

Comment on: Alpha-Klotho protein in systemic lupus erythematosus

Sirs,

We read with great interest the paper “Alpha-Klotho protein in systemic lupus erythematosus” by Martín-González *et al.* published recently in *Clinical and Experimental Rheumatology* (1). In this article, the authors presented comprehensive data, demonstrating that serum alpha-Klotho levels were not significantly different between patients with systemic lupus erythematosus (SLE) and controls, but associated with prednisone treatment and musculoskeletal manifestations (1). However, we wondered whether the control selection in this study was appropriate.

Firstly, 16% of the controls were patients with diabetes mellitus (DM), and also the proportion is far higher than that in SLE patients (5%). Several previous studies indicated that serum alpha-Klotho levels are significantly decreased and associated with diabetic kidney disease (2-4). Therefore, no difference for serum alpha-Klotho levels between SLE patients and controls in this study (1) may be due to DM.

Secondly, their study showed higher body mass index and low-density lipoprotein cholesterol levels and lower high-density lipoprotein cholesterol levels in SLE patients *versus* controls, suggesting the controls could be more likely to have obesity (1). Furthermore, this study also demonstrated that obesity may be closely related to serum alpha-Klotho levels (beta coefficient, 95% confidence interval: 0.66, 0.2–1.11, $p=0.005$) (1). The close

relationship of obesity and serum alpha-Klotho has also been reported in a previous study (5). Therefore, the effect of obesity on the results of this study cannot be ruled out. In these cases, in order to verify whether or not SLE patients actually differ from controls in the serum alpha-Klotho level, the comparisons between SLE patients and controls need to be repeated after exclusion of individuals with DM and obesity in both groups. Otherwise, the conclusion that serum alpha-Klotho levels were not significantly different between SLE patients and controls may be meaningless and even misleading.

In addition, there may be other confounders, such as calcium and vitamin D supplements as stated in this study (1), and exercise and physical activity which may be less common in SLE patients, but increase the serum level of alpha-Klotho (6, 7). These confounders should be investigated or referred to.

L. JIANG¹

Z. YANG², PhD

¹Comprehensive Medical Service Center,

²Department of Laboratory Medicine,
Huangyan Hospital of Wenzhou Medical
University, Taizhou First People's Hospital,
Taizhou, Zhejiang, China.

Please address correspondence to:

Zaixing Yang

Department of Laboratory Medicine,

Huangyan Hospital of Wenzhou

Medical University,

Taizhou First People's Hospital,

218 Hengjie Road,

Taizhou 318020, Zhejiang, China.

E-mail: yangzaixingdiyi@163.com

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