

## Possible association between subclinical hypothyroidism and age at menopause in Colombian women

Álvaro Monterrosa-Castro, Angelica Monterrosa-Blanco & Sandra Sánchez-Zarza

To cite this article: Álvaro Monterrosa-Castro, Angelica Monterrosa-Blanco & Sandra Sánchez-Zarza (2024) Possible association between subclinical hypothyroidism and age at menopause in Colombian women, Gynecological Endocrinology, 40:1, 2334798, DOI: 10.1080/09513590.2024.2334798

To link to this article: <https://doi.org/10.1080/09513590.2024.2334798>



© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group



Published online: 08 Apr 2024.



Submit your article to this journal [↗](#)



Article views: 454



View related articles [↗](#)



View Crossmark data [↗](#)

RESEARCH ARTICLE



## Possible association between subclinical hypothyroidism and age at menopause in Colombian women

Álvaro Monterrosa-Castro<sup>a</sup> , Angelica Monterrosa-Blanco<sup>a</sup>  and Sandra Sánchez-Zarza<sup>a,b</sup> 

<sup>a</sup>Grupo de investigación Salud de la Mujer, Facultad de Medicina, Universidad de Cartagena, Cartagena, Colombia; <sup>b</sup>Instituto de Previsión Social (IPS). Hospital Central, Dr. Emilio Cubas, Facultad de Ciencias de la Salud, Universidad Católica Nuestra Señora de la Asunción, Asunción, Paraguay

### ABSTRACT

**Objective:** To evaluate the association between subclinical hypothyroidism with early menopause, premature menopause, and last menstrual bleeding before the natural age of menopause.

**Methods:** This was a cross-sectional study conducted in 643 postmenopausal women aged 40–69 years. Groups were formed according to last menstrual episode:  $\geq 45$  [Natural age at menopause], 40–44 and [Early menopause],  $< 40$  [Premature menopause], and  $< 45$  [last menstrual episode before the natural age of menopause]. The Zulewski scale was applied to identify manifestations related to hypothyroidism and subclinical hypothyroidism, diagnosed with a serum TSH  $> 4.5$   $\mu\text{IU/mL}$  plus T4-free between 0.7 and 1.9 ng/dL.

**Results:** It was found that 24.4% had the last menstrual episode before the natural age of menopause, 18.6% had early menopause, and 5.7% had premature menopause. Subclinical hypothyroidism was diagnosed in 4.5% of patients. Among women with subclinical hypothyroidism, there was a higher frequency of early menopause, premature menopause, and last menstrual episode before the natural age of menopause, than in women without subclinical hypothyroidism ( $p < 0.05$ ). Paresthesia (50%) and dry skin (40.7%) were the most reported hypothyroidism-related manifestations. Early menopause, premature menopause, and last menstrual episode before the natural age of menopause were associated with subclinical hypothyroidism, OR: 3.37 [95% CI: 1.40–8.10], OR: 4.31 [95% CI: 1.24–14.97], and OR: 3.57 [95% CI: 1.57–8.10], respectively.

**Conclusions:** The last menstrual episode before the natural age of menopause, early menopause, and premature menopause were significantly associated with a higher chance of subclinical hypothyroidism

### ARTICLE HISTORY

Received 29 January 2024  
Revised 14 March 2024  
Accepted 20 March 2024  
Published online 8 April 2024

### KEYWORDS



Age at menopause; early menopause; menopause; premature menopause; climacteric; hypothyroidism; thyroid-stimulating hormone

### Introduction

Subclinical hypothyroidism is characterized by the elevation of the thyroid-stimulating hormone (TSH), with normal preservation of thyroid hormones [1–4]. The condition increases with age and its prevalence may vary from 3 to 18% in the adult population, mainly affecting women, older people, and populations with insufficient iodine intake [2,4,5]. It is a mild thyroid dysfunction, basically asymptomatic, although nonspecific manifestations may occur, such as slow movements or weakness, feeling of thick, dry, or cold skin, weight gain, constipation, decreased sweating, or paresthesia [1,2,4,6]. The importance of subclinical hypothyroidism lies on the potential progression to overt hypothyroidism and the association with lipid alterations, increased coronary risk, congestive heart failure, neuropsychiatric symptoms, and deterioration of muscle strength, especially when blood TSH levels are  $> 10$   $\mu\text{IU/mL}$  [2,3,7,8]. The most common cause of subclinical hypothyroidism is Hashimoto's thyroiditis, a chronic autoimmune disorder [6,9].

Immunological, genetic, benign, or malignant utero-ovarian or pelvic diseases and their surgical interventions are recognized as causes for the last menstrual episode to occur before the natural age of menopause [10–12]. Natural menopause

occurs between 45 and 55 years of age and is the physiological expression of the exhaustion of the ovarian follicles. Ethnic, environmental, geographic, hormonal, genetic, nutritional, and other factors explain the range of the natural age of menopause [13–15]. Menopause occurring between 40 and 44 years is defined as early menopause and before the age of 40 as premature menopause (spontaneous or surgical) [11,13,16]. The cease of menstrual episodes before the natural age of menopause is associated with osteopenia, osteoporosis and fractures, muscle dysfunction, reduction in gait and physical decline, metabolic syndrome, changes in carbohydrate metabolism and diabetes, cardiovascular disease, cerebrovascular, arterial hypertension, dyslipidemia, adverse emotional, psychosocial and global health impact, cognitive decline, and increased mortality from all causes [11,13,17–27]. There are insufficient studies that explore the association between age at menopause and thyroid disorders, and apparently, they have not been evaluated in Latin American women. Thus, the aim of this study was to evaluate the association between subclinical hypothyroidism and the age at menopause onset.

**CONTACT** Álvaro Monterrosa-Castro  [alvaromonterrosa@gmail.com](mailto:alvaromonterrosa@gmail.com)  Grupo de investigación Salud de la Mujer, Facultad de Medicina, Universidad de Cartagena, Cartagena, Colombia

© 2024 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. The terms on which this article has been published allow the posting of the Accepted Manuscript in a repository by the author(s) or with their consent.

## Methods

### Study design and participants

This was a cross-sectional study belonging to the research project 'Menopause and Thyroid' which was approved by the Institutional Ethics Committee of the University of Cartagena, Cartagena, Colombia (Resolution 01385-2021 and minutes 092-2021). The suggestions and recommendations of the STROBE initiative were considered when structuring the research report [28].

In 2022, women aged 40–69 years who were residents of the Caribbean region of Colombia were invited to participate in the study. They had to have one or more years without menstruation and have been considered postmenopausal in their health care services [29], be able to perform daily tasks, be active at the family level and have the perception of having been healthy in the last month. Participation was carried out in person at meetings of fifty women, anonymously, voluntarily, unpaid, and completing the following phases. First, sign written informed consent. Second, complete a sociodemographic and clinical information form. Third, allow measurement of the ankle reflex and collection of 5.0 mL of peripheral venous blood from the non-dominant forearm in order to measure serum TSH and free-T4. Fourth, attend a talk on menopause and thyroid disease. Women were free to leave at any time and those who did not wish to participate, who had visual or literacy deficits, cognitive disability, diagnosis of benign or malignant thyroid pathology, history of surgery or radiotherapy to the neck, intake of iodinated medications, oncological disease, heart failure, and abnormal free-T4 results were excluded. The information was collected by doctors and interviewers, and venous blood sample was taken by nurses. Invitations and meetings were carried out until the forms were completed according to the calculated sample size.

### Used tools and measurements

Measurements were housed in a printed form designed for the study, which had several sections. First, sociodemographic and clinical characteristics were asked: age, occupation, family history of thyroid disease, personal history of high blood pressure, diabetes or dyslipidemia, perception of anxiety or depression in the last month, history of gynecological surgery and age at which the last menstrual episode occurred. Second, the Zulewski scale in Spanish language was applied. This tool assesses manifestations related to hypothyroidism, such as periorbital puffiness, constipation, weight increase, cold skin, paresthesia, hoarseness, dry skin, diminished sweating, impairment of hearing, coarse skin, slow movements, and delayed ankle reflex. One point is assigned to each of the previously mentioned if the manifestation is present and zero when it is absent. Scores are summed and one point is added if the person is <55 years old. The higher the total score, the greater the possibility of hypothyroidism. The tool establishes three categories: euthyroid status [0–2 points], intermediate condition [3–5 points], and possible hypothyroid status [6 and more points]. Sensitivity and specificity of the instrument for the diagnosis of hypothyroidism is 60% [30]. A Kuder–Richardson of 0.56 was calculated among the participants. The third section of the form was reserved to record the ultrasensitive TSH and free-T4 measured serum values, which were performed using third-generation chemiluminescence technique on an Advia Centauros Xp device (Siemens Healthineers Diagnostics Inc., Mishawaka, IN) in the Santa Lucía Clinical Laboratory of Cartagena, Colombia, a

certified institution that meets the criteria established by the Colombian legislation. Criteria of the U.S. Preventive Services Task Force was used to diagnose subclinical hypothyroidism, that is if serum TSH was  $>4.5$   $\mu$ IU/mL with a free-T4 between 0.7 and 1.9 ng/dL [31]. Three groups were established according to the age of the last menstrual episode:  $\geq 45$  years (natural age of menopause), 40–44 years (early menopause), and  $<40$  years (premature menopause) [10,16,17,20,32–34]. In addition, a fourth group was structured that included women with premature menopause and early menopause, that is, those who had menopause  $<45$  years of age. This group was called last menstrual episode before the natural age of menopause.

Forms were reviewed weekly and kept in custody; those correctly completed were numbered and transcribed into a Microsoft Excel® data sheet. Incorrectly completed forms were not considered for analysis.

### Sample size calculation

Sample size was calculated with OpenEpi, using data from the 2005 Colombian population census that projected a national population of 26,442,213 women by 2022, of which 25.6% would be between 40 and 69 years of age and 4.3% would reside in the department of Bolívar. In this department, that is part of the Colombian Caribbean, that was selected by convenience, it is estimated that a total of 1,137,015 women resided in 2022, with 291,075 between 40 and 69 years of age. A sample size of 385 women was calculated, with a confidence level of 95%, with 50% heterogeneity, and a margin of error of 5%. Of 150 (38.9%) were added to replace women who filled out forms incompletely or inconsistent forms. In addition, the same number of participants was added as a precaution, to replace lost forms, since they would be applied in distant populations. Of 685 forms were printed and available, which were applied until they were exhausted.

### Statistical analysis

Statistical analysis was performed with EPI-INFO version 7 (Center for Disease Control and Prevention, Atlanta, GA). Data are presented as continuous variables expressed as mean and standard deviation, and categorical variables expressed as frequencies (%). The significance of the difference between continuous data was calculated with the ANOVA or Kruskal–Wallis test, depending on the distribution of variance based on the Bartlett test. Differences between percentages were evaluated with the Chi-square Mantel–Haenszel test. Bivariate logistic regression was performed between subclinical hypothyroidism (dependent variable) and age at menopause (independent variable). An adjusted logistic regression model was performed with the same variables and also including age, family history of thyroid disease, history of abdominal hysterectomy with or without bilateral oophorectomy, perception of anxiety and depression, and history of diabetes, high blood pressure, and dyslipidemia. For all calculations, a  $p$  value  $< .05$  was considered as statistically significant.

### Ethical considerations

Women were informed of the study, its objectives and tools to be used, after which they gave written consent of participation without receiving any type of incentive in return. The Declaration of Helsinki on human research, the ethical principles of the Belmont Report and Resolution 8430-1993 of the Colombian Ministry of Health was taken into account at all times. Women who had abnormal TSH tests were promptly referred to their health care services.

## Results

A total of 794 women accepted to participate in the study of which 109 (13.7%) had exclusion criteria and 42 (6.1%) form were incorrectly filled out or were incomplete. Finally, analysis was performed on the data of 643 women, a 93.8% of the calculated sample size.

Mean age of the participants was  $55.0 \pm 5.7$  years, average age of menopause onset was  $46.8 \pm 4.0$  years and 75% had their last menstruation at the natural age of menopause. Early menopause was found in 18.6%, premature menopause in 5.7%, and a last menstrual episode before the natural age of menopause in 24.4%. Subclinical hypothyroidism was diagnosed in 4.5% of the participants; these women had a worse score on the Zulewski scale than women without subclinical hypothyroidism. Women with subclinical hypothyroidism had a higher frequency of menopause before the natural age ( $p < .05$ ) (Table 1). Only 5 women (0.7%) had TSH levels  $> 10$   $\mu$ IU/mL. All manifestations

related to hypothyroidism that were explored with the Zulewski scale were more frequent among women with subclinical hypothyroidism as compared to those without ( $p < .05$ ) (Table 2).

The prevalence of subclinical hypothyroidism was 2.9% among participants who had their last menstruation at the natural age of menopause, increasing to 9.1% and 10.8% among those who had early menopause and premature menopause, respectively. When the last menstruation was  $< 45$  years, the prevalence of subclinical hypothyroidism was 9.5%. Upon bivariate and adjusted logistic regression, it was found that early menopause and premature menopause were associated three and four times, respectively, with subclinical hypothyroidism ( $p < 0.05$ ). The last menstrual episode before the natural age of menopause was also associated with subclinical hypothyroidism, OR: 3.57 [95% CI: 1.57–8.10] after adjusting for the chosen covariates (Table 3).

## Discussion

In this group of postmenopausal women residing in Colombia, we found that the frequency of early menopause (18.6%) and premature menopause (5.7%) was higher than the 5% and 1%, respectively, reported by other authors [10,20,22,24,32]. The Study of Women's Health Across the Nation (SWAN) reported a frequency of premature menopause of 1.1% among North American women. Statistical differences were observed according to ethnic groups and the highest frequency (1.4%) was seen among women of Hispanic origin [14]. Our figures are close to those reported by Mishra et al. [15], who in a pooled study of 51,450 postmenopausal women from nine cohort studies, identified early menopause in 7.6% and premature menopause in 2.0%. Golezar et al. [13] in a meta-analysis estimated the global prevalence of early menopause at 12.2% and premature menopause at 3.7%, figures similar to ours. Socioeconomic, nutritional, genetic, ethnic, and lifestyle factors may explain the differences [14,17].

The prevalence of subclinical hypothyroidism of 4.5% found in this study is consistent with that reported by Stuenkel [5], between 4.0 and 8.5%, with an increase to 15% in elderly populations. Likewise, 6.2% has been reported in multiethnic North

**Table 1.** Sociodemographic and clinical characteristics of all women and according to the presence or not of subclinical hypothyroidism.

	All <i>n</i> =643	With subclinical hypothyroidism <i>n</i> =29 (4.5%)	Without subclinical hypothyroidism <i>n</i> =614 (95.5%)	<i>p</i> Value*
Age (years)	$55.0 \pm 5.7$	$53.7 \pm 6.3$	$55.1 \pm 5.6$	.21 <sup>a</sup>
Age at menopause onset (years)	$46.8 \pm 4.0$	$44.0 \pm 3.7$	$47.0 \pm 3.9$	$<.001^a$
Time since menopause (years)	$8.1 \pm 6.4$	$9.7 \pm 6.9$	$8.0 \pm 6.3$	.21 <sup>b</sup>
TSH ( $\mu$ IU/mL)	$2.0 \pm 1.8$	$7.7 \pm 4.0$	$1.7 \pm 1.0$	$<.001^b$
Zulewski Scale Score	$2.7 \pm 2.0$	$6.5 \pm 2.0$	$3.0 \pm 1.8$	$<.001^a$
Last menstrual episode $\geq 45$ years	486 (75.5)	14 (48.2)	472 (76.8)	$<.001^c$
Last menstrual episode between 40 and 44 years	120 (18.6)	11 (37.9)	109 (17.7)	$<.01^c$
Last menstrual episode $< 40$ years	37 (5.7)	4 (13.8)	33 (5.3)	.05 <sup>c</sup>
Last menstrual episode $< 45$ years	157 (24.4)	15 (72.4)	142 (23.1)	$<.001^c$
Work away from home	294 (45.7)	17 (58.6)	277 (45.1)	.15 <sup>c</sup>
Abdominal hysterectomy without bilateral oophorectomy	191 (29.7)	8 (27.5)	183 (29.8)	.79 <sup>c</sup>
Abdominal hysterectomy with bilateral oophorectomy	91 (14.1)	6 (20.6)	85 (13.8)	.30 <sup>c</sup>
Perception of anxiety	107 (16.6)	4 (13.7)	103 (16.7)	.67 <sup>c</sup>
Perception of depression	87 (13.5)	4 (13.7)	83 (13.5)	.90 <sup>c</sup>
Diabetes	69 (10.7)	3 (10.3)	66 (10.7)	.90 <sup>c</sup>
Dyslipidemias	220 (34.2)	9 (31.0)	211 (34.3)	.71 <sup>c</sup>
High blood pressure	191 (29.7)	10 (34.4)	181 (29.4)	.56 <sup>c</sup>
Family history of thyroid disease	114 (17.7)	7 (24.1)	107 (17.4)	.35 <sup>c</sup>

Data are presented as mean  $\pm$  standard deviations or frequencies *n* (%).

\**p* Values as determined with <sup>a</sup>ANOVA, <sup>b</sup>the Kruskal–Wallis test, or the <sup>c</sup>Chi-square – Mantel–Haenszel test.

**Table 2.** Symptoms and signs of hypothyroidism as evaluated with the Zulewski scale among all women and the presence or not of subclinical hypothyroidism.

	All <i>n</i> =643	With subclinical hypothyroidism <i>n</i> =29 (4.5%)	Without subclinical hypothyroidism <i>n</i> =614 (95.5%)	<i>p</i> Value*
Periorbital puffiness	141 (21.9)	11 (37.9)	130 (21.1)	$<.05$
Constipation	165 (26.6)	12 (41.3)	153 (24.9)	$<.05$
Weight increase	138 (21.4)	20 (68.9)	118 (19.2)	$<.001$
Cold skin	78 (12.1)	18 (62.0)	60 (9.8)	$<.001$
Paresthesia	323 (50.2)	20 (68.9)	303 (49.3)	$<.05$
Hoarseness	132 (20.5)	17 (58.6)	125 (20.3)	$<.001$
Dry skin	262 (40.7)	18 (62.0)	244 (39.7)	$<.05$
Diminished sweating	123 (19.1)	10 (34.4)	113 (18.4)	$<.05$
Impairment of hearing	82 (12.7)	11 (37.9)	71 (11.5)	$<.001$
Coarse skin	67 (10.4)	14 (48.2)	53 (8.6)	$<.001$
Slow movements	146 (22.7)	20 (68.9)	126 (20.5)	$<.001$
Delayed ankle reflex	68 (10.6)	12 (41.3)	56 (9.1)	$<.001$
Possible hypothyroid status	85 (13.2)	19 (65.5)	66 (10.7)	$<.001$

Data are presented as frequencies *n* (%); \**p* values as determined with the Chi-square – Mantel–Haenszel test.



**Table 3.** Association between subclinical hypothyroidism and type of menopause.

Type of menopause	Age	Age at menopause	Time in postmenopause	Familial history of thyroid disease	Abdominal hysterectomy without bilateral oophorectomy	Abdominal hysterectomy with bilateral oophorectomy	Subclinical hypothyroidism	Logistic regression	
								Crude	Adjusted*
								Odds ratio	[95% confidence interval]
Last menstrual episode $\geq$ 45 ( $n=486$ )	55.4 $\pm$ 5.1	48.6 $\pm$ 2.4	6.8 $\pm$ 5.1	77 (15.8)	120 (24.6)	58 (11.9)	14 (2.9)	1	
Last menstrual episode between 40 and 44 ( $n=120$ )	53.1 $\pm$ 6.5	42.7 $\pm$ 1.3	10.3 $\pm$ 6.3	27 (22.5)	49 (40.8)	24 (20.0)	11 (9.1)	3.40 [1.50–7.69]	3.37 [1.40–8.10]
Last menstrual episode < 40 ( $n=37$ )	55.6 $\pm$ 8.2	37.2 $\pm$ 3.1	18.3 $\pm$ 9.5	10 (27.0)	22 (59.4)	9 (24.3)	4 (10.8)	4.08 [1.27–13.11]	4.31 [1.24–14.97]
Last menstrual episode < 45 ( $n=157$ )	53.7 $\pm$ 7.0	41.4 $\pm$ 3.0	12.2 $\pm$ 7.9	37 (23.5)	71 (45.2)	33 (21.0)	15 (9.5)	3.56 [1.68–7.56]	3.57 [1.57–8.10]

Data are presented as mean  $\pm$  standard deviation or frequencies,  $n$  (%).

\*Covariates: Age, familial history of thyroid disease, abdominal hysterectomy without bilateral oophorectomy, abdominal hysterectomy with bilateral oophorectomy, perception of anxiety, perception of depression, personal history of diabetes, high blood pressure, and dyslipidemias.

American women aged 42–52 [8]. In our study, women with subclinical hypothyroidism more frequently had manifestations related to hypothyroidism, mainly weight gain, paresthesias, and slow movements, and also had a greater possibility of hypothyroid status as determined with the Zulewski scale than women without subclinical hypothyroidism, 65.5% vs. 10.7%, respectively. Subclinical hypothyroidism is by definition asymptomatic; however, the affected population usually experiences symptoms of hypothyroidism with low frequency or with subtle intensity [1,2,7]. The magnitude of symptoms is influenced by two characteristics of subclinical hypothyroidism. On the one hand, the ability to evolve over months or years to overt hypothyroidism. Aggarwal and Razvi [7] consider that this behavior is an expression of the aging of the hypothalamus-pituitary-thyroid axis. On the other hand, Somwaru et al. [6] indicate that it is potentially a momentary biochemical condition. In adults over 65 years of age, they observed that only 56% still had elevated TSH values after four years of follow-up. A 46% of those with TSH levels between 4.5 and 6.9  $\mu$ IU/mL, 10% between 7.0 and 9.9  $\mu$ IU/mL, and 7% with > 10.0  $\mu$ IU/mL subsequently normalized [6].

In this study, we found a significant association between subclinical hypothyroidism and early menopause, premature menopause, and last menstrual episode before the natural age of menopause. These findings add to those reported in two studies that identified an association between thyroid immunological disturbances and premature ovarian failure. Thyroid autoimmune disease and elevated thyroid peroxidase antibodies were identified in 20–35% of women with premature ovarian failure [33,34]. In subclinical hypothyroidism, same as with menstrual cessation at an early age or before the natural age of menopause, autoimmune disorders underlie as an important etiological factor. More studies are needed reporting on the simultaneity of alterations of the hypothalamic-pituitary-thyroid axis with dysfunction of the hypothalamic-pituitary-ovarian axis in young women. Interestingly, menopause at an earlier age and subclinical hypothyroidism have been associated with cardiovascular, musculoskeletal, and metabolic disease; in addition to various psychobiological conditions that deteriorate quality of life and favor a greater probability of mortality at an early age [7,8,11,13,17–27]. These facts require further research to better explore the relationship between estrogen deprivation, the age of menopause, and thyroid disorders. It is still not clear how estrogens, hormonal factors, and ovarian follicular cells and fluids

are interrelated with thyroid autoimmunity and functional thyroid deficit. However, Kotopoulou et al. [35] pointed out an association between early menarche and a greater risk of subclinical hypothyroidism and Brown et al. [1] noted that altered thyroid function is related to menstrual irregularity, polycystic ovary syndrome, infertility, adverse obstetric outcomes, and premature ovarian failure.

### Strengths, limitations, and recommendations

The strength of this study is evidencing, with the Zulewski scale, the presence of manifestations related to hypothyroidism in a postmenopausal population that seemed to be healthy from a thyroid point of view. It points out the prevalence of subclinical hypothyroidism, early menopause, premature menopause, and last menstrual episode before the natural age of menopause, situations of which many women have little knowledge and need information that could contribute to therapeutic adherence and perception of satisfaction [36]. Our findings seek to raise awareness and draw attention to the potential relationship between two endocrinological conditions that are separately associated with several morbid conditions [7,8,11,17,19,21,24,27]. Despite this, the study has several limitations. Due to the cross-sectional design, although the associations are statistically significant they do not denote causality. No measurement of gonadotropic hormones or estradiol was performed to document the endocrine profile of the participating postmenopausal women. Antithyroid antibodies were not evaluated, we did not ask about morbid conditions present at the moment of their last menstruation, and it was not possible to identify surgical menopause as we did not ask them when the surgery was performed or menopausal status when operated. Among the participants, a low reliability coefficient was found for the Zulewski scale, so new clinical screening tools should be proposed. Although larger studies with other designs are warranted, it is recommended that women who had their last menstruation before the natural age of menopause have their thyroid hormones and antithyroid antibodies evaluated whether thyroid peroxidase or thyroglobulin antibodies [5]. Governmental and non-governmental agencies that dictate health care protocols should bear in mind the age of menopause when making suggestions on screening for thyroid disorders in women who are adult, mid-aged, or older. Health professionals without

distinction of specialty must remember that physical mental tiredness, the perception of fatigue, emotional lability, mood swings, frequent forgetfulness, intolerance to changes in temperature, changes in the skin and integuments, sleep/wake patterns, and the sensation of palpitations, are among the menopausal symptoms but they also reflect thyroid dysfunction [5]. At the same time, doctors should keep in mind that the American Thyroid Association recommends screening all adults starting at the age of 35 and repeating so every five years. The American Association of Clinical Endocrinologists recommends that older adults, but does not specify the age, be evaluated for thyroid function. The American College of Physicians suggests that women aged fifty or older with an incidental finding of thyroid abnormality should be thoroughly evaluated [5,37]. Finally, there is a need for protocols that take into consideration the age of menopause, and indicate when to explore for subclinical hypothyroidism or other thyroid disorders.

In conclusion, in this group of Colombian postmenopausal women who had not previously been diagnosed with thyroid disorders and surveyed in their community, the prevalence of subclinical hypothyroidism was found similar to that reported in other populations. Clinical manifestations related to hypothyroidism were significantly more reported by women diagnosed with subclinical hypothyroidism than among those without the condition. The presence of last menstrual bleeding before the natural age of menopause was high. Early menopause, premature menopause, and the last menstrual episode before the natural age of menopause were significantly associated with subclinical hypothyroidism.

## Acknowledgments

The authors would like to thank the women who accepted and participated in the study, Dr. Jorge Contreras Saldarriaga who was active during the fieldwork phase, Ms. Mabel Vergara Borja, and Ms. Ana Isabel Castro Lagares for their devoted coordination and logistical planning, custody of physical and digital elements and to Ms. Judith Ramos Vásquez for helping in venous blood collection, sample preparation and transfer to the laboratory. In addition, we thank the community associations, senior citizen's center and life center of the city of Cartagena, Colombia, and the management and scientific staff of Laboratorio Clínico Santa Lucía, Cartagena, Colombia.

## Disclosure statement

The author(s) declare having no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Author contributions

AM-C (conceptualization of the 'Thyroid and Menopause' project, definition of its products, data curation, methodology, and statistical analysis, writing and structuring of the initial draft, argument review, and editing of this article). AM-B (conceptualization of the research line of the project, methodology, and statistical analysis, writing, numerical revision of references, and grammatical adjustment, general revision, and editing). S S-Z (data review, writing, English grammar adjustment, networking activities, and international networking). All authors contributed conceptually and approved the final manuscript.

## Funding

The research project 'Menopause and Thyroid' was the winner in the Eleventh Call of the University of Cartagena. Colombia for the financing of research

projects and was approved by Resolution 01385-2021 of the university. Subsequently, the Women's Health Research Group and the Vice-Rector for Research of the University of Cartagena signed the Commitment Act 092-2021 for the realization of the project. The directors of the University of Cartagena, Colombia, did not participate in the design of the study, organization of the fieldwork, conservation, or analysis of the data, or in the writing of the final documents intended for scientific or general publication.

## ORCID

Álvaro Monterrosa-Castro  <http://orcid.org/0000-0002-0686-6468>  
 Angelica Monterrosa-Blanco  <http://orcid.org/0000-0001-5279-7013>  
 Sandra Sánchez-Zarza  <http://orcid.org/0000-0002-6737-6083>

## Data availability statement

All required information regarding the protocol of the study and collected data will be made available upon a reasonable request to the researchers who provide a methodologically sound proposal. Only the analysis required to achieve the aims in the approved proposal will be permitted. Proposals should be directed to [alvaromonterrosa@gmail.com](mailto:alvaromonterrosa@gmail.com)

## References

- [1] Brown EDL, Obeng-Gyasi B, Hall JE, et al. The thyroid hormone axis and female reproduction. *Int J Mol Sci.* 2023;24(12):9815. doi: [10.3390/ijms24129815](https://doi.org/10.3390/ijms24129815).
- [2] Khan SH, Ijaz A. Subclinical-Hypothyroidism: a pathology in evolution. *J Coll Physicians Surg Pak.* 2019;29(2):150–158. doi: [10.29271/jcpsp.2019.02.150](https://doi.org/10.29271/jcpsp.2019.02.150).
- [3] Hashimoto K. Update on subclinical thyroid dysfunction. *Endocr J.* 2022;69(7):725–738. doi: [10.1507/endocrj.EJ22-0182](https://doi.org/10.1507/endocrj.EJ22-0182).
- [4] Baumgartner C, Blum MR, Rodondi N. Subclinical hypothyroidism: summary of evidence in 2014. *Swiss Med Wkly.* 2014;144:w14058. doi: [10.4414/smww.2014.14058](https://doi.org/10.4414/smww.2014.14058).
- [5] Stuenkel CA. Subclinical thyroid disorders. *Menopause.* 2015;22(2):231–233. doi: [10.1097/GME.0000000000000407](https://doi.org/10.1097/GME.0000000000000407).
- [6] Somwaru LL, Rariy CM, Arnold AM, et al. The natural history of subclinical hypothyroidism in the elderly: the cardiovascular health study. *J Clin Endocrinol Metab.* 2012;97(6):1962–1969. doi: [10.1210/jc.2011-3047](https://doi.org/10.1210/jc.2011-3047).
- [7] Aggarwal N, Razvi S. Thyroid and aging or the aging thyroid? An evidence-based analysis of the literature. *J Thyroid Res.* 2013; 2013:481287–481288. doi: [10.1155/2013/481287](https://doi.org/10.1155/2013/481287).
- [8] Sowers M, Luborsky J, Perdue C, et al. Thyroid stimulating hormone (TSH) concentrations and menopausal status in women at the mid-life: SWAN. *Clin Endocrinol (Oxf).* 2003;58(3):340–347. doi: [10.1046/j.1365-2265.2003.01718.x](https://doi.org/10.1046/j.1365-2265.2003.01718.x).
- [9] Ramos-Leví AM, Marazuela M. Pathogenesis of thyroid autoimmune disease: the role of cellular mechanisms. *Endocrinol Nutr.* 2016;63(8):421–429. doi: [10.1016/j.endonu.2016.04.003](https://doi.org/10.1016/j.endonu.2016.04.003).
- [10] Tang VW, Faiman C. Premature ovarian failure: a search for circulating factors against gonadotropin receptors. *Am J Obstet Gynecol.* 1983;146(7):816–821. doi: [10.1016/0002-9378\(83\)91084-0](https://doi.org/10.1016/0002-9378(83)91084-0).
- [11] Torrealday S, Kodaman P, Pal L. Premature ovarian insufficiency - an update on recent advances in understanding and management. *F1000Res.* 2017;6:2069. doi: [10.12688/f1000research.11948.1](https://doi.org/10.12688/f1000research.11948.1).
- [12] Chon SJ, Umair Z, Yoon MS. Premature ovarian insufficiency: past, present, and future. *Front Cell Dev Biol.* 2021;9:672890. doi: [10.3389/fcell.2021.672890](https://doi.org/10.3389/fcell.2021.672890).
- [13] Golezar S, Ramezani Tehrani F, Khazaei S, et al. The global prevalence of primary ovarian insufficiency and early menopause: a meta-analysis. *Climacteric.* 2019;22(4):403–411. doi: [10.1080/13697137.2019.1574738](https://doi.org/10.1080/13697137.2019.1574738).
- [14] Luborsky JL, Meyer P, Sowers MF, et al. Premature menopause in a multi-ethnic population study of the menopause transition. *Hum Reprod.* 2003;18(1):199–206. doi: [10.1093/humrep/deg005](https://doi.org/10.1093/humrep/deg005).
- [15] Mishra GD, Pandeya N, Dobson AJ, et al. Early menarche, nulliparity and the risk for premature and early natural menopause. *Hum Reprod.* 2017;32(3):679–686. doi: [10.1093/humrep/dew350](https://doi.org/10.1093/humrep/dew350).

- [16] “The 2022 Hormone Therapy Position Statement of The North American Menopause Society” Advisory Panel. The 2022 hormone therapy position statement of the North American menopause society. *Menopause*. 2022;29(7):767–794.
- [17] Yang Y, Huang W, Yuan L. Effects of environment and lifestyle factors on premature ovarian failure. *Adv Exp Med Biol*. 2021;1300:63–111.
- [18] Divaris E, Anagnostis P, Gkekas NK, et al. Early menopause and premature ovarian insufficiency may increase the risk of sarcopenia: a systematic review and meta-analysis. *Maturitas*. 2023;175:107782. doi: [10.1016/j.maturitas.2023.05.006](https://doi.org/10.1016/j.maturitas.2023.05.006).
- [19] Gong D, Sun J, Zhou Y, et al. Early age at natural menopause and risk of cardiovascular and all-cause mortality: a meta-analysis of prospective observational studies. *Int J Cardiol*. 2016;203:115–119. doi: [10.1016/j.ij-card.2015.10.092](https://doi.org/10.1016/j.ij-card.2015.10.092).
- [20] Tao XY, Zuo AZ, Wang JQ, et al. Effect of primary ovarian insufficiency and early natural menopause on mortality: a meta-analysis. *Climacteric*. 2016;19(1):27–36. doi: [10.3109/13697137.2015.1094784](https://doi.org/10.3109/13697137.2015.1094784).
- [21] Guo C, Li Q, Tian G, et al. Association of age at menopause and type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Prim Care Diabetes*. 2019;13(4):301–309. doi: [10.1016/j.pcd.2019.02.001](https://doi.org/10.1016/j.pcd.2019.02.001).
- [22] Faubion SS, Kuhle CL, Shuster LT, et al. Long-term health consequences of premature or early menopause and considerations for management. *Climacteric*. 2015;18(4):483–491. doi: [10.3109/13697137.2015.1020484](https://doi.org/10.3109/13697137.2015.1020484).
- [23] Van Ommen CE, King EM, Murray MCM. Age at menopause in women living with HIV: a systematic review. *Menopause*. 2021;28(12):1428–1436. doi: [10.1097/GME.0000000000001871](https://doi.org/10.1097/GME.0000000000001871).
- [24] Shuster LT, Rhodes DJ, Gostout BS, et al. Premature menopause or early menopause: long-term health consequences. *Maturitas*. 2010;65(2):161–166. doi: [10.1016/j.maturitas.2009.08.003](https://doi.org/10.1016/j.maturitas.2009.08.003).
- [25] de Taraciuk MB, Nolting M, Fernandez G, et al. Psychological assessment of patients with premature ovarian failure. *Gynecol Endocrinol*. 2008;24(1):44–53. doi: [10.1080/09513590701668866](https://doi.org/10.1080/09513590701668866).
- [26] Roa-Díaz ZM, Wehrli F, Lambrinoudaki I, et al. Early menopause and cardiovascular risk factors: a cross-sectional and longitudinal study. *Menopause*. 2023;30(6):599–606. doi: [10.1097/GME.0000000000002184](https://doi.org/10.1097/GME.0000000000002184).
- [27] de Souza Macêdo PR, Rocha TN, Gomes Fernandes SG, et al. Possible association of early menopause with worse physical function: a systematic review. *Menopause*. 2021;28(4):467–475. doi: [10.1097/GME.0000000000001712](https://doi.org/10.1097/GME.0000000000001712).
- [28] von Elm E, Altman DG, Egger M, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624):806–808. doi: [10.1136/bmj.39335.541782.AD](https://doi.org/10.1136/bmj.39335.541782.AD).
- [29] World Health Organization. Research on the menopause in the 1990's: a report of the WHO scientific group. Geneva, Switzerland: world Health Organization. 1996. p. 1–7.
- [30] Zulewski H, Müller B, Exer P, et al. Estimation of tissue hypothyroidism by a new clinical score: evaluation of patients with various grades of hypothyroidism and controls. *J Clin Endocrinol Metab*. 1997;82(3):771–776. doi: [10.1210/jcem.82.3.3810](https://doi.org/10.1210/jcem.82.3.3810).
- [31] Ruge JB, Bougatsos C, Chou R. Screening and treatment of thyroid dysfunction: an evidence review for the US preventive services task force. *Ann Intern Med*. 2015;162(1):35–45. doi: [10.7326/M14-1456](https://doi.org/10.7326/M14-1456).
- [32] Nelson HD. Menopause. *Lancet*. 2008;371(9614):760–770. doi: [10.1016/S0140-6736\(08\)60346-3](https://doi.org/10.1016/S0140-6736(08)60346-3).
- [33] Rudnicka E, Kruszewska J, Klicka K, et al. Premature ovarian insufficiency - aetiopathology, epidemiology, and diagnostic evaluation. *Prz Menopauzalny*. 2018;17(3):105–108. doi: [10.5114/pm.2018.78550](https://doi.org/10.5114/pm.2018.78550).
- [34] Jha V, Goswami D, Ayesha. Premature ovarian failure: an association with autoimmune diseases. *J Clin Diagn Res*. 2016;10(10):QC10–QC12. doi: [10.7860/JCDR/2016/22027.8671](https://doi.org/10.7860/JCDR/2016/22027.8671).
- [35] Kotopoulou M, Stratigou T, Antonakos G, et al. Early menarche is independently associated with subclinical hypothyroidism: a cross-sectional study. *Horm Mol Biol Clin Investig*. 2019;38(1):1–7. doi: [10.1515/hmbci-2018-0079](https://doi.org/10.1515/hmbci-2018-0079).
- [36] Yeganeh L, Boyle JA, Johnston-Ataata K, et al. Positive impact of a co-designed digital resource for women with early menopause. *Menopause*. 2022;29(6):671–679. doi: [10.1097/GME.0000000000001972](https://doi.org/10.1097/GME.0000000000001972).
- [37] Garber JR, Cobin RH, Gharib H, et al. American association of clinical endocrinologists and American thyroid association taskforce on hypothyroidism in adults. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American association of clinical endocrinologists and the American thyroid association. *Endocr Pract*. 2012;18(6):988–1028. doi: [10.4158/EP12280.GL](https://doi.org/10.4158/EP12280.GL).