



# Thyroid-Stimulating Hormone Reference Ranges in the First Trimester of Pregnancy in an Iodine-Sufficient Country (*Endocrinol Metab* 2018;33:466-72, Carmen Castillo et al.)

Hyemi Kwon

Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

Since thyroid disease has been associated with adverse pregnancy outcomes, a debate has emerged regarding whether universal thyroid screening in pregnancy should be performed [1,2]. Critical to this debate is the wide range in the prevalence of thyroid disorders reported in the literature. The most serious confounding variable is the difficulty in reaching a consensus regarding ‘normal levels of thyrotropin (thyroid-stimulating hormone [TSH])’ in pregnancy. The recent American Thyroid Association (ATA) guidelines recommended that population-based trimester-specific reference ranges of serum TSH levels should be obtained in a local, euthyroid, pregnant population per trimester, which is considered to be the gold standard [1]. Therefore, the paper of Castillo et al. [3] is a very important study in terms of public health.

Serum TSH level is the most sensitive diagnostic marker of thyroid dysfunction [4,5]. TSH level can be influenced by several factors, such as age, sex, thyroid auto-antibodies, race, smoking status, and intake of dietary iodine [4,5]. Dietary iodine intake is an important contributing factor affecting the distribution of serum TSH levels [5,6]. A Chinese study reported that the reference interval of serum TSH levels in a mildly iodine-deficient area was 0.33 to 3.42 mIU/L, whereas the reference interval in an iodine-excess area was 0.59 to 5.98 mIU/L [7].

Thyroid hormone levels of healthy pregnant women differ from those of non-pregnant women because pregnancy has an impact on the thyroid gland and its function [1]. Moreover, a downward shift of the TSH reference range occurs during pregnancy, especially in early pregnancy [1,2]. For these reasons, the recent ATA guidelines recommended the population-based trimester-specific reference ranges of serum TSH levels [1]. A previous study in Korea, an iodine-replete area, found that the reference ranges of serum TSH were 0.03 to 4.24 mIU/L in the first trimester, 0.13 to 4.84 mIU/L in the second trimester, and 0.30 to 5.57 mIU/L in the third trimester [2].

Castillo et al. [3] investigated the iodine status of healthy first-trimester pregnant women in Chile and proposed TSH reference ranges for this population. The median TSH level was 1.99  $\mu$ IU/mL and the reference range was 0.13 to 5.37  $\mu$ IU/mL in 670 women of the reference population selected according to the National Academy of Clinical Biochemistry guidelines [3]. The authors found adequate iodine intake and a right-shifted distribution of serum TSH levels in first-trimester pregnant women in Chile [3]. Using the above reference range, the prevalence of subclinical and clinical hypothyroidism in pregnant women was 3.92% and 1.76%, respectively [3]. This prospective observational study was valuable and well-designed, and it provided

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Corresponding author: Hyemi Kwon

Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemun-ro, Jongno-gu, Seoul 03181, Korea

Tel: +82-2-2001-2146, Fax: +82-2-2001-1552, E-mail: be02fre@gmail.com

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up-to-date information on the iodine status and thyroid hormone levels of pregnant women in Chile, which has universal salt iodination program.

In the study of Castillo et al. [3], the median urinary iodine (UI) level was 173.45 µg/L in 302 randomly-selected women. Fig. 2 showed the distribution of the various UI levels, indicating that some participants had insufficient iodine intake (UI <150 µg/L), while others had more than adequate iodine intake (UI between 150 to 499 µg/L), and others had excess iodine intake (UI >500 µg/L). I wonder the reason that the UI levels were not measured in all participants of the study, and whether the authors evaluated serum TSH levels in subjects categorized by their UI levels.

A recent meta-analysis on the prevalence of thyroid disease in pregnancy reported that the overall pooled estimates of prevalence for overt hypothyroidism and subclinical hypothyroidism were 0.5% and 3.47%, respectively, among studies using a 2.5th to 97.5th percentile TSH reference range [8]. Based on that result, the prevalence of overt hypothyroidism in Chilean pregnant women seems to be higher than that reported from other countries, despite of the similar prevalence of subclinical disease. Whether this discrepancy is due to differences in the free thyroxine assay or a true increase in prevalence, further researches are needed.

Nonetheless, this study provides important information on the TSH reference range during pregnancy in an iodine-sufficient area. I would like to congratulate the authors on this excellent result and expect many further valuable studies to be conducted in the future.

## CONFLICTS OF INTEREST

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

## ORCID

Hyemi Kwon <https://orcid.org/0000-0003-4257-3133>

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