BALNEO RESEARCH Balneo and PRM Research Journal English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Cognitive dysfunction in patients with major depressive disorder: an observational cross-sectional study in inpatients in a tertiary center in Romania

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Citation: Trifu A.S., Pietreanu A.C., Vasile A.I., Trifu S. – Cognitive dysfunction in patients with major depressive disorder: an observational cross-sectional study in inpatients in a tertiary center in Romania
Balneo and PRM Research Journal **2025**, *16(4): 911*

Academic Editor(s):
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Received: 25.10.2025
Published: 28.12.2025

Reviewers:
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Abstract: Major depressive disorder (MDD) is considered one of the most debilitating psychiatric disorders, with a high rate of relapse and recurrence. Several studies evaluated cognitive dysfunctions in MDD: executive function, decision-making capacity, memory, attention, and processing speed. This study aimed to examine the cognitive dysfunction of patients with MDD. The study was conducted on 81 patients (56 males) aged between 21 and 75 years old with the primary diagnosis of MDD admitted in a psychiatric ward from a tertiary center in Romania. The instruments used were: introductive questionnaire, modified fatigue impact scale, cognitive failures questionnaire, perceived deficits questionnaire, cognitive complaints questionnaire, Hamilton depression scale, decision-making capacity questionnaire, and apathy scale. There are several positive correlations between depression severity and fatigability, apathy and cognitive variables. There are dif-ferences between patients in terms of depression severity depending on: the existence of suicide attempts, mode of presentation, fatigue, apathy and almost all cognitive variables, except decision-making capacity. In almost 36% of the cases, depression severity can be predicted by apathy, cognitive dysfunction, fatigue, personal history and the mode of presentation (admission directly to the ward, admission throught the Emergency Depart-ment, or via Ambulance or Police intervention). Assessing and treating cognitive symptoms in MDD improves functional outcomes. Cognitive deficits exist both in acute phases and remission phases. Most treatment options focus on the affective symptoms, but recently cognitive remission has been set as a new goal for patients with MDD.

Keywords: cognition in depression; major depression; cognitive remission; cognitive failures; cognitive apathy

1. Introduction

Major depressive disorder (MDD) is considered one of the most common and debilitating psychiatric pathologies, being recognized worldwide as a disability [1]. It is associated with a high rate of relapse and recurrence, with chronicity of approximately 20% [2]. MDD is a nervous system disease that influences affect, motivation, cognition, endocrine and behavioral function [3]. The main symptoms of depression are: sleep disorders (hypersomnia or insomnia), loss of interest in previously enjoyed activities, feelings of guilt, low energy, fatigue, apathy, low concentration capacity, modified appetite (increased or decreased), psychomotor slowness, suicidal ideation (plans of suicide, intention of suicide or past attempt of suicide). Insomnia and fatigue can impair cognitive function, contributing to anhedonia, psychomotor slowing, and reduced in-

formation-processing capacity, which complicates diagnosis and delays treatment initiation. These cognitive deficits significantly affect daily functioning, leading to psychosocial impairement marked by absenteeism, reduced productivity, lower quality of life, increased stress, and difficulties in routine and social activities.

Several studies previously evaluated cognitive dysfunction in depression. Roca et al. (2019) examined the link between cognitive disfunction and *suicidal risk* in MDD, showing that **executive impairments** promote maladaptive coping, persistent rumination, reduced positive thinking, and increased suicidal tendencies. They concluded that impulsivity and impaired **decision-making** are key contributors to suicide risk in patients with MDD [4]. Neuringer (1964) showed that rigid thinking is associated with suicidal behavior and emphasized the role of executive functions (such as cortical inhibition, long-term memory, and cognitive flexibility) in preventing self-destructive responses to stress. Neuringer (1964) proposed that cognitive dysfunction may represent a state (present only during acute illness), a trait (predisposing to depression and relapse), or a scar (persistent deficits beginning with early episodes). Recurrent episodes may deepen this scar further worsening cognitive impairement [5].

Zaremba et al. (2019) demonstrated that patients with MDD who are not in remission have a moderately reduced **processing speed**, a moderate deficit in **short-term verbal performance** and **visuospatial memory** compared to a control group. Zaremba et al. (2019) also highlighted that processing speed may have a mediating role between depressive status and deficits in working, visuospatial, and verbal memory [6].

Wang et al. (2020) evaluated quality of life, cognitive deficits, and productivity in patients with depressive disorder and demonstrated the importance of assessing and treating cognitive symptoms to improve *functional outcomes*. Deficits in executive function, memory, and attention negatively impact treatment outcomes in terms of clinical, functional, productivity, and quality of life. On the other hand, it was postulated that cognitive dysfunction may be a key factor that affects the occupational functionality of the patient and their moment of returning to work [8]. There are memory deficits and deficits in executive function, particularly on tasks that involve goal switching and mental flexibility. Additionally, executive dysfunction has been shown to occur also in younger patients with MDD (with ages between 20 and 40 years old), but also in patients with less severe depression (with a Beck Depression Inventory score of 17-21 points) [8].

These cognitive deficits (low concentration, memory deficits, and psychomotor deficits) are moderate and are always less relevant compared to affective impairment. When the patient has both affective changes and cognitive changes, there is a greater risk of misdiagnosis. Previous studies underscored the need to anticipate longer and more intensive treatment in elderly patients with MDD accompanied by cognitive deficits [9]. It was demonstrated that there are different cognitive deficits among patients with MDD compared to Alzheimer's patients [8,10]. Examining the forgetting rate of patients with MDD and patients with Alzheimer's dementia compared to a control group, it was observed that both groups had learning deficits, but the group with dementia showed rapid forgetting, within the first 10 minutes after learning the information [8]. On the other hand, MDD patients demonstrated a normal rate of forgetting, but they required a more prolonged exposure to the stimulus than the control group to be able to memorize it. The prolonged exposure time was needed to compensate for the inefficient learning secondary to a deficit in attention and willpower [10].

Several studies support the idea that cognitive **deficits exist in MDD both in acute phases and remission phases**. Vicent-Gil et al. (2018) found that patients with MDD performed significantly worse than healthy controls in language, attention/working memory, verbal memory, processing speed and executive functioning. Vicent-Gil et al. (2018) highlighted that cognitive performance predicted depressive symptoms at the beginning and follow-up, pointing to the usefulness of cognitive assessment even at the beginning of the illness. Vicent-Gil et al. (2018) also suggested that patients with MDD should be divided into two categories based on the preservation of

cognitive function, because those with preserved cognitive function may recover more quickly and require different treatment strategies than those with cognitive dysfunction.

Most treatments focus on the remission of negative thoughts, emotion regulation strategies, problem-solving skills, communication, resolving interpersonal deficits, or behavioral activation, but cognitive dysfunction remains marginalised from standard treatment [12]. Moreover, cognitive deficits did not automatically resolve with the resolution of affective symptoms [12]. Given the high recurrence rate and the fact that cognitive deficits can increase the risk of relapse, a new goal for the treatment of MDD has been set, namely, **cognitive remission**. Working memory, verbal memory, and verbal fluency were the most sensitive to change with treatment, while executive functions, processing speed, and nonverbal memory were less sensitive to improvement [12]. Interestingly, improvements in verbal memory were more significant among young patients, while improvements in executive functions were more significant among elderly patients [12].

Recent evidence indicates that cognitive rehabilitation can meaningfully improve outcomes in patients with MDD, complementing standard pharmacological and psychotherapeutic care. Meta-analyses and systematic reviews consistently show that cognitive rehabilitation yields moderate improvements in global cognition, particularly in attention, memory, and executive functions [13–15]. Importantly, functional benefits have also been reported when interventions are sufficiently intensive and strategy-based [11,16]. A 2025 study demonstrated that structured cognitive rehabilitation programs delivered in routine services improved cognitive and psychosocial outcomes in MDD, underscoring real-world feasibility [17]. Computerized cognitive training has also been validated, offering scalable tools that may address the cognitive complaints captured in patients with MDD [18].

Beyond pure remediation, integrative approaches targeting motivation and fatigue are gaining traction. Behavioral activation, either automated or therapist-guided, has been shown to reduce depressive symptoms and suicidal ideation, and its combination with cognitive activation appears particularly promising for patients presenting with high apathy [19,20]. Similarly, adjunctive aerobic exercise has been associated with improvements in cognitive control [21], while novel augmentation strategies such as pairing cognitive rehabilitation with neuromodulation show potential in older adults with remitted depression at risk of cognitive decline [22].

Taken together, these findings suggest that cognitive rehabilitation should be considered an adjunctive treatment goal in MDD, alongside symptom remission [23]. For patients with marked cognitive failures, psychosocial fatigue, or behavioral apathy, tailored interventions that combine cognitive training with motivational and physical activation may yield the most robust improvements in both symptoms and functioning.

The present study aimed to examine the cognitive dysfunction of patients with MDD and to see how much of the intensity of depression is based on cognitive dysfunction. We examined cognitive symptoms using self-reported questionnaires that examine self-perceived cognitive dysfunction, alongside apathy and fatigue. We started from the hypothesis that cognitive dysfunction can predict the severity of depression. To this end, we highlighted several hypotheses: 1) There are significant correlations between fatigue, cognitive variables, apathy and depression severity. 2) There are differences in terms of fatigue, cognitive variables and apathy between patients based on their personal history, mode of presentation, number of previous admissions, depression severity, and the existence of a suicide attempt and level of education. 3) We can evaluate depression severity based on fatigue, cognitive variables and apathy.

The present research has an observational, cross-sectional, transversal design.

2. Materials and Methods

2.1. Participants

The study was conducted on 81 inpatients (56 males and 25 females), with ages between 21 and 75 years old. The study was conducted in one of the wards of a monodisciplinary psychiatric hospital. The hospital's organizational structure included gender-specific involuntary admission wards, with separate units for men and women. Our study took place in a ward for male involuntary admission unit, which explains the higher proportion of male participants in our sample.

The first inclusion criteria was: the diagnosis of MDD (patients who were either at their first admission, or patients who had several previous admissions). We included both voluntarily and involuntarily admitted patients. The second inclusion criteria was the need for administering at least one antidepressant drug. We included patients who had no previous psychiatric treatment, but also patients who had previous antidepressant treatment and were not working.

The exclusion criteria were: if they reported a diagnosis of memory-related disorders (such as Alzheimer's disease or any grade of dementia), or if they reported a diagnosis of neurological disorder (such as stroke, multiple sclerosis, Parkinson's disease). We also excluded patients with refractory MDD who needed electroconvulsive therapy. We also excluded patients who opted only for psychotherapy, without any medication treatment.

A priori power analysis was conducted using G*Power (version 3.1) [24] to determine the required sample size for a multiple regression. The analysis was based on an expected effect size of d=0.5 (medium effect, according to Cohen, 1988), an alpha level of 0.05, and a desired statistical power of 0.80. The analysis indicated that a minimum sample size of N=29 would be required to detect a statistically significant effect.

2.2. ***Materials and measured variables***

We used eight questionnaires: introductory questionnaire, modified fatigue impact scale (MFIS), cognitive failures questionnaire, perceived deficits questionnaire (PDQ), cognitive complaints questionnaire (COBRA), Hamilton depression scale, decision-making capacity questionnaire, and apathy scale. We applied the tests only once, at the beginning of the patients' admission.

1) **Introductive questionnaire**: consisted of 18 questions and evaluated factual data of patients: *gender*, *age*, *level of education*, *background*, *marital status*, *employment status* (employed/retired/retired because of a disease), *hereditary-collateral history*, *personal pathological history* (both somatic and psychiatric comorbidities), *type of admission* (voluntary or involuntary), *mode of presentation* (admitted directly to the psychiatric ward, admitted throught the Emergency Room, or admitted via Ambulance or Police intervention), existence of *suicide attempts*, association of *substance use*, existence of previous *treatment*, and *compliance* to previous treatment. For marital status, we divided the group into two categories: patients with social support (those married, with children, or in a relationship) and patients without social support (those who were divorced, unmarried, or alone). For the level of education, we divided the group into two subgroups: the one with a low level of education (less than 12 grades completed), and the one with a higher level of education (university). For personal pathological history, we divided the group into four subgroups: those with no previous comorbidities, those with previous psychiatric comorbidities, those with previous somatic comorbidities, and those with both psychiatric and somatic comorbidities.
2) **Modified fatigue impact scale** [25]: consisted of 21 questions rated on a Likert scale from 0 to 4 (”Never”, ”Rarely”, ”Sometimes”, ”Often”, ”Almost always”). The scale revealed four variables: *fatigue*, *physical fatigue*, *cognitive fatigue* and *psychosocial fatigue*. It is a self-report questionnaire.
3) **Cognitive failures questionnaire** [26]**:** consisted of 25 questions and evaluated minor cognitive failures that the patient had made in the past 6 months, prior to the examination. Every question was rated on a Likert scale from 0 to 4 (”Never”,

"Rarely", "Sometimes", "Often", "Almost always"). The questionnaire revealed four variables: *total cognitive failures*, *forgetting* variable, *distractibility* variable and *false triggering* variable. It is a self-report questionnaire.

4) **Perceived deficits questionnaire** [25]**:** consisted of 20 questions rated on a Likert scale from 0 to 4 ("Never", "Rarely", "Sometimes", "Often", "Almost always"). The questionnaire evaluated self-perceived cognitive dysfunction and revealed five variables: *total perceived deficits*, *attention*, *retrospective memory*, *prospective memory*, and *planning*. It is a self-report questionnaire.
5) **Cognitive complaints questionnaire** [27]**:** consisted of 16 questions and evaluated self-perceived cognitive dysfunction. Every question was rated on a Likert scale from 0 to 3 ("Never", "Rarely", "Sometimes", "Always"). The questionnaire revealed one variable: the *cognitive complaints variable*. It is a self-report questionnaire.
6) **Hamilton depression scale** [28]: consisted of 17 questions and evaluated the *severity of depression*. Every question was rated on a Likert scale from 0 to 5. A score of 8 to 17 reveals minor depression, 18 to 25 reveals moderate depression and over 26 reveals major depression. We divided the group into two subgroups: one with very high scores (over 30 points) and the other with high scores (between 26 and 30 points). It is a clinician-administered questionnaire.
7) **Decision-making capacity questionnaire** [29]: consisted of 14 decisional situations and measured the rationale of the patient and their grade of indecision. Each item describes a situation, and there are two possible answers, or the patient may answer with "I cannot decide". The questionnaire revealed one variable: *decision-making capacity*. It is a self-report questionnaire.
8) **Apathy questionnaire** [30]: consisted of 18 questions rated on a Likert scale from 1 to 4 ("not at all characteristic", "slightly characteristic", "somewhat characteristic", "a lot characteristic"). The questionnaire evaluated the level of apathy and revealed four variables: *apathy*, *behavioral apathy*, *cognitive apathy*, and *emotional apathy*. It is a self-report questionnaire.

The measured variables can be seen in Figure 1.

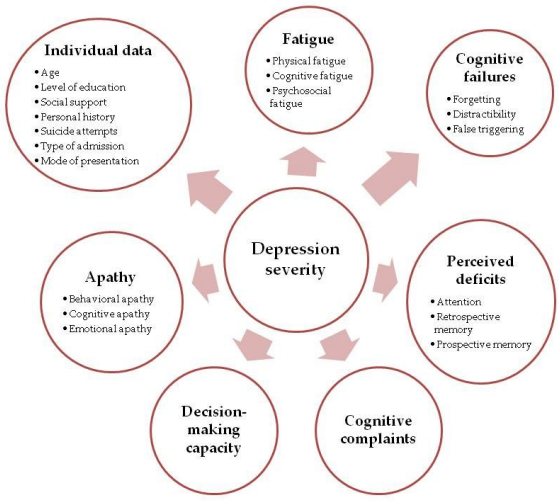

Figure 1. Measured variables in patients with MDD.

2.3. *Methods*

The methods we used to create the database included clinical interviews, a review of previous medical documents, and psychological questionnaires.

The questionnaires were administered between September and November 2020 to patients in a psychiatry ward at a tertiary medical center in Bucharest, Romania.

The entire questionnaire was composed of 124 questions, and the completion time varied according to their compliance and motivation, between 30 and 45 minutes. The

anamnesis and the questionnaire were conducted in the first 3 days after patients' admission. We took care to ensure that each participant fully completed all questionnaires in order to maintain the integrity and completeness of the data.

Patients were informed about the study, its purpose and objectives, and their role in the development of the present research. They were presented with a complete description of the study. They gave their verbal and written consent to participate following research standards for human subjects, and the confidentiality of personal data was guaranteed. Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies (approved by the Ethics Committee of Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, protocol code 1063/ 4.06.2020).

*2.4. **Statistical analysis***

The statistical analyses were designed to explore associations between depression severity and a range of clinical, cognitive, and psychosocial variables, and to identify predictors of depression severity in patients with MDD. Analyses were conducted using SPSS version 22.

The choice of statistical methods was guided by the study's objectives, the measurement level of the variables, and the distributional properties of the data. Descriptive statistics were first used to characterize the sample, including means, standard deviations, ranges, skewness, kurtosis, and Kolmogorov-Smirnov tests for normality. This step ensured appropriate selection of subsequent parametric or non-parametric tests. Correlation analyses were employed to examine bivariate associations between depression severity and cognitive, fatigue, and apathy measures. Pearson correlations were used for normally distributed (parametric) variables, while Spearman correlations were applied to non-normally distributed (non-parametric) variables. This dual approach minimized the risk of violating statistical assumptions and ensured robust identification of linear relationships. Group comparisons were conducted to test whether depression severity differed across subgroups defined by factual characteristics (e.g., suicide attempt history, mode of presentation, personal history, education level). Independent t-tests were used for parametric variables, Mann–Whitney tests for non-parametric variables, and one-way ANOVA for comparisons across more than two groups (e.g., subgroups of medical history). These tests provided a rigorous framework for exploring categorical influences on depression severity. Multiple regression analysis was employed to identify independent predictors of depression severity. This model accounted for potential confounding by simultaneously including multiple candidate predictors, thereby allowing the assessment of their relative contributions.

The dependent variable in the regression model was depression severity, measured with the Hamilton Depression Rating Scale. Independent variables were selected based on results from prior analyses (t-tests, Mann–Whitney tests, and ANOVA), which identified variables showing significant associations with depression severity. This stepwise selection ensured parsimony and relevance of predictors. Candidate predictors included: sociodemographic and clinical factors: personal history (psychiatric and/or somatic comorbidities), mode of presentation (admission directly to the ward, admission throught the Emergency Department, or admission via Ambulance or Police intervention), and history of suicide attempts; cognitive measures: cognitive failures and their subscales, perceived deficits and subscales, cognitive complaints, decision-making capacity; fatigue measures: total fatigue and subscales (physical, cognitive, psychosocial); apathy measures: total apathy and subscales (behavioral, cognitive, emotional). We applied a backward elimination method, starting with all candidate predictors and sequentially removing those with the weakest contributions. This method was chosen because of the large number of potential predictors and the exploratory aim of identifying the most parsimonious set of variables.

Standard regression were considered: linearity between independent variables and depression severity was assumed, consistent with prior correlation analyses; normality and homoscedasticity of residuals were assessed using descriptive statistics and scatterplots; multicollinearity was evaluated with tolerance and variance inflation factor (VIF) values, which were within acceptable limits (tolerance >0.5, VIF <2); independence of errors was tested using the Durbin-Watson statistic, which indicated acceptable values close to 2.

3. Results

3.1. Descriptive statistics

The research group consisted of 81 patients, 25 female (30.86%) and 56 male (69.13%). 52 (64.19%) were from urban areas, 27 (33.33%) were from rural areas, and 2 (2.46%) patients reported that they did not have a place to live at the moment of the examination. The patients were aged between 21 and 75 years, with a mean age of 46.14 and a standard deviation of 13.055. Of the participants, 54 of them had a low and moderate level of education (66.66%), while 27 (33.33%) of them had a higher level of education (graduated from university). The group consisted of 68 (83.95%) patients who were admitted voluntarily, and 13 (16.04%) patients who were admitted involuntarily. 15 (18.51%) of the patients were on their first admission to the psychiatry ward, and 66 (81.48%) had several previous admissions (with an average number of admissions of 8.358 and a standard deviation of 15.15). 25 (30.86%) patients had a suicide attempt. As for personal history, 12 (14.81%) patients had no other comorbidity, 23 (28.39%) patients had associated organic pathologies, 32 (39.5%) patients were known to have a psychiatric disease, and 14 (17.28%) patients suffered from both psychiatric and organic diseases. In terms of social support, we had 50 patients with social support (married, cohabiting or in a relationship) and 31 without social support (divorced, unmarried, single or widowed). More details about the other factual data of the patients can be seen in Table 1.

Table 1. Distribution of factual data among patients with major depressive disorder

Variable	Distribution			
Gender	25 female (30.86%)		56 male (69.13%)	
Background	52 from urban areas (64.19%)	27 from rural areas (33.33%)	2 did not have a place to live at the moment of examination (2.46%)	
Level of education	54 low-moderate level (66.66%)		27 higher level (33.33%)	
Type of admission	68 admitted voluntarily (83.95%)		13 admitted involuntarily (16.04%)	
Mode of presentation	11 arrived by ambulance (13.58%)	9 arrived by ambulance and police (11.11%)	45 admitted directly to the ward (55.55%)	16 admitted through the Emergency Department (19.75%)
Number of previous admissions	15 at their first admission (18.51%)		66 at their multiple admission (81.48%)	
Suicide attempts	25 had (30.86%)		56 had not (69.14%)	
Personal history	12 no other comorbidity (14.81%)	23 had a somatic history (28.39%)	32 had a psychiatric history (39.5%)	14 had both somatic and psychiatric history (17.28%)
Associated addictions	7 alcohol consumption (8.64%)	23 smoking (28.39%)	18 both nicotine and alcohol consumption (22.22%)	
Social support	With social support: 50 patients: 37 (45.67%) married patients, 7 (8.64%) patients in cohabitation, and 6 (7.4%) who were in a relationship		Without social support: 31 patients: 9 (11.11%) were divorced, 5 (6.17%) were unmarried, 17 (20.98%) reported being single, and 1 (1.23%) was widowed	
Retired or not	33 employed (40.74%)	28 retired (34.56%)	17 retired due to psychiatric disorder (20.98%)	
Family history	21 had (25.92%)		60 had not (74.09%)	

The descriptive statistics for the variables that resulted from the questionnaires are presented in Table 2 (mean, standard deviation, minimum, maximum, skewness, kurtosis, Kolmogorov-Smirnov test for normality).

Table 2. Descriptive statistics for cognitive variables

							Kolmogorov-Smirnov normality test		
	Minimum	Maximum	Mean	Std. Deviation	Skewness	Kurtosis	Statistic	Df	Sig.
Age	21	75	46.14	13.05	.07	-.77	.06	81	.200*
Fatigue	0	84	42.16	20.54	-.02	-.81	.06	81	.200*
Physical fatigue	0	36	18.37	9.52	.04	-.86	.05	81	.200*
Cognitive fatigue	0	40	19.33	9.91	-.09	-.90	.10	81	.040
Psychosocial fatigue	0	8	4.43	2.35	-.24	-.95	.15	81	.000
Cognitive failures	3	84	40.02	21.97	.23	-.96	.08	81	.167
Forgetting	1	28	14.33	7.76	.07	-1.18	.10	81	.039
Distractibility	1	29	13.48	7.16	.30	-.77	.10	81	.023
False triggering	0	25	10.31	6.91	.42	-.86	.10	81	.031
Perceived deficits	1	73	29.52	17.65	.33	-.84	.10	81	.040
Attention	0	20	8.60	5.15	.14	-.81	.07	81	.200*
Retrospective memory	0	20	6.63	5.04	.59	-.56	.13	81	.001
Prospective memory	0	15	5.99	4.42	.56	-.79	.12	81	.002
Planning	0	20	8.30	4.92	.16	-.80	.08	81	.200*
Cognitive complaints	1	45	19.01	11.39	.26	-.76	.09	81	.073
Depression severity	12	46	30.23	6.79	.13	.10	.08	81	.200*
Decision-making capacity	0	11	4.68	2.30	.12	-.41	.10	81	.036
Apathy	5	41	19.43	8.71	.45	-.57	.11	81	.009
Cognitive apathy	3	20	9.30	4.23	.65	-.30	.12	81	.005
Behavioral apathy	-5	7	-.69	2.70	.65	.50	.13	81	.002
Emotional apathy	5	21	11.70	3.40	.28	.03	.09	81	.068

3.2. Correlational analysis

The first hypothesis searched for correlations between fatigue, cognitive failures, perceived cognitive deficits, cognitive complaints, decision-making capacity, apathy and depression. To this aim, we ran two correlation analyses.

Using Pearson correlation for the parametrical variables, the results showed that there are significant correlations between depression severity and: fatigue (positive correlation; $r=0.43$; $r^2=0.18$; $p=0.000$); physical fatigue (positive correlation; $r=0.42$; $r^2=0.17$; $p=0.000$); cognitive failures (positive correlation; $r=0.50$; $r^2=0.25$; $p=0.000$); attention (positive correlation; $r=0.33$; $r^2=0.10$; $p=0.002$); planning (positive correlation; $r=0.37$; $r^2=0.13$; $p=0.001$); cognitive complaints (positive correlation; $r=0.37$; $r^2=0.13$; $p=.000$); and emotional apathy (negative correlation; $r=-0.285$; $r^2=0.07$; $p=0.010$).

Using Spearman correlation for the non-parametrical variables, the results showed that there are significant correlations between depression severity and: cognitive fatigue (positive correlation; $r=0.42$; $r^2=0.17$; $p=0.000$); psychosocial fatigue (positive correlation; $r=0.45$; $r^2=0.20$; $p=0.000$); forgetting (positive correlation; $r=0.8$; $r^2=0.23$; $p=0.000$); distractibility (positive correlation; $r=0.48$; $r^2=0.23$; $p=0.000$); false triggering (positive correlation; $r=0.47$; $r^2=0.22$; $p=0.000$); perceived deficits (positive correlation; $r=0.39$; $r^2=0.15$; $p=0.000$); retrospective memory (positive correlation; $r=0.38$; $r^2=0.14$; $p=0.000$); prospective memory (positive correlation; $r=0.33$; $r^2=0.10$; $p=0.000$); apathy (negative correlation; $r=-0.34$; $r^2=0.11$; $p=0.001$); cognitive apathy (negative correlation; $r=-0.35$; $r^2=0.12$; $p=0.001$); and behavioral apathy (negative correlation; $r=-0.38$; $r^2=0.14$; $p=0.000$).

3.3. Group differences analysis

The second hypothesis searched for differences in depression severity based on the factual variables and based on fatigue, cognitive variables and apathy. To this aim,

we ran several independent t-tests for the parametric variables, several Mann-Whitney tests for the non-parametric variables and one ANOVA.

- We searched for any differences in terms of depression severity depending on the factual variables (level of education, social support, type of admission, mode of presentation, existence of a suicide attempt). To this end, we performed independent t-tests, and the results can be seen in Table 3.

Table 3. Independent t-tests for depression severity based on factual variables

	Levene Test for Equality of Variances		T-test for Equality of Means				
	F	Sig.	t	df	Sig (2-tailed)	Mean Difference	Std. Error Difference
Level of education	.80	.372	.33	79	.741	.53	1.61
Social support	.10	.750	-1.04	79	.298	-1.62	1.55
Type of admission	.02	.886	.21	79	.828	.45	2.08
Mode of presentation	2.941	.090	2.090	79	.040	3.60	1.72
Suicide attempt	0.43	.836	2.671	79	.009	4.23	1.58

The result presented in Table 3 means that there are differences in depression severity based only on: mode of presentation (admitted directly to the ward versus admitted throught the Emergency Department or via Ambulance or Police; t (79)=2.941, p=0.040) and suicide attempt (t(79)=2.671, p=0.009).

- We searched for any differences in terms of cognitive variables, apathy and fatigue depending on depression severity. We divided the group of patients into two subgroups: the ones with lower severity depression (with a score on the Hamilton scale lower than 30) and the ones with higher severity depression (with a score on the Hamilton scale higher than 30). To this end, we performed independent t-tests for the parametric variables, and the results can be seen in Table 4. Also, we performed Mann-Whitney tests for the non-parametric variables, and the results can be seen in Table 5.

Table 4. Independent t-tests for parametric variables based on depression severity

	Levene's Test for Equality of Variances		t-test for Equality of Means				
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Fatigue	2.39	.126	4.42	79	.000	18.21	4.11
Physical fatigue	4.33	.040	4.11	74.720	.000	7.88	1.91
Cognitive failures	1.50	.224	5.46	79	.000	22.89	4.18
Attention	2.56	.113	3.31	79	.001	3.58	1.08
Planning	3.97	.050	3.20	75.952	.002	3.29	1.02
Cognitive complains	3.31	.072	3.75	79	.000	8.82	2.34
Emotional apathy	.10	.753	-2.24	79	.028	-1.65	.73

Table 5. Mann-Whitney tests for non-parametric variables based on depression severity

	Mann-Whitney U	Z	Sig.
Cognitive fatigue	400.50	-3.95	.000
Psychosocial fatigue	417.50	-3.83	.000
Forgetting	365.00	-4.29	.000
Distractibility	362.50	-4.32	.000
False triggering	363.50	-4.31	.000
Perceived deficits	451.50	-3.47	.001
Retrospective memory	462.50	-3.37	.001
Prospective memory	494.00	-3.08	.002
Decision-making capacity	731.50	-.835	0.40
Apathy	553.00	-2.51	.012
Cognitive apathy	536.50	-2.68	.007
Behavioral apathy	534.00	-2.72	.007

The results presented in Table 4 and Table 5 mean that there are differences based on the severity of depression (with a Hamilton scale over 30 points and less than 30 points) for all of the fatigue variables, all of the apathy variables and almost all cognitive variables, except decision-making capacity.

- We searched for any differences in terms of depression severity depending on patients' history. We divided the group of patients into four subgroups: the ones with no previous medical history, the ones with psychiatric history, the ones with somatic history and the ones with both somatic and psychiatric history. We performed one-way ANOVA analysis that demonstrated that patients' history had a significant effect on depression severity: F (3, 77) = 3.322; p=0.024.

3.4. Regression analysis

The third hypothesis tried to predict depression severity based on the factual variables, the cognitive variables, the fatigue variable and the apathy variable. To this end, we ran a multiple regression analysis using Backward method. We used this regression method because it starts with all the predictors and removes the least significant gradually at each step. Another argument for using this method was based on the many predictors that we included in the analysis, so we chose the most fitted method. Also, this method does not support bootstrapping and cross-validation in SPSS.

The dependent variable was depression severity (measured by the Hamilton depression scale). The independent variables chosen for the regression model were based on the independent t-tests, Mann-Whitney tests, and one-way ANOVA performed in the second hypothesis. Thus, the independent variables that were submitted in the analysis were: personal history, mode of presentation, the existence of suicide attempts, apathy (and its subscales), fatigue variables (fatigue and its subscales), cognitive variables (cognitive failures and its subscales, perceived deficits and its subscales, cognitive complaints, and decision-making capacity).

The regression analysis generated 17 models, as seen in Table 6. The most relevant models were model 14 (n) and model 15 (o), with a prediction of 35.9%.

Table 6. Regression models for depression severity

Model Summary										
					Change Statistics					
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	R Square Change	F Change	df1	df2	Sig. F Change	Durbin-Watson
1	.66[a]	.44	.265	5.85	.44	2.52	19	61	.003	2.147
2	.66[b]	.44	.277	5.80	.00	.00	1	61	.983	
3	.66[c]	.44	.289	5.76	.00	.00	1	62	.981	
4	.66[d]	.44	.300	5.71	.00	.01	1	63	.910	
5	.66[e]	.43	.310	5.67	.00	.03	1	64	.853	
6	.66[f]	.43	.320	5.63	.00	.04	1	65	.843	
7	.66[g]	.43	.330	5.59	.00	.05	1	66	.811	
8	.66[h]	.43	.339	5.55	-.00	.10	1	67	.744	
9	.66[i]	.43	.346	5.52	-.00	.26	1	68	.607	
10	.65[j]	.43	.352	5.50	-.00	.35	1	69	.554	
11	.65[k]	.42	.354	5.49	-.00	.68	1	70	.410	
12	.64[l]	.42	.356	5.48	-.00	.78	1	71	.378	
13	.64[m]	.41	.356	5.48	-.00	1.01	1	72	.318	
14	.63[n]	.40	.359	5.47	-.00	.67	1	73	.416	
15	.63[o]	.39	.359	5.47	-.00	1.02	1	74	.315	
16	.62[p]	.38	.353	5.49	-.01	1.74	1	75	.190	
17	.61[q]	.37	.347	5.52	-.01	1.63	1	76	.205	

n. Predictors: (Constant), patient history, mode of presentation, behavioral apathy, psychosocial apathy, cognitive complaints, cognitive failures

o. Predictors: (Constant), patient history, mode of presentation, behavioral apathy, psychosocial apathy, cognitive failures

Dependent Variable: depression severity

We also had to check the ANOVA analysis for the relevance of the model (Table 7). We can see in Table 7 that all models are efficient in predicting the dependent variable. Moreover, we can see that both model 14 and model 15 are efficient in predicting depression severity, but the F value is higher in model 15 (F= 9.959). In Table 6, we see that this model explains 35.9% of the variance of depression severity (R = 0.632; R^2 = 0.399; adjusted R^2 = 0.359). Table 8 shows the standardized and non-standardized regression coefficients together with the t-tests, which have helped us develop the multiple regression equation for the dependent variable.

Table 7. ANOVA analysis for the regression model

Model	F	Sig.
1	2.522	.003[b]
2	2.705	.002[c]
3	2.911	.001[d]
4	3.140	.001[e]
5	3.398	.000[f]
6	3.691	.000[g]
7	4.027	.000[h]
8	4.412	.000[i]
9	4.840	.000[j]
10	5.338	.000[k]
11	5.881	.000[l]
12	6.537	.000[m]
13	7.325	.000[n]
14	8.472	.000[o]
15	9.959	.000[p]
16	11.896	.000[q]
17	15.190	.000[r]

a. Dependent Variable: depression severity

n. Predictors: (Constant), patient history, mode of presentation, behavioral apathy, psychosocial apathy, cognitive complaints, cognitive failures

o. Predictors: (Constant), patient history, mode of presentation, behavioral apathy, psychosocial apathy, cognitive failures

Table 8. Coefficients for multiple regression

		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B		Collinearity Statistics	
	Model	B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound	Tolerance	VIF
5	(Constant)	20.22	2.01		10.01	.000	16.20	24.24		
	Mode of presentation	1.94	1.47	.124	1.32	.190	-.99	4.88	.91	1.09
	Psychosocial fatigue	.47	.33	.162	1.42	.158	-.18	1.13	.61	1.62
	Cognitive failures	.07	.03	.229	1.90	.060	-.00	.14	.55	1.80
	Behavioral apathy	-.65	.24	-.258	-2.65	.010	-1.14	-.16	.84	1.18
	Personal history	1.59	.68	.221	2.33	.022	.23	2.95	.89	1.11

Dependent Variable: **Depression severiy**

Based on the results from Table 8, we can highlight the variables that influence the severity of depression the most: firstly, behavioral apathy, followed by personal history, followed by cognitive failures, followed by psychosocial fatigue and, lastly, mode of presentation.

The final model (Model 15) explained 35.9% of the variance in depression severity (adjusted $R^2 = 0.359$). The most significant predictors were: behavioral apathy (negative association, $\beta = –0.258$, $p = 0.010$); personal history (positive association, $\beta = 0.221$, $p = 0.022$), cognitive failures (positive association, $\beta = 0.229$, $p = 0.060$), psychosocial fatigue (positive association, $\beta = 0.162$, $p = 0.158$); mode of presentation (positive association, $\beta = 0.124$, $p = 0.190$). The regression indicated that depression severity in MDD patients is not only linked to affective symptoms but can be significantly predicted by cognitive dysfunction, apathy, fatigue, and contextual clinical factors.

4. Discussion

The present study highlights the significant role of cognitive dysfunction, apathy, and fatigue in shaping the severity of depression among hospitalized patients with MDD. Although affective symptoms remain the primary focus of traditional treatment, our findings underscore the need to broaden the clinical approach to encompass these non-affective dimensions of MDD. A central implication is that cognitive impairments should no longer be regarded as secondary or incidental to mood disturbances.

The first important result of our study was that depression severity positively correlated with fatigue and all its subscales: physical fatigue, cognitive fatigue and psychosocial fatigue. This means that the more severe the major depression is, the more fatigue the patient feels. These robust positive correlations point to fatigue as central clinical target. Fatigue has been linked to poorer treatment adherence, functional impairment, and higher relapse rates. In clinical practice we should routinely evaluate fatigue not only as a symptom of depression but as a predictor of treatment response and quality of life. Interventions may include optimizing antidepressant regimens, considering adjunctive stimulants in carefully selected cases, and implementing lifestyle interventions such as exercise programs, sleep hygiene, and energy-conservation strategies. Addressing psychosocial fatigue specifically may also require family and workplace interventions to reduce the social burden associated with the illness.

The second important result of our study was that depression severity negatively correlated with apathy and all its subscales: emotional apathy, behavioral apathy and cognitive apathy. Our result is different from most studies, which explain that apathy is a common feature of depression and cognitive disorders [31]. However, some previous studies still reported negative correlations between apathy and depression sever-

ity, attributing this finding to the presence of anxiety symptoms and anhedonia in certain patients [32]. The negative association between depression severity and apathy subscales, particularly behavioral apathy, has nuanced clinical relevance. Traditionally, apathy is conceptualized as overlapping with depressive symptoms, yet our findings suggest that apathy may operate as a distinct predictor of depressive severity and prognosis. Behavioral apathy, in particular, emerged as one of the strongest predictors of depression severity in regression models. This highlights the importance of evaluating motivational deficits separately from anhedonia or low mood. From a treatment standpoint, interventions that directly target goal-directed behavior, such as behavioral activation therapy, occupational therapy, or structured psychosocial rehabilitation, may be critical for breaking the cycle of passivity and worsening depression. In pharmacological care, adjunctive agents with pro-cognitive or pro-motivational effects (e.g., dopaminergic enhancers) may warrant consideration in patients with marked apathy.

Third, we found significant differences in depression severity based on mode of presentation (admitted directly to the ward versus admitted throught the Emergency Department or via Ambulance or Police). The patients that need to be admitted throught the Emergency Department or via Ambulance or Police are not aware of the critical state they are in and prefer using denial mechanisms, dissimulation, and minimizing the dangerous situation they are in. They are not aware that their current psychiatric state requires more than a consultation in the Outpatient Clinic or Day Hospitalization. We emphasize that managing acute situations in which patients are brought to the hospital by Ambulance or Police requires involvement of the social support network to help reduce the trauma many patients associate with police-assisted or Ambulance-assisted admissions. We also found significant differences in depression severity based on the existence of a previous suicide attempt, but this result is already proven by multiple previous studies [33].

The fourth important result of our study was that there were differences between patients with more severe major depression and those with less severe major depression in terms of all cognitive variables (except decision-making capacity), all fatigue variables and all apathy variables. The higher the patient's depression score, the higher the subjective deficits regarding the perception of self-image will be, and the patients will become more apathetic, because they no longer feel good about themselves in situations that imply solving tasks.

Lastly, the most important result of our study explained that the severity of depression can be predicted by: **apathy** (behavioral apathy more precisely), **cognitive dysfunction** (measured with the cognitive failures scale), and **fatigue** (psychosocial fatigue more precisely). In addition, two more predictors resulted: one that is about the patient (his **personal history**) and one that is about the **circumstances of their arrival at the hospital** (mode of presentation: directly to the ward, or through the Emergency Ward, or via Ambulance or Police). The result from the regression analysis can be seen in Figure 2.

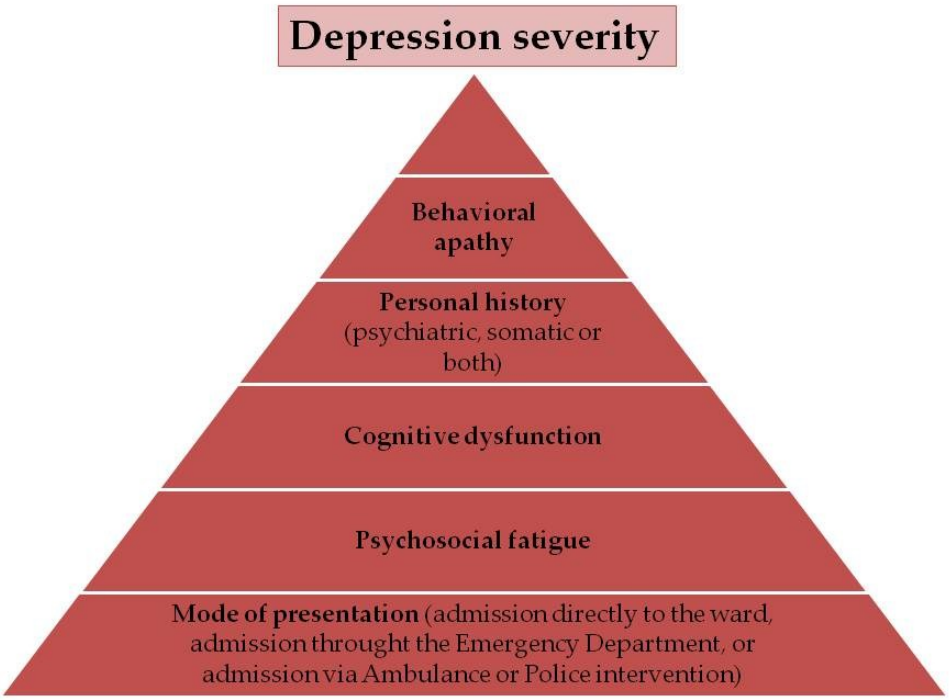

Figure 2. Predictors of depression severity in patients with MDD.

We can conclude that a patient with MDD is in a vicious circle [34]. When recent, unexplained cognitive dysfunction is accompanied by behavioral apathy lasting for more than two weeks, the clinician should consider early depression, since cognitive dysfunction can undermine self-image, reduce motivation, and lead patients to avoid tasks because of fear of a further failure, with important implications for appropriate treatment.

The inclusion of patients' personal history and mode of presentation as predictors in the regression model emphasizes the clinical importance of contextual and background factors. Previous studies, both for somatic illnesses and for psychiatric illnesses validate the personal history of the patient as an important predictor for depression. *Somatic diseases* produce depression in 12-36% of cases through comorbidity or psychological reaction [35,36]. Patients with somatic history will be more depressed with higher levels of fatigue and apathy, just because of their somatic suffering. Similarly, a *personal history of depression* may increase the risk of developing a new depressive episode, especially if the treatment management of reducing the dose by 20% every 2 months was not followed [37]. Patients with psychiatric history have previous psychiatric suffering that affects their quality of life and their ability to plan their future. Moreover, *patients with both somatic and psychiatric history* will be the ones who feel their invalidation, either somatically or psychologically, which changes their self-image, seeing their overall health in a more negative light. Lastly, *patients without any history* will have the most effective adaptive coping mechanisms, which will help them emerge from the current episode and maintain long-term remission [38]. In addition, supporting comprehensive patient health, both physical and psychological, is a core component of health policy in developed countries [39].

Our regression model explained 35.9% of the variance in the depression scale. The apparently low percentage of prediction based on factual variables, cognitive variables, apathy and fatigue is due to the fact that MDD is not reduced only to cognitive dysfunctions (in attention, memory, and thinking). These symptoms are newly evaluated in MDD, because the changes in the motivational-volitional area, the changes in the apathetic behavioral area, along with disturbances in sleep and vital energy, were long

known and validated. Previous studies support that cognitive dysfunctions that persist even during remissions may play a key role in increasing the patient's vulnerability to the recurrence of future depressive episodes [40]. Currently, it has been widely demonstrated that cognitive dysfunction sometimes remains unresolved, even after remission of depressive symptoms.

Another important result of our study was that the level of education did not influence or correlate with cognitive variables or with depression severity. However, we took into account a very raw measurement of patients' level of education, dividing them only into two categories (those with a university degree and those with a maximum of high school education). We searched for associations because previous studies suggested that a lower level of education was correlated with increased risk of depressive symptoms [41].

However, our study had several **limitations**. The design of the study was observational, so we did not have any intervention on the cognitive deficits that we observed in our patients with MDD. In line with this, we could not longitudinally objectify the patients, nor could we dynamically assess their improvement in cognitive deficits. Another limit came from the fact that we used the Hamilton depression scale, which focuses only on the affective components of depression and not on the cognitive components. Another limitation arose from using only self-reported cognitive scales; incorporating neuropsychological objective tests might have provided an alternative perspective on their cognitive dysfunction. Future studies should implement examinations using the Trail Making Test [42], Stroop Color and Word Test [43], digit spam, MoCA [44], MMSE [45] in order to better evaluate the cognitive function of patients with depression. Another limitation arose from the lack of brain imaging, which could have provided information about cortical atrophy and its potential impact on cognitive deficits. In addition to this, we did not make any differences based on the comorbidity with alcohol consumption, even though the rate of this comorbidity is quite high in Romania [46]. Another limitation arose from our analysis of the patients' social support, which focused solely on marital status and childbearing, rather than exploring their relationships with friends and social groups. Another limit of the study came from the group heterogeneity in terms of their level of education; future studies may focus on the cognitive dysfunction in patients with depressive disorder with a specified level of education. A limitation of our regression analysis was that we did not use specialized instruments for the main symptoms of depression (anxiety, insomnia, motivation, energy); adding these scales could have increased the prediction model of depression intensity alongside cognitive deficits. Another limit of our study was the percentage of patients with suicidal attempts (only 30.86% of them); future studies may focus on cognitive dysfunction among suicidal patients. Another limit of our study was the small sample size, which may reduce the generalizability of our findings. Another limit of the study was the ward profile where the study was conducted, which was a ward for involuntarily admitted men. This resulted in a relatively small number of female patients. In addition, another limitation stemmed from the recruitment of patients from a single medical center, which may introduce selection bias and limit the external validity of the study. From a treatment point of view, we did not search for differences between patients based on their previous therapeutic management, whether they had previous medication with antidepressants or not and whether they were compliant to the treatment; future studies should focus on a more specified population, such as patients with refractory MDD or patients taking only one SSRI.

5. Conclusions

The findings collectively argue for the inclusion of cognitive remission as a formal treatment goal alongside affective remission. Persisting cognitive dysfunction after mood recovery has been shown in prior studies to increase vulnerability to relapse; our results reinforce this by demonstrating that cognitive variables independently predict

depression severity. Treatment planning should therefore extend beyond symptom reduction to encompass interventions that promote functional recovery. This could involve cognitive remediation therapies, computerized training programs, or structured problem-solving approaches tailored to deficits in attention, memory, and executive function.

Furthermore, these findings suggest that we should adopt a personalized approach to treatment stratification. Patients presenting with high cognitive burden and behavioral apathy may require more intensive, multimodal interventions, whereas those with preserved cognition may respond well to standard pharmacotherapy or psychotherapy alone. Recognizing these subgroups early in treatment could enhance resource allocation and improve long-term outcomes.

The study highlights the need for healthcare services to incorporate cognitive and functional assessment into routine psychiatric care. This has implications for training, as psychiatrists, psychologists, and allied professionals should be equipped to identify and address cognitive dysfunction in MDD. Service structures may also need to expand to include cognitive rehabilitation units or integrated care pathways that bridge psychiatry, neurology, and rehabilitation medicine.

In summary, the clinical implications of this study emphasize a paradigm shift in the management of MDD. Rather than focusing exclusively on affective symptoms, clinicians must integrate cognitive dysfunction, apathy, and fatigue into diagnostic assessment, treatment planning, and long-term management. By addressing these domains, we can improve functional outcomes, reduce relapse risk, and move closer to the goal of full recovery in patients with MDD, including both affective and cognitive remission.

Cognitive rehabilitation represents a promising adjunctive intervention in MDD, addressing the often overlooked cognitive dimension of the disorder. By targeting deficits in memory, attention, and executive function, rehabilitation strategies can break the cycle of dysfunction, reduce apathy, improve fatigue management, and ultimately enhance both symptomatic and functional outcomes. As our study suggests, integrating cognitive rehabilitation into treatment plans could shift clinical practice toward a more holistic model of recovery that recognizes cognitive remission as a vital endpoint alongside mood improvement.

Author Contributions: Conceptualization, AST, ACP, AIV, ST; methodology, AST, ACP, AIV, ST; validation, AST, ACP, AIV, ST; formal analysis, AST, ACP, AIV, ST; investigation, AST, ACP, AIV, ST; resources, AST, ACP, AIV, ST; writing—original draft preparation, AST, ACP, AIV, ST; writing—review and editing, AST, ACP, AIV, ST; visualization, AST, ACP, AIV, ST; supervision, AST, ACP, AIV, ST; project administration, AST, ACP, AIV, ST. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, protocol code 1063/ 4.06.2020) for studies involving humans.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The raw data supporting the conclusions of this article will be made available by the authors on request.

Acknowledgments: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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