Clinical features of atypical depression in bipolar and recurrent affective disorders, psychogenic depression

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Objective: *to perform a comparative study of the clinical features of atypical depression (AtD) in affective disorders of various origins: in bipolar affective disorder (BAD), recurrent depressive disorder (RDR) and psychogenic depression (PD).*
Patients and methods. *A sample of 250 depressed patients aged 18 to 65 years were examined, of which 77 participants (50 women and 27 men) with symptoms of AtD were included to the study. Group 1 included 35 patients with BAD, group 2 – 18 patients with RDR, and group 3 – 24 patients with diagnoses including PD. The patients' condition was assessed using the diagnostic criteria for affective disorders according to ICD-10 and DSM-5 with a Montgomery-Asberg Depression Rating Scale (MADRS).*
Results and discussion. *AtD detection rate was 30.8%, including 45.4% in BAD, 23.4% – in RDR, and 31.2% – in PD. AtD manifested at the age of about 20 years, and was more common in women. AtD in BAD occurred more often in individuals with cycloid, hyperthymic, and hysterical features. Affective fluctuations before the disease onset, a significantly greater number of depressive episodes in history were characteristic. The most frequent typical depressive symptoms included: daily and seasonal mood fluctuations, morning deterioration of well-being, decreased appetite. High comorbidity with metabolic endocrine diseases was observed. AtD in RDR often began spontaneously in individuals with emotionally labile, psychasthenic, and hysterical features. The most common typical depressive symptoms included melancholy, derealization, weakness, ideas of self-accusation, suicidal thoughts and attempts. A high comorbidity with cardiovascular diseases was found. AtD in PD occurred more often in psychasthenic individuals. The most characteristic symptoms included: increased appetite, anxiety, asthenia, superficial night sleep, hypochondriacal inclusions. Comorbidity with skin and gastrointestinal diseases was observed.*
Conclusion. *The identified features of the clinical picture and course of AtD in BAD, RDR, and PD can be used for earlier and more accurate evaluation of affective disorders and the adequate treatment administration.*

Keywords: *atypical depression; recurrent depressive disorder; bipolar affective disorder; psychogenic depression.*
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In the middle of the 20th century, a special type of depression was identified, called atypical, due to its resistance to therapy, more pronounced anxiety and agitation compared with classical depression, and possible presence of psychotic episodes in its structure [1]. Klein D.F. and Davis J.M. [2] described symptoms of low mood, hypersomnia, hyperphagia, weight gain, increased libido, as well as "anxious-phobic tendencies", with "hysteroid dysphoria", occurring more often in females, with a "fragile, superficial" mood, which lacked "the essential characteristics of a pathological depressive state, as well as a tendency to sleep and overeating." These criteria were provisional and needed to be clarified. Therefore, in 1982 Davidson J.R. and colleagues [3] proposed one of the first classifications of AD, including: 1) patients with agitation and psychotic symptoms responding to electroconvulsive therapy (ECT); 2) outpatients with mild non-psychotic symptoms, "phobic anxiety", tension and pain who responded to monoamine oxidase inhibitors MAOIs; 3) patients with autonomic symptoms such as increased appetite, mood lability and irritability responding to MAOIs; 4) patients with residual depressive states, including secondary depression in schizophrenia; and 5) patients with bipolar depression and autonomic symptoms responding to MAOIs. Many experts [4–9] emphasized the key role of anxiety in the clinical picture of AD.

Currently, the relevance of the topic is growing along with a significant increase in the detection of AD cases among young people, in whom it is often associated with traumatic life events [10–13].

Symptoms of AD, according to the DCM-5, include an obligatory feature of mood reactivity (increased response to external factors while maintaining the ability to receive pleasure and satisfaction in response to positive events) and at least two of the following symptoms: hyperphagia and / or body weight gain (at least 3–5 kg in the last 3 months), hypersomnia (sleep more than 10 hours a day at least 3 days a week for at least 3 months), lead paralysis (heaviness in the arms and legs for at least 1 hour a day, not less than 3 days a week for 3 months) and sensitivity (increased sensitivity to ongoing events and interpersonal communication) [14].

Despite the general criteria for diagnosing AD, certain features of it are noted within individual disorders. Most often, AD occurs in the structure of bipolar disorder (up to 50%) and is characterized by a high level of psychomotor retardation and lead paralysis [15], emotional lability, hyperphagia accompanied by weight gain, and hypersomnia [15–17], a higher frequency of psychotic symptoms and suicidal behavior [18]. AD in the structure of RDD is detected in approximately 20% of patients [19]

Table 1. Socio-demographic characteristics of patients

Indicator	Group			Total (n=77)
	BD (n=35)	RDD (n=18)	PD(n=24)	
Average age of inclusion in the study, years, Me [25th; 75th percentile]	32.4 [19.0; 53.0]	27.6 [18.0; 45.0]	24.5 [18.0; 35.0]	28.8 [18.0; 53.0]
Gender, n (%):				
men	17 (48.6)	4 (22.2)	6 (25.0)	27 (31.9)
women	18 (51.4)	14 (77.8)	18(75.0)	50 (68.1)
Level of education, n (%):				
higher incomplete	21 (60.0)*	8 (44.4)*	7 (29.2)	36 (46.8)
higher education	7 (20.0)	7 (38.9)	13 (54.2)*	
secondary vocational	4 (11.4)	1 (5.6)	3(12.5)	27 (35.1)
incomplete secondary vocational				8 (10.4)
	3 (8.6)	2 (11.1)	1 (4.2)	6 (7.8)
Employment status, n (%): employed	16 (45.7)	7 (38.9)	9 (37.5)	32 (41.6)
unemployed	19 (54.3)	11 (61.1)	15 (62.5)	45 (58.4)
Marital status, n (%):				
married	15 (42.9)*	5 (27.8)	3 (12.5)	23 (29.9)
single	16 (45.7)	13 (72.2)	20 (83.3)*	49 (63.6)
divorced	4 (11.4)	–	1 (4.1)	5 (6.5)

Note. * – $p<0.05$.

Table 2. Hereditary burden of mental disorders, n (%)

Heredity	BD (n=35)	RDD (n=18)	PD (n=24)
• affective disorders;	17 (48.6)*	8 (44.4)*	3 (12.5)
• schizophrenia spectrum disorders;	4 (11.4)	2 (11.1)	–
• alcoholism/alcohol abuse;	3 (8.6)	1 (5.6)	2 (8.3)
• substance abuse;	1 (2.9)	1 (5.6)	1 (4.2)
• no burden	10 (28.6)	6 (33.3)	18 (75)
Suicidal attempts in the family	5 (14.3)	3 (16.7)	3 (12.5)

Note. *– $p<0,01$.

and is often considered as a kind of "bridge" from unipolar depression to bipolar II [20]. It is characterized by algia and senestopathies, atypical panic disorder with inclusion of conversion symptoms [19]. However, comparative studies of AD in various affective disorders, including PD, have not been conducted, which is important for timely diagnosis and selection of adequate therapy.

The purpose of this work is a comparative study of the clinical features of atypical depressive syndrome in affective disorders of various origins: bipolar disorder, RDD, and PD.

Patients and research methods. The study was conducted in the period from 2019 to 2021 on an outpatient and inpatient basis at S.S. Korsakov Psychiatric Clinic of Sechenov University. 250 patients with depression were randomly examined by clinical and clinical follow-up methods, of whom 77 patients with symptoms corresponding to AD (50 women and 27 men) were selected. Among them, there were 35 patients with bipolar disorder (F31.3–F31.5), 18 patients with RDD (F33.0–F33.3, F33.8–F33.9), 24 patients with a diagnosis including PD (F32, F34.1, F41.2, F43.1–F43.2). (ICD-10).

Inclusion criteria: written informed consent of a patient to participate in the study; the presence of symptoms of an atypical depressive episode within the framework of bipolar disorder, RDD, PD at the time of the examination; age 18–65 years at the time of entry into the study; absence of severe somatic pathology.

Exclusion criteria: depression within the framework of schizophrenia spectrum disorders; organic depressions; depressions combined with alcoholism and drug addiction; unwillingness or inability of a patient to sign an informed consent to participate in the study; pregnancy, breastfeeding.

The condition of the patients was assessed in accordance with the ICD-10 and DSM-V diagnostic criteria for affective disorders using a specially designed clinical examination card. The Montgomery–Asberg Depression Rating Scale (MADRS) was used to assess the severity of depression. Statistical processing of the obtained results was carried out using Statistica 13.0 software (StatSoft Inc., USA). Comparison of the three groups on quantitative scales was carried out on the basis of Kruskal–Wallis nonparametric analysis of variance.

Research results. A comparative study of patients suffering from AD in the framework of bipolar disorder, RDD and PD revealed a number of significant differences both in socio-demographic parameters (Table 1) and in the clinical picture of the disease. The average age of the patients at the time of inclusion in the study was significantly lower in the PD group (24.5 years) compared to the BD group (32.4 years) ($p<0.01$). Women predominated among the surveyed (BD – 51.4%, RDD – 77.8%, PD – 75.0%). There were more patients with higher education in the BD group (60%) than in the PD group (29.2%) ($p<0.05$). Accordingly, there were more patients with incomplete higher education in the PD group than in the BD group (54.2% and 20%, respectively; $p<0.01$), which can be explained by the younger age of patients with PD. In terms of the level of family adaptation, the BD group favorably differed: there were significantly more married individuals (42.9%) than in the RDD group and, especially, PD group (12.5%) ($p<0.01$), and there were significantly more singles in the PD group, which can also be associated with a younger age of the latter. There were no cases of dis-

ability in any group, however, the unemployment rate was high, which may be due to various factors (BD – 54.3%, RDD – 61.1%, PD – 62.5%).

Heredity in the BD and RDD groups was significantly more often burdened with affective disorders (48.6% and 44.4%), compared with the PD group (12.5%; p<0.01). Disorders of the schizophrenic spectrum in an equal proportion (11.1% each) occurred in families of patients with bipolar disorder and RDD and were absent in the PD group. Abuse of alcohol, psychoactive substances, as well as suicides in the families of patients of all groups were noted approximately equally (Table 2).

In the structure of premorbid personality traits (Fig. 1) in the bipolar group, cycloid, hyperthymic, hysterical (28.6%, 22.9%, 17.1%, respectively) features were distinguished with the same frequency; in the RDD group, the emotionally labile type was more common than the hysterical type (50% and 11.1%, respectively; p<0.05), and the psychasthenic type was also distinguished (27.8%); in the PD group, the psychasthenic type prevailed compared with the hysterical type of personality (83.3%, 8.3%, respectively; p<0.001).

Patients in the groups differed in a number of indicators of the disease course. Before the onset of the disease, affective fluctuations of the subclinical level were significantly more common in patients of the BD group than in the RDD group (65.6% and 22.2%, respectively; p<0.01).

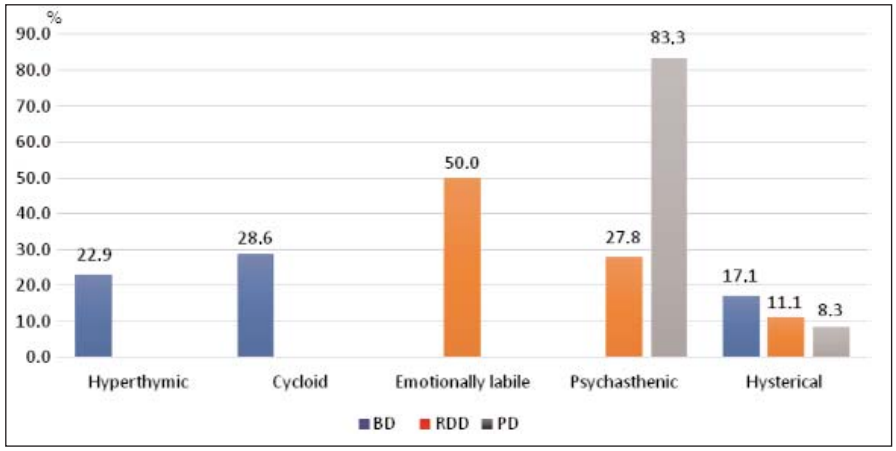

Fig. 1. *Premorbid personality traits in patients of three groups*

Table 3. Clinical and dynamic characteristics of AD

Indicator	BD (n=35)	RDD (n=18)	PD (n=24)
The characteristic of depression according to ICD-10, n (%):			
mild	0	0	0
moderate	21 (60.0)	9 (50.0)	19 (79.2)*
severe	14 (40.0)	9 (50.0)*	5 (20.8)
Number of depressive episodes in history, n (%):			
from 1 to 5	13 (37.1)	10 (55.6)	16 (66.7)*
from 5 to 10	6 (17.1)	4 (22.2)	7 (29.2)
from 10 to 20	12 (34.3)**	4 (22.2)	1 (4.2)
more than 20	4 (11.4)	0	0
Average duration of a depressive episode (M±δ), months	3.8±2.1	5.4±3.4	8.5±5.3**
Average duration of remission (M±δ), months	1.99±1.54	3.89±1.57	7.67±5.51**

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

The manifestation of the disease in the RDD and BD groups could be due to traumatic events / stress (33.3% and 8.6%, respectively; p<0.05). Over the past two years, a large proportion of stress factors was associated with the Covid-19 epidemic; these stressors did not only provoke the onset of the depressive phase, but also affected the structure and severity of depression, and were one of the leading psychogenic factors in the development of PD, contributing to its prolongation and recurrence. The proportion of factors associated with coronavirus infection in the PD group was 66.7%, which is significantly higher than in the RDD group (16.7%; p<0.001) and in the BD group (40.0%; p<0.05).

The average age of onset of the disease in all groups was about 20 years and did not differ significantly (BD – 21.6±6.9, RDD – 20.4±6.9, PD – 19.8±5.4 years). As for the course of the diseases (Table 3), there were certain differences between the groups: before the start of treatment, moderate severity of depression was more often detected in the PD group compared with the RDD group (79.2% and 50%, respectively; p<0.05); a severe course was more often detected in the RDD group than in the PD group (50% and 20.8%, respectively; p<0.05). Comparison of the number of depressive episodes in history showed the following: the number of episodes from 1 to 5 was more common in the PD group compared with BD (66.7% and 37.1%; p<0.05); the number of episodes from 5 to 10 was equal in both groups; from 10 to 20 episodes were significantly more common in the BD group than the PD group (34.3% and 4.2%; p<0.01); more than 20 episodes occurred only in the BD group (11.4%). The average duration of a depressive episode was the longest in the PD group (8.5±5.3 months) and the shortest in the BD group (3.8±2.1 months; p<0.05), which may be due to the persistence and duration of such a traumatic factor as the pandemic. The maximum mean duration of remission was also noted in the PD group (7.67±5.51 months), the shortest – in the BD group (1.99±1.54 months; p<0.05).

The duration of the current episode (r=-0.268, p<0.05), the severity of depression according to the MADRS scale (r=0.249, p<0.05), and BMI (r=0.295, p<0.05) correlated with the number of depressive episodes, i.e. the less frequently there were exacerbations, the longer was the average duration of the episode; the more depressive episodes there were in the anamnesis, the higher the severity of depression according to the MADRS scale, and also, the more frequent exacerbations and the shorter the remissions, the higher the BMI index (r=-0.238, p<0.05).

Table 4. Clinical features of AD in patients of three groups, n (%)

Atypical symptoms	**BD (n=35)**	**RDD (n=18)**	**PD (n=24)**
Mood reactivity	35 (100)	18 (100)	24 (100)
Sensitivity	22 (62.9)	15 (83.3)	18 (75.0)
Lead paralysis	25 (71.4)	11 (61.1)	15 (62.5)
Vegetative symptoms	25 (71.4)	11 (61.1)	16 (66.7)
Increased appetite	20 (57.1)	11 (61.1)	20 (83.3)*
Weight with BMI:			
norm	11 (31.4)	7 (38.9)	8 (33.3)
overweight	16 (45.7)	7 (38.9)	11 (45.8)
obesity degree I	5 (14.3)	3 (16.7)	3 (12.5)
obesity degree II	2 (5.7)	1 (5.6)	2 (8.3)
Hypersomnia	27 (77.1)	12 (66.7)	15 (62.5)
Typical Symptoms	**BD (n=35)**	**RDD (n=18)**	**PD (n=24)**
Yearning	20 (57.1)	14 (77.8)**	7 (29.2)
Anxiety	19 (54.3)**	13 (72.2)*	23 (95.8)
Adynamia	13 (37.1)	10 (55.6)*	6 (25.0)
Anhedonia	2 (5.7)	1 (5.6)	1 (4.2)
Ideas of self-blame	23 (65.7)	13 (72.2)*	9 (37.5)
Decreased appetite	12 (34.3)	6 (33.3)*	2 (8.3)*
Decreased libido	25 (71.4)	14 (77.8)	16 (66.7)
Early awakenings	13 (37.1)	6 (33.3)	6 (25.0)
No sense of sleep	20 (57.1)	13 (72.2)	16 (66.7)
Superficial night sleep	10 (28.6)	9 (50.0)	18 (75.0)**
Difficulty falling asleep	14 (40.0)	10 (55.6)	11 (45.8)
Sleep-wake cycle inversion	4 (11.4)	2 (11.1)	3 (12.5)
Daily fluctuations:			
worse in the morning	10 (28.6)	4 (22.2)	2 (8.3)**
worse in the evening	5 (14.3)	5 (27.8)	–
Seasonal fluctuations:			
autumn winter	15 (42.9)*	7 (38.9)*	3 (12.5)
spring	3(8.6)	–	–
Depersonalization	8 (22.9)	6 (33.3)	3 (12.5)
Derealization	2 (5.7)	7 (38.9)***	1 (4.2)
Hypothymia	35 (100)	18 (100)	24 (100)
Ideation inhibition	12 (34.3)	11 (61.1)	9 (37.5)
Decreased attention	24 (68.6)	13 (72.2)	21 (87.5)
Decreased memory	10 (28.6)	6 (33.3)	12 (50.0)
Suicidal thoughts	21 (60.0)	13 (72.2)*	10 (41.7)
History of suicidal attempts	9 (25.7)	8 (44.4)*	4 (16.7)
Comorbid symptoms	**BD (n=35)**	**RDD (n=18)**	**PD (n=24)**
Asthenia	22 (62.9)	15 (83.3)	23 (95.8)**
Obsessive Compulsive Symptoms	4(11.4)	1(5.6)	2 (8.3)
Obsessive-phobic symptoms	6 (17.1)	3 (16.7)	4 (16.7)
Irritability	18 (51.4)	9 (50.0)	8 (33.3)
Tearfulness	16 (45.7)	9 (50.0)	11 (45.8)
Panic attacks	18 (51.4)*	6 (33.3)	5 (20.8)
Hypochondriacal inclusions	5 (14.3)	5 (27.8)	9 (37.5)*

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

Analysis of the structure of the depressive syndrome in patients of the three groups (Table 4) showed that differences in the frequency of atypical symptoms were not statistically significant, with the exception of increased appetite, which was more common in the PD group compared with the BD group (83.3% and 57.1%, respectively; p<0.05). As for the main manifestations of depression, a number of significant differences were revealed: in patients with RDD, complaints of melancholy were noted more often than in the PD group (77.8% and 29.2%; p<0.01). Anxiety was observed more frequently in the PD group than in the RDD group (95.8% and 72.2%, respectively; p<0.05) and BD group (54.3%; p<0.01). Complaints of adynamia prevailed in the RDD group compared with the PD group (55.6% and 25%; p<0.05). The ideas of self-blame in patients with bipolar disorder (65.7%) were as common as in the RDD group (72.22%), which exceeded these figures in the PD group (37.5%; p<0.05). In the BD (34.3%) and RDD (33.3%) groups, patients with reduced appetite were more common than in the PD group (8.3%; p<0.05). In the PD group, patients with superficial nocturnal sleep were more common than in the BD group (75% and 28.6%, respectively; p<0.01). Daily fluctuations in well-being with worsening in the morning in bipolar disorder were 28.6%, RDD – 22.2%, which significantly differed from PD (8.3%); deterioration in well-being in the evening in the RDD group was detected more often than in the BD group (27.8% and 14.3%; p<0.01). Patients with seasonal fluctuations with a predominance of deterioration in well-being in the autumn-winter period prevailed in the BD (42.9%) and RDD (38.9%) groups, the number of such patients was much lower in the PD group (12.5%; p<0.05). Seasonal fluctuations with deterioration in spring were noted only in the BD group (8.6%). In patients with RDD, complaints of derealization were recorded significantly more often than in the BD and PD groups (38.9%; 5.7% and 4.2%, respectively; p<0.001). Suicidal thoughts occurred more often in the RDD group than in the PD group (72.2% and 41.7%; p<0.05), as well as the history of suicide attempts (44.4% and 16.7%; p<0.05). In the PD group, patients with asthenia (95.8%) were more common than in the BD group (62.9%; p<0.01). Panic attacks were more common among patients in the BD group than in the PD group (51.4% and 20.8%; p<0.05). Hypochondriacal inclusions were more often recorded in the PD group than in the BD group (37.5% and 14.3%; p<0.05).

When assessing the somatic status of patients (Table 5), it was found that in all three groups, metabolic-endocrine (19.5%) and cardiovascular diseases (14.3%) prevailed. In the BD group, metabolic-endocrine diseases were significantly more common (31.4%; p<0.05), in the RDD group – cardiovascular diseases (38.9%; p<0.05), in the PD group – skin and diseases associated with the gastrointestinal tract (25%; p<0.05). There were no significant differences in the frequency of alcohol and substance abuse.

Discussion

The results obtained in the study indicate that AD has both common features of clinical manifestations and course, as well as differences associated with the nosological affiliation of the disease in which it is observed. As a whole, AD is characterized by a high prevalence (30.8%) which, however, does not go beyond these indicators in other studies (18–36%) [21–22]). The early onset of the disease at about 20 years of age does not contradict the previously obtained results [20, 23–24], and also confirms the opinion of J.W. Stewart [25] that "the onset of the disease before 20 years of age" is a diagnostic criterion for atypical depression. The predominance of women in our sample is consistent with the data of other authors [26–28]. Despite the high level of education, more than a half of the patients did not work, which may be due to various factors, including the course of AD [29]. The presence of hysterical accentuations in the premorbid is regarded by some authors

as a manifestation of AD itself [30], however, in our study, they were not as widely represented as the premorbid features characteristic of individual affective disorders, although they could play the role of a certain predictor. Overweight occurred in almost a half of the patients (44.2%), which is typical of AD [31], as well as a high percentage of complaints of asthenia [32–33]. Our study revealed a high comorbidity of AD with metabolic-endocrine, cardiovascular and skin diseases. Some studies also noted a close relationship between AD and metabolic syndrome and cardiovascular diseases [34–35].

Along with atypical symptoms, the structure of depressive syndromes also included signs of classical depression, as pointed out by other researchers [11, 21, 36–37], who called such symptoms melancholic inclusions.

Table 5. Comorbid somatic pathology and use/abuse in patients of the three groups, n (%)

Disorders	BD (n=35)	RDD (n=18)	PD(n=24)	Total (n=77)
Somatic pathology:				
metabolic-endocrine	11 (31.4)*	3 (16.7)	1 (4.2)	15 (19.5)
cardiovascular	3 (8.6)	7 (38.9)*	1 (4.2)	11 (14.3)
skin	3 (8.6)	1 (5.6)	6 (25.0)*	10 (13.0)
diseases of the gastrointestinal tract	–	–	6 (25.0)*	6 (7.8)
Use/abuse during depression:				
alcohol	6 (17.1)	4 (22.2)	2 (8.3)	12 (15.6)
psychoactive substances	1 (2.9)	1 (5.6)	3 (12.5)	5 (6.5)
alcohol and psychoactive substances	4 (11.4)	-	-	4 (5.2)

Note. *– p <0,05.

AD in the structure of BD was characterized by the highest detection rate (45%). Such a relationship between AD and BD is confirmed by the results of studies over the past 20 years, especially with BD II, where the prevalence of symptoms of atypical depression is 32.5%, and in the group of bipolar spectrum disorders – 39.5% [38]. Other studies have also indicated a more frequent detection of AD in BD II compared to RDD [39–40]. For patients from the BD group, as well as for RDD, a hereditary burden of affective diseases was characteristic, which is consistent with the data available in the literature [20, 23–24]. In the structure of premorbid personality traits, cycloid, hyperthymic and hysterical character traits were predominant. A number of authors [41–42] also noted cyclothymic temperament in premorbid AD patients, which, in their opinion, is a diathesis not only for AD, but also for bipolar disorder, anxiety disorders, and borderline personality disorder. Patients with AD within bipolar disorder were characterized by affective fluctuations before the manifestation of the disease, a greater number of depressive episodes in history, including those provoked psychogenically. Of the typical depressive symptoms, the following were more often noted: diurnal mood swings with a deterioration in well-being in the morning and seasonal depressions [43], complaints of reduced appetite. A high comorbidity with metabolic-endocrine diseases was revealed.

AD within RDD was less common than in other groups (23%), which coincides with the data of other studies, where this figure reached 20% [19]. Depression often began spontaneously. Premorbid was characterized by emotional lability, psychasthenic and hysterical accentuations. Of the typical depressive symptoms, melancholy, adynamia, derealization, and ideas of self-accusation were more often recorded. Suicidal thoughts and attempts in the anamnesis, high comorbidity with cardiovascular diseases were noted much more often.

Patients with AD in the PD group accounted for 31.2% of the entire sample and were the youngest at the time of inclusion in the study, which could account for the smallest number of people with higher education and those who were married. They had a significantly lower hereditary burden of mental illness. For the premorbid, psychasthenic accentuation of the personality was most characteristic. The patients significantly more often complained of increased appetite, anxiety (a number of studies [4–9, 24, 29, 44] noted a comorbidity of anxiety and AD), weakness, rapid fatigue, superficial night sleep; hypochondriacal inclusions were also revealed more often. Comorbidity has been identified with skin and gastrointestinal diseases.

Thus, the identified markers of AD, including the premorbid personality, features of psychopathological symptoms, comorbidity with other diseases, the course of the disease, and correlations between individual characteristics and nosological affiliation, will allow for an earlier and more accurate diagnosis of AD and administration of adequate therapy.

REFERENCES

1. West ED, Dally PJ. Effect of iproniazid in depressive syndromes. *Br Med J.* 1959 Jun 13;1(5136):1491-4. doi: 10.1136/bmj.1.5136.1491
2. Klein DF, Davis JM. Diagnosis and Drug Treatment of Psychiatric Disorders. Baltimore: Williams & Wilkins; 1969.
3. Davidson JR, Miller RD, Turnbull CD, Sullivan JL. Atypical depression. *Arch Gen Psychiatry.* 1982 May;39(5):527-34. doi: 10.1001/archpsyc.1982.04290050015005
4. Sovner RD. The clinical characteristics and treatment of atypical depression. *J Clin Psychiatry.* 1981 Jul;42(7):285-9.
5. Lojko D, Rybakowski JK. Atypical depression: current perspectives. *Neuropsychiatr Dis Treat.* 2017 Sep 20;13:2447-56. doi: 10.2147/NDT.S147317
6. Buzuk G, Lojko D, Owecki M, et al. Depression with atypical features in various kinds of affective disorders. *Psychiatr Pol.* 2016;50(4):827-38. doi: 10.12740/PP/44680
7. Koyuncu A, Ertekin E, Binbay Z, et al. The clinical impact of mood disorder comorbidity on social anxiety disorder. *Compr Psychiatry.* 2014 Feb;55(2):363-9. doi: 10.1016/j.comppsych.2013.08.016. Epub 2013 Oct 19.

8. Koyncu A, Ertekin E, Ertekin BA, et al. Relationship between atypical depression and social anxiety disorder. *Psychiatry Res.* 2015 Jan 30;225(1-2):79-84. doi: 10.1016/j.psychres.2014.10.014. Epub 2014 Nov 11.

9. Tav A, Demir Berkol T, Yildirim YM, et al. Can Comorbid Bipolar Disorder Be Associated with Atypical Depression in Patients with Social Anxiety Disorder? *J Neurobehav Sci.* 2019;6(1):130-5.

10. Matza LS, Revicki DA, Davidson JR, Stewart JW. Depression with atypical features in the national comorbidity survey: classification, description, and consequences. *Arch Gen Psychiatry.* 2003 Aug;60(8):817-26. doi: 10.1001/archpsyc.60.8.817

11. Angst J, Gamma A, Benazzi F, et al. Melancholia and atypical depression in the Zurich study: epidemiology, clinical characteristics, course, comorbidity and personality. *Acta Psychiatr Scand Suppl.* 2007;(433):72-84. doi: 10.1111/j.1600-0447.2007.00965.x

12. Lee S, Ng KL, Tsang A. Prevalence and correlates of depression with atypical symptoms in Hong Kong. *Aust N Z J Psychiatry.* 2009 Dec;43(12):1147-54. doi: 10.3109/00048670903279895

13. Тювина НА, Балабанова ВВ, Воронина ЕО. Гендерные особенности депрессивных расстройств у женщин. *Неврология, нейропсихиатрия, психосоматика.* 2015;7(2):75-9. doi: 10.14412/2074-2711-2015-2-75-79
[Tyuvina NA, Balabanova VV, Voronina EO. Gender features of depressive disorders in women. *Nevrologiya, neiropsikhiatriya, psikhosomatika = Neurology, Neuropsychiatry, Psychosomatics.* 2015;7(2):75-9. doi: 10.14412/2074-2711-2015-2-75-79 (In Russ.)].

14. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington: American Psychiatric Publishing; 2013.

15. Benazzi F. Atypical bipolar II depression compared with atypical unipolar depression and nonatypical bipolar II depression. *Psychopathology.* Mar-Apr 2000;33(2):100-2. doi: 10.1159/000029128

16. Тювина НА, Коробкова ИГ. Сравнительная характеристика клинических особенностей депрессии при биполярном аффективном расстройстве I и II типа. *Неврология, нейропсихиатрия, психосоматика.* 2016;8(1):22-8. doi: 10.14412/2074-2711-2016-1-22-28
[Tyuvina NA, Korobkova IG. Comparative clinical characteristics of depression in bipolar affective disorders types I and II. *Nevrologiya, neiropsikhiatriya, psikhosomatika = Neurology, Neuropsychiatry, Psychosomatics.* 2016;8(1):22-8. doi: 10.14412/2074-2711-2016-1-22-28 (In Russ.)].

17. Mitchell PB, Wilhelm K, Parker G, et al. The clinical features of bipolar depression: a comparison with matched major depressive disorder patients. *J Clin Psychiatry.* 2001 Mar;62(3):212-6; quiz 217.

18. Bowden CL. Strategies to reduce misdiagnosis of bipolar depression. *Psychiatr Serv.* 2001 Jan;52(1):51-5. doi: 10.1176/appi.ps.52.1.51

19. Петрунько ОВ, Швецова АВ, Магонова ЕГ, Хамарханова АА. Атипичная симптоматика в клинике монополярной депрессии. *Сибирский медицинский журнал.* 2009;(5):72-5.
[Petrun'ko OV, Shvetsova AV, Magonova EG, Khamarkhanova AA. Atypical symptoms of bipolar depression. *Sibirskii meditsinskii zhurnal.* 2009;(5):72-5 (In Russ.)].

20. Akiskal HS, Benazzi F. Atypical depression: a variant of bipolar II or a bridge between unipolar and bipolar II? *J Affect Disord.* 2005 Feb;84(2-3):209-17. doi: 10.1016/j.jad.2004.05.004

21. Gold PW, Chrousos GP. Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs low CRH/NE states. *Mol Psychiatry.* 2002;7(3):254-75. doi: 10.1038/sj.mp.4001032

22. Blanco C, Vesga-Lopez O, Stewart JW, et al. Epidemiology of major depression with atypical features: results from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *J Clin Psychiatry.* 2012 Feb;73(2):224-32. doi: 10.4088/JCP.10m06227. Epub 2011 Sep 6.

23. Novick JS, Stewart JW, Wisniewski SR, et al. Clinical and demographic features of atypical depression in outpatients with major depressive disorder: preliminary findings from STAR*D. *J Clin Psychiatry.* 2005 Aug;66(8):1002-11. doi: 10.4088/jcp.v66n0807

24. Stewart J. Atypical depression: history and future. *Psychiatr Ann.* 2014;44:557-62.

25. Brailean A, Curtis J, Davis K, et al. Characteristics, comorbidities, and correlates of atypical depression: evidence from the UK Biobank Mental Health Survey. *Psychol Med.* 2020 May;50(7):1129-38. doi: 10.1017/S0033291719001004. Epub 2019 May 2.

26. Agosti V, Stewart JW. Atypical and nonatypical subtypes of depression: comparison of social functioning, symptoms, course of illness, co-morbidity and demographic features. *J Affect Disord.* 2001 Jun;65(1):75-9. doi: 10.1016/s0165-0327(00)00251-2

27. Stewart JW, Mcgrath PJ, Fava M, et al. Do atypical features affect outcome in depressed outpatients treated with citalopram? *Int J Neuropsychopharmacol.* 2010 Feb;13(1):15-30. doi: 10.1017/S1461145709000182. Epub 2009 Apr 3.

28. McGinn LK, Asnis GM, Suchday S, Kaplan M. Increased personality disorders and Axis I comorbidity in atypical depression. *Compr Psychiatry.* Nov-Dec 2005;46(6):428-32. doi: 10.1016/j.comppsych.2005.03.002

29. Lasserre AM, Glaus J, Vandeleur CL, et al. Depression with atypical features and increase in obesity, body mass index, waist circumference, and fat mass: a prospective, population-based study. *JAMA Psychiatry.* 2014 Aug;71(8):880-8. doi: 10.1001/jamapsychiatry.2014.411. Erratum in: *JAMA Psychiatry.* 2014 Sep;71(9):1079.

30. Соколовская ЛВ. Астения – типология, динамика (пограничные состояния и эндогенные заболевания): Автореф. ... дис. канд. мед. наук. Москва; 1991. 17 с.
[Sokolovskaya LV. *Asteniya – tipologiya, dinamika, pogranichnyye sostoyaniya i endogennyye zabolevaniya. Avtoref. ... diss. kand. med. nauk* [Asthenia – typology, dynamics (borderline states and endogenous diseases): Author's abstract. Dis. Cand. Med. Sci.]. Moscow; 1991. 17 p. (In Russ.)].

31. Зеленина ЕВ. Соматовегетативный симптомокомплекс в структуре депрессий (типология, клиника, терапия): Автореф. ... дис. канд. мед. наук. Москва; 1997. 23 с.
[Zelenina YeV. *Somatovegetativnyy simptomokompleks v strukture depressiy (tipologiya, klinika, terapiya): Avtoref. ... diss. kand. med. nauk* [Somatovegetative symptom complex in the structure of depression (typology, clinic, therapy): Author's abstract. Dis. Cand. Med. Sci.]. Moscow; 1997. 23 p. (In Russ.)].

32. Lasserre AM, Strippoli MF, Glaus J, et al. Prospective associations of depression subtypes with cardio-metabolic risk factors in the general population. *Mol Psychiatry.* 2017 Jul;22(7):1026-34. doi: 10.1038/mp.2016.178. Epub 2016 Oct 11.

33. Лапин ИА, Рогачева ТА. Атипичная депрессия (анализ взаимосвязей отдельных атипичных симптомов с социально-демографическими и клиническими переменными). *Социальная и клиническая психиатрия.* 2020;30(3):17-25.
[Lapin IA, Rogacheva TA. Atypical depression (analysis of links between individual atypical symptoms and sociodemographic and clinical variables). *Sotsial'naya i klinicheskaya psikhiatriya.* 2020;30(3):17-25 (In Russ.)].

34. Angst J, Gamma A, Benazzi F, et al. Atypical depressive syndromes in varying defi nitions. *Eur Arch Psychiatry Clin Neurosci.* 2006 Feb;256(1):44-54. doi: 10.1007/s00406-005-0600-z. Epub 2005 Jul 27.

35. Perugi G, Akiskal HS, Lattanzi L, et al. The high prevalence of "soft" bipolar (II) features in atypical depression. *Compr Psychiatry.* Mar-Apr 1998;39(2):63-71. doi: 10.1016/s0010-440x(98)90080-3

36. Benazzi F. Testing DSM-IV definition of atypical depression. *Ann Clin Psychiatry.* 2003 Mar;15(1):9-16. doi: 10.1023/a:1023272408562

37. Seemüllera F, Riedela M, Wickelmaiera F, et al. Atypical symptoms in hospitalised patients with major depressive episode: frequency, clinical characteristics, and internal validity. *J Affect Disord.* 2008 Jun;108(3):271-8. doi: 10.1016/j.jad.2007.10.025. Epub 2007 Dec 31.

38. Смулевич АБ. Депрессии в общей медицине: Руководство для врачей. Москва: МИА; 2007. 256 с.
[Smulevich AB. *Depressii v obshchei meditsine:*

Rukovodstvo dlya vrachei [Depression in General medicine: a guide for doctors]. Moscow: MIA; 2007. 256 p. (In Russ.)].

39. Pae CU, Tharwani H, Marks DM, et al. Atypical depression: a comprehensive review. *CNS Drugs*. 2009 Dec;23(12):1023-37. doi: 10.2165/11310990-000000000-00000

40. Stewart JW, Mcgrath PJ, Quitkin FM, Klein DF. DSM-IV depression with atypical features: is it valid? *Neuropsychopharmacology*. 2009 Dec;34(13):2625-32. doi: 10.1038/npp.2009.99. Epub 2009 Sep 2.

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