Maturitas 61 (2008) 323–329

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

# Impaired quality of life among middle aged women: A multicentre Latin American study

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ARTICLE INFO

*Article history:*
Received 1 August 2008
Received in revised form
23 September 2008
Accepted 24 September 2008

*Keywords:*
Menopause
Quality of life
Menopause rating scale
Latin America

ABSTRACT

*Background:* Several studies indicate that quality of life (QoL) is impaired in middle aged women. Assessment of QoL using a single validated tool in Latin American climacteric women has not been reported to date at large scale.
*Objective:* The Menopause Rating Scale (MRS) was used to assess QoL among middle aged Latin American women and determine factors associated with severe menopausal symptoms (QoL impairment).
*Methods:* In this cross-sectional study, 8373 healthy women aged 40–59 years, accompanying patients to healthcare centres in 18 cities of 12 Latin American countries, were asked to fill out the MRS and a questionnaire containing socio-demographic, female and partner data.
*Results:* Mean age of the entire sample was 49.1 ± 5.7 years (median 49), a 62.5% had 12 or less years of schooling, 48.8% were postmenopausal and 14.7% were on hormonal therapy (HT). Mean total MRS score ($n$ = 8373) was 11.3 ± 8.5 (median 10); for the somatic subscale, 4.1 ± 3.4; the psychological subscale, 4.6 ± 3.8 and the urogenital subscale, 2.5 ± 2.7. The prevalence of women presenting moderate to severe total MRS scorings was high (>50%) in all countries, Chile and Uruguay being the ones with the highest percentages (80.8% and 67.4%, respectively). Logistic regression determined that impaired QoL (severe total MRS score ≥17) was associated with the use of alternatives therapies for menopause (OR: 1.47, 95% CI [1.22–1.76], $p$ = 0.0001), the use of psychiatric drugs (OR: 1.57, 95% CI [1.29–1.90], $p$ = 0.0001), attending a psychiatrist (OR: 1.66, 95% CI [1.41–1.96], $p$ = 0.0001), being postmenopausal (OR: 1.48, 95% CI [1.29–1.69, $p$ = 0.0001]), having 49 years or more (OR: 1.24, 95% CI [1.08–1.42], $p$ = 0.001), living at high altitude (OR: 1.43, 95% CI [1.25–1.62, $p$ = 0.0001]) and having a partner with erectile dysfunction (OR: 1.69, 95% CI [1.47–1.94, $p$ = 0.0001]) or premature ejaculation (OR: 1.34, 95% CI [1.16–1.55, $p$ = 0.0001]). Lower risk for impaired QoL was related to living in a country with a lower income (OR: 0.77, 95% CI [0.68–0.88], $p$ = 0.0002), using HT (OR: 0.65, 95% CI [0.56–0.76], $p$ = 0.0001) and engaging in healthy habits (OR: 0.59, 95% CI [0.50–0.69], $p$ = 0.0001).
*Conclusion:* To the best of our knowledge this is the first and largest study assessing QoL in a Latin American climacteric series with a high prevalence of impairment related to individual female and male characteristics and the demography of the studied population.


## 1. Introduction

The female climactic is associated to significant biological, psychological and social changes which may lead to impaired quality of life (QoL) [1–3]. This impairment has been assessed with various instruments specifically designed for the purpose [4–8]. In this sense one can mention the Menopause Rating Scale (MRS), a menopause specific health related QoL scale which was initially developed in the early 1990s to measure the severity of age-/menopause-related complaints by rating a profile of symptoms [9–11]. Factorial analysis and statistical methods were applied to finally identify three dimensions of symptoms/complaints: a psychological, a somatic-vegetative, and a urogenital factor that explained 59% of the total variance. This is indicative for a high

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doi:10.1016/j.maturitas.2008.09.026

efficiency of a scale requiring only 11 items—compared to other international scales [12]. This scale has recently been validated in healthy Latin American climacteric populations, where age, the menopause, sexual inactivity and educational level have been determined to be risk factors predicting more severe menopausal symptoms and thus impaired QoL [13,14]. Despite this, up-to-date, assessment of QoL using one validated tool has not been performed at large scale within the Latin American climacteric population.

The objective of the following research was to assess QoL among middle aged Latin American women with the MRS and determine factors associated with its impairment (severe menopausal symptoms).

## 2. Methods

### 2.1. Participants

From November 2006 to February 2007 a cross-sectional study was carried out in 22 healthcare centres of 18 cities with a population of more than 500,000 inhabitants in 12 Latin American countries (see "List of Participating Countries and Investigators"). Sample size was established based on the fact the menopause, affects all women and occurs approximately between 40 and 59 years of age. Using statistical software a minimal sample size of 380 per centre was calculated considering that each centre covered an estimated population of 50,000 women [15] and assuming that 50% of the surveyed population would present menopausal symptoms [13] with an estimated 5% error and a 95% confidence interval.

To record all data, an itemized questionnaire was previously constructed and validated in 50 women before implementation at the Latin American centres affiliated to the Collaborative Group for Research of the Climacteric in Latin America (REDLINC) participating in this study the called the REDLINC IV study intended to assess QoL among middle aged women. Methodological aspects as well as the results of studies I and II have recently been published [16,17]. The inclusion criteria were healthy Hispanic women (non-black) aged 40–59 years who were accompanying patients attending health centres. Indigenous populations, pregnant women, and those who did not consent to participate or were incapable of understanding the items included on the questionnaire were excluded. Women fulfilling inclusion criteria were requested to fill out the MRS and a general data questionnaire after being informed about the research, its purpose, the MRS and its content. After consenting to participate and upon filling out the questionnaire they received additional support. Research protocol of this study was reviewed and approved by the Bioethics Committee of the PROSAM Foundation, Santiago de Chile, Chile.

### 2.2. Variables included in the general questionnaire

#### 2.2.1. General data

Age (years), parity, REDLINC centre number (city and country), menopausal status (pre, peri or post), marital status, educational level (expressed in years of schooling), accessed healthcare system (free-minimal cost [<25% of private consultation fee], or paid [paying more than the minimal cost]). Country geographical location (high or low altitude) and per capita gross domestic product (GDP) was assessed and recorded. This GDP was used to evaluate economic differences between centres [18] (Table 1). High altitude and lower country income have been reported as factors related to earlier age at menopause presentation [16]. Female age and menopausal status have been reported to be factors involved in QoL impairment [5,19]. Insufficient educational level (women or partner) was considered as 12 years or less of study [20].

#### 2.2.2. Lifestyle and other personal factors

Included in this section were smoking habit (current, sometime, non-smoker), church attendance, history of sexual abuse and if currently having one partner or engaged in healthy habits. Healthy lifestyles have been related to better QoL [21].

#### 2.2.3. Medical care and drug

Depressive symptoms and hormone therapy (HT) use are factors predicting QoL during the menopausal transition [22,23]. Hence rate of women seeking psychiatric attention as well as the use of psychotropic drugs and HT/alternative therapies for the menopause was assessed.

#### 2.2.4. Data related to partner

Partner age (years), years of schooling (total years), healthiness, faithfulness, presence of alcoholism, or sexual dysfunction (erectile or premature ejaculation) was assessed. Erectile dysfunction was defined as the persistent or recurrent incapacity to achieve or maintain an erection to allow satisfactory sexual intercourse [24] whereas premature ejaculation as the persistent or recurrent ejaculation after minimal sexual stimulation before, during or shortly after penetration or before the individual's desire to do so [25].

### 2.3. Menopausal status definitions

Concerning the menopausal status the following definitions were used: premenopausal (women having regular menses); perimenopausal (irregularities >7 days from their normal cycle) and postmenopausal (no menses in the last 12 months) [26]. Those with bilateral oophorectomy were considered as postmenopausal.

### 2.4. The menopause rating scale

The MRS is composed of 11 items assessing menopausal symptoms divided into three subscales: (a) *somatic*: hot flushes, heart discomfort, sleeping problems and muscle and joint problems (items 1–3 and 11, respectively); (b) *psychological*: depressive mood, irritability, anxiety and physical and mental exhaustion (items 4–7, respectively); and (c) *urogenital*: sexual problems, bladder problems and dryness of the vagina (items 8–10, respectively). Each item can be graded by the subject from 0 (not present) to 4 (1 = mild; 2 = moderate; 3 = severe; 4 = very severe). For a particular individual, the total score per each subscale is the sum of each graded item contained in that subscale. Total MRS score is the sum of the scores obtained for each subscale. A total score of 9 to 16 was considered as moderate and ≥17 severe [27]. The MRS scale has been translated to more than 27 languages. For the purpose of this research the Spanish version of the MRS was used [28], which has been validated in Ecuador and Chile [13,14]. More details of the scale, punctuation and scoring is detailed elsewhere [11,27].

### 2.5. Statistical analysis

Analysis was performed using EPI-INFO 2000 statistical software (Centres for Disease Control, Atlanta, GA, USA; WHO, Basel, Switzerland). Data is expressed as mean ± standard deviations (S.D.), medians and percentages. Chi-square calculation was used to compare categorical data. Risk factors for higher total MRS scorings, and thus impaired QoL, were analyzed using logistic regression. For this, total MRS scorings, as continuous variables, were transformed into a categorical one, now considered as cases those exhibiting scores ≥17 (severe MRS scoring). Independent variables to be entered in the regression model were: high altitude residency (≥2000 m above sea level), country with low per capita

**Table 1**
Sociodemography, HT use and smoking rate among different centres ($n = 8373$).

| Investigator (country, city) | GDP US$ (million) | Education ≤12 years (%) | Free healthcare (%) | Smoking (%) | HT use (%) | Postmenopausal (%) |
|---|---|---|---|---|---|---|
| All ($n = 8373$) | 4281[a] | 62.5 | 56.2 | 17.4 | 14.7 | 48.8 |
| Argentina | 4747 | | | | | |
| Buenos Aires | | 70.4 | 51.9 | 40.3 | 9.8 | 58.5 |
| Bolivia | 990.1 | | | | | |
| Santa Cruz | | 63.7 | 22 | 20.7 | 26.6 | 40.1 |
| Cochabamba (centre 1) | | 38.4 | 21.8 | 27.4 | 24.7 | 51.1 |
| Cochabamba (centre 2) | | 32.1 | 54.5 | 7.1 | 1.6 | 34.5 |
| Colombia | 2663.2 | | | | | |
| Cali | | 76.9 | 46.2 | 13.4 | 20.7 | 52 |
| Cartagena | | 93.6 | 67.3 | 17.3 | 5.6 | 42.8 |
| Bogota (centre 1) | | 84.9 | 71 | 10.7 | 12.3 | 46.5 |
| Bogota (centre 2) | | 92.2 | 90.1 | 12.3 | 3.9 | 26.1 |
| Chile | 7084.8 | | | | | |
| Santiago | | 69.5 | 79.2 | 51.4 | 6.2 | 45.1 |
| Cuba | 2850.2 | | | | | |
| La Habana | | 62.4 | 100 | 34.9 | 4.5 | 45.9 |
| Dominican Republic | 3815.1 | | | | | |
| Santiago de Los Caballeros | | 68.5 | 47.4 | 15.6 | 8.5 | 51.1 |
| Ecuador | 2761.2 | | | | | |
| Quito | | 57.4 | 72.1 | 7.9 | 17.9 | 45 |
| Guayaquil (centre 1) | | 44.8 | 64.4 | 13.1 | 19.3 | 39.7 |
| Guayaquil (centre 2) | | 33.6 | 0 | 19.8 | 15.3 | 40.2 |
| Mexico | 7239.4 | | | | | |
| Mexico City | | 62.4 | 67.9 | 32.9 | 8.4 | 50.3 |
| Panama | 4796.6 | | | | | |
| Panama City | | 48.5 | 69.7 | 6.8 | 13.9 | 49.5 |
| Peru | 2840.5 | | | | | |
| Piura | | 77.6 | 100 | 6.3 | 16.9 | 46.6 |
| Cuzco | | 45.1 | 64.2 | 13 | 19.4 | 39.6 |
| Lima (centre 1) | | 48.1 | 0 | 9.8 | 26.2 | 82 |
| Lima (centre 2) | | 81.6 | 72.4 | 8.2 | 8.7 | 47.4 |
| Uruguay | 4860.2 | | | | | |
| Montevideo | | 58.9 | 0.5 | 1.6 | 38.9 | 77.1 |
| Venezuela | 5274.9 | | | | | |
| Caracas | | 65.3 | 73.2 | 13.9 | 13.4 | 63.2 |

[a] Adjusted gross domestic product (GDP) for year 2005 from participating countries is given: source CEPAL [18]. Adjusted median GDP: US$ 4281 million.

GDP (≤4281 million US dollars, median) and access to free healthcare (*socio-demographical*); older age (≥49, median), higher parity (≥2, median), low schooling (≤12 years), marital status (married or not), postmenopausal status, smoking status, medication use (HT, menopause alternatives, psychiatric) and if attending a psychiatrist, engages in healthy habits and/or currently having one stable partner (*female*); and partner age, low schooling (≤12 years), alcoholism, healthiness, faithfulness, precocious ejaculation, erectile dysfunction (*male*). Entry of variables into the model was considered with a 20% significance level and the stepwise procedure performed. A $p$ value of <0.05 was considered as statistically significant.

## 3. Results

During the study period a total of 8394 women fulfilled inclusion criteria and were surveyed. Of these, 21 were excluded due to incomplete data leaving a total of 8373 surveys for statistical analysis. Mean age of the entire sample was 49.1 ± 5.7 years (median 49) and the mean educational level 11.6 ± 4.4 years. The use of alternative therapies for the menopause and psychotropic drugs was 7.6% and 8%, respectively. Socio-demographics (GDP, attained education, type of healthcare), smoking and rate of HT use in participating centres are given in Table 1. Of the entire sample, 54.5% were married and 62.5% had 12 or less years of education. Significant differences were observed between centres from different cities, i.e. 32.1% had 12 years or less of education in Cochabamba (Bolivia centre 2), whereas in Cartagena (Colombia), this figure was 93.6%. More than half (56.2%, range: 0–90.1%) of surveyed women were affiliated to free or partially subsidized healthcare systems. Regarding the menopausal status of the whole series, 31.6% were premenopausal, 19.6% perimenopausal, 48.8% postmenopausal, 7.7% had history of bilateral oophorectomy and 16.3% only hysterectomy. Additionally, 27.4% of participating centres were located at high altitude (≥2000 m above sea level) and 72.7% had a GDP below the median for Latin America (4281 US$ million, year 2005). Of the whole sample, 17.4% were current smokers and 14.7% were on HT. These figures varied among centres, i.e. from 1.6% in Montevideo (Uruguay) to 51.4% in Santiago de Chile (Chile) for smoking and from 1.6% Cochabamba (Bolivia centre 2) to 38.9% Montevideo (Uruguay) for HT use.

Other aspects related to surveyed women include: engaged in healthy habits (90.5%), regular church attendance (57.9%), attended a psychiatrist (11.6%) and had a history of sexual abuse (4.4%). Regarding the partner ($n = 6,909$) it was found that mean age was 51.6 ± 8 years (median: 51, range 19–90), mean educational level 12.4 ± 4.6 years (54.2% had 12 or less years), 11.5% had alcoholism, 68.5% were healthy, 60.8% were faithful

**Table 2**
Total and subscale MRS scorings and prevalence of moderate–severe total scorings in relation to studied country.

| Country | Total MRS score | Somatic score | Psychological score | Urogenital score | Moderate score 9–16 (%) | Severe score ≥17 (%) | Moderate–severe (%) |
|---|---|---|---|---|---|---|---|
| All ($n$ = 8373) | 11.3 ± 8.5[a] | 4.1 ± 3.4 | 4.6 ± 3.8 | 2.5 ± 2.7 | 30.5 | 24.9 | 55.4 |
| Argentina ($n$ = 378) | 10.7 ± 8.7 | 3.9 ± 3.5 | 4.6 ± 4.0 | 2.2 ± 2.5 | 27.2 | 26.5 | 53.7 |
| Bolivia ($n$ = 1132) | 10.0 ± 7.7 | 3.5 ± 3.1 | 4.0 ± 3.0 | 2.4 ± 2.5 | 31.8 | 20.4 | 52.2 |
| Colombia ($n$ = 1523) | 11.0 ± 9.7 | 4.3 ± 3.8 | 4.4 ± 4.4 | 2.2 ± 2.7 | 23.6 | 24.7 | 48.3 |
| Chile ($n$ = 370) | 16.3 ± 8.5 | 5.8 ± 3.5 | 7.7 ± 4.4 | 2.7 ± 2.9 | 39.7 | 41.1 | 80.8 |
| Cuba ($n$ = 375) | 12.0 ± 9.4 | 4.5 ± 3.5 | 5.2 ± 4.4 | 2.3 ± 2.7 | 26.9 | 28.8 | 55.7 |
| Dominican Republic ($n$ = 378) | 10.9 ± 7.8 | 4.4 ± 3.4 | 4.0 ± 3.2 | 2.4 ± 2.4 | 34.1 | 22.5 | 56.6 |
| Ecuador ($n$ = 1146) | 11.8 ± 8.2 | 4.2 ± 3.2 | 4.6 ± 3.5 | 3.0 ± 2.9 | 34.4 | 25.7 | 60.1 |
| Mexico ($n$ = 380) | 9.4 ± 7.7 | 3.4 ± 3.0 | 3.8 ± 3.5 | 2.2 ± 2.4 | 31.1 | 18.4 | 49.5 |
| Panama ($n$ = 396) | 11.5 ± 8.1 | 4.9 ± 3.7 | 4.3 ± 3.5 | 2.3 ± 2.5 | 30.1 | 26.5 | 56.6 |
| Peru ($n$ = 1535) | 10.7 ± 8.0 | 3.5 ± 2.9 | 4.3 ± 3.4 | 2.9 ± 2.9 | 29.3 | 22.3 | 51.6 |
| Uruguay ($n$ = 380) | 13.0 ± 7.9 | 4.5 ± 2.8 | 5.6 ± 3.9 | 2.9 ± 2.6 | 36.3 | 31.1 | 67.4 |
| Venezuela ($n$ = 380) | 12.4 ± 8.1 | 5.0 ± 3.4 | 4.9 ± 3.8 | 2.5 ± 2.7 | 36.1 | 26.6 | 62.7 |

[a] Mean ± standard deviation (S.D.).

and 17.6% had erectile dysfunction and 16% premature ejaculation.

Mean total and subscale MRS scorings and the prevalence of moderate to severe total scores in relation to country are depicted in Table 2. As one can observe, in general more than 50% of women of all countries present moderate to severe scorings, Chile and Uruguay being the countries with the highest percentages (80.8% and 67.4%, respectively). Mean total MRS score ($n$ = 8373) was 11.3 ± 8.5 (median 10, range 0–44); somatic subscale: 4.1 ± 3.4 (median 4, range 0–16); psychological subscale: 4.6 ± 3.8 (median 4, 0–16) and the urogenital subscale: 2.5 ± 2.7 (median 2, range 0–12). Total, somatic and psychological MRS scores were highest in Chile whereas the urogenital mean score was highest in Ecuador.

Logistic regression determined that impaired QoL (severe total MRS score ≥17) was associated to using alternatives therapies for the menopause (OR: 1.47, 95% CI [1.22–1.76], $p$ = 0.0001), the use of psychiatric drugs (OR: 1.57, 95% CI [1.29–1.90], $p$ = 0.0001), attending a psychiatrist (OR: 1.66, 95% CI [1.41–1.96], $p$ = 0.0001), being postmenopausal (OR: 1.48, 95% CI [1.29–1.69, $p$ = 0.0001]), having 49 years or more (OR: 1.24, 95% CI [1.08–1.42], $p$ = 0.001), living in high altitude (OR: 1.43, 95% CI [1.25–1.62, $p$ = 0.0001]) and having a partner with erectile dysfunction (OR: 1.69, 95% CI [1.47–1.94, $p$ = 0.0001]) or premature ejaculation (OR: 1.34, 95% CI [1.16–1.55, $p$ = 0.0001]). Lower risk for impaired QoL was related to living in a country with a lower income (OR: 0.77, 95% CI [0.68–0.88], $p$ = 0.0002), using HT (OR: 0.65, 95% CI [0.56–0.76], $p$ = 0.0001) and engaging in healthy habits (OR: 0.59, 95% CI [0.50–0.69], $p$ = 0.0001) (Table 3).

**Table 3**
Socio-demographic and female/male factors associated to impaired QoL (severe total MRS score: ≥17): logistic regression analysis.

| Factors | Odds ratio (CI 95%) | $p$ value |
|---|---|---|
| Socio-demographic | | |
| Living in high altitude | 1.43 (1.25–1.62) | 0.0001 |
| Country with lower GDP | 0.77 (0.68–0.88) | 0.0002 |
| Female | | |
| Alternative therapies for the menopause | 1.47 (1.22–1.76) | 0.0001 |
| Use of psychiatric drugs | 1.57 (1.29–1.90) | 0.0001 |
| Attending a psychiatrist | 1.66 (1.41–1.96) | 0.0001 |
| Postmenopausal status | 1.48 (1.29–1.69) | 0.0001 |
| Older age (≥49 years) | 1.24 (1.08–1.42) | 0.001 |
| HT use | 0.65 (0.56–0.76) | 0.0001 |
| Engaging in healthy habits | 0.59 (0.50–0.69) | 0.0001 |
| Male | | |
| Premature ejaculation | 1.34 (1.16–1.55) | 0.0001 |
| Erectile dysfunction | 1.69 (1.47–1.94) | 0.0001 |

## 4. Discussion

The demographic panorama of Latin America and the Caribbean is currently evolving at a pace expected to increase in forthcoming years. As life expectancy increases in our population, women are expected to spend a significant proportion of their lives deprived of estrogens [3]. To make matters worse, age at menopause presentation in Latin America has been determined to occur earlier than in women from USA and Europe [16]. Therefore the earlier the onset of the menopause the longer the exposition to the negative effects of hypoestrogenism and hence QoL is subject to be impaired earlier. Under this scenario together with the fact of a rapidly evolving population, delineating risk factors for health related QoL impairment becomes an urgent necessity for the designing of preventive strategies. Although the World Health Organization (WHO) has defined QoL as "individual's perceptions of their position in life in the context of the cultural and value systems in which they live and in relation to their goals, expectations, standards and concerns" [29], in most cases rigid application of this nomenclature is not feasible as the term encompasses several constructs including physical, functional, emotional, social and cognitive variables, thus QoL, health related one included, varies from individual to individual and from one population to another.

Health related QoL, and specifically that related to menopausal symptoms, has been extensively studied in the developed world [6–8]. Contrarily, assessment of QoL in relation to the menopause in Latin America has been performed upon small series, in which several QoL assessment tools have been validated [3–5,13,14,30]. To the best of our knowledge, the present cross-sectional study, constitutes the first and largest Latin American QoL assessment series, involving many countries of the region and utilizing a specific validated menopausal QoL assessing tool, the so-called MRS. The total and subscale MRS scores found in this large series correlate with those previously found in smaller Latin American series using the same instrument in Ecuador [13] and Colombia [31]. Despite this, important to highlight in this series is the high prevalence of women found to have moderate to severe total MRS scorings (impaired QoL), situation that was the highest in Uruguay (67.4%) and Chile (80.8%). The MRS standards found for Chile (Santiago de Chile) in the present series correlate well with those previously found by Aedo et al. [14], which are higher than the international MRS standards reported for Latin America [27]. The higher total MRS scores found for Chile and Uruguay was due to higher scorings in the psychological subscale (7.7 ± 4.4 and 5.6 ± 3.9, respectively), also higher when compared to the rest of participating countries. Urbanization, as reported by others [32,33], increases the prevalence of depressive and anxiety symptoms. This could possibly

explain, at least in part, the increased MRS standards for Chile, moreover if one bears in mind that Santiago de Chile is a highly urbanized and developed city if compared to other cities of Latin America and to the fact that prevalence of depression in this city (perhaps due to its development) is near 30% [34]. Montevideo (Uruguay) has a similar profile as Santiago de Chile, however contradictory as it may seem HT use for Uruguay was highest of the series. More research is needed in this regard, moreover if one bears in mind the diverse demographic conditions (educational level, type of accessed healthcare, HT use, smoking habit, national GDP and geographical city location) found in many of the participating countries of this Latin American series.

In regard to altitude, our regression model found that women living at higher altitude were at higher risk for impaired QoL (more severe menopausal symptoms). One explanation could be drawn from the observation that the percentage of perimenopausal women among those living at high altitude cities (Quito, Cochabamba, Cuzco, Bogota, $n = 2292$) was higher than those living at sea level (23.7% vs. 18%, $p < 0.0001$), hence it would be expected that these women (perimenopausal) be more symptomatic as it has been previously reported by others using the same tool [31]. The mentioned trend (higher rate of perimenopausal at high altitude) remained equal when each high altitude city was compared to their sea level counterparts for that country. Data linking high residency altitude with more severe menopausal symptoms (impaired QoL) is lacking in the literature. Despite our preliminary finding, more research is warranted to establish a valid pathophysiologic mechanism, rather than just the higher rate of perimenopausal women found among those living in high altitude cities which could be the consequence of selection bias. In this sense, important to mention is that our first REDLINC study [16] established that women aged 49 living in cities at an elevation of more than 2000 m above sea level had a higher risk of being menopausal and that the age at menopause was earlier in those women. This data is in accordance with the findings of others for high altitude cities in Peru [35] and the Tibet [36]. One could hypothesize that women living at high altitude are becoming postmenopausal earlier, consequently the rate of perimenopausal women would be higher and thus more symptomatic which would explain impaired QoL (Higher MRS scorings). The reason for earlier age at menopause in women living at higher altitudes is unknown. One must mention that the diameter of preovulatory follicles is smaller in women living at a high altitude [37], hypothesizing that high altitude may influence follicle development. Hypoxia affects follicle metabolism, stimulating endothelin-1, which inhibits oocyte luteinization [38], and increasing interleukin-6 secretion [39], a cytokine involved in follicle development. Additionally, as a result of hypoxia, women having a blood oxygen saturation level below 85% have decreased estradiol [40] and progesterone [37] levels. Clearly, time of residency in the altitude (antiquity) and genetics are important components in determining survival and QoL at high altitude [41].

Contrary to previous reports drawn upon Hispanic and non-Hispanic middle aged women supporting the fact that low socio-economic status and lower education increases severity of menopausal symptoms [3,13,42–44] and sexual dysfunction [45], the present study demonstrated that climacteric women coming from countries with a lower GDP decreased the risk of presenting higher MRS scores and thus impaired QoL. Due to the multidimensional nature of risk factors predicting menopausal symptoms, a single explanation for this contradictory finding is difficult to ascertain; however important to mention is the fact that in a recent study, the prevalence of overweight and obesity in women aged 20–45 years was found to be higher among those of higher socio-economical status [46]. Obesity, on the other hand, has been determined to be a risk factor for increased menopausal symptoms in Hispanic [47] and non-Hispanic series [48,49]. In a recent study using the MRS tool, Kakkar et al. [50] determined that Indian working women seem to suffer more from psychological symptoms whereas non-working women showed a greater incidence of somatic symptoms. Educated women showed a lower incidence of psychological and somatic symptoms, situation that correlates with the findings of the present research. Contrary to this, others have determined that low educational level, suggesting low socio-economic status, and either dissatisfaction with present life or feeling of poor health, have been reported to correlate with women presenting severe climacteric symptoms, whereas low self-esteem, anxiety about the future and few intimate friends, suggesting a lack in social support, have been associated with mild symptoms and complaints [51,52].

The present study determined that female age and the menopause were risk factors for severe total MRS scorings (impaired QoL), situation that confirms previous reports using diverse scales (MRS included) in Hispanic [3,5,13,14] and non-Hispanic series [53–55].

In the present series, women who were on psychiatric consultation and using psychotropic drugs (mainly antidepressants) were at higher risk for presenting severe MRS scores. The prevalence of depression and depressive and anxiety symptoms increase during the menopausal transition [22,56,57]. Moreover, it has been determined that increased menopausal symptoms (vasomotor related) are directly related to depressive symptoms [30,58]. To better highlight the latter, a recent study performed among middle aged women (40–59 years) found that increased depressive and anxiety symptoms (higher Hamilton Depressive Rating Scale scorings), directly correlated with higher MRS scorings [56]. According to our regression model, HT use and engaging in healthy habits were found to decrease the risk of presenting severe menopausal symptoms, situation that confirms the findings of others [31,59–61]. Contrary to this, the use of alternatives for the treatment of the menopause was related to more severe menopausal symptoms. The significance of this finding remains unclear. However one must bear in mind that causality cannot be determined in a cross-sectional design.

Male sexual dysfunction (erectile and ejaculatory) was found to be a significant risk factor for impaired QoL in this middle aged female series. The exact mechanism through which masculine sexual dysfunction (SD) exerts increased menopausal symptoms remains unclear but it could be possible that male SD imposes increased anxiety and depressive symptoms or female sexual dysfunction which can *per se* increase total menopausal scorings. Several of our previous preliminary observations seem to support this hypothesis in terms of male [62,63] or female SD [64] imposing higher grade of menopausal symptoms. Although these findings are interesting, analysis was based only on the total MRS score, determining what group of menopausal symptoms (somatic, psychological or urogenital) is being impacted would seem even more interesting however the focus of a separate manuscript.

Finally regarding the limitations of the present study one can mention its cross-sectional nature. Despite this, the great amount of obtained information regarding this middle aged female series and that of their socio-demographic background and partner constitutes an important tool for comparison purposes with other Hispanic populations, not to mention the consequently important increase in scientific data and contributions. Not determining body mass index (overweight and obesity) is another drawback important to mention in the present series, moreover if obesity (among women with the metabolic syndrome), using the MENQOL questionnaire, has recently been determined to be an implicated factor related to more severe menopausal symptoms [47]. Ethnicity is another issue taken into account when comparing populations in

terms of severity of menopausal symptoms (impaired QoL). Despite the fact that surveyed women in the present series were Hispanic/mestizo type (non-black), in a recent report, using the MRS instrument, Monterrosa et al. [31] determined that Afro-Colombian women in comparison to non-black (Hispanic/mestizo) were at higher risk for impaired QoL (more severe menopausal symptoms), thus extrapolation of the results of the present series must be confined to the mestizo (non-black) population of the Latin American region.

In conclusion, in this Latin American middle aged series there was a high prevalence of QoL impairment which depended upon individual female and male characteristics and the demography of the studied population. Due to the wide diversity of the population (GDP variance, educational level, geographical location, habits etc) findings cannot be generalized to one Latin American country or population. Despite the outlined limitations to the best of our knowledge this is the first and largest study assessing QoL in a Latin American climacteric series.

## Appendix A. List of participating countries and investigators

*Argentina*: Monique Royer; *Bolivia*: Maria T. Espinoza, Desire Mostajo, Edwin Soto; *Chile*: Juan E. Blümel, Daniel Flores; *Colombia*: German Baron, Gustavo Gomez, Alvaro Monterrosa, William Onatra, *Cuba*: Daysi Navarro; *Dominican Republic*: Ascanio Bencosme; *Ecuador*: Peter Chedraui, Andres Calle, Patricia Leon-Leon; *Mexico*: Jose A. Hernandez-Bueno; *Panama*: Konstantinos Tserotas; *Peru*: Luis Danckers, Eliana Ojeda, Humberto Izaguirre, Edward Mezones-Holguin; *Uruguay*: Selva Lima; *Venezuela*: Emma Belzares.

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