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COMORBIDITY AND MULTIMORBIDITY IN PATIENTS WITH SCHIZOPHRENIA AND BIPOLAR DISORDER: SIMILARITIES AND DIFFERENCIES

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SUMMARY

Background: *There is a need for better understanding and research of the comorbidity structure in schizophrenia and bipolar disorder.*

Objective: *To assess the prevalence of somatic and psychiatric comorbidity in schizophrenia and bipolar affective disorder treated at the University Hospital Centre Zagreb.*

Method*: This retrospective study compares the prevalence of comorbid diagnosis of somatic and psychiatric disorders in 192 patients with schizophrenia and 97 patients with bipolar disorder. The diagnoses were established according to ICD-10 criteria. The data were collected from hospital medical documentation.*

Results: *Patients with bipolar disorder had more both somatic (67.1% vs. 50.6%) and psychiatric (29.9% vs. 10.9%) comorbidity than patients with schizophrenia. The three most prevalent somatic comorbidites in patients with bipolar disorders were cardiovascular (22.6%), endocrinological (22.6%), and gastrointestinal (16.4%) disorders while neurological (11.4%), gastrointestinal (10.9%) and endocrinological (9.3%) disorders were the most frequent in patients with schizophrenia.*

Conclusion*: The exact prevalence and nature of the somatic and psychiatric comorbidity in patients with schizophrenia and bipolar disorder is still unclear and further research is needed.*

Key words: *schizophrenia - bipolar disorder - comparative comorbidity*

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INTRODUCTION

Schizophrenia and bipolar disorder are two of the most incapacitating and life shortening mental disorders. Comparative study of psychiatric and somatic comorbidity in schizophrenia and bipolar disorder could have theoretical and practical implications (Jakovljević & Crnčević 2012). Possible differences in comorbidity profile may be related to specific psychopathology in these two diagnostic entities (Jakovljević et al. 1993). From the Kraepelin's time psychiatrists have debated whether schizophrenia and bipolar disorder were the two distinct mental disorders with different etiopathogenesis, course and prognosis or were more connected mental disorders including that they could represent different ends of the common pathophysiological processes.

Patients with schizophrenia as well as patients with bipolar disorder have higher mortality rates in comparison with general population, both as a result of natural and unnatural causes (Hoang et al 2011). The contribution of the natural causes to excess mortality has been increasingly recognized, particularly due to coronary heart disease, stroke, and cancer. The simultaneous presence of multiple pathological conditions in the form of comorbidity and multimorbidity is more a rule than an exception in all populations of psychiatric patients, particularly in those with schizophrenia or bipolar disorder (see Jakovljević & Crnčević 2012). Chronic somatic diseases accounted for half of the excess mortality in patients with schizophrenia or bipolar disorder (Laursen et al. 2011). In clinical practice comorbidity is underrecognized, underdiagnosed, underestimated and undertreated so that we can speak about comorbidity anosognosia. Although it is generally accepted that somatic and psychiatric comorbidity is associated with both schizophrenia and bipolar disorder, the exact prevalence/epidemiology and nature of these phenomena are still unclear.

The aim of this preliminary study was to assess differences and similarities in comorbidity prevalence and structure between schizophrenia and bipolar disorder.

SUBJECTS AND METHODS

Data source and study population

The data were collected from hospital medical documentation. The sample comprised of consecutively admitted patients with the diagnosis of schizophrenia and bipolar disorder on the Department of Psychiatry, University Hospital Center Zagreb in 2011. Altogether 289 patients (141 males and 148 females) were included, and each patient was not included if rehospitalised. The mean age of the sample was 43.03±13.94 years.

Table 1. Distribution of age and gender in the sample and the differences between the groups based on gender (N=289)

	Age Mean (SD)	Age by gender Male	Female	t	p
General	43.03(13.94)	41.39(12.8) n=141	44.5(14.80) n=148	1.962	0.051
Shizophrenia (n=192)	39.5 (12.03)	37.4(10.06) n=95	41.6(13.44) n=97	2.409	0.017
Bipolar (n=97)	49.8 (14.97)	49.4(14.23) n=46	50.24(15.7) n=51	0.262	0.794

The sample consisted of 192 patients (95 males and 97 females) with the diagnosis of schizophrenia and 97 patients (46 males and 51 females) with the diagnosis of bipolar disorder established by the ICD-10 criteria by the attending psychiatrist.

The groups did not differ in frequency of male and female patients but female patients were older than male in the group of schizophrenia. Distribution by age and gender in the whole sample and in the group of schizophrenia and bipolar patients and the differences between the groups is shown in table 1.

Males were younger than females in both groups.

Statistical analysis

Percentages were used to describe categorical variables, and means and standard deviations to summarize continuous variables. T-test and chi square test were performed for comparisons between the groups.

RESULTS

The prevalences of comorbid medical disorders by category and differences between the groups of schizophrenia and bipolar disorder were assessed with chi-square test and shown in table 2.

The comorbidity (somatic or psychiatric) was present in 58.4% of patients with schizophrenia and 80.5% of patients with bipolar disorder. The groups significantly differed in the presence of psychiatric, cardiovascular and endocrinological disorders. Psychiatric comorbidity, as well as cardiovascular and endocrinological disorders were more prevalent in the group of bipolar disorders.

The most prevalent somatic disorder in comorbidity with schizophrenia was group of neurological disorders, followed by gastrointestinal disorders. The most prevalent comorbidity in bipolar patients were cardiovascular and endocrinological disorders.

Table 2. Differences in comorbidity between patients with schizophrenia and bipolar disorder

	Schizophrenia n (%)	Bipolar n (%)	*x*	*p*
Psychiatric disorders	21 (10.9)	29 (29.9)	16.190	0.0001
Cardiovascular disorders	14 (7.2)	22 (22.6)	13.994	0.0001
Gastrointestinal disorders	21 (10.9)	16 (16.4)	1.783	0.1950
Tumors	4 (2.08)	5 (5.1)	2.015	0.1680
Endocrinological disorders	18 (9.3)	22 (22.6)	9.567	0.0030
Diabetes	8 (4.1)	9 (9.2)	3.041	0.1100
Thyroid dysordes	13 (6.7)	13 (13.4)	3.461	0.0810
Respiratory disorders	8 (4.1)	1 (1.03)	2.100	0.2810
Neurological disorders	22 (11.4)	8 (8.2)	0.714	0.5400
Epilepsy	8 (4.1)	1 (1.03)	2.100	0.2810
Locomotor system disorders	9 (4.6)	8 (8.2)	1.475	0.2890
Gynecologic disorder	7 (3.6)	2 (2.06)	0.536	0.7230
No somatic comorbidity	95 (49.4)	32 (32.9)	7.113	0.0080
No psychiatric comorbidity	171 (89)	68 (70.1)	16.190	0.0001
No comorbidity in general	80 (41.6)	19 (19.5)	13.949	0.0001

Table 3. Metabolic disorders in schizophrenia and bipolar disorder

	Schizophrenia n (%)	Bipolar n (%)	*x*	*p*
Arterial hypertension	11 (5.7)	18 (18.5)	11.746	0.001
Diabetes	8 (4.1)	9 (9.2)	3.041	0.110
Hypercholesterolemia	85 (44.2)	53 (54.6)	3.237	0.079
Decreased HDL	98 (51)	38 (39.1)	3.283	0.078
Hypertrigliceridemia	86 (44.7)	49 (50.5)	0.854	0.381

Table 4. Gender differences in metabolic disorders in schizophrenia and bipolar disorder

Metabolic disorder	Schizophrenia		*x*	*p*	Bipolar		*x*	*p*
	Male n (%)	Female n (%)			Male n (%)	Female n (%)		
Arterial hypertension	1 (1.0)	10 (10.3)	7.614	0.0100	11 (23.9)	7 (13.7)	1.6610	0.290
Diabetes	2 (2.1)	6 (6.1)	2.001	0.2790	5 (10.8)	4 (7.8)	0.2630	0.732
Hypercholesterolemia	41 (43.1)	44 (45.3)	0.765	0.7710	25 (54.3)	28 (54.9)	0.0350	1.000
Decreased HDL	46 (48.2)	40 (41.2)	0.765	0.4660	23 (50)	26 (50.9)	0.0001	1.000
Hypertrigliceridemia	63 (66.3)	35 (36.1)	16.006	0.0001	25 (54.3)	13 (25.4)	10.3260	0.002

Table 5. Gender differences in comorbidity between patients with schizophrenia and bipolar disorder

	Schizophrenia		*x*	*p*	Bipolar		*x*	*p*
	Male n (%)	Female n (%)			Male n (%)	Female n (%)		
Psychiatric disorders	16 (16.8)	5 (5.1)	6.7300	0.0110	12 (26)	17 (33.3)	0.606	0.500
Cardiovascular disorders	3 (3.1)	11 (11.3)	4.7530	0.0490	15 (32.6)	7 (13.7)	4.918	0.031
Gastrointestinal disorders	13 (13.6)	8 (8.2)	1.4560	0.2550	8 (17.3)	8 (15.5)	0.051	0.990
Tumors	0	4 (4.2)	4.0010	0.1210	2 (4.3)	3 (5.8)	0.116	1.000
Endocrinological disorders	2 (2.1)	16 (16.4)	11.6970	0.0010	5 (10.8)	17 (33.3)	6.960	0.014
Diabetes	2 (2.1)	6 (6.1)	2.0010	0.2790	5 (10.8)	4 (7.8)	0.263	0.732
Thyroid disorders	0	13 (13.4)	13.6570	0.0001	1 (2.1)	12 (23.5)	9.504	0.002
Respiratory disorders	2 (2.1)	6 (6.1)	2.0010	0.2790	0	1 (1.9)	0.911	1.000
Neurological disorders	13 (13.6)	9 (9.2)	0.9180	0.3710	3 (6.5)	5 (9.8)	0.344	0.718
Epilepsy	2 (2.1)	6 (6.1)	2.1750	0.1670	1 (2.1)	0	1.120	0.474
Locomotor disorders	3 (3.1)	6 (6.1)	0.9850	0.4790	3 (6.5)	5 (9.8)	0.344	0.718
No somatic comorbidity	53 (55.7)	42 (43.2)	2.9950	0.1120	14 (30.4)	18 (35.2)	0.255	0.669
No psychiatric comorbidity	79 (83.1)	92 (94.8)	6.7300	0.0110	34 (73.9)	34 (66.6)	0.606	0.508
No comorbidity in general	40 (42.1)	40 (41.1)	0.0151	1.0000	11 (23.9)	8 (15.6)	0.263	0.798

The differences between metabolic disorders in the group of schizophrenia and bipolar disorder are presented in table 3.

Arterial hypertension was significantly more often diagnosed in the group of patients with bipolar disorders. The groups did not differ in the presence of diabetes, hypercholesterolemia, decreased HDL and hypertrigliceridemia. We also assessed if the differences in metabolic disorders in the groups were based on gender (Table 4).

The group differences based on gender were present for hypertriglicidemia. Males had hypertriglicidemia more often than females in both groups. In the group of schizophrenia females had hypertension in comorbidity more often than males.

The gender differences based on comorbidity in both groups of the patients were also assessed using chi-square test and presented in the table 5.

In the group of schizophrenia patients, males and females differed in the presence of psychiatric, endocrinologic and cardiovascular comorbidity. Females had more cardiovascular and endocrinologic disorders, but males had more psychiatric disorders in comorbidity.

In the group of bipolar patients, the males and females significantly differed in the presence of cardiovascular and endocrinological disorders. Endocrinological disorders were more present among females, but males had more cardiovascular disorders in comorbidity.

DISCUSSION

The prevalence and structure of the comorbidity in schizophrenia and bipolar disorder has been the subject of increasing interest. Our preliminary study corroborated high rates of somatic and psychiatric comorbidity in patients with schizophrenia and particularly in those with bipolar disorder. Patients with bipolar disorder had more both somatic (67.1% vs. 50.6%) and psychiatric (29.9% vs. 10.9%) comorbidity than patients with schizophrenia. According to some authors psychiatric comorbidity is a prevailing hallmark of bipolar disorder (Kemp et al. 2010) because 50-97% of patients with bipolar I meet criteria for a concurrent mental disorder (Krishnan 2005, Kemp et al. 2010). The lower prevalence of psychiatric comorbidity in our study may be explained with a general psychiatrists' tendency of use only one main diagnosis for clinically complex and polymorphic syndromes. Psychiatric comorbid syndromes may be considered as integral to bipolar disorder or schizophrenia (Buckley et al. 2009). Psychiatric comorbidity is a very intriguing issue and raises many fundamental questions about the nature of psychopathology in schizophrenia and bipolar disorder. For longer than a century psychiatrists have debated whether schizophrenia and bipolar disorder were two distinct mental disorders or were more connected. The phenomenon of high rates of psychiatric comorbidity may indicate that psychiatric classification systems are not optimal yet (see Jakovljević & Crnčević 2012).

According to the definition of comorbidity as „the statistical association of two distinct diseases in the same individual at a rate higher than expected by chance"(see Bonavita & de Simone 2008), it is plausible to compare our results with the relevant literature. Beyer et al. (2005) described the next distribution of the comorbid systemic illnesses in 1379 bipolar outpatients: endocrine and metabolic diseases (13.6%), diseases of the circulatory system (13.0%), the diseases of the nervous system and sense organs (10.7%), diseases of the musculosceletal system and injury (10.7%), infectious and parasitic disease (7.6%), disease of respiratory system (7.3%), diseases of the digestive system (7.3%), diseases of genitourinary system (3.7%), neoplasm (2.8%), the diseases of the skin and subcutaneous tissues (2.0%), disease of blood (1.5%), complications of pregnancy, childbirth, and the puerperal (0.4%) and other (0.9%). The most common specific diseases included cardiovascular diseases/hypertension (10.7%), COPD/asthma (6.1%), diabetes (4.3%), HIV infection (2.8%) and hepatitis C infection (1.9%). In this study 56% of bipolar patients did not have any significant comorbid medical conditions, 26% had one comorbid medical condition, 13% had two, 3% had three, and 2% had four or more conditions. According to Moreira et al. (2011) the most prevalent conditions in 195 outpatients with bipolar disorder were: migraine (31.8%), hypothyreoidism (24.1%), hypertension (11.3%), traumatic brain injures (10.3%), asthma (9.7%), epilepsy (8.2%), diabetes (5.1%), stroke (2.1%) and hyperthyreoidism (1%)

According to the literature, somatic comorbidity was found in 20 to 74% patients with schizophrenia (Oud & de Yong 2009). It seems that diabetes mellitus, cardiovascular disease, hypertension, osteoporosis, respiratory disease, obesity and metabolic syndrome are among the most common medical comorbidities in patients with schizophrenia (Iacovides & Siamouli 2008), but it is not confirmed in all studies (see Harris 1988). Nasrallah et al. (2006) reported that 33.2% of the 1448 patients with schizophrenia in the CATIE trial had hypertension, 10.4% diabetes mellitus, 47.3% dyslipidemia when defined by elevated serum triglycerides and 48.3% when defined as low serum HDL. In one of the largest study with 4,721 patients with schizophrenia, and 2,176 patients with bipolar disorder, bipolar patients were 19% more likely to have diabetes, 44% more likely to have coronary artery disease , and 18% more likely dyslipidemia (Kilbourne et al. 2007). According to Jukić et al. (2009) the leading somatic disorders in inpatients with schizophrenia in the year 2008 were: endocrinological disorders 22%, anemia 20%, cardiovascular disease 18%, infectious diseases 17%, skin and subcutaneous diseases 10%, gastrointestinal diseases 6% what was significantly different with the year 1955 when the leading somatic diseases were infectious diseases 17%, tuberculosis 15%, the lower respiratory system chronic illnesses 10%, bone and muscle diseases 8% and cardiovascular disease.

In our study cardiovascular disorders were statistically more common in patients with bipolar disorders (22.6%) than in patients with schizophrenia (7.2%). Arterial hypertension was statistically more frequent in patients with bipolar patients (18.5%) than in patients with schizophrenia (5.7%). Diabetes was also more frequent in patients with bipolar disorder (9.2%) than in patients with schizophrenia (4.1%), but without statistical significance. Our results are opposite to those of Coclami & Cross (2011) who found schizophrenia to be the most common diagnosis with diabetes. The estimated prevalence of cardiovascular disease risk factors varies widely in the literature (see table 6).

Disturbances in lipid homeostasis are excellent candidates for a pathological role in both schizophrenia and bipolar disorder as well as in their somatic comorbidity since cholesterol play important roles in constituting the cell membrane, myelination and synaptogenesis (Vila-Rodriguez et al. 2011). As a universal precursor of steroidgenesis cholesterol can regulate gen transcriptions indirectly via steroid receptors and also it can promote selective and efficient signal transduction (Hayashi T & Su TP 2010). Higher comorbidity is generally associated with some personality traits like high harm-avoidance and low self-directedness (Aukst-Margetić et al. 2009).

The prevalence of specific comorbidity with regards to gender in schizophrenia and bipolar disorder appears with conflicting results. Generally, medical and psychiatric comorbidity is more common in women than in man (Krishnan 2005). In schizophrenia group, cardiovascular disorders were more common in females than in males (11.3% vs. 3.1%), while the opposite was found in bipolar disorder: cardiovascular disorders were more frequent in males than in females (32.6% vs. 13.7%). The prevalence of endocrine disorders in general was statistically higher in females than in males in both groups (schizophrenia 16.4% vs. 2.1%; bipolar disorder 33.3% vs. 10.8%) In both groups thyroid disorders were

T**able 6**. Estimated prevalence and relative risk of modifiable cardiovascular disease risk factors in schizophrenia and bipolar disorder compared to the general population (from De Hert et al. 2009)

Modifiable risk factors	Schizophrenia	Bipolar disorder
Smoking	50-80% RR: 1.5-2	54-68% RR: 1-2
Hypertension	19-58% RR: 2-3	35-61% RR: 2-3
Dyslipidemia	25-69% RR up 5	23-38% RR:up 3
Diabetes	10-15% RR 2	8-17% RR:1.5-2

more common in females (schizophrenia 13.4% vs. 0, and bipolar disorder 23.5% vs. 2.1%). Hypertriglyceridemia was found statistically more frequently in males than in females in both schizophrenia (66.3% vs. 36.1%) and bipolar disorder (54.3% vs. 25.4%) groups.

Somatic comorbidity in schizophrenia and bipolar disorder may be or may be not etiologically related so that theoretically three types can be recognized: etiological, interactional and coincidental type (Jakovljević 2009, Jakovljević et al. 2010; Jakovljević & Crnčević 2012). Our preliminary study was not designed to differentiate comorbidity types what is very important issue for the future research. Future research should reveal whether comorbidity in schizophrenia and bipolar disorder has a real specific and stable structure or the structure of comorbidity is variable and coincidental. Very important issue is also how to distinguish pathogenic from pathoplastic factors in comorbidity.

This preliminary study represents only an initial step and has many limitations. The cross-sectional data obtained retrospectively from medical records are not as accurate as information obtained in prospective and more structured research settings. Some crucial variable such as comorbidity onset could not be obtained. Differences in age between patients with schizophrenia and bipolar patients may contribute to the differences in comorbidity results. Patients with bipolar illness due to its better functioning may seek help for various somatic complains more often than patients with schizophrenia. A larger sample size of the both groups, particularly of the bipolar disorder group would be more beneficial.

CONCLUSSION

Our study offers just a glimpse in the comparative comorbidity in schizophrenia and bipolar disorder. The exact prevalence and nature of the somatic and psychiatric comorbidity in patients with schizophrenia and bipolar disorder is still unclear and further research is needed. Future research will require a prospective, longitudinal study comparing simultaneously comorbidity in patients with different major psychiatric disorders.

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