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Lifetime anxiety and substance use disorder comorbidity in bipolar disorder and its relationship to selected variables. Gender and bipolar subtype differences in comorbidity.

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Summary

Aim. The main objective of the presented study was to investigate relationships between lifetime comorbidity in bipolar disorder to demographic and clinical variables and level of functioning in current remission. The prevalence of comorbidity and gender and bipolar subtype differences were also assessed.
Subjects and methods. Seventy three bipolar I or II outpatients in remission (Hamilton Depression Rating Scale < 9, Young Mania Rating Scale < 7) were assessed by means of the Composite International Diagnostic Interview (CIDI) in order to detect possible anxiety and substance use comorbid diagnoses. The sample was split according to the presence of different classes of comorbid disorders and the groups were compared.
Results. Lifetime psychiatric comorbidity (anxiety and substance use disorders) was 71.2%. The only significant differences between sexes were found in general substance use disorders, alcohol and nicotine use disorder comorbidities. Only panic disorder with or without agoraphobia and nicotine use disorders were significantly more prevalent in BP I than in BP II. Significant differences between non-comorbid group and comorbid groups were found in some investigated variables.
Conclusions. Lifetime psychiatric comorbidity is a common phenomenon in bipolar disorder associated with some demographic and clinical variables.

bipolar disorder / anxiety disorders / substance use disorders / comorbidity

INTRODUCTION

Comorbidity has been defined as the presence of more than one specific disorder in a person in a defined period of time. This definition extends the perspective of comorbidity to a lifetime perspective and is the most commonly used in research [1].

The data from both epidemiological and clinical studies indicate that comorbidity is a common phenomenon among bipolar patients with a possible negative impact on clinical characteristics of bipolar disorder (BP). The rates of comorbidity reported by various authors have been as diverse as ranging from 31 to 68% [2, 3, 4, 5], though in the National Comorbidity Survey (NCS) all the individuals diagnosed as having bipolar I disorder suffered from at least one psychiatric disorder in their lifetimes [6]. The re-

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ported differences might possibly be explained by differences in the characteristics of groups of patients studied: bipolar subtype (I, II, or both), current psychopathological status (inpatient, outpatient, or both; in an acute phase, in remission, or both), population (clinical, general), or in variety of diagnostic instruments and diagnostic criteria employed.

Other aspects of comorbidity, i.e. gender and subtype differences, have been less extensively investigated and require further research due to inconsistent and insufficient data.

Comorbidity has also been described in terms of its relationships to less favourable clinical characteristics of BP and various other variables characterizing patients [2, 4, 5, 7].

Relative lack of cross-cultural data on comorbidity in bipolar disorder justifies undertaking this issue in our preliminary study.

SUBJECTS AND METHODS

Seventy three bipolar outpatients who fulfilled the inclusion criteria were recruited from a group of eighty consecutive bipolar patients who visited three outpatient psychiatric settings in Krakow. The inclusion criteria were: 1) DSM-IV diagnosis of BP I or BP II; 2) remission confirmed by the Hamilton Depression Rating Scale (HDRS) scores less than 9 and Young Mania Rating Scale (YMRS) scores less than 7; 3) age at least 18 years; and 4) written informed consent obtained before participation in the study. The only exclusion criteria were: 1) prominent intellectual or cognitive difficulties that hindered the participation in the study; and 2) withdrawal of the consent in the course of the study. Seven out of eighty consecutive patients did not meet the full criteria of remission and were not included in the study. All of the included 73 patients completed the study.

The diagnosis of DSM-IV BP I or BP II were confirmed using sections E and F of the Polish translation of the Munich Version of the Composite International Diagnostic Interview for lifetime assessment (M-CIDI-LT). Lifetime anxiety and substance use disorders comorbidities were diagnosed using sections D, I, K, L, N of the M-CIDI-LT. The computerized version of M-CIDI-LT was used. All the assessments with M-CIDI-LT were performed by the first author, who had been trained in the use of CIDI in a WHO-approved training centre in Wroclaw [8, 9, 10]. The choice of CIDI was dictated by lack of the other structured diagnostic instruments (i.e. SCID for DSM-IV), which have not been translated into Polish.

Demographic, clinical and the other selected variables were obtained from an interview conducted using a self-constructed semi–structured questionnaire. Whenever needed, the missing data were completed with information obtained from outpatient and inpatient medical records and treating psychiatrists.

In the total of 73 patients enrolled in the study, five groups were distinguished to perform comparisons: BP patients without comorbidity (group 1), BP patients with any kind of comorbidity (anxiety or substance use disorders) (group 2), BP patients with comorbid anxiety disorders (group 3), BP patients with comorbid substance use disorders (group 4), and BP patients with comorbid anxiety and substance use disorders (group 5). The whole group was also split and compared according to gender and bipolar subtype.

Group 1 consisted of twenty one patients (28.8%), group 2 of fifty two patients (71.2%), group 3 of twenty five patients (34.2%), group 4 of six patients (8.2%), and group 5 of twenty one patients (28.8%).

Statistics

The $\chi 2$ test with Yates' correction or Fisher's exact test were used to analyze categorical variables. Kruskall-Wallis' *H*-tests and one-way analysis of variance (ANOVA) were performed for continuous variables when comparing many groups. Student's *t*-tests and Mann-Whitney's *U*-tests were then performed for direct comparisons between groups. All statistics were two-tailed, and significance was set at $p< 0.05$.

RESULTS

Seventy three bipolar patients completed the study. Fifty (68.5%) fulfilled the diagnosis of DSM-IV BP I. Thirty one (42.5%) were men; the mean age was 44.6 years (SD=11.0, range=21.0-67.0).

Table 1. Lifetime prevalence of comorbid disorders in the whole group of BP patients.

Comorbid diagnosis	All patients with bipolar diagnosis	
	n	%
All disorders (without nicotine use disorders)	52	71.2
Anxiety disorders	46	63.0
PD ± Ago	13	17.8
GAD	23	31.5
SAD	14	19.2
SP	20	27.4
Ago	7	9.6
OCD	3	4.1
PTSD	3	4.1
Substance use disorders (without nicotine)	27	37.0
Alcohol	22	30.1
Sedatives and hypnotics	10	13.7
Drugs	2	2.8
Nicotine	43	58.9
Substance use disorders (with nicotine)	49	67.1

Ago = agoraphobia, OCD=obsessive-compulsive disorder, PTSD = post traumatic stress disorder

Table 1 shows comorbidities in all BP-I and BP-II cases. Lifetime psychiatric comorbidity (with the exclusion of nicotine use disorders) was 71.2%. The comorbid lifetime anxiety disorders were found in 63% of the sample, and substance use disorders in 37%. After inclusion of nicotine use disorders the SUDs comorbidity reached 67.1%.

The most prevalent anxiety disorders were generalized anxiety disorder (GAD) (23 patients, 31.5%), simple phobias (SP) (20 patients, 27.4%), social anxiety disorder (SAD) (14 patients, 19.2%), and panic disorder with or without agoraphobia (PD±Ago) (13 patients, 17.8%). The most prevalent SUDs were alcohol use disorders (22 patients, 30.1%) and nicotine use disorders (43 patients, 58.9%).

Table 2 shows comparisons of comorbidities between sexes and BP subtypes. Although the rate of comorbidity was higher in men (80.6%) than in women (64.3%), it did not reach statistical significance. The only significant differences between sexes were found in general SUDs comorbidity (58.1% in men vs. 21.4% in women), alcohol use disorders (54.8% in men vs. 11.9% in women) and nicotine use disorders (74.2% in men vs. 47.6% in women).

There were no statistical differences in comorbidity between BP I and BP II. Only PD±Ago (24% vs. 4.3%) and nicotine use disorders (72%

Table 2. Lifetime prevalence of comorbid disorders in BP men and BP woman and BP I and BP II – comparisons.

COMORBID DIAGNOSIS	MEN (N=31)		WOMAN (N=42)		(X2) p	BP I (N=50)		BP II (N=23)		(χ^2) p
	n	%	n	%		n	%	n	%	
All disorders (without nicotine use disorders)	25	80.6	27	64.3	NS	37	74.0	15	65.2	NS
Anxiety disorders	20	64.5	26	62.0	NS	31	62.0	15	65.2	NS
PD ± Ago	6	19.3	7	16.7	NS	12	24.0	1	4.3	<0.05
GAD	12	38.7	11	26.2	NS	17	34.0	6	26.1	NS
SAD	8	25.8	6	14.3	NS	8	16.0	6	26.1	NS
SP	8	25.8	12	28.6	NS	12	24.0	8	34.8	NS
Ago	3	9.7	4	9.5	NS	3	6.0	4	17.4	NS
OCD	1	3.2	2	4.8	NS	1	2.0	2	8.7	NS
PTSD	0	0	3	7.1	NS	3	6.0	0	0.0	NS

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Substance use disorders (without nicotine)	18	58.1	9	21.4	<0.05	20	40.0	7	30.4	NS
Alcohol	17	54.8	5	11.9	<0.001	18	36.0	4	17.4	NS
Sedatives and hypnotics	4	12.9	6	14.3	NS	6	12.0	4	17.4	NS
Drugs	2	6.7	0	0	NS	2	4.1	0	0.0	NS
Nicotine	23	74.2	20	47.6	<0.05	36	72.0	7	30.4	<0.01
Substance use disorders (with nicotine)	25	80.7	24	57.1	<0.05	40	80.0	9	39.1	<0.01

vs. 30.4%) were significantly more prevalent in BP I than in BP II.

The direct comparison of the group without comorbid disorders (group 1) with the group with any comorbid disorder (group 2) revealed no significant differences in most investigated variables. Bipolar patients with any kind of comorbidity were employed significantly less often and more frequently were dependant on disability pension uptake. Nineteen of them (36.5%), in comparison to only two (9.5%) patients without comorbidity, reported at least one traumatic event (this difference was statistically significant). The mean GAF score in the comorbid group was 74.4, compared to 88.2 in the non-comorbid group, a difference that was highly significant ($p<0.01$). The patients from the comorbid group also more often reported current tobacco smoking (Tab. 3).

To detect other possible associations of comorbidity with the investigated variables, the direct comparisons of non-comorbid group (group 1) with two other comorbid groups, i.e. with comorbid anxiety disorders (group 3) and with comorbid both anxiety and SUDs (group 5) were conducted. Group 4 (patients with comorbid SUDs only) was not included in the comparisons due to the very limited number of subjects (n=6).

The comparison of the non-comorbid group with group 3 revealed significant differences in

Table 3. Comparison of the group of BP patients without comorbidity (group 1) with the group of BP patients with any comorbidity (group 2) – categorical and continuous variables

VARIABLE	GR 1 (N= 21)	GR 2 (N=52)	P
	N (%)		(χ^2)
Sex Male Female	 6 (19.3) 15 (35.7)	 25 (80.7) 27 (64.3)	NS
Place of residence City Country	 18 (85.7) 3 (14.3)	 40 (76.9) 12 (23.1)	NS
Education Primary Vocational High school College/University	 0 (0.0) 2 (33.3) 9 (23.7) 10 (37.0)	 2 (3.8) 4 (7.7) 29 (55.8) 17 (32.7)	NS
Marital status (married)	13 (61.9)	34 (65.4)	NS
Full or part time employment	17 (81.0)	26 (50.0)	< 0.05
Disability pension	7 (33.3)	32 (61.5)	< 0.05

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Bipolar subtype I II	 13 (61.9) 8 (38.1)	 37 (71.1) 15 (28.9)	NS
First episode Depressive (Hypo-) manic	 14 (66.7) 7 (33.3)	 39 (75.0) 13 (25.0)	NS
History of rapid cycling*	7 (33.3)	22 (42.3)	NS
Lifetime suicidal ideation	11 (52.4)	35 (67.3)	NS
Lifetime suicide attempts	3 (14.3)	14 (26.9)	NS
Switch after antidepressants	9 (42.9)	29 (55.7)	NS
Family history of mood disorders	12 (57.1)	28 (53.8)	NS
SUDs in family	5 (23.8)	19 (36.5)	NS
Suicide attempts in family	4 (19.1)	12 (23.1)	NS
Committed suicides in family	3 (14.3)	8 (15.4)	NS
Comorbid somatic conditions	9 (42.9)	20 (38.5)	NS
Head traumas	1 (4.8)	10 (19.2)	NS
Lifetime traumatic events	2 (9.5)	19 (36.5)	< 0.05
Tobacco smoking	7 (33.3)	34 (65.4)	< 0.05
Intimate relationships ever	19 (90.5)	50 (96.1)	NS
Children	14 (66.7)	36 (70.6)	NS
MEAN (SD)			
Age**	42.7 (9.8)	45.3 (11.5)	NS
Onset of BP (age)	28.5 (8.7)	28.0 (9.8)	NS
Age at first suicide attempt	30.3 (8.3)	31.4 (12.2)	NS
Age at first hospitalization	33.2 (9.7)	33.6 (10.4)	NS
No. of hospitalizations	4.1 (3.7)	6.0 (5.8)	NS
Longest hospitalizations (months)	2.3 (1.7)	2.7 (1.8)	NS
Max. ann. no. of hospitalizations	1.4 (0.7)	1.7 (0.9)	NS
GAF	88.2 (12.0)	74.4 (15.3)	< 0.01

* Rapid cycling – four or more episodes per year

** Student's *t*-test was performed for normally distributed variables

mean GAF-scores (88.2 vs. 75.0, p<0.01) and employment status, with 81% of the patients from the non-comorbid group being currently employed, and only 44 % from the anxiety comorbid group (p<0.05) (Tab. 4).

The non-comorbid group and group 5 (with comorbid both anxiety and SUDs) varied in the greatest number of variables. The patients with comorbid disorders from both diagnostic groups had significantly more lifetime suicidal ideation (85.7% vs. 52.4%, p<0.05) and lifetime suicide attempts (42.9% vs. 14.3%, p<0.05) than did bipolar patients without comorbidity. They also had a higher mean number of psychiatric hospitalizations (6.9 vs. 4.1, p<0.05) and lower mean GAF-

Table 4. Comparison of the group of BP patients without comorbidity (group 1) with the group of BP patients with anxiety disorders comorbidity (group 3).

VARIABLE	GR 1 (N = 21)	GR 3 (N = 25)	P
	N (%)		(χ^2)
Full or part time employment	17 (81.0)	11 (44.0)	< 0.05
Tobacco smoking	7 (33.3)	15 (60.0)	= 0.08
	MEAN (SD)		(U)
Max ann. no. of hospitalizations	1.4 (0.7)	1.6(0.6)	= 0.07
GAF	88.2 (12.0)	75.0 (14.6)	< 0.01

Table 5. Comparison of the group of BP patients without comorbidity (group 1) with the group of BP patients with both anxiety disorders and SUDs comorbidity (group 5).

VARIABLE	GR 1 (N = 21)	GR 5 (N = 21)	P
	N (%)		(χ^2)
Sex Male Female	 6 (28.6) 15 (71.4)	 13 (61.9) 8 (38.1)	< 0.05
First episode Depressive (Hypo-) manic	 14 (66.7) 7 (33.3)	 20 (95.2) 1 (4.8)	< 0.05
Lifetime suicidal ideation	11 (52.4)	18 (85.7)	< 0.05
Lifetime suicide attempts	3 (14.3)	9 (42.9)	< 0.05
Lifetime traumatic events	2 (9.5)	10 (47.6)	< 0.05
Tobacco smoking	7 (33.3)	15 (71.4)	< 0.05
	MEAN (SD)		(U)
No. of hospitalizations	4.1(3.7)	6.9 (5.1)	< 0.05
GAF	88.2 (12.0)	72.2 (17.3)	< 0.01

scores (72.2 vs. 88.2, p<0.01). Comorbid group 5 patients more often reported having experienced a traumatic event (47.6% vs. 9.5%, p<0.05), more often had a depressive onset (95.2% vs. 66.7%, p<0.05), and were more often male (61.9%vs 28.9%, p<0.05) (Tab. 5).

To assess possible relationships between the type of comorbid disorders and investigated variables, the comorbid anxiety group and comorbid "mixed" group (anxiety + SUDs) were also compared. The "mixed" group patients were significantly more often men (61.9% vs. 28 %, p<0.05) and had more often a depressive onset (95.2% vs. 68%, p<0.05). The "mixed" group reported more often having experienced traumatic events (47.6% vs. 20%, p<0.05), had a higher mean number of psychiatric hospitalizations (6.9 vs. 5.2, p<0.05) and a tendency (p=0.052) to report suicidal ideation more often (85.7% vs. 56%, p<0.05).

DISCUSSION

The comorbidity was high and reached 71.2% in the studied group. Similar results have also been reported in many clinical studies. McElroy et al. [2] assessed comorbidity in a group of 288 BP I and BP II patients, using DSM-IV criteria, as high as 65%, with the prevalence of both anxiety and SUDs of 42%. Suppes et al. [3] studied a heterogeneous group of 261 BP I, BP II, BP

NOS and bipolar schizoaffective patients, and assessed DSM-IV comorbidity at 67%. The prevalence rate of anxiety disorders was 44% and of SUDs 41%. In the epidemiological NCS, where CIDI was also applied, all the patients with BP I fulfilled the diagnostic criteria for at least one comorbid diagnosis. The prevalence of comorbid anxiety disorder was similarly higher (93%) than SUDs (71.1%) [6, 11].

In our study, GAD was the most prevalent anxiety disorder (31.5%). Many other authors have also confirmed its frequent association with BP. In NCS, 42.4% of BP patients fulfilled GAD criteria [12, 13].

The high prevalence rate of SP (27.4%) is somewhat surprising. The reported rates by other authors are lower (10-20%) [2, 14, 15, 16]. Only Taman and Ozpoyraz, in a group of 70 BP I patients in remission, reported a similar rate (25.7%) [17]. It might be possible that our result is higher due to patients mistakenly attributing the criterion of impaired professional, social or interpersonal functioning (criterion E) that was actually the result of the basic disorder to the fact of experiencing phobic anxiety.

SAD was the third most prevalent anxiety disorder in the studied group (19.2%). Although clinical studies assessed SAD in as broad a range as from 1.55% to 31.1%, it was the most prevalent comorbid disorder in NCS, with a rate of 47.2%. Our study suggests, however, the increased prevalence of this disorder in BP cases compared to the general population (3-13%) [18].

The frequent comorbidity of PD±Ago with BP is consistently reported across different studies. In many studies it is the most prevalent comorbid disorder [2, 4, 16, 19, 20]. We have assessed this comorbidity to be 17.8%, which is quite similar to the results of Henry et al. (16%) [19], Simon et al. (17.3%) [21], Cosoff and Hafner (15%) [14], and McElroy et al. (20%) [2] in clinical samples, and those of Chen and Dilsaver (20.8%) [22], who analyzed data from Epidemiologic Catchment Area Study (ECA), or those of Angst (12.5%) in the Zurich Cohort Study [23]. All presented results are much higher than the rates reported for the general population, both of PD (1.5-5%) and of panic attacks not meeting the full criteria of PD (3-5.6%) [18]. Only Vieta et al. assessed the PD-BP comorbidity at 2.32%, but still since the results were low for all the anxiety disorders (7%), PD was the most frequent comorbid anxiety diagnosis [4].

The comorbidity of OCD in BP has been assessed in many clinical and epidemiological studies. Whereas in ECA it reached 21% [24], in the Hungarian epidemiological study [25] and in the Swiss study conducted by Angst [23], it was much lower (respectively 3.2 and 5.4%). Some clinical research reported high rates of comorbidity between BP and OCD (21.1-38.6%) [14, 17, 20, 26], whereas another set of studies reported moderate or low rates (3-13.4%) [2, 16, 19, 21]. Our results (4.1%) do not confirm the very frequently reported phenomenon of BP-OCD comorbidity, and are similar to those obtained by Henry et al. in the group of 318 hospitalized BP patients (3%) [19].

In our sample, alcohol use disorders were very common (30.1%), which is consistent with the results of other clinical (20-33%) [2, 5, 27] and epidemiological (21.4%) [23] studies. It should be mentioned that some studies revealed significantly higher (61.2-66.7%) [11, 26, 28] or lower (6.9%-15.2%) [4, 7, 29] rates, but the studies were quite heterogeneous in many aspects (e.g. base population or diagnostic tools and criteria employed).

In our study, sedatives and hypnotics abuse or dependence was similarly or less prevalent (13.7%) than in groups studied by other authors (2.5-10%), who used structuralized diagnostic tools [2, 5, 7, 23, 27]. On the contrary, Muesser et al. revealed the comorbid sedatives and hypnotics abuse or dependence in a group of 41 BP inpatients to be 20% using a non-structured clinical interview [26]. This may confirm the hypothesis that the use of structured diagnostic tools may be blind to the subgroup of abusing patients in which the sedative-hypnotic use disorders have clearly iatrogenic provenance.

The comorbidity of drugs abuse or dependence in our study, which is lower than cited in the literature, is possibly due to limited access or the high black market price of the substance of abuse in Poland, especially cocaine, which is very often abused by BP patients.

Our research is probably one of very few studies that assessed the comorbidity of nicotine use disorders in BP. We assessed this comorbidity to be 58.9%, which is within the boundaries of that given by Kaplan and Sadock's Synopsis of Psy-

chiatry (70%) [18] and those obtained by Angst in his epidemiological study (46.4%) [23]. Smoking can therefore be a very serious medical issue in this population.

We did not confirm the higher rates of comorbidity in bipolar women than men reported by some authors [30]; moreover, we found comorbidity to be higher in men (80.6%) than in women (64.3%), but the difference was statistically insignificant. We did not confirm the increased prevalence of comorbid anxiety disorders in women either, as did some other authors [30, 31], but it was not the case with SUDs. SUDs with or without inclusion of nicotine use disorders were significantly more prevalent in bipolar men than women (80.7% vs. 57.1% and 58.1% vs. 21.4% respectively). The most prominent difference that was highly significant ($p<0.001$) between sexes was in alcohol use disorder comorbidity. 54.8% of men and only 11.9% of women with BP met the abuse or dependence criteria. Similarly highly significant ($P<0.001$) differences in alcoholism were observed by Henrick et al. (48.4% vs. 20.3%) [32] and Frye et al. (49.1% vs. 29.1%) [33]. Both groups of researchers noticed, however, that the prevalence of alcohol use disorders was approximately 2.5 times higher in bipolar men than men from the general population (in ECA: 23.8% [34]), and 4 to 7 times higher in bipolar women than women from the general population (in ECA: 4.6%[34]). Our results, although confirming the higher alcohol use disorders comorbidity in men, do not support the thesis that it is bipolar women who are more in danger of developing SUDs in comparison to women from the general population.

The next significant difference between sexes concerned nicotine use disorders, which were more prevalent in bipolar men (74.2%) than bipolar women (47.6%). We do not know of other studies that have explored this issue.

We did not find significant differences between bipolar subtypes in general rates of comorbidity, nor did we find any differences in the comorbidity of the whole group of anxiety disorders and SUDs. The lack of statistically significant differences in comorbidity between BP subtypes was also reported by Simon et al [21], McElroy et al. [22] and Suppes et al. [3], who studied relatively large groups. Our results, although statistically insignificant, show slightly higher rates of general and SUDs comorbidity in BP I than in BP II, but lower rates of comorbid anxiety disorders in BPI. This might indicate a possible relationship of SUDs with manic episodes [35, 36], and of some anxiety disorders or their subtypes with bipolar spectrum [37, 38, 39], which have been reported in the literature. The only significant differences between BP subtypes were found in PD-BP comorbidity (24% vs. 4.3%, $p<0.05$) and in nicotine use disorder comorbidity (72% vs. 30.4%, $p<0.01$), which were both more prevalent in BP I. This may indicate the existence of a special relationship of PD with BP I, but not BP II, and requires further research. Other authors have not confirmed this association [2, 23], although in the group studied by Simon et al. [16] 18.3% of BP I patients and 13.9% of BP II patients met the criteria for PD±Ago, but the difference was not significant.

The direct comparisons of non-comorbid BP cases with the "all comorbid" BP cases revealed that the latter were less frequently employed and more often took disability pension, as well as had lower GAF scores, which may represent a worse quality of remission. The "all comorbid" group patients experienced traumatic life events more often and smoked more often.

Further comparisons that were performed confirmed lower employment rate and GAF scores, as well as more frequent smoking and higher maximal annual number of psychiatric hospitalizations, in the group of "anxiety comorbid" patients.

The largest total number of significant differences, also in critical clinical variables, was detected between the non-comorbid BP group and the "mixed comorbid" group. The latter had more frequent suicidal ideations and attempts in anamnesis, a higher total number of psychiatric hospitalizations, lower GAF scores, more traumatic life events, and more often smoked. The patients from the "mixed" comorbid group also more often had a depressive onset of BP.

Our findings of lower employment rates and more frequent disability pension uptake in comorbid BP patients are in congruence with the results of McElroy et al. [2] and Simon et al. [21], who reported poorer professional functioning of BP patients with comorbidity.

Lower GAS scores in BP patients with comorbidity were registered by Young et al. [40], and

some other groups reported poorer functioning or worse quality of remission in those patients [32].

The association of traumatic life events with comorbidity in BP patients detected in our study has not been reported so far. It should be mentioned that the assumed definition of a traumatic event was very broad and not specific. A "traumatic event" had been defined as an experience of sexual, physical or verbal abuse. The results should be therefore treated as explorative and require further research.

The association of comorbidity with suicidality has been also confirmed by many other authors. The increased rates of suicidal ideation or attempts were reported in studies that had taken into account anxiety disorders and SUDs comorbidity with BP only, as well as many different classes of comorbid disorders summarized in one comorbid group.

Our findings that BP patients with comorbid both anxiety and SUDs disorder are particularly suicidal are similar to those of Pini et al., who compared four groups of BP patients: with comorbid SUDs, with comorbid SUDs and other psychiatric disorders, with comorbid non-SUDs, and without comorbidity. In the logistic regression model, they detected a significant relationship of comorbidity with disorders from both diagnostic groups (i.e. SUDs and other psychiatric disorders) with attempted suicide rate [31].

Our results also confirmed the relationship of comorbidity in BP with higher hospitalization rates, a fact observed by some other authors [41, 42, 43].

To our knowledge, the association of comorbidity with smoking has not been reported so far. If this result were replicated, and the character of this relationship further clarified, it would be of great clinical significance.

The main limitations of the present study are: 1) a relatively small group of outpatients, which prevents undertaking a multivariate analysis and make the findings of preliminary rather than confirmatory character, 2) the lack of a control group, which disallows comparisons with a normal population or another psychiatrically ill group, 3) retrospective assessment of comorbidity and investigated variables, which may influence the reliability of the analyzed data, 4) possible biases (Berkson's bias [44], interviewer's bias) that also decrease reliability and prevent the generalization of the results. Our study has, however, some noticeable strengths, which are: 1) the relative heterogeneity of the studied group (only BP I and BP II patients were assessed), 2) the use of structured assessment instruments and DSM-IV criteria, which increase the reliability and comparability of the results, 3) the inclusion of patients in remission only, which supports good compliance and possibly positively influences the reliability of the data.

CONCLUSIONS

Lifetime psychiatric comorbidity is a widespread problem in BP. It is associated with less favourable clinical characteristics of BP, but the character of these associations and the nosological status of comorbid cases require further research. There may exist gender – and BP subtype – specific patterns of comorbidity in BP which need to be further clarified.

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