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10.2478/AMB-2024-0015

ORIGINAL ARTICLE

CLINICAL AND PSYCHOLOGICAL FACTORS INFLUENCING THE PERCEIVED STRESS AMONG PATIENTS WITH ANXIETY AND DEPRESSION IN REMISSION DURING THE COVID-19 PANDEMIC

V. Stoyanova, I. Kamenova, R. Vladimirova

Department of Psychiatry and Medical Psychology, Medical University – Sofia, Bulgaria

Abstract. Background and objectives: *The COVID-19 pandemic has turned into a crisis with serious direct medical influence, and also with enormous indirect socio-psychological consequences. The study, which is part of a larger one, aimed to assess the perceived stress after the first COVID-19 wave in patients with depression and anxiety in remission and healthy controls and to evaluate clinical-psychological factors as predictors for moderate/high Perceived Stress (MH-PSS-10).* ***Methods:*** *The study was cross-sectional, with 120 participants, grouped into four categories: anxiety in remission, depression in remission, healthy controls, and healthy first-degree relatives to patients with depression/anxiety. Self-assessment scales for depression and anxiety – Hospital Anxiety and Depression Scale (HADS), The UCLA Loneliness Scale – 3-point scale (UCLA-LS3), Perceived Stress Scale (PSS-10), and the State – Trait Anxiety Inventory (STAI-T, STAI-S) were used.* ***Results:*** *The groups did not differ in the level of PSS-10. Using the ROC curve analysis, significant threshold values for HADS-A (≥ 6.50), HADS-D (≥ 2.50), STAI-T (≥ 38.5), STAI-S (≥ 39.5) ($p < 0.001$), and UCLA-LS3 (≥ 3.50) ($p = 0.007$) were determined. Using the multiple binary logistic analysis, depression (OR = 2.42), loneliness (OR = 2.36), STAI-S (OR = 6.55), and STAI-T (OR = 3.43) significantly increased the risk of MH-PSS-10.* ***Conclusion:*** *Patients with complete remission of anxiety and depressive disorders did not differ from healthy controls in stress perception during the COVID-19 pandemic. Subthreshold values of depression, anxiety, and loneliness increased the feeling of moderate/high stress irrespective of the psychiatric history.*

Key words: *COVID-19, PSS-10, depression, anxiety, remission*

Corresponding author: *Assos. Prof. Vessela Stoyanova, Department of Psychiatry and Medical Psychology, Medical University, 1 Sv. Georgi Sofiiski Str., 1431 Sofia, Bulgaria, e-mail: vesstoyan@yahoo.com, ORCiD: 0000-0003-4865-1753*

Received: *01 August 2023;* ***Accepted:*** *25 October 2023*

INTRODUCTION

The COVID-19 pandemic in recent years, in addition to a serious biomedical problem (direct influence), has caused many economic and socio-psychological consequences (indirect influences). These consequences could be referred to as a "crisis" [1], which in turn resulted in a growing need for psychiatric care [2]. It is spoken about as "the new normal" [3], which implies redefining a lot of psychosocial factors that determine physical and mental health as well as overall well-being. Last, but not least, coping with death is a very critical moment for mental health globally, especially in neoliberal societies.

Considering all of the above, mental health professionals will have to cope with this relatively new and complex form of stress and trauma. The so-called bio-psycho-social and spiritual model should be applied to protect mental health in risky groups and in the general society as well [4]. In addition, COVID-19 was a global and inevitable event that has been perceived by everyone uniquely. Social restrictive measures have been known to cause psychological discomfort with a lasting effect because of their duration of months and even years after their initiation [5]. Therefore, the perceived stress should be considered as a result of the complex interplay between the traumatic situation, personality characteristics based on genetic and epigenetic factors, and the ability to use coping strategies and/or resilience [6]. Furthermore, the perceived stress could be a reason for subsequent psychosocial, mental, and somatic problems, both in the general population and in risk groups [7]. The prevailing opinion is that patients with mental disorders represent a risk group and mental problems before the pandemic could contribute to increased anxiety, depression, and stress [8,9]. At the same time, the states of anxiety and depression, including subthreshold states [10,11], as well as loneliness [12], could intensify the experience of one situation as stressful.

The current study was performed between the first and second COVID-19 "waves", a period of relatively low morbidity and mortality and therefore, low direct influences on the pandemic. Most of the stress during this time was caused by the measures and the received information about the pandemic, which makes these indirect influences interesting for analysis.

The study aims to define the levels of perceived stress in risk groups of patients with mental disorders in complete remission, compare them with healthy controls, and determine the complex impact of clinical-psychological and sociopsychological factors acting simultaneously on COVID-19-related perceived stress. We analyzed whether or not the psychiatric diagnosis acts as a risk factor for the psychological perception of stress.

MATERIALS AND METHODS

The study was cross-sectional, non-interventional, and a part of a bigger one that included a sample, recruited from July 2020 to October 2020 in the outpatient service of the Psychiatric Clinic of University Hospital "Aleksandrovska" in Sofia, Bulgaria. Overall, 120 persons were included on a consecutive principle – 30 patients with a depressive disorder in remission (MDD-R), 30 patients with an anxiety disorder in remission (AD-R), as well as 60 healthy controls – 30 first-degree relatives to patients with a history of depressive or anxiety disorder (HC-FDR) and 30 controls without a family history (HC). The participants in the study were aged ≥ 18 and have not been infected by COVID-19 till the beginning of the study. The patients were previously diagnosed to suffer from Depression (F32, F33) and Anxiety Disorder (F4), defined by the diagnostic criteria of ICD-10, and at present in remission. Clinical remission was defined as a stable condition, with a duration of at least 6 months that does not imply a change in the maintained treatment and is objectified by the Clinical Global Impression scale – Severity (CGI-S) with a score ≤ 2. The healthy controls and HC-FDR were recruited on a consecutive basis and carefully matched for age and gender with the patients.

We analyzed used media sources, and the concerns raised by the pandemic related to its medical, economic, and psychological consequences. The participants answered the question "Does the COVID-19 pandemic concern you in terms of medical, economical, and psychological (due to restraint measurements and lifestyle changes) aspects?" Three answers were available: yes, no, and can not decide. In addition, self-assessment scales for the level of anxiety, depression, perceived stress and perceived loneliness, and state, and trait anxiety were completed. We used the following instruments:

HADS (Hospital Anxiety and Depression Scale) consists of 14 items: seven items for anxiety (HADS-A), which focus mainly on symptoms of generalized anxiety with scores from 0 to 21, and seven items for depression (HADS-D), focused on anhedonia, also with scores from 0 to 21 [13]. An optimal balance between sensitivity and specificity was found using a cut-off score of 8 or above for both HADS-A and HADS-D [14].

PSS-10 (Perceived Stress Scale – 10-point variant) assesses the perceived stress in terms of the COVID-19 pandemic. The assessment is made by a 5-point Likert scale (from 0 to 4) as the values from 0 to 13 represent low levels of stress, from 14 to 26 – moderate, and from 27 to 40 – high levels of stress [15].

UCLA-LS3 (The UCLA Loneliness Scale – 3-point scale) is used to assess loneliness [16]. Values lower than 3 are considered as absent perceived loneliness, 4-5 points – moderate, and 6-9 points – marked loneliness.

STAI (State-Trait Anxiety Inventory) consists of 40 values of which 20 represent state-anxiety in terms of COVID-19 and 20 assess trait-anxiety [17]. The val-

ues of the two subscales are assessed by a 4-point Likert scale (from 1 to 4).

The evaluation and self-assessment scales were completed on the day of the examination in the outpatient service by an independent psychiatrist, who was not familiar with the patients so that the bias of the investigators to be avoided. All procedures of the study were performed after an oral and written acquaintance with the objectives of the study and written informed consent was obtained. The Commission on Ethics of Scientific Research of the Medical University of Sofia had approved the study (No. 4298/ 03/07/2020).

The clinical-psychological values from the self-assessed tests and the socio-psychological factors in terms of used media sources and the medical, economical, and psychological concerns, raised by the pandemic were analyzed.

STATISTICAL ANALYSIS

Statistical analysis was performed using the IBM SPSS Statistics 25.0. The level of significance, in which the null hypothesis was rejected, was accepted at $p < 0.05$. Descriptive methods for distribution of the considered variables, nonparametric test of Kolmogorov-Smirnov and Shapiro-Wilk for testing the distribution of normality, One-way analysis of variance (ANOVA) for testing the hypothesis of difference between means in several independent samples, Student's t-test, and nonparametric test of Mann-Whitney U for the hypothesis of difference between two independent samples, ROC curve (Receiver operating characteristic) analysis for defining threshold values of quantitative variables, binary logistic regression to define the quantitative value of the influence of the studied factors were performed. For defining the validity of the used scales, several criteria were calculated: sensitivity, specificity, positive predictive value, negative predictive value, and accuracy (% of correct answers).

RESULTS

The studied groups were well balanced *with* respect to *patient* sex and there was no difference between patient and control groups according to age. However, there was an age difference between the two patient groups. The mean age of the AD-R patient group was significantly lower by 13.5 years than that of the MDD-R patient group. Gender, age, psychometric characteristics, and socio-psychological factors of the participants are represented in Table 1.

The levels of stress, measured both as qualitative and quantitive values, were comparable among the four studied groups. Differences in the subthreshold value of anxiety have been observed, which were significantly higher in MDD-R, in comparison to HC. The difference between state- and trait- anxiety was greatest in HC-FDR, as well as the presence of a larger proportion of people with medical worries, which distinguishes this group significantly only from MDD-R.

For a regression model all individuals with values of PSS ≤ 13 (n = 37; 31%) were defined to have low and/or absent stress and those with PSS ≥ 14 (n = 83; 69%) with moderate and high levels of stress (MH/PSS-10) [18]. The quantitative values of HADS-A; HADS-D; UCLA-LS3; STAI-T, STAI-S, and the difference between the two types of anxiety STAI (S-T) as well as the categorical values of mass media and assessments of the medical, economic, and psychological concerns related to the pandemic were included in the regression model.

The values of STAI (S-T) were the only ones from the quantitative values with a normal distribution. For the rest of the metrics, a ROC curve analysis was performed to identify statistically significant threshold values that distinguish the individuals with and without stress. The areas under the curves and the level of significance have shown that significant threshold values for distinguishing low from MH/PSS-10 can be established for all of the five studied indicators.

The following rule was used in their selection:

Youden index [maximum (sensitivity + specificity−1)]

Based on this analysis significant threshold values for HADS-A ≥ 6.50 (AUC 0.726, $p < 0.001$) HADS-D ≥ 2.50 (AUC 0.722, $p < 0.001$), UCLA-LS3 ≥ 3.50 (AUC 0.651, $p = 0.007$) STAI-T ≥ 38.5, (AUC 0.815, $p < 0.001$) and STAI-S ≥ 39.5 (AUC 0.830, $p < 0.001$) were determined.

The results, displayed in Table 2, show a significant decrease in the threshold values in comparison with the results already established in the general population, especially regarding HADS [14].

To quantify the impact of the studied indicators on the risk of MH/PSS-10, a binary logistic regression analysis was applied and the results are shown in Table 3.

Table 1. Comparative analysis of demographic, psychometric, and socio-psychological characteristics of the studied groups

Characteristics	AD-R	MDD-R	HC	**HC-FDR**	Statistics
Age $\overline{X}$ ± SD	37.93 (± 8.971)	51.43 (± 14.431)	43.73 (± 15.456)	45.53 (± 15.511)	AD-R/MDD-R Independent samples t-test, F = 5.606, df = 58, p < 0.001 Mann-Whitney p = n.s.
Gender n (%) Male Female	 12 (40) 18 (60)	 9 (30) 21 (70)	 12 (40) 18 (60)	 13 (43.3) 17 (56.7)	Pearson Chi-square test = 1.269; df = 3; p = 0.810
HADS-A $\overline{X}$ ± SD	5.67 (± 3.262)	7.23 (± 4.116)	5.07 (± 2.864)	6.43 (± 4.240)	Student's t-test Mann-Whitney MDD-R/HC p = 0.021
HADS-D $\overline{X}$ ± SD	3.20 (± 2.235)	4.33 (± 3.325)	2.73 (± 1.818)	4.13 (± 3.350)	Student's T-test; Mann-Whitney p = n.s.
UCLA-LS3 $\overline{X}$ ± SD	3.87 (± 1.224)	4.60 (± 1.831)	4.27 (± 1.461)	3.90 (± 1.470)	Kruskal-Wallis H test = 4.817; df = 3; p = 0.186
PSS-10 $\overline{X}$ ± SD	14.97 (± 6.060)	17.10 (± 7.581)	16.13 (± 4.967)	16.07 (± 6.528)	ANOVA F = 0.565; df = 3; p = 0.639
Stress n (%) Low Moderate High	 13 (43.3) 16 (53.3) 1 (3.3)	 7 (23.3) 19 (63.3) 4 (13.3)	 9 (30.0) 20 (66.7) 1 (3.3)	 8 (26.7) 20 (66.7) 2 (6.7)	Fisher-Freeman-Halton Exact Test = 5.186, p = 0.530
STAI-S $\overline{X}$ ± SD	42.90 (± 10.012)	45.37 (± 10.685)	45.10 (±9.803)	48.07 (± 11.262)	ANOVA F = 1.230; df = 3; p = 0.302
STAI-T $\overline{X}$ ± SD	40.50 (± 10.207)	43.53 (± 9.769)	39.47 (±8.589)	40.73 (± 10.654)	ANOVA F = 0.938; df = 3; p = 0.425
STAI(S-T) $\overline{X}$ ± SD	2.4000 (± 7.38871)	1.8333 (± 8.20043)	5.6333 (± 6.12222)	7.3333 (± 7.21748)	ANOVA F = 3.911; df = 3; MDD-R/HC-FDR p = 0.011
Used media sources n (%) Social media Classical media Combination	 10 (33.3) 4 (13.3) 16 (53.3)	 5 (16.7) 4 (13.3) 21 (70)	 10 (33.3) 0 (0) 20 (66.7)	 7 (23.3) 1 (3.3) 22 (73.4)	Fisher-Freeman-Halton Exact Test = 8.858, p = 0.158
Medical worries n (%) Yes No Cannot decide	 22 (73.3) 6 (20.0) 2 (6.7)	 19 (63.3) 11 (36.7) 0 (0)	 20 (66.7) 6 (20.0) 4 (13.3)	 27 (90.0) 2 (6.7) 1 (3.3)	Fisher-Freeman-Halton Exact Test 13.247 df = 6 MDD-R/HC-FDR p = 0.034
Economical worries n (%) Yes No Cannot decide	 16 (53.3) 13 (43.3) 1 (3.3)	 20 (66.7) 9 (30.0) 1 (3.3)	 21 (70.0) 6 (20.0) 3 (10.0)	 21 (70.0) 6 (20.0) 3 (10.0)	Fisher-Freeman-Halton Exact Test = 6.410 p = 0.368
Psychological worries n (%) Yes No Cannot decide	 12(40.0) 15 (50) 3 (10)	 16 (53.3) 13 (43.3) 1 (3.3)	 15 (50.0) 9 (30.0) 6 (20.0)	 17 (56.7) 10 (33.3) 3 (10.0)	Fisher-Freeman-Halton Exact Test = 6.458 p = 0.371

Abbr.: AD-R – Anxiety Disorder-Remission; MDD-R – Major Depressive Disorder-Remission; HC – Healthy Controls; HC-FDR – Healthy Controls – First Degree Relatives; HADS-A – Hospital Anxiety and Depression Scale – Anxiety subscale; HADS-D – Hospital Anxiety and Depression Scale – Depression subscale; UCLA-LS3 – UCLA 3-items Loneliness Scale; PSS-10 – Perceived Stress Scale – 10-point variant; STAI-S State-Trait Anxiety Inventory- State-anxiety subscale; STAI-T State-Trait Anxiety Inventory- Trait-anxiety subscale; STAI(S-T) – the difference between State and Trait anxiety

Table 2. Threshold values of HADS-A, HADS-D, UCLA-LS, STAI–S and STAI–T for identifying individuals with and without stress and values of the criteria for validation of screening tests

Indicator	Threshold value	Sensitivity %	**Specificity** %	Positive predictive value (PPV) %	Negative predictive value (NPV) %	Accuracy %
HADS-A	≥ 6.50	53	85	88	46	63
HADS-D	≥ 2.50	73	67	82	54	71
UCLA-LS	≥ 3.50	59	67	79	44	62
STAI–S	≥ 39.5	85	67	84	68	79
STAI–T	≥ 38.5	75	77	87	60	76

HADS-A – Hospital Anxiety and Depression Scale – Anxiety subscale; HADS-D – Hospital Anxiety and Depression Scale – Depression subscale; UCLA-LS3 – UCLA 3-items Loneliness Scale; STAI-S State – Trait Anxiety Inventory – State-anxiety subscale; STAI-T State-Trait Anxiety Inventory- Trait-anxiety subscale;

Table 3. Risk ratios and 95% CI of the investigated psychological values as predictors of MH/PSS-10

Indicator	Comparison	Single				Multiple			
		OR	95% CI		p	OR	95% CI		p
			Lower limit	Upper limit			Lower limit	Upper limit	
STAI–S-T	Increase with 1	1.018	0.967	1.071	0.505				
HADS-A	≥ 6.50/ < 6.50	6.224	2.352	16.470	< 0.001				
HADS-D	≥ 2.50/ < 2.50	5.364	2.347	12.257	< 0.001	2.418	0.870	6.723	0.091
UCLA-LS	≥ 3.50/ < 3.50	2.909	1.307	6.473	0.009	2.362	0.849	6.572	0.100
STAI–S	≥ 39.5/ < 39.50	11.500	4.652	28.427	< 0.001	6.548	2.260	18.973	0.001
STAI–T	≥ 38.5/ < 38.50	10.167	4.134	25.005	< 0.001	3.427	1.183	9.933	0.023
Psychological worries	Yes /No	2.423	1.067	5.501	0.034				
	Can not decide /No	2.692	0.656	11.056	0.169				
Used media sources	Social media /Both	0.469	0.469	0.469	0.469				
	Classical media /Both	0.856	0.856	0.856	0.856				
Medical worries	Yes /No	1.506	0.601	3.778	0.383				
	Can not decide /No	1.667	0.269	10.334	0.583				
Economical worries	Yes /No	2.263	0.982	5.213	0.055				
	Can not decide /No	6.222	0.689	56.203	0.104				
Diagnosis	Controls-relatives/ Healthy controls	0.857	0.288	2.547	0.781				
	Anxiety-remission/ Healthy controls	0.560	0.193	1.623	0.286				
	Depression-remission/ Healthy controls	1.408	0.445	4.453	0.560				

Abbr. MH/PSS-10 – Moderate or High levels of stress/Perceived Stress Scale – 10-point variant; HADS-A – Hospital Anxiety and Depression Scale – Anxiety subscale; HADS-D – Hospital Anxiety and Depression Scale – Depression subscale; UCLA-LS3 – UCLA 3-items Loneliness Scale; STAI-S State-Trait Anxiety Inventory- State-anxiety subscale; STAI-T State-Trait Anxiety Inventory-Trait-anxiety subscale; STAI(S-T) – the difference between State and Trait anxiety

The risk in the study participants was the highest, with values higher than or equal to the threshold values of STAI-S (OR = 11.5) and STAI-T (OR = 10.2), and the lowest in psychological worries (OR = 2.4). Applying multiple analysis of statistically significant factors in the regression equation (Backward conditionally procedure) in step 4, four of them remain, as the values of OR decrease their value, and in some the level of significance exceeds 0.05. However, as the influence of these factors retains its direction of impact, ORs are considered statistically significant.

DISCUSSION

The present study covers the period after the first COVID-19 isolation, which was characterized by some normalization of the situation, after a period of forced isolation, restrictions, conflicting messages, and lack of sufficient information. This period was chosen to integrate all coping mechanisms for adapting to the situation. Moreover, there are data from studies that show peak anxiety and depression at the beginning of isolation and subsequent reduction in healthy individuals in longitudinal follow-ups [19]. In the investigated sample, the patients with AD-R were the youngest but differed significantly only from the group of patients with MDD-R. The probable reason for this is the earlier onset of anxiety disorders in the general population compared to recurrent depression, as well as the higher chance of achieving remission at a younger age with maintenance therapy [20]. An additional group HC-FDR, which combines both genetic predisposition and specific psychosocial factors that are different from those in the general population (coexistence with and/or taking care of the mentally ill) was formed. This group aimed to assess what distinguishes it from healthy controls as well as from patients and to what extent.

Anxiety and depression were measured by HADS, which is an appropriate tool in the general population as well as among psychiatric patients [21]. It is comparable to other tools for depression, is short, accessible, and is used to evaluate both depression and anxiety [22]. The mean scores of HADS-A, even subthreshold were higher in MDD-R patients, which differed them significantly only from HC. Similar results are reported in other studies [2]. However, it seems that the anxiety identified in this way is rather non-specific, transitory, and not necessarily related to COVID-19. The mean values of HADS-D were also subthreshold and highest in MDD-R, but the groups did not differ from each other. Comparable values in terms of anxiety and depression of the analyzed groups show that there are no significant differences in these psychometric indicators between patients in remission, healthy controls, and controls-relatives. These results do not support the prevailing literature that patients with pre-existing mental illnesses have higher levels of anxiety and depressive symptoms during a pandemic than non-psychiatric participants [8,9]. It should be noted that several studies have reported a significant increase in stress, anxiety, and depression in healthy individuals compared to the pre-pandemic period, which may also explain the similar results in our study [23]. There were no significant differences in perceived stress in the different groups, but approximately 2/3 of the participants were with MH/PSS-10.

The quantitative indicators included in the logistic regression show that the threshold values of the used self-assessment tools are lower than the accepted ones in the general population under normal conditions [14,16]. The pandemic situation in connection with its comprehensiveness and intensity causes moderate/high stress at much lower thresholds, and their predictive value is moderate to high. Probably, in the „new normal“ [3] we may need to redefine the thresholds for anxiety, depression, and loneliness in the population, as much lower values seem to have a significant predictive value for the occurrence of moderate/high stress, the consequences of which may result in impairment in mental and/or physical health. The threshold values determined by HADS decreased significantly (Table 2). To their analysis, the presence of such anxiety and depressive values increased the risk of MH/PSS-10 more than 6 and 5 times, respectively. Evaluating them by multiple analysis, anxiety is eliminated as a risk factor. Depression retains its impact, with values above certain thresholds increasing the risk 2.5 times. It seems that anxiety does not necessarily cause stress, especially when it is diffuse, but it is possible to mobilize coping strategies in a pandemic situation. These results contradict others published in the literature that anxious patients have higher levels of stress, more socioeconomic consequences, and more fears related to the medical aspects of COVID-19 than controls and patients with depression [24]. On the other hand, mild depressive symptoms make individuals more vulnerable to pandemic stress, whether or not there is a history of depression or anxiety [9]. We can conclude, like other authors, that depression, even below the threshold, is a predictor of a more intense perception of stress [25].

Even before the coronavirus crisis, loneliness was a public health problem, as it was widespread and associated with an increased risk of morbidity and mortality [26]. The experience of loneliness did not differ in the four studied groups. Evidence from the literature suggests that emotional loneliness during the pandemic was growing deeper, although the ability to maintain virtual social contacts was preserved and even increased. Loneliness plays a key role in the presence of symptoms of anxiety and depression during a pandemic [27]. Predictive values of loneliness for MH/PSS-10 are ≥ 3.50 and individually increase the risk by almost 3 times and after multiple analisis more than 2 times so even relatively low values of loneliness increase the risk

of moderate or severe stress. If anxiety can initially have adaptive characteristics, depression and loneliness are always maladaptive [28] and are predictors of a more intensive perception of stress in a pandemic situation [29].

Anxiety levels as a personality trait and as related to COVID-19 also did not differ in the compared groups. When applying the logistic analysis, however, the factors with the most serious predictive value were STAI-S and STAI-T. Probably important for the state of intensive stress is not just the presence of anxiety as a momentary state, which could be due to other factors, but the specific anxiety associated with the pandemic situation and anxiety as a personality trait. Moreover, previous studies have found that the correlation for STAI-T was higher with depression than with anxiety [30]. In addition, situational anxiety increased more in the control groups, and the difference between STAI-S and STAI-T was the greatest in HC-FDR and significantly distinguished this group only from MDD-R. Based on previous studies non-psychiatric controls may have a more significant worsening of psychological distress than patients with severe mental illness [9]. However, this indicator does not affect the level of stress in the application of logistics analysis. The probable explanation is that anxiety is adaptive and leads to the inclusion of coping strategies, which, despite the significant increase in situational anxiety, compared to anxiety as a personality trait lead to the normalization of perceived stress in healthy individuals. Our results show that relatives who are often caregivers seem to be experiencing the pandemic situation with the greatest increase in anxiety. This is probably due to the more responsibilities and expectations for dealing with the pandemic in people without mental health problems and especially in those who have mentally ill relatives. In the multiple analysis, STAI-S ≥ 39.5 and STAI-T ≥ 38.5 values increased the risk of MH/PSS-10 nearly 6.5-fold and 3.5-fold, respectively.

Attitudes toward the pandemic were largely determined by the information received. Media information and misinformation have a serious impact on stress levels [7]. It is noteworthy that a relatively small proportion of the participants (up to 33.3%) in the groups received information only from social media, which is considered the main source of fake news. The predominant share received information from both social and traditional media. In our study, the sources of information did not affect the level of stress, which in other studies is highlighted as a risk factor, especially when information comes from social media provoking the so-called “infodemic” [7].

Groups did not differ in the levels of economic and psychological concerns. However, there are differences in the medical concerns, with the highest share in the HC-FDR group, which distinguishes it significantly only from MDD-R. This corresponds to the significant increase in state-anxiety in this group. Probably medical concerns more than economic and psychological ones are the reason for the bigger difference between state- and trait-anxiety during this early phase of the pandemic. Of the categorical values in their analysis, only the psychological concerns related to isolation and limitations increase the risk by almost 2.5 times for MH/PSS-10, but in the multiple analysis, they are eliminated as a risk factor.

A previous history of depression and anxiety did not appear to increase the risk of MH/PSS-10. This shows that individuals in complete remission are just as resilient as healthy controls and first-degree relatives. Most studies show that patients with severe mental illness have higher levels of perceived COVID-19-related stress, anxiety, and depressive symptoms than non-psychiatric participants [8, 9]. However, these studies do not specify whether patients are in remission and how stable and long-lasting it is. We could assume that the similar results for PSS-10 in the studied groups are probably due to different mechanisms. In healthy individuals, there is a lack of experience, which leads to an initial increase in situational anxiety and the inclusion of coping strategies that successfully affect stress levels. In persons with a psychiatric history, existing experience of illness or social isolation caused by a previous mental illness may lead to more experience with adverse events and resilience, leading to less increase in situational anxiety [19]. In this sense, we must be careful when we attribute the deterioration of patients with anxiety and depression to the pandemic alone [27].

It should be noted that the study has some limitations. The study was cross-sectional, the sample was formed by the outpatient service of one medical institution and may not be representative of the general population. Another possible limitation is the size of the groups although all statistical analyses were consistent with this fact. At the same time, the included patients can be followed prospectively, and the inclusion of healthy relatives provides an opportunity to consider the perceived stress in a bio-psycho-social aspect.

In conclusion, patients with complete remission of anxiety and depressive disorders with regular access to outpatient services and good therapeutic maintenance control had no differences in stress perception during COVID-19 in comparison to healthy controls. Psychiatric history should be viewed not only as a

risk factor but also as a source of experience and wisdom in dealing with a crisis. Subthreshold values of depression and loneliness increase the feeling of moderate/high stress irrespectively to the psychiatric history.

Ethical considerations: *The Commission on Ethics of Scientific Research of the Medical University of Sofia had approved the study (No. 4298/ 03/07/2020) and all procedures of the study were performed after written informed consent.*

Funding: *The authors have received an educational grant from The Medical University of Sofia, Bulgaria (№114/04.06.2021).*

Conflict of interests/Acknowledgments: *The authors report no conflict of interest. Some results of the study have been presented during a poster session on the 35th ECNP Congress.*

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