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Is There a Regional Difference in Symptoms Perception Associated with Pre-Menstrual Syndrome? Results from a National Study among Reproductive-Age Women in Brazil

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Abstract

Background: Evaluate the prevalence, intensity and regional distribution of premenstrual syndrome (PMS) symptoms reported by reproductive age Brazilian women.Methods: An observational and retrospective study was conducted analyzing data of women from the five Brazilian regions. Women aged 20 to 49 years who consulted at private healthcare services filled up a self-reported questionnaire about the prevalence and intensity of somatic and psychoemotional pre-menstrual symptoms.Results: A total of 23104 women stated to have premenstrual symptoms, of which 38.91

Index terms— premenstrual syndrome, Brazilian women, regional study, premenstrual severity symptoms.

Is There a Regional Difference in Symptoms Perception Associated with Pre-Menstrual Syndrome? Results from a National Study among Reproductive-Age Women in Brazil There are several different psycho-emotional and physical symptoms associated with PMS as depression, angry outbursts, irritability, anxiety, confusion, social withdrawal, breast tenderness, abdominal bloating, headache and swelling of extremities [2]. These symptoms are cyclic and recurrent and can change in extent and intensity during different menstrual cycles [2]. According to the World Health Organization, "Premenstrual Tension Syndrome" is characterized by certain environmental, metabolic, or behavioral symptoms that occur during the luteal phase of the menstrual cycle, and lead to cyclic emotional, physical, or behavioral symptoms that interfere with an individual's lifestyle [3]. The American College of Obstetrics and Gynecology and the Royal College of Obstetricians and Gynecologists' criteria describe PMS as any number of psychoemotional or physical symptoms and functional impairment is required [4].

Since PMS is a global problem, it has been studied worldwide to understand its effects on daily life [5,6]. The first global meta-analysis reported the pooled prevalence of PMS at values around 47.8% worldwide, although most of the included studies were heterogeneous, involving several confounding factors within and between studies, and a limited sample size [7]. Some studies suggested that the prevalence of PMS is higher in Latin-American countries when compared to Europe [8].

In Brazil, there are few published studies on the prevalence, symptoms characteristics, and detailed information about the premenstrual syndrome in women of reproductive age. In addition, the correlation with socio-demographic, socioeconomic, and sociocultural conditions of the affected women is not established [9][10][11][12]. However, a study in the Brazilian population showed that when using criteria for the diagnosis of PMS, the prevalence of the syndrome was lower than the self-reported [9]. Therefore, nationwide studies looking at regional differences involving a large sample size among sufferers of PMS are scarce, and new data will contribute to demystifying PMS and help health professionals to assist affected women.

This study aimed to evaluate the prevalence, intensity and regional distribution of PMS symptoms reported by the Brazilian female population and the information generated may help to rethink mechanisms to improve the health and quality of life of PMS suffering women and offer decision-making tools related to the need for early and effective treatment of PMS.

1 II.

2 Methods

3 a) Study design and sample selection

It was an observational and retrospective study. All data were collected from a database with information stored by the Market Research Programs (MRP) and anonymized to ensure the data subjects' confidentiality and the study's security and confidentiality.

A self-reported questionnaire was answered by women aged 20 to 49 years from all Brazilian regions: South, Southeast, North, Northeast, and Midwest, between February 2019 and March 2020.The invitation to participate was made through an electronic device (cell phone or tablet). As soon as the woman requested access to the clinic's wireless network, she was invited to participate in the research and received information about the content and purpose of the research. This study was free from a consent form. The duration of the questionnaire filling out was around five to ten minutes.

Next, the participants were categorized as having PMS or not, according to the ACOG diagnostic criteria [2]. To evaluate functional impairment, the participants were asked how much the PMS symptoms disturbed their daily life (not at all, a little, or a lot) and those who answered "a lot" were considered as having a functional impairment.

Those who accepted to participate voluntarily were directed to the questionnaire adapted from the PSST -Premenstrual Symptoms Screening Tool -version validated in Brazil (Annex 1) [13].PSST is a retrospective questionnaire that can be completed during clinical consultation which is well established for PMS symptoms. It has demonstrated high sensitivity (79%) for PMS diagnosis and, in addition, identified women who suffer from severe PMS [14].

A 4-point Likert scale was used to measure the intensity of psychoemotional (irritability, anxiety and tension, decreased interest in routine activities, depression and sadness, overeating, concentration difficulties, emotional instability) and physical(headache, acne and oily skin, edema, weight gain, breast tenderness, exacerbation of immunoallergic conditions) symptoms according to intensity (0 = none; 1 = mild; 2 = moderate; 3 = severe). Also, demographic data of the participants were collected, and they were asked whether they would take oral contraceptives as a treatment option for PMS.

To have representativeness according to regional population, the respondent women were randomly selected according to the population proportions by region, based on the latest published demographic Census (2010) **??**15]. The study flow chart is represented in Figure 1.

The study protocol was submitted to the Research Ethics Committee under the registration number 33794520.1.0000.8098.

4 b) Sample Calculation

To calculate the sample size, an estimation formula was used for a descriptive study with a categorical qualitative variable [16][17][18]. In this case, the premenstrual syndrome (PMS) estimate was obtained from the literature [10].The level of significance alpha or type I error was set at 5% (or 95% confidence interval) and the sampling error at 3% (d=0.03). According to the results, a minimum sample of n=1022 was obtained. The program used was SAS (Statistical Analysis System), version 9.4 (SAS Institute Inc, 2002-2012, Cary, NC, USA).

According to the 2010 Demographic Census data, **??**15] the Brazilian female population aged 20 to 49 years was distributed as follows: 42.4% in the Southeast, 26.9% in the Northeast, 14.1% in the South, 8.9% in the Midwest and 7.7% in the North region. A specific procedure was used for this selection that randomly shuffles and chooses lines among those available in each region, using the SAS statistical software.

5 c) Statistical methods

According to the variables under study, the sample characteristics are shown as frequency tables of categorical variables with absolute (n) and percentage (%) frequency values.

Comparisons among regions concerning the response of each question were analyzed using Pearson's Chi-Square test or Analysis of Variance (ANOVA). If a significant difference was found at 5% in the first test, multiple comparisons were performed so that each region was compared. Bonferroni's correction test was used for multiple comparisons.

The p-value was considered significant at 0.8%, resulting from the significance level of 5% divided by 6.We used Poisson Regression to compare regions regarding the number of moderate or severe symptoms, an appropriate statistical test for numerical data. All analyzes were performed using SAS software version 9.4 and Excel.

6 III.

7 Results

A total of 56,948 women responded to the initial questionnaire. Of these, 8,990 were aged between 20 and 49 years and met the diagnostic criteria for PMS (any number of psycho-emotional or physical symptoms with functional

impairment). Among them, 5,121 participants agreed to answer a detailed anamnesis about their symptoms, characterizing the target population of the study.

After that, 2,475 respondents were randomized respecting the proportionality of the female population of each state, according to the 2010 census(Table 1).

The mean age of participants was 30.8 ± 7.4 years. Women between 20 and 29 years represented 47.8% of the sample, corresponding to the larger age group. The participants aged between 40 to 49 years represented the lowest proportion of respondents (14.4%).The mean age was higher in the southeast region (31.4, p=0.0003). Among the different Brazilian regions, the proportion of respondents in each age group was uniform (Table 2).

The profile of the participants who did not accept to respond to the questionnaire was similar to participants who accepted to respond, regarding the Brazilian regions and age group. Half of the participants in each profile agreed to answer the questionnaire.

By analyzing the total prevalence of symptoms and the distribution of severe physical symptoms, it was observed no significant differences between the regions of Brazil, except for the lower prevalence of weight gain in the northeast region (Table 3).

Headache was the most prevalent physical symptom (86.2%) in the Brazil average, as well as in the South and Midwest regions, and 41% of the women with headaches presented the symptom with severe intensity. The second most prevalent symptom in the Brazil average was acne and oily skin (85.8%), with 32.3% of severe intensity, followed by edema (85% prevalence, 25.5% with severe intensity). Acne and oily skin were also the most prevalent symptom in the Southeast and Northeast regions. In the North region, edema was the most prevalent physical symptom (Table 3).

Weight gain was the only physical symptom with a statistically significantly lower prevalence in the northeast region compared to other regions of the country (Table 3).

The least prevalent and severe symptom was an exacerbation of immunoallergic conditions (78.8% and 15.4%) respectively (Table 3).

When focusing on the psychoemotional symptoms, the most prevalent symptom in the country was irritability (98.5%) with 61.7% of women presenting the symptom in severe intensity. Anxiety and tension were the second most prevalent psychoemotional symptom in the Brazilian population (98.4%) and 54.2% of the participants presented it in severe intensity (average). The most prevalence of this symptom was observed in the south region. Regarding intensity, it was statistically significant in the northeast and southeast regions. In the South region, both symptoms (irritability / Anxiety and tension) showed the same higher prevalence (99.4%). The third most prevalent symptom in the country was decreased interest in routine activities (94.5%) and 39% of women considered it to be of severe intensity (Table **??**).

Overeating was the only symptom was observed with a statistically significant difference between regions for prevalence and intensity.

On average, 74.3% of women with PMS stated they would take contraceptivesas an option for PMS symptoms treatment (Table **??**).

IV.

8 Discussion

Our investigation showed a high prevalence of physical and psychoemotional symptoms in all Brazilian regions, with the average prevalence of these symptoms in Brazil being 83.6% and 94.2%, respectively.

In a study in southern Brazil 1395 women aged 15 to 49 years were evaluated. The main premenstrual physical symptoms found in this study were abdominal discomfort, headache and breast pain. Among the psychoemotional symptoms, the most prevalent were irritability, nervousness and fatigue. [9] In our study the most prevalent physical symptoms were headache (86.2%), acne and oily skin (85.8), and edema (85%) and the psychoemotional symptoms were irritability (98.5%), anxiety and tension (98.4%) and decreased interest in routine activities (94.5%).

In a multicenter Brazilian study that aimed to describe the perspectives and attitudes of Brazilian women toward premenstrual syndrome,1053 women, separated by regions, between 18 and 40 years, lived in 6 Brazilian cities, 1 in each geographic region of the country and the Federal District were interviewed [10]. Results showed that most women (78.1%) stated that PMS is related to emotional symptoms, and 24.3% said that it is related to physical symptoms [10]. The emotional symptoms most frequently mentioned by the participants were nervousness/anxiety, irritability/anger/ aggressiveness and mood swings/crying, whereas the most common physical symptoms were headache, cramps and breast pain, swelling, and tenderness [10]. On the other hand, in our investigation we observed that irritability and anxiety/tension were the most prevalent psychoemotional symptoms.

When evaluating the prevalence of symptoms with severe intensity, our study showed a higher prevalence of psychoemotional symptoms over physical symptoms, reaching 60% for irritability versus 40% for headache, which was the most severe physical symptom.

In a study across several countries, including Brazil, with a total of 7226 women (400-500 women from each country) aged 15-49, it has been reported a higher frequency of physical symptoms, as assessed by severity and number of menstrual cycles affected [6]. In this global study, Brazil was characterized by the second-largest values of severity and duration of symptoms, staying only behind the UK. The high prevalence of severe symptoms

observed in our study corroborates these findings. However, when evaluating the global population, among the 5 most prevalent symptoms, 4 were physical [6]. In our study, psychoemotional symptoms were a higher prevalence and severity. It is important to highlight that these data were collected before the pandemic of COVID-19, so these results were not influenced by the psychological effects seen during the pandemic. We continue to collect data during the pandemic, and it will be interesting to compare this issue.

The lower severity of overeating in the northeast region may be related to the lower severity of anxiety and tension during the premenstrual period.

Previously studies showed that among Brazilian women, 52.3% stated that physicians prescribed hormones as a strategy for dealing with premenstrual syndrome, [10] and PMS symptoms severity was inversely associated with oral contraceptive use (emotional symptoms) and better-perceived health (physical symptoms) [19].In our investigation, among respondents who met the diagnostic criteria for PMS (n=2.475), 74.3% would take oral hormonal contraceptives as a treatment option for PMS. This is an important finding since the combined oral contraception for women of reproductive age is one of the effective options used for the treatment of PMS, mainly for women who seek contraception counseling. [20] The strength of this study includes the use of a questionnaire validated in Brazil that is commonly used for population studies, the large number of women included, and the national scope of the study. In addition, the participating women included in our study were selected in a private healthcare system to minimize bias-related the socioeconomic status of participants. A limitation of this study is that data such as education and family income of the participants were not collected.

V.

9 Conclusion

Psychoemotional symptoms are more frequent and severe than somatic symptoms. There were a lot of similarities in women's experiences of these symptoms across Brazilian regions. Symptoms had a frequency and intensity regardless of the region, which makes many women states that would be willing to take a contraceptive that reduces TPM symptoms. It is important for healthcare professionals, to make screening symptoms associated with SPM during contraception counseling to choose the most proper option.

10 List of abbreviations

Premenstrual syndrome; MRP: Market Research Programs; PSST: Premenstrual Symptoms Screening Tool [1]

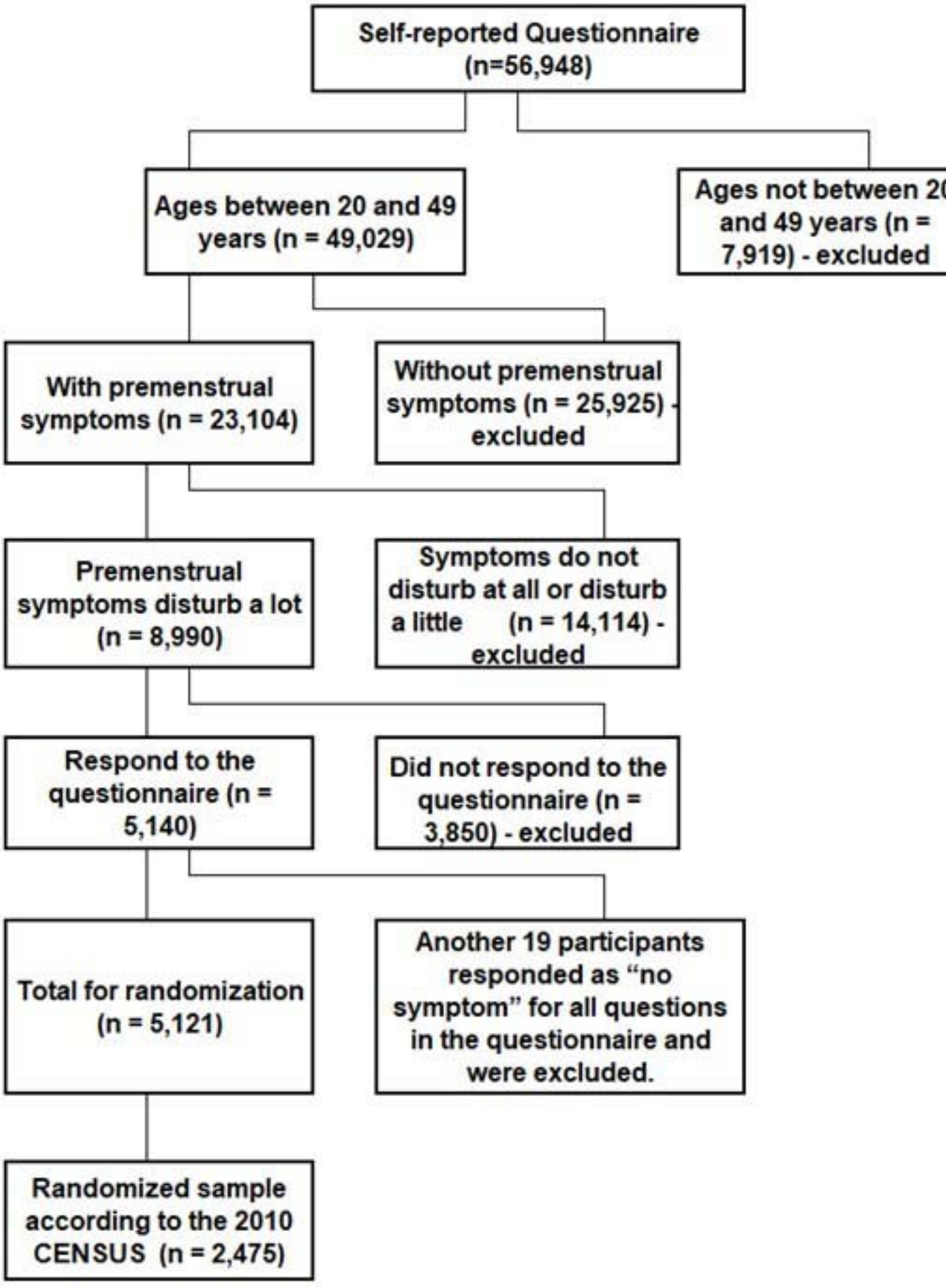

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Figure 1: Figure 1 :

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Region	State	Distrito Federal Goiás Mato Grosso		Rando
		Target Population 91 (35.3%) 94 (36.4%) 54 (20.9%)		
Mid-west	Mato Grosso do Sul	19	(7.4%)	17
	Total	258	(100%)	221
North	Amazonas	114	(57.6%)	108
	Pará	41	(20.7%)	40
	Tocantins	43	(21.7%)	42
	Total	198	(100%)	190

Figure 2: Table 1 :

2

Region of Brazil	(n=221) Midwest		North (n=190)		Northeast (n=666)		South (n=348)	
Profile -n (%)								
20 to 29 years	107	(48.4)	106	(55.8)	341	(51.2)	168	(48.3)
30 to 39 years	80	(36.2)	63	(33.2)	247	(37.1)	128	(36.8)
40 to 49 years	34	(15.4)	21	(11.1)	78	(11.7)	52	(14.9)
Total of participants	221	(100%)	190	(100%)	666	(100%)	348	(100%)
Mean (S.D.)	30.7 (7.4)		29.8 (7.2)		30.2 (7.3)		30.5 (7.5)	
Median (Min -Max)	30 (20 -49)		28 (20 -49)		29 (20 -49)		30 (20 -49)	
p (Anova Region * Age) = 0.0043	p = 0.9641		p = 0.0645		p = 0.0222		p = 0.4165	

Multiple comparisons: each region with the rest of country (? for Bonferroni correction = 0.008)
* numbers means statistical significance compared with the others.

Figure 3: Table 2 :

3

Region of Brazil		Midwest North (n=221) (n=190)
		Physical symptoms (%)
Headache	Prevalence	86.8
	Severe intensity	43.2
Acne and oily skin	Prevalence	85.1
	Severe intensity	33.0
Edema	Prevalence	84.2
	Severe intensity	23.1
Weight gain *	Prevalence	84.6
	Severe intensity	32.6

Year Prevalence Severe intensity Prevalence Severe intensity * numbers means statistical significance compared
2022

8

Figure 4: Table 3 :

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.2 Authors contribution

Adriana O. Pedro contributed to the design, writing and revision of the manuscript; Samantha B. O. Silva contributed to the design, data analysis and wrote the manuscript; Maura G. Lapa contributed to data analysis; Juliana D. P. Brandao contributed to data analysis and wrote the manuscript and Vivienne C. Castilho contributed to the design and revision of the manuscript.

All authors discussed the results and contributed to the final manuscript.

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.4 Availability of data and materials

The data generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

.5 Declarations

All procedures performed in this research were in accordance with the ethical standards and approved by Research Ethics Committee in all participating sites and was conducted following the ethical standards outlined in the Helsinki Declaration ??1983).

.6 Competing interests

Adriana O. Pedro has served on advisory boards or has been a consultant for Libbs Farmacêutica, Abott, Achè, Amgen, EMS, Eurofarma, Grumenthal, Mantecorp-Farmasa, and Sanofi. She has also served on the speaker's bureau for Libbs Farmacêutica, Abott, Achè, Amgen, EMS, Eurofarma, Grumenthal, Mantecorp-Farmasa, and Sanofi-Aventis. Samantha B. de Oliveira, Maura G. Lapa, Juliana D. P. Brandao and Vivienne C. Castilho are employed at Libbs Farmacêutica, Medical Affairs Division.

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