1. Introduction
Premenstrual syndrome (PMS) is a disorder that encompasses clinically significant somatic and psychological symptoms during the luteal phase of the menstrual cycle, leading to substantial distress and impairment in functional capacity disappearing within a few days of the onset of menstruation [1]. In different countries, the prevalence of PMS ranges 12 % [2] to 86 % [3] of the female population, with the pooled worldwide prevalence at 48 % [4].

The most common symptoms of PMS include mood swings, decreased concentration, aggression, irritability, depression, anxiety, tearfulness, breast tenderness, abdominal and/or low back pain, swelling, weakness, sweating, headache, vomiting, nausea, diarrhea, and some else psychological and physical symptoms [5, 6]. Thus, PMS is both a medical problem and a social one due to the deterioration of women’s quality of life, the development of family and intimate maladaptation, the worsening of relationships with others, and decreased efficiency of working or study activities [7]. Numerous factors, such as stress level, age, body mass index, and marital status, impact the severity of PMS [8].

Different approaches are used for the management of PMS [8]. Although recent studies [9, 10] observed the effectiveness of drug-free treatment of PMS (for instance, exercises, swimming), women still widely use medications to alleviate symptoms of PMS [5, 8]. Nonsteroidal anti-inflammatory drugs [5, 6], antidepressants, oral contraceptives, vitamins, and herbal supplements are the most common drug classes used for this purpose [2].

In Ukraine, numerous studies have been conducted on the problem of PMS. However, they are mainly concerned with studying hormonal disorders and pathology of the reproductive system [11, 12], the effectiveness of some medications [13], the impact of PMS on quality of life [14], etc. There is limited data about both (1) the prevalence of PMS symptoms among women of reproductive age and (2) the evaluation of its drug management in Ukraine, which determined the relevance and purpose of this study.

The aim of the study. To establish the prevalence of PMS symptoms and evaluate the medication management of this disorder in Lviv.

Materials and methods. The objects of the study were: scientific publications related to the problem of PMS; the results (n=105) of the survey. Methods applied: systematization, generalization, comparison, questionnaire. The statistical analyses (descriptive statistics, univariable analysis using simple logistic regression, multiple logistic regression) were performed with SPSS Trial.

Results. The prevalence of PMS among the surveyed was high (83.8 %). The most common complaints are abdominal and/or low back pain (46.6 %) and increased irritability/aggression (43.2 %). Almost half (46.6 %) of women who experienced PMS consult a pharmacist, and only 23.9 % seek medical advice. At the same time, 87.5 % (n=77) of women (among those suffering from PMS) use medicines to alleviate/eliminate the symptoms of PMS. Nonsteroidal anti-inflammatory drugs (77.6 %), sedatives (36.8 %), and complex herbal remedies that affect the genital system (18.4 %) are the most common drugs for PMS.

Choosing the way of PMS management, 44.8 % of women would prefer herbal medicines to synthetic ones. Both previous using of synthetic drugs for PMS and adverse drug reactions to synthetic drugs have a statistically significant contribution to a positive attitude towards herbal remedies (p=0.004 and p=0.026, respectively).

Conclusion. PMS is a common medical and social issue. Achieving effective and safe medication management of PMS requires the joint participation of a physician, pharmacist, and the patient in terms of compliance and lifestyle adjustments.

Keywords: premenstrual syndrome, symptoms, management, questionnaire, pharmacotherapy, nonsteroidal anti-inflammatory drugs, herbal remedies, risk factors

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Step 1. Goal setting and design of the study (literature search and analysis of worldwide publications on PMS, defining the purpose of the study, definition of objects and methods of the research, development of a survey instrument, content validation, and adjustment of the first version of questionnaire, approval the final version of survey instrument).

Step 2. Data collection and preliminary processing (survey of study participants, analysis of fulfillment of questionnaires, exclusion of the questionnaires from the final analysis due to missing information, entering the data into a customized database in SPSS).

Step 3. Statistical analysis and interpretation (analysis of the survey results with appropriate statistical and mathematical methods: descriptive statistics, univariable analysis, multiple logistic regression; presenting the results).

Step 4. Drafting the manuscript and critical revision (systematization and analysis of the results, comparing these findings with other studies, making conclusions, and defining recommendations to improve the PMS medication management).

3. Materials and methods

The questionnaire-based study was conducted in 3 pharmacy networks in Lviv, Ukraine, from June to December 2020. Totally 116 women of different ages, places of residence, professions, and fields of activity agreed to be included in the study sample. However, data from 105 questionnaires were included in the final analysis (11 questionnaires were excluded because of missing responses).

The survey instrument was a questionnaire of 20 questions related to the problem of PMS. A panel of 10 experts (gynecologists and pharmacists) examined the survey instrument for content validity. After calculating the indexes of validity, two questions were eliminated from the questionnaire. Thus, the final version of the survey instrument included 18 questions.

The statistical analyses were performed with SPSS Trial. Descriptive statistics described the qualitative (presented as frequencies and percentages) and quantitative (presented as mean±standard deviation (SD)) variables. To figure out the factors that contribute to women’s adherence to herbal remedies, a univariable analysis was conducted using simple logistic regression on each independent variable (age, employment, number of symptoms of PMS, using synthetic medications for alleviation/elimination the symptoms of PMS in the past, adverse drug reaction occurrence after using synthetic medications for alleviation/elimination the symptoms of PMS in the past). Variables with a P≤0.25 was considered statistically significant and were included in the multiple logistic regression. Multiple logistic regression was performed with forward and backward Wald tests. Results were presented as adjusted odds ratio (OR), 95% confidence interval (CI) for OR, and P-value for the variables included in the final model. A value of P<0.05 was statistically significant.

Ethics approval.

The study received ethical approval from the Human Research Ethics Committee of Danylo Halytsky Lviv National Medical University No. 10 in December 2019.

4. Results

The average age of respondents was 26.4±8.6 years (range 19–48), with the prevalence of women under 25 years. Among the 105 females involved into the final analysis, 83.8% experienced PMS. Out of them, 48.9% of participants had at least one symptom of PMS regularly (monthly), 33.0% – irregularly, and 18.1% – rarely (Table 1). Women complained mainly of 1–3 symptoms of PMS, which occurred 2–14 days before menstruation (Table 1).

<table>
<thead>
<tr>
<th>Main characteristics</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>18–25</td>
<td>75 (71.4)</td>
</tr>
<tr>
<td>26–40</td>
<td>19 (18.1)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>11 (10.5)</td>
</tr>
<tr>
<td>Employment:</td>
<td></td>
</tr>
<tr>
<td>study and/or work</td>
<td>75 (71.4)</td>
</tr>
<tr>
<td>unemployed</td>
<td>30 (28.6)</td>
</tr>
<tr>
<td>PMS symptoms:</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>88 (83.8)</td>
</tr>
<tr>
<td>monthly</td>
<td>43 (48.9)**</td>
</tr>
<tr>
<td>irregularly</td>
<td>29 (33.0)**</td>
</tr>
<tr>
<td>rarely</td>
<td>16 (18.1)**</td>
</tr>
<tr>
<td>no</td>
<td>17 (16.2)</td>
</tr>
<tr>
<td>Number of symptoms of PMS</td>
<td></td>
</tr>
<tr>
<td>1–3</td>
<td>46 (52.3)**</td>
</tr>
<tr>
<td>4–6</td>
<td>22 (25.0)**</td>
</tr>
<tr>
<td>7–9</td>
<td>9 (10.2)**</td>
</tr>
<tr>
<td>≥10</td>
<td>7 (8.0)**</td>
</tr>
</tbody>
</table>

Table 1

Note: * – SD standard deviation; ** – women (n=88) who had PMS were considered as 100%.

The most common symptoms of PMS were: (1) abdominal and/or low back pain and (2) increased irritability/aggression, observed in 46.6% and 43.2% of study participants, respectively. Increased appetite and changes in taste (36.4%), apathy, tearfulness (33.0%), loss of emotional self-control (33.0%), breast tenderness (31.8%), and depressed mood (30.7%) were also common (Fig. 1).

Much fewer women complained of (1) decreased attention, (2) isolation, (3) nightmares (11.5% among those suffering from PMS each), (4) high blood pressure, (5) headache, (6) pain radiating to the eyeballs (10.2% each), (7) bone pain (9.0%), (8) heart pain (8.0%) (9) and nausea/vomiting (3.4%).

According to the survey results, 68.6% and 31.4% of participants consider (1) chronic stress and (2) inflammatory diseases of the genital system to be the main factors contributing to the occurrence of PMS, respectively. At the same time, both frequent pregnancy (8.6% of study participants) and late reproductive age (6.7%) have the fewest influence on the development of PMS.

We found that almost half (46.6%) of women who experience PMS symptoms consult a pharmacist,
and only 23.9% seek medical advice. However, 87.5% (n=77) of respondents (among those suffering from PMS) use medications for the management of PMS. Most of them (67.6%) take drugs periodically (for severe pain or other symptoms that are “annoying”), 27.3%–monthly, and 5.2% of respondents – use medicines for a long time (Fig. 2).

More than half of the respondents (54.5%) take medicines from their own experience, 26.0% of patients – according to the pharmacist’s recommendations, 11.7% – to the doctor’s advice, and 7.8% – to the Internet. Nonsteroidal anti-inflammatory drugs (most often ibuprofen) are the most frequently used for the medication management of PMS (77.6%), followed by sedatives (36.8%), complex herbal remedies that affect the genital system (18.4%), estrogens (15.8%), hemostatic drugs (10.5%), hormonal contraceptives (7.9%), and folk remedies (5.3%) (Fig. 3).

**Fig. 1.** The most common symptoms (n=13) of PMS in the study participants: * the total percentage does not equal 100% because the responders could choose a few answers simultaneously

- Abdominal and/or low back pain: 35.1%
- Increased appetite and changes in taste: 33.0%
- Anxiety: 28.4%
- Increased body weight: 27.3%
- Skin changes, acne: 29.5%
- Depressed mood: 30.7%
- Breast tenderness: 31.8%
- Loss of emotional self-control: 33.0%
- Apathy, tearfulness: 33.0%
- Increased appetite and changes in taste: 36.4%
- Increased irritability/aggression: 43.2%
- Abdominal and/or low back pain: 46.6%

**Fig. 2.** The frequency distribution of using medications for the management of PMS

- Periodically (against severe pain): 35.1%
- Periodically (against "annoying" symptoms): 27.3%
- Monthly: 32.5%
- Regularly for a long time: 5.2%

**Fig. 3.** The distribution of the medications used for the treatment of PMS: the total percentage does not equal 100% because the responders could choose a few answers simultaneously

- Nonsteroidal anti-inflammatory drugs: 77.6%
- Sedatives: 36.8%
- Complex herbal remedies that affect the genital system: 18.4%
- Estrogens: 15.8%
- Hemostatic medications: 10.5%
- Hormonal contraceptives: 7.9%
- Folk remedies: 5.3%
81.8% (n=63) of study participants observed the effectiveness of the medicines. At the same time, 18.2% of women reported that their condition did not improve. Moreover, 28.6% of study participants had different adverse drug reactions.

According to our findings, 52.4% (n=55) of respondents believe that herbal remedies are effective. In addition, 44.8% (n=47) of women would prefer herbal remedies to synthetic medications choosing the way of PMS management. It was determined that factors contributing to women’s adherence to herbal remedies include: (1) using synthetic medications for alleviation/elimination of the symptoms of PMS in the past (OR=0.234; 95% CI 0.095–0.642, p=0.004) and (2) adverse drug reaction occurrence after using synthetic medications for alleviation/elimination the symptoms of PMS in the past (OR=3.192; 95% CI 1.152–8.848, p=0.026) (Tables 2, 3).

The study found that 53.3% of women need different information on PMS. Evidence-based data about the effectiveness of medications and the principles of rational pharmacotherapy of PMS were the most frequently required, which reported 35.7% and 32.1% of women, respectively (Fig. 4).

5. Discussion

The prevalence of PMS in Ukrainian women is high and in this study was about 84%. The rates of PMS vary significantly across different countries and study populations [2, 3, 5]. For instance, the prevalence of PMS in France is 12% [15], in Poland – 42% [16], Brazil – 47% [17], Ethiopia – 53% [18], Nigeria – 69% [19], Nepal – 72% [20], Spain – 73% [21], Iran – 74% [5], Thailand – 86% [3]. A wide range of prevalence rates in different studies might be due to using various tools of measurement and data collection methods [3, 4, 6]. Moreover, attitude and perception of PMS by women can lead to overestimating the symptoms [2, 3, 22].

More than half (52.3%) of participants complained of 1 to 3 symptoms of PMS, 25% – from 4 to 6 simultaneously. At the same time, about 18% of the female population experienced seven or more symptoms. The most common manifestations of PMS were both physical and psychological disorders, including abdominal and/or low back pain (46.6%), increased irritability and aggression (43.2%), followed by tearfulness, apathy (33.0%) and loss of emotional self-control (33.0%). This distribution confirms the results of the previous study in Iran, where low back pain and mood swings were the main complaints of PMS (59.1% and 64.9%, respectively) [5]. However, other studies established a considerably high proportion of other disorders. For instance, in Pakistan the most common symptoms were irritability, anger, depression, breast tenderness and gastrointestinal disorders [6], in Thailand – breast tenderness and angry outbursts [3].

According to our findings, 68.6% and 31.4% of respondents consider constant stress and inflammatory diseases of the genital system as the main risk factors of PMS, respectively. A lot of studies have investigated the risk factors of PMS so far [18]. As described in scientific literature, the presence of PMS is associated with age [16, 17, 23], lower education and unemployment [17], early menarche (<12 years) [23], sedentary lifestyle [17, 24, 25], stress and depression [17, 24, 26]. Also, there is a statistically significant association between the

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Table 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>Crude OR (95% CI)</th>
<th>Wald Statistics (df)</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.991 (0.950–1.034)</td>
<td>0.168 (1)</td>
<td>0.682</td>
</tr>
<tr>
<td>Number of symptoms of PMS</td>
<td>0.992 (0.871–1.128)</td>
<td>0.016 (1)</td>
<td>0.898</td>
</tr>
</tbody>
</table>

Employment:

- unemployed: 1.000
- study and/or work: 0.898 (0.384–2.101), 0.062 (1), 0.804

Using synthetic medications for alleviation/elimination the symptoms of PMS in the past:

- yes: 1.000
- no: 0.336 (0.136–0.826), 5.652 (1), 0.017

Adverse drug reaction occurrence after using synthetic medications for alleviation/elimination the symptoms of PMS in the past:

- no: 1.000
- yes: 2.082 (0.800–5.414), 2.260 (1), 0.133

Note: * – simple logistic regression (P-values by Wald test), significant at P<0.05

Table 3

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted OR (95% CI)</th>
<th>Wald Statistics (df)</th>
<th>P valuea</th>
</tr>
</thead>
</table>
| Using synthetic medications for alleviation/elimination the symptoms of PMS in the past:
- yes: 1.000
- no: 0.234 (0.095–0.642), 8.234 (1), 0.004

Adverse drug reaction occurrence after using synthetic medications for alleviation/elimination the symptoms of PMS in the past:

- no: 1.000
- yes: 3.192 (1.152–8.848), 4.978 (1), 0.026

Note: Multicollinearity and interaction term were checked and were not found. Hosmer-Lemeshow test, classification table and the area under the ROC-curve were applied to check the model fitness and reported to be fit; a – adjusted to account for other predictors in the model; b – multiple logistic regression (P-values by forward and backward Wald tests), significant at P<0.05
According to the evidence-based search, nonsteroidal anti-inflammatory drugs are effective against pain in women with PMS (level of evidence A) [29]. However, this group of drugs has a pronounced ulcerogenic effect on the mucous membrane of the gastrointestinal tract [27]. Therefore, the duration of nonsteroidal anti-inflammatory drugs usage (particularly in self-medication) should not exceed three days [29]. Herbal remedies with chasteberry (Vitex Agnus-castus) inhibit the secretion of dopamine and follicle-stimulating hormone, normalize the hormonal imbalance of the estrogen-progesterone system, and reduce prolactin secretion [30, 31]. Medications containing St. John’s wort (Hypericum perforatum) are effective in eliminating behavioral disorders in PMS (level of evidence C) [32–34]. Medicines based on black cohosh (Cimicifuga racemosa) facilitate “hot flashes”, reduce sweating, normalize nervous stress, and eliminate headaches, depression, anxiety, and insomnia (level of evidence C) [35, 36].

**Study limitations.** All data were obtained from retrospective self-reporting survey. Thus, original information was based on the participant’s subjective assessment which could result in over- or underestimation of some findings.

**Further prospective studies** are needed to avoid bias.

Only 5 factors were included in the regression analysis to establish the women’s adherence to herbal remedies for medication management of PMS. Hence, future studies are needed to explore the impact of other characteristics on adherence.

Other important limitations of this study were the sample size and carrying out the survey only in one city which limits the generalizability of our findings. However, this study provides valuable results for evaluating the prevalence of PMS and its management.

7. **Conclusions**

1. The prevalence of PMS was high (83.8 %). The most common symptoms of PMS were abdominal and/or low back pain (46.6 %), followed by increased irritability/aggression (43.2 %).

2. More than 87 % of women who experienced at least one symptom of PMS used medications for the management of PMS: nonsteroidal anti-inflammatory drugs (77.6 %), sedatives (36.8 %), complex herbal remedies that affect the genital system (18.4 %). This distribution indicates the multicomponent use of drugs and, hence, the need for clinical and pharmaceutical evaluation of drug management of PMS.

3. Self-medication of PMS is a common problem because 88 % of women take drugs without medical advice. At the same time, more than half of the respondents (53.3 %) would like to receive additional information on PMS. Thus, we believe that achieving effective and safe medication management of PMS requires the joint work of a physician, pharmacist, and the patient (in terms of compliance and lifestyle adjustments).

### Table 4

**Clinical efficacy of medicines for PMS**

<table>
<thead>
<tr>
<th>Medications/plants</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal anti-inflammatory drugs [29]</td>
<td>A</td>
</tr>
<tr>
<td>Chasteberry (Vitex Agnus-castus) [30, 31]</td>
<td>B</td>
</tr>
<tr>
<td>St. John’s wort (Hypericum perforatum) [32–34]</td>
<td>C</td>
</tr>
<tr>
<td>Black cohosh (Cimicifuga racemosa) [35, 36]</td>
<td>C</td>
</tr>
</tbody>
</table>
4. Women with PMS have a positive attitude towards herbal remedies. Both previous using of synthetic drugs for PMS and adverse drug reactions to synthetic drugs have a statistically significant contribution to a positive attitude towards herbal remedies (p=0.004 and p=0.026, respectively).

5. The literature analysis showed that drugs commonly used for PMS (nonsteroidal anti-inflammatory drugs) have the level of evidence A. At the same time, herbal remedies based on chasteberry have level B, black cohosh – level C, and St. John’s wort – level C.

Conflict of interest
The authors declare that they have no conflicts of interest.

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References


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