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**On the Cover:**

**ION ȚUCULESCU (1910-1962)**

Portretul soției  
*Portrait of the wife*

## BIPOLAR FEMALE INPATIENTS AND THEIR SEXUALITY

Laura Damian<sup>1</sup>, Ioana Miclutia<sup>2</sup>

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### **Abstract**

*Introduction: The extent of impairment in sexual function in bipolar female patients is quite common and underestimated (Dell'Osso et al., 2009), comparable with other psychosis (Mahmoud et al., 2012).*

*Method: 173 female were enrolled, 112 being admitted to the Second Psychiatric Clinic, Cluj-Napoca, diagnosed according to ICD-10 criteria with bipolar disorder (81 were depressive and 31 manic); the remaining 61 subjects were matched controls. Sexual practices were assessed by a questionnaire regarding sexuality, and bipolar patients completed YMRS, and BDI for severity.*

*Results: Female subjects were homogenous regarding age means and education. The majority of depressed, manic patients, and controls were married, had a partner. 54.4% of manic, 43.3% of depressive female inpatients were sexual active, being significantly inferior to controls 86.9%. The frequency of sexual intercourse/week was: 1.38 (SD=2.47) in depression, 2.38 (SD=2.95) in mania and 2.42 (SD=1.5) in controls, being non-significant within groups. There could not be established any correlations between the severity of mania/ depression and sexuality.*

*Discussion: Difficulties in accurate assessment of sexual disorder rely on several factors, among them the intrinsic pattern of the disease itself, the deterioration of social and interpersonal relationships, medication (Montejo et al., 2001), age decline. The majority of studies focused on the effects and hierarchy of antidepressant, especially of the SSRIs (Montejo et al., 2001, Brill 2004); few studies being performed prior to any treatment initiation (Kennedy et al., 1999).*

*Conclusion: Both patient groups were less sexual active than controls, depressive patients being even less sexual involved than manic inpatients. The frequency of sexual intercourse showed the following hierarchy: depressive inpatients had sex 1.38 times /week, manic patients 2.38 times, and controls 2.42, being non-significant. No significant correlation to the severity of depression or mania and the degree of sexual involvement could be established.*

**Key words:** bipolar, female, sexuality.

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## **Introduction**

The issue of detection and assessment of sexual problems in psychiatric patients, especially schizophrenia (Miclutia et al, 2008), bipolar patients is rather neglected, although sexuality may be an important aspect of intimacy, source of noncompliance, many of the antipsychotics (Smith, 2007), mood stabilizers (Ketter, 2010) or antidepressants (Smith, 2007) being responsible of sexual side effects (Brill, 2004). While physicians feel uncomfortable and rushed asking direct questions about sexuality, patients expect to clarify their doubts about the safety of the recommended medication and openly discuss their problems regarding sexuality.

In spite of the fact that there could be recorded few studies regarding this topic in bipolar female patients (Hartmann, 2007, Mazza et al., 2011), the extent of impairment in sexual function is quite common and underestimated (Dell’Osso et al., 2009).

The two polarities of bipolarity imply different sexual patterns in the sexual response cycle (desire, arousal, orgasmic capacity, resolution): hypersexuality, promiscuous behavior, risk for sexual transmitted diseases, hallmark and diagnosis criterion for manic episode (APA, 2000), quite frequent even in hypomanic or mixed episodes; reduced sexual interest and engagement in sexuality, less sex drive, arousal difficulties and erectile dysfunctions in men and less vaginal lubrication and engorgement in women; orgasm and ejaculation difficulties, and some degree of resolution and refractoriness (Seidman & Roose, 2001) during depression.

Prevalence data of sexual dysfunctions in bipolar seem to be difficult to be clearly ascertained, being common, more frequent than in normal controls (Hartmann, 2007) and comparable with other psychosis (Mahmoud et al., 2012). While sexual dysfunction range between 10-52% in men and 25-63% in the general population, this disorder may reach up to 83% in inpatient bipolar patients (Marzani-Nissen & Clayton, 2004), being more extended in men.

## **Material and methods**

This is a prospective study that aims to detect the sexual dysfunctions in female bipolar patients, to compare their sexuality to matched healthy control subjects, and to evidence the relationship between the severity of psychopathology, and sexual function.

From the total of 173 female enrolled subjects, 112 being admitted to the Second Psychiatric Clinic, Cluj-Napoca, diagnosed according to ICD-10 criteria with bipolar disorder , 81 were depressive and 31 manic; the remaining 61 subjects were matched controls non randomly selected from the periodical visits to the GP (Fig. 1).

Inclusion criteria of the bipolar sample: age range-18-62 years; diagnosis of depressive or manic episode according to ICD-10 criteria, more than three episodes of any polarity.

Exclusion criteria: other important psychiatric comorbidity, personality disorder, mental retardation, alcohol and/or substance abuse/dependence; diabetes mellitus; neurological diseases or brain injuries; endocrine diseases; local genital infections, diseases, treatment with antihypertensive medication, oral contraception, hormonal substitution.

After contact and the explanation of the psychometrical procedures, all subjects signed and informed consent and underwent a questionnaire regarding sexual practices; bipolar patients were rated by Young Mania Rating Scale – YMRS (Young et al., 1978) and by Beck Depression Inventory – BDI (Beck et al., 1961) in order to assess the severity of psychopathology (Fig. 2). The protocol has been submitted for approval to the Local Ethics Committee.

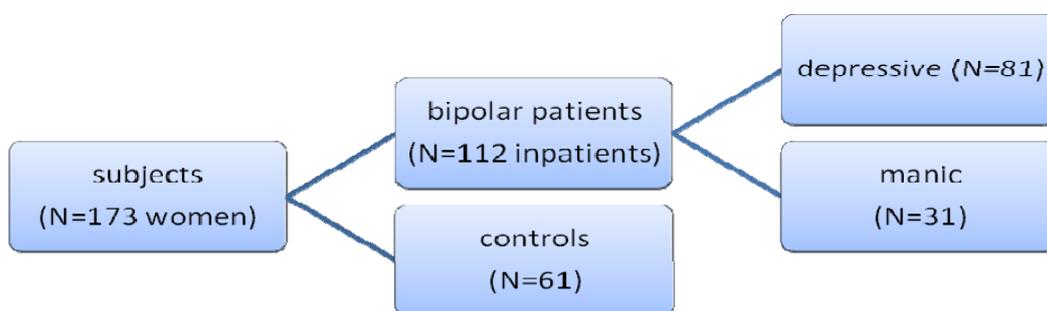


Fig. 1. Subjects' distribution

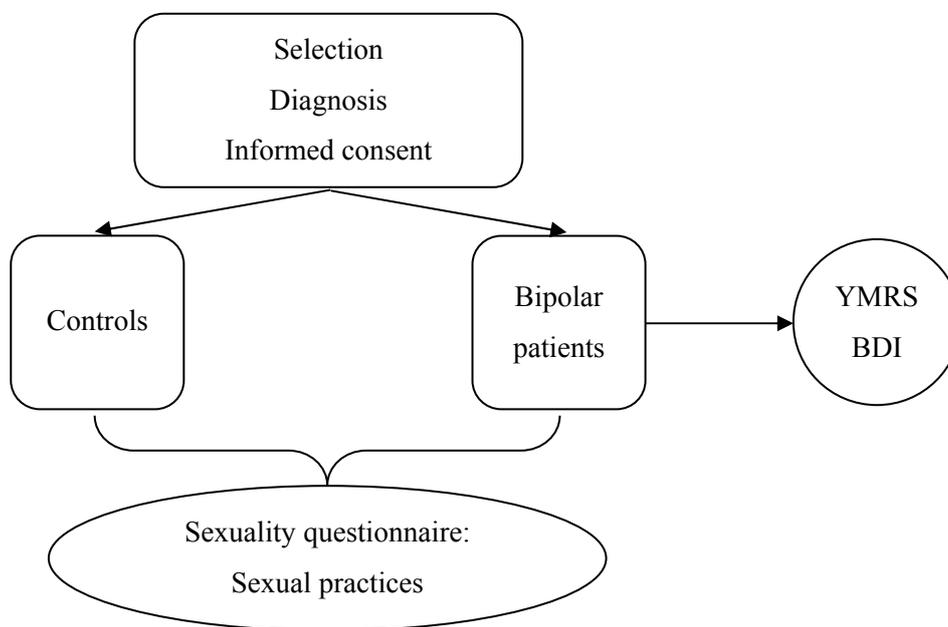


Fig. 2. Procedures and psychometrical assessment of the samples

Following statistic methods have been employed: significance testing, considering the level of significance –p value <0.005; distribution under the null hypothesis-F-test; analysis of variance (ANOVA), permitting the comparison of the difference between group means, chi-square  $\chi^2$  test that explores the sampling distribution.

## Results

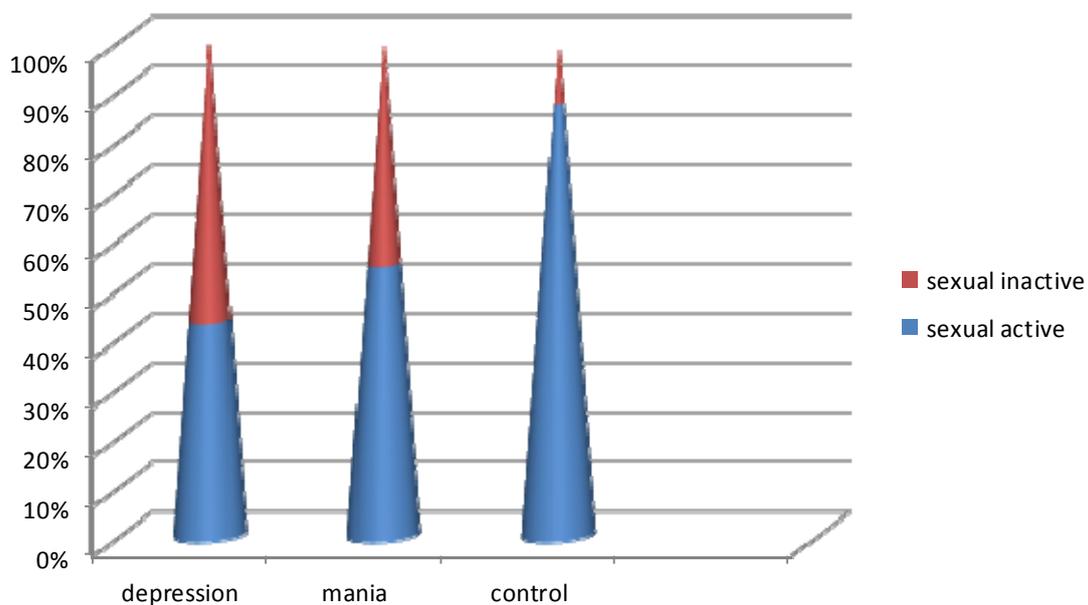
Demographic data of the samples revealed the following: age means-40.39 years in depression (SD=8.94), 42.12 years in mania (SD=11.4), and 37.63 years in controls (SD=9.36), demonstrating a homogenous group sampling ( $F=2.67, p>.05$ ) and education ( $F=5.25, p>.05$ ).

Regarding the marital status, the majority of depressed, manic and euthymic controls were married, without significant differences (Table 1). Taking into consideration the fact that these subjects had access to a sexual partner, the investigation of different aspects of sexuality may be reasonable.

**Table 1.** Marital status of bipolar female patients and controls

	Depression (N=81)		Mania (N=31)		Control (N=61)		F	p
	mean	SD	mean	SD	mean	SD		
Marital status	N	%	N	%	N	%	chi square	p
single	7	8.6	1	3.2	9	14.8	16.47	>.05
married	49	60.5	21	67.7	43	70.5		
divorced	12	14.8	5	16.1	8	13.1		
co-habited	0	0	1	3.2	0	0		
separated	10	12.3	2	6.5	0	0		
widowed	3	3.7	1	3.2	1	1.6		

54.4% (N=17) of manic, 43.3% (N=31) of depressive female inpatients were sexual active, being significantly inferior to controls 86.9% (N=53), chi-square-28.35,  $p<.001$  (Fig. 3).



**Fig. 3.** The sexual involvement of depressive, manic patients and controls

Another aspect that has been investigated constituted the frequency of sexual intercourse/week: 1.38 (SD=2.47) in depressive patients, 2.38 (SD=2.95) in manic patients and 2.42 (SD=1.5) in controls, being non-significant within groups  $F=4.17, p<.05$ .

The ultimate aim of the current study aimed to emphasize the relationship between the severity of psychopathology, depression being assessed by BDI, mania measured by YMRS, and the sexual activity, respective inactivity (Table 2).

**Table 2.** The severity of depression, mania, and sexual activity

	sexually inactive		sexually active		T	p
	mean	SD	mean	SD		
BDI	21.8	13.1	19.34	11.51	0.18	>.05
YMRS	18.53	12.0	16.85	10.96	0.43	>.05

## Discussion

There could be named as limitation of the current study the small sample size, the exploration of the sexual activity while being manic /depressive as inpatients having temporary restricted access to their partners. The age limits were chosen broadly, of sexual active women, taking into account the possible decline of various aspects of sexuality due to menopause as pointed by da Silva Lara et al., 2009. Another important confusing factor could be the current and previous treatment with antidepressants, antipsychotics, mood stabilizers, that could produce important sexual side effects (Brill, 2004).

Increased sexuality and promiscuity is common during a manic episode, being part of the diagnosis criteria (Mazza et al., 2011).

Difficulties in accurate assessment of sexual disorder rely on several factors, among them the intrinsic pattern of the disease itself, the deterioration of social and interpersonal relationships, medication (Montejo et al., 2001), age decline.

The majority of studies have focused on the effects and hierarchy of antidepressant, especially of the SSRIs (Montejo et al., 2001, Brill 2004); few studies were performed prior to any treatment initiation (Kennedy et al., 1999), explaining the paucity of epidemiological researches (Hartman, 2007).

Other methodological inconveniences of the studies refer to the type of enquiry, heterogeneity of the mood episodes, explored time span of sexual experience, personal expectancies regarding sexuality, and the willingness and sincerity to report (Baldwin, 2001).

## Conclusions

The homogenous structure of the samples permitted the exploration of potential sexual active women regarding mean age group, and the availability of a sexual partner.

In spite the myth that manic patients could be hypersexual, the current study revealed the fact that both patient groups were less sexual active than controls, depressive patients being even less sexual active than manic inpatients.

The frequency of sexual intercourse showed the following hierarchy: depressive inpatients had sex 1.38 times /week, manic patients 2.38 times, and controls 2.42, being non-significant.

No significant correlation to the severity of depression or mania and the degree of sexual involvement could be established.

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## QUETIAPINE AS AN ADJUNCTIVE THERAPY IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER AND INADEQUATE RESPONSE TO SSRI

Theodor Moica<sup>1,2</sup>, Iosif Gabos Grecu<sup>1,2</sup>, Cristian Gabos Grecu<sup>1,2</sup>, Gabriela Elena Buicu<sup>2,3</sup>, Octavian Cosmin Popa<sup>3</sup>, Szilard Sebesi<sup>2</sup>, Marieta Gabos Grecu<sup>1,2</sup>

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### **Abstract**

*Objective:* The objective of the study was to demonstrate the efficacy of quetiapine used as an augmentation treatment to 3 SSRIs - paroxetine, sertraline and escitalopram, respectively, in patients with major depressive disorder (MDD), single or recurrent episode without psychotic symptoms and inadequate response to monotherapy with a SSRI.

*Method:* In this 8-week prospective study we included 70 patients, hospitalized in Clinica Psihiatrie I Tirgu Mures between July 1<sup>st</sup>, 2011 and July 1<sup>st</sup>, 2012 for MDD, recurrent episode (N=63; 90%) and MDD (N=7; 10%), with incomplete response to the SSRI treatment. All patients received treatment with paroxetine, sertraline or escitalopram. To evaluate the efficacy of quetiapine XR as augmentation treatment we divided the sample into two groups: group A (N=35) receiving augmentation therapy with quetiapine 150mg daily and group B (N=35) remaining on monotherapy. In both groups, the score of the Hamilton Rating Scale for Depression (HAM-D-17) at Week 0 and Week 8 was used to assess the efficacy of the augmentation treatment.

*Results and Discussion:* Group A consisted of 22 women, mean age = 41.73 and 13 men with mean age = 44.15. At Week 0 (baseline), the average HAM-D score was 22.2 (SD=4.35) and at Week 8, the average score was 8 (SD=4.75). In group B we included 22 women, mean age = 44.32 and 13 men with mean age = 43.15. The average score on the HAM-D scale was 21.8 (SD= 4.03) at baseline and 10.6 (SD=4.85) at week 8. At the end of the study (Week 8), the difference of means between the two groups was 2.571 (SD=1.148; 95% CI). The mean scores on HAM-D scale at the end were significantly different between the two groups (t= 2.24; DF=68; two-tailed; p<0.05).

*Conclusion:* In major depressive disorder, quetiapine 150 mg administered once daily may be effective as an augmentation treatment in patients with incomplete response to the SSRI monotherapy.

**Key words:** depression, SSRI, quetiapine, inadequate response.

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## Introduction

In patients with Major Depressive Disorder (MDD), even if antidepressant treatment is correctly managed, only 1/3 of patients reach remission. Augmentation strategies using atypical antipsychotics proved to be a viable option in this case. Quetiapine seemed to be safe and effective as an augmentation agent to Selective Serotonin Reuptake Inhibitors (SSRIs) in patients with an inadequate response to antidepressant monotherapy. The objective of the study is to demonstrate the efficacy of quetiapine as augmentation therapy to 3 SSRIs (paroxetine, sertraline and escitalopram) in patients with Major Depressive Disorder, single or recurrent episode, without psychotic symptoms and inadequate response to the SSRI monotherapy.

## Method

We have evaluated the efficacy of quetiapine as augmentation therapy to SSRI on 70 patients diagnosed with major depressive disorder (DSM-IV-TR, American Psychiatric Association), single episode (N=7) and recurrent (N=63), without psychotic features, hospitalized in Clinica Psihiatrie I Tîrgu Mureş between July 1<sup>st</sup>, 2011 and July 1<sup>st</sup>, 2012. The participants had an inadequate response to antidepressant treatment of the current depressive episode. Inadequate response requires a score  $\geq 14$  on the Hamilton Rating Scale for Depression (HAM-D-17).

Adequate antidepressant treatment for the current episode involves the use of minimal doses accepted as effective for a period of at least 4-6 weeks. Patients had at least one SSRI dose increased before study entry and at the time of enrollment were treated with: Paroxetine 40 mg per day, Sertraline 100 mg per day or escitalopram 20 mg daily. Quetiapine XR dose was 50 mg for the first two days, then 150 mg per day until the end of the study.

Efficacy was evaluated based on the mean changes of scores on the HAM-D 17 at 5 consecutive visits conducted at Weeks 0, 1, 2, 4 and 8. Evaluations at Weeks 4 and 8 were made after the patients were discharged from the hospital, but were followed-up as outpatients. We compared two groups of patients: group A (35 patients) with incomplete response that used quetiapine XR 150 mg daily as augmentation therapy in addition to paroxetine, sertraline or escitalopram and group B (35 patients) with incomplete response who continued antidepressant monotherapy with SSRI. For the statistical analyses and interpretation of data we used SPSS 11 for Windows and GraphPad Prism version 6. The inclusion criteria were: a) signed informed consent; b) adults between 18 and 55 years old; c) inpatients diagnosed with major depressive disorder, single or recurrent episode, without psychotic features; d) patients with inadequate response to current treatment with SSRI; e) patients with at least one increase of the SSRI dose before entering the study; f) no concomitant benzodiazepines (BZD) unless initiated before the study entry and unchanged dosage throughout the study. The exclusion criteria were: a) patients with other axis I disorders, including anxiety

disorders, personality disorders or disorder associated with substance use; b) patients with unstable medical conditions such as thyroid dysfunction; c) patients with treatment-resistant depression (with no response to more than two antidepressants from different classes, given in adequate dose and for a sufficient period of time).

## Results

Main characteristics of the samples are those referring to: sex, age, educational level and the diagnosis of MDD. In total, a number of 70 patients, hospitalized in Clinica Psihiatrie I Tîrgu Mures between 01 July 2011 and 01 July 2012 were included in the study. 63 (90%) of them have the diagnosis of MDD, recurrent episode, and 7 (10%) MDD, single episode.

In group A (patients receiving augmentation) 35 patients were included in the study, 22 of them being females,  $Mage = 41.73$  and 13 males  $Mage = 44.15$  years. The general average of the entire sample was  $Mage = 42.63$ ,  $SD = 9.87$  years. In group B we included 35 patients, 22 of them being females,  $Mage = 44.32$  and 13 males.  $Mage = 43.15$ . The general average of the entire sample was  $Mage = 43.9$ ,  $SD = 7.19$ .

**Statistics Age Group A**

		M	F
N	Valid	13	22
	Missing	9	0
Mean		44.15	41.73
Sum		574	918

Table 1. Statistic results for group A

**Statistics Age Group B**

		M	F
N	Valid	13	22
	Missing	9	0
Mean		43.15	44.32
Sum		561	975

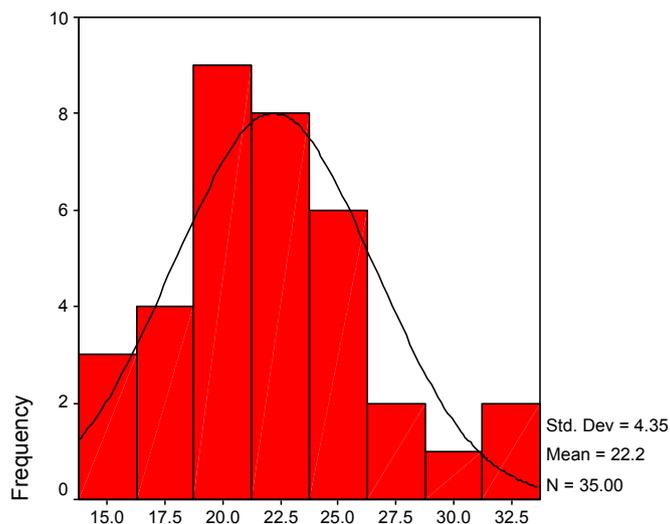
Table 2. Statistic results for group B

With regard to education, in group A 6 (17.1%) patients had a Bachelor's degree, 20 (57.1%) had graduated from high school and 9 (25.7%) had graduated from a vocational school. In group B 9 (25.7%) patients had a Bachelor's degree, 15 (42.9%) had graduated from high school and 11 (42.9%) had graduated from a vocational school.

In group A at Week 0 (baseline) a level of depression was revealed on HAM-D scores, where  $M = 22.2$ ,  $SD = 4.35$  (Fig. 1). At Week 8, the level of depression showed the next results:  $M = 8.0$ ,  $SD = 4.75$  (Fig. 2).

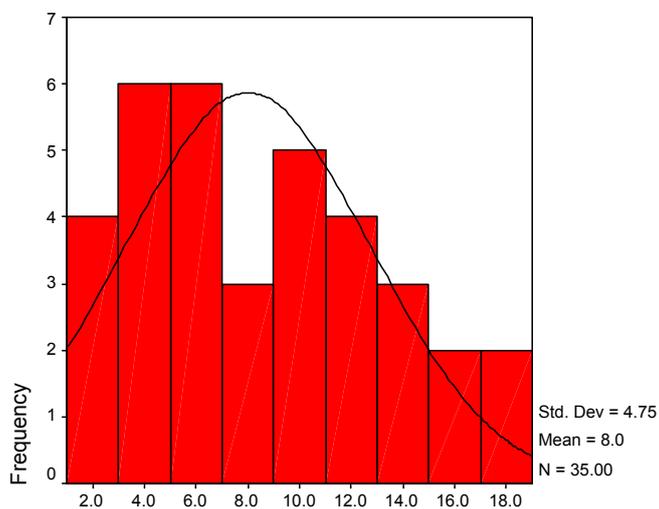
In group B at Week 0 (baseline) a level of depression was revealed on HAM-D, where  $M = 21.8$ ,  $SD = 4.03$ , and at Week 8, where  $M = 10.6$ ,  $SD = 4.85$ .

As it can be seen into the above 4 histograms, when analyzing the frequency distribution of the scores obtained by the patients, in all situations the dates tends to have a symmetrical and normal distribution (bell-form). We can say that there is a normal distribution of data. Applying the D'Agostino & Pearson normality test confirmed that our data respected the normal, Gaussian distribution (Table 1).



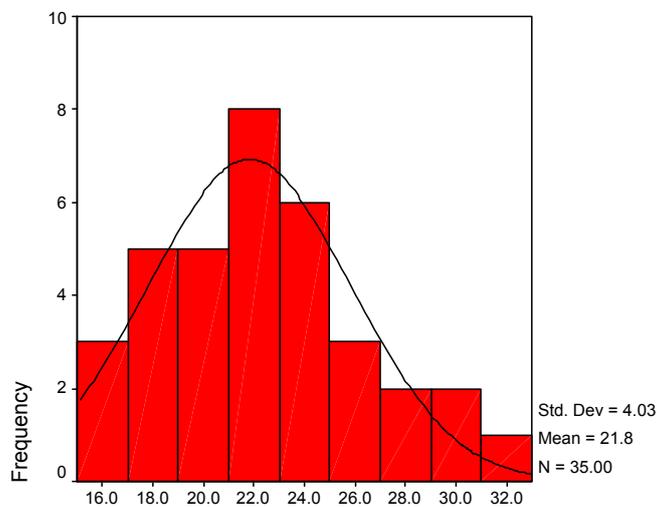
Group A, Week 0

**Fig. 1.** Mean distribution of HAM-D scores in group A at Week 0 (baseline)



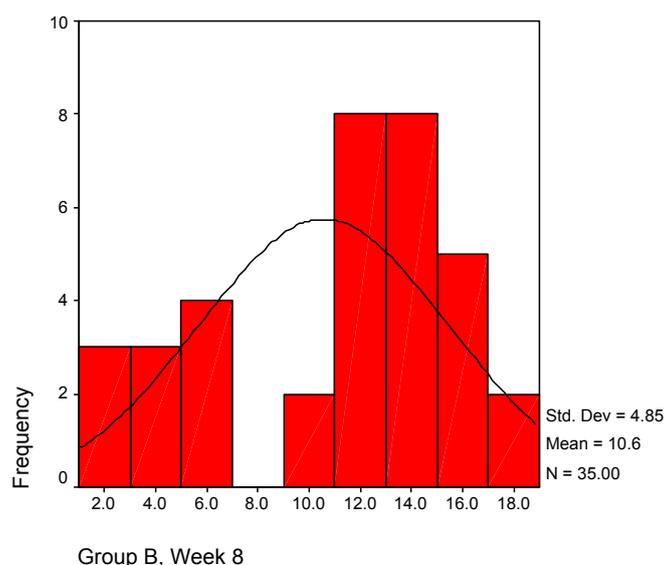
Group A, Week 8

**Fig. 2.** Mean distribution of HAM-D scores in group A at Week 8



Group B, Week 0

**Fig. 3.** Mean distribution of HAM-D scores in group B at Week 0 (baseline)



**Fig. 4.** Mean distribution of HAM-D scores in group B at Week 8

**Table 1.** D'Agostino & Pearson normality test for mean scores of HAM-D at week 8

	Group A	Group B
Mean	8.000	10.57
Std. Deviation	4.753	4.852
Std. Error of Mean	0.8034	0.8202
Lower 95% CI of mean	6.367	8.905
Upper 95% CI of mean	9.633	12.24
K2	3.671	4.690
P value	0.1595	0.0958
Passed normality test (alpha=0.05)?	Yes	Yes

When we apply unpaired t-test, the difference of means between the two groups was 2.571 (SD=1.148). The 95% confidence interval for this difference is from 0.28 to 4.86. The means of the group A and the group B at week 8 scores differ in a significant statistic manner,  $t = 2.24$ ,  $DF = 68$ , two-tailed where  $p < 0.05$ .

**Table 2.** Unpaired t-test for mean scores of HAM-D at week 8 (Group A vs. Group B)

Parameter	Value
P value	0.0284
t, df	$t = 2.240$ ; $df = 68$
Mean $\pm$ SEM of group A	$8.000 \pm 0.8034$ , $N = 35$
Mean $\pm$ SEM of group B	$10.57 \pm 0.8202$ ; $N = 35$
Difference between means	$2.571 \pm 1.148$
95% confidence interval	0.2805 to 4.862
R square	0.06870

This means that at week 8 there is a statistically significant difference between the level of depression in group A – 35 patients with incomplete response that used quetiapine XR 150 mg daily as augmentation therapy in addition to paroxetine, sertraline or escitalopram, and the level of

depression in group B – 35 patients with incomplete response who continued antidepressant monotherapy with SSRI.

## **Discussion**

Major Depressive Disorder (MDD) is a chronic and debilitating disease characterized by a wide range of emotional and physical symptoms that coexist during a depressive episode and may reoccur at some point. It is considered that by 2020 depression will be the second leading cause of morbidity worldwide after cardiovascular disease. For patients with a major depressive episode, the possibility of experiencing another episode at some point in the future is 85% (Mueller et al., 1999). Remission rates after the first antidepressant treatment are small (less than 30%) and incomplete or suboptimal response is frequently encountered (Trivedi et al., 2006).

Strategies adopted for patients with incomplete response to antidepressant treated, may include: optimizing the dose, switching to another antidepressant, combinations of antidepressants, augmentation with carbamazepine, lithium, buspirone, thyroid hormones or an atypical antipsychotic, pharmacotherapy combined with psychotherapy, deprivation of sleep, light therapy, electroconvulsive therapy (ECT), vagus nerve stimulation, transcranial magnetic stimulation and deep brain stimulation (Bauer et al., World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Unipolar Depressive Disorders in Primary Care, 2007; Gabos-Grecu I., Actualitati in terapia depresiilor, 2007).

The actual research demonstrates that quetiapine used as augmentation therapy is effective as an augmentation therapy to 3 Selective Serotonin Reuptake Inhibitors (SSRIs) - paroxetine, sertraline and escitalopram, in patients of the studied group. Our data are consistent with the literature which supports the use of this drug in patients with MDD with an inadequate response to SSRI monotherapy. Our study is the first study in Romania that evaluated the efficacy of quetiapine as an augmentation therapy in MDD, with an inadequate response to monotherapy with SSRI.

Numerous studies have shown that atypical antipsychotics, in addition to their antipsychotic effect, have also an antidepressive affect, initially observed in patients with schizophrenia and schizoaffective disorders (Tollefson et al., 1998; Keck, 2000; Emsley, 2003, Cheer et al., 2004, Levinson et al., 1999; Khouzam, 2000, Babinkostova et al., 2011).

Also, in a series of randomized, placebo-controlled trials, the authors concluded that the use of atypical antipsychotics (olanzapine, risperidone, quetiapine, ziprasidone) as an adjunct to antidepressant monotherapy may be a viable option in major depressive disorder for treatment-resistant patients (Matthews et al., 2002; Barbee et al., 2004; Papakostas et al., 2008, Ravindran et al., 2007).

In a study published in 2006, McIntyre et al. have shown that augmentation with quetiapine is significantly more effective compared with placebo in patients with MDD, on therapy with SSRI or

SNRI, with an inadequate response to antidepressant monotherapy, administered at least 6 weeks (McIntyre et al., 2006). Similar results were obtained another trial on patients with depression resistant to SSRI or SNRI, which used augmentation with quetiapine compared with placebo. Efficacy was evaluated in both studies using the HAM-D scale (Mattingly et al., 2006).

Bauer et al. published a meta-analysis of two randomized, placebo-controlled studies, proving the efficacy and safety of quetiapine XR as adjunctive therapy in patients with MDD, with incomplete response to antidepressant monotherapy (Bauer et al., 2010).

In the study we have conducted, quetiapine XR used as augmentation therapy at a dose of 150 mg daily, resulted in improvement of most symptoms of MDD between Week 0 and Week 8. Efficacy, as measured by the HAM-D, showed a significant improvement in depressive symptoms in patients with adjunctive therapy compared to patients who continued antidepressant monotherapy. Changes in HAM-D were significantly higher at week 8 in patients with augmentation therapy compared to patients who continued antidepressant monotherapy.

## **Conclusion**

Following the interpretation of the results we showed that there is a statistically significant difference between the mean scores obtained by patients in the level of depression, at week 8, between the group that used quetiapine XR for augmentation and the group that continued antidepressive monotherapy (2.571 to 1.148 at 95% CI,  $t = 2.24$ ,  $DF = 68$ , two-tailed where  $p < 0.05$ ). This indicates that quetiapine XR 150 mg daily is effective as an augmentation treatment to paroxetine, sertraline or escitalopram, in patients with Major Depressive Disorder, Major depressive episode, single or recurrent, without psychotic symptoms, with inadequate response to monotherapy with these 3 SSRIs.

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## THE SOCIO-OCCUPATIONAL STATUS AT FIVE YEARS FOLLOW-UP AFTER THE FIRST EPISODE OF SCHIZOPHRENIA

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### **Abstract**

*Introduction: The onset of psychotic disorder significantly disrupts the educational and vocational pathway of the affected individual. The capacity to be involved in a partner relationship and to interact within the social network e.g. the social status, to attain school or other academic facility, e.g. the working status may be relevant evolution predictors after the first episode of schizophrenia.*

*Method: This is a naturalistic follow-up study of patients treated for first episode of schizophrenia-FEP and followed up for 5 years in the Psychiatric Hospital Bistrita. Therefore 86 patients who met ICD-10 diagnosis criteria for an acute psychotic disorder were enrolled and evaluated by psychometrical methods at baseline and 5 years later in order to assess severity of symptoms, relapse and general functioning as primary outcome measure and to explore the social and professional impact of the disorder/ relapse.*

*Results: After a general overview of the demographic data of the sample at baseline, the evolution of the marital status as the occupational status will be presented, taking into consideration the educational background and the relapses. Being single at disease onset was significantly related to relapse after FEP. Those patients who could keep their jobs, experienced less relapses.*

*Discussion: Relapse rates may offer a more realistic picture of the general long term outcome of FEP patients than response and remission. The social adjustment, as stable and functional partner keeping, suggest a robust index of a good outcome; occupational status is considered to be even a more reliable outcome index, less influenced by medication or by other confounding factors, reflecting the social functioning*

*Conclusion: Patients showed significant higher rate of divorce in comparison to the baseline evaluation, and relapses were more common in single patients.*

*There could be observed a more obvious drift during the survey of the occupational status: from skilled work towards semi-skilled worked and more alarming to sick leave*

**Key words:** first episode of schizophrenia, marital, occupational status.

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## **Introduction**

The capacity to keep a job, to attain school or other academic facility, to be involved in a partner relationship and to interact within the social network, reflects cognitive flexibility, symptom remission, adequate adjustment, and functionality. Various studies have focused especially on the premorbid adjustment, understood as the individual's social, interpersonal, academic, and occupational functioning prior to the onset of psychotic disorder (Addington and Addington, 2005). This capacity is far from being unitary, encompassing at least two components: academic and social functioning: the first being related to intelligence, executive function, verbal memory while the later to symptom related variables (Monte et al., 2008).

Working status may be a relevant evolution predictor in several psychiatric diseases. Among them, schizophrenia seems the most disabling, with a chronic course. Therefore, all efforts concentrate towards and adequate management of the first episode of schizophrenia, which may be considered more responsible to treatment and improve long term outcome.

Among predictive factors of working disability are: cognitive factors, especially memory, and less important-age of the onset of the psychosis, substance abuse, premorbid social attainment, affective versus non affective predominance (Dickerson et al., 2008).

Completing education and keeping employment are relevant for young adults and are important for identity and general well-being. The onset of psychotic disorder significantly disrupts the educational and vocational pathway of the affected individual. Consequently, vocational outcomes are poorer for people with first-episode psychosis (FEP) relative to the general population (Killackey et al, 2006).

## **Method**

The principal aims were to assess pre-morbid adjustment and clinical profile at the onset of psychosis that could influence risk of relapse in the first 5 years of treatment and follow-up. The secondary objectives of this study are to compare the impact of psychosis on socio-economic status of the patients who relapsed or not.

This is a naturalistic follow-up study of patients treated for first episode of schizophrenia-FEP and followed up for 5 years in the Psychiatric Hospital Bistrita. Consecutive patients admitted for treatment, as in- or out-patients between January 2006 and February 2007, were treated and followed for a period of 5 years. 86 patients who met ICD-10 diagnosis criteria for a acute psychotic disorder were enrolled and evaluated by psychometrical methods at baseline and 5 years later in order to assess severity of symptoms (PANSS), relapse, general functioning (GAF) (procedures and results are recently published (Stefanescu et al., 2013).

## Results

Regarding the demographic profile of the sample, the gender distribution was: female 51 (59.3%) to male 35 (40.7%), with the following marital status (Table 1).

**Table 1.** The course of marital status of the sample

Marital status	Onset		After 5 years	
	N	%	N	%
Single	39	45.3	34	40.7
Married	38	44.2	38	45.3
Divorced	0	0	9	10.5
Non-married couple	9	10.5	3	3.5
Total	86	100.0	84	100.0

A further aspect that has been investigated was the relationship between the evolution of the marital status and relapses (Table 2).

**Table 2.** The relationship between marital status at onset and relapse

Marital status at onset	Relapse		$\chi^2$	DF	p
	Yes	No			
Without a partner	41.7%	30.8%	4.64	1	<.05
With a partner	58.3 %	69.2%			

Marital status at onset (being single) was significantly related to relapse after FEP.

In order to offer an overview of professional network, the occupational status, the educational background will be presented (Table 3).

**Table 3.** The educational level of the sample

Education (N, %)	
Elementary education	44 (51.2%)
High school completed	22 (25.6%)
College or university diploma	20 (23.2%)

**Table 4.** Occupational status at the onset of the disorders and after 5 years

	onset		after 5 years	
	N	%	N	%
Unemployed	31	36.6	2	2.3
Work in agriculture	0	0	8	9.3
Unskilled work	12	14	0	0
Semi-skilled work	16	18.6	30	34.9
Skilled work	13	15.1	0	0
Student	6	7.0	0	0
Illness pension	0	0	52	60.5
Missing data	2	2.3	2	2.3
Total			86	100.0

The occupational status at onset was not significantly related to relapse after FEP.

**Table 5.** The relationship between occupational status and relapse after 5 years

Occupational status after 5 years	Relapse		$\chi^2$	DF	p
	Yes	No			
Unemployed or illness pension	54 75.0%	0 0.0%	25.20	1	.000
Work	18 25.0%	12 100.0%			
Total	72 100.0%	12 100.0%			

Patients who didn't relapse were able to keep their jobs.

## Discussion

While symptomatic remission criteria (fulfillment of symptom relief) have been clearly established and operational in multiple studies (Andreasen et al., 2005), it seems more relevant for practical issues the concept of enduring remission, that specifies also the time criterion (more than 6 months period), due to the fact that first episode of schizophrenia patients may exhibit heterogeneous course, being prone to side effects of antipsychotics, persistent negative symptoms, substance abuse, adherence difficulties, especially in the critical period (Gaebel et al., 2013). Besides response, remission (Leucht and Lasser, 2006) and treatment outcome which might be better in FEP patients than in multiple episode schizophrenia patients (Watt et al., 1983), partly to better response to low dosages of antipsychotics, relapse rates may offer a more realistic picture of the general long term outcome. Recovery, on the other hand implies rather a long term functional outcome goal, referring besides symptom relief, autarchy. Therefore, a follow up analysis after the first episode of schizophrenia outline rather on a short term measurable outcomes (Addington et al., 2003, Rodriguez-Sanchez et al., 2008, Ventura et al., 2011, Gaebel et al., 2013 after one year, Chen et al., 2005 after three years) and seldom after five years (Bertelsen et al., 2008, Bertelsen et al., 2009, Barder et al., 2013) and scarce after ten years (Stirling et al., 2003, Uçoc et al., 2011). These are large cohort studies, difficult to organize and keep patients active in the follow-up.

The social adjustment, as stable and functional partner keeping, suggest a robust index of a good outcome after the first episode of schizophrenia (Albert et al., 2011), although low GAF scores and the persistent negative symptoms may still be crucial in modest outcomes. Middle age females seem to keep their partners or find new ones, especially when raising (Albert et al., 2011). The partner evolution in FEP patients tends towards divorce and or separation soon after the onset of the disorder with a relative stability trend in time. Age, gender and professional implication may be interwoven.

Occupational status is considered to be a more reliable outcome index, less influenced by medication or by other confounding factors, reflecting the social functioning. This index may vary during the evolution of the disorder: nearby the onset of the disorder there could be already recorded a poor social attainment; the further professional attainment is related more to certain cognitive, depressive

factors and less to medication adherence, e.g. after two years 36% of patients could not keep their jobs (Dickerson et al., 2008). Other studies (Albert et al., 2011) outlined the fact that even though full recovery could not be reached, some isolated psychotic symptoms being still present after five years; job could be kept with the condition of a stable and supportive environment.

## Conclusions

On a five years follow up, patients significantly divorced in comparison to the baseline evaluation, and relapses were more common in single patients.

There could be observed a more obvious drift during the survey of the occupational status: from skilled work towards semi-skilled worked and more alarming to sick leave (60.5%). If academic attainment had been fulfilled, there could not be stressed if after words the professional inclusion had been at the same level or below. Never the less, there could be outlined the clear relation between relapses and poor professional inclusion.

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## CLINICAL DIFFERENTIAL ASPECTS OF THE QUALITY OF LIFE IN PATIENTS WITH SCHIZOPHRENIA

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### **Abstract**

*Introduction:* We aimed to explore the potential association between medical-clinical variables and scales measuring the severity of symptoms in patients with schizophrenia and to identify a predictive model of the "quality of life" concept for people with this disorder based on scales measuring the severity of schizophrenic patients' symptoms and the treatment side effects.

*Method:* We performed a statistical analysis using mean scores and standard deviation for descriptive analysis of medical-clinical characteristics. The relationships between clinical-medical characteristics and the scales of the instruments rating schizophrenia severity and associated symptoms (PANSS, LUNSERS, WHODAS) identification was performed using the Pearson's Product-Moment Correlation. Multiple linear regressions were used to test the predictive models included in this study. In our research were included 110 patients with ages between 18 and 65 years, diagnosed with schizophrenia according to DSM-IV-TR, who gave their consent to participate. Assessment tools: WHO DAS II (World Health Disability Assessment Schedule-Second Organization Version) Romanian version, WHO-QOL, short form, and standard scales for pathology: PANSS, LUNSERS (The Liverpool University Neuroleptic Side Effects Rating Scale) and socio-demographic characteristics.

*Results:* The illness onset age is a significant negative predictor of schizophrenic symptoms measured by PANSS scale, and the treatment side effects, evaluated by LUNSERS. The total duration of hospitalizations is a negative predictor of the degree of disability measured by general WHODAS scale, and the treatment side effects, evaluated by LUNSERS. The number of treatment schemes is a positive predictor of schizophrenic symptoms measured by PANSS scale. The quality of life, assessed by WHO-QoL-BREF, for patients with different forms of schizophrenia, can be predicted based on the knowledge of scales measuring the severity of schizophrenic patients' symptoms and the treatment side.

*Conclusion:* In this context, increasing the intensity of side effects (LUNSERS) predicts a decrease in quality of life perceived by WHO-QoL-BREF. Increasing general pathology symptoms (PANSS) will predict a quality of life negative evolution. Similarly, increased disability (WHODAS) will negatively predict evolution for quality of life, regarding the patients with schizophrenia.

**Key words:** schizophrenia, quality of life, predictors.

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## **Introduction**

During the last years, the quality of life of the schizophrenia patients has become a major subject of interest for researchers due to the negative impact this condition has on the quality of life of the individual.

Evaluating the quality of life in the context of this condition has been met with numerous controversies due to the lack of consensus regarding its definition and the existence of generally accepted models, which could explain the totality of the specific factors that may influence the quality of life in this group of patients (Awad et al., 1997; Meltzer, 1999).

Disability in schizophrenia patients has been reported in many studies, some even on patients in remission (Harvey et al., 2009). In the present context, which tend towards resource efficiency, measuring quality of life and disability in patients with schizophrenia has established itself, aiming this way to obtain a remission not only in terms of symptomatology and cognition (Ventura et al., 2009), but also in terms of patient functioning.

In order to obtain broader and more accurate view on the impact of the condition and the results of the programs we must resort to both objective and subjective measurements (Kayes, 2010).

Despite the fact that the subjective perspective of the patients with schizophrenia is questionable in terms of validity, because it can be influenced by psychotic symptoms or adaptation to the condition, it still remains basis of the concept of quality of life (Lehman et al., 1993).

The first objective of this study was to explore the potential association between medical-clinical variables and scales measuring the severity of schizophrenic patients' symptoms. Medical-clinical variables included in the study: Age (years), Illness onset age (years), Duration of illness (years), Total duration of hospitalizations, Treatment Duration, Number of treatment schemes. Rating severity of schizophrenia and associated symptoms was achieved through scales – PANSS (Kay, 1987, 2000), LUNSERS (Day, 1955) and WHODAS II (WHOQOL Group, 2000)

The second objective of this study was the identification of a predictive model of the "quality of life" concept for people suffering of schizophrenia, based on scales measuring the severity of schizophrenic patients' symptoms and the treatment side effects. The quality of life assessment for schizophrenic patients was performed using WHOQOL-BREF scale (WHOQOL Group 1993, 1998).

## **Method**

### ***Sample characteristics***

#### *Socio-demographic characteristics:*

The research took place between October 1<sup>st</sup>, 2011 and October 1<sup>st</sup>, 2012 on a total number of 143 people diagnosed with schizophrenia who were hospitalized in psychiatric wards of the Psychiatric Hospital "Prof. Dr. Alexandru Obregia". All persons participated to the study based on their

expressed consent. The research included only individuals with a certain diagnosis of schizophrenia according to DSM IV-TR criteria.

Successive implementation of the criteria allowed the retention in this study of a total number of 110 people (65 women, 45 men) according to DSM-IV-TR. The percentage of female persons is 59.1%. Age of subjects varies between 20 years and 58 years, with an average age of 40.2 years (SD = ±10.36 years). Most subjects had completed secondary and post-secondary (42.7%) education levels, followed by those who have graduated from a vocational school (21.8%) and the subjects with higher education (19.1%) The subjects completing just the primary level of education totals 16.4% percent.

## Results and Discussion

The majority of patients included in the study were diagnosed with paranoid form of schizophrenia (75.3%) or an undifferentiated form (14.7%). A small percentage of patients suffer from residual schizophrenia (5.4%) or hebephrenic (4.5%). The Illness Onset Age for the subjects included in the study varies between 18 years and 37 years, with an average of 24.13 years (SD= 4.57 years). Duration of illness for the subjects is 16.19 years with a standard deviation of 9.73 years. It ranges from one year to 38 years. Regarding the total duration of hospitalization, it varies between 1 and 6 years, recording an average value of 2.79 years with a standard deviation of 1.81 years.

As shown in Table 1, the treatment duration in years has a mean value of 9.07 years with a standard deviation of 5.34 years. It varies from 6 months to 25 years. The number of treatment schemes varies between one and 40 treatment schemes, with a mean of 11.43 treatment schemes (SD= 9.63).

**Table 1.** Medical-clinical characteristics of the patients' sample

	N		Mean	Std. Deviation	Minimum	Maximum
	Valid	Missing				
Age (years)	110	0	40.18	10.37	20	58
Illness onset age (years)	110	0	24.14	4.57	18	37
Duration of illness (years)	110	0	16.19	9.75	1.0	38
Total duration of hospitalizations	110	0	2.79	1.81	1	6
Treatment Duration	110	0	9.07	5.34	.5	25.0
Number of treatment schemes	110	0	11.43	9.63	1.0	40.0

### **O1. Relations between the medical-clinical variables and scales scales measuring the severity of schizophrenic patients' symptoms**

First objective is to explore the potential association between medical-clinical variables and scales measuring the severity of schizophrenic patients' symptoms.

The practicability of this objective is given the fact that allows understanding how variations in medical-clinical variables produce variation in the symptoms of schizophrenia, neuroleptic

treatment-related side effects or consecutive disability associated with schizophrenia. Rating severity of schizophrenia and associated symptoms was achieved through scales – PANSS, LUNERS și WHODAS.

PANSS (Positive and Negative Syndrome Scale): is meant to evaluate the symptom severity of patients with schizophrenia, schizoaffective disorder and other psychoses are present positive and negative symptoms. PANSS comprises three subscales: 1. Positive symptoms subscale (P); 2. Negative symptoms subscale (N); 3. General psychopathology subscale (G).

As shown in Table 2. "Correlation coefficients between medical-clinical variables and PANSS scale", statistical significant correlations were recorded between the instrument's specific subscales and two of the medical-clinical characteristics: Illness onset age (n=110,  $r=-.20$ ,  $p<.05$ ) and number of treatment schemes (n=110,  $r=.25$ ,  $p<.01$ ).

**Table 2.** Correlation coefficients between medical-clinical variables and PANSS scale

		Positive Score	Negative Score	General psychopathology Score	Total Score
Illness onset age	Pearson Correlation	-.197*	.005	-.240*	-.197*
	Sig. (2-tailed)	.039	.960	.012	.039
	N	110	110	110	110
Total duration of hospitalization	Pearson Correlation	.018	.192*	.101	.135
	Sig. (2-tailed)	.851	.044	.293	.161
	N	110	110	110	110
Number of treatment schemes	Pearson Correlation	.095	.237*	.239*	.254**
	Sig. (2-tailed)	.325	.013	.012	.007
	N	110	110	110	110

\*Correlation is significant at the 0.05 level (2-tailed).

\*\*Correlation is significant at the 0.01 level (2-tailed).

The illness onset age negatively correlates at low magnitude with positive symptoms subscale ( $r = -.20$ ,  $p <.05$ ), general psychopathology subscale ( $r = -.24$ ,  $p <.05$ ) and PANSS Total score ( $r = -.20$ ,  $p <.05$ ). A statistically significant relationship interpretation of this fact is that an increased illness onset age is accompanied by a decrease in positive symptoms, general pathology and also the severity of psychopathology.

Total duration of hospitalizations positively correlates with negative symptoms subscale ( $r=.19$ ,  $p<.05$ ). This translates into a negative symptoms growth trend with increasing duration of schizophrenic patients' hospitalization.

The number of treatment schemes positively correlates with the negative symptoms scale ( $r = .24$ ,  $p <.05$ ), with general psychopathology subscale ( $r = .24$ ,  $p <.05$ ) and with PANSS total score ( $r = .25$ ,  $p <.01$ ). This correlation means an increase in these types of symptoms with increasing number of treatment schemes. For the other medical-clinical characteristics were not observed statistical significant correlations: patient's age ( $r = -.04$ ,  $p > .05$ ), duration of illness ( $r = .06$ ,  $p > .05$ ),

treatment duration ( $r = -.04$ ,  $p > .05$ ). The two medical-clinical variables, for which we obtained significant correlations with PANSS total score, were tested in a regression model. Regression procedure validated that the illness onset age and the number of previous treatment schemes correctly predict about 10% ( $R^2 = .096$ ,  $F(2, 107) = 5.71$ ,  $p < .01$ ) of the variance from the total score of the PANSS scale.

As shown in Table 3. "Prediction coefficients for the PANSS scale", it was found that the number of previous treatment schemes predict part of the psychotic symptoms ( $\beta = .24$ ,  $t(108) = 2.61$ ,  $p < .05$ ), as the illness onset age predicts ( $\beta = -.18$ ,  $t(108) = -1.94$ ,  $p = .055$ ). For the latter variable, the threshold is marginally, which, in practice, is to be interpreted with caution, more as a trend.

Table 3. Prediction coefficients for the PANSS scale

		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	100.429	6.223		16.138	.000
	Illness onset age	-.473	.244	-.179	-1.943	.055
	Number of treatment schemes	.303	.116	.240	2.608	.010

a. Dependent Variable: PANSS Total Score

Interpretation of these data is that when the number of previous treatment increases by one standard unit, the psychotic symptoms increases with .24 standard units, while the other predictors in the model remain constant. When illness onset age increases by one standard unit, PANSS psychotic symptoms will decrease by -.22 standard units, while the other predictors in the model remain constant.

Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS): is a self-assessment scale, comprehensive and fully validated for measuring the impact and severity of the medication side effects. The scale measures the severity of recognized side effects of neuroleptics, including irrelevant items, however, to distinguish where many medicinal effects are attributed incorrectly. LUNSERS scale evaluates six subcategories of medication-induced side effects: 1. Psychic; 2. Extra pyramidal; 3. hormonal; 4. Anticholinergic; 5. Autonomic; 6. Allergic reaction; 7. Other effects. The high values obtained in the subscales indicate higher degrees of this type of side effect.

As shown in Table 4, statistical significant correlations were recorded between the instrument's specific subscales and three of the medical-clinical characteristics: illness onset age, treatment duration and number of treatment schemes.

The illness onset age negatively correlates with Extrapyramidal side-effects ( $r = -.22$ ,  $p < .05$ ), Autonomic ( $r = -.23$ ,  $p < .05$ ) and psychic side-effects ( $r = -.20$ ,  $p < .05$ ). Such, as early illness onset occurs, the greater will be the impact of these side effects experienced by patients. There is a low magnitude positive correlation between Treatment duration and the occurrence of the anticholinergic side effects ( $r = .19$ ,  $p < .05$ ). Thus, as the number of years of treatment increases, it grows the intensity of anticholinergic side effects reported by patients. The number of treatment schemes

positively correlates with Hormonal side-effects ( $r=-.24, p<.05$ ). All the observed correlations have a low magnitude, but there are statistically significant. So, it is expected that the hormonal side-effects produced by medication will be more obvious as the patient's history includes a higher number of prescribed treatment schemes. For the other medical-clinical characteristics were not observed statistical significant correlations: patient's age ( $p>.05$ ), total duration of hospitalizations ( $p>.05$ ), and duration of illness ( $r = .06, p>.05$ ). To calculate a regression model, it was used a composite score to aggregate all LUNSERS subscales (sum of scales). Regression procedure validated a model based on one predictor, namely the illness onset age ( $R^2=.05, F(1, 108)=5.01, p < .05$ ).

**Table 4.** Correlation coefficients between medical-clinical variables and LUNSERS scale

		Extrapyramidal Score	Anticholinergic Score	Autonomic Score	Allergic reaction Score	Psychic Score	Hormonal Effects Score	Other effects Score
Illness onset age	Pearson Correlation	-.220*	-.169	-.228*	-.012	-.200*	-.060	.044
	Sig. (2-tailed)	.021	.077	.017	.901	.037	.530	.645
	N	110	110	110	110	110	110	110
Treatment duration	Pearson Correlation	.038	.190*	.128	.128	.015	.162	.025
	Sig. (2-tailed)	.694	.047	.184	.181	.875	.091	.793
	N	110	110	110	110	110	110	110
Number of treatment schemes	Pearson Correlation	.070	.103	-.004	.116	.177	.242*	.043
	Sig. (2-tailed)	.469	.282	.964	.226	.064	.011	.656
	N	110	110	110	110	110	110	110

\*Correlation is significant at the 0.05 level (2-tailed).

\*\*Correlation is significant at the 0.01 level (2-tailed).

**Table 5.** Prediction coefficients for the LUNSERS scale

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	47.678	8.439		5.650	.000
	Illness onset age	-.773	.344	-.212	-2.250	.026

a. Dependent Variable: LUNSERS Total Score

As shown in Table 5, part of the neuroleptics side effects intensity can be predicted based on the illness onset age ( $\beta=.21, t(108) = -2.25, p < .05$ ). When illness onset age increases by one standard unit, neuroleptics side effects intensity will decrease by  $-.24$  standard units, while the other predictors in the model remain constant.

WHODAS (World Health Organization Disability Assessment Schedule) II: measures functioning and disability in accordance with prescriptions issued by World Health Organization in International Classification of Functioning, Disability and Health (ICF), being a standardized trans-cultural instrument. Based on 36 items, WHODAS II covers 6 domains: Cognition (understanding

& communicating); Mobility (moving & getting around); Self-care (hygiene, dressing, eating & staying alone); Getting along (interacting with other people); Life activities (domestic responsibilities, leisure, work & school) and Participation (joining in community activities).

As shown in Table 6, statistical significant correlations were recorded between the instrument's specific subscales and four of the medical-clinical characteristics: illness onset age, duration of illness, total duration of hospitalizations and number of treatment schemes.

**Table 6.** Correlation coefficients between medical-clinical variables and WHODAS scale

		Cognition	Mobility	Self-care	Getting along	Life activities	Participation
Illness onset age	Pearson Correlation	-.208*	-.097	-.066	-.010	-.159	-.187
	Sig. (2-tailed)	.029	.312	.492	.921	.097	.051
	N	110	110	110	109	110	110
Duration of illness	Pearson Correlation	.218*	.245**	-.020	.152	.105	.156
	Sig. (2-tailed)	.022	.010	.834	.115	.276	.103
	N	110	110	110	109	110	110
Total duration of hospitalizations	Pearson Correlation	.309**	.164	.110	.163	.194*	.300**
	Sig. (2-tailed)	.001	.087	.252	.090	.043	.001
	N	110	110	110	109	110	110
Number of treatment schemes	Pearson Correlation	.269**	.268**	.083	-.015	.174	.120
	Sig. (2-tailed)	.004	.005	.391	.877	.069	.210
	N	110	110	110	109	110	110

\*. Correlation is significant at the 0.05 level (2-tailed).

\*\*. Correlation is significant at the 0.01 level (2-tailed).

Illness onset age correlates negatively with the difficulties of understanding and communication ( $r = -.21$ ,  $p < .05$ ). Consequently, as the illness onset age is lower the greater will be the understanding and communication difficulties experienced by the individual.

Duration of illness correlates positively with both understanding and communication difficulties ( $r = .22$ ,  $p < .05$ ) and with movement difficulties ( $r = .25$ ,  $p < .01$ ). Therefore, these two types of difficulties may be expected to be obvious to those individuals whose disease has been going on for many years, as compared to those in which the disease lasts for a few years. The total duration of hospitalizations correlated positively with difficulties of understanding and communication ( $r = .31$ ,  $p < .01$ ), with difficulties to participate in society ( $r = .30$ ,  $p < .01$ ), and life activities ( $r = .19$ ,  $p < .05$ ). Thus, the higher the duration of hospitalization was, the greater the difficulties will be experienced in each of the three areas of activity.

The number of treatment schemes positively correlated with difficulties in understanding and communication ( $r = .27$ ,  $p < .01$ ) and with movement ( $r = .27$ ,  $p < .01$ ). In this case, the persons who

followed a high number of treatment schemes are expected to accommodate greater difficulties in terms of communication and the movement. To calculate a regression model, it was used a composite score to aggregate all WHODAS subscales (sum of scales). Regression procedure revealed that total duration of hospitalizations is the only medical-clinical variable that significant predicts WHODAS scale total score ( $R^2 = .070$ ,  $F(1, 108) = 8.11$ ,  $p < .01$ ).

**Table 7.** Prediction coefficients for the WHODAS scale

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
1	(Constant)	76.832	3.259	23.572	.000
	Total duration of hospitalizations	2.793	.981	2.848	.005

a. Dependent Variable: Scor total WHODAS

As shown in Table 7, total duration of hospitalizations will predict a part of functioning and disability ( $\beta=26$ ,  $t(108) = 2.85$ ,  $p < .01$ ). When total duration of hospitalizations by one standard unit, functioning intensity will increase by .26 standard units, respectively disability will decrease.

In conclusion, the illness onset age is a significant negative predictor of schizophrenic symptoms measured by PANSS scale, and the treatment side effects, evaluated by LUNSERS. The total duration of hospitalizations is a negative predictor of the degree of disability measured by general WHODAS scale, and the treatment side effects, evaluated by LUNSERS. The number of treatment schemes is a positive predictor of schizophrenic symptoms measured by PANSS scale.

## **O2. Predictive model of the „quality of life” concept for people suffering of schizophrenia**

The second objective of this study is to identify a predictive model of the "quality of life" concept for people suffering of schizophrenia, based on scales measuring the severity of schizophrenic patients' symptoms and the treatment side effects. The quality of life assessment for schizophrenic patients was performed using WHO-QoL-BREF scale.

Practical utility of this objective is the validation of a prediction model for schizophrenic patients' quality of life, based on symptom severity scales for the assessment of schizophrenia.

WHO-QoL-BREF: WHOQOL is designed to measure four domains of quality of life: 1. Physical 2. Psychological; 3. Social; 4. Environmental. Quality of life is measured by the respondent reference frame or as the individual's perception over a number of life aspects.

High values correspond to a high level of satisfaction with quality of life.

As shown in Table 8, there were statistically significant correlations between total scores of the instruments' scales measuring schizophrenia symptoms and treatment side effects severity and the scale of the instrument that measure quality of life (WHO-QoL-BREF).

It was recorded a statistically significant negative correlation between total PANSS score and WHOQOL total score ( $r = -.357, p < .001$ ). Therefore, for schizophrenic patients with psychotic symptoms are more severe as the level of quality of life is reduced.

**Table 8.** Correlation coefficients between PANSS, LUNERS, WHODAS scale and WHO-QoL-BREF

		PANSS Total Score	LUNERS Total Score	WHODAS Total Score
WHOQoL-BREF Total Score	Pearson Correlation	-.357**	-.347**	-.357**
	Sig. (2-tailed)	.000	.000	.000
	N	110	110	110

\*\*Correlation is significant at the 0.01 level (2-tailed).

LUNERS total score significant negatively correlates with WHOQOL-BREF total score ( $r = -.347, p < .001$ ). In this case, people with high treatment side effects are expected to record low quality. WHODAS II total score significant negatively correlates with WHO-QoL-BREF total score ( $r = -.357, p < .001$ ). Therefore, for schizophrenic patients the degree of disability is higher the level of quality of life is reduced. Multiple linear regression procedure was used to determine which of these assessments scales of severity of symptoms associated with schizophrenia, may be retained in a valid prediction model.

**Table 9.** Prediction coefficients for the WHO-QoL-BREF scale

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	
	B	Std. Error	Beta			
1	(Constant)	105.491	8.356		12.625	.000
	PANSS Total Score	-.216	.095	-.216	-2.272	.025
	Luners Total Score	-.143	.069	-.198	-2.070	.041
	WHODAS Total Score	-.127	.061	-.201	-2.073	.041

a. Dependent Variable: WHO-QoL-BREF Total Score

In this case, the regression procedure validates all three scales as significant predictors of WHOQOL scale total score. They explains up to 22% ( $R^2 = .22, F(3, 106) = 9.83, p < .001$ ) of the variance in quality of life assessment scale (dependent variable) for the schizophrenic patients sample. As shown in Table 9, it was found that psychotic symptoms rating scale predict the quality of life ( $\beta = -.22, t(108) = -2.27, p < .05$ ), as well as happens with treatment side effects assessment scale ( $\beta = -.20, t(108) = -2.07, p < .05$ ) and with the disability assessing scale ( $\beta = -.20, t(108) = 2.07, p < .05$ ). Interpretation of these data is that when the value of psychotic symptoms scale increases by one standard unit, the quality of life (WHO-QoL-BREF) will decrease by  $-.22$  standard units, while the other predictors in the model remain constant. When the value of the treatment side effects scale increases by one standard, the quality of life (WHO-QoL-BREF) will decrease by  $-.20$  standard

units, while the other predictors in the model remain constant. Also, when the disability scale increases by one standard unit, the quality of life (WHOQOL) will decrease by - .20 standard units, while the other predictors in the model remain constant.

These data allow writing a regression equation, based on which the quality of life measured by WHOQOL can be predicted for schizophrenic patients. The form of this equation is:

$$Y (\text{quality of life WHO-QoL-BREF}) = 105.49 + (-22 * \text{PANSS Total Score}) + (-.20 * \text{LUNSERS Total Score}) + (-.20 * \text{WHODAS Total Score})$$

## Conclusion

Practical utility of this model is that the quality of life, assessed by WHO-QoL-BREF, for patients with different forms of schizophrenia, can be predicted based on the knowledge of the scales measuring the severity of schizophrenic patients' symptoms and the treatment side effects. In this context, increasing the intensity of side effects (LUNSERS) predicts a decrease in quality of life perceived by WHO-QoL-BREF. Increasing general pathology symptoms (PANSS) will predict a quality of life negative evolution. Similarly, increased disability (WHODAS) will negatively predict evolution for quality of life, regarding the schizophrenic patients.

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## GENDER DIFFERENCES IN THE PREVALENCE OF DEPRESSION AND ITS CLINICAL FEATURES

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### **Abstract**

*Introduction: Nowadays the psychical illnesses mean the most considerable burden to the society. The frequency of psychiatric clinical pictures is in growing. The examination of the gender differences gained increasingly larger space in the past decades literature. It is for a long time known, that certain illnesses turn with different frequency in the two genders, this is most characteristic for example in the case of the distressful illnesses and depression. Method: We made our examination on the section of the Targu Mures, Psychiatry Clinic Nr 1, collected the material of patients who were taken on the section in the retrospective examination, and who were issued according to the DSM-IV diagnostic system with a diagnosis of unipolar major depression. Results and discussion: Between the depressed patients (female/male proportion 1:1.42) the higher female proportion was typical, beside all in the other available factors. The men's five most frequent complaints were: self-reproach, self-evaluation disturbance negative future vision, negative present picture and sexual disturbance, while the women's five most frequent complaints were: bad morning mood, sexual disturbance, negative future vision, dejection, unable of decision. Conclusions With the description of the characteristics of male depression provides help for the recognition of male depression, which is really important, since the male depression is more often fatal than the females, because of the mortality deriving from the higher suicide rate.*

**Key words:** depression, gender differences, male suicide.

### **Introduction**

Nowadays the psychical illnesses mean the most considerable burden to the society. The frequency of psychiatric clinical pictures is in growing. Kessler found the prevalence of lifetime referred to the totality of psychiatric illnesses 48.7%, while the totalized point-prevalence in other examinations was between 9% (Australia) and 11.2 % (USA) (1). The mood illnesses all in their frequency, all in their significance excel from among psychiatric illnesses; most of the epidemiological examinations confirm the high frequency of the depression. In Hungary, Szadocky found 15.1% lifetime-prevalence regarding depression (2). The examination of the gender differences gained increasingly

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bigger space in the past decades literature. It is for a long time known, that certain illnesses turn with different frequency in the two genders, this is most characteristic for example in the case of the distressful illnesses and depression (3). In the analyzing examinations of the prevalence of the depression according also to the surveys, in the unipolar depression of lifetime prevalence it was demonstrable the female's 2:1 proportion predominance (Table 1) (4).

**Table 1.** Gender proportion between the handled patients suffering from depression

Place of examination	Time of examination	Female/male proportion
United States	1970	2.1:1
Poland	1969	1.4:1
Canada	1971	1.7:1
Czechoslovakia	1971	2.1:1
Italy	1988-1990	2.2:1

A lot of research examined the reasons of the gender differences which can be found in the frequency of the depressed sickness, for the explanation of this were born many theories, which partly explain, partly are questioning again the statements from above.

Kornstein (5) classes the reasons of the female predominance which can be found in the depressed patients' proportion into three groups: Biological factors, psychosocial factors and artefacts (Table 2) (5).

**Table 2.** The reasons of gender differences which can be experienced in the prevalence of the depression

Biological factors	Psychosocial factors	Artefacts
Brain structures	Socialization	Searching for help- behaviour
Brain functions	Social status	Symptom presentation
Gene transmission	The role of life events	Diagnose problems
Reproduction functions	Coping-mechanizms	
	Victimization	

### Biological factors

The biological theories explain the gender differences in depression by the differences in the male and female brain structure and its function, in the neuroendocrine and neurotransmitter systems and in the gene transmission. The literature is not uniform in the judgment of the role of the genetic factors. According to the Kendlers (6) the genetic vulnerability of the two gender considering depression is identical. Other examinations found different results: at female patients who have depressed relatives it developed rather depression, while the male became rather alcoholics (7). Nowadays it is proved that it is a considerable biological factor the effect of the gender hormones in the mood and distressful disturbances. This supports that the frequency of the depression is powerfully age pendant. In childhood it is very rare, if it appears after all than we rather find the

male children's mild overweight between the depressed patients (8, 9). The characteristic higher female proportion starts evolving in puberty (10), and in the reproductive age throughout it can be detected. After menopause in the female/male proportion we may experience again a decrease because of which finally the proportion changes into its contrary (11, 12, 13). The above changes may be primarily the consequences of the effect of the female hormones. All the estrogen, all the progesterone may influence the mood and the behavior (14, 15).

### **Social factors**

Many researchers examined the effects of the social factors onto the gender proportion which can be experienced in the depression and distressful illnesses. The fact that the women's social status is lower generally, than the men's, many people connected it with the outstanding frequency of the depression (16, 17). According to international examinations young women are exposed to a stress effect more often, than men with an identical age (18). Women become the victims of sexual abuse, assault, violence more frequently (19), in this case the probability of the appearance of the later depression grows (20). Psychic factors. The women's bigger psychic tendency may play a role in their increased tendency for the depression. Among women the depressed behavior pattern is much more accepted, than among men. Algood- Merten (21) found the women's reduced self-confidence an important factor in the development of depression. Warren pointed out that the men are more inclined to obscure their depression, because this does not get on with the man role and contradicts with the man socialization samples (22). According to some examinations the women are significantly more sensitive opposite the environmental effects (23), because they depend more emotionally from their environment, they internalize better their feelings, and they blame themselves for the mistakes more often than the men (24), that's why they become depressed more often in the case of a stress effect (25).

### **Artefacts**

Already Angst suggested that the gender proportion depends on the definition of the depression. The symptom doctrine of the depression writes down primarily the characteristics of the female depression, and accordingly to this as more superficial the diagnosis creation of the depression is, the male depression is rather lost, for example on the level of the primary care on the effect of other (masking) factors (26). In the case of the depressed women the considerable part of the examinations found significantly higher co-morbidity compared to the men (27). In the depressed women's case the co-morbid phobias (28), generalized anxiety and panic illness (29), bulimia nervosa (30) are significantly more frequent, while in the men's case the alcohol and drug abuse (30) altogether is more probably, onto so much, that according to some assumptions it counts as equivalent of the depression at men (31).

## Gender differences in the clinical appearance of the depression

For the clinicians it is known for a long time, that characteristic differences can be found at the comparison of the male and female depression. Differences which can be seen in the Table 3, support the experience of most clinicians. Of course it's possible, that man depressed patient comes with symptomatic picture typically dominant onto women, respectively woman depressed patient comes with symptomatic picture typically dominant onto man. We can see that about the daily depression in the people (and in the colleagues standing less near to the profession) took shape a picture which primarily tallies with the description of the female depression. Because of all these they made a separate scale (Gotland Scale for Assessing Male Depression), which one makes easier the recognition of the male depression (32).

**Table 3.** The male and female depression's differences (33)

<b>Male depression</b>	<b>Female depression</b>
	rather
Blames others	Blames herself
Angry, irritable	Sad, apathy
To high Ego	Devaluating herself
Suspicious	Anxious, timid
Searching for conflicts	Avoids conflicts
Hostile	Polite, delicate
By insult aggressive	By insult retreating
Waiting for respect from others	Struggling with an own acknowledgement
For a failure blaming the environment	For a failure blaming herself
Excited, agitated	Slowed down, nervous
Compulsively time holder	Chronic procrastinator
Less sleeping	More sleeping
Control ambitious	Runs out at the borders
Feeling ashamed	Feeling guilty
Desiring praise	By praise confused
Speaks hardly from weakness	Speaks easily about weakness
Is afraid from failure	Is afraid from success
Sense of security/power	Sense of security /subjected to sg
Alcohol, TV, sport, sex	Food, friend, love
Better treatment/from others	Better behaviour/ from herself
Do they love me sufficiently?	Am I sufficiently likeable?

## Aims

The main aim of the work was, that starting-up with the literature up to now to examine in domestic sample (depressed patients) the gender differences which appear in depressed sicknesses according to the under mentioned two main dimensions:

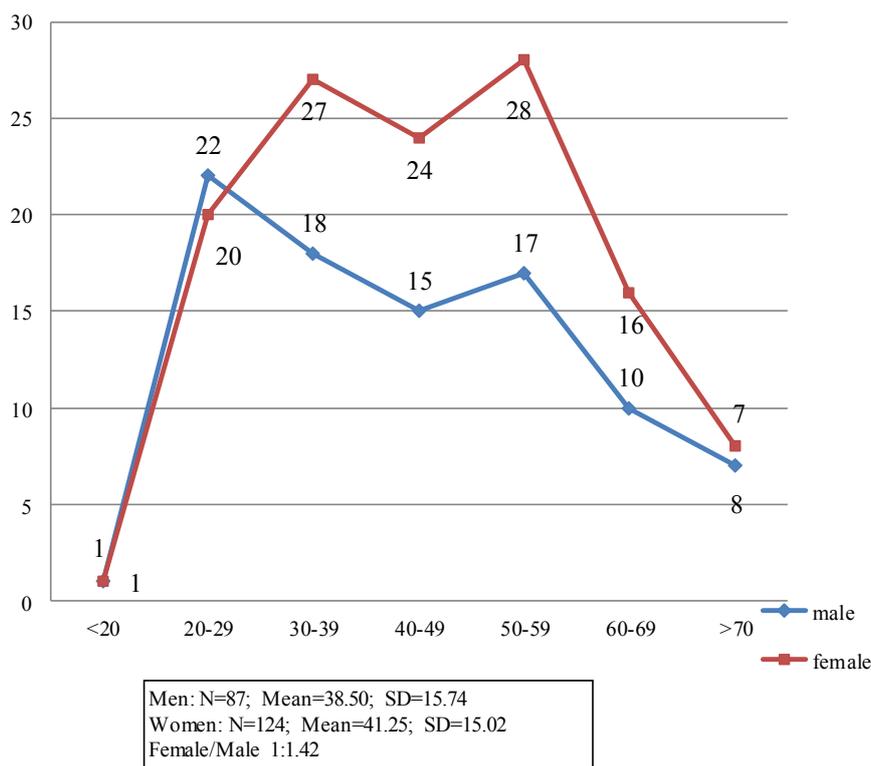
- The examination of the gender differences in the frequency of appearance of depressed illnesses.
- The examination of the gender differences in the clinical appearance of depressed illnesses.

## Material and method

We made our examination on the section of the Targu Mures, Psychiatry Clinic Nr 1, collected the material of patients who were taken on the section in the retrospective examination, and who were issued according to the DSM-IV diagnostic system with a diagnosis of unipolar major depression. The sampling happened in the months of May and April 2012. We used Zung Scale as a measuring device in the examination (Self Rating Depression Rating Scale-SDS). It belongs between the so-called self-completing scales, that means the patient marks, that the statement written down in the questionnaire (which one writes down practically a characteristic symptom, syndrome of the depression) how typical onto him is.

## Results

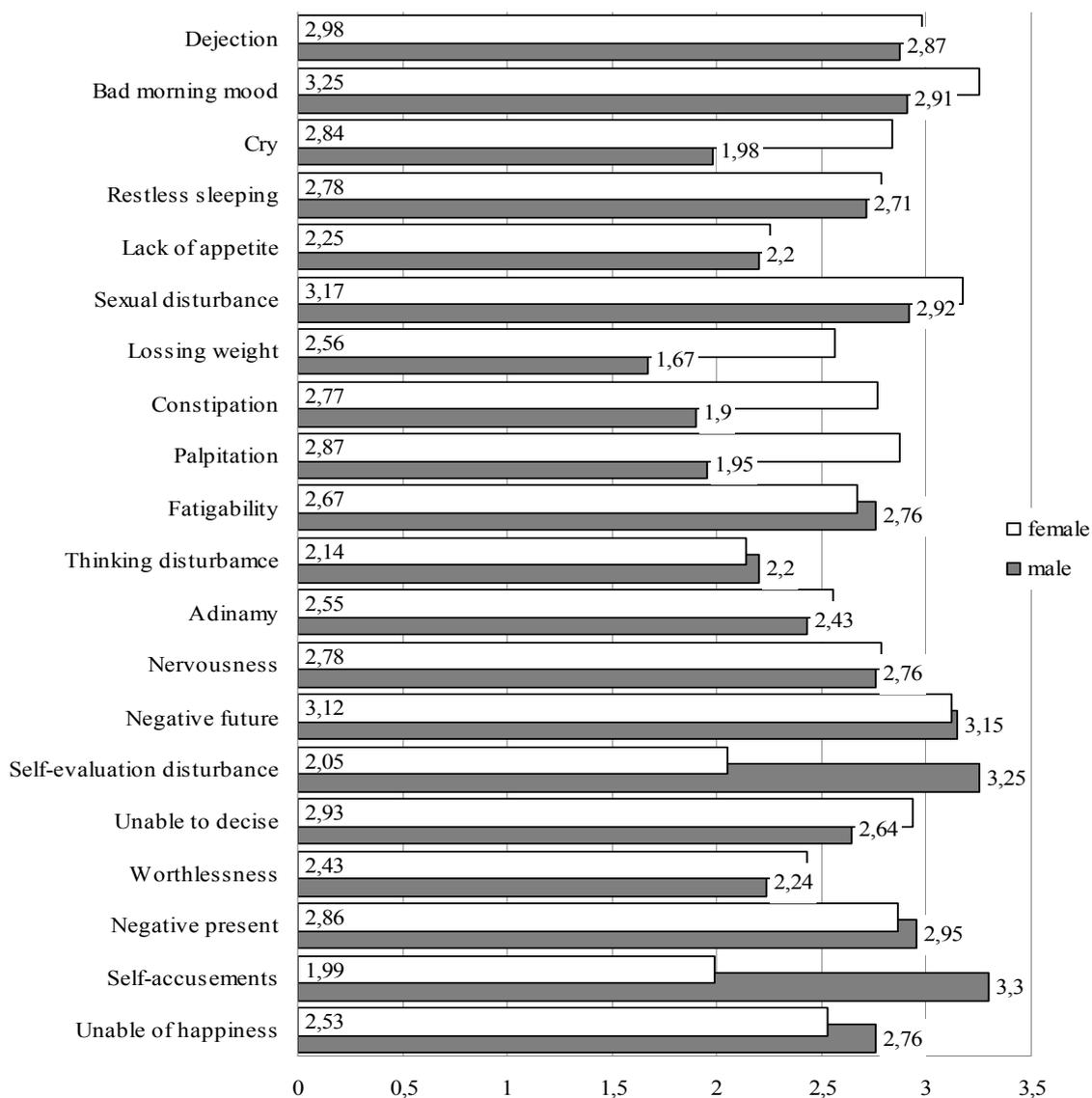
Between the depressed patients (female/male proportion 1:1.42) the higher female proportion was typical, beside all in the other available factors, for example in the age (men: 38.5 years. women: 41.2 years,  $p= 0.29$ ), we did not find significant differences.



**Fig. 1.** The gender distribution of depressed patients according to the age (years old)

In the course of the examination 30.6% of the patients had Zung points higher than 55 points, it can be said it is serious depression, (men: 28.7%. women: 32.5%). According to the results although the male and female symptom representation are similar, certain characteristic differences are demonstrable (Fig. 2). The men's five most frequent complaints were: self-reproach, self-evaluation disturbance negative future vision, negative present picture and sexual disturbance, while the

women's five most frequent complaints were: bad morning mood, sexual disturbance, negative future vision, dejection, unable of decision. Women complained more frequently about somatic symptoms (palpitations, lack of appetite, constipation, and losing weight) which are in good harmony with the literature data.



**Fig. 2.** Zung average score according to the single symptoms by genders

## Conclusions

In the examination according to the literature data (34,35), we found the female proportion higher between depressed patients (female/male proportion: 1.42) We may tell that the serious depression prevalence (as long as as I mentioned it already in the method, that those who have Zung score higher than 55 points we consider them serious depressed ones) in the examined population was 30.6 %. What concerns the gender differences in the gravity of the depression as we know, women are more inclined to suffer more from their psychic symptoms in case of identical gravity (36,37)

and like this it is not surprising that on the Zung scale, which appears to be more subjective, their state appears more severe (Zung scale average score of the men is: 51.55, till of the women is: 53.52). The research sheds light on the clinical differences between the male and female depression. With the description of the characteristics of male depression provides help for the recognition of male depression, which is really important, since the male depression is more often fatal than the females, because of the mortality deriving from the higher suicide rate.

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## EXPLORING QUALITY OF LIFE IN PATIENTS WITH LIVER TRANSPLANTATION

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### **Abstract**

*Introduction: The quality of life, self-esteem and rehabilitation of patients following liver transplantation is essential for the team of medical professionals, the families and, of course, for the patients themselves.*

*Method: We assessed 10 patients with liver transplantation who were at different recovery periods, from six months to three years after transplantation. All patients having had the surgery were treated and monitored by a team within the Military Medical Academy.*

*Results: The overall assessment of the health and quality of life (joy of life, energy and vitality, satisfaction with personal relationships and minimization of negative feelings) was encouragingly positive for almost all patients. Concerning the possibilities for self-determination, self-realization, dedication to work and dealing with problems alone, a significant proportion of patients showed that they can handle them only "somewhere", corresponding to the pursuit of paid employment.*

*Discussion: The findings of the study are related to the enormous impact on the patients with transplant of the opportunities for self-realization and return to work or training that induce the feel of being "useful, successful and independent". This premise is the foundation of the patients' physical and mental well-being, good adaptation and good self-esteem.*

*Conclusions: The results of the study are significant for further research on the specific problems and lack of experience with the mental status of the patient with liver transplant, thus offering the opportunity for developing more efficient and targeted services for this category of patients.*

**Key words:** liver cirrhosis, liver transplantation, quality of life, adaptation and rehabilitation, self-esteem.

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## **Introduction**

The authors of this article are specialists in the field of mental health and work specifically with patients who are about to undergo liver transplants or have been already successfully transplanted. Monitored patients are mainly suffering from cirrhosis resulting from alcohol abuse or hepatitis B and a minority with autoimmune disease. In most cases, patients address their liver disease when they already have liver cirrhosis. A group of patients were not even on any treatment. Regardless of detailed discussions about the possibility of liver transplantation and the necessary research, several patients experience psychological crises in various degrees [1, 2].

Upon receiving a severe and definitive diagnosis of "cirrhosis", patients find themselves in a position similar to that described for the loss of a loved one: the original emotions and feelings are denial, anger, despair and frustration. Most often, patients seek answers from doctors when and how they have gone through all the stages of liver disease without feeling any particular physical pain. The majority feel some deceptiveness and hopelessness that trigger a psychological crisis dominated by the emotional instability and several other approaches such as a new perspective on life, priorities, people or bad habits, all aiming towards a different strategy for the future. All important physical and mental changes that take place are mostly against the lack of a specific life experience in this type of crisis, which further weakens the protective and adaptive capacity and resilience of the psychophysical personality. All these changes have a significant impact on the emotional sphere, thus expressing the most common disorders ranging from diffuse anxiety to explosive reactions. There is often a well-marked emotional perception of the individual all-around and pointed his emotional response, including the direction of decisions. Typical is the perception and evaluation of events and situations only in black and white version with a reduced ability to perceive the nuances [3, 4, 5].

Liver transplantation is a complex medical procedure that requires a serious psychological capacity of the patient to continue to live fruitful. Therefore, a psychological-psychiatric evaluation of the patient's willingness to participate in the program for liver transplantation, along with other clinical research becomes compulsory. If necessary, the psychosocial support is continued in order to accelerate the emotional acceptance and the management and development of new coping strategies.

Liver cirrhosis is a serious disease with a fatal outcome, but an alternative is the liver transplantation. The transplant and the subsequent recovery period do not pose fewer risks associated with the "adoption" of the "new" body and the patient's adherence to the "new life." If the fears of the patient before transplantation are most often associated with the procedure such as finding a suitable donor in due time and the surgery outcome, new fears appear after the procedure that are related to whether the body will not reject the organ, how will be the immunosuppressive treatment tolerated, when the money will be refunded or whether work and life will be fulfilled [6].

For all these reasons, assessing the psychological state of the patient before and after transplantation becomes a priority, as well as offering professional emotional support and treatment, if needed.

## **Objective**

The aim of the study is to establish the psycho-emotional state and social functioning of patients after liver transplantation. Their assessments are important for their quality of life, level of self-esteem and future prospects. The results serve as a "starting point" for psychotherapeutic work with these patients. The basic assumption is related to the sighting of positive change, quality of life and rehabilitation after transplantation.

## **Methods**

Four methods were used to study the condition of patients after liver transplantation: 1) the psychological interview; 2) the self-assessment questionnaire for social adaptation (adapted after Weissman) consists of 54 questions divided into several categories including work/school, leisure, family and finances, with each question having five possible responses; 3) the self-assessment scale for self-esteem (Rosenberg) consists of 10 statements with four choices of "totally agree" to "totally disagree"; and 4) the WHO questionnaire for quality of life consisting of 31 questions concerning 24 areas of life relating to mental, physical and social functioning. The patient is assessed individually provided with five choices from "none" to "very much".

These research methods were selected to identify and track potential psychological and social recovery of patients after liver transplantation.

Ten patients were examined - nine men and one woman aged 27 to 52. They were diagnosed and treated in the department of Gastroenterology and Hepatology at the Military Academy and underwent transplant liver from a cadaveric donor.

## **Results**

The study of quality of life, level of self-evaluation and adaptation of patients after liver transplantation helps to understand their assessment of satisfaction/dissatisfaction in terms of their physical and mental health options for coping and social acceptance or isolation. The results of such studies provide an opportunity to help patients by offering psychological techniques to cope with distress, depression and symptoms of social withdrawal.

After the administration of the quality of life questionnaire, six key areas were selected.

The processing of responses to the WHO quality of life assessment were selected six key areas of life to the categories of issues such as the following results:

1. Overall assessment of the health and quality of life of patients. With regard to this category of questions, most of the respondents (70%) answer "good" or "very good", while only 30% believe they have an average or below average, "neither good nor bad" (Fig. 1).

2. Joy of life and filled with meaning. With regard to this category of questions, all patients responded in the upper positive level, "very much" (40%) and "extremely" (60%) (Fig. 2).

3. Satisfaction with sleep, ability to perform work in the everyday level of performance - energy and vitality. With regard to this category of questions 70% of patients responded positively, "satisfied" and "very satisfied", while only 30% are in the "dissatisfied" or "moderate" levels (Fig. 3).

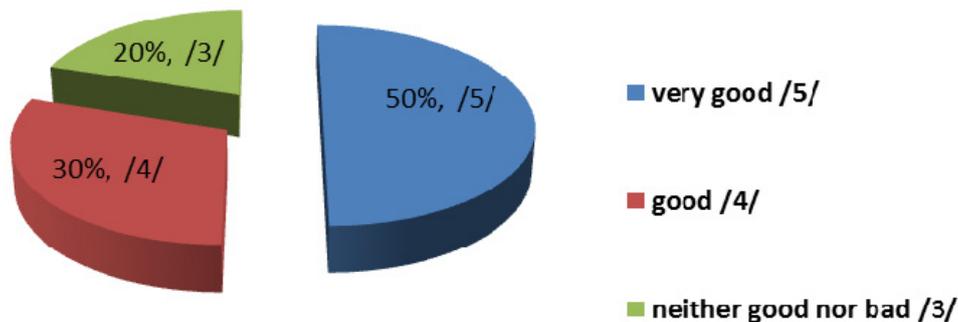


Fig. 1. Overall assessment of the health and quality of life of patients

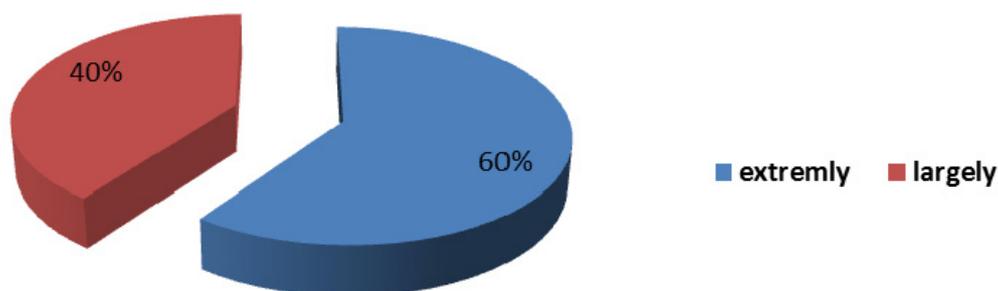


Fig. 2. Joy of life and filled with meaning.

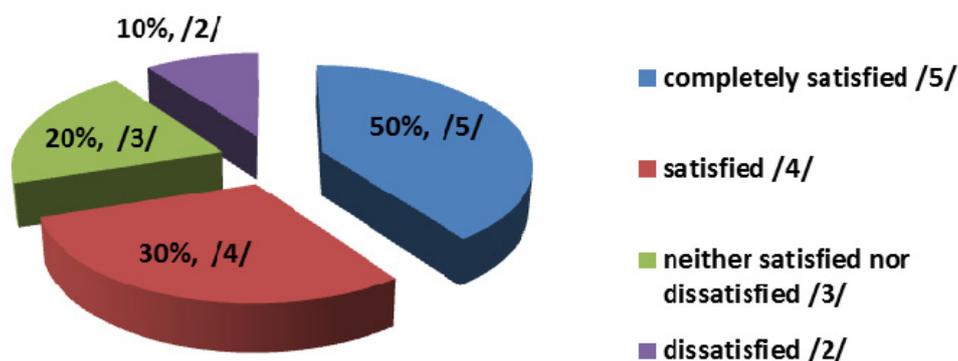


Fig. 3. Level of performance, energy and vitality

4. Testing of negative feelings such as sadness, anxiety, depressions, despair, and deal with them. With regard to this category of questions, all patients reported that this only happens "sometimes" or "neither fair nor less"(Fig. 4).

5. Satisfaction with personal relationships, support from friends, hospital care. With regard to this category of questions, 80% of patients feel "satisfied" and 20 percent are more "satisfied" (Fig. 5).

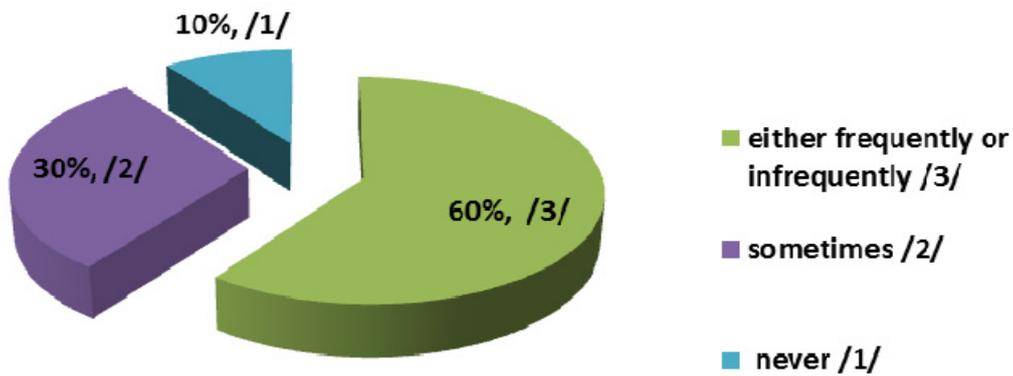


Fig. 4. Negative feelings in studied sample

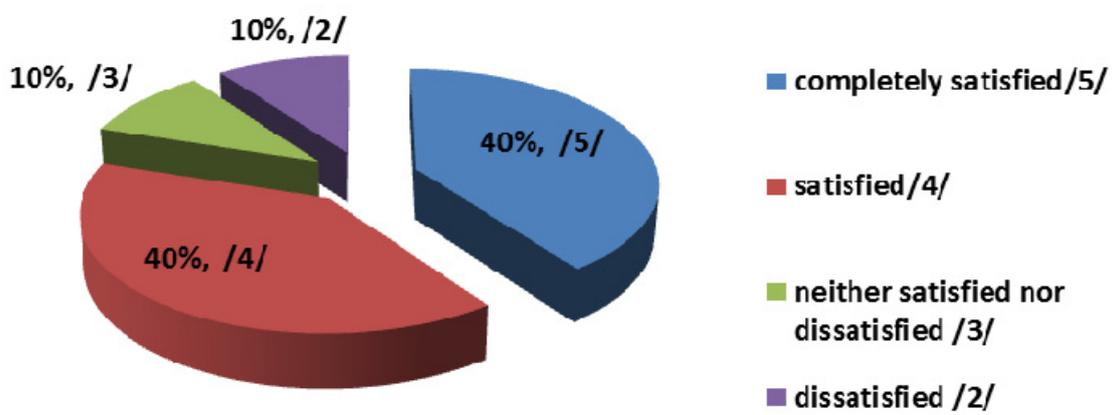


Fig. 5. Satisfaction with personal relationships, support from friends and hospital care.

6. Ability to self-determination, self-realization and dedication to an activity, independently deal with problems. With regard to this category of questions, 60% of patients considered that handle only "somewhat" and "moderate," while 40% have a strong positive self "largely" and "very much" (Fig. 6).

Regarding the questionnaire level of self, we can say that 30% of those surveyed had a rather low self-esteem, other 30% is slightly reduced, while 40% of those surveyed - is good for self-esteem high.

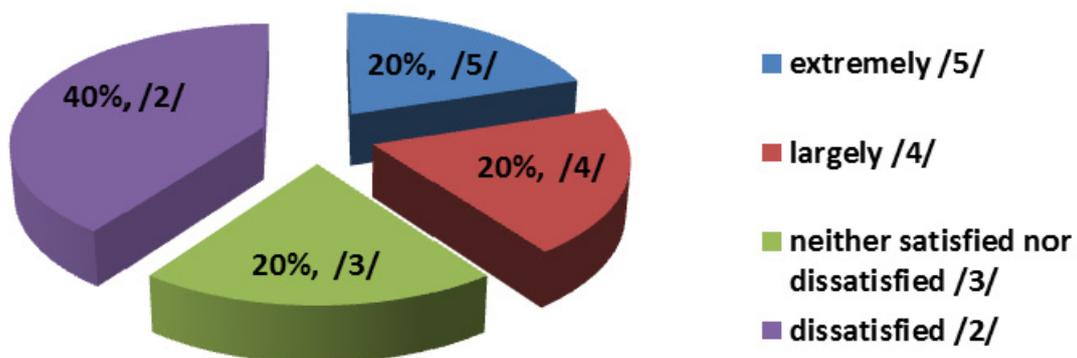


Fig. 6. Ability to self-determination at patients from studied sample.

In terms of social adaptation questionnaire it should be noted that fully 70% of the patients had no work for months or even years before transplantation because some disability. They were retired due to illness or simply stopped training or employment. They note that "hosts" often feel "led" and "addicted" to his family and "insufficient income", which makes them dissatisfied and poorly adapted. Another 20% of the daily team work and earn money, which was a major reason for better adaptation and 10% of patients feel dissatisfied and poorly adapted, although still working the same job that worked before transplantation (Fig. 7).

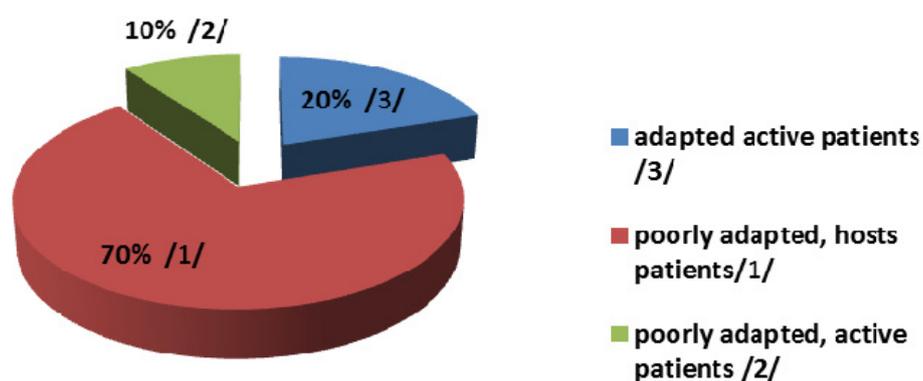


Fig. 7. Level of social adaptation.

## Discussion

According to the qualitative and quantitative analysis of the instruments all patients with liver transplant experience joy and pleasure in life. This is due to the "proximity" with the jeopardized severe disease that gave them the opportunity to truly appreciate life and enjoy it. Almost all patients appreciated the support of relatives, friends and health care professionals caring for them, and the importance of personal relationships.

Almost all have good sleep, performance/energy, vitality and the way they carry out their daily activities.

The above probably help them to feel negative emotions such as sadness, despair, depression, anxiety - only "sometimes" and easy to deal with them.

Patients who for various reasons / most early retirement due to illness / no fee work anywhere - stay home and do chores - in most of the others feel dependents, dissatisfied, led by struggling to cope with their problems. They tend to have low self-esteem, and share their feelings that they are related to their low income or lack thereof.

Patients who have kept their jobs than before liver transplantation and after subsequent recovery period have returned to work, feel most fulfilled and realized in life independently solve problems and deal with negative feelings. They feel good and able to deal with challenges in your life.

These results demonstrate the great importance of social activity and social inclusion for people, particularly for transplant patients. They have expressed a need to achieve in your life, which largely means work for pay and define their self-esteem and desire to feel independent, financially independent, useful and meaningful.

These findings enable a wealth of medical professionals who care for these patients to promote, support and engage in the recovery process of their performance and return to work. It also emphasized the need for taking active roles and positions - as opposed to disability and isolation.

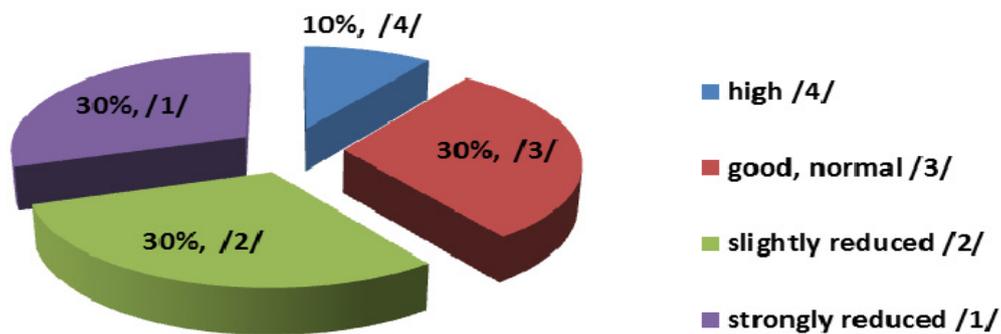


Fig. 8. Level of self-esteem.

## Conclusion

In conclusion it can be said that this study revealed the issues regarding quality of life, self-esteem and adjustment in patients with liver cirrhosis after liver transplantation. This in turn contributes to the timely intervention of specialists caring for their mental and physical health by supporting - minimizing disability and their problems, improve their access to roles, relationships and activities within their families, the working environment and society as a whole. The results can obtain diversity of professionals dealing with issues of transplantation, with a structured framework within which they will acquire the skills to acquire knowledge and develop attitudes necessary to provide effective support and treatment to the needy patients.

It is known that the competence of healthcare professionals represent a set of skills necessary for the effective implementation of psychosocial interventions, including care for individuals with serious health problems resulting in psychological problems. Such competences in patients undergoing transplantation should include a) Perception and involvement of the individual; b) Collecting information with a focus on details; c) Organizing and formulating information involve the patient; d) Family interventions; e) Formation and development of staff and f) Participation in a teamwork.

A team of professionals able to carry out all these activities could provide excellent service aimed at restoring mental well-being in patients with liver transplants.

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## PATTERNS OF PSYCHOACTIVE DRUGS CONSUMPTION HABITS AT PENINSULA FESTIVAL 2011 - TARGU MURES

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### **Abstract**

*Introduction: According to National Anti-Drug Agency (2010) the prevalence of psychoactive substances consumption traded under the name of “legal highs” or “etnobotanics” is 6.7% among young people aged 15-35 years. As a consequence of the drug use increase Romania occupied in 2010 the tenth place in the EU regarding deaths related to consumption of such substances.*

*Method: 256 participants at the 2011 Peninsula Music Festival in Targu Mures were interviewed using a questionnaire of 45 questions referring to knowledge, attitudes and habits of psychoactive substance use on.*

*Results: In this study we found that the prevalence of drug (legal or illegal) consumption in the group age 15-35 years is increasing. The most commonly used illegal drug is cannabis followed by ecstasy. In the prevalence of alcohol and tobacco consumption there was no significant change, but in the prevalence of etnobotanics consumption and use of medicines (anxiolytics or anaesthetics) combined with alcohol there was an increase compared to the previous years (2009 and 2010). On the other hand, we evaluated the level of information of target group related to the possibilities of treatment provided in the public health system in Romania (pharmacological treatment with methadone or naltrexone; social and psychological therapies).*

*Conclusions: This study underlines the importance of prevention, health education and information programs especially for most vulnerable groups.*

**Key words:** *etnobotanical herbs, legal drugs, methadone.*

### **Introduction**

Since 1990, Romania's political, economic and social situation has changed a lot. These changes, together with other factors, favored the marketing of legal and illegal drugs. The most important conditions and factors that sustained the development of this market are a) the geographic position, with opened borders after 2007 when Romania became an EU member and thus a bridge between the East and the West; b) the lack of laws in this field, older technical tools that sometimes fail to detect drugs; c) the delayed answer of the authorities confronting with fast changes in the economic and social life, such as labor migration, break of the families or poverty and sudden enrichment.

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Romania shifted quickly from a transit country into a target country. Experiences of recent years, particularly concerning synthetic drugs (amphetamines, MDMA, LSD and others) showed that the prevalence of drug use has increased also in East European countries. The illegal market moved from western countries (Netherlands, Belgium and Germany), transforming Romania in one of its target countries [1].

In 2008, the so-called “spice shops” were approved to sell legally the new psycho-active substances named “etnobotanical herbs”. Two types of these are well known: 1) mixtures of plants and chemical substances used for smoking – the “spice”- type products and 2) mixtures of chemical powders that can be sniffed or injected – synthetic psycho-active substances with energizing or hallucinogen effects, alone or mixed with well-known energizers such as caffeine or creatine and are traded under different names [2].

A large number of products designed for inhaling/smoking, branded as “spices” were detected: Spice Silver, Spice Gold, Spice Diamond, Spice Arctic Synergy, Spice Tropical Synergy, Spice Egypt, Spice Maraciuca, Ganja, M6, Diesel and Katana [2].

According to the 2010 report of Romanian Health Ministry in 2009 there were 1300 persons mainly of young age taken to hospital with intoxication symptoms due to the use of legal spices. The report stated that these psychoactive substances are harmful to health, most important symptoms being confusion, perception disorder, attention disorder, severe headaches, anxiety, panic disorder, hypertonia, tachycardia and fever. The ministry changed the laws by enlarging the list of forbidden psycho-active substances and increased the severity the penalties: prison sentence from 3 to 15 years for cultivation, production, storage, trading and buying of drugs with a low or medium risk; 10-20 years prison for drug use with a high risk. There are few examples of psycho-active substances that are on the forbidden list: 1) Herbs: *Salvia divinorum* (causes acoustic and visual hallucinations), *Mitragynaspeciosa* (Kratom) (with similar effects to cocaine); 2) Mushrooms: *Amanita muscaria*, *Amanita pantherina* (with similar effects to LSD, causing mainly hallucinations); 3) Synthetic substances: LSD (Lysergic Acid Diethylamide), Piperazine derivatives (causing mostly hallucinations), Ketamine (causing strong addiction) with two fatal overdoses between 2008-2010; 4) Bath salts (mefedrone) with several fatal overdoses reported between 2008-2010 [3].

In 2011, as a consequence of law enforcements “spice shops” or “dream stores” have been closed, but during the three previous years when they were active, the prevalence of these psycho-active substances increased (Table 1). According to 2010 data, the users of legal substances represented 2% among the general population in Romania.

The main target of this study is to follow-up the changes of drug use, detecting the risk factors and assessing the level of knowledge in vulnerable groups about drug laws and therapeutic possibilities.

**Table 1.** Lifetime prevalence of psychoactive substances in Romania (2004-2010)

	2004	2007	2010
SNPP (new substances with psycho-active properties: “legal highs” or “etnobotanics”)	-	-	2.0
Cannabis	1.7	1.5	1.6
Ecstasy	0.8	0.3	0.7
Cocaine	0.4	0.1	0.3
Heroin	0.2	0.1	0.3
Amphetamines	0.3	-	0.1
LSD	0.2	-	0.1
Ketamine	-	-	0.1

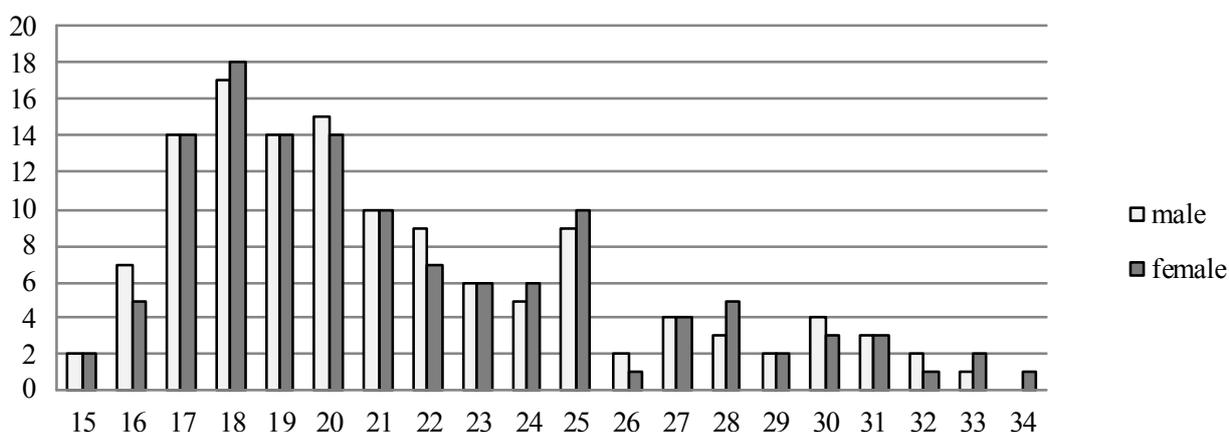
## Method

The target group was the population that attended the Peninsula Music Festival. We decided to focus on this population because our previous study showed that at this festival there is a direct access to the users of legal and illegal drugs.

Data collection took place in 2011 in Targu Mures at the Peninsula Music Festival. The interviewers (residents in psychiatry) were previously trained in using the study questionnaire. The sample size and structure was representative for the festival visitors. We randomly select the participants until fulfilling the sample criteria. The questionnaire was validated for Romanian and Hungarian population in previous study. The questionnaire has 46 items that explore gender, family status, educational level, drug use habits, legislation and mental health system. A special attention was focused in identifying the knowledge and attitudes toward psychiatric treatment.

## Results and discussion

The sample size is 256 participants adjusted for gender, age and educational level. Descriptive statistical characteristics: gender distribution was 50.39 % men and 49.61 % women. Age distribution: Mean age 21.42 years, Median 21, Standard deviation 4.32, Minimum 15, Maximum 34. Sample characteristics are depicted in Fig. 1.



**Fig. 1.** Distribution of sample by age and gender

In Table 2 we summarize the socio-demographic indicators of drug use prevalence in the last 12 months. In our sample the drugs called “legal spices” has the highest prevalence (19.8%), while the lowest prevalence is observed in heroin and inhaled organic solvent (0.8%). The first two rows compare our data with the 2010 data measured among general population. Our sample’s drug use prevalence is higher showing that young people attending the festivals represent a vulnerable subpopulation with a higher risk of drug abuse than general population.

**Table 2.** Socio-demographic indicators of drug use prevalence of last twelve months

Characteristics of substance users	„legal spices” or „ethnobotanical herbs”	cannabis	ecstasy	amphetamines	cocaine	heroin	LSD	ketamine	BZD combined with alcohol	inhaled organic solvent
<b>Absolute value</b>	(51)	(42)	(13)	(12)	(3)	(2)	(3)	(4)	(5)	(2)
<b>Percentage in our sample</b>	19.8%	16.6%	5.0%	4.6%	1.2%	0.8%	1.2%	1.6%	2.0%	0.8%
<b>Romanian general population</b>	2.0%	1.6%	0.7%	0.1%	0.3%	0.3%	0.1%	0.1%	5.4%	
<b>Gender</b>										
Male	72.6%	69.4%	61.5%	83.3%	66.6%	100%	66.6%	75.0%	60.0%	50.0%
Female	27.4%	30.6%	38.5%	16.7%	33.3%	0%	33.3%	25.0%	40.0%	50.0%
<b>Age</b>										
15-24 years old	54.6%	32.6%	30.8%	33.3%	0%	0%	33.3%	50.0%	80.0%	100%
25-34 years old	45.4%	67.4%	69.2%	66.6%	100%	100%	66.6%	50.0%	20.0%	0%
<b>Residence</b>										
Urban	73.7%	80.4%	76.9%	75.0%	100%	100%	66.6%	75.0%	60.0%	100%
Rural	26.3%	19.6%	23.1%	25.0%	0%	0%	33.3%	25.0%	40.0%	0%
<b>Education</b>										
Primary school	50.4%	28.8%	15.5%	16.8%	0%	0%	0%	25.0%	20.0%	100%
High school	26.5%	37.8%	30.7%	41.6%	66.6%	100%	66.6%	50.0%	60.0%	0%
University	23.1%	33.4%	53.8%	41.6%	33.3%	0%	33.3%	25.0%	20.0%	0%

We have also evaluated the participants’ the level of knowledge about the legislation concerning the drug use. 39.25% had sufficient information, 28% had an incorrect or insufficient knowledge of existing laws, while 32.75% has no knowledge about legislations (Table 3).

An important objective of this study was to evaluate the knowledge of participants regarding drug abuse consequences on health and therapeutic possibilities. Four items referred to this purpose. An average of 58.7% of participants believed that “they know” and 41.2% have not reported proper knowledge about these domains.

The concept of vulnerability has been underlined in a number of publications issued by EU institutions and EMCDDA [4]. In vulnerable groups, the preventive measures proved their efficiency. In the scientific literature multiple levels of intervention are described. Firstly, the

individual preventive intervention aiming to increase attachment and commitment to school are often accompanied by reductions in problem behaviors [5]. However, interventions are effective when they address motivation, skills, and decision-making, as well as erroneous normative beliefs, in a similar way to effective universal interventions [6]. Secondly, the intervention at the family level is based on the development of strong connections between young people and their family. Finally, the intervention at the community level, based on specific programs aim to improve general social environment, community cohesion and group identity. We can achieve these aims by focusing on improving interpersonal communication, social skills, expression of feelings, and social support in primary environments: school, work place and family.

**Table 3.** The knowledge level about legislation

Items related with legislation	Prison punishments	Penalty	Without penalties	I don't know
Cultivation, production, storage, trading and buying of drugs with a low or medium risk	47%	23%	2%	28%
Cultivation, production, storage, trading and buying of drugs with a high risk	73%	5%	2%	20%
Buying and storage for personal uses of drugs with a low or medium risk	16%	18%	30%	36%
Buying and storage for personal uses of drugs with a high risk	21%	30%	2%	47%

**Table 4.** Knowledge related to risks of drug abuse and possibilities of therapy

Characteristics	Yes	No	I don't know
Legal highs or ethnobotanical drugs cause dependency	36%	38%	26%
Drugs may have severe side effects: confusion, hallucinations, delirium and intoxication	77%	6%	17%
Romanian healthcare system provides drug addicts biological therapy: drug withdrawal therapy, substitution therapy (Methadone, Naltrexone)	12%	34%	54%
Romanian healthcare system provides other therapeutic possibilities than medical treatment (psychotherapy, sociotherapy, ergotherapy)	5%	27%	68%

## Conclusion

An important result of our survey is that drug use among music festival visitors is averagely 3.6 times higher than the national (Romanian) prevalence in the same age group. This is why we consider them a vulnerable group with high risk. The music festival could be an "hot" point for education, research and intervention in this vulnerable group. In order to be able to make an efficient intervention we consider it important to research the protective and risk factors.

The sample's knowledge of existing legislation regarding drugs, drug abuse risks and therapeutic possibilities provided by Romanian health care system is in great proportions incomplete or can be considered at fault. This is why we consider that the primary, secondary and tertiary prevention is important among this specific population.

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## ADAPTATIVE CAPACITIES IN THE REMISSION STAGE OF ALCOHOL DEPENDENCE

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### **Abstract**

*Introduction: Initial stage of alcohol addiction remission (first 6 months of absolute abstinence) is an extremely difficult period for the organism of any patient. At this stage in the course of disease, there are several factors that can cause early relapse of alcohol dependence. The aim of the research was to study the role of affective disorders of different intensity (at clinical or sub-clinical level) in triggering early relapses in patients with alcohol dependence.*

*Method: This study included 155 patients with alcohol addiction during the onset of remission stage of the disease. Clinical examination (clinical and psychological tests) and laboratory measurements (hormones blood level: adrenocorticotrophic, cortisol, prolactin) showed the presence of unlike affective disorders (anxiety, depression, dysphoria), as well as endocrine disturbances, compared with people from the control group (20 healthy persons matched for age and gender).*

*Results: 83.02% of the patients associated anxiety with either dysphoria or moderate depression. Early relapses were found in patients with anxiety associated with depression or pronounced dysphoria at clinical level, with a higher frequency when anxiety was associated with other affective disorders at subclinical level. Early alcoholic relapses were more frequent when anxiety was associated with pronounced pathological compulsion for alcohol (69.23%). In patients with predominantly clinical anxiety, the levels of ACTH ( $p < 0.05$ ) and cortisol ( $p < 0.001$ ) were significantly higher, while in those with moderate anxiety and no compulsion (at subclinical level) only the cortisol level was increased significantly ( $p < 0.001$ ). On the other hand, in patients with severe depression, the ACTH level ( $p < 0.001$ ) was significantly decreased, while the levels of other hormones remained unchanged ( $p > 0.05$ ).*

*Discussion: The results suggest that the patients with anxiety have an overactive stress system, while the function of anti-stress system remained without considerable changes. Thus, in patients with clinically manifest alcoholic depression, the pituitary component of the hypothalamus-pituitary-adrenal stress system remains underactive. That point out towards the existence of a functional-dynamic imbalance regarding the stress and anti-stress systems of the body.*

*Conclusion: In early period of remission, there is a functional-dynamic imbalance in the activity of stress and anti-stress systems in alcohol addicts, which correlates with prevalent affective disorders. In early period of remission, patients have various affective mood disorders (anxiety, depression, dysphoria), which trigger the compulsion for alcohol consumption.*

**Key words:** alcohol dependence, adaptative mechanisms, affective disorders.

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## Introduction

Initial stage of alcohol addiction remission (first 6 months of absolute abstinence) is an extremely difficult period for the organism of any patient. At this stage of disease evolution, there are several factors that can cause early relapse of alcohol dependence. Among these factors are: the phenomenon of co-dependency, anosodiaphoria, anosognosia of the disease, ignorance of social norms, low self-control, intrapsychic and interpersonal conflicts, somatic disorders, psychoendocrine disorders etc. A role in relapse to alcohol addiction is compulsion to alcohol consumption and affective mood disorders (anxiety, depression, dysphoria), which persist in these patients not only during relapse period, but also in the remission stage. Modern scientific research dedicated to alcohol dependence [4, 5, 7] demonstrated the negative impact of affective disorders on the remission of the disease.

The mood disturbances in alcohol addicts have some specific features in the early period of disease remission: 1) usually, spontaneously installed; 2) intensified in early stage of remission, reduced by abstinence evolution; 3) multiple and polymorphous, 4) patients perceive this as a psychological discomfort and the cause of this discomfort is referred to alcohol ingestion refraining; 5) frequently, it is found a positive correlation between the emotional disturbances intensity, compulsion to alcohol addiction and early recurrence of alcohol addiction [1, 2, 21].

Scientific literature [3, 4, 7, 12, 15, 20] tended to systematize the existing mood affective disorders in early remission stage. From many psychopathological disorders characteristic to alcohol dependence, as common at the early remission, are emphasized the following syndromes: depression, dysphoria, cognitive impairment [12, 18]. Another study showed that the prevalent syndromes are the depressive, dysphoric and neurotiform types [11; 19]. A large number of researchers [3, 10, 11, 16, 17, 20, 21], studying affective disorders characteristics for the early period of remission from alcohol dependence, reported that they are polymorphic, undifferentiated, more commonly depressive syndrome, often being a starting point for early recurrence of the disease. Depressive manifestations in most cases are associated with anxiety, with asthenic component, dysphoria or hypochondria [3, 12, 20].

Clinical analysis of alcoholic remission period, revealed the following types of subdepressive state, in patients with initial stage of remission: 1) astheno-vegetative 2) dysphoric, 3) dissociative, 4) sadness type, deep sorrow [11, 23]. Markovskaia (1987) reported in early remission period in alcohol dependent people the following types of affective disorders: asthenic depression (as hypo- and hypersthenic), dysphoric depression, hypochondriac depression; "typical" depression symptoms characteristic for endogenous depression. The author noted that asthenic type disorders have positive impact in maintaining remission stability and that dysphoric type is often the cause of early relapse [15]. There are also opinions, according to which, depression in the stage of remission of alcohol dependency, is more likely to be of psychogenic origin [8, 10].

The analysis of literature data concerning affective disorders, in the remission stage of alcohol dependency, allows us to conclude that in most cases the following psychopathological syndromes persist: 1) anxiety 2) depression, 3) dysphoria.

In some patients, during the initial period of remission of alcohol dependency, there are various deviations in psychological status: mild hypothyria, anxiety and mild dysphoria. In most cases, the spectrum of affective disorders does not reach the level of clinical manifestation, or are so vague, and often, neither patients, nor doctors take it in consideration or don't assess them adequately. Frequently, we can notice them before disease recurrence. Alcohol ingestion induces short-term improvements in patients' emotional state, so that they can be classified as factors predisposing to recurrence of alcohol dependence.

The aim of the research was to study the role of affective disorders of different intensity (at clinical or subclinical level) in triggering early relapses in alcohol dependent people.

## **Method**

155 patients with alcohol addiction during the onset of remission stage of the disease (first 6 months after discharge from hospital) were investigated clinically, paraclinically (radioimmunoassay methods and Hardware test standards: ACTHK-PR - company "Cis" - to assess blood levels of ACTH, СтероH-K125-J - to estimate the level of cortisol, HPRLK-PR - Cis company "- to assess blood levels of prolactin). The hormones of blood mentioned levels were investigated in all subjects included in the study and also in 20 healthy individuals (men of the same age) as a reference group (blood levels of these hormones were: for ACTH -  $40.43 \pm 3.21$  pg / ml for cortisol -  $420.80 \pm 25.88$  nm / l for PRL -  $154.70 \pm 8.78$   $\mu$  k a. / L). Taking into account the particularities of hormone secretion biorhythm, blood levels of all hormones studied, were assessed at the same time of the day (in the morning, between 8 and 9 a.m., fasting). Depending on the clinical and physiological indices (affective disorders), the study sample was divided into three groups: 1) with prevalence of anxiety, 2) with prevalence of depression, 3) with prevalence of dysphoria. Each of the study groups, depending on the intensity of affective disorders was divided into two subgroups: a) affective disorders at sub-clinical (can be detected only through psychological testing) and b) people showing clinical affective disorders.

## **Results and discussions**

This study demonstrated that patients with anxiety prevalence at a subclinical level presented some deviations in their behavior, especially on social networking. These patients lacked the initiative, could be easily influenced from psychological point of view, avoided difficulties in habitual and critical situations, performed pedantic other people's instructions, living acute any failure, which was

immediately subjected to detailed analysis. Frequently they considered themselves inferior, unhappy, compared to other people. Also, these patients presented persisting unjustified fear and anxiety.

The indifferent attitude or accusing entourage causes them anxiety. In such cases, we have resorted to painstaking analysis of interpersonal relations. These patients often seemed to be alarmed by possible failures, showing distrust in their own abilities. In discussions, they accused the inability to master emotions, telling that tendencies to control emotions result in headache, fatigue, rapid exhaustion. Anxiety level, according to Ch. Spilbergher scale in this group of patients was within 31 to 45 points inclusive.

Patients with clinical-level anxiety have persistent discomfort, tension and inner unrest. These patients analyzed in detail their behavior during alcohol abuse, exposing thoughts with obsessive character, psychological climate in the family, social relations, both related to fortification period and the "future without alcohol". They had characteristic feeling of inferiority. In situations that implied the probability of alcohol intake, they became overly cautious, clumsy, hesitant and incapable to make decisions independently. Due to the presence of self-untrust, they could be easily influenced by others, including former "carousing companions." They avoided situations involving responsibility, preferring to carry out the orders of others, a fact that probably explains the possible negative influence of peers in the sense of resuming drinking. In the early establishing remission, patients from this group were seeking for support, continuous compassion, showing desperation in cases of absence of attention. Also, they felt internal psychological pressure, fear of new lifestyles, which excluded systematic fortification, and had already become a habit. The search of moral support was felt in their behavior and relationships with family members. Usually they were pedantic and cautious. Conscientious enough, and fulfill their service obligations. They are generally very responsible, for fear of "not wrong" lacked their own initiative. In all failures, they were likely to accuse or looked for entire systems of explanations, in order to get calm. Anxiety level, according to Ch. Spilbergher scale was more than 45 points.

Early relapse of alcoholism in this population usually were caused by the negative influence of peers supervisor, friends parties, or failures in solving daily problems difficult.

Referring to the data obtained from clinical investigations and clinical-psychological tests performed, we can mention that in most cases, early disease recurrence in patients of this group developed when it was present anxiety at clinical level (Table 1).

It should be noted that not all patients with anxiety at clinical level developed recurrences. Seeking explanation for this phenomenon, it was examined the influence of other affective disorders (dysphoria, depression) associated anxiety, and the instinct of addiction to alcohol, on developing early alcohol relapse in patients with predominance of anxiety. To achieve the objectives of the study, patients were divided into the following groups: 1) dysphoria of clinical level and 2)

dysphoria of subclinical level, 3) depression of clinical level, and 4) with depression of subclinical level; 5) with marked addiction to alcohol and 6) moderate alcohol addiction.

**Table 1.** Frequency of early relapse in alcohol dependence, depending on clinical levels of anxiety

Groups of patients	No early relapses	Early relapses
Anxiety of clinical level (n=25)	$\frac{13}{52.0}$	$\frac{12}{48.0}$
Anxiety of subclinical level (n=28)	$\frac{25}{89.29}$	$\frac{3}{10.71}$

**Note:** - the numerator - number of patients, the denominator - their percentage.

**Table 2.** The early onset of alcohol relapses depending on the character of affective disorders and compulsion for alcohol addiction in patients with prevalence of anxiety (n = 53)

Groups of patients	Number of patients with:	
	Affective disorder	Early relapses
Anxiety + marked dysphoria	$\frac{9}{16.98}$	$\frac{1}{11.11}$
Anxiety + moderate dysphoria	$\frac{44}{83.02}$	$\frac{14}{31.81}$
Anxiety + marked depression	$\frac{9}{16.98}$	$\frac{1}{11.11}$
Anxiety + moderate depression	$\frac{44}{83.02}$	$\frac{14}{31.81}$
Anxiety + marked compulsion for alcohol addiction	$\frac{13}{24.52}$	$\frac{9}{69.23}$
Anxiety + moderate compulsion for alcohol addiction	$\frac{40}{75.47}$	$\frac{6}{15.0}$

Data presented in Table 2 demonstrate that, most frequently, the anxiety was associated with dysphoria or moderate depression. The percentage of patients with such combinations of affective disorders was - 83.02%. The same regularity was highlighted and in the case of compulsion for alcohol addiction, at the majority of patients with predominance of anxiety was detected the presence of moderate compulsion to alcohol addiction.

Studying the early alcohol relapses in these patients, despite the expected results, as that, the early relapses will be initiated in patients with anxiety associated with depression or pronounced dysphoria (clinical level), it was detected a higher frequency of these namely then, when the anxiety was associated with other affective disorders at subclinical level. Therefore, the percentage of relapses in the case of combination, anxiety with depression or moderate dysphoria, (of subclinical level) was higher (31.81%) than, when the anxiety was associated with dysphoria or pronounced depression (11.11%). The affective disorders mentioned, being of subclinical level, are often not considered by practicing physicians, a fact, which may explain the high frequency of early recurrence of alcohol addiction to patients with affective disorders at the subclinical level. *It follows that in the early period of establishing remission for alcohol dependence, it is absolutely necessary*

*to undergo clinical-psychological testing of all the patients, in order to detect early the affective disorders at subclinical level*, in order to manage a complex treatment, clinical argued, that would prevent the early relapses. As regards, the compulsion for alcohol addiction, the early alcoholic relapses were more frequent, when the anxiety was accompanied by pronounced pathological compulsion for alcohol (69.23%). In most cases the compulsion for alcohol, in these patients, is manifested by obsessive thoughts with reference to the situations related to the alcohol intake. It was often like "the confrontation of the motivations" (type affective ambivalence, ideation, behavioral). Very often the update of pathological impulse for alcohol was preceded by dreams, with alcoholic theme. Therefore, the probability of early relapse of the alcohol addiction was higher in patients with prevalence of anxiety, when it was associated with depression, dysphoria at subclinical level or with pronounced pathological compulsion for alcohol (of clinical level).

It should be mentioned that, in alcohol addicts, manifesting various affective disorders, at the same time, multiple somato-vegetative, vascular, neurological, neuro-endocrine etc. disturbances are present. [1,12,24]. There are described several mechanisms underlying neuro-endocrine disturbances arising as a consequence of chronic alcoholism: 1) ethanol disturb hormone metabolism in the liver 2) blocks biosynthetic processes acting directly toxic to the glands of internal secretion 3) acts on pituitary gland inhibiting the synthesis and / or secretion of pituitary hormones; 4) alcohol influences on hypothalamus by inhibiting the secretion of liberine, causing secondary changes in pituitary and peripheral endocrine glands [2, 25].

Some scientists consider that for patients with alcoholism, various hypothalamic syndromes are characteristic. One of the pathogenic mechanisms of damage to the hypothalamus is the brain catecholamine system dysfunction. Rich blood supply of hypothalamus facilitates the action of toxic ethanol metabolites and ethanol on hypothalamus. Advanced degree of alcoholism affecting different brain structures, and primarily the hypothalamus, leads to disruption of peripheral endocrine function [27] both transpituitary and direct due to toxic action of alcohol and its metabolites on endocrine glands [9]. Neurochemical research on the mechanisms of development alcoholism is based on the concept of stress, particularly emotional stress [2]. For these reasons, most scientific research aimed for studying the biochemical indices of disease and neuro-endocrine function provides the analysis of the main "axes of stress' pituitary - adrenal, pituitary - thyroid, hypophysis - gonads.

Neuro-endocrine disorders occurring in alcohol dependent patient body are present both, in recurrence period and in remission. Clinical and experimental studies [11, 26] have shown that chronic alcohol abuse causes a number of endocrinopathies. The first undergone changes in neuroendocrine axis control system are: hypothalamus - pituitary - adrenal and hypothalamus - pituitary - gonads [11]. Depending on premorbid deviations of androgen status were divided into

two clinical forms of the disease present especially in men: 1) alcoholism in men "hiperandroids" and 2) alcoholism in men "hypoandroids" [11]. Other scientists studying neuroendocrine changes in patients with alcoholism [26] proposed a separation of alcohol dependence that evolves hyperadrenocorticotropinemia because in these patients was found extremely strong alcoholic motivation for hiperproduction of ACTH [11, 12, 26]. Ethanol action on axis hypothalamus - pituitary - adrenal occurs through activation of [6, 9, 11] its function [6; 9; 11] phenomenon that induced ACTH hypersecretion and oxy cetosteroides.

Another group of researchers [14] presented data on the reversibility of these neuroendocrine changes after a long period (more than 1 year) of total abstinence, which is argued by restoring hypothalamic control of endocrine function.

**Table 3.** Hormonal status of patients with different affective disorders

Groups of patients with:	Baseline hormone		
	ACTH (M±m; P) (pg/ml)	Cortisol (M±m; P) (nmol/L)	PRL (M±m; P) (µk un./L)
Moderate anxiety (n=28)	30.80±4.45 P>0.05	566.12±26.26 P<0.001	133.31±15.85 P>0.05
Pronounced anxiety (n=25)	72.65±12.64 P<0.05	586.83±26.65 P<0.001	158.18±24.66 P>0.05
Moderate depression (n=35)	42.59±4.77 P>0.05	371.74±21.40 P>0.05	182.94±35.38 P>0.05
Pronounced depression (n=20)	17.25±4.77 P<0.001	384.07±19.62 P>0.05	132.38±15.06 P>0.05
Moderate dysphoria (n=25)	43.61±8.93 P>0.05	339.99±15.13 P<0.02	110.79±9.92 P<0.01
Pronounced dysphoria	39.61±7.12 P>0.05	336.05±20.56 P<0.02	105.01±6.22 P<0.001
Reference group	40.43±3.21	420.80±25.88	154.70±8.78

The data above show increased interest in neuro-endocrine disturbances present in alcohol addicts, in order to reveal pathogenic mechanisms that underlie the clinical manifestations of the disease. However, so far, poorly studied endocrine disturbances in patients with different clinical expression level of affective disorders make impossible the development of pathogenesis-based appropriate methods of therapy and prevention of the disease. These were the premises of the present research, which aimed to study the endocrine disturbances during incipient remission and the dependency of early alcohol relapses on these disturbances. To achieve the purpose of this work, we studied the level of ACTH, cortisol and PRL in patients presenting predominantly anxiety, depression or dysphoria with different grade of clinical manifestation. The results of these studies are summarized in Table 3.

The data acquired allow us to state that in patients with predominantly clinical anxiety, the levels of ACTH (P<0.05) as well as of cortisol (P<0.001) increases in a statistically significant way, the blood level of PRL being normal (P>0.05), while in those with moderate anxiety (subclinical level) only cortisol significantly increased (P<0.001). So we can mention that in patients with anxiety, the stress system is overactive, while the function of anti-stress system remained without considerable changes.

In the group of patients with depression prevalence, the hormonal status had its characteristic peculiarities and namely: in patients with severe depression, the ACTH level ( $P < 0.001$ ) was substantially reduced, while the levels of other hormones did not change statistically significant ( $P > 0.05$ ). Thus, in patients who clinically manifest alcoholic depression, the pituitary component of the hypothalamus-pituitary-adrenal stress system remains underactive.

In the group of patients with dysphoria predominance, markedly decreased blood levels of PRL ( $P < 0.001$ ) and cortisol ( $P < 0.02$ ) were found, ACTH levels had no statistically significant deviations compared with controls ( $P > 0.05$ ). Based on the above data, it can be stated that in patients with affective disorders with dysphoria prevalence, the anti-stress system function is considerably changed. This is not so obviously observed in patients with predominance of anxiety and depression.

The above data highlights the existence of a functional-dynamic imbalance regarding the stress and anti-stress systems of the body. Using the data presented in Table 3 (absolute values that reflect the blood levels of hormones), the S/As ratio was calculated, which is a relative index that indicates the interaction between functional status of stress (represented by blood levels of ACTH) and anti-stress (represented by blood levels of PRL) systems. We studied this ratio because we assume that the relapse of alcohol addiction does not depend significantly on the absolute value of studied hormone levels, as on disparity between the functional state of the stress and anti-stress systems in alcohol addicted patients (Table 4).

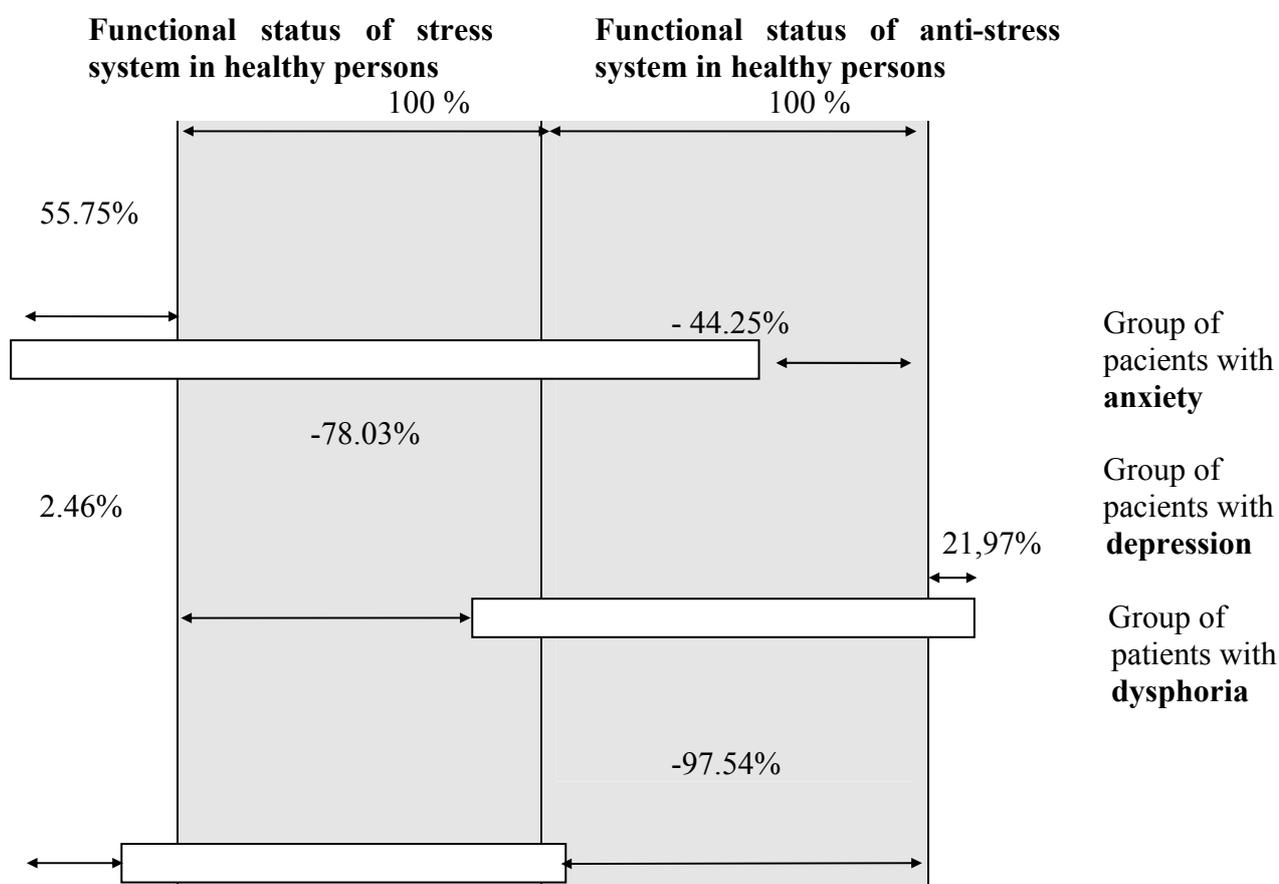
**Table 4.** Frequency of early alcohol relapses in dependency on ratio S/As in patients with different affective disorders

Groups of patients	S/As ratio	Early relapses *
<b>Anxiety</b> (n=53)	0.354	$\frac{15}{28.3}$
<b>Depression</b> (n=55)	0.189	$\frac{19}{34.54}$
<b>Dysphoria</b> (n=50)	0.385	$\frac{23}{46.0}$

Note: \* - in numerator - number of relapses, in denominator - percentage of relapses. The S/As ratio in healthy individuals is 0.261.

Table 4 shows that the S/As ratio in all patient groups is different from that found in individuals from the control group. In addition, it can be mentioned that this ratio is different in different patient groups. For a clearer statement of received data, the S/As ratio was represented graphically (Figure 1). Thus, it is obvious that in patients with anxiety prevalence, the S/As ratio is different from that found in healthy individuals due to the hyperfunction of stress system and hypofunction of the anti-stress system. But it is interesting that in patients with anxiety, the stress system is functionally elevated to the same level to which the functional activity of the anti-stress system is diminished [ (+ 55.75%) and (-44.25%) respectively]. So, we can conclude that in this group of patients the stress

- anti-stress balance is shifted towards the increase of stress system activity. Thus, we can assume that the function of these two systems is not essentially disintegrated but is shifted towards the stress system overactivity. Perhaps, the lowest percentage of early alcohol relapses in group of patients with anxiety compared with other groups included in the study is determined by this displacement of functional-dynamic balance between the stress/anti-stress systems of the body. In patients with predominance of depression, hypofunction of stress system and, at the same time, hyperfunction of the anti-stress system is observed, but unlike to patients with anxiety, functional disintegration between those two studied systems is obvious [(-78.03%) and (+ 21.97%) respectively]. Eventually, the percentage of relapses was higher, too.



Referring to patients with prevalence of affective disorders of dysphoria type, it can be observed that the S/As ratio is changed due to essential increase of the stress system activity (+ 2.46%) and obvious hypofunction of the anti-stress system (- 97.54%). So, in this group functional disintegration of stress – anti-stress systems is mostly expressed. As a result, the highest percentage of early alcohol relapses was present in patients with dysphoria prevalence.

Thus, the psycho-endocrine disorders in alcohol addicts may be one of the essential causes of early alcohol relapses.

## Conclusions

In early period of remission establishing of alcohol addiction, patients presented various affective mood disorders (anxiety, depression, dysphoria), which update the compulsion for alcohol addiction. During the first 6 months of remission of alcohol addiction, patients presented different hormonal changes according to prevalent affective disorder and their intensity. Psycho-endocrine disorders present during early remission of alcohol addiction need to be taken into account for the successful prevention of early alcohol relapses. In early period of remission, there is a functional-dynamic imbalance in the activity of stress and anti-stress systems in alcohol addicts, which correlates with prevalent affective disorders, the imbalance that reflects the adaptive capabilities of the body.

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