

**Craiova University of Medicine and Pharmacy  
DOCTORAL SCHOOL**

**DOCTORAL THESIS  
ABSTRACT**

**SOMATIC COMORBIDITIES IN MAJOR AFFECTIVE  
DISORDERS**

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## **CONTENTS**

<b>INTRODUCTION. IMPORTANCE OF THE ISSUE</b>	<b>3</b>
<b>UNIPOLAR DEPRESSIVE DISORDER</b>	<b>3</b>
<b>BIPOLAR AFFECTIVE DISORDER</b>	<b>4</b>
<b>SOMATIC COMORBIDITIES</b>	<b>4</b>
<b>RESEARCH HYPOTHESIS. PURPOSE OF THE PAPER</b>	<b>5</b>
<b>RESEARCH OBJECTIVES</b>	<b>5</b>
<b>METHODOLOGICAL COORDINATES</b>	<b>5</b>
<b>RESULTS</b>	<b>6</b>
<b>Somatic comorbidities in unipolar depressive disorders</b>	<b>6</b>
<b>Somatic comorbidities in bipolar affective disorders</b>	<b>7</b>
<b>DISCUSSION</b>	<b>7</b>
<b>CONCLUSIONS</b>	<b>9</b>
<b>BIBLIOGRAPHY</b>	<b>11</b>

## **INTRODUCTION. IMPORTANCE OF THE ISSUE**

*Depression* is a major psychiatric disorder with the most common incidence and high severity and recurrence, disease which increases the number of somatic comorbidities and correlates directly with lowering the overall functioning, physical and social [1] as well as of the quality of life of the patient and his family [2]. The prevalence and incidence are currently estimated reaching a total of over 350 million people affected globally, the depressive disorder having become in recent decades a real public health problem, accounting currently as the leading cause of disability expressed in lost years of life due to premature mortality (Years of Life Lost - YLL) [3]. *Bipolar disorder* leads to a major impact on the condition of the affected person, affecting both individually the quality of life of patients and their family as well as socially, through the economic burden caused by the disease. Disabilities caused by bipolar disorder places it among the top ten disabling medical conditions, with a percentage of 2.5% of total YLD [4]. The most important somatic comorbidities of the two affective disorders are the cardiovascular diseases, diabetes, stroke, cancer, chronic pain, viral hepatitis, obesity and neurodegenerative diseases.

This paper attempts to assess somatic comorbidities associated with the two major affective disorders, depression and bipolar disorder, as well as how hospitalization indicators are influenced correlated with socio-demographic features of the individuals diagnosed and hospitalized for treating these diseases.

## **UNIPOLAR DEPRESSIVE DISORDERS**

Through symptoms and consequences, through the development of recurrent or chronic types, the depressive disorder represents one of the psychiatric disorders that lead to significant changes in the life and socio-professional status of the patients. Symptoms of depressive disorder indicate depressed mood most of the day, almost every day, without being influenced by definite or specific circumstances and continuously present in at least for the last two weeks, loss of interest or pleasure in activities that were normally enjoyable, asthenia, fatigue. Additional symptoms that may commonly be present in the case of depression are loss of self-confidence, feelings of guilt, culpability, recurrent thoughts of death or suicide, suicidal behaviour, diminished focus of attention and concentration, sleep disturbances (insomnia, hypersomnia, superficial sleep, poor quality sleep), changes in appetite (decrease or increase in appetite) resulting in changes of body weight ( $\pm 5\%$  in comparison with the previous

month). Current treatment guidelines suggest both psychopharmacological option as well as psychological or socio-therapeutic options, by having taken into account both the characteristics and needs of the patient [5, 6, 7].

The evolution of depressive disorder is marked by intensity and severity of symptoms, with a maximum duration of clinical and therapeutic expectancy ranging from four weeks up to two years, divided into premorbid stage, prodromal stage, depressive episode, remission, relapse and recurrence.

## **BIPOLAR AFFECTIVE DISORDER**

Type I Bipolar disorder affects approximately 0.8% of the adult population, epidemiological data ranging between 0.4% and 1.6%, with variations arising from ethnic and cultural diversity, [8], while for type II bipolar disorder, currently being estimated a 0.5% frequency of this diagnosis in the adult population.

As major psychiatric disorder, the bipolar disorder shows a chronic course, alternating episodes of mania, characterized by mental and physical hyperactivity, exaggerated optimism and self-confidence, excessive irritability, aggressive behavior, reduced sleeping needs, grandeur illusions, thoughts loss, unorganized speech, impulsiveness, rational and attention incapacity, excessive social decisions, and in the most severe cases, delusions and hallucinations [9] and depressive for intervals from several days to several months. Through dramatic or subtle mood changes, this condition has major consequences on both individual and social levels, especially due to behavioral expressions generated by intense emotional cycles that do not follow a regular pattern.

Although current therapies do not provide complete solutions for bipolar disorder, their efficient use can diminish morbidity and mortality associated with the disease, the specific objectives of the management of bipolar disorder requiring establishment and maintenance of adherence and compliance with the therapy, patient monitoring for early identification of new episodes, reduction of hetero- and self-harm risks and minimizing functional deficiencies [10]

## **SOMATIC COMORBIDITIES**

Epidemiological surveys have shown, both for unipolar depressive disorder and bipolar affective disorder, high rates of comorbid associations with various medical conditions which significantly complicate prognosis and psychopharmacological intervention as well as quality of response. The occurrence of somatic comorbidity represents a major risk factor for the development of psychiatric disorders, studies in the field indicating a significant increase of 1.6 to 3 times in the mortality rate among patients with mental illness and associated medical conditions [11]. These data raise the question of specific

care needs for such patients, both at primary and general medical level, requiring a consensus on the care priorities.

### **RESEARCH HYPOTHESIS. PURPOSE OF THE PAPER**

Psychiatric epidemiology research places major affective disorders on first place both in terms of the proportion of hospital admissions and frequency of comorbidities. Somatic comorbidities interact in an important measure with the clinic and especially with the evolution of these sufferings. Evaluation and analysis of comorbidities cannot be separated from hospitalization indicators or from socio-demographic characteristics of patients.

The overview research of these data, as well as emphasizing clinical-evolutionary course correlations, could help to improve development and planning strategies and measures of primary and secondary psycho-prophylaxis, but also of the discovery of predictive factors. The current research aims at assessing somatic comorbidity in relation to hospitalization and socio-demographic indicators in the case of major affective disorders, as well as the importance of their clinical course.

### **RESEARCH OBJECTIVES**

- Evaluation of somatic comorbidities in patients hospitalized for major affective disorders.
- Study of hospitalization indicators and socio-demographic characteristics of patients hospitalized for major affective disorders.
- Highlighting relationships of somatic comorbidity and socio-demographic characteristics with the evolution of major affective disorders.

### **METHODOLOGICAL COORDINATES**

The retrospective clinical study of patients hospitalized in Craiova Neuropsychiatry Hospital with a diagnosis of unipolar depressive disorders and bipolar affective disorders, between 1 January 2008 - 31 December 2012. The study was conducted in accordance with ethical clinical research and approval from Ethics Committee of the Hospital Clinic of Neuropsychiatry Craiova. The data were drawn from observation sheets.

Having applied inclusion and exclusion criteria, there were established two working groups, the working group A = 5054 patients diagnosed with unipolar depressive disorders, hospitalized in Craiova Neuropsychiatric Hospital between 1 January 2008 - 31 December 2012 and working group B = 270 patients diagnosed with bipolar disorder hospitalized in Craiova Neuropsychiatric Hospital between 1 January 2008 - 31 December 2012.

For data processing we used Microsoft Excel (Microsoft Corp., Redmond, WA, USA) with XLSTAT suite for MS Excel (Addinsoft SARL, Paris, France). The parameters measured for subjects included in this study were stored in Microsoft Excel files (\* .xls).

## RESULTS

In the Neuropsychiatric Hospital Craiova there were made a number of 18 306 hospital admissions, out of which 11168 - 61.01% with the diagnosis of unipolar depressive disorder (TDU), 687 - 3.75% for the diagnosis of bipolar disorder (TAB), and 6451 - 35.24% for other diseases. It can be observed an upward trend in terms of admissions for the diagnosis of TDU, from 1841 to 57.17% in 2008 to a peak of 2741 in 2011 - 66.06%), while the TAB, the same year - 2011, there was recorded a maximum number of hospitalizations, 168 - 4.05%). There is a differential distribution of the two sexes, with a clear dominance of women diagnosed with major affective disorders (57.76%), consistent with epidemiological data from specialized literature and a report reversed for other psychiatric diagnoses, the predominant male patients (62.28%). ( $p < 0.001$ ). Distribution of hospital admissions for diagnoses of major affective disorders according to age of patients showed a clear majority of the age group 45-64 years (88.94%) for both sexes (males - 38.65% and women - 50.29) ( $p < 0.001$ ). It has been noticed a prevalence of urban environment, explained by the level of addressability to the two hospitals. Among patients hospitalized with a diagnosis of major affective disorder, the most numerous were those active in the labor market (3097 patients - 58.17%), followed by those withdrawn from professional activity due to disability caused by mental illness (1189 patients - 22.33%).

Unfavorable evolution of major affective disorders caused repeated hospitalizations in psychiatric clinics of patients with these diagnoses, in the five years included in our study more than half of them (51.48%) were hospitalized more than twice, out of which 557 - 10.46 % recorded in the source having more than 5 admissions. It has also been noted that there is an approximately equal distribution on the sex of patients and the number of admissions that they had. The most common duration of hospitalization for the treatment of major affective disorder in the Neuropsychiatric Hospital Craiova was between more than one week and one month (81.25%), followed by short-term, up to 7 days (16.10 %), while the long-term hospitalization, more than 1 month, accounted for only 2.65%.

### **Somatic comorbidity in unipolar depressive disorders**

From a quantitative point of view, it has been emphasized a predominance of patients who had no associated somatic disease (2653 patients - 52.49%), whereas

patients who had multiple diagnoses, most were those with one comorbidity (935 patients - 18.50%) or two associated somatic diseases (900 patients - 17.81%).

Cardiovascular comorbidities (myocardial infarction, hypertension, coronary artery disease, heart failure) were mentioned in the medical records for 1923 admissions (17.22%) achieved in the studied time frame, 10.01% being females and 21.7% males. Diabetes was present during the five years of study in the documentation completed for 1055 admissions (9.45%), women being more than twice as many (6.52%) than men (2.93%) ( $p < 0.001$ ). Neurological and neurodegenerative disorders were recorded in the 895 admissions (8.01%) of patients diagnosed with this disease category.

Other somatic disorders (endocrine, digestive, blood dyscrasias, and malignancies) highlighted in medical records and which were not individually significant clinical entities were grouped according to the methodology named as "other comorbidities" and were present in the case of 2345 (21.00%) hospital admissions carried out in the two hospitals during the time studied.

### **Somatic comorbidities in Bipolar Affective Disorder**

Somatic comorbidities related to bipolar disorder were present in half of patients of the group B=270 (37.41%). Cardiovascular diseases represented the main comorbidity related to bipolar affective disorder, being registered in source documents made for 98 – 14.26% of the 687 hospitalizations made. Diabetes mellitus, both type 1 and type 2, was mentioned as somatic comorbidity related to psychiatric diagnosis of bipolar disorder in the case of 51 hospitalizations (7.42%), and, neurological and neurovegetative disorders were present in the case of 37 hospitalizations made for patients from group B=270, and in a number almost double for women patients (3.49%), compared to men (1.89%). The other somatic disorders related to the diagnosis of Bipolar Affective Disorder diagnosis were mentioned in medical documents for 88 hospitalizations (12.81%).

## **DISCUSSIONS**

Thus, we could see a more reduced frequency of comorbid medical conditions for bipolar patients in group B=270 (27.41%), compared to depressive patients in group A=5054 (47.51%), and the frequent association of two or even more somatic diseases in the same patients psychiatrically diagnosed with Unipolar Depressive Disorder. A remarkable difference was registered in the case of patients in whom documents two somatic diseases related to psychiatric diagnosis were mentioned (17.81% - TDU vs. 11.11% TAB).

Thus, the presence of these related medical conditions constitutes a risk factor for the evolution of both nosologic entities, the progressive complications being met both in the case of psychic disease and somatic disease, leading to high mortality rates and special care needs. By comparing the number of related comorbidities, between the two pathologies, we saw that patients with TDU are inclined to have more comorbid associations than those with TAB, almost half of them having at least other somatic pathology, compared to less than 40% of those with TAB ( $p < 0,05$ ). The difference between the two psychiatric entities, concerning the presence of cardiovascular comorbidities is statistically significant ( $p < 0,05$ ).

Data obtained concerning cardiovascular disorders in bipolar patients from the studied group also underline the important role that cardiovascular diseases have concerning the evolution of the psychic disease, mentioned in previous studies [12, 13], highlighted by the average length of stay almost 50% higher in bipolar patients, compared to depressive patients, the difference being highly statistically significant ( $p < 0,001$ ).

We identified a difference concerning the average length of stay for patients with major affective disorders and comorbid diabetes mellitus, the data obtained showing for depressive patients in group A=5054 an average length of hospitalization of  $12.01 \pm 6.14$  days, while for bipolar patients from group B=270, the average length of stay was  $15.31 \pm 10.64$  days, the difference being statistically significant ( $p < 0,05$ ).

The higher frequency of neurological complications in the case of group A=5054 is statistically significant ( $p < 0,05$ ), being able to exist a higher influence of this somatic comorbidity on TDU psychiatric pathology. The effects of this risk potential for the comorbid association between neurological diseases and bipolar affective disorder was also highlighted by the sensibly higher average length of hospitalization for patients in group B=270 ( $15.05 \pm 8.27$  days), compared to those in group A=5054 ( $12.31 \pm 5.84$  days), the difference being significant ( $p < 0,05$ ).

We found a higher frequency of the association of some somatic comorbidity with TDU than with TAB ( $p < 0,01$ ). However, all the other somatic comorbidities related to both unipolar depressive disorder (21.00%) and bipolar affective disorder (12.81%) were constituted in prognostic factors of the unfavorable evolution of psychic disorders (Test  $p < 0,05$ ).

For both patients with TDU ( $p < 0.001$ ) and those with TAB ( $p < 0.001$ ), there are highly significant differences between the frequency of comorbidities in patients with a different number of hospitalizations, the tendency being that patients with several hospitalizations have an increased number of related somatic diseases. Thus we can statistically maintain the statement that the accumulation of some other comorbidities aggravate the psychiatric disease, determining frequent re-hospitalizations, with the amplification of clinical, social and economic effects generated by these, aspect also confirmed in the specialized literature [14, 15].

### CONCLUSIONS

1. During the period January 1<sup>st</sup>, 2008 – December 31<sup>st</sup>, 2012, between the two Psychiatry clinics of the Craiova Clinical Neuropsychiatry Hospital, were made 18.306 hospitalizations, of which 11.168-61,01% with the diagnosis of unipolar depressive disorder (TDU) and 687 – 3,75%, with the diagnosis of bipolar affective disorder (TAB).
2. The number of hospitalizations for major affective disorders recorded an increasing tendency, highly statistically significant ( $p < 0,001$ ), with maximum values in 2011: 2741 hospitalizations – 66,06% for TDU and 168 hospitalizations – 4,05% for TAB, with an average age of  $52,19 \pm 6,65$  years old (men –  $53,73 \pm 6,25$  years old, women –  $51,07 \pm 6,73$  years old).
3. The number of hospitalizations for major affective disorders was highly significantly ( $p < 0,01$ ) related to female gender – 57,76%, age group 45-64 years old – 88,94% (men – 38,65%, women – 5,29%), urban environment – 59,07%, employee status for women – 60,93% and disability retiree for men.
4. The same socio-demographic characteristics maintain their significant influence on the frequency of hospitalizations for the two entities: TDU ( $p < 0,001$ ) and TAB ( $p < 0,05$ ).
5. Somatic comorbidities were recorded in 2401 patients with TDU – 47,51%, more frequent in women ( $p < 0,05$ ), and in 101 patients with TAB – 37,41%, also more frequent in women ( $p < 0,05$ ).
6. The main somatic comorbidities were cardiovascular diseases, for both TDU – 17,22% and TAB – 14,26% ( $p < 0,05$ ).

7. Diabetes mellitus was more frequent in patients with TDU – 9,45% than TAB – 7,42%, the difference not being statistically significant.
8. Neurological comorbidities were more frequent in patients with TDU – 8,01% than in those with TAB – 5,39% ( $p < 0,05$ ), the situation being similar for other somatic comorbidities: 21,00% for TDU and 12,81% for TAB ( $p < 0,01$ ).
9. The unfavorable evolution of major affective disorders, expressed by the number of hospitalizations and average length of stay was more important in patients with TAB in the presence of somatic comorbidities: vascular ( $p < 0,001$ ), diabetes mellitus ( $p < 0,001$ ), neurological ( $p < 0,05$ ), other comorbidities ( $p < 0,01$ ). In patients with TDU and somatic comorbidities, the increase of the average length of stay was highly significantly related to the high number of hospitalizations ( $p < 0,001$ ).
- 10. Female gender, age group 45-64 years old and urban residence environment are highly significantly ( $p < 0,01$ ) related to the unfavorable evolution of the unipolar depressive disorder and bipolar affective disorder just like the presence of somatic comorbidities ( $p < 0,05$ ), translated mainly by the increase of the number of hospitalizations and their length, which requires a different and multidisciplinary therapy management.**

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