



## ORIGINAL ARTICLE

# Determination of thyrotropin reference values in an adult Mexican population



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### KEYWORDS

Thyrotropin;  
Reference values;  
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Thyroid ultrasound

### Abstract

**Background and objective:** The upper limit of TSH reference level is controversial. The purpose of our study was to determine TSH reference values in a Mexican population in accordance with the National Academy of Clinical Biochemistry (NACB) criteria and in correlation with thyroid ultrasound (US) examination.

**Patients and methods:** The study was conducted in volunteers with no known thyroid disease. We recruited 482 subjects, most of them medical or administrative staff from our hospital. They answered a questionnaire on demographic data, family history, co-morbidities, and drug use. Their thyroid hormone levels and thyroid antibodies were determined, and a complete physical examination and thyroid US were performed. The population used to establish the TSH reference intervals was selected according to the NACB criteria and their normal thyroid structural and echogenic characteristics in US examination.

**Results:** Among 482 subjects (209 males) with a median age of 26 years, prevalence rates of TPOAb and TgAb were 9.3% and 10.3% respectively. Mean TSH level in the overall population was  $1.90 \pm 1.94$ , with a 97.5th percentile of 6.76 mIU/L. The reference population was limited to 282 subjects (41.5% were excluded) with a mean TSH of  $1.86 \pm 1.63$  and a 97.5th percentile of 4.88 mIU/L. No sex difference was found ( $p = 0.287$ ). Median urinary iodine level in the reference population was 267  $\mu\text{g/L}$  IQR (161.3–482.5).

**Conclusions:** The TSH reference interval in the reference population was 0.71 (CI 0.65–0.77) to 4.88 mIU/L (CI 4.5–5.3); these limits may be influenced by iodine nutritional status in this population.

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**PALABRAS CLAVE**

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Valores de referencia;  
Anticuerpos  
antiperoxidasa  
tiroideo;  
Anticuerpos  
antitiroglobulina;  
Ultrasonido tiroideo

**Determinación de los valores de referencia para la tirotropina en una población mexicana adulta****Resumen**

*Antecedentes y objetivo:* Existe controversia respecto al límite superior de referencia para TSH. El objetivo del estudio fue determinar los valores de referencia para TSH en una población mexicana de acuerdo con los criterios de la National Academy of Clinical Biochemistry (NACB) y en correlación con el examen ultrasonográfico (US) tiroideo.

*Pacientes y métodos:* El estudio se realizó en voluntarios sin enfermedad tiroidea conocida. Se reclutaron 482 individuos, personal sanitario y administrativo del hospital, que respondieron un cuestionario sobre datos demográficos, antecedentes familiares, co-morbilidades y medicamentos consumidos, y a los que se les practicó determinación de hormonas tiroideas, anticuerpos anti-tiroideos, exploración y US tiroideo. La población escogida para establecer los intervalos de referencia de TSH fue seleccionada con los criterios de la NACB más la normalidad estructural y ecogénica del tiroides por US.

*Resultados:* En los 482 sujetos (209 hombres) con mediana de edad de 26 años, la prevalencia de TPOAb fue de 9,3% y TgAb 10,3%. La media de TSH para la población total fue  $1,90 \pm 1,94$ , con percentil 97,5 de 6,76 mUI/L. La población de referencia se limitó a 282 sujetos (41,5% fueron excluidos); la TSH media de esta población fue de  $1,86 \pm 1,63$ , con percentil 97,5 de 4,88 mUI/L, sin diferencia entre géneros ( $p=0,287$ ). La mediana para la yoduria de la población referencia fue 267  $\mu\text{g/L}$  RIQ (161,3-482,5).

*Conclusiones:* El intervalo de referencia para la TSH fue de 0,71 (IC 0,65-0,77) a 4,88 mUI/L (IC 4,5-5,3); el resultado posiblemente está influido por el estado nutricional de yodo de esta población.

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**Introduction**

An intense debate over the upper TSH reference limit in adults<sup>1-3</sup> has taken place in the past few years. This resulted because of a publication by the National Academy of Clinical Biochemistry (NACB) that suggested decreasing it to 2.5 mIU/L.<sup>4</sup> As with any reference value, this is pivotal in daily clinical practice. The prevalence of spontaneous hypothyroidism is 1–2% in populations with sufficient iodine intake but it increases in the elderly, especially up to 10-fold in females; moreover, the prevalence of subclinical hypothyroidism ranges between 4.0 and 8.5%.<sup>5</sup> The NACB also suggested that in order to establish TSH reference intervals, these should be determined on the basis of 95% confidence intervals of the transformed logarithmic values obtained, in at least 120 normal volunteers rigorously selected for their euthyroid status and with no detectable antithyroid antibodies, no personal or family history of thyroid disease, a normal thyroid gland on examination and no drug intake other than estrogen.<sup>4</sup> Ultrasound has proved useful as a screening tool because abnormal echogenicity correlates with thyroid autoimmunity,<sup>6,7</sup> so that ultrasonographic evaluation has been added to the NACB criteria in several studies determining TSH reference intervals.<sup>8,9</sup> Most studies establishing TSH reference intervals in adult populations in accordance with the NACB criteria have been conducted in developed countries. In Mexico there is no information on TSH reference intervals in healthy adult populations or studies based on the NACB criteria.

The purpose of this study was to determine TSH reference intervals in a normal healthy population following

the NACB's guidelines in association with ultrasound thyroid screening.

**Materials and methods**

This study was approved by the Ethics Committee of the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán".

This cross-sectional study included healthy adults over the age of 18 with no previous history of thyroid disease; they were all recruited among the hospital's administrative personnel, nurses, and physicians (residents and undergraduate students). All participants signed an informed consent form for enrollment. All the volunteers filled out a questionnaire on their family history of thyroid disease, personal pathological history and co-morbidities, as well as the use of drugs and contrast material for radiological studies. Thyroid ultrasound was performed with a portable unit (7.5 MHz lineal transducer) by a single investigator (AFR), an endocrinologist with experience in thyroid sonography. This evaluation took place before thyroid examination and the operator had no access to each volunteer's information. The volume of each thyroid lobe was calculated with the following formula (mL): width  $\times$  height  $\times$  length  $\times$  0.52; the sum of both lobes yields the total thyroid volume.<sup>7</sup> Ultrasound gain was adjusted so as to keep operating conditions constant and until the internal jugular vein and carotid artery lumens were free of echoes. Normal or decreased echogenicity was determined by comparison with the surrounding neck muscles; thyroid hypoechogenicity was graded as 1 or mild,

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