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Association between anxiety and severe quality-of-life impairment in postmenopausal women: analysis of a multicenter Latin American cross-sectional study

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Abstract

Objective: To evaluate associations between anxiety and severe impairment of quality of life (QoL) in Latin American postmenopausal women.

Methods: This was a secondary analysis of a multicenter cross-sectional study among postmenopausal women aged 40 to 59 from 11 Latin American countries. We evaluated anxiety (The Goldberg Depression and Anxiety Scale), and QoL (Menopause Rating Scale [MRS]), and included sociodemographic, clinical, lifestyle, and anthropometric variables in the analysis. Poisson family generalized linear models with robust standard errors were used to estimate prevalence ratios (PRs) and 95% CIs. There were two adjusted models: a statistical model that included variables associated with the outcomes in bivariate analyses, and an epidemiologic model that included potentially confounding variables from literature review.

Results: Data from 3,503 women were included; 61.9% had anxiety (Goldberg). Severe QoL impairment (total MRS score $\geq$17) was present in 13.7% of women, as well as severe symptoms (MRS subscales): urogenital (25.5%), psychological (18.5%), and somatic (4.5%). Anxiety was independently associated with severe QoL impairment and severe symptoms in the epidemiological (MRS total score: PR 3.6, 95% CI, 2.6-5.0; somatic: 5.1, 95% CI, 2.6-10.1; psychological: 2.8, 95% CI, 2.2-3.6; and urogenital: 1.4, 95% CI, 1.2-1.6) and the statistical model (MRS total score: PR 3.5, 95% CI, 2.6-4.9; somatic: 5.0, 95% CI, 2.5-9.9; psychological: 2.9, 95% CI, 2.2-3.7; and urogenital: 1.4; 95% CI, 1.2-1.6).

Conclusions: In this postmenopausal Latin American sample, anxiety was independently associated with severe QoL impairment. Hence, screening for anxiety in this population is important.

Key Words: Anxiety – Climacteric – Latin America – Menopause – Quality of life – Symptoms.

Menopause marks the end of the female reproductive period. During the menopausal transition there is a progressive and irreversible decline of ovarian function, which causes an array of symptoms.[1,2] These can be severe enough to negatively impact female health and quality of life (QoL).[3-5] QoL encompasses several factors that require assessment and objective measuring for both epidemiological and clinical purposes, particularly during and after menopause.[6] Indeed, hormonal changes may impact several domains such as the somatic-vegetative, psychological, and urogenital.[7]

Aside from hormonal changes, age,[3,5,8] socioeconomic status,[3,9] altitude of residency,[3] ethnicity, and cultural aspects[10,11] may also correlate with more intense menopausal symptoms and hence impaired QoL. On the other hand, lifestyle factors such as cigarette smoking,[12] alcohol consumption,[13] sedentary lifestyle, obesity,[13,14] and mental illnesses, especially mood disorders such as anxiety and depression[3] are also important.

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Of the above-mentioned features, mood problems are of particular importance as they increase during the menopausal transition.[15] In particular, the association between anxiety and QoL during female midlife is a topic of growing interest.[16] Anxiety is highly prevalent during the peri- and early postmenopausal stage,[15] mainly due to hormonal changes.[17,18] In addition, other aspects seem to explain the association between anxiety and QoL including inflammation,[19] the presence of hot flashes,[20] and certain neurotransmitters.[21,22] However, there are some controversies regarding the explanation of the biological and psychological plausibility of these associations. There are authors who claim that severe menopausal symptoms predispose to more anxiety and/or depression,[20,23] whereas others argue the opposite, that it is the hot flashes and sleep disturbances that lead to depression and anxiety in postmenopausal women.[24,25] Furthermore, research suggests that social and even geographical patterns may influence this association.[3] Thus, it becomes relevant to investigate these relations in a population with particular characteristics.

Despite the fact that Latin American women have certain features that typify them as a particular group such as an earlier onset of menopause and therefore a higher exposure to hypoestrogenism,[26] as well as a high prevalence of anxiety,[27] we have not found research analyzing the influence of anxiety on the QoL of postmenopausal Latin American women residing in their countries of origin. Hence, the aim of the present secondary analysis was to ascertain whether there is an association between anxiety and severe QoL impairment in this postmenopausal population, controlling for demographic, clinical, anthropometric, and lifestyle variables. The results of this research may provide useful information for the comprehensive clinical management of postmenopausal women.

METHODS

Study design and selection of participants

The present document is a secondary data analysis of a cross-sectional, multicenter study from the Collaborative Group for Research of the Climacteric in Latin America (REDLINC V), which included women (pre-, peri-, and postmenopausal) residing in 11 Latin American countries and analyzed sleep problems.[28] However, for this subanalysis we only included postmenopausal women: (1) 12 months or more of absent menses or (2) those post bilateral oophorectomy, as defined by the Executive Summary of Stages of Reproductive Aging Workshop.[29]

Participants were randomly selected from those accompanying family members seeking health care in 22 hospitals from 11 countries: México, Panamá, Paraguay, Dominican Republic, Perú, Bolivia, Chile, Ecuador, Colombia, Argentina, and Uruguay. Those aged 40 to 59 years were included and requested to fill out the surveys after being informed about the research and providing written consent. Individuals with the following conditions were excluded from the analysis: psychiatric illness under drug treatment, mental retardation, stroke sequelae, malignancy, or chronic kidney disease on hemodialysis, peritoneal dialysis or having had a kidney transplant. More details regarding the methodology used in the REDLINC V study can be consulted elsewhere.[28]

A total of 6,598 women were invited to participate in the REDLINC V study. 7.9% declined participation, leaving 6,079 who gave consent and provided complete records for analysis.[28] Only the data of those defined as postmenopausal were included for this secondary analysis (n = 3,503).

Sample size and statistical power calculation

NQuery Advisor Software version 6.0 (Statistical Solutions, Cook, Ireland) was used to calculate statistical power with a two-tailed, 95% CI, and an estimated prevalence ratio (PR) of 1.66 based on the report of Joffe et al[16] that addresses the association between anxiety and QoL in 425 mid-aged women of the Study of Women's Health Across the Nation.[16] Taking into account, a 24.9% prevalence of severe QoL impairment reported by Chedraui et al[3] for mid-aged Latin American women, a statistical power of 92% was estimated with 3,503 participants.

Variables and measurements

Exposure variable: Anxiety

The validated Spanish language version of the Goldberg Anxiety and Depression Scale was used to measure anxiety (anxiety subscale).[30] This instrument consists of two subscales, one for depression and one for anxiety, each with nine items, all having dichotomous responses (yes/no). The two subscales have the same structure: four screening items and then five items that are answered only if two or more positive screening responses are encountered. Anxiety was identified as five or more positive responses including minimum two items from the screening section. The Goldberg Scale has a reported sensitivity of 0.82, specificity of 0.91 (for either anxiety or depression) and a positive predictive value of 0.56.[30,31]

Response variable: quality of life

The Menopause Rating Scale (MRS) was used to assess QoL. The tool has been translated to more than 27 languages and used worldwide.[7,32] For the present research we used the Spanish language version validated in various Latin American studies.[3,8,11]

The MRS consists of 11 items that assess menopausal symptoms which are grouped into three subscales: (a) somato-vegetative—vasomotor symptoms (hot flashes), heart discomfort, sleeping problems, and muscle and joint problems; (b) psychological—depressive mood, irritability, anxiety, physical and mental exhaustion; and (c) urogenital—sexual problems, bladder problems and vaginal dryness. Each item has a Likert scale score from 0 to 4 (0 = not present, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe). Scores achieved for each item are added to provide the total score of its corresponding subscale. The total MRS score is the sum of the subscale scores. A total MRS score $\geq$17 was defined as

severe QoL impairment.[33] Heinemann et al[7,32] have proposed cutoff values to define severe symptoms according to each subscale: somatic (>8), psychological (>6), and urogenital (>3). Regarding the internal consistency of the MRS, as measured by Cronbach α, coefficients have been found between 0.80 and 0.85 in the countries where the tool has been validated.[34]

Measurement of control variables

Sociodemographic variables included age (years), educational level, parity, and presence of a steady partner (yes/no). Clinical variables related to menopause included (1) the type of menopause defined as natural or surgical (by bilateral oophorectomy), (2) the postmenopausal stage was categorized as early (≤5 years since menopause onset) or late (>5 years since menopause onset) according to Stages of Reproductive Aging Workshop criteria,[29] (3) the history of hysterectomy (yes/no), and (4) the current use of hormone therapy (HT) (yes/no). Other clinical variables included diabetes mellitus (yes/no), hypertension (yes/no), or arthrosis (yes/no).

Depression was measured using the depression subscale of the Goldberg Anxiety and Depression Scale (four screening items and five items to be answered only if two or more positive screening responses are encountered). Depression was defined if four or more of the responses were positive, including at least two of the screening items.[30]

Tobacco and alcohol consumption were included as life style variables. Smoking was categorized as never, quit a year or more ago, quit less than a year ago, and currently smokes. Alcohol habit was assessed using the Short Scale of Abnormal Drinking (Spanish acronym EBBA), which was designed to detect risky drinking through seven dichotomous (Yes/No) response items. Individuals with three or more positive responses were defined as problem drinkers.[35]

Body mass index (BMI) was calculated as weight in kilograms over squared height in meters (kg/m^2). According to this, BMI was categorized as normal (18-24.99 kg/m^2) or increased (≥25 kg/m^2). Individuals with an increased BMI were further subcategorized as being overweight (25-29.99 kg/m^2) or obese (≥30 kg/m^2).[36]

Ethical aspects

The research protocol of the REDLINC V study was reviewed and approved by the Bioethics Committee of the Pro Salud de la Mujer Foundation, Santiago de Chile, Chile. The present secondary analysis was approved by the Ethics Committee of Universidad Peruana de Ciencias Aplicadas (UPC) of Lima, Perú. The primary data collection included the signing of an informed consent and the fulfillment of the guidelines recommended in the Declaration of Helsinki.[37]

Statistical analysis

STATA software version 11.0 (Stata Corp., College Station, TX) was used for analysis. Data are presented as mean ± standard deviations for numeric variables (ie, age, BMI) or absolute and relative frequencies for categorical variables. The normality of the data distribution of numerical variables was assessed with the Shapiro-Wilk test. The crude association between anxiety and severe QoL impairment and severe symptoms (according to each MRS subscale) was measured with the χ^2 test, with previous assessment of assumptions based on expected values.

Generalized linear models with a Poisson link function and robust standard errors were used to estimate prevalence ratios and 95% CIs. A total of 12 models were developed for the four outcomes: severe QoL impairment, severe somatic symptoms, severe psychological symptoms, and severe urogenital symptoms. For each of the outcomes we performed a crude model, a statistically adjusted model (adjustment included the variables with statistically significant associations with each of the outcomes in the bivariate analysis) and an epidemiologically adjusted model (adjustment included potentially confounding variables according to the reviewed literature and directed acyclic graphs). The Newton-Raphson method was used for the measurement of maximum likelihood. For all calculations, a P value of <0.05 was defined as statistically significant.

RESULTS

General characteristics of the postmenopausal women included in the analysis are depicted in Table 1. Mean age of the sample was 52.5 ± 4.7 years, 77.6% had a secondary or higher education, 8.2% had no children, and 33.4% reported having a steady partner. Also, 10.4% had diabetes mellitus, 28.0% hypertension, and 10.5% arthrosis. Nearly 60% of surveyed women were overweight or obese and 18.4% reported HT use. According to the Goldberg Scale, almost half had depression and 61.9% anxiety. 21.3% currently smoked and 2.7% were problem alcohol drinkers. 13.7% displayed severe QoL impairment (total MRS score ≥17); and according to each MRS subscale: women presented severe symptoms in 4.5% (somatic), 18.5% (psychological) and 25.5% (urogenital).

Frequency of severe QoL impairment (total MRS score ≥17) and severe symptoms (for each MRS subscale) among studied women according to the presence or absence of anxiety is displayed in Fig. 1. Women with anxiety showed significantly higher rates of severe QoL impairment and more severe symptoms.

Upon bivariate analysis, severe QoL impairment was positively associated with anxiety, depression, education, parity, having a steady partner, past or current smoking, higher BMI, hypertension, and arthrosis (Table 2). Bivariate analyses of factors associated with severe symptoms (according to each MRS subscale) are presented in Table 3. Anxiety, depression, past or current smoking, higher BMI, hypertension, and arthrosis were independently and positively associated with severe symptoms of all three subscales. Severe somatic symptoms were positively associated with having a steady partner and a history of hysterectomy. Severe urogenital symptoms were positively associated with education,

TABLE 1. *General characteristics of the postmenopausal women included in the analysis (n = 3,503)*

	n (%)
Age, y	52.5 ± 4.7
40-44	249 (7.1)
45-49	605 (17.3)
50-54	1,198 (34.2)
55-59	1,451 (41.4)
Educational level	
Primary	784 (22.4)
Secondary	1,197 (34.2)
Non-university higher education	621 (17.7)
University	901 (25.7)
Has children	3,217 (91.8)
Has a stable partner	1,171 (33.4)
Surgical menopause	434 (12.4)
Postmenopausal stage, y	
Early (≤5)	1,758 (50.2)
Late (>5)	1,745 (49.8)
History of hysterectomy	956 (27.3)
HT use	645 (18.4)
BMI, kg/m^2	26.6 ± 0.8
Normal (18-24.99)	1,429 (40.8)
Overweight (25-29.99)	1,403 (40.1)
Obesity (≥30)	671 (19.2)
Diabetes mellitus	365 (10.4)
Hypertension	981 (28.0)
Arthrosis	368 (10.5)
Smoking	
Never	2,521 (72.0)
Quit a year or more ago	175 (5.0)
Quit smoking <1 year ago	378 (10.8)
Currently smokes	429 (21.3)
Problem drinker	94 (2.7)
Depression[a]	1,720 (49.1)
Anxiety[a]	2,167 (61.9)
Quality of life (MRS)	
Severe impairment of quality of life (total score ≥17)	478 (13.7)
Severe somatic symptoms (score >8)	156 (4.5)
Severe psychological symptoms (score >6)	648 (18.5)
Severe urogenital symptoms (score >3)	893 (25.5)

Information are presented as mean ± standard deviations or frequencies *n* (%).
BMI, body mass index; HT, hormone therapy; MRS, Menopause Rating Scale.
[a]As determined with the Goldberg Anxiety and Depression Scale.

HT use, parity, having a steady partner and being in an early postmenopausal stage. Finally, severe psychological symptoms were positively associated with educational level (Table 3). Generalized linear models revealed an independent positive association between anxiety and severe QoL impairment and severe symptoms, according to epidemiological (MRS total score: PR 3.6, 95% CI, 2.6-5.0; somatic: 5.1, 95% CI, 2.6-10.1; psychological: 2.8, 95% CI, 2.2-3.6, and urogenital: 1.4, 95% CI, 1.2-1.6) and statistical criteria (MRS total score: PR 3.5, 95% CI, 2.6-4.9; somatic: 5.0, 95% CI, 2.5-9.9; psychological: 2.9, 95% CI, 2.2-3.7, and urogenital: 1.4; 95% CI, 1.2-1.6) (Table 4).

DISCUSSION

These findings shows that in this postmenopausal female Latin American sample anxiety was associated with severe QoL impairment, independent of other sociodemographic, clinical, and psychological variables. It should be pointed out that this association was observed both globally (using total MRS scores to define QoL impairment) and for each of the three studied subscales of the MRS: somatic, psychological, and urogenital, although the magnitude of the association was higher with the first subscale.

Although previous studies have assessed such an association mainly among perimenopausal women, to the best of our knowledge this is the first to use the MRS to evaluate the potential influence of anxiety over QoL specifically in postmenopausal Latin American women. Therefore, it is difficult to directly compare our results with those of other studies. However, since the MRS is based on the presence and severity of a particular symptom profile, we performed an indirect analysis, focusing on the independent value of each subscale that represents a group of symptoms. As stated above, we found that the strongest association was between anxiety and severe somatic symptoms.

Our study shows that the prevalence of severe somatic symptoms in postmenopausal women with anxiety was five times higher than that observed among those without anxiety. This is consistent with results described in other studies in which a significant association between anxiety and somatic-vegetative symptoms, particularly hot flashes, has been found.[20,38] For example, Juang et al[20] reported a strong association between anxiety and vasomotor symptoms in postmenopausal women, regardless of the presence of a sleep disorder. Mechanisms explaining this association are still not well established. However, anxiety had been correlated to increased levels of norepinephrine and serotonin, which in turn can increase the frequency of vasomotor symptoms due to their important role in thermoregulation.[21] Similarly, increased proinflammatory cytokine interleukin-6 levels had been found in mid-aged women with psychological symptoms.[19] This cytokine has the ability to stimulate the hypothalamic-pituitary-adrenocortical axis with the consequent release of corticotropin releasing factor,[39] which could explain increased menopausal symptoms as well as cardiovascular risk.[40] In fact, some studies have correlated anxiety with increased cardiovascular morbidity and mortality.[41] To note, as already mentioned, is the fact that unlike our study, the association between anxiety and impaired QoL had mostly

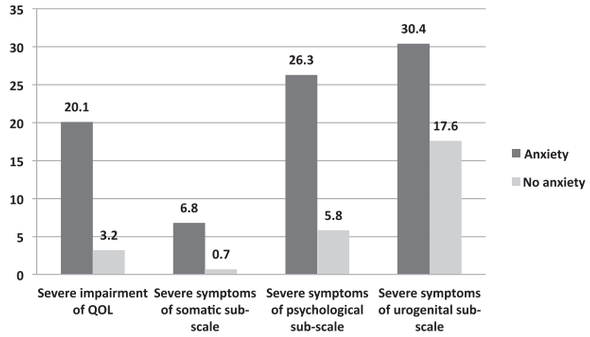

FIG. 1. Frequency of severe QoL impairment (total MRS score ≥17) and severe symptoms (for each MRS subscale) among studied postmenopausal women (n = 3,503) in accordance to the presence or not of anxiety. MRS, Menopause Rating Scale; QoL, quality of life.

TABLE 2. *Factors associated with severe QoL impairment according to the MRS in women included in the analysis (n = 3,503)*

	QoL		
	With severe QoL impairment[a] $n = 478$	Without severe QoL impairment $n = 3,025$	P^b
Anxiety			
Without anxiety (n = 1,336)	43 (3.2)	1.93 (96.8)	<0.001
With anxiety (n = 2,167)	435 (20.1)	1,732 (79.9)	
Depression			
Without depression (n = 1,783)	91 (5.1)	1,692 (94.9)	<0.001
With depression (n = 1,720)	387 (22.5)	1,333 (77.5)	
HT use			
No (n = 2,858)	393 (13.8)	2,465 (86.3)	0.700
Yes (n = 645)	85 (13.2)	560 (86.8)	
Age (years)			
40-44 (n = 249)	26 (10.8)	214 (89.2)	0.132
45-49 (n = 605)	89 (14.5)	525 (85.5)	
50-54 (n = 1,198)	181 (15.1)	1,017 (84.9)	
55-59 (n = 1,451)	182 (12.5)	1,269 (87.5)	
Education level			
Primary (n = 784)	111 (14.2)	672 (85.8)	0.009
Secondary (n = 1,197)	167 (14.0)	1,030 (86.0)	
Non-university higher education (n = 621)	105 (16.9)	516 (83.1)	
University (n = 901)	95 (10.5)	806 (89.5)	
Parity			
No children (n = 286)	25 (8.2)	261 (91.3)	0.012
Parous (n = 3,217)	453 (14.1)	2,764 (85.9)	
Has a steady partner			
No (n = 2,332)	129 (11.0)	1,042 (89.0)	<0.001
Yes (n = 1,171)	349 (14.9)	1,983 (85.0)	
Type of menopause			
Surgical (n = 434)	67 (15.4)	367 (84.6)	0.245
Natural (n = 3,079)	411 (13.4)	2,658 (86.6)	
Postmenopausal Stage			
Early (n = 1,758)	246 (14.0)	1,512 (86.0)	0.547
Late (n = 1,745)	232 (13,3)	1,513 (86.7)	
Hysterectomy			
Yes (n = 956)	141 (14.8)	815 (85.3)	0.244
No (n = 2,547)	337 (13.2)	2,210 (86.8)	
BMI			
Normal (n = 1,429)	148 (10.4)	1,281 (89.6)	<0.001
Overweight (n = 1,403)	181 (12.9)	1,222 (87.1)	
Obesity (n = 671)	149 (22.2)	522 (77.8)	
Diabetes mellitus			
Present (n = 365)	51 (14.0)	314 (86.0)	0.847
Absent (n = 3,138)	427 (13.6)	2,711 (86.4)	
Hypertension			
Present (n = 981)	170 (17.3)	811 (82.7)	<0.001
Absent (n = 2,522)	308 (12.2)	2,214 (87.8)	
Arthrosis			
Present (n = 368)	88 (23.9)	280 (76.1)	<0.001
Absent (n = 3,135)	390 (12.4)	2,745 (87.6)	
Smoking habit			
Never (n = 2,521)	315 (12.5)	2,206 (87.5)	0.017
Quit ≥1 year ago (n = 175)	28 (16.0)	147 (84.0)	
Quit <1 year ago (n = 378)	64 (16.9)	314 (87.1)	
Currently smokes (n = 429)	71 (16.6)	358 (83.5)	
Alcohol habit			
Absent (n = 3,409)	460 (13.5)	2,949 (86.5)	0.115
Present (n = 94)	18 (19.2)	76 (80.9)	

Information are presented as frequencies *n* (%).
BMI, body mass index; HT, hormone therapy; MRS, Menopause Rating Scale; QoL, quality of life.
[a]Total MRS scores ≥17.
[b]*P* values obtained by the χ^2 test.

been studied among pre- and perimenopausal women,[16,42] probably because some studies reported that vasomotor symptoms were associated with fluctuating estrogenic levels.[22,43] However, other authors conclude that affective disorders and vasomotor symptoms (during the menopausal transition) are associated with an imbalance of neurotransmitters[21,22] caused by estrogenic deficiency; hence, the greatest impact is expected during the postmenopausal stage. Thus, our findings, as that of others, suggest an interrelationship between anxiety and vasomotor symptoms during the

TABLE 3. *Factors associated with severe symptoms according to the subscales of the MRS (somatic, psychological and urogenital) (n = 3,503)*

	Severe somatic symptoms			Severe psychological symptoms			Severe urogenital symptoms		
	Yes $n = 156$	No $n = 3,347$	P^a	Yes $n = 648$	No $n = 2,855$	P^a	Yes $n = 893$	No $n = 2,610$	P^a
Anxiety									
No	9 (0.7)	1,327 (99.3)	<0.001	78 (5.8)	1,258 (94.2)	<0.001	235 (17.6)	1,101 (82.4)	<0.001
Yes	147 (6.8)	2,020 (93.2)		570 (26.3)	1,597 (73.7)		658 (30.4)	1,509 (69.6)	
Depression									
No	23 (1.3)	1,760 (98.7)	<0.001	145 (8.1)	1,638 (91.9)	<0.001	338 (19.0)	1,445 (81.0)	<0.001
Yes	133 (7.7)	1,587 (92.3)		503 (29.2)	1,217 (70.8)		555 (32.3)	1,165 (67.7)	
HT use									
No	129 (4.5)	2,729 (95.5)	0.716	522.(18.3)	2,336 (81.7)	0.453	693 (24.3)	2,165 (75.7)	<0.001
Yes	27 (4.2)	618 (95.8)		126 (19.5)	519 (80.5)		200 (31.0)	445 (69.0)	
Age, y									
40-44	8 (3.3)	232 (96.7)	0.07	49 (20.4)	191 (79.6)	0.051	55 (22.9)	185 (77.1)	0.295
45-49	29 (4.7)	585 (95.3)		124 (20.2)	490 (79.8)		169 (27.5)	445 (72.5)	
50-54	67 (5.6)	1,131 (94.4)		238 (19.9)	960 (80.1)		316 (26.4)	882 (73.6)	
55-59	52 (3.6)	1,399 (96.4)		237 (16.3)	1,214 (83.7)		353 (24.3)	1,098 (75.7)	
Education level									
Primary	44 (5.6)	740 (94.4)	0.183	154 (19.7)	630 (90.3)	0.014	192 (24.6)	592 (75.4)	0.019
Secondary	50 (4.2)	1,147 (95.8)		231 (19.3)	966 (80.7)		294 (24.6)	903 (75.4)	
Non-university higher education	32 (5.2)	589 (94.9)		130 (20.9)	491 (79.1)		191 (30.8)	430 (69.2)	
University	30 (3.3)	871 (96.7)		133 (14.8)	768 (85.2)		216 (24.0)	685 (76.0)	
Parity									
No children	12 (4.2)	274 (95.8)	0.826	41 (14.3)	245 (85.7)	0.058	58 (20.3)	228 (79.7)	0.035
Parous	144 (4.5)	3,073 (95.5)		607 (8.9)	2,610 (81.1)		835 (26.0)	2,382 (74.0)	
Has a steady partner									
No	38 (3.3)	1,133 (95.8)	0.014	217 (18.5)	954 (81.5)	0.972	203 (17.3)	968 (82.7)	<0.001
Yes	118 (5.1)	2,214 (94.9)		431 (18.5)	1,901 (81.5)		690 (29.6)	1,642 (70.4)	
Type of menopause									
Surgical	23 (5.3)	411 (94.7)	0.361	95 (21.9)	339 (78.1)	0.052	116 (26.7)	318 (73.3)	0.528
Natural	133 (4.3)	2,936 (95.7)		553 (18.0)	2,516 (82.0)		777 (25.3)	2,292 (74.7)	
Postmenopausal stage									
Early	81 (4.6)	1,677 (95.4)	0.657	331 (18.8)	1,427 (81.2)	0.614	475 (27)	1,283 (73)	0.037
Late	75 (4.3)	1,670 (95.7)		317 (18.2)	1,428 (81.8)		418 (24)	1,327 (76)	
Hysterectomy									
Yes	66 (6.9)	890 (93.1)	<0.001	195 (20.4)	761 (79.6)	0.076	256 (26.8)	700 (73.2)	0.285
No	90 (3.5)	2,457 (96.5)		453 (17.8)	2,094 (82.2)		637 (25.0)	1,910 (75.0)	
BMI									
Normal	43 (3.0)	1,386 (97.0)	<0.001	225 (15.8)	1,024 (84.3)	<0.001	336 (23.5)	1,093 (76.5)	0.004
Overweight	64 (4.6)	1,339 (95.4)		255 (18.2)	1,148 (81.8)		354 (25.2)	1,049 (74.8)	
Obesity	49 (7.3)	622 (92.7)		168 (25.0)	503 (75.0)		203 (30.3)	468 (69.7)	
Diabetes mellitus									
Absent	137 (4.4)	3,001 (95.6)	0.462	571 (18.2)	2,567 (81.8)	0.177	789 (25.1)	2,349 (74.7)	0.165
Present	19 (5.2)	346 (94.8)		77 (21.1)	288 (78.9)		104 (28.5)	261 (71.5)	
Hypertension									
Absent	99 (3.9)	2,423 (96.1)	0.015	443 (17.8)	2,079 (82.4)	0.023	619 (24.6)	1,903 (75.5)	0.039
Present	57 (5.8)	924 (94.2)		205 (20.9)	776 (79.1)		274 (27.9)	707 (72.1)	
Arthrosis									
Absent	119 (3.8)	3,016 (96.2)	<0.001	554 (17.8)	2,581 (82.3)	<0.001	767 (24.5)	2,368 (75.5)	<0.001
Present	37 (10)	331 (90)		94 (25.5)	274 (74.5)		126 (34.2)	242 (65.8)	
Smoking habit									
Never has smoked	98 (3.9)	2,423 (96.1)	0.015	424 (16.8)	2,097 (83.2)	0.001	629 (25)	1,892 (75)	0.013
Quit ≥1 year	15 (8.6)	160 (91.4)		37 (21.1)	138 (78.9)		41 (23.4)	134 (76.6)	
Quit <1 year	21 (5.6)	357 (94.4)		84 (22.2)	294 (77.8)		122 (32.3)	256 (67.7)	
Currently smokes	22 (5.1)	407 (94.9)		103 (24.0)	326 (76.0)		101 (23.6)	328 (76.5)	
Alcohol habit									
Absent	148 (4.3)	3,261 (95.7)	0.053	625 (18.3)	2,784 (81.7)	0.131	866 (25.4)	2,543 (74.6)	0.466
Present	8 (8.5)	86 (91.5)		23 (24.5)	71 (75.5)		27 (28.7)	67 (71.3)	

Information are presented as frequencies *n* (%).
BMI, body mass index; HT, hormone therapy; MRS, Menopause Rating Scale
[a]*P* values obtained by the χ^2 test.

postmenopausal stage. This leads us to speculate that they have similar pathophysiological mechanisms.

Similarly, a significant association between anxiety and the presence of severe urogenital symptoms was found in our study. Interestingly, although the frequency of severe urogenital symptoms was higher in women with anxiety, as compared to somatic and psychological ones (30.4% vs 6.8% and 26.3%, respectively, Fig. 1); regression models found that the association between urogenital symptoms and anxiety was the weakest (Table 4). There is no defined mechanism to

TABLE 4. *Association between anxiety and severe QoL impairment and symptoms severity (MRS) in the studied population (n = 3,503)*

	Crude		Adjusted reduced (epidemiological models)			Adjusted reduced (statistical models)		
	PR	95% CI	PR	95% CI	*P*	PR	95% CI	*P*
Anxiety and severe QoL impairment (total MRS score ≥17)								
Without anxiety	Base		Base			Base		
With anxiety	6.2	4.6-8.5	**3.6**[a]	2.6-5	<0.001	**3.5**[b]	2.6-4.9	<0.001
Anxiety and presence of severe somatic symptoms (score >8)								
Without anxiety	Base		Base			Base		
With anxiety	10.1	5.2-19.7	**5.1**[c]	2.6-10.1	<0.001	**5**[d]	2.5-9.9	<0.001
Anxiety and presence of severe psychological symptoms (score >6)								
Without anxiety	Base		Base			Base		
With anxiety	4.5	3.6-5.7	**2.8**[e]	2.2-3.6	<0.001	**2.9**[f]	2.2-3.7	<0.001
Anxiety and presence of severe urogenital symptoms (score >3)								
Without anxiety	Base		Base			Base		
With anxiety	1.7	1.5-2	**1.4**[g]	1.2-1.6	<0.001	**1.4**[h]	1.2-1.6	<0.001

The bold values represent the prevalence ratio (PR) adjusted to the epidemiological and statistical model.
BMI, body mass index; HT, hormone therapy; MRS, Menopause Rating Scale; PR, prevalence ratio; QoL, quality of life.
[a]Epidemiological model adjusted as per age, educational level, presence of diabetes, hypertension, arthrosis, menopausal stage, BMI, smoking habit, and depression.
[b]Statistical model adjusted per variables that had a significant association with severe QoL impairment during bivariate analysis (QoL impairment: educational level, having a partner, parity, BMI, hypertension, arthrosis, smoking habit, and depression).
[c]Epidemiological model adjusted as per age, educational level, presence of diabetes, hypertension, arthrosis, menopausal stage, BMI, smoking habit, and depression.
[d]Statistical model adjusted by the variables that had a significant association with severe somatic symptoms (MRS) in bivariate analysis (partner, hysterectomy, BMI, hypertension, arthrosis, smoking habits, and depression).
[e]Epidemiological model adjusted as per age, educational level, presence of diabetes, hypertension, arthrosis, menopausal stage, BMI, smoking habit, and depression.
[f]Statistical model adjusted by the variables that had a significant association with severe psychological symptoms (MRS) in bivariate analysis (educational level, BMI, hypertension, arthrosis, smoking habits, and depression).
[g]Epidemiological model adjusted as per age, educational level, presence of diabetes, hypertension, arthrosis, menopause stage, BMI, smoking habit, and depression.
[h]Statistical model adjusted by the variables that had a significant association with severe urogenital symptoms (MRS) during bivariate analysis (HT use, educational level, parity, has a partner, menopausal stage, BMI, hypertension, arthrosis, smoking habit, and depression).

explain this association; however, Alexander et al[40] had reported that stress, through corticotropin-releasing hormone and peptides derived from proopiomelanocortin, inhibits the release of gonadotropin-releasing hormone, thus decreasing estrogen levels and its action at the tissue level. This may partially explain our findings. On the other hand, one should recall that vaginal dryness has an inverse relationship to serum estradiol levels.[2] Nevertheless, this is a relatively understudied topic that requires further research.

Regarding the limitations of our study, first, its cross-sectional design does not allow establishing causality. Second, our study focused on native Spanish-speaking women; hence, results cannot be extrapolated to other populations. Nevertheless, it provides a baseline for future studies. There are reports suggesting that ethnicity influences QoL within the mid-aged female Latin American population.[10,11] However, ethnicity was not considered in our study, and therefore may also be considered a potential limitation. Also important is the fact that the Goldberg Scale, used to measure anxiety, is a screening one; hence, our results should be interpreted with caution as the scale could over- or underestimate its actual frequency in our population. Finally, one must mention a possible existing colinearity between MRS and Goldberg Scale scores, especially the psychological MRS subscale that includes two items that assess the presence of depression and anxiety. Nevertheless, first, analysis was carried out with total MRS scores and also independently with subscale scores, after which the strongest association was observed between anxiety and severe somatic symptoms; and second, statistical analysis evaluating possible collinearity of the generalized linear models yielded negative results.[44]

Despite the aforementioned limitations, to the best of our knowledge, the present study is the first to evaluate the association between anxiety and QoL in a large sample of postmenopausal women using a specific tool to assess menopausal symptoms, the MRS. Due to obvious implications, studying factors affecting QoL is highly relevant; moreover, if we bear in mind that in this population menopause onset had been reported to occur earlier than in other populations.[3,26] In addition, the high number of studied women gives our study a further added value.

CONCLUSIONS

Anxiety was independently associated with severe QoL impairment in this postmenopausal Latin American sample. A strong association was found between anxiety and severe somatic symptoms, which include hot flashes, sleep disorders and muscle and joint complaints. Thus, screening for anxiety in this population becomes relevant in clinical practice. However, there is a need to conduct longitudinal studies to

determine the causality of this association and the benefit of early detection of anxiety in this group of women.

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