding author
Joon Young Kim

https://orcid.org/0000-0003-0448-1684

Center for Pediatric Research in Obesity and Metabolism, Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center and Department of Medicine, Division of Endocrinology and Metabolism, University of Pittsburgh School of Medicine, 4401 Penn Ave, Faculty Pavilion 6th floor, Pittsburgh, PA 15224, USA
Tel: +1-412-692-5239
Fax: +1-412-692-8531
E-mail: joon.kim@chp.edu

Given the ever-escalating rates of type 2 diabetes and high prevalence of vitamin D deficiency in South Korea, Choi et al.[1] studied the relationship of vitamin D status, determined by the serum level of 25-hydroxyvitamin D (25(OH)D), to visceral adipose tissue and nonalcoholic fatty liver disease (NAFLD) in adult patients with type 2 diabetes. This study reported that low vitamin D levels are associated with greater visceral fat thickness and higher prevalence of NAFLD.[1] Despite the significance of this study with respect to public health implications, we have some concerns and additional points needed further clarification.

First, it is likely that three comparison groups (vitamin D deficient, insufficient, and sufficient groups) represent distinct patient characteristics with respect to the study outcome measures (i.e., visceral adiposity and NAFLD) due to the different treatment modalities including oral hypoglycemic agent, insulin, or combined across the groups as reported by the authors.[1] There might be different effects of diverse treatment approaches and various treatment duration (which were not shown in this study) on glucose metabolism and insulin dynamics.[2] Importantly, insulin resistance is considered a major contributor in the pathogenesis of NAFLD[3], and each antidiabetic medication has a distinct effect on adipose tissue distribution and insulin sensitivity.[4] Accordingly, the association between vitamin D level and visceral adiposity and prevalence of NAFLD could be potentially influenced by the different treatment modalities in this study. Therefore, additional covariate adjustment should be reconsidered when visceral adiposity and NAFLD are compared by vitamin D status. Furthermore, discussion of contradicting findings observed in this study is needed: (1) vitamin D sufficient group tended to have higher fasting insulin (12.6 ± 12.5 μIU/mL) and higher fasting plasma glucose (209.8 ± 120.5 mg/dL), but showed numerically lower homeostasis model assessment of insulin resistance (HOMA-IR, 3.6 ± 3.1) than those of vitamin D deficient group (fasting insulin, 7.6 ± 6.7 μIU/mL; fasting plasma glucose, 185.5 ± 69.9 mg/dL; HOMA-IR, 4.4 ± 5.4), and (2) type 2 diabetic adults with NAFLD versus without NAFLD had higher 25(OH)D level (as stated in the Results), which is conflicting to the finding of higher prevalence of NAFLD in the vitamin D deficiency group (as stated in Fig. 2 of Ref. 1).

Further, it is interesting that vitamin D level positively correlates with systolic blood pressure (as stated in Table 2 of Ref. 1), despite lower vitamin D status is often associated with hypertension in the literature.[5] Taken together, deeper exploration into the clinical characteristics in the studied patients and better analytical approach would be critical to understand these observations.

Second, it is important to determine whether the effect of vitamin D on the prevalence of NAFLD is independent of visceral fat thickness in addition to the given logistic regression model.[1] Adipocyte dysfunction followed by visceral adipose tissue expansion, and its consequential alteration of adipokine release has been implicated in the pathogenesis of NAFLD. Several animal studies attested to this pathogenic mechanism along with vitamin D deficiency: (1) low vitamin D intake correlates with increased proinflammatory adipokines and severity of NAFLD[6], and (2) artificial sunlight therapy attenuates hepatic inflammation and enhances adiponectin secretion in rats with nonalcoholic steatohepatitis.[7] Similarly, a large cohort study in adults exhibited that serum vitamin D correlates positively with serum adiponectin and negatively with serum leptin.[8] However to date, it is yet to be determined whether vitamin D involves in the pathogenesis of NAFLD since beneficial effects of vitamin D supplement on both visceral adiposity and NAFLD in human are still controversial. Hence, it would be much informative if visceral adiposity is considered a modulating component in the association of vitamin D status to the prevalence of NAFLD.

Lastly, there is a lack of explanation for the finding that vitamin D deficiency group has increased visceral fat accumulation compared with vitamin D sufficient group. It is interesting that vitamin D deficiency group has greater visceral fat thickness than other groups despite having similar body mass index and subcutaneous fat thickness. Recently, the association of low vitamin D status with several metabolic conditions has been increasingly reported, suggesting that vitamin D may play a beneficial role in metabolism and adipose tissue distribution. However, it is also possible that adipose tissue may act as a reservoir for vitamin D, thereby simply having an inverse relationship between vitamin D level and amount of body fat by volumetric dilution[9], without any significant effect on insulin sensitivity and NAFLD.[10] In addition, although Choi et al.[1] acknowledged the lack of data in relation to outdoor physical activity, dietary habits, and seasonal variations, potential confounding effects of these factors should be discussed more in depth. Especially, physical activity is highly effective in prevention of NAFLD by improving liver fat metabolism, and concurrently impact serum vitamin D level. Further, given four distinct seasons in South Korea, it has been documented that there is a significant seasonal variation in serum vitamin D level.[11] As a result, a question arises as to whether the association found by the authors[1] was largely driven by these confounders. Collectively, more comprehensive explanations for the study findings and limitations are critical to understand the association between vitamin D and visceral adiposity and NAFLD in this study.

In conclusion, Choi et al.[1] reported that vitamin D deficiency is associated with increased visceral fat thickness and elevated prevalence of NAFLD in Korean adults with type 2 diabetes. Despite the nature of retrospective study, in-depth discussion is required to address the aforementioned issues with respect to the association between vitamin D, visceral adiposity, and NAFLD in diabetes mellitus. A further multi-center study with large sample size is warranted to identify the role of vitamin D in the pathogenesis of NAFLD, one of the most common metabolic diseases.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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