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Thyroid Stimulating Hormone Reference Range and Prevalence of Thyroid Dysfunction in the Korean Population: Korea National Health and Nutrition Examination Survey 2013 to 2015 (*Endocrinol Metab* 2017;32:106-14, Won Gu Kim et al.)

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We would like to thank Dr. Young Ki Lee and Professor Dong Yeob Shin for reading our article and providing insightful comments regarding our study.

In our article published in volume 32, issue 1 of *Endocrinology and Metabolism*, we reported that the reference interval of thyroid stimulating hormone (TSH) in the Korean population was between 0.62 and 6.68 mIU/L, which is higher than that of Western countries [1]. This was the first nationwide cross-sectional study to evaluate the distribution of serum TSH levels in the Korean population using data from the Korea National Health and Nutrition Examination Survey (KNHANES) from 2013 to 2015. Based on that reference interval, the prevalence of subclinical hypothyroidism was 3.10%, and the corresponding value from the U.S. National Health and Nutrition Examination Survey (NHANES) III was 4.3%, with a cutoff serum TSH value of ≥ 4.5 mIU/L [1,2]. However, the previously reported prevalence of subclinical hypothyroidism in Korea was very high, and was determined without considering the distribution of serum TSH in the reference population. For example, the prevalence of subclinical hypothyroidism in the Ansung cohort and Korean Longitudinal Study on Health and Aging study was 11.7% and 17.3%, respectively [3]. If we use a lower reference value of serum TSH, there is a possibility of overestimating the prevalence of subclinical hypothyroidism. Therefore, our study provided important information about the distribution of serum TSH in Korean reference population using KNHANES data.

In our study, the definition of the reference population was subjects with no prior history of thyroid disease, no history of taking medication that could influence thyroid function, no family history of thyroid disease, negative anti-thyroid peroxidase antibody (TPOAb) results and serum free thyroxine levels in the reference range [1]. This definition of the disease-free population was adopted from a previous study that analyzed thyroid function in the U.S. NHANES III data [2]. Our definition was stricter than that of the National Academy of Clinical Biochemistry guidelines [4]. Essentially, our approach was to conduct a direct comparison of the KNHANES with the U.S. NHANES III.

In the data used in our study, information regarding neck ultra-

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sonography (US) or anti-thyroglobulin antibody (TgAb) status was not available. Previously, Kim et al. [5] reported the reference interval of TSH in 19,465 subjects, including normal US findings in the definition of the reference population. The reference interval of that study was between 0.73 and 7.06 mIU/L, which is similar to our findings. In the U.S. NHANES III data, positive TPOAb results were detected in 13% of the total population, and positive TgAb results were detected in 11.5% [2]. TPOAb and TgAb were detected together in 6.9% of subjects, and TgAb alone was positive 3.4% [2]. However, only TPOAb was significantly associated with hypothyroidism, while TgAb was not [2]. These findings suggest that only a small number of subjects were positive for TgAb only and that the impacts of those with positive TgAb results on the distribution would be limited.

In our study, the median urinary iodine concentration in the Korean population was 299.4 μg/L, suggesting more than adequate iodine intake in Korea [1]. Iodine intake is known to be associated with thyroid disease and serum TSH levels. Recently, Jeon et al. [6] found that the TSH reference interval in a Korean reference population was right-shifted in the iodine-excessive groups using KNHANES data, and that the prevalence of overt and subclinical hypothyroidism was associated with nutritional iodine status. That finding suggests that higher iodine intake in the Korean population could be the reason for a higher reference interval of serum TSH concentrations. However, we did not have a clear answer about the long-term consequences of higher serum TSH levels in the Korean population.

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CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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