MEDICAL UNIVERSITY PLEVEN

DEPARTMENT OF PSYCHIATRY AND MEDICAL PSYCHOLOGY

ABSTRACT
OF DISSERTATION
FOR ACQUIRING AN EDUCATIONAL AND SCIENTIFIC DEGREE
„DOCTOR OF MEDICINE”

„Clinical and epidemiological aspects of Premenstrual syndrome and characteristics cases of comorbidity with Depressive and Panic disorders"

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Scientific field: 03.01.20 Psychiatry

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The dissertation consists of 150 pages and is illustrated with 49 tables and 22 colour figures. The supplements include: A questionnaire card, evaluating the awareness of women of PMS and their attitudes towards its treatment; A scale, evaluating PMS/PMDD - PSST; Mini International Neuropsychiatric Interview (M.I.N.I. 6.0.0.).

The Reference list includes 246 authors, 6 of whom in Cyrillic and 23% published after 2012. The dissertation was discussed and proposed for defense at a Board meeting of the Department of psychiatry and medical psychology, Medical university – Pleven, that took place on 19.11.20.

The official defence will take place on 29 Apr 2021 at 12:30 PM at Ambroise Paré Hall – Medical University, according to Decision of the Rector of MU Pleven № 289/02 Feb 2021 before a scientific committee:

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Materials, related to the defence are published on the internet site of MU – Pleven.

Note: The numbering of the tables and figures in this abstract do not correspond to those in the dissertation.

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LIST OF ABBREVIATIONS:

ACOG – American College of Obstetrics and Gynaecology
APA – American Psychiatric Association
MDE – Major depressive episode
DD – Depressive disorder
IAPMD – International Association for Premenstrual Disorders
ICD-10 – International Classification of Disease, 10th ed
PMD – Premenstrual disorders
PMS – Premenstrual syndrome
PMDD – Premenstrual dysphoric disorder
PMS-N – Premenstrual syndrome with no psychiatric comorbidity
PMS-DD – Premenstrual syndrome, comorbid with depressive disorder
PMS-PD – Premenstrual syndrome, comorbid with panic disorder
PD – Panic disorder
MDD – Major depressive disorder
WHO – World Health Organisation
SSRI – Selective inhibitors of serotonin re-uptake
COPE – Calendar of Premenstrual Experience
DRSP – Daily Record of Severity of Problems
DSM-IV – Diagnostic and Statistical Manual of Mental Disorders, 4th ed
DSM-5 – Diagnostic and Statistical Manual of Mental Disorders, 5th ed
PAF – Premenstrual Assessment Form
PSST – Premenstrual Symptoms Screening Tool

I. INTRODUCTION

For many women the reproductive years are related to exhausting premenstrual symptoms, that can impair their quality of life and relationships with their closest. Premenstrual syndrome (PMS) can be defined as every set of psychological and somatic symptoms, that appear regularly during the luteal phase of the menstrual cycle, cause functional impairments, and disappear during menstruation. The psychological symptoms include depression, anxiety, anger, and irritability, swift mood changes, lack of interest towards usual activities, and impaired concentration. Common expressions are also fatigue, appetite changes, indisposition, abdominal bloating and/or breast swelling, stomach aches, headache. The individual differences in the symptoms presentation, their severity and variations between cycles show, that the defining characteristic of this syndrome is its clear manifestation within exact timeframe (Rapkin A, 2003). The diagnosis Premenstrual dysphoric disorder (PMDD) also requires that the symptoms have been present only during the luteal phase in the course of several successive months, and have been prospectively confirmed. Women have to experience difficulties with at least one emotional symptom (for example, low spirit, irritability, etc.). Their complaints have to be of enough severity so that they interfere with some aspects of their psychosocial functioning (APA, 1994; APA, 2011).

Distinct premenstrual symptoms are registered in approximately 80% of women in the general population, 20 to 40% report on more disturbing symptoms, that clearly affect the overall well-being, as well as the interpersonal relationships at home and work, defined as PMS. Between 2% and 6% of women experience severe PMDD symptoms, that substantially impair their health (Sveindorttir H, Backstrom T, 2000; Connolly M, 2001).

The estimates on the prevalence of PMS show significant differences among different cultures and ethnic groups. Shershah and co-authors conducted a demonstrative in that respect study, in which they report, that PMS was registered in 37% of the Pakistani women, living in the Mohajir and Punjabi regions and in only 11,6% of those, living in Baluchistan (Shershah S. et al.,1991). At the other extreme are the very low levels of prevalence in Japanese women reported by Takeda – 1,2% of the participants were identified as having PMDD, and 5,3% with PMS (Takeda T. et al., 2007). The exactly opposite results are registered in Mianmar – the prevalence of PMS there reaches up to 54,4% (Htet Htet Oo et al., 2016).

As PMS manifests within at least two decades of the lifetime of women, the expected comorbidity with other psychiatric disorders is high. The studies that examine the concomitant existence of both panic disorder (PD) and PMS/PMDD show, that this comorbidity is very common – between 1% and 9% of women with PMS also fulfil the diagnostic criteria for PD (Pearlstein T. et al.,1990; Chandraiah S. et al., 1991; Stout A.,1986). Interestingly, among women with prospectively confirmed premenstrual difficulties, the simultaneous presence of PMS and PD is registered in 16% to 25% (Harrison W. et al., 1989; Fava M. et al., 1992).

Female gender is related to nearly twice as high risk of Major depressive disorder (MDD) compared to male gender (Halbreich U., 2003). This between gender difference is registered first after the menarche and dissipates after the menopause (Lasiuk G., 2007). The considerable rate of major depressive episode (MDE) in women increases the probability of also being diagnosed with PMS and PMDD. Furthermore, according to DSM-IV, PMDD

should be classified as "depressive disorder, not otherwise specified" (APA, 1994). In DSM-5 PMDD is classified among the depressive disorders as a comorbidity of affective disorders or a deterioration of current affective disorder (APA, 2011). This categorisation demonstrates, that the overall medical characteristics and symptoms of PMDD are closely related to depression.

The knowledge of PMS has gone through different phases - from its complete denial and attitudes as if it was an attempt of the female population from Western Europe to set themselves on a pedestal (Johnson S. et al.,1988) to an over diagnosed condition in some communities (Rasheed P. et al., 2003). And because of that in 2007 Halbreich and an expert group in the field of PMS propose a diagnostic consensus and recommend a new set of criteria for research purposes (Halbreich U. et al, 2007). They do not offer a list of major symptoms but on the contrary - they broaden to largely the reference range in that for the purpose of scientific research they include all kinds of symptoms or clusters of symptoms as long as they appear mostly during the luteal phase of the menstrual cycle, disappear right after the end of menstruation, and are not simply deterioration of other disorders. In the above-mentioned diagnostic recommendations the cyclic manifestation/disappearance of PMS/PMDD is explicitly stated, and the clear transition from asymptomatic to symptomatic, and then again to asymptomatic phase is specifically underlined. These enriched criteria are in accordance with the ideas of leading experts like Young S. et al. (1998), Freeman E et al. (2004), Walsh S. et al. (2015), who persistently and continuously ask the question whether there are multitude differing premenstrual syndromes, that include various premenstrual phenotypes. They step on the conception of liability and menstrually related symptom groups, necessary for the manifestation of PMS. The liability changes over time and can be increased or diminished according to hormonal changes, stress levels, exhaustion, live events, etc. But is it possible that this liability is related to concomitant psychic disorders, sharing common biochemistry? The clarification of that question could aid the understanding of the aetiology and pathobiology of PMS, and the discovery of effective treatment. Currently, only the selective serotonin re-uptake inhibitors (SSRI) are recognised as effective psychopharmacological agents for that indication, even though they are better than placebo by only around 20% (Halbreich U. et al., 2006; O'Brien P. et al., 2011; Walsh S. et al., 2015).

The different variants of PMS continue to be the in focus of the researchers. In 2015 the International Association for Premenstrual Disorders (IAPMD) review and define all types of premenstrual disorders and divide PMS into core (typical) and variant PMS (Walsh S. et al., 2015). The typical PMS is related to spontaneous ovulatory menstrual cycles, which can be subdivided to a type with dominating physical, psychological, or mixed symptoms, but it remains unclear why the expression of symptoms is so variable.

The aim of this study to search for subgroups of PMS with comorbid DD or PD was our humble attempt to help discerning this problem. PMS with comorbid anxiety or depressive disorders creates additional diagnostic difficulties and sometimes complicates the treatment and slows the alleviation of both disorders. Considering that, this patients population needs to be the subject of targeted research.

Many studies show that PMS is related to considerable indirect economic losses for the affected women. The researchers detect substantial effect on the productivity, quality of life,

and level of functioning of the women with PMS/PMDD, which is comparable to other severe diseases like diabetes, hypertension, depressive disorder (Sternfeld B. et al., 2002; Chawla A. et al., 2002; Halbreich U. et al., 2008; Borenstein D., 2004; Yang M. et al., 2008; Robinson R. et al., 2012). At the same time, the syndrome remains hardly recognised by physicians and patients and because of that women do not seek help for its alleviation (Robinson R. et al., 2000; Sinclair K., 2018; Janda C. et al., 2019). This necessitates taking measures for their active education and searching for adequate therapeutic methods.

II. HYPOTHESIS

PMS and its severe form - PMDD are common disorders among women in fertile age, but certain specific features have been described in different nationalities and ethnic groups. However, there is no data on the prevalence and clinical picture of PMS in the Bulgarian population.

Although there is evidence in the literature on the serious socio-economic effects of the disorder, it often goes unrecognised, is not acknowledged as medical problem and people do not seek help for its treatment, which probably also holds true for Bulgarians.

The question remains, if there are different types of PMS. High levels of comorbidity with depressive and anxiety disorders have been described. It is possible, that there are distinct subgroups of PMS depending on the comorbidity.

III. AIMS AND TASKS

The fundamental aim of the present work is the evaluation of the prevalence and the main symptoms of PMS in the Bulgarian population, and the quest for characteristic features of subgroups of PMS in cases of comorbidity depressive and panic disorder. That necessitated the formation of three groups to be evaluated and compared – women with PMS and no comorbidity (PMS-N); women with PMS and comorbid depressive disorder (PMS-DD); women with PMS and comorbid panic disorder (PMS-PD).

A. Aims and tasks in the group of PMS and no psychiatric comorbidity (PMS-N)

Aim:

1. To evaluate the prevalence of PMS in a randomly recruited sample of Bulgarian women in fertile age;

2. To delineate the most common symptoms and their severity in the Bulgarian sample;

3. To explore the rate of help-seeking behaviour in relation to PMS, as well as the attitudes towards its overcoming in the examined Bulgarian sample.

For that purpose the following **tasks** were set:

1. To evaluate by means of a screening scale the presence of PMS in a randomly recruited sample of mentally healthy women, aged between 18 and 50 with regular menstrual cycles;

2. To systematically examine and evaluate the clinical characteristics, severity of the symptoms, and the ratio somatic/psychological symptoms, as well as the overall severity of the syndrome in women suffering PMS;

3. To evaluate the influence of age on the expression and severity of the symptoms;

4. To evaluate the characteristics and the prevailing manifestations in sub-threshold PMS (regular premenstrual indisposition) and to compare them to the clinical characteristics of PMS;

5. To elucidate the attitudes towards treatment and the readiness to initiate one in the examined sample of Bulgarian women.

Б. Aims and tasks in the group of PMS and comorbid depressive disorder (PMS-DD)

Aim:

1. To evaluate the possible pathoplastic alterations in the clinical picture of PMS in women, who sought treatment for first or consecutive episode of MDD;

2. Comparative analysis of PMS with comorbid depressive disorder and PMS with no psychiatric comorbidity.

For that purpose the following **tasks** were set:

1. To evaluate the clinical characteristics, severity of symptoms, and the ration somatic/psychological symptoms in women suffering PMS aged between 18 and 50 with regular menstrual cycles and concomitant first or consecutive depressive episode;

2. To evaluate the severity of PMS in patients with first or consecutive depressive episode;

3. To systematically compare the clinical picture of PMS with DD (PMS-DD) and PMS with no comorbidity (PMS-N).

В. Aims and tasks in the group of PMS and comorbid panic disorder (PMS-PD)

Aim:

1. To evaluate the possible pathoplastic alterations in the clinical picture of PMS in women, who sought treatment for PD;

2. Comparative analysis of PMS with comorbid panic disorder and PMS with no psychiatric comorbidity.

For that purpose the following **tasks** were set:

1. To evaluate the clinical characteristics, severity of symptoms, and the ration somatic/psychological symptoms in women suffering PMS aged between 18 and 50 with regular menstrual cycles and concomitant panic disorder;

2. To evaluate the severity of PMS in patients with PD;

3. To systematically compare the clinical picture of PMS with PD (PMS-DD) and PMS with no comorbidity (PMS-N).

IV. MATERIALS AND METHODS

4.1. Study design

This study has complex design, encompassing:

1. An analytic, observational (non-interventional) study, that includes three cross-sectional analyses with retrospective gathering of part of the data in women with PMS and no psychiatric co-morbidity, women with PMS and co-morbid depressive disorder, and women with PMS and co-morbid Panic disorder;

2. Descriptive data analysis of the attitudes of women with PMS towards its presence and treatment.

The study design, the inform consent form, and the utilised scales were granted permission by the independent ethics committee of UHATNP "Sveti Naum" Ltd-Sofia and all study procedures were conducted in accordance with the requirements of the Declaration of Helsinki and the regulations for good clinical practise. The anonymity of the participants was preserved.

4.2. Study subjects

1. Women, screened for the presence of PMS. They formed 2 subgroups - women with and women without PMS. The group of women with PMS was further divided according to the age of the participants into a group of women below 35 years of age and a group of women over 35 years of age, respectively. The data was gathered from 305 women altogether.

1.1.Women with PMS and MDD, current depressive episode. The data was gathered in a group of 31 women.

2. Women with PMS and current first or consecutive episode of PD. The data, obtained from 30 women with PMS and PD was analysed.

4.2.1 Inclusion and exclusion criteria for the group with PMS and no co-morbidity

Inclusion criteria

▪ Mentally healthy women with Bulgarian ethnicity, aged between 18 and 50 years with regular menstrual cycles of 21 to 35 days duration, who do not use oral contraceptives or psychotropic medications.

Exclusion criteria

▪ Women, who are currently breast-feeding or have been breast-feeding in the preceding 3 months, as well as pregnant women over 12th pregnancy week.

▪ Women, who use oral contraceptives.

▪ Women, who suffer psychiatric disorders and use psychopharmacological medications for any reason.

▪ Women, who have been subjected to hyster- or ovariectomy, who suffer other gynaecological conditions (as for example, uterine bleedings, hormonally determined

gynaecological diseases), or who are taking hormonal preparations, that could alter the natural cyclicality of female sex hormones.

- Grouping criteria

- The group of women with PMS was defined as women, who have regularly experienced premenstrual symptoms in the preceding 12 months.

- The group of women without PMS was defined as women, who do not experience premenstrual symptoms or who do experience such symptoms but they were not related to disfunction in the preceding 12 months.

4.2.2 Inclusion criteria for the group of women with PMS and co-morbid Depressive disorder (PMS-DD)

Inclusion criteria

- Patients, who were diagnosed with first or consecutive MDD depressive episode and are suffering concomitant PMS, that was regularly present in the preceding 12 months.

- Somatically and gynaecologically healthy women aged between 18 and 50 years with regular menstrual cycles with 21 to 35 days duration.

Exclusion criteria

- Women, who are currently breast-feeding or who have been breast-feeding in the preceding 3 months.

- Women, who use oral contraceptives.

- Women, who have been subjected to hyster- or ovariectomy, who suffer other gynaecological conditions (as for example, uterine bleedings, hormonally determined gynaecological diseases), or who are taking hormonal preparations, that could alter the natural cyclicality of female sex hormones.

4.2.3 Inclusion and exclusion criteria for the group of women with PMS and co-morbid Panic disorder (PMS-PD)

Inclusion criteria

- Patients, who were diagnosed with PD and are suffering concomitant PMS.

- Somatically and gynaecologically healthy women aged between 18 and 50 years with regular menstrual cycles with 21 to 35 days duration.

Exclusion criteria

- Women, who are currently breast-feeding or who have been breast-feeding in the preceding 3 months.

- Women, who use oral contraceptives.

▪ Women, who have been subjected to hyster- or ovariectomy, who suffer other gynaecological conditions (as for example, uterine bleedings, hormonally determined gynaecological diseases), or who are taking hormonal preparations, that could alter the natural cyclicality of female sex hormones.

5. Procedures

5.1 Methodology for the PMS-Non group

The questionnaire for the evaluation of premenstrual syndrome was distributed to mentally healthy Bulgarian women aged between 18 and 50 years, who had regular menstrual cycles, and were living and working in city environment. The women were recruited by visiting randomly chosen companies, administrative institutions, universities. The participants were thoroughly informed about the за essence and the clinical presentations of the premenstrual syndrome. After signing the informed consent form they filled-in a PMS questionnaire based on the Premenstrual Symptoms Screening Tool (PSST). They evaluated retrospectively their premenstrual symptoms in the preceding 12 months. Afterwards they filled-in a questionnaire card asking for their attitudes towards PMS and the need for treatment.

5.2 Methodology for the PMS-DD

Patients aged between 18 and 50 years with regular menstrual cycles, no gynacologic conditions, and not taking any hormonal preparations were examined, who were diagnosed according to ICD 10 criteria with a current first or consecutive depressive episode. The sample was recruited in clinical as well as outpatient conditions among consecutively admitted for the treatment of a first of consecutive depressive episode women in fertile age (18 - 50 years old). The depressive episode was diagnosed by administration of the M.I.N.I. 6.0, as it strictly follows the ICD 10 diagnostic criteria. Those women, who were diagnosed with a current depressive episode were first informed essence of PMS and after they declared informed consent to participate in the study, they were asked to fill-in a PMS questionnaire based on the PSST. They evaluated retrospectively their premenstrual symptoms during the preceding 12 months.

5.3 Methodology for the PMS-PD

Examined were patients, who were diagnosed according to the criteria of ICD 10 with panic disorder and concomitant PMS. Furthermore, they were aged between 18 and 50, had regular menstrual cycles, no gynaecological conditions, and no intake of hormonal preparations. The sample was recruited in outpatient and hospital conditions among consecutively visiting women in fertile age with PD. panic disorder was diagnosed by means of M.I.N.I. 6.0, as it strictly follows ICD 10 diagnostic criteria. Those women, who were diagnosed with current panic disorder, were offered to fill-in a questionnaire on PMS based on the PSST, but only after they were informed on the essence of the syndrome and declared their informed consent for participation. They evaluated retrospectively their premenstrual symptoms during the previous 12 months.

5.4 Tools

5.4.1 Scale for evaluation of PMS/PMDD

We used the modified Premenstrual Symptoms Screening Tool – PSST. The somatic symptoms were extracted in separate questions for the sake of their more accurate evaluation. The choice of this tool was motivated by the fact, that it is user-friendly, fast to complete screening instrument, that was developed by Steiner (Steiner M. et al., 2003) to aid the identification of women, suffering PMS/PMDD. It consists of twenty questions, tapping on psychological and somatic symptoms, that persisted every the 2 weeks before menses during the preceding year. The presence of questions also on impairments in the social and occupational fields turns the questionnaire into a clinically important tool. Furthermore, it corresponds the latest research guidelines, that require the inclusion of the broadest possible spectrum of symptoms for the longest possible time period. It includes clear set of criteria for diagnosing PMS/PMDD. The severity grades are 4: absent, mild, moderate, and severe symptom. The following criteria are used for diagnosing mild to moderate PMS: 1. At least one of 1^{-st}, 2^{-nd}, 3^{-d} или 4^{-th} questions should be rated as mild/moderate; 2. In addition at least four of the questions 1 to 19 should be rated as mild/moderate; 3. Question 20 should be rated as mild/moderate. The criteria for diagnosing PMDD are as follows: 1. At least one of 1^{-st}, 2^{-nd}, 3^{-d} или 4^{-th} questions should be rated as severe; 2. In addition at least four of the questions 1 to 19 should be rated as severe; 3. Question 20 should be rated as severe.

5.4.2. A questionnaire card, evaluating the awareness of women of PMS and their attitudes towards its treatment

The questionnaire card was created specifically for the purpose of this study. It included questions on the help-seeking behaviour for PMS up to the present moment; the medication intake for relieving the condition; by what medical specialist were those medications prescribed; the attitudes towards consultation with medical specialist; the reasons for avoiding a consultation (for example, the idea that the syndrome is in fact normal part of women's life and not a pathological condition; the idea, that it has to be borne despite it causes suffering; the complaints are not always severe); the attitudes towards treatment; presence of relatives (mother, grandmother, sisters, other related women), who have or had similar problems before menses between 20 and 40 years of age.

5.4.3 Mini International Neuropsychiatric Interview; M.I.N.I. 6.0.0.

M.I.N.I. Is a brief, structured, diagnostic interview, that was developed for the purpose of diagnosing disorders according to DSM and ICD 10. Its administration takes around 25 minutes. It is suited for clinical, as well as research settings. It was validated according to the Structured clinical interview for DSM (SCID), The composite international diagnostic interview for ICD 10 (CIDI) and the opinion of experts' panel [229]. It encompasses the diagnostics of major depressive episode, dysthymia, suicidal behaviour, hypo-/manic episode, panic disorder, agoraphobia, social phobia, obsessive-compulsive disorder, generalised anxiety disorder, post-traumatic stress disorder, psychotic disorders, eating disorders, abuse disorders, and antisocial personality disorder.

6. Statistical methods

6. 1. Descriptive statistics.

- ✓ Variation analysis (quantitative variables) - mean, standard deviation, mediane, minimum, maximum.
- ✓ Frequency analysis (nominal and rang variables) - *absolute frequencies* – the number of entities in a certain group; *relative frequencies* – the number of entities in the total entity
- ✓ Graphic images - bar charts.

6. 2. Methods for testing hypotheses.

- ✓ Kolmogorov - Smirnov Test and Shapiro - Wilk Test – for testing hypotheses of normality of the distribution of quantitative variables;
- ✓ Chi-square test or Fisher's exact test – for looking for a relationship between two categorical variables;
- ✓ Mann-Witney Test – for comparison of two independent groups in case of rang variables or when the normality of distribution and/or the homogeneity of variations is breached;
- ✓ Kruskal-Wallis Test – for comparing of more than two independent groups in case of rang variables or when the normality of distribution and/or the homogeneity of variations is breached.

$\alpha = 0,05$ was considered statistically significant. The corresponding null hypothesis is rejected, when the p-value is smaller than α for the Kruskall-Wallis Test, and smaller than 0.0167 for the Mann-Whitney Test.

The data was analysed by means of the specialised statistics package SPSS, version 13.0.

V. RESULTS

5.1 Prevalence of PMS

The primary analysis included descriptive statistics and comparisons of the mean/frequency distributions of basic characteristics of the syndrome in the examined groups. The data was gathered by 305 women in total. In 67,9% (N=207) of them PMS was not present and they formed the group of women with no PMS and in 32,1% (N=98) PMS was registered, so they were included in the group of women, suffering PMS. The mean age of the women with PMS was 31.04 ±6.31 and the mean age of women without PMS was – 30.22 ±5.37. Both groups did not differ significantly by age (t(303)=1.174, p=0.241).

The syndrome was mild in 15,4% (N=47), moderate in 13,4% (N=41), and severe, corresponding the criteria for PMDD in 3,3% (N=10), (Fig.1).
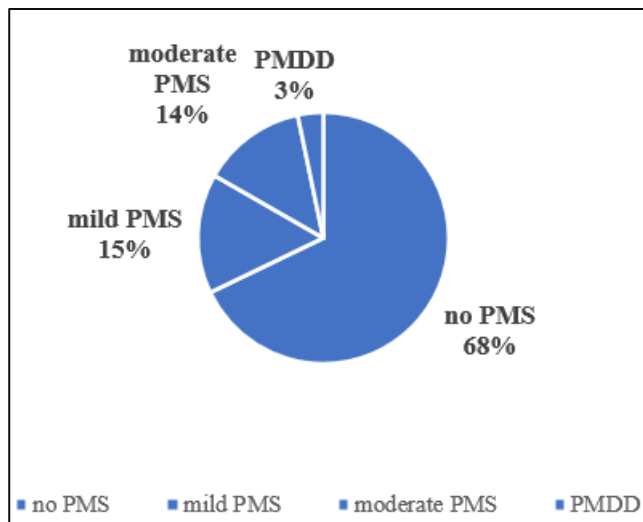
Figure 1. Percentage of women **with** and **without** PMS

5.2 Symptom analysis of the subgroup without PMS:

In 6,3% (N=13) of the women without PMS there were no symptoms, and in 93,7% (N=194) of them there were sub-threshold ones or the so-called "normal" premenstrual complaints.

Psychological symptoms were registered with differing frequency, as follows: *irritability* – in 49,7% (N=103), *sweets craving* – 47,7% (N=99), *increased appetite* – 58,5% (N=121), *fatigue* – 43,5% (N=90), and 17,4% (N=36) of the inquired women define the appetite change they experience as severe. These were followed by *absent-mindedness* – 29,5% (N=61), *grief* – при 26,1% (N=54), *mood swings* –25,6% (N=53). Of the women without full blown PMS 9,2% (N=19) experienced also *changes in their sleep pattern*, 9,1% (N=19) *anxiety*, and 3,4% (N=7) *despair* (fig. 13 and 15).

Somatic symptoms: 81,1% (N=168) of the women in our sample reported on *breast tension and tenderness*, moreover in equally 33,8% (N=70) this symptom was mild and moderate, resp., and in 13,5% (N=28) – severe. *Abdominal bloating* was experienced by 74,4% (N=154), in 39,6% (N=82) of whom it was mild, in another 19,3% (N=40) – moderate, and in 15,5% (N=32) - severe. Of all examined women 41,1% (N=85) suffered *headache*, which was rated as severe by 10,1% (N=21). 35,3% (N=73) of the women had *gained weight*. *Joint aches* suffered 16,4% (N=34), *muscle aches* – 14% (N=29), *palpitations* – 8,2% (N=17), *shivering, hot and cold flashes* – 14,5% (N=30) (Fig. 14 and 16).

The ratio of psychological to somatic symptoms was 34,8%: 65,2% (Fig. 17).

5.3 Clinical characteristics of the subgroup with PMS:

Severity: 32,1% (N=98) of the whole sample fulfilled the criteria for PMS, moreover in 15,4% (N=47) it was mild, in 13,4% (N=41) – moderate, and in 3,3% (N=10) severe (Fig. 1)

In women with full blown PMS the psychological symptoms were represented as follows: the most prevalent symptom was *irritability* (87,8%; N=86), followed by *fatigue* – 79,6% (N=78), *mood swings* – 76,5% (N=77), *sadness* – 78,7% (N=77), *absent-mindedness* – 60,2% (N=59) and *anxiety* – 70,4% (N=69). *Changes in appetite* were registered in 79,6% (N=78). *Sweets craving* was present in 69,4% (N=68). *Changes in the sleep pattern* reported

42,9% (N=42). *Despair* and *apathy* were recorded in 35,7% (N=35) and 30,6% (N=30) of the participants, resp. (Fig. 2)

Figure 2. Distribution of the psychological symptoms by prevalence in the group **with** PMS
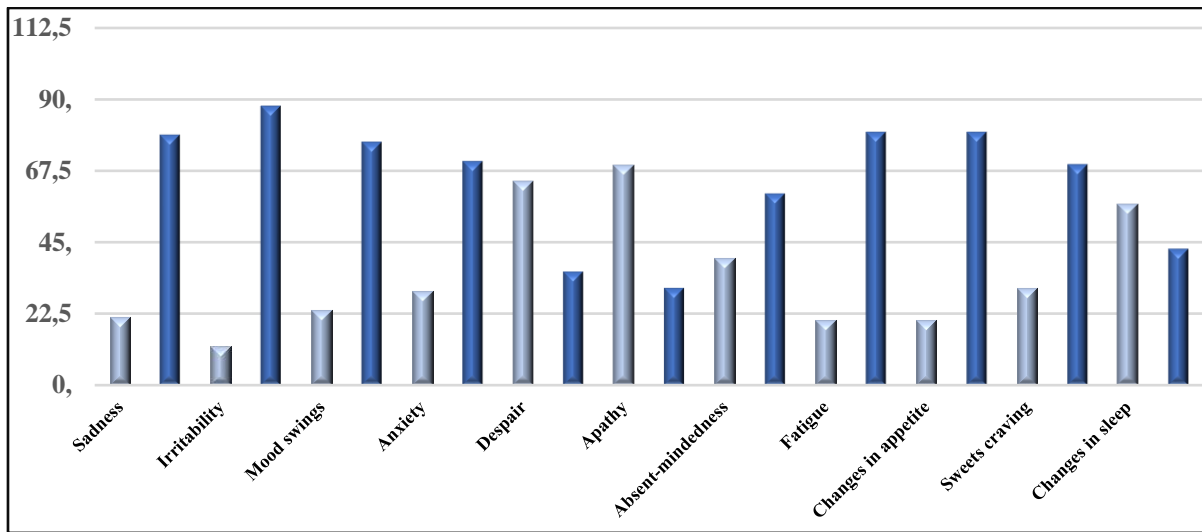
The severity of irritability was mild in 28,6% (N=28), in 32,7% (N=32) it was moderate, and in 26,5% (N=26) it was severe. The fatigue is equally distributed: mild in 26,5% (N=26) of the participants, moderate in – 30,6% (N=30), and severe in – 22,4% (N=22). Regarding the variable „mood swings" a slight prevalence of the moderate cases was detected – 35,7% (N=35) and equal parts of mild and severe ones – 20,4% (N=20). With the symptom "sadness" the mild and moderate forms prevail, in 37,8% (N=37) and 27,6% (N=27), resp., and severe were 13,3% (N=13) of the cases. The symptom „absent-mindedness" was distributed as follows: mild in 28,6% (N=28), moderate – 21,4% (N=21), and severe – 10,2% (N=10). The anxiety was also more frequently mild or moderate, in 33,7% (N=33) and 26,5% (N=26), resp., and severe in 10,2% (N=10). Changes in appetite: in 10,2% (N=10) of the cases it was mild, 41,8% (N=41) were moderate, and 27,6% (N=27) were severe (Fig. 3).

Figure 3. Distribution psychological symptoms by severity in the group **with** PMS
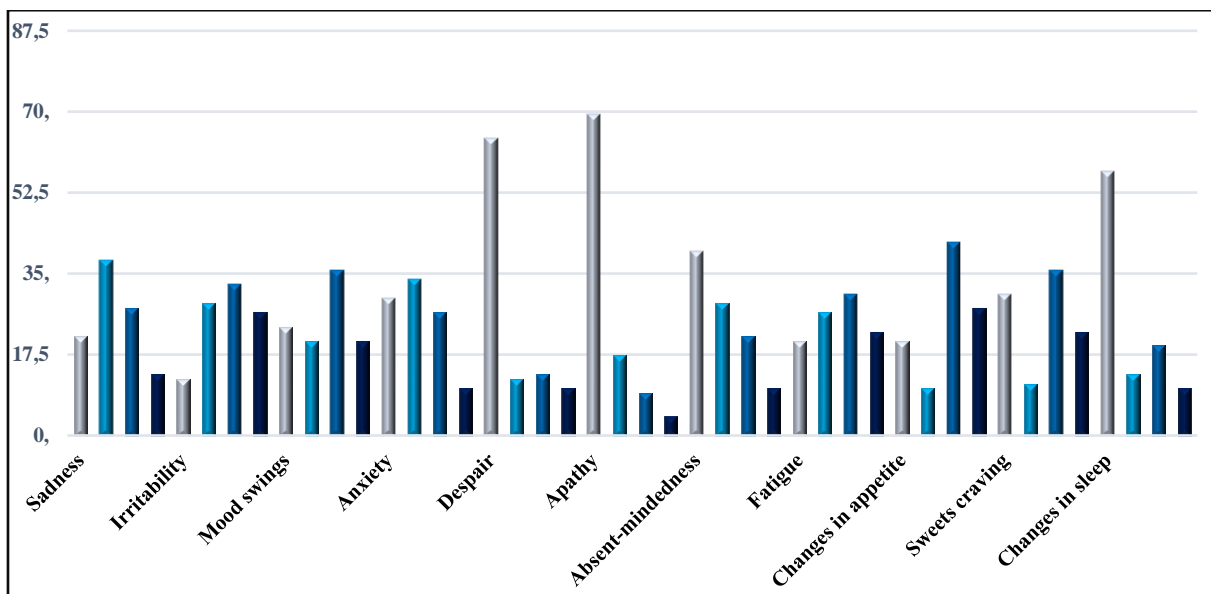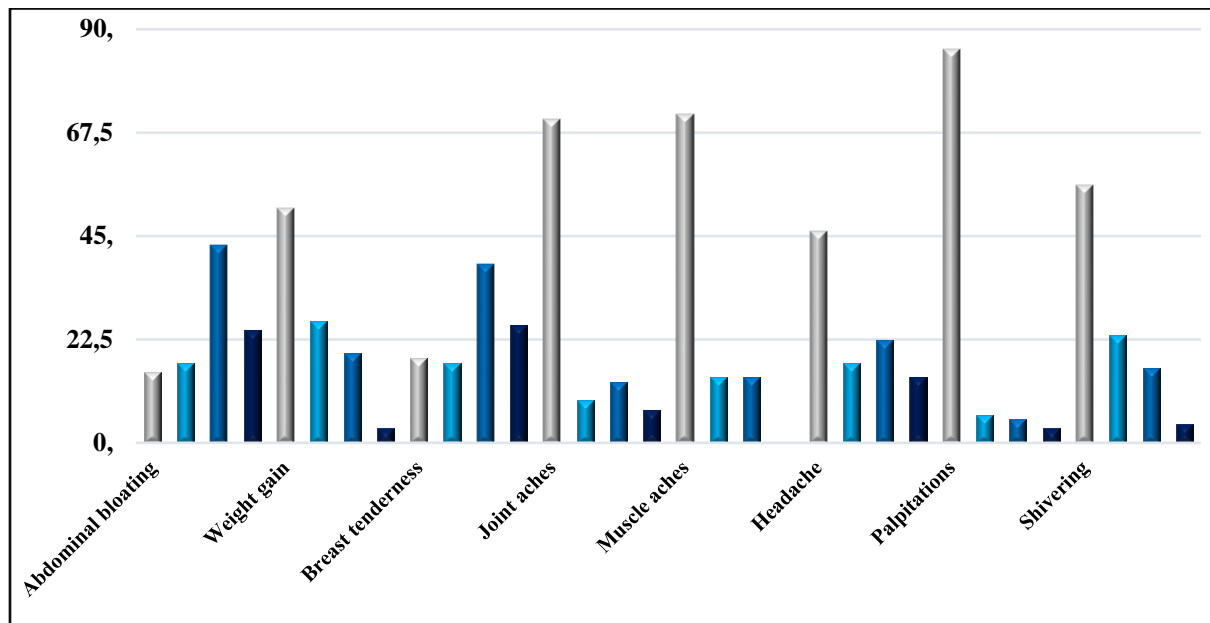
Somatic symptoms

Prevalence of somatic symptoms: the symptoms „breast tension" and „breast tenderness by touch" were detected in 81,6% (N=80), and the symptom „abdominal bloating" experienced 84,7% (N=83) of the examined women. For headache report 54,1% (N=53), for shivering – 43,9% (N=43), and for changes in weight – 49% (N=48). Joint aches were registered in 29,6% (N=29), muscle aches – 28,6% (N=28), and palpitations – 14,3% (N=14) (Fig. 4).

Figure 4. Distribution of the somatic symptoms by prevalence in the group **with** PMS
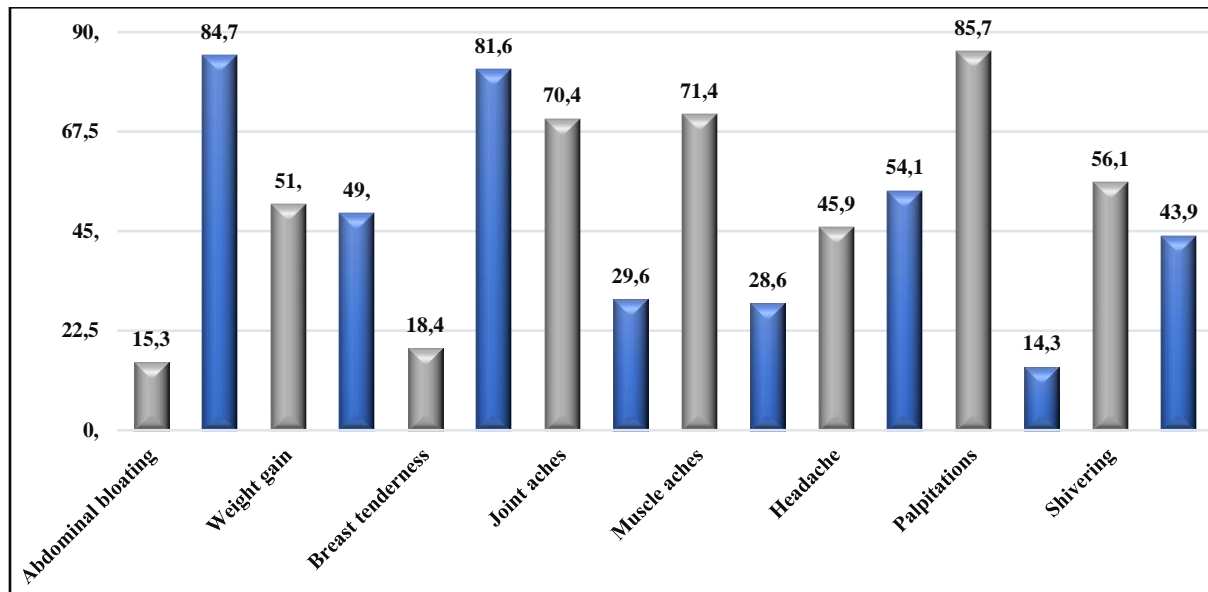
Severity of somatic symptoms: the severity of "breast tension and tenderness" was mostly moderate – 38,8% (N=38), mild in 17,3% (N=17) and severe in 25,5% (N=25). Similar results were evident for the symptom "abdominal bloating" – in 42,9% (N=42) it is moderate, in 17,3% (N=17) – mild, and in 24,5% (N=24) severe. Headache is evenly distributed in severity – 17,3% (N=17) mild, 22,4% (N=22) moderate, and 14,3% (N=14) severe. Regarding the symptom "shivering" most prevalent were the mild and moderate degrees, 23,5% (N=23) and 16,3% (N=16), resp., and in 4,1% (N=4) severe. Likewise, the severity of the symptom "weight gain" was mainly distributed in the regions of the mild and moderate degrees, 26,5 (N=26) and 19,4% (N=19), resp., and 3,1% (N=3) severe. Moderately severe joint aches report 13,3% (N=13) of the women, mild ones – 9,2% (N=9) of them, and severe – 7,1% (N=7). With respect to the symptom "muscle aches" there were no severe and equal number mild and moderate cases – 14,3% (N=14). Regarding the symptom "palpitations" there was near even distribution: mild degrees of severity in 6,1% (N=6); moderate ones in 5,1% (N=5), and severe in 3,1% (N=3) (Fig. 5).

Figure 5. Distribution somatic symptoms by severity in the group **with** PMS

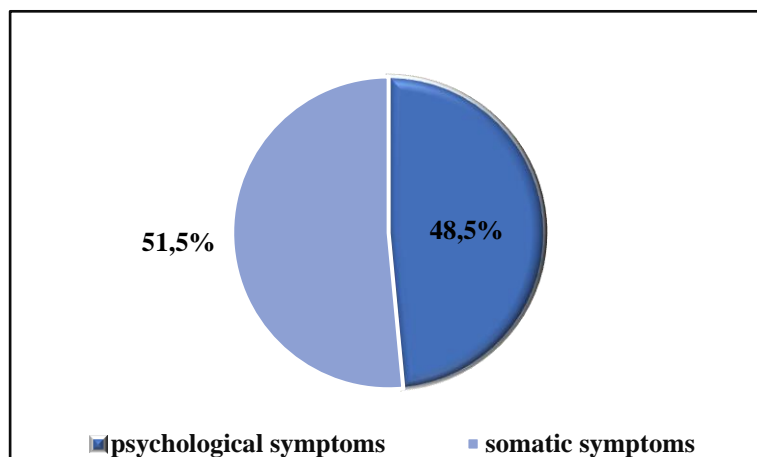The <u>ratio</u> of psychological to somatic symptoms was 51,5% : 48,5% (Fig. 6).

Figure 6. Ratio of psychological to somatic symptoms in women with PMS

*5.3.1 Clinical characteristics of the subgroup **with** PMS by age*

The subgroup of women with PMS was divided into two groups depending on the age of the participants:

> **1. Women, aged ≤35 years**
> **2. Women, aged >35 years**

In the present study are described the data, acquired from 76 women with PMS in the age group 20 - 35 and 22 women in the age group 36 - 48 years.

***Psychological** symptoms in the **younger** women's group: irritability* recorded 92,1% (N=67), moreover the symptom was severe in 25% (N=19); for *change in appetite* reported 78,9% (N=60), of which 30,3% (N=23) severe; *fatigue* – 77,6% (N=59), in 21,1% (N=16) it was severely expressed; *sadness* and *mood swings* – 76,3% (N=58) each, and in 11,8% (N=9) and 19,7% (N=15) severe, resp., *anxiety* – 73,7% (N=56); *sweets craving* – 64,5% (N=49); *apathy*

– 34,2% (N=22) and *absent-mindedness* – 57,9% (N=34) (Fig. 7 and 8).

In the group of the **older** women most prevalent were *sadness, fatigue* and *sweets craving* – 86,4% (N=19) each. Severely expressed were *sadness* in 18,2% (N= 4), *fatigue* – 27,3% (N= 6), and *sweets craving* – 18,2% (N=4). The frequency of the symptoms: *changes in appetite* - 81,8% (N=18), *mood swings* – 77,3% (N=17), *irritability* – 72,7% (N=16), *changes in sleep* – 72,7% (N=16). For *anxiety* reported 59,1% (N=13), for *despair* – 40,9% (N=9), and for *apathy* – 36,4% (N=8) (Fig. 7 and 8).

Figure 7. Distribution of the psychological symptoms by prevalence in women **with** PMS, depending on age
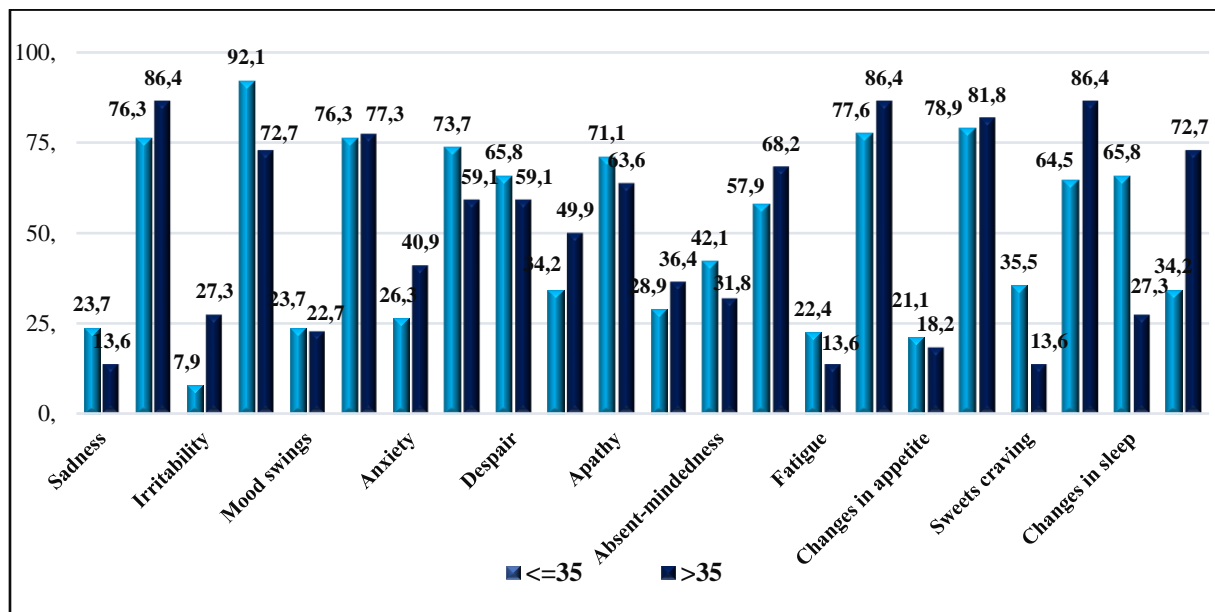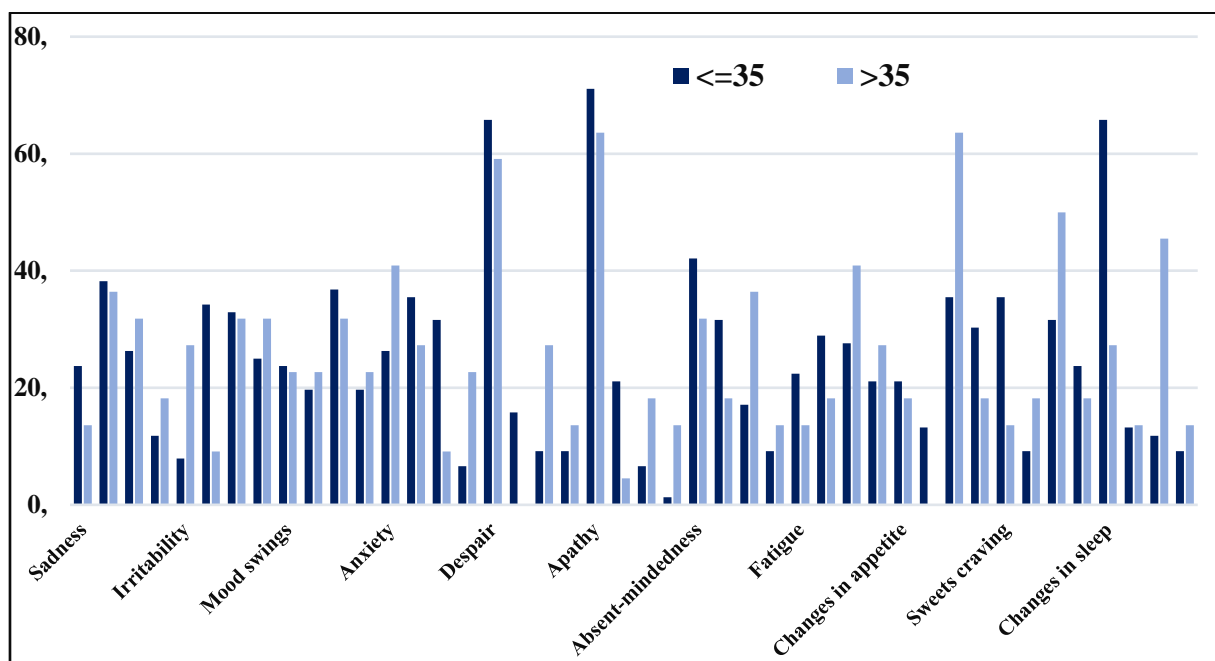

Figure 8. Distribution of the psychological symptoms by severity in women **with** PMS, depending on age

The *somatic* symptoms in women *younger than 35 years* were: breast tension and tenderness by touch in 84,2% (N=65); 85,5% (N=64) experienced abdominal bloating; weight gain detected 50% (N=38); shivering, hot and cold flashes – 44,7% (N=34), headache – 42,1% (N=30); joint and muscle aches – 28,9% (N=22) each; palpitations – 10,5% (N=8). The prevalence of the severe degree of breast tension and tenderness was 26,3% (N=20), of the abdominal bloating 23,7% (N=18), of headache 6,6% (N=5) (Fig. 9 and 10).

In the group of women *over 35 years* for headache reported 95,5% (N=21), for abdominal bloating – 86,4% (N=19), for breast tension and tenderness – 68,2% (N=15), for weight gain – 45,5% (N=10), for shivering, hot and cold flashes – 40,9% (N=9), for joint aches – 31,8% (N=7), for muscle aches – 27,3% (N=6), for palpitations – 27,3% (N=6). The headache was severe in 40,9% (N=9), the breast tenderness in – 22,7% (N=5), and the abdominal bloating in 27,3% (N=6) (Fig. 9 and 10).

Figure 9. Distribution of somatic symptoms by prevalence in women **with** PMS, depending on age
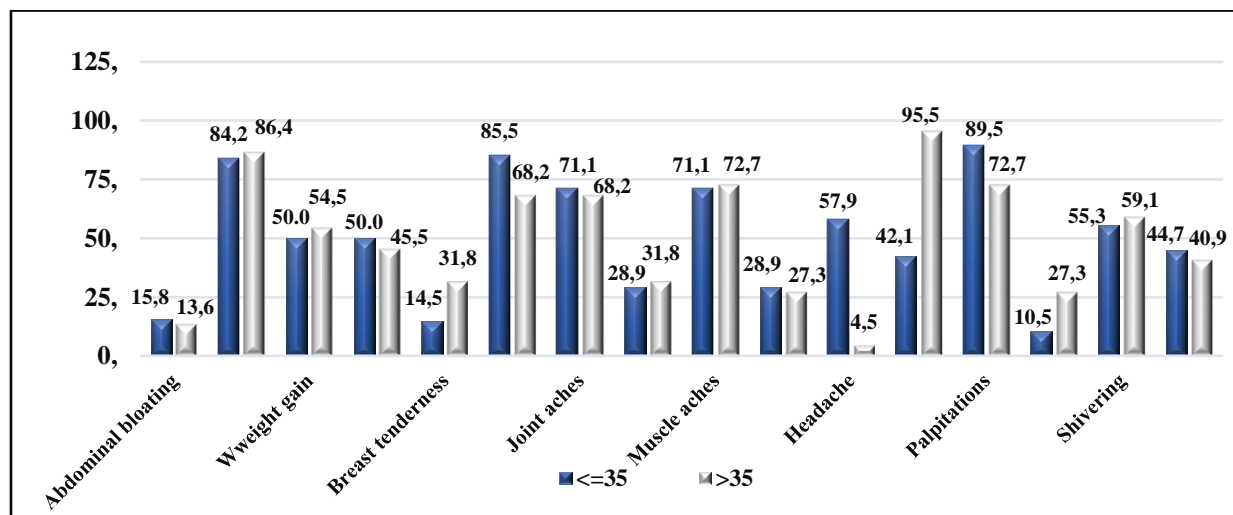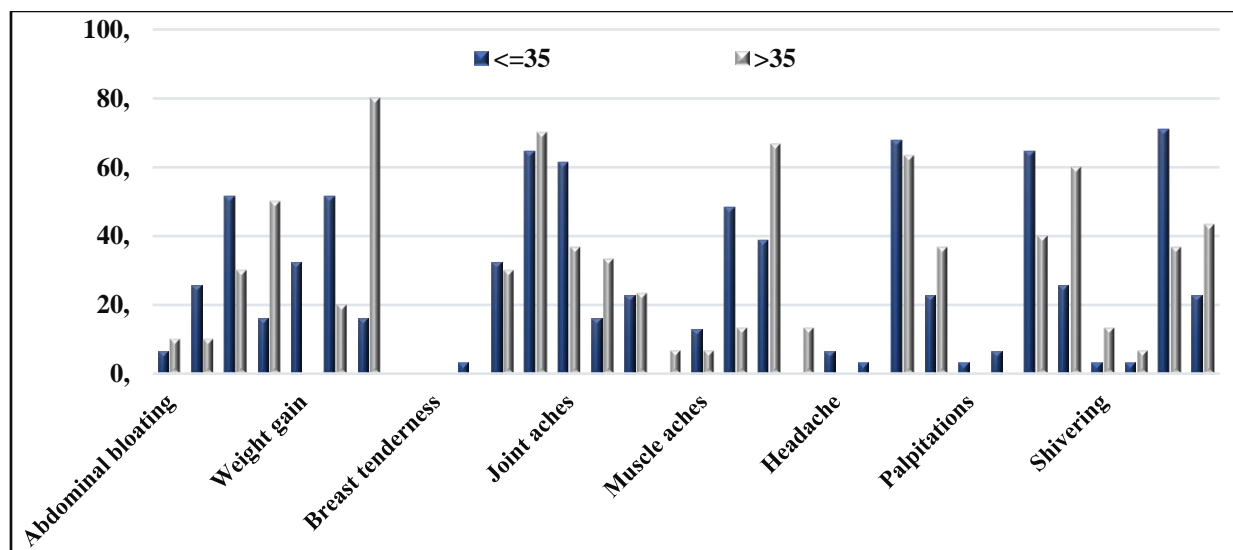

Figure 10. Distribution of somatic symptoms by severity in women **with** PMS, depending on age

The <u>ratio</u> of psychological to somatic symptoms is equal in both groups (Fig. 11)
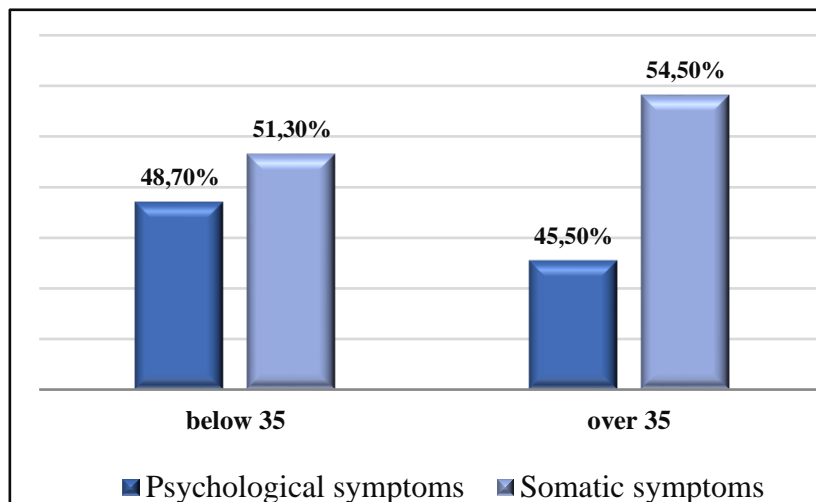

Figure 11. Ratio of psychological to somatic symptoms in both age groups of women **with** PMS

5.3.2. Comparative analysis of the symptoms by severity and prevalence in both age groups of women with PMS

Prevalence: for the comparison of the prevalence of the symptoms we used the Mann - Whitney test, which is used for analysing variables between two independent groups in cases of non-normal distribution.

According to the results of the between-group comparison increasing age is not related to change in prevalence of the psychological symptoms except insomnia, which was statistically significant increased (Z = -3,245, p = 0,001) (Table 1). In the case of somatic symptoms with the increase of age most drastic and statistically significant increase was registered for the prevalence of headache – from 42,1% to 95,5% (Z = -4,732, p < 0.001). Statistically significant increase in prevalence was also detected for palpitations (Z = -2,004, p = 0.041) (Table 1).

Table 1. Comparison of the prevalence of the symptoms in both age groups of women **with** PMS

With PMS		
Symptom	*Z*	*p*
Changes in appetite	-0,063	0,950
Sweets craving	-0,895	0,371
Insomnia	-3,245	**0,001**
Abdominal bloating	-1,078	0,281
Weight gain	-0,121	0,904
Breast tension and tenerness	-0,668	0,504
Joint aches	-0,423	0,672
Muscle aches	-0,300	0,764
Headache	-4,732	**<0,001**
Palpitations	-2,044	**0,041**
Shivering	-0,237	0,813

Mann-Whitney test

The severity of the symptoms was compared between the two groups by the Fisher's exact test. It is a non-parametric test, used for comparisons of categorical variables. We used this test instead of Pearson's chi-square test as the latter would normally require all values of each variable be at least 5 and this was not the case with our data.

The between-group comparison demonstrated that getting older was related to worsening of the psychological symptoms, moreover for the symptoms irritability ($p = 0,024$, FET), anxiety ($p = 0,026$, FET), despair ($p = 0,034$, FET), apathy ($p = 0,009$, FET), and insomnia ($p = 0,002$, FET) to a statistically significant degree (Table 2). With respect to the somatic symptoms the comparison showed, that the muscle aches ($p = 0,018$, FET) and the headache ($p < 0,0001$, FET) were significantly more severe in women over 35 (Table 2).

Table 2. Comparison of the severity of psychological and somatic symptoms in the subgroups **below** and **over** 35 years

Psychological symptoms	Fisher's exact Test-value	p
Sadness	1,631	0,696
Irritability	9,089	**0,024***
Mood swings	0,442	0,948
Anxiety	8,884	**0,026***
Despair	8,085	**0,034***
Apathy	10,371	**0,009***
Absent-mindedness	4,694	0,182
Fatigue	2,568	0,482
Changes in appetite	6,614	0,075
Sweets craving	5,854	0,113
Insomnia	13,826	**0,002***
Somatic symptoms	Fisher's exact Test-value	P
Abdominal bloating	3,772	0,297
Weight gain	3,741	0,247
Breast tension and tenerness	5,447	0,131
Joint aches	1,497	0,666
Muscle aches	7,664	**0,018***
Headache	27,535	**0,000****
Palpitations	5,469	0,087
Shivering	6,314	0,084

*p<0,05; ** p<0,001

The psychological and somatic symptoms were equally distributed in the two groups and there was no statistically significant difference in their prevalence ($p = 0,953$) (Table 3).

Table 3. Comparison of the ratio psychological to somatic symptoms in both age groups of women **with** PMS

With symptoms of PMS	Age groups				p
	≤ 35		> 35		
	N	%	N	%	
Psychological symptoms	37	48,7	10	45,5	*0,953*
Somatic symptoms	39	51,3	12	54,5	

Severity: in the group of women, younger than 35, PMS was mild in 47,4% (N=36), moderate in 46,1% (N=35), and severe in 6,6% (N=5). In the group of women older than 35 the prevalence of the mild PMS was 50% (N=11), moderate - 27,3% (N=6), and severe – 22,7% (N=5). The between-group comparison demonstrated statistically significant difference in the prevalence – X^2 (2)=5, 82; p=0,054 (Table 4, Figure 12).

Table 4. Comparison of the severity of PMS in both age groups

PMS severity	Age groups				X^2	df	p
	≤ 35		> 35				
	N	%	N	%			
MILD	36	47,4	11	50,0	5,82	2	*0,054*
MODERATE	35	46,1	6	27,3			
SEVERE	5	6,6	5	22,7			
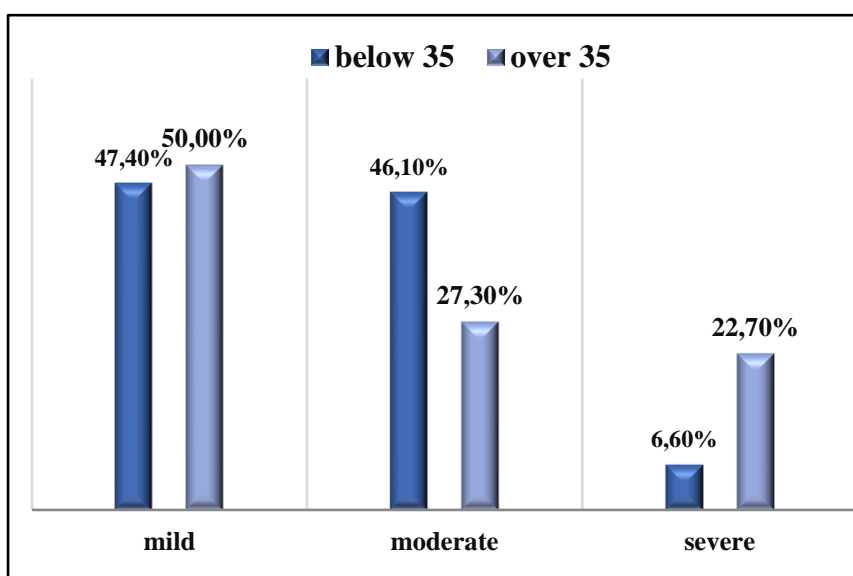
Figure 12. Severity of PMS in both age groups

*5.4 Comparative analysis of the symptoms in the groups **with** and **without** PMS*

Psychological symptoms: the prevalence of all psychological symptoms was statistically significant higher in the participants with PMS compared to those without PMS ($p < 0.001$) (Fig 13, Table 5).

Figure 13. Distribution of psychological symptoms by prevalence in women **with** and **without** PMS
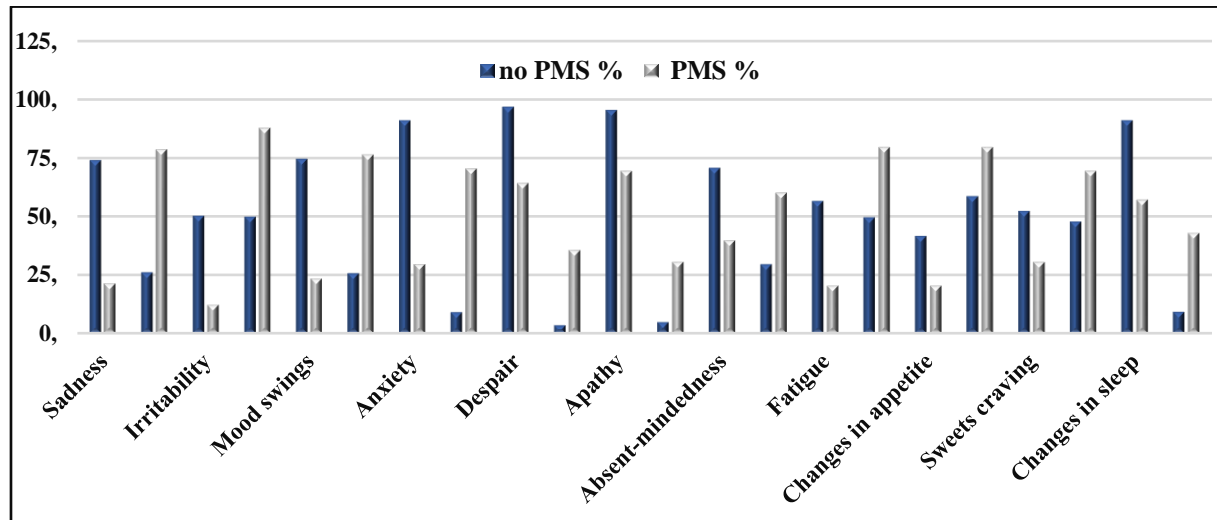
Somatic symptoms: we registered a significant increase in the prevalence of the symptoms „abdominal bloating" ($Z = -4,250$, $p < 0.001$) and „shivering" ($Z = -5,418$, $p < 0.001$) in women with PMS. Although with smaller statistical significance the symptoms „weight gain" ($Z = -2,634$, $p = 0.008$), „breast tension and tenderness" ($Z = -2,555$, $p = 0.011$), „joint aches" ($Z = -2,706$, $p = 0.007$), „muscle aches" ($Z = -3,010$, $p = 0.003$), and „headache" ($Z = -2,382$, $p = 0.017$) also became more common when the syndrome was present. Only the symptom "palpitations" was not differing significantly between the two groups ($Z = -1,716$, $p = 0.086$) (Table 5, Fig. 14).

Figure 14. Distribution of somatic symptoms by prevalence in women **with** and **without** PMS
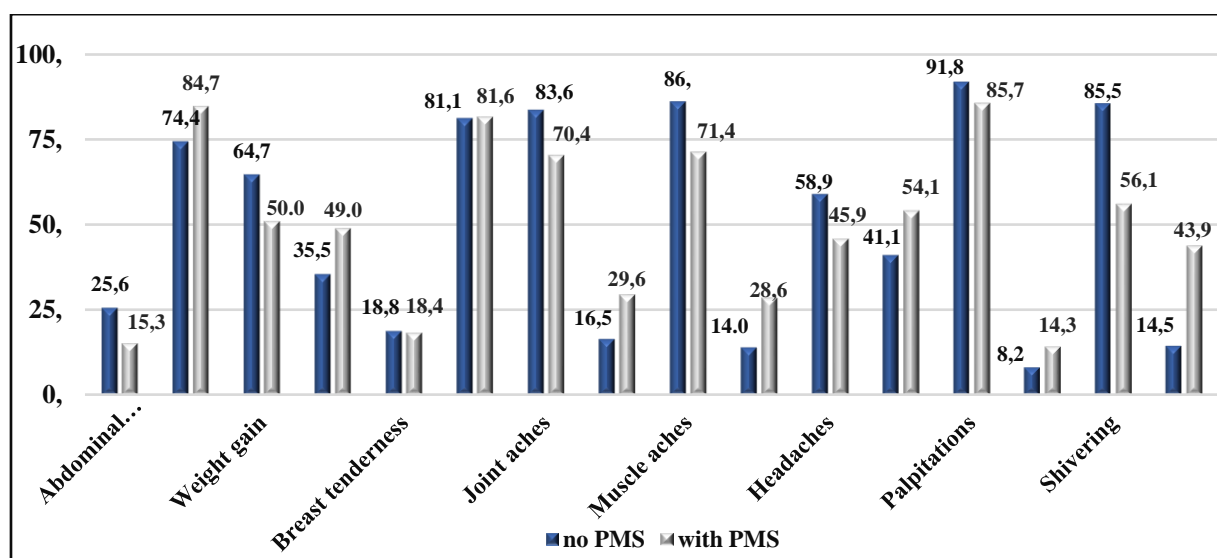
Table 5. Comparative analysis of the prevalence of the symptoms in the groups **with** and **without** PMS

Symptom	Z	p
Sadness	-8,945	<0,001
Irritability	-6,877	<0,001
Mood swings	-9,828	<0,001
Anxiety	-11,227	<0,001
Despair	-7,744	<0,001
Apathy	-6,359	<0,001
Absent-mindedness	-5,337	<0,001
Fatigue	-6,884	<0,001
Changes in appetite	-4,803	<0,001
Sweets craving	-4,219	<0,001
Insomnia	-7,006	<0,001
Abdominal bloating	-4,250	<0,001
Weight gain	-2,634	0,008
Breast tension and tenderness	-2,555	0,011
Join aches	-2,706	0,007
Muscle aches	-3,010	0,003
Headache	-2,382	0,017
Palpitations	-1,716	0,086
Shivering	-5,418	<0,001

Mann-Whitney Test

The severity of psychological symptoms was significantly greater in the group with PMS (p < 0,001, FET) (Table6, Fig. 15). With regard to somatic symptoms the situation was similar - they all were more severe in the PMS group (p < 0,001, FET) (Table 6, Fig. 16).

Figure 15. Distribution of psychological symptoms by severity in the groups **with** and **without** PMS
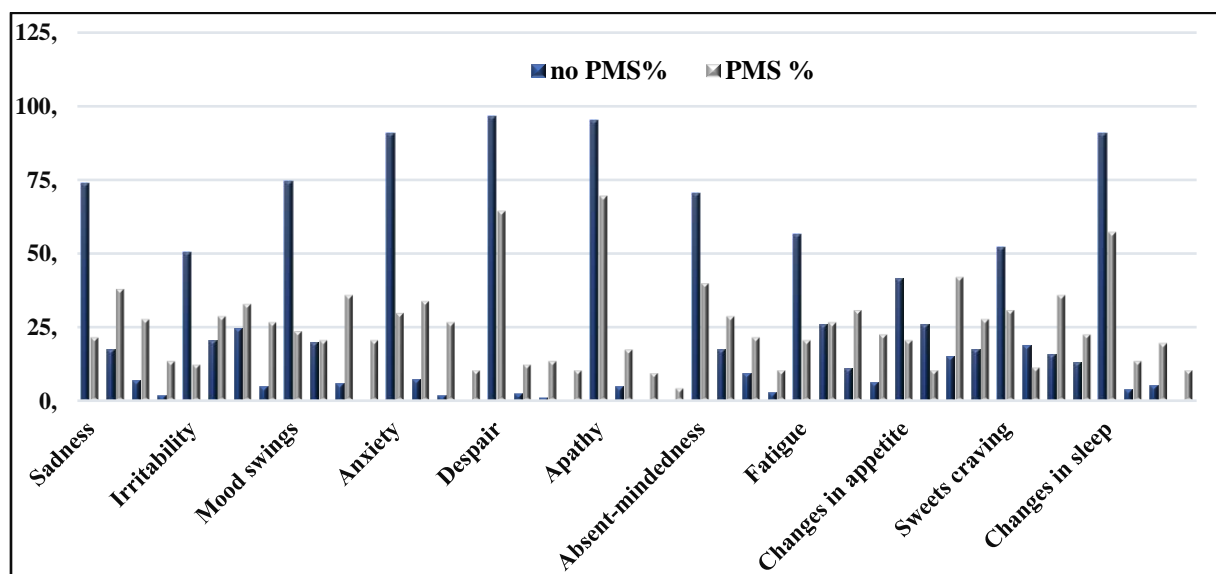
Figure 16. Distribution of somatic symptoms by severity in the groups **with** and **without** PMS
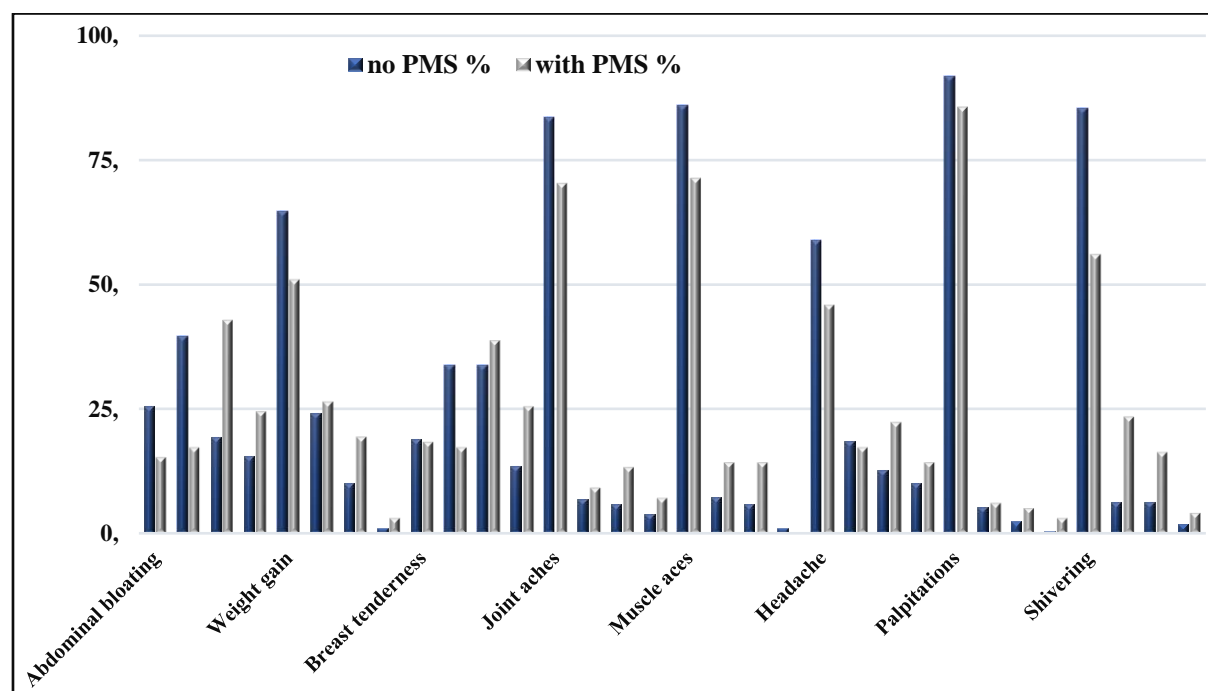
Table 6. Comparison of the severity of psychological and somatic symptoms in the groups **with** and **without** PMS

Psychological symptoms	Fisher's exact Test-value	p
Sadness	95,543	0,000**
Irritability	69,897	0,000**
Mood swings	120,418	0,000**
Anxiety	137,987	0,000**
Despair	72,260	0,000**
Apathy	58,931	0,000**
Absent-mindedness	43,308	0,000**
Fatigue	62,362	0,000**
Changes in appetite	54,126	0,000**
Sweets craving	38,452	0,000**
Insomnia	65,914	0,000**

Somatic symptoms	Fisher's exact Test-value	P
Abdominal bloating	44,272	0,000**
Weight gain	24,673	0,002*
Breast tension and tenderness	26,502	0,000**
Joint aches	24,315	0,003*
Muscle aches	29,378	0,000**
Headache	21,965	0,004*
Palpitations	25,525	0,004*
Shivering	47,224	0,000**

*p<0,05; ** p<0,001

The prevalence of the psychological and somatic symptoms was nearly equal in the PMS group – 48,5% / 51,5%. In women without PMS the somatic symptoms were more prevalent – 34,8% / 65,2%. The psychological symptoms in women with PMS were 1,4 times more common than in those without the syndrome, and the somatic symptoms were almost equally distributed in the two groups. All variables differed statistically significant between the two groups ($X^2(1) = 22,97$, p= 0,580, p < 0.001) (Table 7, Fig. 17).

Table 7. Comparative analysis of the ratio psychological to somatic symptoms in women **with** and **without** PMS

PMS – symptoms		(+) PMS	(–) PMS	Total	X^2	df	p
Psychological symptoms	N	72	48	120	22,9	1	**<0.001**
	%	34,8%	48,5%	39,3%			
Somatic symptoms	N	135	50	185	7		
	%	65,2%	51,5%	60,7%			
Total	N	207	98	305			
	%	100,0%	100,0%	100,0%			

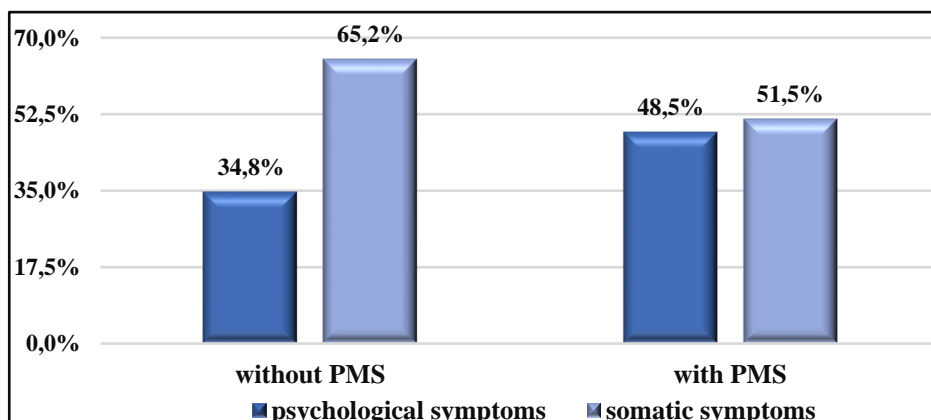**Figure 17.** Distribution of psychological and somatic symptoms in women **with** and **without** PMS

5.5 Clinical picture of PMS in the group of women with comorbid DD (PMS-DD)

We analysed the data, acquired from 31 women with PMS and DD, aged between 25 and 48 years (mean age 39,32 ± 6,91).

Severity: 25,8% (N=8) of the women suffered mild PMS; 58,1% (N=18) of them – moderate, and 16,1% (N=5) – severe PMS, which corresponds to the criteria for PMDD (Table 12, Fig. 23).

Psychological symptoms: The prevalence of sadness was 87,1% (N=27). This symptom was most commonly mild – 41,9% (N=13). Moderately and severely expressed it was in 29% (N=9) and 16,1% (N=5), resp. The prevalence of irritability was high: 96,8% (N=30), moreover it was severe in 35,5% (N=11), moderate in 48,4% (N=15), and mild in 12,9% (N=4). On mood swings reported 100% (N=31) of the participants and this symptom was severe in 35,5% (N=11) of them, moderate in 45,2% (N=14), and mild in 19,4% (N=6). The prevalence of anxiety was also 100% (N=31). In 45,2% (N=14) of the cases it was severe, in 41,9% (N=13) - moderate, and in 12,9% (N=4) - mild. Despair – prevalence of 71% (N=31). The moderate severity of the symptom dominated – 32,3% (N=10), followed by the mild – 29% (N=9), and severe - 9,7% (N=3). Apathy – prevalence of 87,1% (N=27) with moderate severity in 48,4% (N=15), mild severity in another 48,4% (N=15), and severe expression in 3,2% (N=1). The prevalence of the symptom absent-mindedness was 93,5% (N=29) and it was moderate in 74,2% (N=23), and mild and severe in 9,7% (N=3) each. The prevalence of *fatigue* was 100% (N=31). The moderate severity of that symptom prevailed – 58,1% (N=18), followed by mild – 22,6% (N=7), and severe expression - 19,4% (N=6). Changes in appetite had prevalence of 96,8% (N=30) with dominating moderate severity – 45,2% (N=14). The severe cases were – 38,7 (N=12) and the mild ones - 12,9% (N=4). Sweets craving - prevalence of 87,1% (N=27). The symptom was most commonly moderately severe – 35,5% (N=11) or mild – 32,3% (N=10), severe was it in 19,4% (N=6). For insomnia reported 96,8% (N=30). Most of them complained of moderately expressed symptom – 58,1% (N=18), and equal number of women suffered mild or severe symptom – 19,4% (N=16) (Tables 8 and 9, Figures 18 and 19).

Somatic symptoms: abdominal bloating was frequent symptom – 93,5% (N=29). It was most commonly moderate – 51,6% (N=16), followed by mild – 25,8% (N = 8)and severe – 16,1% (N=5). The prevalence of the symptom weight gain was 67,7% (N=21) and it was most often mild – 51,6% (N=16). The moderate degree of expression reached 16,1% (N=5). There were no severe cases. Breast tenderness experienced all participants - 100% (N=31). The severe degree of expression dominated - 64,5% (N=20). It was moderately expressed in – 32,3% (N=10), and rarely mild - 3,2% (N=1). Joint aches suffered 38,7% (N=12). The symptom was most often moderately severe 22,6% (N=7). The mild forms encompassed 16,1% (N=5), and severe ones were lacking. Muscle aches reported 87,1% (N=27) of the women, of which 48,4% (N=15) were mild, 38,7% (N=12) - moderate, and severe forms were once again not registered. Headache was another common symptom with its prevalence of – 93,5% (N=29). It was most often moderate – 67,7% (N=21). Severe cases were detected in 22,6% (N=7), and mild ones in 3,2 (N=1). The prevalence of palpitations was high - 96,8% (N=30). Its severity was most commonly moderate – 64,5% (N=20). The severe cases were 25,8% (N=8) and the mild ones - 6,5% (N = 2). Similar distribution was registered for shivering – 96,8% (N=30). The moderate

forms of the symptom prevailed - 71% (N=22), the severe ones were 22,6% (N=7), and the mild ones - 3,2% (N=1) (Tables 8 and 9, Figures 20 and 21).

The <u>ratio</u> psychological to somatic symptoms was 74,2% : 25,8% (Fig. 22).

Table 8. Distribution of the symptoms by prevalence in the PMS-N, PMS-DD, PMS-PD groups

Symptom		PMS-N (N=98)	PMS-DD (N=31)	PMS-PD (N=30)
		N / %	N / %	N / %
Sadness	absent	21 (20,4)	4 (12,9)	6 (20,0)
	present	77 (79,6)	27 (87,1)	24 (80,0)
Irritability	absent	12 (12,2)	1 (3,2)	0 (0,0)
	present	86 (87,8)	30 (96,8)	30 (100,0)
Mood swings	absent	23 (23,5)	0 (0,0)	3 (10,0)
	present	75 (76,5)	31 (100,0)	27 (90,0)
Anxiety	absent	29 (29,6)	0 (0,0)	3 (10,0)
	present	69 (70,4)	31 (100,0)	27 (90,0)
Despair	absent	63 (64,3)	9 (29,0)	8 (26,7)
	present	35 (35,7)	22 (71,0)	22 (73,3)
Apathy	absent	68 (69,4)	4 (12,9)	7 (23,3)
	present	30 (30,6)	27 (87,1)	23 (76,7)
Absent-mindedness	absent	39 (39,8)	2 (6,5)	5 (16,7)
	present	59 (60,2)	29 (93,5)	25 (83,3)
Fatigue	absent	20 (20,4)	0 (0,0)	3 (10,0)
	present	78 (79,6)	31 (100,0)	27 (90,0)
Changes in appetite	absent	20 (20,4)	1 (3,2)	0 (0,0)
	present	78 (79,6)	30 (96,8)	30 (100,0)

Sweets craving	absent	30 (30,6)	4 (12,9)	8 (26,7)
	present	68 (69,4)	27 (87,1)	22 (73,3)
Insomnia	absent	56 (57,1)	1 (3,2)	4 (13,3)
	present	42 (42,9)	30 (96,8)	26 (86,7)
Abdominal bloating	absent	15 (15,3)	2 (6,5)	3 (10,0)
	present	83 (84,7)	29 (93,5)	27 (90,0)
Weight gain	absent	50 (51,0)	10 (32,3)	0 (0,0)
	present	48 (49,0)	21 (67,7)	30 (100,0)
Breast tension and tenderness	absent	18 (18,4)	0 (0,0)	0 (0,0)
	present	80 (81,6)	31 (100,0)	30 (100,0)
Joint aches	absent	69 (70,4)	19 (61,3)	11 (36,7)
	present	29 (29,6)	12 (38,7)	19 (63,3)
Muscle aches	absent	70 (71,4)	4 (12,9)	2 (6,7)
	present	28 (28,6)	27 (87,1)	28 (93,3)
Headache	absent	45 (45,9)	2 (6,5)	0 (0,0)
	present	53 (54,1)	29 (93,5)	30 (100,0)
Palpitations	absent	84 (85,7)	1 (3,2)	0 (0,0)
	present	14 (14,3)	30 (96,8)	30 (100,0)
Shivering	absent	55 (56,1)	1 (3,2)	4 (13,3)
	present	43 (43,9)	30 (96,8)	26 (86,7)

Table 9. Distribution of the symptoms by severity in the PMS-N, PMS-DD, PMS-PD groups

Psychological symptoms		PMS-N (N=98)	PMS-DD (N=31)	PMS-PD (N=30)
		N / %	N / %	N / %
Sadness	absent	21/21,4	4/12,9	6/20,0
	mild	37/37,8	13/41,9	5/16,7
	moderate	27/27,6	9/29,0	14/46,7
	severe	13/13,3	5/16,1	5/16,7

30

Irritability	absent mild moderate severe	12/12,2 28/28,6 32/32,7 26/26,5	1/3,2 4/12,9 15/48,4 11/35,5	0/0,0 0/0,0 4/13,3 26/86,7
Mood swings	absent mild moderate severe	23/23,5 20/20,4 35/35,7 20/20,4	0/0,0 6/19,4 14/45,2 11/35,5	3/10,0 4/13,3 10/33,3 13/43,3
Anxiety	absent mild moderate severe	29/29,6 33/33,7 26/26,5 10/10,2	0/0,0 4/12,9 13/41,9 14/45,2	3/10,0 0/0,0 5/16,7 22/73,3
Despair	absent mild moderate severe	63/64,3 12/12,2 13/13,3 10/10,2	9/29,0 9/29,0 10/32,3 3/9,7	8/26,7 11/36,7 8/26,7 3/10,0
Apathy	absent mild moderate severe	68/69,4 17/17,3 9/9,2 4/4,1	4/12,9 15/48,4 11/35,5 1/3,2	7/23,3 8/26,7 15/50,0 0/0,0
Absent-mindedness	absent mild moderate severe	39/39,8 28/28,6 21/21,4 10/10,2	2/6,5 3/9,7 23/74,2 3/9,7	5/16,7 2/6,7 21/70,0 2/6,7
Fatigue	absent mild moderate severe	20/20,4 26/26,5 30/30,6 22/22,4	0/0,0 7/22,6 18/58,1 6/19,4	3/10,0 4/13,3 12/40,0 11/36,7
Changes in appetite	absent mild moderate severe	20/20,4 10/10,2 41/41,8 27/27,6	1/3,2 4/12,9 14/45,2 12/38,7	0/0,0 1/3,3 19/63,3 10/33,3
Sweets craving	absent mild moderate severe	30/30,6 11/11,2 35/35,7 22/22,4	4/12,9 10/32,3 11/35,5 6/19,4	8/26,7 4/13,3 6/20,0 12/40,0
Insomnia	absent mild moderate severe	56/57,1 13/13,3 19/19,4 10/10,2	1/3,2 6/19,4 18/58,1 6/19,4	4/13,3 2/6,7 15/50,0 9/30,0

Somatic symptoms		PMS-N (N=98) n / %	PMS-DD (N=31) N / %	PMS-PD (N=30) N / %
Abdominal bloating	absent	15/15,3	2/6,5	3/10,0
	mild	17/17,3	8/25,8	3/10,0
	moderate	42/42,9	16/51,6	9/30,0
	severe	24/24,5	5/16,1	15/50,0
Weight gain	absent	50/51,0	10/32,3	0/0,0
	mild	26/26,5	16/51,6	6/20,0
	moderate	19/19,4	5/16,1	24/80,0
	severe	3/3,1	0/0,0	0/0,0
Breast tension and tenderness	absent	18/18,4	0/0,0	0/0,0
	mild	17/17,3	1/3,2	0/0,0
	moderate	38/38,8	10/32,3	9/30,0
	severe	25/25,5	20/64,5	21/70,0
Joint aches	absent	69/70,4	19/61,3	11/36,7
	mild	9/9,2	5/16,1	10/33,3
	moderate	13/13,3	7/22,6	7/23,3
	severe	7/7,1	0/0,0	2/6,7
Muscle aches	absent	70/71,4	4/12,9	2/6,7
	mild	14/14,3	15/48,4	4/13,3
	moderate	14/14,3	12/38,7	20/66,7
	severe	0/0,0	0/0,0	4/13,3
Headache	absent	45/45,9	2/6,5	0/0,0
	mild	17/17,3	1/3,2	0/0,0
	moderate	22/22,4	21/67,7	19/63,3
	severe	14/14,3	7/22,6	11/36,7
Palpitations	absent	84/85,7	1/3,2	0/0,0
	mild	6/6,1	2/6,5	0/0,0
	moderate	5/5,1	20/64,5	12/40,0
	severe	3/3,1	8/25,8	18/60,0
Shivering	absent	55/56,1	1/3,2	4/13,3
	mild	23/23,5	1/3,2	2/6,7
	moderate	16/16,3	22/71,0	11/36,7
	severe	4/4,1	7/22,6	13/43,3
Impairment in functioning	absent	0/0,0	0/0,0	0/0,0
	mild	49/50,0	0/0,0	0/0,0
	moderate	29/29,6	25/80,6	17/56,7
	severe	20/20,4	6/19,4	13/43,3

5.6 Clinical picture of PMS in the group of women with comorbid PD (PMS-PD)

We analysed the data from 30 women with PMS and PD, aged between 23 and 43 years (mean age 31,2 ±7,89).

Severity: 56,7% (N=17) of the women suffered moderate PMS, and 43,3% (N=13) pf them – severe PMS, corresponding to the criteria for PMDD. No cases of mild PMS were registered (Table 12, Fig. 23).

Psychological symptoms: The prevalence of sadness was 80% (N=24). The symptom was most commonly moderate - 46,7% (N=14). The severe and mild cases were equally distributed – 16,1% (N=5) each. The prevalence of irritability was high - 100% (N=30). None of the particpiants suffered mild form of that symptom and the severe and moderate cases were 86,7% (N=26) and 13,3% (N=4), resp. For mood swings reported 90% (N=27). The severe cases were 43,3% (N=13), the moderate ones - 33,3% (N=10), and the mild ones - 13,3% (N=4). Anxiety – 90% (N=27). It was most often severe – 73,3% (N=22). The moderate forms were 16,7 (N=5), and mild forms were not registered. Despair – 73,3% (N=22). Most prevalent were the mild degrees – 36,7% (N=11). The moderate ones were – 26,7 % (N=8) and the severe ones - 10% (N=3). Apathy – 76,7% (N=23). It was moderately severe in 50% (N=15), mild in 26,7% (N=8), and severe cases were lacking. The prevalence of absent-mindedness was – 83,3% (N=25), of which most common was the moderate degree – 70% (N=21). The mild and severe forms were equally distributed – 6,7% (N=2) each. Fatigue was commonly reported – 90% (N=27). It was most often moderately – 40% (N=12) and severely expressed – 36,7% (N=11), and mild one experienced 13,4% (N=4). Changes in appetite had prevalence of 100% (N=30). The moderate degree of expression dominated – 63,3% (N=19), the severe was 33,3% (N=10) and the mild - 3,3% (N=1). Sweets craving experienced 73,3% (N=22) and the symptom was severe in 40% (N=12), moderate in 20% (N=6), and mild in 13,3% (N=4). For insomnia reported 86,7% (N=26). It was moderate in 50% (N=24) and severe in 30% (N=6) (Tables 8 and 9, Figures 18 and 19).

Somatic symptoms: abdominal bloating was a common symptom – 90% (N=27). The severe degree of expression dominated – 50% (N=15), moderately severe it was in 30% (N=9), and mild - in 10% (N=3). The prevalence of the symptom weight gain was 100% (N=30). It was moderate in severity in most of the cases – 80% (N=24), mild in 20% (N=6), and severely expressed forms were not registered. Breast tenderness – 100% (N=30). The severe forms dominated – 70% (N=21), moderate severity - 30% (N=9), mild forms were lacking. From joint aches suffered 63,3% (N=19). They were mild in 33,3% (N=10), moderate in 23,3% (N=7), severe in 6,7% (N=2). On muscle aches reported high percentage of women – 93,3% (N=28). Most common were the moderate degrees of severity 66,7% (N=20), and mild and severe symptom suffered equal number of women – 13,3% (N=4) each. Headache was another frequent symptom – 100% (N=30). The moderate degrees were most prevalent – 63,3% (N=16), the severe were 36,7% (N=11). Palpitations – 100% (N=30). It was moderate in 40% (N=12) and severe in 60% (N=18). Shivering was present in 86,7% (N=26) and it was severe in 43,3% (N=13), moderate in 36,7% (N=11) (Tables 8 and 9, Figures 20 and 21).

The <u>ratio</u> of psychological to somatic symptoms was 30%: 70% (Fig. 22).

5.7 Comparative analysis of the clinical characteristics of PMS in the groups without psychiatric comorbidity (PMS-N), with comorbid DD (PMS-DD), and with comorbid PD (PMS-PD)

To search for pathoplastic changes in the clinical picture of PMS in cases of comorbidity the women with PMS and no comorbidity were compared to women with PMS and comorbid DD or PD. For the purpose of the comparison the distribution of the syndrome severity and the prevalence and severity of the its symptoms in the group of women with no comorbidity were recalculated as parts of 100% (Tables 8 and 9). After the recalculation 10,2% of the women with no comorbidity suffered severe syndrome, 41,8% - moderate and 47,9% – mild.

For the purposes of the between group comparison in addition to descriptive statistics and comparisons of the means/frequency distributions of basic symptoms between the groups we also used the Kruskal-Wallis test to compare categorical variables between more than two independent groups or when the frequency distribution was different from normal and/or there the condition for homogeneity of variations was violated. As post hoc analysis we used the Mann-Whitney test with Bonferroni's correction.

<u>Psychological symptoms</u>: *sadness* – no significant between group difference was registered neither in its prevalence ($X^2(2) = 1,090$, p = 0,580) (Table 10), nor in its severity ($X^2(2) = 2,394$, p=0,302) (Table 11). The prevalence of *irritability* also did not demonstrate between group difference ($X^2(2) = 5,807$, p = 0,550) (Table 10). The initial comparison of its severity by the Kruskal-Wallis Test demonstrated significant difference ($X^2(2) = 35,511$, p < 0,001). The post hoc analysis by the Mann-Whitney test with Bonferroni correction showed significant differences between the groups PMS-PD/PMS-DD and PMS-N/PMS-PD (p < 0,001) and no significant difference between the groups PMS-N/PMS-DD (p= 0,035) (Table 11). The symptom is most severe when comorbid with PD, followed by DD, and it is most mild when no comorbidity is present. *Mood swings* – we found significant difference regarding its prevalence ($X^2(2) = 10,508$, p = 0,005). The post hoc analysis demonstrated no significant difference between PMS-PD/PMS-DD (p = 0,073) and PMS-N/PMS-PD (p= 0,110) and only between PMS-N/PMS-DD (p = 0,003) (Table 10). The symptom is most common in PMS-DD – 100%, followed by PMS-PD – 90% and PMS-N – 76,5% (Table 10). Regarding it severity again a significant difference was present ($X^2(2) = 12,083$, p= 0,002). The post hoc analysis showed no such difference between PMS-PD/PMS-DD (p = 0,896), but found significant difference between PMS-N/PMS-DD (p = 0,004) and PMS-N/ PMS-PD (p = 0,009) (Table 11). The symptom *anxiety* also showed significant difference between the three groups ($X^2(2) = 15,092$, p = 0,001). No statistically significant difference was present between PMS-PD/PMS-DD (p = 0,073) and PMS-N/PMS-PD (p = 0,031), but between the groups PMS-N/PMS-DD the prevalence was significantly higher in the group with DD (p = 0,001) (Table 10). It severity was also statistically significant between the groups ($X^2(2) = 51,109$, p < 0,001). We did not register difference in severity between both groups with comorbidity but we did find such difference between the remaining groups - PMS-N/PMS-DD (p < 0,001) and PMS-N/PMS-PD (p < 0,001) (Table 11). The between group analysis on the prevalence of *despair* demonstrated statistically significant difference ($X^2(2) = 19,854$, p < 0,001). The post hoc analysis by Mann-

Whitney test found no difference between both groups with comorbidity (p = 0,838), but did find such between PMS-N/PMS-DD (p = 0,001) and PMS-N/PMS-PD (p < 0,001) – significantly lower in PMS-N. The difference in its severity between the three groups was significant (X^2(2) = 13,269, p = 0,001) and again in the groups with comorbidity it was not significant (p = 0,904) and it was significant between PMS-N/PMS-DD (p = 0,003) and PMS-N/PMS-PD (p = 0,003) (Table 11). *Apathy* also demonstrates significant between group difference (X^2(2) = 40,074, p < 0,001). Again, between the groups with comorbidity there was no significant difference (p = 0,293) but between PMS-N/PMS-DD and PMS-N/PMS-PD there was significant difference (p < 0,001) (Table 10). The severity of the symptom repeats the same pattern – statistically significant difference between the three groups (X^2(2) = 36,292, p < 0,001), lack of difference between the groups with comorbidity (p = 0,904) and significant difference between PMS-N/PMS-PD and PMS-N/PMS-DD (p < 0,001) (Table 11). The prevalence of the symptom *absent-mindedness* was significantly different between the three groups (X^2(2) = 15,343, p< 0,001), between the comorbid groups and PMS-N/PMS-DD there was no difference (p = 0,215; p = 0,020), but there was such between PMS-N/PMS-DD (p = 0,001). Its severity follows the same pattern - significant difference between the three groups X^2(2) = 23,782, p < 0,001), no statistical difference between the groups with comorbidity (p = 0,385) and significant differences between the rest of the groups - PMS-N/PMS-PD (p = 0,001) and PMS-N/PMS-DD (p < 0,001). *Fatigue* differed significantly between the three groups (X^2(2) = 8,470, p = 0,014). Such difference was not evident between the PMS-DD/PMS-PD groups (p = 0,073) and the PMS-N/PMS-PD groups (p = 0,196), but was present between PMS-N/PMS-DD (p = 0,006). Its severity also demonstrated significant between group difference (X^2(2) = 7,176, p = 0,028), which was evident only between the PMS-N/PMS-PD (p = 0,026) and not in the rest of the comparisons (PMS-DD/PMS-PD (p = 0,444); PMS-N/PMS-DD (p = 0,056)). The prevalence of *changes in appetite* demonstrated statistically significant difference (X^2(2) = 11,619, p = 0,003). The post hoc analysis showed no statistical difference between both groups with comorbidity (p = 0,325) as well as between PMS-N/PMS-DD (p = 0,024). It was only present between PMS-N/PMS-PD (p = 0,007). Its severity also demonstrated between group difference (X^2(2) = 6,599, p = 0,037), which was only present between PMS-N/PMS-PD (p = 0,030) (PMS-DD/PMS-PD (p = 0,796); PMS-N/PMS-DD (p = 0,068). Regarding the symptom *sweets craving* there was no statistically significant difference neither in its prevalence (X^2(2) = 3,777, p = 0,151), nor in its severity (X^2(2) = 1,202, p = 0,548). *Insomnia* on the other hand, differed significantly (X^2(2) = 38,507, p < 0,001), not between the groups with comorbidity (p = 0,154) but between each of them and the PMS-N group (PMS-N/PMS-DD (p < 0,001); PMS-N/PMS-PD (p < 0,001). It was also evident regarding the severity (Tables 10 and 11).

Table 10. Comparison of the prevalence of the symptoms between the groups (PMS-N, PMS-PD, PMS-DD)

Psychological symptoms	X^2	df	p*	PMS-N/PMS-DD**	PMS-N/PMS-PD**	PMS-DD/PMS-PD**
Sadness	1.090	2	.580	.297	.867	.458
Irritability	5.807	2	.055	.148	.045	.325
Mood swings	10.508	2	**.005**	**.003**	.110	.073
Anxiety	15.092	2	**.001**	**.001**	.031	.073
Despair	19.854	2	**.000**	**.001**	**.000**	.838
Apathy	40.074	2	**.000**	**.000**	**.000**	.293
Absent-mindedness	15.343	2	**.000**	**.001**	.020	.215
Fatigue	8.470	2	**.014**	**.006**	.196	.073
Changes in appetite	11.619	2	**.003**	.024	**.007**	.325
Sweets craving	3.777	2	.151	.052	.680	.180
Insomnia	38.507	2	**.000**	**.000**	**.000**	.154

Somatic symptoms	X^2	df	p*	PMS-N/PMS-DD**	PMS-N/PMS-PD**	PMS-DD/PMS-PD**
Abdominal bloating	1.891	2	.389	.206	.466	.616
Weight gain	25.775	2	**.000**	.069	**.000**	**.001**
Breast tension and tenderness	12.555	2	**.002**	**.010**	**.012**	1.000
Joint aches	11.075	2	**.004**	.344	**.001**	.056
Muscle aches	57.040	2	**.000**	**.000**	**.000**	.417
Headache	32.926	2	**.000**	**.000**	**.000**	.161
Palpitations	106.207	2	**.000**	**.000**	**.000**	.325
Shivering	37.182	2	**.000**	**.000**	**.000**	.154

Kruskall-Wallis; p*< 0.05;   Mann-Whitney; p**< 0.0167

Table 11. Comparison of the severity of the symptoms between the groups (PMS-N, PMS-PD, PMS-DD)

Psychological symptoms	X^2	df	p*	PMS-N/PMS-DD**	PMS-N/PMS-PD**	PMS-DD/PMS-PD**
Sadness	2.394	2	.302	.427	.144	.904
Irritability	35.511	2	**.000**	.035	**.000**	.895
Mood swings	12.083	2	**.002**	**.004**	**.009**	.385
Anxiety	51.109	2	**.000**	**.000**	**.000**	.444
Despair	13.269	2	**.001**	**.003**	**.003**	.796
Apathy	36.292	2	**.000**	**.000**	**.000**	.550
Absent-mindedness	23.782	2	**.000**	**.000**	**.001**	.557
Fatigue	7.176	2	**.028**	.056	.026	
Changes in appetite	6.599	2	**.037**	.068	.030	
Sweets craving	1.202	2	.548	.724	.273	
Insomnia	37.240	2	**.000**	**.000**	**.000**	

Somatic symptoms	X^2	df	p*	PMS-N/PMS-DD**	PMS-N/PMS-PD**	PMS-DD/PMS-PD**
Abdominal bloating	6.266	2	**.044**	.824	.021	.026
Weight gain	36.514	2	**.000**	.322	**.000**	**.000**
Breast tension and tenderness	35.287	2	**.000**	**.000**	**.000**	.596
Joint aches	7.719	2	**.021**	.522	**.006**	.089
Muscle aches	62.265	2	**.000**	**.000**	**.000**	**.001**
Headache	39.792	2	**.000**	**.000**	**.000**	.103
Palpitations	112.015	2	**.000**	**.000**	**.000**	**.004**
Shivering	61.227	2	**.000**	**.000**	**.000**	.515

Kruskall-Wallis; p*< 0.05; Mann-Whitney; p**< 0.0167

The difference in the prevalence and severity of psychological symptoms is illustrated in Figures 18 and 19.

Figure 18. Distribution of psychological symptoms by prevalence (PMS-N, PMS-DD, PMS-PD)
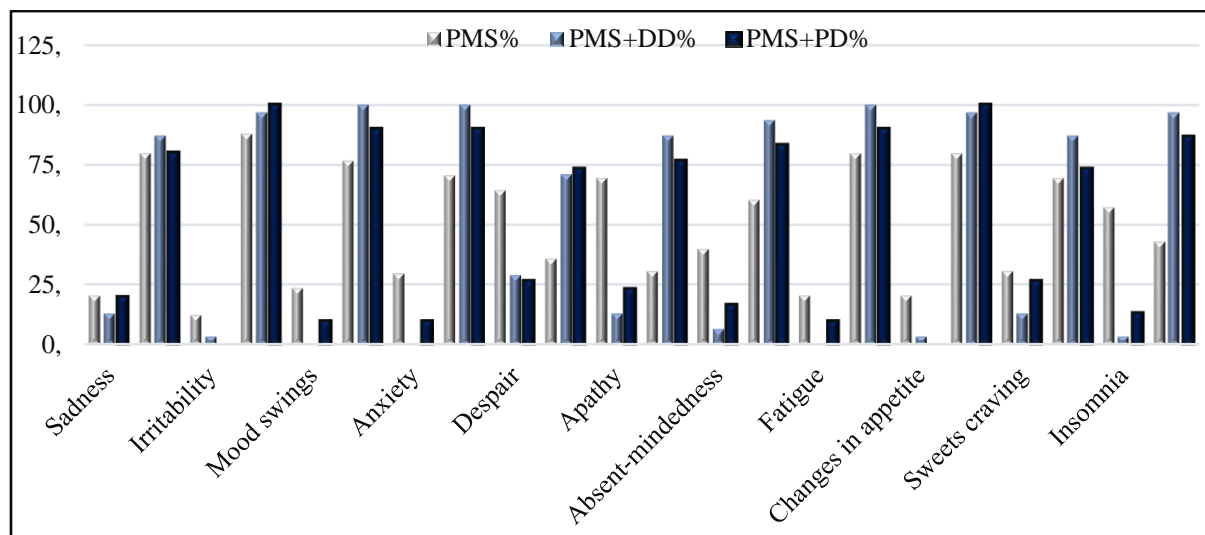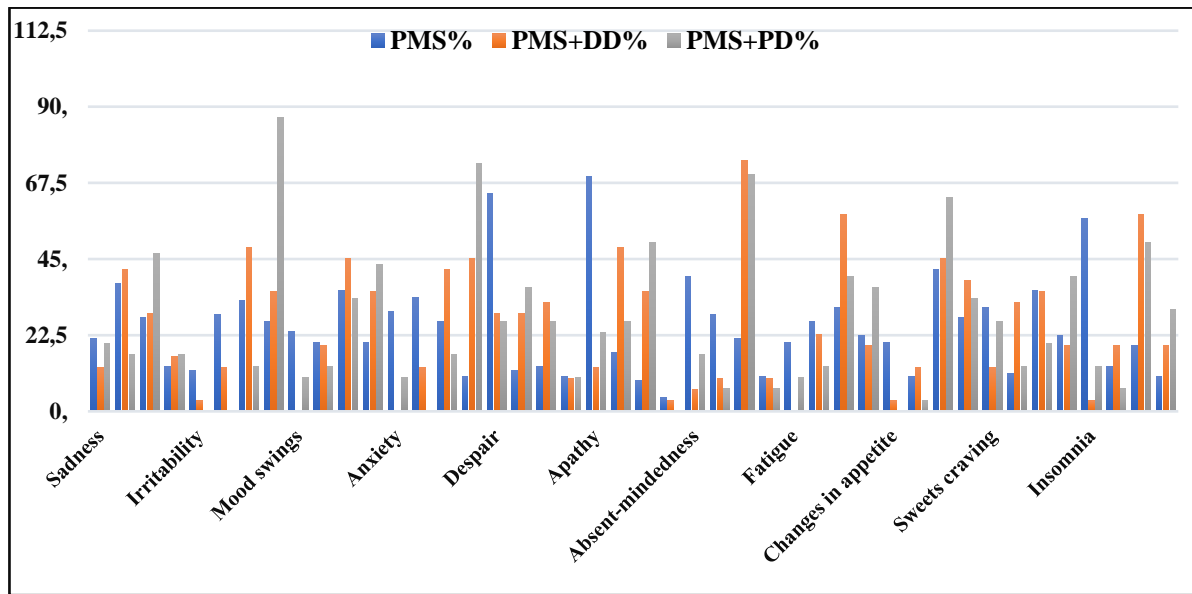
Figure 19. Distribution of psychological symptoms by severity (PMS-N, PMS-DD, PMS-PD)

Somatic symptoms: there was no statistically significant difference in the frequency of *abdominal bloating* ($X^2(2) = 1,891$, p = 0,389), but there was a small one in its severity ($X^2(2) = 6,266$, p = 0,044). The prevalence of *weight gain* did also show significant between group difference ($X^2(2) = 25,775$, p < 0,001). According to the post hoc analysis it was between both groups with comorbidity (p = 0,001) and between PMS-N/PMS-PD (p < 0,001) and no difference of statistical significance between PMS/N/PMS-DD (p = 0,069). Exactly the same hold true for its severity - significant between group difference ($X^2(2) = 36,514$, p < 0,001) and significant one between both groups with comorbidity (p < 0,001) and between PMS-N/PD (p < 0,001) and no difference between PMS-N/PMS-DD. The prevalence of *breast tension* also was statistically significant different ($X^2(2) = 12,555$, p = 0,002). The post hoc analysis did not show one only between the groups with comorbidity but demonstrated difference between PMS-N/PMS-DD (p = 0,010) and PMS-N/PMS-PD (p = 0,012). The prevalence of the symptom *joint aches* was statistically significant different between the groups ($X^2(2) = 11,075$, p = 0,004), but only between PMS-N/PMS-PD – p = 0,001. The same was true about its severity: statistically significant difference between the three groups ($X^2(2) = 7,719$, p = 0,021) and statistically significant one only between PMS-N/PMS-PD (p = 0,006). The symptom *muscle aches* was statistically significantly different between the groups ($X^2(2) = 57,040$, p < 0,001) and the difference was greatest in the comparison PMS-N/PMS-DD and PMS-DD/PMS-PD (p < 0,001 for both comparisons). The severity of the symptom was statistically different ($X^2(2) = 62,265$, p < 0,001) between every two groups - PMS-N/PMS-DD, PMS-DD/PMS-PD (p < 0,001), PMS-DD/PMS-PD (p = 0,001). *Headache* followed the same order – statistically significant difference in the prevalence between the three groups ($X^2(2) = 32,926$, p < 0,001). The post hoc analysis found differences between PMS-N/PMS-DD and PMS-N/PMS-PD (p < 0,001) and lack of difference between the comorbid groups (p = 0,161). The severity of that symptom also demonstrated statistically significant difference ($X^2(2) = 32,926$, p < 0,001) and it was again between PMS-N/PMS-DD and PMS-N/PMS-PD (p < 0,001) but also between the groups with comorbidity (p = 0,001). *Palpitations*: with regard to its prevalence, there was statistically significant between group difference ($X^2(2) = 106,207$, p < 0,001), that after the post hoc analysis was positioned between PMS-N/PMS-DD and PMS-N/PMS-PD (p < 0,001), but there was no difference between both groups with comorbidity (p = 0,325). The severity of the symptom showed statistically significant difference ($X^2(2) = 112,015$, p < 0,001), which again

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was between PMS-N/PMS-DD and PMS-N/PMS-PD (p < 0,001) and also between the comorbid groups (p = 0,004). The prevalence of *shivering* also differed statistically significant between the groups ($X^2(2)$ = 37,182, p < 0,001). It was between PMS-N/PMS-DD and PMS-N/PMS-PD (p < 0,001) and the comorbid groups did not differed statistically significant (p = 0,154). There was significant difference in the severity of the symptom ($X^2(2)$ = 61,227, p< 0,001). The post hoc analysis showed that it was between PMS-N/PMS-DD and PMS-N/PMS-PD (p < 0,001) but there was no difference between the groups with comorbidity (p = 0,515) (Tables 10 and 11).

The difference in the prevalence and severity of somatic symptoms in the three groups is illustrated in Figures 20 and 21.

Figure 20. Distribution of somatic symptoms by prevalence (PMS-N, PMS-DD, PMS-PD)
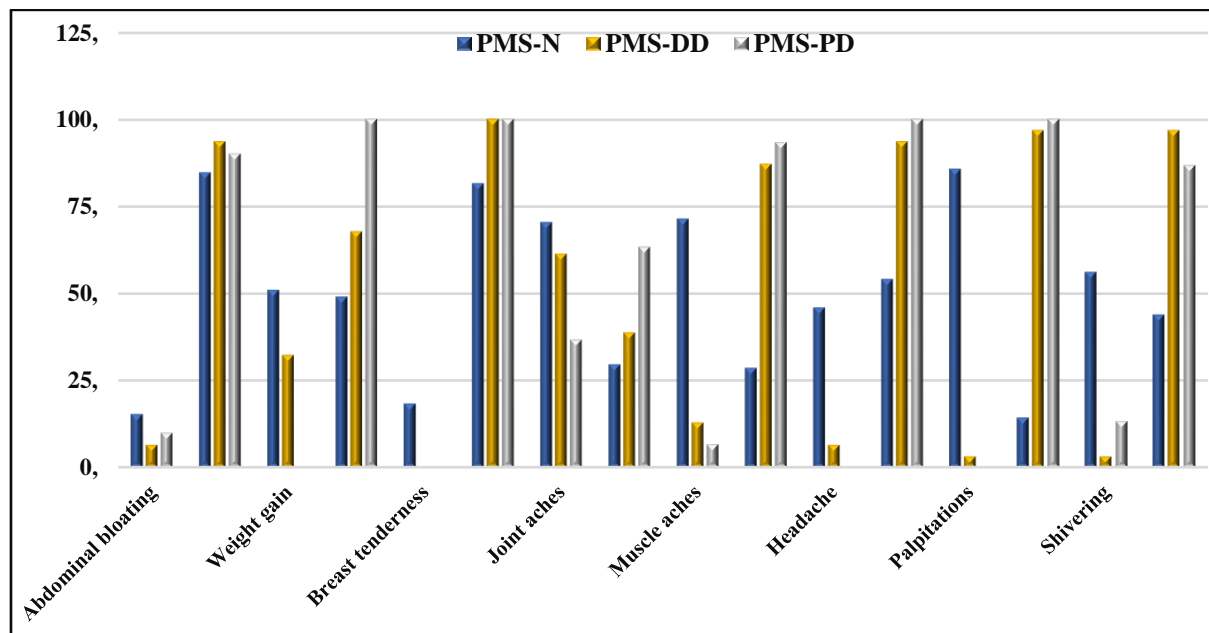
Figure 21. Distribution of somatic symptoms by severity (PMS-N, PMS-DD, PMS-PD)
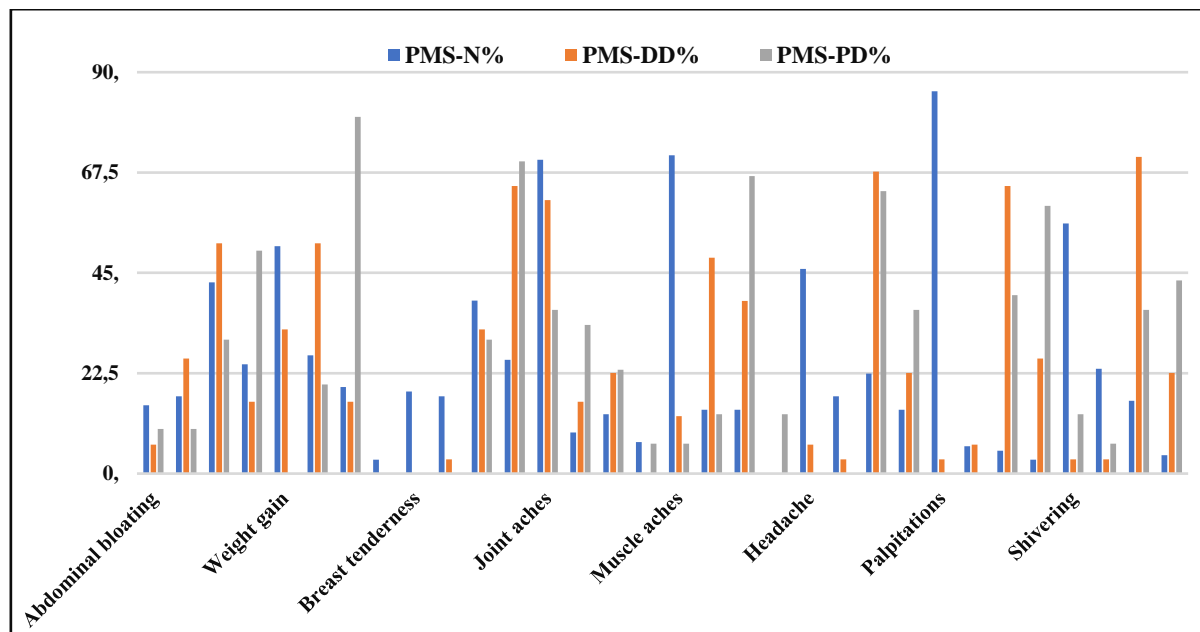
The ratio psychological to somatic symptoms was nearly equal in the PMS-N (48,5 : 51,5); in those women with comorbid PD the somatic symptoms were dominant (30 : 70) and nearly threefold more common than in women with comorbid DD (74,2 : 25,8). Psychological symptoms, on the other hand, were most prevalent in women with comorbid DD, followed by those without comorbidity, and relatively mildly present in women with comorbid PD (Fig. 22).

Figure 22. Ratio psychological to somatic symptoms in the three groups (PMS-N, PMS-PD, PMS-DD).
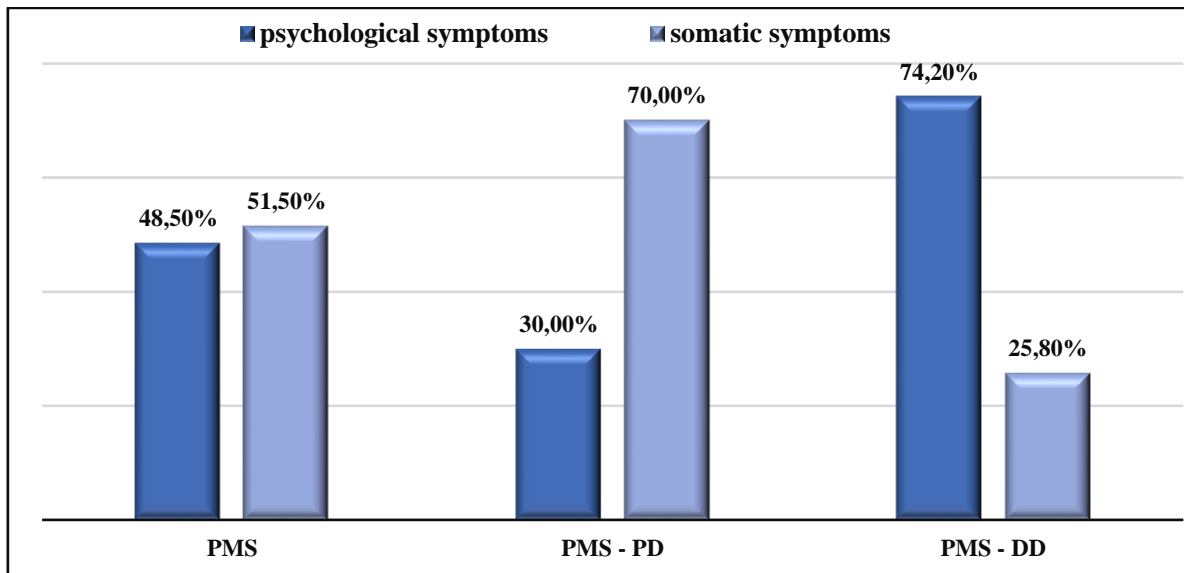
Severity: The difference in severity between the three groups was statistically significant $(X^2(2) = 30,906, p < 0,001)$. The conducted post hoc analysis demonstrated statistically significant difference between PMS-DD/PMS-PD (p = 0,002) and even more marked one between PMS-N/PMS-PD (p < 0,001). No significant difference was found between PMS-N/PMS-DD (p = 0,034) (Table 31). PMS was most severe in the group PMS-PD, followed by groups PMS-DD and PMS-N. PMS was most commonly severe in group PMS-PD - 43,3%, and in group PMS-N (10,20%) and PMS-DD (16,1%) – around twice less common. The mild cases were most prevalent in PMS-N (47,9%), followed by PMS-DD (25,8%), and in PMS-PD there were none. The moderate cases prevailed in both groups with comorbidity, and in the group PMS-N most prevalent was the mild form (Table 12, Figure 23).

Table 12. Comparison of the severity of PMS

Severity	X2	df	p*	PMS-N/PMS-DD**	PMS-N/PMS-PD**	PMS-DD/PMS-PD**
	30.906	2	.000	.034	.000	.002

Kruskall-Wallis; p*<0.05; Mann-Whitney; p**<0.0167
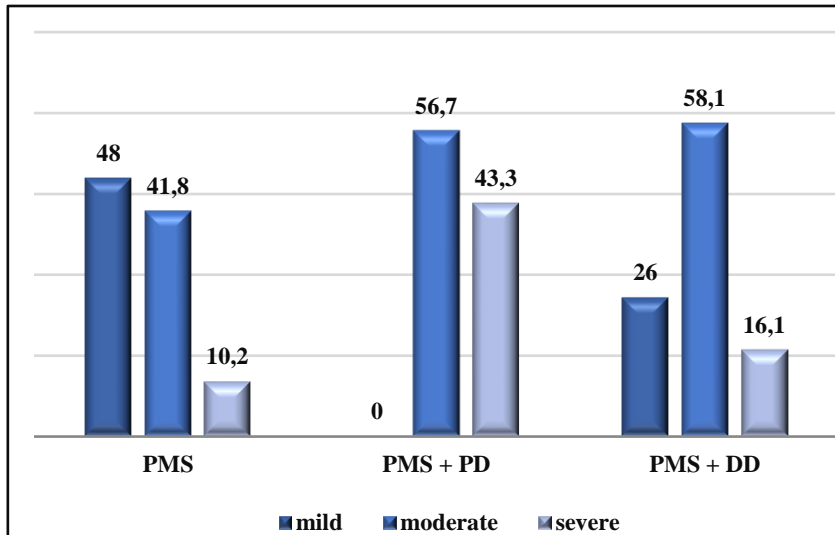
Figure 23. Severity of PMS in the groups

5.8 Attitudes towards PMS as a health problem and medical assistance seeking

All participants, who were screened for PMS also filled-in additional questionnaire card, related to their knowledge of the syndrome, its acknowledgement of as a medical problem, and their help-seeking behaviour.

Of those women without PMS 73,4% (N=152) believed, that it was not necessary to seek medical consultation for that problem, moreover 32,3% (N=67) of them assumed it was normal part of women's life and not a medical condition, 12,1% (N = 25) believed it needed to be born regardless its negative influence on their everyday routine, 23,2% (N = 48) accepted it as a tolerable condition and 5,9% (N = 12) found no point in searching for help as they did not believe there was any way of releasing it. Of the women with PMS 51% (N = 50) had never sought help, and of them 4,1% (N = 4) believed it was normal part of their lives, 27,5% (N = 27) – because they believed they should bear it, 8,2% (N = 8) did not experience severe complaints, and 11,2% (N = 11) did not believe that they could be helped. Of all women with PMS 45,9% (N = 45) would not take medications, and 54,1% (N = 53) would concoct medication treatment in future.

Up to the moment of the study only 17,3% (N = 17) of the women with PMS had already searched for medical help and the remaining 82,7% (N = 81) – had not (Fig. 24). 34,7% (N = 34) of the women with PMS had taken medications and of them 67,6% (N = 23) had chosen those medications by themselves, 26,5% (N= 9) got prescription from a gynecologist, and 5,9% (N= 2) – from their general practitioner (Fig. 25).
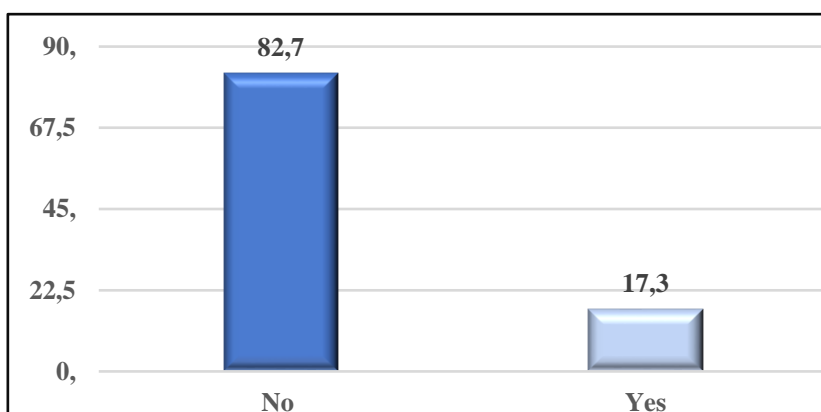
Figure 24. Help-seeking behaviour in the past
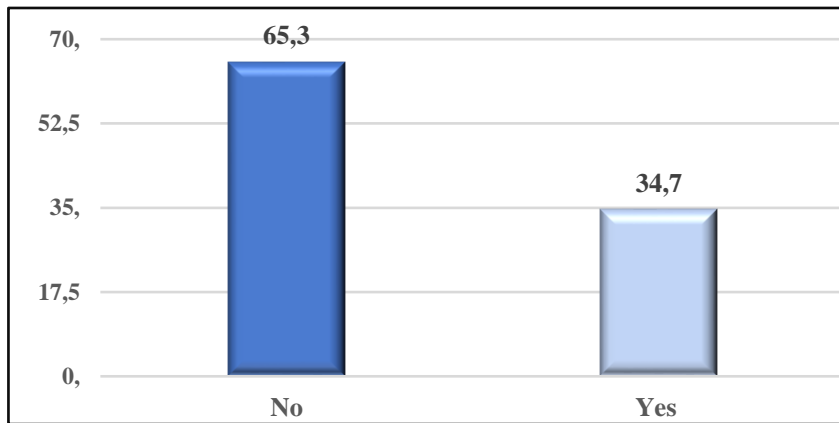
Figure 25. Medication intake in the past

More women who in the past had conducted consultations were in the age group over 35 years – 22,7% (N= 5) to 15,8% (N= 12) of the younger women. On the contrary, more women below 35 years had taken medications in the past – 35,5% (N= 27) to 31,8% (N= 7) of the older women. Those medications were prescribed by a physician in 8 women below 35 (30,8%) and in 3 women over 35 (12,5%). Women with PMS over 35 were more inclined to consult a physician (68,2%, N = 15) in the future, than younger ones – 43,4% (N = 33) (Fig. 26). With age the willingness to medication intake grew - from 48,7% (N= 37) of the women below 35 to 72,7% (N= 16) of the women over 35 (Fig. 27).
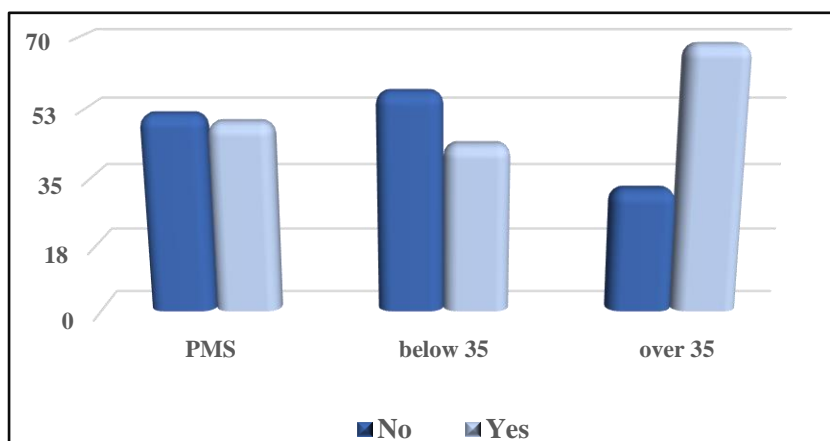
Figure 26. Willingness to conduct a consultation in future in women with PMS altogether and depending on age
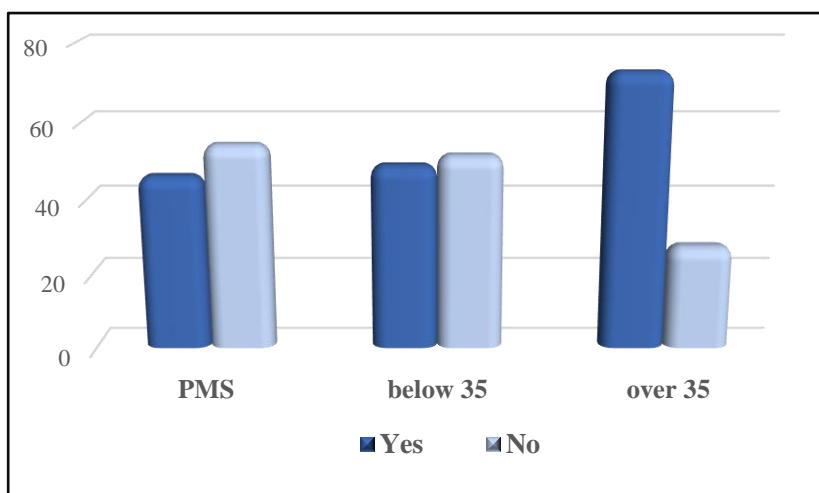
Figure 27. Willingness to conduct treatment in future in women with PMS altogether and depending on age

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VI. DISCUSSION

6.1 Prevalence of PMS

In the presented study on the prevalence of PMS in a randomly recruited sample of Bulgarian women we found, that 67,9% of the inquired women did not suffer PMS and in 32,1% the syndrome was present. The mild and moderate cases of PMS were nearly equally distributed – 15,4% and 13,4%, resp., and the severe ones (PMDD) were 3,3%. The diagnostics of PMS in our study was conducted by gathering retrospective data and did not differ from the way most studies worldwide gathered their data. Nevertheless, this method despite being fast, holds some risk of falsely increasing the numbers. This problem has been repeatedly discussed by the world's leading experts in PMS research and despite the recommendations for prospective follow-up (Bancroft J, Backstrom T., 1985; Cohen L.et al., 2002) studies with such design are scarce. Two studies that used retrospective evaluation and prospective follow-up within one menstrual cycle (Wittchen H. et al.,2002; Potter J. et al., 2009) and two prospective studies (Cohen L. et al., 2002; Henshaw C.et al., 2007) were conducted. They recruited small number of participants and are related more with the problems of the diagnostic evaluation than with evaluation of the prevalence of PMS. In those studies the method was still the retrospective evaluation. Because of the problems of the retrospective evaluation Rapkin and his team already in 1988г proposed when using this type of evaluation the registered shares be corrected by 30 to 50%, so that the subjectivity of women be avoided. In their research they compared retrospective and prospective evaluations and they found that retrospective evaluations correlate with the prospective ones in only 50% of the cases. Severino and Moline (1990) also detected that only in 30% of their sample of women with PMDD the results of the retrospective evaluations corresponded to prospective observation of the symptoms. The same tendency is evident in more studies. Lu, who worked with a group of 30 young Taiwanese women of mean age 24,4 found that the retrospective evaluation of the severity of the symptoms was much higher – 57% of the participants evaluated their symptoms as severe, whilst during a prospective evaluation only 33% of the women suffered significant symptoms during the luteal phase (Lu Z. Et al., 2001). Other investigators confirm that when it is relied on remembering a higher rate of severity is registered (Connolly M., 2001; De Souza M. et al., 2000). Considering these recommendations we corrected our results by 50%: this way 16,1% of the women fulfilled the criteria for PMS and 7,7% of them suffered mild syndrome, 6,7% - moderate, and 1,7% - severe (e.g.PMDD). These results are not contrary to results in the literature worldwide which point prevalence of 20 – 40% (Matsumoto T. et al., 2013).

In the different studies on the prevalence of PMS it varies considerably depending on the type of the study and the utilised methodology and tools (Hariri F. et al., 2013; Crow E. et al., 2017; Htet Htet Oo et al., 2016; Khodjaeva N. et al., 2013; ReuveniI D. et al., 2013). For exapmle, in a study of 83 women that gathered prospective data during 1 to 7 cycles Sveindottir and Bäckström (2000) focused only on the symptom count. They found that 80,7% experienced symptoms but only 2% fulfilled the criteria for PMDD. We adopted more detailed set of criteria and not just the presence/absence of symptoms and this way we detected prevalence of PMS of 32,1%, but regarding PMDD the corrected results were similar – 1,7%. If we compare our group of Bulgarian women to the summarised data of Rapkin (Rapkin A. et al., 1988) and Collins (Collins A. et al., 1993) it could be seen that the results are comparable – 3,6% of the samples

in those studies and 3,3% of our sample suffered PMDD. In our sample the shares of mild and moderate cases are smaller (13,4% and 15,4%, resp.) than the ones published by the above-mentioned authors (29,6% and 23,7%, resp.), and that can be explained by the strict criteria we used in our study. In a study of Johnson and co-authors (1988) 3,2% of the women were evaluated as suffering from severe symptoms, 13,4% as having moderate complaints, in 25,6% the symptoms were considered moderate, 39,6% were with mild syndrome, and 12,7% of the women had no premenstrual symptoms.

Also important is the question on the definition that the researchers use. When in research on the prevalence of PMS the definition of DSM-IV is used, the prevalence varies from 1,2% in the Japanese community to 17,9% among Brazilian students (Takeda T.et al., 2006; Teng C. et al., 2005). Studies based on DSM-IV definition in recent years were conducted in Ukraine (Crow E., Jeannot E., 2017) and Mianmar (Htet Htet Oo et al., 2016) and the reported prevalence were very similar – 29% and 37,3%, resp. The present study is also based on the definition of DSM, as it used larger symptom group and clear diagnostic criteria. When comparing those data to ours (32,1%) it is clear that the prevalence of PMS in Bulgarian women is no different from the rest. When using the definition of the ACOG the lowest numbers come from the USA, where 8,3% of the female students suffer PMS (Deuster P. et al., 1999), and the highest prevalence is in Saudi Arabia, where 38% of young women were affected (Rasheed P. et al., 2003). Despite the differences in the definitions used in the study of PMS, it is clear that our results are not largely different (32,1%, 16,1% after correction). The prevalence of PMS increases when the definition of IVD 10 is used, which is more descriptive than the DSM-IV definition and that is a possible explanation for that evident difference. Demonstrative example are two consecutive studies in Pakistan. The first one detected prevalence of 92,4 % (Rizwan H. et al, 2014), which was then confirmed by the second study, which reported prevalence of 98,2% (Ghani S. et al., 2016). The authors themselves recognised the possible influence of the definition they used on the high prevalence they detected.

The tools that are used also influence the results on the prevalence of PMS. In the research recommendations there is no list of the main symptoms that are diagnostically important (Halbreich U. et al., 2007; Matsumoto T. et al., 2012). The number of symptoms as well as the multitude of combinations between them that are possible has contributed to the invention of different evaluation tools. Most questionnaires focus on twenty symptoms, which have been appointed as the most prevalent by many research teams (Halbreich U. et al., 1982; Woods N. et al., 1982; Freeman E., 1997). There are over 20 evaluation scales, most of which were created in accordance to the hypothesis of the author of the corresponding study. We chose Premenstrual Symptoms Screening Tool (PSST). It is easily applied screening tool, that was developed by Steiner and co-authors (2003) to identify women suffering from PMS/PMDD, following the DSM-IV criteria. In this questionnaire there is only one item on somatic symptoms that unifies all of them. Because we wanted to gain more precise evaluation of those symptoms, we extracted every somatic symptom in a separate question, which gave us the opportunity to arrive at more detailed clinical picture. PSST works with strictly defined criteria for diagnostics and evaluation of the different severity grades of the syndrome. Not least, the questions on the impairments in the social and occupational functioning make the questionnaire clinically important. We analysed other studies that also used PSST for evaluation of PMS. The

results of an Israeli team (ReuveniI D. Et al., 2016) showed 25,6% prevalence of PMS and 9,9% of PMDD, an Indian team (Raval C. et al., 2016) reported prevalence of 18,4% of PMS, 14,7% moderately severe and 3,7% PMDD. An Iranian team of researchers (Hariri F. et al., 2013) registered reverence of PMS of 30,7% and of PMDD of 12,9%. This way our results are obviously corresponding the previously published in literature but also show that PSST allows satisfactory detecting of the syndrome in different ethnic groups. Another commonly used questionnaire is the Premenstrual Assessment Form (PAF). It was developed by Halbreich and is the most comprehensive evaluation tool. It includes 95 items, that cover alterations in mood, behaviour, and somatic state (Halbreich U. et al., 1982), but is time-consuming and women do not often agree to participate in such a study. The results of two recent studies that used the PAF were conducted in the Turkey (Özcan H. et al., 2013) and Uzbekistan (Khodjaeva N. et al., 2013). The reported prevalence of PMS was 16% and 28,1%, resp. Irrespective of the large variety of symptoms, included in this scale, the results did not differ from the rest of the data in literature, as well as from the data on the prevalence of PMS in the Bulgarian population (32,1%).

Another assumption is that the prevalence of PMS differ in people of different culture and ethnical background. For example, Shershah and co-authors (1991) interviewed 1600 women from five different regions in Pakistan, including women with very low educational grade, who filled-in the questionnaires with the help of trained staff. It turned out that symptoms of PMS experienced 37% of the women living in the Mohajir and Punjabi regions compared to 11,6% living in the region of Baluchistan. In 2014 a report came out from the same country which stated that the prevalence of PMS in their community was 92,4% (Rizwan H. et al., 2014). These results were confirmed two years later by a second Pakistani study (Ghani S. et al., 2016). It again recorded high prevalence of PMS – 98,2%. Severe PMDD was detected in 10%, moderate in 25%, and mild in 63% of the examined women. Interestingly, high percentage of women with mild PMS, and similar to the other countries percentage of women with moderate and severe PMS and PMDD. According to the authors a possible explanation would come from the definition that they used (ICD10). Exploring the prevalence of PMDD among Japanese women Takada found, that only 1,2% of the participants suffered from PMDD, and 5,3% experienced moderate PMS. Takada speculated that the lower prevalence of PMDD might have been a function of the traditional Confucian ethics, according to which the individual well-being of women is subordinate to the group prosper and women, who experience difficulties in verbalising their complaints (Takeda T. et al., 2006). The link between ethnicity and prevalence of PMS is also visible in a Canadian study which explores the prevalence of PMS in the general population and amongst the main ethnic groups (Caroline A. et al., 2017). The researchers examined 1102 women, categorised in four ethnic groups based on their own self-determination: Caucasian (n = 514), East-asian (n = 401), South-asian (n = 105), and others (n = 82). The team reported that the prevalence of premenstrual symptoms did not differ significantly among the ethnic groups (p = 0,11). The authors believed that this result could be explained by the unification of the life-style and the health attitudes in the contemporary society. The results from the Bulgarian sample do not differ from those in the literature so far and do not point to specifics of the Bulgarian ethnicity. We were also interested in comparing our results to the data from other Balkan countries. Only a Greek team reports on the prevalence

of PMS, and the results are similar to ours - 25,7% (Karaoulanis S.et al., 2010).

Our results on the prevalence of PMDD are also similar to those in the literature. Two studies that used the DSM-IV definition but used prospective confirmation of the symptoms, and also used different evaluation tools found similar shares of women with PMDD: 5,3% in the study of Wittchen in the USA (Wittchen H. et al., 2002) and 4,1% in a study in France by Potter (Potter J. et al., 2009). In the Bulgarian sample this percentage is 3,3%, which is confirmed by other studies, reporting prevalence of around 3 – 8% (Rapkin A. et al., 1988; Collins A. et al., 1993; Sternfeld B. et al., 2002; Rivera-Tovar A. et al., 1990; Hariri F. et al., 2013; Htet Htet Oo et al., 2016; ReuveniI D. et al., 2016; Ghani S. et al., 2016; Raval C. et al., 2016). In recent years there are reports on much higher prevalences of 20,9% in the Indian community up to 54,4% in Mianmar, which the authors relate to the very high levels of stress in their sample (Htet Htet Oo et al., 2016).

The evidence in the available literature on the prevalence of PMS are gathered from studies that encompassed several thousands of women by the use of different criteria, depending on the chosen definition. They used different methods of evaluation. In summary, the results show that around 20 – 40% of women suffer PMS, and 2 – 8% - PMDD (Matsumoto T. et al., 2013). Our data relatively well replicates what is known from previous research. Despite the use of different evaluation tools the reported prevalence is completely comparable to our 32,1%.

6.2 Clinical characteristics of the PMS group

In the ICD 10, DSM-IV and DSM 5 diagnostic criteria (APA, 1994; APA, 2011; WHO, ICD – 10, 1992) the most prevalent premenstrual symptoms are summarised in two categories:

1. Somatic symptoms – headache, breast tension and tenderness, back pain, abdominal bloating and cramps, weight gain, swelling of hands and feet, water retention, muscle and joint aches;

2. Psychological symptoms – irritability and anger, worries, depressive mood, mood swings and crying spells, anxiety and tension, absent-mindedness, loneliness, lowered self-esteem, fatigue, insomnia, dizziness, altered sexual interest, hunger, appetite changes, social distancing.

In the scientific literature so far around 300 symptoms have been described. In 2007 Halbreich and a group of experts proposed for research purposed to qualify s PMS any kind of symptoms and symptom groups as long as they follow the menstrual cycle and are not just a deterioration of other disorders (Halbreich U. et al., 2007). But still the symptom analysis is limited by the tools and their usual division into psychological and somatic remains.

The questionnaire that we used is a modified version of the Premenstrual Symptoms Screening Tool – PSST (Steiner M. et al., 2003), but the somatic symptoms were extracted into separate items each so that they could be more precisely evaluated. It consists of twenty items, corresponding to the both symptom types – 11 psychological and 8 somatic ones. This strategy corresponds to the latest recommendations for conducting clinical studies that require the inclusion of broad symptom spectrum (Halbreich U. et al., 2007). The severity grades were 4: no, mild, moderate, and severe syndrome.

According to our results the most common symptoms were irritability, followed by mood swings, sadness, fatigue, and anxiety. The most severe symptoms were anxiety (26,5%)

and changes in appetite (27,6%). Despair, decreased interests, and changes in the sleep pattern were more rare. The most common as well as most severe somatic symptoms were breast tension and tenderness and abdominal bloating. Half of the women experienced headache, followed by shivering, hot and cold flashes, and weight gain. A quarter of the women suffered joint and muscle aches, palpitations. The psychological and somatic symptoms were nearly equally distributed.

Similar results were also reported by Woods and co-authors (1982), who informed on a retrospective community based study in the USA. 179 women took part in it. The symptom, that most commonly was identified as severely impairing was irritability (12%). In the Bulgarian sample the leading role of irritability was once more confirmed but its prevalence was higher – 26,5%. In the above-mentioned study 46% of the women reported on mild to moderate changes in mood. Further common symptoms were anxiety, fatigue, depression, and tension, which were also found in our sample. The most prevalent somatic symptoms were headache, face swelling, cramps, breast tenderness, weight gain, swelling of the extremities. According to Joshi and co-authors (2010) the most common symptom is mastalgia or breast tension. The Bulgarian sample definitely confirmed that the symptom breast tension and tenderness (81,6%) along with the symptom abdominal bloating (84,7%) are among the leading somatic symptoms. An Australian study also found that breast pain, abdominal bloating, and weight gain are the most commonly reported symptoms, but followed by affective symptoms (Treloar S. et al., 2002). In our sample the both somatic and psychological symptoms were equally represented.

In a study on the core symptoms of PMS the leading experts Freeman and Halberstadt (2011) analysed 1081 women by daily evaluation on a 17-item diary, including also prospective follow-up for several months. The statistical analysis identified 6 main symptoms: anxiety and tension, mood swings, pain, increased appetite and specific foods craving, spasms, and reduced interest in activities. The authors believed that the clinical diagnosis of PMS may focus around this complex. Our results point to similar conclusions – the most common symptoms were irritability, mood swings, sadness, fatigue, and anxiety. Budeiri and co-authors (1994) defined tension, anger, irritability, low spirits, mood swings, headache, abdominal bloating, changes in appetite and sleep as most common symptoms. These studies bring somatic symptoms to the front as the leading symptom type.

The studies from recent years give similar results, despite certain specifics. For example, in the Canadian population the most common symptoms were cramps (75%), abdominal bloating (75%), mood swings (73%), increased appetite (64%), and acne (62%). But the prevalence of cramps differs among different ethnic groups, and specifically East Asian women report it significantly less than Caucasian and South Asian women ($p < 0,05$) (Caroline A. et al., 2017). In German women the five most significant symptoms were headache, which evaluated as the most severe symptom (33%), follows by irritability (27,3%), low self-esteem (23.5%), depressed mood (22.9%), and emotional lability (11.1%) (Schmelzer K. et al., 2015). Similar results were also published for Indian women. The authors reported on dominating somatic symptoms like back and joint pain (Kumari S., Hindawi A., 2016). From the review above it is obvious that divergent information is distributed with regard to the ratio of psychological to somatic symptoms. Some authors register more psychological symptoms and

others - more somatic, but it seems that this depend a lot on the evaluation tools they use. The scale we used is well balanced with regard to both types of symptoms. We registered nearly equal distribution of the psychological and somatic symptoms.

The summary of the literature data shows, that despite the use of different questionnaires, the results are comparable and reveal that symptoms like irritability, anxiety, headache, and abdominal bloating are the most common premenstrual complaints (Halbreich U. et al., 2007; Borenstein J. et al., 1997; Ghani S. et al., 2016; Raval C.et al., 2016; Özcan H. et al., 2013; Abdelmoty H. et al., 2015; Guler T. et al., 2013). The results for the Bulgarian sample confirm this data but breast tension and tenderness turn out to be a core somatic symptom.

6.2.1 Clinical characteristics of PMS, depending on age

As already known, most disease deteriorate with age. Approaching the age of menopause and the related hormonal changes gives reason to expect deterioration in PMS with advancing age. For detailed clarification of the course of the syndrome in a longitudinal plane the group of women with PMS was divided according to the age of the participants - below and over 35 years. Our results show that in women below 35 the most common psychological symptom (experienced by nearly all women) is irritability, followed by changes in appetite, fatigue, sadness, and mood swings. Nearly half of the women reported on absent-mindedness. Little less prevalent were despair, apathy, and changes in sleep. Similar results were reported in a study among 30 Japanese women aged between 18 and 35 years. The most common premenstrual symptoms were anger or irritability (70,6%), anxiety (68,5%), and fatigue (52%) (Takeda T. Et al., 2006). Another study among girls, mean age $14,67 \pm 1,7$, reported as most common psychological symptoms fatigue in 68% and mood disturbances in 55% (Abdelmoty H. et al., 2015). Further studies in patients aged between 18 and 24 and between 18 and 30 detected as common symptoms anxiety, tension, swift emotional changes and crying spells, anger, irritability, sleepiness, low energy levels, headache (Raval C. et al., 2016; Özcan H. et al., 2013). In a detailed study among patients, mean age 21,7 the mood changes (91,9%), irritability (79,4%), and aggression (77,9%) were the most prevalent psychological symptoms (Ghani S. et al., 2016). The psychological symptoms that we detected in our sample of young women exactly replicate what was already published in literature.

In our study with advancing age irritability (72,7%) was replaced by sadness, fatigue, and increased consumption of sweet foods (equal frequency) – 86,4%. Around half of the women experienced anxiety and despair and least - apathy. The prevalence and severity of psychological symptoms did not change with the exception of that of insomnia which was significantly increased. Altogether, psychological symptoms were equally distributed un both groups. This data was supported by a study that analysed the age differences in PMS presentation among 150 women aged between 20 and 45. The group was divided into three subgroups: 22 women (14.2%) aged between 15 and 25, 78 (52.0%) – between 26 and 35, and 50 (33,3%) - between 36 and 50. The single significant correlation with age that was found was for irritability, which was found to be more common in women in the higher-age group compared to the rest of the groups ($p < 0,05$). There were no significant differences in the rest of the psychological symptoms in those age groups (Kumari S. et al., 2016). Despite the fact

that in our sample the prevalence of irritability decreases with age, the difference between both groups was not significant. The observation that psychological symptoms in general do not change with age was confirmed.

Among the younger Bulgarian women the somatic symptoms were breast tension and tenderness and abdominal bloating. Half of them experienced also weight gain, shivering, hot and cold flashes. A quarter of them also complained of joint and muscle aches and palpitations. With increasing age most drastically and statistically significant increased the percentage of headache, which became a major symptom. Statistically significant increase was also registered for the prevalence of palpitations. Common remained the symptom breast tension and tenderness. Half of the women suffered weight gain, shivering, hot and cold flashes. The psychological and somatic symptoms were nearly equally distributed and identical in both age groups. Similar results on the symptoms of PMS were published in a study in students, mean age 20,5 ±2,1, in which somatic symptoms outnumbered psychological ones. The most common complaints were breast tension and tenderness (68,6%), back pain (67,4%), abdominal bloating (60,5%) were designated as most impairing the everyday functioning, although they reported also psychological symptoms - sadness and crying (56,4%) and irritability (76,7%) (Guler T. et al., 2013). Another study of young women (mean age 21,7) also confirmed our findings: the most common physical symptoms were abdominal spasms (84%), body aches (78%), abdominal bloating (66%) (Ghani S. et al., 2016).

According to our results in the subgroup of the younger women PMS was in nearly equal shares mild and moderate. With advancing age the syndrome became either milder (in half of the cases) or more severe (in ¼ of the women), and was more rarely moderately expressed. The number of the severe cases increased statistically significantly – from 6,6% to 22,7% at the expense of the moderate cases, which became less common with age. The prevalence of mild PMS remained unchanged – around 50%. Our results confirm the reports from the world literature. For example, in the study of Warner and Bancroft (1990) the women over 35 and those with larger number natural menstrual cycles experienced more premenstrual symptoms. Cohen examined older women – 36 – 44 years. In a sample of 513 women 6,4% fulfilled the criteria for PMDD (Cohen L. et al., 2002). Similar data reported a team from Uzbekistan, that analysed the data of 276 patients with PMS aged between 21 and 30 (56,4%) and 146 (29,8%) women over 30 years of age. Mild PMS was more often registered in the group 21–30 years (61,5% vs 38,5% p < 0,0001) and moderate PMS was most often detected in women over 21 (92,3% vs 7,7%, p < 0,0001). As far as women with severe PMS are concerned, most of them (70,8% vs 29,2% p = 0,009) were over 30. Moreover, in women between 18 and 30 the symptoms of PMS apparently disappeared around the first or second day of the menstruation, but in those over 30 the symptoms persisted until the 4th and 5th day (Khodjaeva N. et al., 2013). To summarise, our results confirm the already observed deterioration of the PMS severity with age, and furthermore the prevalence of PMDD in the Bulgarian sample was even higher. A possible explanation could be the retrospective gathering of the data.

6.3 Symptom analysis of the subgroup of women without PMS. Comparative analysis of the symptoms between the groups with and without PMS

The bigger part of the women in the Bulgarian sample (67,9%) experience distinct symptoms in the two weeks preceding menstruation. They are its precursors and cause significant level of discomfort in everyday life of women and can be defined as premenstrual indisposition. Their detailed analysis showed that most of the women in the group without PMS had complaints. Only 6,3% of women had no symptoms. Studies on the prevalence of the premenstrual symptoms in other countries also found that the number of women that experienced at least one symptom two weeks before menstruation varied between 50% and 97% (Rasheed P. et al., 2003; Tschudin S. et al., 2010; Takeda T. et al., 2006; Matsumoto T. et al., 2013). Takada, for example, published evidence on higher prevalence – 91% of the examined Japanese women reported on at least one symptom (Takeda T. et al., 2006). The team of Joshi (2010) conducted a study based on 107 women, who evaluated 35 symptoms. Their report stated that 61,7% of the women fulfilled the criteria for PMS, 38,3% of them suffered 3 or more symptoms, 14,0% experienced 5 or more symptoms. This study includes markedly larger number of symptoms – 35, compared to ours, nevertheless the results do not differ. The authors reported that 95% of the women without OMS experienced at least one premenstrual symptom (93,7% in our sample). Studies from recent years also find sub-threshold premenstrual symptoms in 64,5% in Israeli women (ReuveniI, D. et al., 2016) up to 99% in Canadian women (Caroline A. et al., 2017) and this high prevalence was also registered in the Bulgarian sample. In summary, the results show that up to 90% of women in fertile age experience at least several premenstrual symptoms, which vary from mild to severe (Matsumoto T. et al., 2013), and that is also true for the Bulgarian population.

The available literature almost completely lacks information on the manifestation of sub-threshold PMS. Authors generally report symptoms like mood swings, anxiety, changes in sleep and appetite, mild abdominal pain, palpitations, headache, and breast tenderness (Woods N. et al.,1982; Takeda T. et al., 2006).

Our team decided to analyse the symptoms of premenstrual indisposition in women without PMS in more detail, as this could aid in clinical aspect the discrimination of the normal experiences that do not need therapeutic interventions in PMS. In our sample the most common symptoms were irritability, fatigue, increased appetite, and sweets craving. Most commonly as severe was reported the change in appetite. These psychological symptoms are accompanied by breast tension and tenderness, abdominal bloating, which are seen in two thirds of the women. Many of them suffer also headache and severe one, followed by weight gain. Somatic symptoms in fact prevail and are five times more common than psychological.

The comparison of the symptoms in women with and without PMS could in our opinion help to better understand how and when the premenstrual indisposition transforms into fully blown PMS. We did not find such kind of analysis in the literature despite the fact that the early diagnosis of the syndrome could prevent serious impairments in the functioning of the affected women. When comparing the symptoms of the women with and without PMS the overlapping of the psychological symptoms stands out. In both group we found irritability, fatigue and increased appetite, but the full manifestation of the syndrome was related to increasing the severity of the complaints and the expression of additional symptoms like anxiety, mood swings, sadness, fatigue, and changes in appetite. Women in both groups experienced breast tension and tenderness, abdominal bloating, and headache. Again, as it was the case with

psychological symptoms, the full blown PMS was related to more severe expression of the complaints. In PMS the percentages of both types of symptoms were nearly equal. In women without PMS somatic symptoms were more prevalent. There was statistically significant difference in the prevalence of of each symptom type. We believe, that there is a regularity showing deterioration and enrichment of the premenstrual complaints in manifest PMS.

6.4 Clinical picture in women with comorbid DD

One of the aims of this study was to examine the clinical picture of PMS in cases of concomitant depressive episode. For that purpose we evaluated 31 women with PMS and DD and the results were compared to those of the group of patients with PMS and no psychiatric comorbidity. A study by Lane and Francis already searched for similar relationship. According to them the percentage of women with a history of affective disorder which also experienced premenstrual complaints was roughly 60% (Landen M., Eriksson E., 2003). Halbreich and Endicott explored the concomitant psychiatric diagnoses and premenstrual dysphoria in 170 women and 84% of the women who fulfilled the criteria for MDD experienced depressive changes of mood during their menstrual period. Only 9% of the women who had no psychiatric diagnosis experienced such mood changes (Ito et al., 2006). A Swiss study evaluated 3518 women in reproductive age with the purpose to search for possible link between PMS and severe depression. This study examined the relationship between moderate to severe PMS and depression. MDE was diagnosed in 11,3% of the women with moderate PMS and in 24,6% of the women with severe PMS (Yonkers K. et al., 1997). Richards and co-authors (2006) also reported that premenstrual syndrome of moderate severity is common among women with depression during the perimenopausal period. The severity of PMS in women with DD in our study was distributed as follows: 25,8% mild PMS, 58,1% moderate PMS, and 16,1% severe PMS. Women with DD show high prevalence of PMDD. But this is not surprising as in previous international studies the results were similar. For example, a study on the prevalence of PMDD in women in Sub-Saharan Africa also reported on concomitant diseases and significantly higher prevalence of MDD, PD, and generalised anxiety disorder in women with PMDD, compared to women with normal premenstrual experience (Lane T. et al., 2003). This high comorbidity between PMS/PMDD and MDE was documented by many researchers (Cohen L. et al., 2004; Yonkers K., 1997; Kim D. et al., 2004; Breaux C. et al., 2000; Hsiao M. et al., 2004). Ito and Matsubara reported that 31% of the women with DD suffer PMDD (Hsiao M. et al., 2004). In a Japanese study Miyaoka and her team (2011) found significantly higher prevalence than that in the Bulgarian sample – 43,1%, while PMDD was registered in only 5,9% of the women without DD (Halbreich U. et al., 1985). In that respect our study gave additional information on the severity of PMS with comorbid DD by comparing it to the severity of PMS with no psychiatric comorbidity. This way again was confirmed its significant deterioration – 16,1% of the women suffer PMDD. The mild PMS was also more common in the comorbid cases. The moderate cases with comorbid DD were 4 times more common, and the severe ones - 5 times more common than in PMS with no comorbidity.

Systematised data in the literature on the specifics of PMS comorbid with DD are rather scarce. The Bulgarian sample provided detailed information on each symptom. The psychological symptoms in women with PMS and DD were highly prevalent. All women

suffered mood swings, anxiety and fatigue, followed by irritability and changes in appetite and sleep. Highly prevalent were also absent-mindedness, sadness, apathy, despair, sweets craving. The most severe symptoms were anxiety, changes in appetite, mood swings, and irritability. The team of Siegel also detected, that women with DD experienced mostly fatigue, changes in appetite, swelling of the extremities, weight gain, irritability, tension, mood swings, depression, impaired concentration, excessive worries (Siegel J. et al., 1986). We acquired additional information from the comparison of the ratio psychological to somatic symptoms in women with PMS and no comorbidity and those with comorbid DD. It was evident, that in the latter the psychological symptoms were greatly predominant (3 times more common). The most severe somatic symptom in the women with PMS and DD was breast tension and tenderness, followed by palpitations, shivering, abdominal bloating, and headache. As already stated, somatic symptoms were three times less common than psychological ones. These results are in accordance with a previous report that found greater prevalence of psychological and behavioural than somatic symptoms in women with DE (Clare A., 1983). A Turkish team published in 2016 data stemming from a study, aiming at clarifying the comorbidity of PMS with BAD and DD. The comparison was between women with BAD who were euthymic during the duration of the study (n = 23), women with MDD who were in remission (n = 23), and healthy controls (n = 23). It turned out that premenstrual syndrome was more common in the group with MDD than both the control group and the group with BAD. Moreover in the group with PMS and MDD depressed mood, lack of pleasure, hostility, anger, impulsivity, absent-mindedness were more common than in the control group (p < 0.05) (Adewuya A. et al., 2008). Our results completely confirm the findings of this study with regard to the comorbidity between PMS and MDD.

6. 5 Clinical picture in women with comorbid PD

One of the purposes of our study was to clarify the clinical picture of PMS comorbid with PS. We examined 30 women with an episode of PD and comorbid PMS. In fact many researchers have searched the biological relationship between PD and PMDD through administration of anxiety and panic attack provoking agent (Choudhari S. et al., 2017; McNally Ret al.2004; Le Melledo J. et al.,1995; Le Melledo J. et al., 2000). Gorman examined the effects of inhaling 5–7% carbon dioxide in patients with PD, PMDD, severe MDE, and healthy women. The results showed that the patients with severe depression are indistinguishable from asymptomatic controls regarding their reaction to inhalation of carbon dioxide. In contrast to them, the patients with PMDD and those with PD significantly more common had panic attacks when inhaling carbon dioxide (Gorman J.et al., 2001). In addition, women with PMS/PMDD were inclined to catastrophically wrong interpretations of physical sensations and increased disposition to concerns, characteristic of both disorders (Vickers K. et al., 2004). These observations were also confirmed in clinical environment. Several studies demonstrated high prevalence of PMS among patients with PD. most researchers used retrospective evaluation of PMS/PMDD and a structured interview for PD. They detected that between 1 and 9% of the women with PMS/PMDD fulfilled the criteria for PD (Pearlstein T. et al., 1990; Chandraiah S. et al., 1991; Stout A. et al., 1986). Prospective studies detected simultaneous existence of PD and PMS in even higher percentage of the affected women (16 – 25%) (20 Harrison W. et al., 1989; Fava M. et al., 1992). 56,7% of the Bulgarian sample with PMS suffered moderate PMS

and 43,3% - severe. We did not detect women with mild PMS and that was not the result of purposeful exclusion of such cases.

From our results it is apparent that in the clinical picture of PMS comorbid with PD somatic symptoms dominate significantly being twice more common than psychological. Nearly all women in the group PMS-PD experienced somatic symptoms like breast tension and tenderness, abdominal bloating, headache, palpitations, and weight gain. All patients suffered irritability and changes in appetite, followed by mood swings, anxiety and fatigue, changes in sleep. The most severe somatic symptoms were irritability and anxiety and apathy on the contrary - was not defined as severe by no patients.

6.6 Comparative analysis of PMS with no comorbidity and PMS with comorbid DD or PD

Examining three distinct groups gave us the opportunity to follow the specific differences in PMS in the cases of comorbidity. Base on our data for the Bulgarian population we were able to discern three subtypes of PMS depending on the presence or absence of comorbidity. The search for subgroups required analysis of the between group differences. This way we were able to find out that the most common psychological symptoms in PMS without comorbidity were irritability, changes in appetite, mood swings; almost the same results were also found for the group with comorbid PD. in contrast, the women with comorbid DD suffered most commonly mood swings, anxiety, apathy, absent-mindedness, and fatigue. The statistical analysis showed that the mood swings, anxiety, apathy, absent-mindedness, fatigue, and insomnia were most common in the group with DD, while in the group with PD most common were despair and changes in appetite. The prevalence of irritability and sadness did not differ among the groups. The severity of the psychological symptoms was greater in the groups with compared to the group without comorbidity, with the exclusion of the sadness and sweets craving. The severity of the psychological symptoms was equal between the two groups with comorbidity, with the exclusion of the symptom irritability (more severe in the group with comorbid PD).

In all three groups leading somatic symptoms were breast tension and tenderness and abdominal bloating. These symptoms were statistically significant most severe in the women with comorbid PD, followed by DD, and in the group with no comorbidity they were least severe.

The distribution of psychological and somatic symptoms was nearly equal in women with PMS without comorbidity; in women with comorbid PD the somatic symptoms were leading and 3 times more common than in women with comorbid DD and slightly dominated the psychological symptoms in PMS without comorbidity. On the other hand, the psychological symptoms were most prevalent in women with DD, followed by women with no comorbidity, and relatively least common in women with PD.

In other words, somatic symptoms were leading symptoms in PMS and PD, psychological symptoms - in PMS and DD, and in PMS and no comorbidity both symptom types followed near equal distribution.

Obviously in the presence of comorbidity PMS was more severe regardless the comorbid condition, but twice more - in comorbid PD and in that group namely PMS turned

out to be most severe. The severity of PMS was intermediary in comorbid DD, and it was the mildest in the group with no comorbidity.

Searching for subgroups within PMS was in accord with the contemporary research aims at clarifying the essence of PMS. The premenstrual disorders continue standing in the focus of the researchers. In 2015 the International Association for Premenstrual Disorders (IAPMD) reviewed and defined all premenstrual disorders and divides PMS into core (typical) and variant PMS (Walsh S. et al., 2015). Typical PMS is related to spontaneous ovulatory menstrual cycles, that can be divided into such with dominant somatic, psychological, or mixed symptoms. Women with predominantly psychological or mixed may fulfil the criteria for PMDD. Our findings confirm this idea and make obvious that in PMS comorbid with DD the psychological symptoms prevail and the prevalence of PMDD is high. And in comorbid PD dominated somatic symptoms. Our data in fact answer the question where should we search PMS with dominating somatic symptoms - in patients with comorbid PD; with dominating psychological symptoms - in patients with comorbid DD; and the mixed variant - in those with PMS with no psychiatric comorbidity. The question of the existence of various premenstrual syndromes, which include multitude divergent premenstrual phenotypes has for long engaged the attention of the leading experts (Young S. et al., 1998; Freeman E et al., 2004; Walsh S. et al., 2015), but even at present there is still no unanimous understanding. The theories lie on the idea of susceptibility and menstrually related symptom groups, necessary for manifesting PMS. The susceptibility change over time and can be increased or decreased parallel to hormonal changes, stress levels, exhaustion, etc. the susceptibility may also be related to psychiatric disorders, having similar pathobiochemistry. In our results this differing susceptibility according to the differing comorbid conditions was clearly visible. We discerned different subgroups of PMS depending on the comorbid DD or PD, which was exactly the purpose of our research.

6.7. Attitudes towards PMS as health related problem and help-seeking behaviour

The poor awareness and the extremely low visits to healthcare professionals on the background of existing treatment options, motivated us to examine the attitudes and willingness to get treatment of Bulgarians with PMS and to direct the attention towards the syndrome and the opportunities for its alleviation. The women in our sample demonstrated poor health knowledge in regard to PMS. Up until the moment of the study a very low percentage of women had sought medical assistance to alleviate it. Only ⅓ of them had taken medications which were moreover not prescribed by a physician but unwarranted chosen by themselves. They even had not visited their GP. A glimpse on the reasons why, we found in their answer of the question on help-seeking willingness in future. Half of the women considered PMS as normal part of their lives, that it has to be put up with and bared, or that there were no methods for alleviation of that problem. Half of the sample would not take medications in future. The age analysis showed, that women over 35 years of age are less inclined to seek help which we consider being related to the deteriorating in the clinical condition with age. But this constellation is not typical only for the Bulgarians. Here is what Robinson and Swindle registered in 2000 in regard to the reasons for help seeking (Robinson R. et al, 2000): they examined 1022 participants and found out that older age, greater

recurrence of the premenstrual symptoms, the symptoms severity, the level of functional impairment were related to a less negative attitudes towards help seeking and the use of healthcare services, which was also registered in our sample. They discovered that women have negative attitudes towards PMS as a health related problem, that they did not seek help because they considered it inappropriate and a sign of weakness, which is identical to the conclusions from the Bulgarian sample. In 2012 a multinational study was conducted, which aimed to evaluate the effect of PMS on the capacity for work and other daily activities. 4,032 women aged between 15 and 45 years from 19 countries in North America, Latin America, Europe, Asia, and Australia were screened for PMS/PMDD. The women with moderate to severe PMS usually reported more frequent work absenteeism - more than 8 hours per cycle, severe impairment in the work productivity, as well as in other everyday activities, in their social contacts and relationships (Robinson R. et al., 2012). These results were confirmed several times in the following years – Heshmatian и Akbari (2015), Naeimi (2015) (Naeimi N., 2015), Mohebbi и Akbari (2017) (Mohebbi M. et al., 2017). PMS also affects the relationships with the family members (Dennerstein L. et al., 2010), and the relationships with the spouse of women with PMDD are even more affected than those of women with recurrent episodes of MDD. Furthermore, the effects of PMDD on social activities was comparable to those of chronic depression (Ballagh S. et al., 2008).

Regardless the systematic efforts for proving the serious socio-economic consequences of PMS, the results in recent years still show that it is often unrecognised and not regarded as medial problem and that women do not seek help for its alleviation (Sinclair K., 2018; Janda C. et al., 2019). Our results as well as the evidence in the literature worldwide unambiguously show the need for popularisation of PMS and motivating women for treatment. Efforts to increase the knowledge of women for that condition would change these negative results.

VII. SUMMARY

The presented study aimed to evaluate the prevalence of PMS in the Bulgarian population and look for characteristic features of subgroups in cases of comorbid depressive or panic disorder, as well as to examine the attitudes of the Bulgarians towards to syndrome and the ways for its alleviation. We included three groups of women – **with** and **without** PMS, women with current DE and PMS, and women with current episode of PD and PMS.

Our results (like many others in literature) clearly showed that the Bulgarians do not differ from the other ethnic groups in regard to the prevalence of PMS. 32% of the sample fulfilled the criteria for PMS and in the majority of them the syndrome was mild, and the lowest share was for the severe PMS, corresponding to the criteria for PMDD. To preserve the objectivity of the research guidelines for investigating the prevalence of PMS when using retrospective evaluation the relative shares were corrected by 50%, regardless the fact that most authors did not consider this condition. This way we found that 16,1% of the examined women fulfilled the criteria for PMS and 1,7% - for PMDD.

The detailed evaluation of women without premenstrual symptoms showed that nearly all of them experience certain symptoms, which did not reach syndrome level. They preceded the menstruation and were considered as natural part of the menstrual cycle. In women without

PMS the most common symptoms in the premenstrual period were irritability, fatigue, increased appetite, breast tension and tenderness, abdominal bloating, headache, and shivering. Somatic symptoms prevailed. The correlation with age showed that ageing is related to more greater prevalence of psychological symptoms and greater severity of somatic symptoms. We found a relationship between the enrichment of the typical premenstrual complaints with psychological symptoms and increase in severity of both psychological and somatic symptoms the manifestation of PMS.

The analysis of the clinical picture of PMS in the Bulgarian sample showed that most common symptoms were irritability, changes in appetite, breast tension and tenderness, abdominal bloating. The psychological and somatic symptoms were equally represented. With increasing age the changes in sleep, headache, and palpitations became the most common and most severe symptoms and the syndrome became more severe.

Commonly discussed in literature are the questions weather a simultaneous existence of PMS and affective or anxiety disorder is possible, if their symptoms overlapped or the described premenstrual complaints were just deterioration of the existing psychiatric condition. Regardless the expectation of overlap of symptoms between PMS and the accompanying psychiatric disorder, the most common symptoms of PMS in the cases with comorbid PD in our sample were irritability and changes in appetite. In women with PMS and comorbid DD the most common symptoms were mood swings, fatigue, and anxiety. In this group psychological symptoms were clearly dominant. In all three examined groups the most common somatic symptoms were breast tension and tenderness and abdominal bloating. But somatic symptoms were definitely more both prevalent and severe in women with comorbid PD.

According to our results there were three distinct subgroups of PMS depending on the comorbidity with DD or PD, or the lack of comorbidity. There was obvious difference depending n the type of the comorbid condition. In comorbid PD somatic symptoms dominated and in comorbid DD the psychological ones were more prevalent, and when no comorbidity was present both symptom types were equally distributed. PMS was more severe in both types of comorbidity. The syndrome was most commonly severe in PMS and comorbid PD and it was most commonly mild in the group with no comorbid conditions.

The literature in recent years shows that PMS often remains unrecognised, is not regarded a medical problem, and no help is sought for its treatment. In the Bulgarian sample it is clearly seen that women are overall willing to bear the condition and not to search help for its treatment and alleviation. In that regard we found no difference with the world tendencies.

VIII. CONCLUSIONS

1. In most of the women complaining of symptoms of PMS, these symptoms do not reach syndrome level. Nonetheless, they precede the menstruation and are considered by women as normal part of their monthly cycle.

2. In women without PMS the most common symptoms in the premenstrual period are irritability, fatigue, increased appetite, breast tension and tenderness, abdominal bloating, headache, and shivering. Somatic symptoms prevail.

3. Increasing the prevalence and severity of psychological symptoms and the severity also of somatic symptoms leads to manifested PMS.

4. A third of all women fulfil the criteria for PMS. In most of them the syndrome is mild, and the smallest share of them suffer from severe PMS.

5. In manifested PMS the most common symptoms are irritability, changes in appetite, breast tension and tenderness, abdominal bloating. Psychological and somatic symptoms are equally distributed. With increasing age the changes in sleep, the headache, and the palpitations become most prevalent and most severe and the syndrome's severity also increases.

6. In women with PMS and comorbid DD most common symptoms are mood swings, fatigue, anxiety, breast tension and tenderness. In this group there is considerable preponderance of psychological symptoms.

7. In women with PMS and comorbid PD the most common symptoms are irritability and breast tension and tenderness. Somatic symptoms are markedly predominant.

8. PMS with comorbid DD as well as with comorbid PD is more severe. It is most severe in the case of comorbidity with PD and least severe in the group without comorbid disorder.

9. Three distinct subgroups of PMS can be discerned: PMS with no comorbidity of mixed type with equal portions of psychological and somatic symptoms; in the cases of comorbid DD psychological symptoms prevail; in the cases with comorbid PD somatic symptoms prevail.

10. A big portion of the Bulgarians take PMS as part of their lives and not as a medical problem. Only half of them are willing to seek help and take medications but with ageing their share grows.

IX. CONTRIBUTIONS, LIMITATIONS, AND POSSIBILITIES FOR FUTURE RESEARCH

Contributions

1. Theoretical

Original

1) The study provides detailed description of the clinical picture of PMS and its prevalence in the Bulgarian population. We made a profile of the syndrome in women below and over 35 and described the changes related to age.

2) We made an analysis of the premenstrual complaints of women in the Bulgarian population and a comparative analysis of the symptoms in women with and without PMS, which gives opportunity to evaluate the predictors of manifestation of PMS.

3) We made analysis of PMS with comorbid PD and DD. We found a clear difference in its clinical picture in both cases of comorbidity.

4) Three subgroups of PMS were delineated depending on the lack or the presence of comorbidity.

5) We made an evaluation of the attitudes of Bulgarian women towards PMS as a health problem and the level of help-seeking behaviours.

Confirmatory

1) We confirmed the already known from literature prevalence of PMS as well as its clinical characteristics.

1. Practical

1) A PMS questionnaire, which gives a detailed and fast evaluation of PMS and can be easily applied in everyday practise.

2) The analysis on the help-seeking behaviour may serve as a pilot study in a program for expanding the health education and knowledge of Bulgarian women and improving their quality of life.

Limitations and possibilities for future research

The randomly recruited sample of women for screening for PMS was too small, despite the consumer-friendly questionnaire. The questionnaire itself examines in detail a comprehensive number of psychological and somatic symptoms, but an expansion in its part evaluating the psychosocial functioning would give opportunity to calculate the direct and indirect losses.

It was clearly established that PMS is not recognised and accepted as medical problem. Obvious is also the unwillingness to seek help and the mistrust to possible medical treatment. Targeted efforts towards making PMS more familiar and its defining as health problem could lead to higher recognition of the syndrome and seeking treatment for it – drug, as well as non-drug, that would allow the avoidance of somatic and psychological distress, healthcare expenses, and lost gains for the suffering women.

The main flow of the current study is the lack of prospective confirmation of PMS. We made an analysis of the clinical picture by gathering data retrospectively. The prospective confirmation of symptoms for two consecutive months would give opportunity for more precise diagnosis and symptom evaluation. This is to some extent compensated by correcting the shares by 50%. This concerns also the patients with comorbid conditions, but on the other hand it would be unethical to delay the treatment of the main disease for 2 months, although theoretically it leads to inaccurate evaluation of PMS.

The better understanding of PMS and its role in women's life would probably give an opportunity for its diagnosing as early as possible, best at the very first presentation and diagnosing of a depressive or panic episode and would this way aid the choice of antidepressant, that would alleviate both PMS and the comorbid condition at the same time.

The recruited groups of patient with comorbid panic and depressive disorder are relatively small – around 30 women each. PD and DD were diagnosed according to the ICD 10 criteria but no scales for evaluation of the severity of PD and DD were used. It would be appropriate for future studies to search for a relationship between the severity of the depressive

or anxiety syndrome and the severity of PMS, which could further aid the analysis of the subgroups of PMS.

X. FINAL

Our results show that the prevalence and clinical characteristics of PMS in Bulgarian women do not differ from what was reported in other nationalities and ethnicities. Its simultaneous coexistence with panic and depressive disorder, as well as the specifics in its clinical picture are important for the clinicians and could aid the choice of medications, appropriate for the treatment of both disorders. The detected unrecognition of the syndrome and the low levels of help-seeking behaviours of women can be altered through active spreading of information on its essence and the ways to attenuate it and that could improve the quality of life of the Bulgarian women in the future.

PUBLICATIONS, RELATED TO THE DISSERTATION

I. Publications in referenced and indexed in Scopus and Web of science periodicals

1. **Rossitza Iakimova**, Maya Stoimenova-Popova, Petranka Chumpalova, Milena Pandova, Maria Stoyanova. Clinical characteristics of PMS co-morbid with MDD and effectiveness of SSRIs in its treatment. 2020. Acta medica bulgarica, 4/2020; XLVII: 24-31.

II. *Publications in Bulgarian periodicals, that are <u>not</u> referenced or indexed in Scopus or Web of science*

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2. **R. K. Iakimova**, D. C. Aptalidis, M. S. Pandova, M. B. Stoyanova, M. Y. Stoimenova-Popova 2019. Clinical characteristics of Premenstrual syndrome/Premenstrual Dysphoric Disorder co-morbid with Panic Disorder and the effectiveness of Selective Serotonin Reuptake Inhibitors in its treatment. J Biomed Clin Res Volume 12 Number 1,40-46 ISSN 1313-6917 ISSN 1313-6917 (Print), ISSN 1313-9053 (On-line). 2019.

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1. **Iakimova R**, Stoyanova M,, Stoimenova-Popova M, Chumpalova P, Veleva I, Tumbev L. Clinical and therapeutic aspects of premenstrual syndrome comorbid with panic disorder. 27-th EPA Congress, April 6-9, 2019, Warsaw, Poland. E-PP0266

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Abstract

Introduction: Premenstrual syndrome (PMS) can be defined as every collection of psychological and somatic symptoms that recur regularly during the luteal phase of the menstrual cycle, cause functional impairments, and disappear during menstruation.

Isolated premenstrual symptoms are registered in nearly 80% of women in the general population, 20% to 40% of them suffer from PMS, and 2% to 6% experience a severe form of PMS, that corresponds to the criteria of premenstrual dysphoric disorder (PMDD). The estimates on the prevalence of PMS demonstrate significant differences in distinct cultures and ethnic groups but data, regarding the Bulgarian population is missing. The syndrome often remains unrecognised by doctors and patients which is the reason why women do not seek help regardless its substantial influence on their quality of life and functioning.

A number of authors support the concept of the existence of a variety of premenstrual phenotypes based on the liability, which varies according to hormonal levels, levels of experienced stress, life events, exhaustion, etc. But the question remains, if this could also be related to concomitant mental disease with similar pathobiochemistry. The clarification of this problem would assist with the elucidation of the ethology and pathobiology of PMS and with discovering effective treatment.

Aim: Evaluation of the prevalence and the basic symptoms of PMS among Bulgarian women; looking for specific characteristics of subgroups of PMS in cases of comorbidity with depressive or panic disorder.

Materials and methods: A total of 366 women were examined in this cross-sectional non-interventional study. They were divided into three groups: 1 group - 305 women, screened for PMS, further subdivided into 2 groups - women with and without PMS; 2 group - 31 women with PMS and current depressive episode, part of major depressive disorder (MDD); 3 group - 30 women with PMS and current first or consecutive episode of panic disorder (PD). A modified version of the Premenstrual Symptoms Screening Tool (PSST) was used for evaluation of PMS. Episodes of depressive and panic disorders were diagnosed by means of the Mini international neuropsychiatric interview (M.I.N.I.), version 6.0. a questionnaire card on the attitudes of women towards PMS and the need for treatment was also used. The Statistical Package for Social Sciences (SPSS) версия 13.0 was used for the analyses of the data.

Results: We found PMS in 32.1% of the examined women. In 15,4% of them it was mildly expressed, in another 13.4% it was moderate, and in 3.3% it corresponded to the criteria for PMSS. In 67.9% of the participants there was no PMS, although 93.7% of them experienced sub-threshold symptoms.

In the manifested PMS the most common symptoms were irritability (87.8%), severe in 26.5%; changes in appetite (69.4%), severe in 27.6%; breast tension and tenderness (81.6%), severe in 25.5%; abdominal bloating (84.7%), severe in 24.5%. Psychological and somatic symptoms were equally distributed - 51.5%/48.5%. With the advance of age the prevalence and severity of the changes in sleep, the headache, the palpitations and the severity of the syndrome itself increased statistically significant.

In women with PMS and comorbid MDD the most common (100%) and severe (45,2%) psychological symptom was anxiety, followed by the changes in appetite. Most prevalent and severe of the somatic symptoms was breast tension and tenderness (64.5%). The ratio psychological to somatic symptoms was: 74.2% / 25.8%. Severity of the syndrome: mild in 25.8%, moderate in 58.1% and severe in 16.1%.

In women with PMS and comorbid PD the most common and severe psychological symptom was irritability (86.7%), followed by anxiety (73.3%), and sweets craving (40%). The most prevalent ad severe somatic symptom was breast tension and tenderness (70%), followed by palpitations (60%), abdominal bloating (50%), and shivering (43,3%). The somatic symptoms dominated: 70% / 30%. Cases of mild PMS were not registered, moderate ones were found in 56.7%, and severe - in 43.3%.

The comparative analysis between the three groups demonstrated clear differences. The leading symptoms in PMS comorbid with PD as well as in PMS without psychiatric comorbidity were irritability and changes in appetite, but in PMS with comorbid MDD they were mood swings and anxiety. In all three groups the most common and severe somatic symptoms were breast tension and tenderness and abdominal bloating. The ratio of psychological to somatic symptoms also differed among the groups: in the cases with comorbid PD somatic symptoms dominated, while in those with comorbid MDD psychological symptoms prevailed. In women with no comorbidity both symptom types were nearly equally distributed. The difference in the syndrome severity was also statistically significant: the syndrome was most severe when comorbid with PF and least severity when no comorbidity was present.

The conviction of 37% of Bulgarian women was that it was normal art of their lives. 25% of them believed they should endure the syndrome regardless it caused them problems, 34% considered it bearable, and 51% were inclined to seek help.

Conclusion: A third of the evaluated Bulgarian women fulfilled the criteria for PMS, moreover in the larger part of them the syndrome was mild, and the smallest proportion suffered from severe PMS (PMDD). In the majority of the women the manifestations did not reach syndromal level. The most common symptoms among Bulgarian women were irritability, changes in appetite, breast tension and tenderness, abdominal bloating. Both symptom types were equally distributed.

Our results corroborate the idea that the clinical picture of PMS vary depending on the comorbidity. Three distinct subgroups formed: PMS of mixed type with no comorbidity, PMS with comorbid MDD - dominance of psychological symptoms, PMS with comorbid PD - dominance of somatic symptoms. PMS is most severe when comorbid with PD, and least severe when no comorbidity is present.

Large part of Bulgarian women consider PMS part of their lives and not a medical problem.