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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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Clinically, whether a patient has thyroid dysfunction is primarily screened for based on whether his or her thyroid stimulating hormone (TSH) level is within the normal range [1]. Therefore, the validity of the reference range of TSH is very important for ensuring informed clinical judgments. A previous report indicated that the reference range of TSH was higher in areas with high iodine intake [2]. Since iodine intake has been reported to be high in Koreans [3], it seems plausible that the serum TSH reference range would be somewhat high in the Korean population. However, no nationwide study had previously been conducted on the reference range of TSH in Korea.

Recently, Kim et al. [4] evaluated the Korean reference range of serum TSH using Korea National Health and Nutrition Examination Survey (KNHANES) data from 2013 to 2015 and reported that the serum TSH reference range in Korea (0.62 to 6.86 mIU/L) was higher than the corresponding ranges in Western countries. This result was in line with that of a previous study by Kim et al. [5], in which the reference interval for TSH was reported to be 0.73 to 7.06 mIU/L. These results suggest that subclinical hypothyroidism in Korea may be overdiagnosed due to an inappropriately low TSH reference range. Nevertheless, applying the TSH reference values reported in this study directly to real clinical practice must be prudent with the following considerations.

The National Academy of Clinical Biochemistry (NACB) suggested that the serum TSH reference range should be established in rigorously screened euthyroid volunteers who do not have goiter, anti-thyroid peroxidase antibody (TPOAb), or thyroglobulin antibody (TgAb) [1]. The KNHANES data provided information on TPOAb, but information on the results of ultrasonography or TgAb was not available. Therefore, it is possible that the high reference range could be attributed to the unintentional inclusion of persons with mild thyroid dysfunction induced by TPOAb-negative occult thyroiditis in this population. In this study, the mean TSH level was higher in females than in males. In contrast, in a previous United States study on this topic, the gender difference in the mean TSH level, which was significant in the disease-free population, disappeared in the reference population. These discrepancies may also indicate the possibility that mild thyroid dysfunction was not sufficiently ex-

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cluded in this study [6]. The NACB also suggested that age-related normal reference limits should be used in children [1], but subjects aged 10 to 19 years were analyzed together with adults.

In addition, the results of this study raise another question. If high iodine intake increases the estimated reference value of TSH, can we be sure that this is not because of the increased prevalence of iodine-associated hypothyroidism? Excess iodine intake may lead to hypothyroidism and autoimmune thyroiditis [7], and because we do not have a perfect way to screen for thyroid dysfunction, if the prevalence of thyroid dysfunction in the population is high, the proportion of misclassified subjects with occult thyroid dysfunction may also be high, even in the selected reference population.

Therefore, although this study is valuable and important for understanding the patterns of thyroid hormone profiles in Korea, its results should be interpreted with caution. If we cannot suggest a complete explanation for the reason for the higher cut-off levels in the TSH reference interval of the Korean population, further studies with a more thorough exclusion of occult thyroid disease will be required to "re-define" the normal TSH level in Korea.

CONFLICTS OF INTEREST

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

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