

THYROID-STIMULATING HORMONE AND FOLLICLE-STIMULATING HORMONE STATUS IN HISPANIC WOMEN DURING THE MENOPAUSE TRANSITION

Introduction: Few studies exist on thyroid status and ovarian dysfunction, although the prevalence of thyroid disease, particularly hypothyroidism, increases with advanced age and is more common in women. Loss of ovarian function is a lengthy process, and it is well known that follicle-stimulating hormone (FSH) increases with age and is correlated with loss of ovarian reserves. Limited information is available on FSH and thyroid-stimulating hormone (TSH) status in healthy euthyroid women in pre- and postmenopause states. We propose that patterns in FSH levels depend on the menopause state and that a possible relationship with TSH is present in mature women.

Methods: Baseline data from the study Health and Menopause in Hispanic Women in Puerto Rico were used. Eligible women were 30–84 years old. Demographic data and lifestyle and health information were collected through a questionnaire, and blood chemistries were analyzed.

Results: In women without thyroid disease, the median TSH was 1.97 mIU/L, and for euthyroid women the median was 1.84 mIU/L; no difference was observed between pre- and postmenopause states. A positive tendency was found between FSH levels and age in this group.

Conclusions: This report compares the value of TSH in Puerto Rican women during pre- and postmenopausal states, and our findings are different from those in other ethnic groups. FSH levels correlate with age, and the general tendency of FSH to increase with age differs according to menopause state. No correlation between TSH and FSH levels was found in this study. (*Ethn Dis.* 2008;18[Suppl 2]:S2-230–S2-234)

Key Words: FSH, TSH, Puerto Rico, Menopause

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INTRODUCTION

Typically, menopause induces changes in the ovary, the most striking of which is a profound decline in follicle numbers. In both natural and surgical menopause, follicle-stimulating hormone (FSH), which is an indirect marker of follicular activity, increases noticeably.¹

Marked alterations in steroid metabolism have been observed during hyper- and hypothyroid states.² The altered thyroid status could contribute to variations in hormone levels, as has been reported during the menopause transition.^{2,3} In these studies, overt thyroid failure and subclinical hypothyroidism can be associated with infertility and menstrual irregularities.³ Although the discussion about the normal ranges of thyroid-stimulating hormone (TSH) is still open,^{4,5} TSH is the preferred test to assess thyroid function as stated by the National Academy of Clinical Biochemistry.⁶ Abnormal thyroid function has public health consequences,⁷ but few studies relate TSH status to the menopause transition.²

Several studies have shown that overt thyroid failure and subclinical hypothyroidism are associated with abnormal lipid disorders, fatigue, depression, and weight gain,⁷ all of which are important factors during menopause. On the other hand, the relationship between TSH and low- and high-density lipoprotein and cholesterol levels is not clear.^{8–10} Furthermore, elevation of plasma triglycerides is associated with hypothyroidism. Nevertheless, the molecular mechanism by which TSH may regulate lipase activities and circulating thyroid-binding globulin levels in humans remains to be defined.¹¹

At present, analyses carried out in Puerto Rican women of menopausal age are limited, although a recent study has established the average age of onset of menopause.^{12,13} The objective of the present cross-sectional study was to evaluate the patterns of FSH levels in the menopause state and a possible relationship with TSH in pre- and postmenopausal Puerto Rican women without thyroid disease.

METHODS

To accomplish the objectives of this study, we used the baseline data from the longitudinal study Health and Menopause in Hispanic Women in Puerto Rico. This longitudinal study recruited 299 women aged 30–84 years who were followed annually for three years. A systematic selection by age was used initially to invite a random sample of participants from the Puerto Rico Teachers Association. The second wave of participants was obtained by using the snowball sampling technique, that is, every participant in the first group identified a colleague who was invited to participate in the study. Once a new participant was identified, a similar evaluation was performed. The third group of participants came from the second group of participants, again using the snowball technique. Written informed consent was obtained from each participant before admission to the study. The study design was approved by the institutional review board of the Medical Sciences Campus of the University of Puerto Rico. Each of the three evaluations included blood chemistries, anthropometric measurements, and an interviewer-administered questionnaire on

Table 1. TSH values by menopause stage for the total sample and for the sample without thyroid disease, among all women and the subset with normal TSH values

	Total Sample				Sample without Thyroid Disease			
	Premenopause	Postmenopause (Natural)	Postmenopause (Surgical)	Total	Premenopause	Postmenopause (Natural)	Postmenopause (Surgical)	Total
All TSH values								
Mean±SD	2.52±1.90	2.80±2.31	2.29±1.27	2.42±1.90	2.28±1.53	2.60±1.99	2.16±1.13	2.35±1.61
Median	2.05	2.17	2.04	1.94	1.99	2.05	1.94	1.97
n*	107	72	40	299	87	56	37	199
TSH in normal range .4–4.0 mIU/L								
Mean±SD	2.00±.88	2.08±.80	2.03±.90	1.96±.83	1.99±.84	2.05±.78	1.99±.90	2.00±.83
Median	1.83	1.91	1.94	1.79	1.83	1.88	1.77	1.84
n*	88	62	37	258	79	50	35	181

SD = standard deviation.

* Includes women who could not be classified as to menopause stage.

demographics, lifestyle and health characteristics.

Participants were classified into two groups, those who were in a premenopausal phase (who had at least one menstrual episode in the last 12 months) and those who were in a postmenopausal phase (natural, with ≥ 12 consecutive months of amenorrhea, or surgical, as indicated in the questionnaire). Participants without thyroid disease who were not taking thyroid-replacement therapy, as reported in the questionnaire ($n=199$), were considered for the analyses. Euthyroid participants were defined as having a TSH level of .4–4.0 mIU/L. Other variables considered in this analysis included age, body mass index (BMI), FSH, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and total cholesterol.

To describe the quantitative characteristics of the study group, means, medians, and standard deviations (SD) were computed. To compare the means in different conditions, *t* test, analysis of variance, and regression models were used. For the purpose of analyzing the data with these statistical procedures, a square root transformation was applied for variance homogeneity. The correlation among variables was performed by using the Pearson correlation coefficient when normality assumption was satisfied, and for non-normal variables a Spearman

correlation coefficient was used. A lowest method (local weighted regression model) was used to assess the trend in the association of FSH and age. All statistical analyses were performed by using GraphPad Prism 4 (GraphPad Software, Inc., San Diego, Calif) or STATA 8.0 (Stata-Corp LP, College Station, Texas).

RESULTS

The number of women considered for this study was 299. The average (\pm SD) age was 51.53 (± 9.84) years. Of the 299 women, 199 (67%) reported no thyroid problems, and of this group, 181 (91.0%) were euthyroid, 17 (8.5%) had TSH >4.0 mIU/L, and 1 (0.5%) had TSH <0.4 mIU/L. Table 1 shows TSH values for the total sample and in the sample without self-reported thyroid disease. Of the 199 women who did not report a diagnosis of thyroid problems, 43.7% were premenopausal, 46.7% were postmenopausal (28.1% natural and 18.6% surgical), and 9.6% did not report menstrual frequency and could not be classified. No significant differences were found in TSH levels between pre- and postmenopausal participants ($P=.05$).

The distribution of normal TSH (.4–4.0 mIU/L) per age group (30–39, 40–49, 50–59, and >60 years) is shown in Figure 1. Among the total

sample, the distribution of women within each age group was 11.7%, 30.4%, 39.3%, and 18.7%, respectively. Average TSH values increased with age, although the changes between groups were not significant ($P > .005$).

Figure 2 shows the relationship between FSH and age among women without self-reported thyroid disease. A positive tendency was observed for the total sample, as shown in Figure 2A. A further analysis dividing the population into pre- and postmenopausal groups showed two tendencies. For the premenopausal group (Figure 2B), the increase of FSH with age was monotonic, while the postmenopausal group (Figure 2C) showed a biphasic pattern.

Mean (\pm SD) BMI was 29.35 (± 6.10) kg/m² ($n=294$) in the overall sample. Lipid profile indices in the same group ($n=293$) were total cholesterol 205.8 (± 44.75) mg/dL, HDL cholesterol 55.89 (± 32.03), and LDL cholesterol 120 (± 32.03) mg/dL. An asymmetrical distribution of triglycerides was observed. The median and mean (\pm SD) for triglycerides ($n=292$) were 122.59 mg/dL and 132.6 (± 72.62) mg/dL, respectively.

DISCUSSION

Thyroid status during the menopause transition has not been extensively

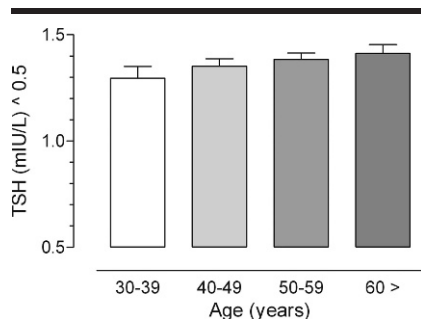


Fig 1. Thyroid-stimulating hormone (TSH) dependence by age group among women without thyroid dysfunction (n=199). Bars represent the normalized average of TSH in each group. A square root transformation was used. The means (\pm SD) of TSH concentrations for women aged 30–39, 40–49, 50–59, and \geq 60 years were 1.77 (\pm .77), 1.92 (\pm .83), 2.00 (\pm .85), and 2.08 (\pm .81) mIU/L, respectively.

studied, although the prevalence of thyroid disease, particularly hypothyroidism, increases with advanced age.^{2,7} Recent studies have characterized the distribution of age at menopause among Puerto Rican women;^{12,13} this criterion, together with menstrual history, is a powerful predictor of menopausal status.¹⁴ The present report is a first effort at describing TSH and FSH levels, BMI, triglycerides, and cholesterol in pre- and postmenopausal Hispanic women residing in Puerto Rico.

In women without self-reported thyroid disease the median TSH was higher than the median value reported in the Third National Health and Nutrition Examination Survey (NHANES-III) (1.50 mIU/L) for women without thyroid disease. Dividing our sample into the same age groups (by decade, from 30 to 79 years), we show a median value for each group higher than that in NHANES-III.¹⁵ Sowers et al² reported a median TSH value of 1.89 mIU/L from women aged 42–52 in premenopause and early perimenopause, which is also lower than the one found in this study (1.97 mIU/L) for the same age group. These results suggest that it is relevant to evaluate TSH levels within

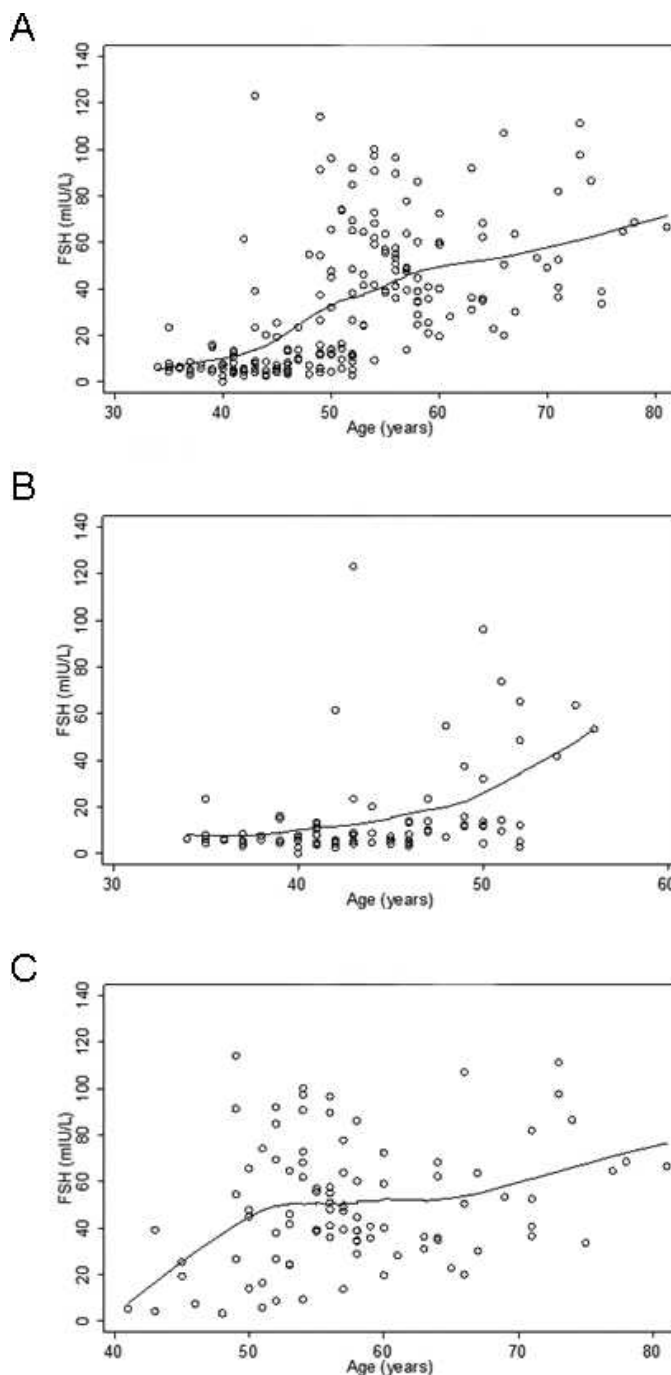


Fig 2. Relationship between follicle-stimulating hormone (FSH) and age among women with no self-reported thyroid disease. A) Total sample. B) Premenopausal sample. C) Postmenopausal sample. Lines represent the lowest analysis for a bandwidth of .8.

groups and within locations to establish appropriate baseline levels. Several considerations come to mind as necessary to have appropriate basal TSH values or interval ranges for popula-

tions; these should include a series of exclusion criteria for compensated subclinical thyroid pathology, such as thyroid ultrasonography, as well as the standard blood chemistry.⁴

While the median value of TSH in our sample was different from that of women living in the United States,¹⁵ we found a tendency for the average TSH to increase with age. However, separation of euthyroid participants by age groups did not show significant differences in the average value of TSH (Figure 1). The positive marginally significant ($P<.048$) relationship between TSH with age was found in women without self-reported thyroid dysfunction. This correlation is similar to that reported by other researchers.^{6,15} However, Dhatt et al¹⁶, have reported that TSH levels did not correlate with age or sex in an ambulatory Arab population, while Kratzsch et al⁴ showed an inverse association of TSH with age, specifically in healthy male and female blood donors. We understand that other analyses, including thyroxine, thyroid-binding globulin, and thyroid antibody levels may help yield a more complete scenario to clarify the discrepancies observed between TSH levels and age.

We observed no significant difference between TSH levels and menopausal stage. This result is consistent with the reports by Sowers et al² and Massoudi et al.¹⁹ In the group of participants without thyroid dysfunction, we found a small tendency toward an inverse relationship between FSH and TSH ($P=.095$). Sowers et al also report a slight negative nonsignificant correlation between these variables.²

We found a positive correlation of FSH with age. This correlation has been frequently observed and is considered the norm in women approaching menopause and during menopause. Our data show, however, that the general tendency for FSH to increase with age differs according to menopause state. Premenopausal women show a shallow tendency, with a gradual increase in FSH with age more evident after age 50. Postmenopausal women show an increase in FSH levels with age up to 50, then the level plateaus up to age 65,

and gradually increases again after age 70.

Implications of thyroid function are varied, and one of the most discussed is the relationship with cardiovascular disease in which lipid metabolism is a key factor. In our study, mean BMI was comparable to that reported in the literature,¹⁷ and no correlation between BMI and TSH was found ($P>.05$). Knudsen et al¹⁸ report a positive correlation between TSH and BMI levels ≥ 30 kg/m². However, the study sample in this case comprised women aged 18–65 and men aged 60–65 years. Our data support the results of Massoudi et al,¹⁹ which show no association between TSH and BMI in healthy perimenopausal women. In addition, we found that total cholesterol, HDL cholesterol, and LDL cholesterol levels and TSH did not show significant correlations ($P>.05$). Although some studies indicate that TSH is related to lipid levels,⁷ our results support other studies that indicate no relationship between TSH and lipid levels.^{8,10} In contrast, our analysis of triglyceride levels shows a significant correlation with TSH ($P=.0167$). This result supports the literature that suggests TSH is important for triglyceride metabolism, although the molecular mechanisms are still unclear.¹¹

There is a paucity of literature on racial/ethnic variations in TSH level. In many cases, the normal values of TSH are adopted from analyses of populations of different origins and demographic characteristics that may not be necessarily comparable. More information on the effect of ethnic background on basal TSH levels may be important to support effective public health policies for women. Our finding of increasing FSH with age is in agreement with the literature; in addition, our data suggest that the increments in FSH may vary between age groups in the postmenopausal population. It would be of interest to further explore this relationship in larger representative

samples of Hispanic women and women of other ethnicities. More information is needed to elucidate the roles of thyroid hormones and gonadotropins on reproductive status.

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