Gender differences in the clinical course of depression in bipolar disorder

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Objective: *to investigate gender differences in patients with depression and bipolar disorder (BPAD) and their impact on the clinical course of the disease.*
Patients and methods. *50 women and 50 men with bipolar disorder (BPAD) (F31 according to the International Classification of Diseases, 10th revision – ICD-10) were examined using a specially developed survey. Patients' symptoms were assessed in accordance with the diagnostic criteria of affective disorders according to ICD-10 and DSM-V, MADRS (Montgomery-Asberg Depression Rating Scale) and Q-LES-Q-SF (Scoring the Quality of Life Enjoyment and Satisfaction Questionnaire).*
Results and discussion. *Gender differences in the clinical course of BPAD were revealed. In men the disease usually starts with a mania phase followed by a marked mood increase in BPAD-I, a shorter period before the first mania (hypomania) if the onset is with the depression phase, mood swings and substance use disorders in puberty, which makes the diagnosis easier. In women BPAD diagnosis may be harder due to higher frequency of BPAD-II, clinical presentation with depression, longer period before the first mania (hypomania). Therefore, the most important clinical markers of BPAD in women include the early onset of the disease, its association with neurohormonal factors, history of affective variability, substance use disorders, schizophrenia, hereditary or comorbid eating disorder in puberty or later in life. The most common clinical features during the depression phase in men include: seasonal fluctuation (worsening of symptoms in autumn and winter) and diurnal variations (improvement of symptoms in the evening), numbed emotions, depersonalization-derealization syndrome, decreased libido, difficulty in falling asleep and increased appetite and/or body mass, comorbid depression, panic attacks and alcohol and substance abuse. The depression in women with BPAD is characterized by a higher prevalence of apathy, tearfulness, self-harm, body dysmorphic disorder, decreased appetite. Both male and female patients with depression and BPAD have a high level of anxiety, presence of psychomotor retardation, self-accusation and irritancy, 10% had atypical features according to the DSM-V criteria. Women have a higher proportion of depressive episodes (including rapid cycling BPAD) and a higher risk of suicidal behavior, and men, due to a higher frequency of manic phases, change partners and have a history of divorce significantly more often.*
Conclusion. *The revealed features of psychopathological symptoms, comorbid disorders, the course of the disease and correlations between individual characteristics and factors due to gender differences, can be used as markers of bipolarity, which will allow to diagnose BPAD earlier and more accurately and prescribe adequate therapy.*

Keywords: *depression, bipolar affective disorder, BPAD, gender, bipolar depression in women, bipolar depression in men.*
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Bipolar affective disorder (BPAD) occurs in approximately 2.6% of the population [1]. The prevalence rate is even higher and reaches 6.4%, if we take into account the entire spectrum of bipolar disorders according to the criteria for the diagnosis of BPAD according to DSM-III-R and DSM-IV [1, 2, 3, 4]. In a 20-year prospective Zurich study by Jules Angst, which involved 406 patients with a major depressive episode, 1% per year had a change of diagnosis to BPAD I, 0.5% – to BPAD II. At the same time, a further change in the diagnosis of BPAD II to BPAD I was observed in 2% of patients per year [5]. This is consistent with Hirshfeld's data that 67% of patients with BPAD receive incorrect diagnoses at the first visit, and a third of patients wait for10 years or more for a correct diagnosis, which also affects the prevalence of the disease in the population [6, 7].

Despite the importance of identifying hypo-and manic phases for determining BPAD, it is depressive episodes that make a significant contribution to the disease burden and correlate with the quality of life indicators [8, 9]. This can be explained by worse tolerance of the depressive state; longer duration and frequency of relapses; more pronounced social maladaptation; high risk of comorbid somatic diseases and suicide [11, 12, 13].

In recent decades, there has been an increased interest in gender studies in psychiatry. The obtained data reflect the features of unipolar depression or BPAD as a disease in general, both in men and women, but do not give an idea of gender differences in depression within BPAD [9, 14].

Nevertheless, knowledge of the main markers of bipolarity, clinical features and the course of depression within BPAD in men and women will contribute to the correct diagnosis, prognostic assessment of the disease course and administration of an adequate therapy.

The purpose is to study gender characteristics of depression within BPAD and their influence on the course of the disease.

Patients and methods. The study was conducted from 2018 to 2020 in outpatient and inpatient settings of S. S. Korsakov Psychiatric Clinic of Sechenov University. One hundred patients with a diagnosis of F31.3 – F31.5 according to ICD 10, including 50 women and 50 men, were examined by clinical and clinical-catamnestic methods. At the time of inclusion in the study, the mean age of women was 33.0 [23.0; 50.2] years, the mean age of men – 37.5 [29.5; 47.2] years ($p>0.05$). The duration of the disease in the group of women was 9.5 [5.3;18.8] years, in men – 15.5 [4.3; 22.8] years ($p>0.05$). Thus, the groups did not significantly differ in the age and duration of the disease.

Inclusion criteria: current depressive episode within BPAD; written informed consent of the patient to participate in the study; absence of decompensated severe somatic pathology.

Exclusion criteria: depressive state within other nosologies (recurrent depressive disorder (RDD), depression in schizophrenia, organic and somatogenic depressions, reactive depressive states); unwillingness or inability of the patient to sign an informed consent to participate in the study; pregnancy, breastfeeding.

The patients' condition was assessed in accordance with the diagnostic criteria of affective disorders according to ICD-10 and DSM-V using a specially developed clinical examination card. The MADRS scale (Montgomery-Asberg Depression Rating Scale) was used to assess the severity of depression, and the Q-LES-Q-SF scale (Scoring the Quality of Life Enjoyment and Satisfaction Questionnaire) was used to assess the quality of life and social functioning.

Statistical processing of the obtained results was carried out using the program Statistica 10 and SAS JMP 11. The comparison of the two groups on quantitative scales was carried out on the basis of the nonparametric Mann–Whitney test. The statistical significance of different values for binary and nominal indicators was determined using Pearson's Chi-square with Yates correction and Fisher criterion, the determination of the odds ratio (OR) with a 95% confidence interval (95% CI). The conclusion about the correlation between quantitative indicators was determined on the basis of Spearman's correlation coefficient (r-coefficient), and qualitative indicators – Pearson's contingency coefficient (χ-coefficient). Qualitative indicators are presented in the form of absolute and relative (%) indicators. Since most quantitative features did not meet the laws of normal distribution, they were described using the median (Me) and quartiles (Me [25%; 75%]). The level of statistical significance was fixed at the level of error probability 0.05.

Table 1. *Socio-demographic characteristics of study participants*

Criteria	Men (n=50)	Women (n=50)
Age at the time of inclusion in the study, years, (Me [25%; 75%])	37.5 [29.5; 47.2]	33.0 [23.0; 50.2]
Family status, n (%):		
not married	19 (38.0%)	20 (40.0%)
married	20 (40.0%)	18 (36.0%)
divorced	11 (22.0%)	12 (24.0%)
Education, n (%):		
secondary	0 (0.0%)	1 (2.0%)
vocational education	6 (12.0%)	2 (4.0%)
incomplete higher education	8 (16.0%)	14 (28.0%)
higher education	36 (72.0%)	33 (66.0%)
Employment status, n (%):		
working/studying	29 (58.0%)	24 (48.0%)
not working/not studying	18 (36.0%)	19 (38.0%)
retired	3 (6.0%)	7 (14.0%)

Results.

A comparative clinical and catamnestic examination of patients with depression within the framework of BPAD did not reveal statistically significant differences in socio-demographic characteristics (Table 1), however, there were more working men than women. There were more pensioners among women due to earlier retirement age.

There were differences in the course of the disease (Table 2). Women had a later onset of the disease, (mean age 22.5 [17,0; 28,0] years) compared with men (mean age 21 [19,0; 29,0] years), but the differences were not significant ($p>0.05$).

The probability of a BPAD I was higher in men, while BPAD II – in women, but the differences did not reach the statistical significance ($p>0.05$).

The majority of men and women had an alternating course of the disease. Women were significantly more likely to have a rapid-cycle course (OR: 3.9; 95% CI (1.1–15.2), $p<0.05$).

The number of manic episodes at the time of the survey was 1.3 times higher in men, while the number of depressive episodes were 1.2 times higher in women. This is confirmed by the distribution into groups: men significantly more often fell into the group of «1 to 5 depressive episodes», while women – in the group of «11 to 20 depressive episodes» ($p<0.05$).

The first phase was depressive more often in women than in men (OR: 3,0; 95% CI (1.2–7.6), $p<0.05$). At the same time, the period before the first mania (or hypomania) was 2 times longer in women, and women had twice as many depressive episodes as men.

The onset of the disease had a certain trigger in 46% of men and 48% of women ($p>0.05$). Both men and women associated the first phase of depression with the presence of a traumatic event (26% and 22%, respectively, $p>0.05$). In men, the most common trigger was the use of psychoactive substances (14% compared to 4%, $p>0.05$). In 18% of women, the first episode of depression was associated with the influence of neurohormonal factors: menarche, childbirth, abortion, perimenopause, hormone therapy ($p<0.05$).

The first visit to a psychiatrist in the vast majority of patients with BPAD was about depression (98% and 92%, respectively, $p<0.001$), although in 40% of men the disease began with a manic phase (compared with 8% of women). In addition, in men manic phases occurred much earlier, their number was greater than in women, while the number of depressive phases both before the onset of mania, and in for the entire period of the disease, was less than in women.

The mean age of men at the first treatment was 29.5 [23.0; 36.6] years, women – 25.0 [20.3; 33.0] years, that is, the average time from the onset of the disease was 7.26±8.38 years and 4.74±5.45 years, respectively. Thus, we can assume a later referral of men to a psychiatrist, although the differences did not reach the level of statistical significance.

Hereditary burden was detected in 50% of men and 42% of women (p>0.05) and was mainly represented by disorders of the addictive and affective spectra (including established diagnoses of BPAD, RDD, subclinical affective disorders, postpartum, reactive or late-age depression), less often – by schizophrenia, anxiety or obsessive-compulsive disorders (OCD). Men with a family history were equally likely (22%) to have affective disorders, alcohol and substance abuse. Women had the same ratio of affective/ addictive disorders and schizophrenia (12%). No statistically significant differences were found in the hereditary burden of anxiety and OCD.

The structure of premorbid features in the examined patients included hyperthymic, cyclothymic, anxious and demonstrative traits. At the same time, men were more likely to have psychasthenic premorbidity (52% compared to 28% of women, OR: 2.8; 95% CI (1.2–6.4), p<0.05), while women – demonstrative premobidity (22% compared to 4% of men, OR: 6.8; 95% CI (1.4–32.4), p<0.05).

Previous mental disorders in puberty were more common in men (72% of men and 44% of women, OR: 3.6; 95% CI (1.6–8.4), p<0.01). There were no significant differences in the presence of adolescent affective fluctuations (30% of men, 16% of women, p>0.05) and OCD (12% of men and women, p>0.05). In men, alcohol and substance abuse were observed (20% in men and 0% in women, p<0.05), while eating disorders were noted only in women (12% and 0%, respectively, p<0.05).

Assessment of the severity of a current depressive episode on the MADRS scale (Table 3) showed that, on average, depression in women was milder (28.0 points [24.0; 28.0]) than in men (30.0 points [24.5; 34.0]) (p>0.05).

Women had moderate depressive phases (p<0.05), while men were more likely to be diagnosed with a «severe depressive episode» (OR: 3.4; 95% CI (1.4–8.0), p<0.05). A correlation was established between the severity of depression (MADRS scores) in men with ideas of self-blame (r=0.31), decreased libido (r=0.42), decreased appetite (r=0.49), and shortened sleep duration (r=0.31).

In the clinical picture of depression in both groups, anxiety, ideatory inhibition, and irritability were almost equally likely to occur. A third of men and women were characterized by motor inhibition and ideas of self-blame.

With the general predominance of anxiety affect (more than 50%), apathy was significantly more common in women (OR: 2.4; 95% CI (1.1–5.9), p<0.05). Decreased appetite was typical of the majority of patients, but significantly more often occurred in women (OR: 3.7; 95% CI (1.4–10.6), p<0.05). Self-harm and dysmorphophobic syndrome were found only in women. At the same time, a statistical relationship was determined between self-harm in women and BPAD II (φ=0.35), mental disorders in puberty (φ=0.49), substance abuse in the depressive phase (φ=0.31), longitudinal course (φ=0.41) and suicidal attempts in the anamnesis (φ=0.54).

Men were significantly more likely to have sensory anesthesia (OR: 3.5; 95% CI (1.2–10.6), p<0.05), depersonalization-derealization syndrome (OR: 4.9; 95% CI (1.3–18.8), p<0.05), decreased libido (OR: 3.0; 95% CI (1.3–6.8), p<0.05). They were more frequently characterized by diurnal and seasonal mood swings. Thus, in men, depression occurred more often in the autumn-winter period (OR: 2.8; 95% CI (1.1–7.0), p<0.05) and was accompanied by a deterioration in the morning (OR: 3.3; 95% CI (1.3–8.2), p<0.05).

In both groups of patients, sleep disorders were characterized by difficulty falling asleep, shortening of sleep duration with frequent and early awakenings, lack of sense of sleep, and hypersomnia. Men were significantly more likely to have difficulty falling asleep (OR: 3.5; 95% CI (1.6–10.6), p<0.05).

In men and women depression was atypical (according to the DSM-V criteria, which require the mandatory presence of mood reactivity and at least two of the following symptoms:

Table 2. *Main characteristics of the disease course*

Criteria	Men (n=50)	Women (n=50)
Duration of the disease at the time of inclusion in the study (Me [25%; 75%]), years	15.5 [4.3; 22.8]	9.5 [5.3;18.8]
Age of onset, (Me [25%; 75%]), years	21 [19; 29]	22.5 [17; 28]
Type BPAD:		
BPAD I, n (%)	20 (40.0%)	13 (26.0%)
BPAD II, n (%)	30 (60.0%)	37 (74.0%)
Course:		
alternating, n (%)	38 (76.0%)	36 (72.0%)
longitudinal, n (%)	7 (14.0%)	4 (8.0%)
rapid-cyclic, n (%) *	3 (6.0%)	10 (20.0%)
ultra-rapid-cyclic, n (%)	2 (4.0%)	0 (0.0%)
Number of manic episodes for the entire period of the disease, n, (Me [25%; 75%])	4.0 [2.0; 6.0]	3.0 [2.0; 3.0]
Number of depressive episodes for all time of disease, n, (Me [25%; 75%])	5.50 [3.0; 14.25]	7.0 [4.0; 35.0]
Including		
from 1 to 5, n (%) **	25 (50.0%)	15 (30.0%)
from 6 to 10, n (%) **	6 (12.0%)	16 (32.0%)
from 11 to 20, n (%) **	8 (16.0%)	1 (2.0%)
more 21, n (%) **	11 (22.0%)	18 (36.0%)
First phase *		
depression, n (%)	30 (60.0%)	41 (82.0%)
mania, n (%)	20 (40.0%)	9 (18.0%)
Period from the beginning of the disease to the first mania passed (M±m), years	0.06±7.90	3.50±7.52
Number of depressive phases before the first mania (M±m), episodes	1.08±0.99	2.06±3.15

Note. * – p<0,05; ** – p<0,01

increased appetite and/or weight gain, hypersomnia, lead paralysis, sensitivity) with an equal frequency (10%). The following correlations of the atypical course were established: in women – with a longer duration of the depressive episode (r=0.3) and frequent job changes (φ=0.32), in men – with a rapid-cyclic variant of BPAD (φ=0.33) and a lower degree of severity according to MADRS (r=-0.3).

There were significant differences in suicidal activity in men and women with BPAD. Suicidal attempts in the anamnesis were more common in women (OR: 3.5; 95% CI (1.6–10.6), p<0.05).

With regard to mental disorders concurrent with depression (Table 4), men were more likely to have panic attacks (OR: 4.0; 95% CI (1.2–13.4), p<0.05), while eating disorders were noted only in women (p<0.05).

High burden of metabolic-endocrine and cardiovascular diseases was noted in both sexes. In men, gastrointestinal diseases were significantly more common (OR: 4.4; 95% CI (1.1–17.0), p<0.05).

To assess the quality of life, the life satisfaction assessment scale was used (Table 5). There were no significant differences between the groups of men and women (p>0.05): the score for men was 42.0 [36.0; 46.75]; for women – 41.0 [37.25; 43.75] [13], which conditionally corresponds to the average level of social functioning. A higher level of social adaptation in men (scores on the Q-LES-Q-SF scale) correlated with hyperthymic character traits (r=0.31), family status («married») (r=0.36), later age at the onset of the disease (r=0.29).

Men were more likely to divorce and change partners (OR: 2.3; 95% CI (1.1–5.4), p<0.05). This correlated with hyperthymic premorbidity (φ=0.299) and a history of substance abuse (φ=0.32). In women, the relationship between the frequency of divorce/separation with BPAD I (φ=0.41) and the atypical course of depression (φ=0.32) was revealed.

Men were more likely to quit their jobs due to illness than women, but the differences were not statistically significant (p>0.05). We also determined the correlation between dismissal due to the condition in men and cyclothymic premorbidity (φ=0.31), frequent job changes and the presence of disorders in puberty (φ=0.4).

Discussion. Thus, the data obtained in the study indicate that the clinical features of depression and the course of BPAD have both common characteristics and certain gender differences. Both men and women are characterized by: early

Table 3. *Main characteristics of the depression episode*

Criteria	Men (n=50)	Women (n=50)
Duration of the depressive phase, days, (Me [25%; 75%])	90.0 [60.0; 180.0]	90.0 [60.0; 165.0]
The severity of depression on the MADRS scale, points, (Me [25%; 75%])	30.0 [24.5; 34.0]	28.0 [24.0; 28.0]
Including		
severe, n (%) *	26 (52.0%)	12 (24.0%)
moderate, n (%) *	11 (26.0%)	23 (46.0%)
mild, n (%)	11 (22.0%)	15 (30.0%)
subdepression, n (%)	2 (4.0%)	0 (0.0%)
Predominant affect, n (%):		
anxiety, n (%)	28 (56.0%)	26 (52.0%)
apathy, n (%) *	12 (24.0%)	22 (44.0%)
longing, n (%)	8 (16.0%)	3 (6.0%)
Ideatory inhibition, n (%)	20 (40.0%)	26 (52.0%)
Motor inhibition, n (%)	14 (28.0%)	18 (36.0%)
Ideas of self-accusation, n (%)	14 (28.0%)	16 (32.0%)
Anesthesia of senses, n (%) *	11 (22.0%)	5 (10.0%)
Irritability, n (%)	22 (44.0%)	22 (44.0%)
Tearfulness, n (%) **	10 (20.00%)	24 (48.00%)
Self-harm, n (%) *	0 (0.0%)	13 (26.0%)
Depersonalization-derealization syndrome, n (%) *	8 (16.0%)	3 (6.0%)
Dysmorphophobic syndrome, n (%) *	0 (0.0%)	5 (10.0%)
Hypochondriac inclusions, n (%)	5 (10.0%)	4 (8.0%)
Somatic complaints, yes, n (%) including pain syndrome, n (%)	15 (30.0%) 11 (22.0%)	13 (26.0%) 7 (14.0%)
Sleep disturbance, n (%):		
difficulty falling asleep, n (%) *	12 (24.0%)	5 (10.0%)
early awakenings, n (%)	6 (12.0%)	6 (12.0%)
frequent awakenings, n (%)	10 (20.0%)	20 (40.0%)
lack of sleep feeling, n (%)	6 (12.0%)	4 (8.0%)
hypersomnia, n (%)	11 (22.0%)	12 (24.0%)
undisturbed, n (%)	5 (10.0%)	3 (6.0%)
Impaired appetite, n (%):		
reduced, n (%) **	38 (76.0%)	44 (88.0%)
increased, n (%)	6 (12.0%)	3 (6.0%)
normal, n (%)	6 (12.0%)	3 (6.0%)
Change in body weight, n (%):		
decrease, n (%)	9 (18.0%)	7 (14.0%)
increase, n (%)	5 (10.0%)	2 (4.0%)
Decreased libido, n (%) **	28 (56.0%)	15 (30.0%)
Suicidal thoughts, n (%)	20 (40.0%)	18 (36.0%)
Suicide attempts, n (%) *	6 (12.0%)	12 (24.0%)
Seasonality of depressive phases, n (%)		
none, n (%)	27 (54.0%)	34 (68.0%)
autumn–winter, n (%) *	19 (38/0%)	9 (18/0%)
spring–summer, n (%)	4 (8.0%)	7 (14.0%)
Daily fluctuations, n (%)		
none, n (%) ***	21 (42.0%)	38 (76.0%)
worse in the morning, n (%) *	21 (42.0%)	9 (18.0%)
worse in the evening, n (%)	8 (16.0%)	3 (6.0%)
Atypical course, n (%)	5 (10.00%)	5 (10.00%)

Continuing of Table 3

Note. * – p<0.05; ** – p<0.01; *** – p<0.001

age of onset of the disease; hereditary burden of mainly affective disorders, schizophrenia and alcoholism; development of the disease in persons with predominantly hyperthymic and cycloid premorbidity; high frequency of atypical sleep disorders, changes in appetite and body weight; prevailing anxiety affect; seasonal exacerbations of the condition (more often in autumn and winter); high comorbidity with metabolic diseases, substance abuse, panic attacks; high level of suicidal activity; a more pronounced decrease in social and family adaptation, which mainly confirms the results of previous studies [9, 14].

Due to the numerous data on the complexity of making a correct diagnosis of BPAD, especially in the early stages of the disease, it is important to identify gender-specific markers that would help clinicians suspect a bipolar course and prescribe adequate therapy.

Despite the absence of pronounced differences in the age of the onset of BPAD and earlier treatment of women by a psychiatrist, it was found that it is women who later receive the correct diagnosis and, accordingly, treatment: up to 11 years, compared with a 7-year delay in men [3, 15].

According to our research, this may be due to a number of reasons. In women, BPAD II was significantly more common, and hypomanic conditions were not considered painful by patients for a long time and, therefore, were not noted by a doctor. In addition, in women the disease debuted with the depressive phase, and the period before the first mania was on average 3.5 years, which is consistent with the literature data [16, 17, 18].

According to some authors, in the presence of early onset of the disease and hereditary burden of affective disorders (especially BPAD), any depressive episode, even in the absence of a hypo-and manic phase in the anamnesis, should be considered as bipolar [19]. A number of large-scale studies, including those involving twin pairs, have shown that in the case of a burdened family history, genetic predisposition to mania and depression are inherited with different probabilities (the mania gene predominates), while psychosocial factors play a key role in the development of depression [20, 21]. In our study, men were twice more likely than women to have a family history of affective spectrum disorders, including BPAD. In addition, in men, the disease more often began with a manic phase and/or proceeded according to the type of BPAD I: this combination increases the likelihood of an earlier correct diagnosis [22, 23]. Besides, according to our data, in men and women, the first depressive episode was almost equally likely to have an endoreactive beginning.

In a significant proportion of women, the first and subsequent depressions were triggered by periods of hormonal changes (menarche, childbirth, abortion, hormone therapy), which is consistent with the data of other studies [10, 14].

Such indicators of bipolarity as seasonality (deterioration in autumn-winter time) and daily fluctuations in the state with an improvement in the evening were more pronounced in men [24, 25].

A predictor of bipolarity can also be pre-existing disorders in puberty. Men were characterized by alcohol and / or substance abuse in adolescence, while women had eating disorders that accompanied depression in later life. Eating disorder is the rarest comorbid mental disorder in patients with BPAD (0.1% of men and 0.6% of women), but women have an 11-fold higher risk of developing it [26].

As for the clinical picture of depression, both groups were characterized by a fairly high level of associative and motor inhibition, the presence of ideas of self-blame and irritability. Many authors consider anxiety as the predominant affect in depression within BPAD [27]. This is consistent with our findings: anxiety depressions occurred in more than a half of the patients in both groups. Apathy with a decrease in the volitional component, tearfulness, self-harm, dysmorphophobic inclusions and eating disor-

Table 4. *Comorbid disorders, n (%)*

Criteria	Men (n=50)	Women (n=50)
Mental disorders		
Panic attacks, n (%) *	12 (24.0%)	4 (8.0%)
Alcohol abuse, n (%)	14 (28.0%)	9 (18.0%)
Substance abuse, n (%)	5 (10.0%)	3 (6.0%)
OCD, n (%)	5 (10.0%)	6 (12.0%)
Eating disorder, n (%) *	0 (0.0%)	6 (12.0%)
Somatic diseases		
Metabolic and endocrine, n (%)	4 (8.0%)	7 (14.0%)
Cardiovascular, n (%)	6 (12.0%)	5 (10.0%)
Gastrointestinal, n (%) *	11 (22.0%)	3 (6.0%)
Urogenital, n (%)	2 (4.0%)	1 (2.0%)
Skin, n (%)	2 (4.0%)	1 (2.0%)
Autoimmune, n (%)	0 (0.0%)	2 (4.0%)
Respiratory, n (%)	2 (4.0%)	0 (0.0%)

Note. * – p<0.05

Table 5. *Quality of life assessment*

Criteria	Men (n=50)	Women (n=50)
Quality of life assessment on the Q-LES-Q-SF scale, points, (Me [25%; 75%])	42.0 [36.0; 46.75]	41.0 [37.25; 43.75]
Frequent changes of partners/ divorce, n (%) *	21 (42.00%)	12 (24.00%)
Number of days of disability per year, days, (Me [25%; 75%])	30.0 [14.0; 60.0]	30.0 [21.0; 60.0]
Frequent job changes, n (%)	17 (34.00%)	17 (34.00%)
Dismissed for health reasons, n (%)	12 (24.00%)	9 (18.00%)
Disability, n (%)	2 (4.00%)	1 (2.00%)

Note. * – p<0,05

ders are characteristic features of bipolar depression in women. The structure of depression in men more often included melancholy, anesthesia of the senses, depersonalization-derealization, decreased libido, difficulty falling asleep, increased appetite and body weight.

According to a number of authors, depression in BPAD is quite often characterized by hypersomnia, hyperphagia with changes in body weight, and mood reactivity, which allows us to attribute it to an atypical variant, which, according to some data, is more typical of women [9, 28]. In our study, a combination of the corresponding symptoms was equally likely to occur in patients of both sexes. However, in women, the atypical course correlated with a longer duration of the depressive episode and social maladaptation (frequent job changes, a large number of marriages and divorces), while in men it prevailed within the framework of the rapid-cyclical BPAD variant and was characterized by a lower degree of severity according to MADRS.

According to the literature, the number of anxiety disorders is 1.42 times higher in women, and men are more prone to addiction diseases [29, 30]. In our study, men were significantly more likely to have panic attacks in the structure of the depressive phase, substance abuse, and diseases of the gastrointestinal tract. The absence of any sex differences in the comorbidity of OCD in the depressive phase, according to our results, is consistent with the literature data [12].

Gender is one of the risk factors that increases the likelihood of suicidal thoughts and attempts. In a study of 247 patients with bipolar disorder, it was shown that women had suicidal thoughts 2 times more often than men, and they were 3 times more likely to try to commit suicide [31]. According to our data, depression is highly likely to be accompanied by suicidal thoughts in patients of both sexes, but women were twice more likely to make suicidal attempts, some of which included a demonstrative component. Only women inflicted self-harm.

In addition to the fact that BPAD is associated with comorbid diseases, high risk of suicide and mortality, it has significant socio-economic consequences [26].

In women, depressive phases constitute a greater part of the disease [32, 33, 34]. This affects the total number of days of disability per year, social functioning and quality of life [26, 35]. In addition, apathy in the structure of the depressive state in women is a factor that weakens volitional self-regulation, which leads to a decrease in social functioning [36]. In the study, no significant differences were found between men and women in the Q-LES-Q-SF quality of life and social functioning scale scores, in relative indicators of dismissal due to health conditions and frequent job changes; however, men changed partners much more often and had a history of divorce. In women, predictors of lower quality of life (frequent changes of jobs and partners) included an atypical course and abuse during the depression phase; in men – mental disorders in puberty and substance abuse.

Conclusion

Thus, the study of the clinical features of depression within BPAD, gender differences in the structure of the depressive syndrome and the course of the disease as a whole is an urgent problem that requires further research. Nevertheless, the identified markers of BPAD, features of psychopathological symptoms, comorbid mental and somatic disorders, the course of the disease and correlations between individual characteristics and factors, taking into account gender differences, will allow for an earlier and more accurate diagnosis of BPAD and administration of an adequate therapy.

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