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THE INFLUENCE OF ANXIETY LEVEL AND PAST COVID-19 ON SLEEP QUALITY AND INSOMNIA SEVERITY

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Based on recent studies, we put forward a hypothesis about the synergistic effect of anxiety disorders and previous COVID-19 on the deterioration of the quality of sleep and occurring of insomnia. The purpose of the study was to investigate the impacts of anxiety disorders, and COVID-19 on anamnesis and its combined effect on sleep disturbances. We conducted a case-control study, which included 60 patients, who were divided into 3 groups depending on the occurrence of anxiety disorders and COVID-19 in their medical history during the last 6 months. Patients were assessed by the Beck anxiety inventory, Pittsburgh Sleep Quality Index, and the Insomnia Severity Index. We found a worsening sleep quality and a higher frequency of insomnia in patients with COVID-19. Along with this, concomitant anxiety disorders worsened both the quality of sleep and the level of insomnia in these respondents. It was determined that patients with an anxiety disorder with a history had a lower subjective assessment of sleep quality, higher sleep latency, and more pronounced diurnal dysfunction, while patients without a history had better sleep efficiency and a lower frequency of sleeping pills. Anxiety disorders and having experienced COVID-19 are associated with poorer sleep quality and more severe insomnia. Their combination significantly reduces the quality of sleep and increases the degree of insomnia. These findings suggest a potential role for COVID-19 in exacerbating the association between anxiety and sleep disorders.

Key words: anxiety, mood disorders, sleep disorders, insomnia, sleep quality, COVID-19.

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ВПЛИВ РІВНЯ ТРИВОГИ ТА ПЕРЕНЕСЕНОГО COVID-19 НА ЯКІСТЬ СНУ ТА ТЯЖКІСТЬ ІНСОМНІЇ

На підставі останніх досліджень, нами було висунуто гіпотезу про синергічний вплив тривожних розладів та перенесеного COVID-19 на погіршення якості сну та виникнення безсоння. Метою дослідження було вивчення впливу тривожних розладів, COVID-19 в анамнезі та їх комбінованого впливу на порушення сну. Ми провели дослідження «випадок-контроль», яке охопило 60 осіб, що були розділені на 3 групи залежно від наявності тривожних розладів та COVID-19 в анамнезі протягом останніх 6 місяців. Пацієнти були оцінені за допомогою опитувальника тривожності Бека, Пітсбургського індексу якості сну та Індексу тяжкості безсоння. Нами було виявлено погіршення якості сну та вищу частоту безсоння у пацієнтів, що перехворіли на COVID-19. Поряд з цим супутні тривожні розлади погіршували як якість сну, так і рівень безсоння у цих респондентів. Було визначено, що у пацієнтів з тривожним розладом та перенесеним в анамнезі нижча суб'єктивна оцінка якості сну, вища його латентність та більш виражена добова дисфункція, в той час як пацієнти без в анамнезі мали кращу ефективність сну та нижчу частоту використання снодійних. Виявлено, що тривожні розлади та перенесений COVID-19 мають зв'язок із погіршенням якості сну та більш важким безсонням. Їх поєднання суттєво знижує якість сну та підвищує ступінь безсоння. Ці результати вказують на потенційну роль COVID-19 у посиленні зв'язку між тривогою та розладами сну.

Ключові слова: тривога, розлади настрою, розлади сну, інсомнія, якість сну, COVID-19.

The study is a fragment of the research projects: "The study of the pathogenetic role of the circadian molecular clock in the development of metabolic diseases and systemic inflammation and the development of treatment methods aimed at these processes", state registration No. 0120U101166 and "Clinical-psychopathological and paraclinical examinations and optimization of medical and rehabilitation measures at the common forms of mental and comorbid disorders", state registration No. 0121U108235.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes a coronavirus respiratory disease (COVID-19) with a variety of clinical syndromes and severity that has affected health systems worldwide [6].

In the early stages of studying treatments for COVID-19, many researchers explored the possibility of non-pharmaceutical interventions to limit the spread of SARS-CoV-2, for example, attempts were made to study the effect of heliometeorological factors, such as sunlight and temperature, on virus strains [5].

There are studies that show a correlation between risk of mental illness and heliometeorological factors such as the level of solar activity, which reduce the effectiveness of mechanisms of psychological adaptation and promote the development of affective disorders, autoaggressive behavior, neurotic disorders, alcoholic psychoses and others. Recently it was assumed that the fluctuating of biological rhythms is associated with endogenous rhythms, that are genetically fixed [15].

It has shown that clock genes play the main role in regulating circadian rhythm of biological process in eukaryotic organisms. Clock genes demonstrated association with mood disorders, cognitive impairments and insomnia, which indicate possible common pathways in its pathogenesis [4, 13].

During COVID-19 pandemic increasing of the prevalence of anxiety levels was registered from 20 to 60 % in different population [3]. COVID-19-related anxiety makes a unique contribution to the somatization of patient complaints. Moderate and severe levels of anxiety associated with COVID-19 have been shown links to more severe somatic symptoms in a large representative sample of adults in United Kingdom [11]. This feature indicates a significant role of mood disorders in the course of COVID-19.

Life in a pandemic of COVID-19 is filled with stress, which is associated with the uncertainty in many industries due to this situation. All of this can contribute to the development of insomnia and disruption of the sleep structure. An association has been demonstrated between COVID-19-related anxiety and insomnia through the mechanism of anxiety-induced cognitive arousal [14]. Insomnia can change the state of immune homeostasis of the body and have a negative impact in viral infections [8]. On the other hand, the development of a somatic disease can lead to sleep disturbance due to acute stress. Thus, we put forward a hypothesis about the synergistic effect of anxiety disorders and previous COVID-19 on the deterioration of the quality of sleep and occurring of an insomnia.

The purpose of the study was to investigate the impacts of anxiety disorders, COVID-19 in anamnesis and its combined effect on sleep disturbances.

Materials and methods. We performed a case-control study, which included 60 males and females, aged 18 to 59 years. All respondents were divided into 3 groups according to the anamnesis data and clinical interview with psychiatrist, namely:

- group 1 – patients who has anxiety disorders and became ill with COVID-19 during the last 6 months (n=20);
- group 2 – patients who has anxiety disorders and was not ill with COVID-19 during the last 6 months (n=20);
- group 3 (control) – persons who were not ill with COVID-19 during the last 6 months and have not anxiety disorders (n=20).

Criteria for inclusion was anxiety disorders according to International classification of diseases-10 (F 40, F41). For group 1 we have additional inclusion criteria, which were exclusion criteria for groups 2 and 3: COVID-19 in the anamnesis, confirmed by PCR testing, post-COVID syndrome (5-24 weeks from the onset of symptoms of COVID-19), age from 18 to 59 years. The criteria for inclusion in the control group was the absence of COVID-19 in the anamnesis and anxiety disorders. The criteria for exclusion were the presence of concomitant severe somatic pathology, a history of mental disorders before COVID-19, including anxiety disorder at the time of the onset of coronavirus infection, the appearance of symptoms of coronavirus infection 5 weeks ago and later. Patients with COVID-19 were surveyed on the severity of the clinical course and awareness of the previous contact with an infected person.

The study was conducted in accordance with the principles of Good Clinical Practice and the Helsinki Declaration of the World Medical Organization. All patients provided informed consent to participate in the study. During the visit patients were interviewed by psychiatrists for collecting data about medical history and mental status. To assess the overall level of anxiety, the Beck anxiety inventory (BAI) was used, according to which the sum of scores less than 22 indicates low anxiety, 22-35 – moderate, and 36-63 – potentially concerning levels of anxiety. For measurement sleep quality we used the Pittsburgh Sleep Quality Index (PSQI). Score less than 5 means good sleep quality. The Insomnia Severity Index was used for assessment degree of insomnia. Total score can be in the following range: 0-7 = no clinically significant insomnia, 8-14 = subthreshold insomnia, 15-21 = clinical insomnia (moderate severity), 22-28 = clinical insomnia (severe).

Data processing. Microsoft Statistical Excel 2019 software (Microsoft Corp., USA) and IBM SPSS Statistic 26.0 (IBM Corp., USA) were used for statistical analysis of the obtained data. The normality of the distribution was evaluated according to the Shapiro-Wilk test with considering values of asymmetry and excess. The quantitative data were presented as arithmetic mean (M) and standard error (m) or medians (Me) and interquartile range (Q1-Q3) depending on type of distribution. We used one-way analysis of variance (ANOVA), the Kruskal-Wallis criterium with post hoc analysis by Steell-Dwass test, Yates-

corrected and χ^2 test, the Cramer's V criterium, multivariate analysis of variance (MANOVA) with post hoc analysis by Scheffe's method. The effect size was measured by η^2 . The critical p-value was 0.05.

Results of the study and their discussion. The mean age of patients of group 1 was 39.3 ± 6.1 years, group 2 – 34.9 ± 7.8 years and group 3 – 36.2 ± 6.7 years. Group 1 included 8 (40 %) men and 12 (60 %) women, group 2 – 9 (45 %) men and 11 (55 %) women, and group 3 – 6 (30 %) men and 14 (70 %) women. No statistically significant age ($p=0.703$) and gender ($p=0.611$) differences were found.

In group 1 7 patients (35 %) reported a mild course of the COVID-19, 9 (45 %) – moderate and 4 (20 %) – severe. The low level of anxiety was found in 4 (20 %) patients of group 1 and 6 (30 %) in group 2, mild – in 7 (35 %) of group 1 and in 9 (45 %) of group 2, and moderate in 9 (45 %) and 5 (25 %) respectively. There are no significant differences between anxiety severity between group 1 and 2 ($\chi^2 = 1.79$, $df=2$, $p = 0.409$).

We have investigated that total score's medians of PSQI was 14.0 (8.0–19.8) points in group 1, 6.5 (1.3-15.8) points in group 2 and 3.5 (1.0-7.5) points in group 3. It was shown statistically significant difference between groups ($H=12.7$, $df=2$, $p=0.002$). In groups 1 and 2 we have found poor quality of sleep. In patients from group 1 quality of sleep was worse compare to group 3 ($p=0.001$). We have analyzed all components' spectrum by PSQI in studied groups (Table 1).

Table 1

Differences between components of Pittsburgh sleep quality index in patients with anxiety disorders after COVID-19, abs. (%)

Component of PSQI score		Groups			p-value
		Group 1 (n=20)	Group 2 (n=20)	Group 3 (n=20)	
C1	0	3 (15 %)	6 (30 %)	11 (55 %)	0.002
	1	3 (15 %)	5 (25 %)	3 (15 %)	
	2	2 (10 %)	4 (20 %)	6 (30 %)	
	3	12 (60 %)	5 (25 %)	0 (0 %)	
C2	0	1 (5 %)	5 (25 %)	9 (45 %)	0.005
	1	6 (30 %)	4 (20 %)	7 (35 %)	
	2	2 (10 %)	6 (30 %)	3 (15 %)	
	3	11 (55 %)	5 (25 %)	1 (5 %)	
C3	0	6 (30 %)	7 (35 %)	5 (25 %)	0.143
	1	5 (25 %)	7 (35 %)	12 (60 %)	
	2	3 (15 %)	3 (15 %)	3 (15 %)	
	3	6 (30 %)	3 (15 %)	0 (0 %)	
C4	0	7 (35 %)	9 (45 %)	16 (80 %)	0.008
	1	2 (10 %)	5 (25 %)	4 (20 %)	
	2	3 (15 %)	3 (15 %)	0 (0 %)	
	3	8 (40 %)	3 (15 %)	0 (0 %)	
C5	0	5 (25 %)	8 (40 %)	10 (50 %)	0.074
	1	2 (10 %)	4 (20 %)	4 (20 %)	
	2	6 (30 %)	6 (30 %)	4 (20 %)	
	3	7 (35 %)	2 (10 %)	2 (10 %)	
C6	0	4 (20 %)	10 (50 %)	16 (80 %)	0.010
	1	5 (25 %)	4 (20 %)	2 (10 %)	
	2	5 (25 %)	4 (20 %)	2 (10 %)	
	3	6 (35 %)	2 (10 %)	0 (0 %)	
C7	0	4 (20 %)	5 (25 %)	9 (45 %)	0.025
	1	4 (20 %)	7 (35 %)	9 (45 %)	
	2	4 (20 %)	5 (25 %)	2 (10 %)	
	3	8 (40 %)	3 (15 %)	0 (0 %)	

Note. C1 – subjective sleep quality, C2 – sleep latency, C3 – sleep duration, C4 – habitual sleep efficiency, C5 – sleep disturbances, C6 – use of sleeping medication, C7 – daytime dysfunction.

Our study shows statistically significant differences between groups by following components: subjective sleep quality ($\chi^2=20.45$, $df=6$, $p=0.002$), sleep latency ($\chi^2=18.52$, $df=6$, $p=0.005$), habitual sleep efficiency ($\chi^2=17.37$, $df=6$, $p=0.008$), use of sleeping medication ($\chi^2=16.74$, $df=6$, $p=0.010$) and daytime dysfunction ($\chi^2=14.42$, $df=6$, $p=0.025$). It had been detected that patients from group 1 are more inclined to lower subjective quality of sleep, higher latency of sleep and more severe daily dysfunction, while groups 2 and 3 had better habitual sleep efficiency and less frequency of sleeping medications' usage.

We found a relatively strong link between the type of groups and subjective sleep quality (Cramer's $V=0.413$, $p=0.002$). At the same time there are detected a moderate link with sleep latency (Cramer's

V=0.393, p=0.005), habitual sleep efficiency (Cramer’s V=0.380, p=0.008), use of sleeping medication (Cramer’s V=0.374, p=0.010) and daytime dysfunction (Cramer’s V=0.347, p=0.010). It means that patients of group 1 have the tendency to have worse sleep quality while group 3 is more inclined to have better one.

Our analysis shows a statistically significant impact on sleep quality as anxiety disorders (p<0.001), as COVID-19 in medical history for the last 6 months (p=0.038). By the way, the contribution of anxiety was higher than COVID-19, because η^2 was 37.3 % and 7.9 % respectively. Furthermore, the relationship between these factors was significant (p=0.019) and conditioned 13.8 % of general dispersion. We have compared PSQI scores depending on the level of anxiety and presence of COVID-19 during the last 6 months of medical history (Fig.1).

After post hoc analysis of the total score of PSQI with considering anxiety level, we defined that patients with a low level of anxiety or its absence have lower PSQI scores than those who have mild or moderate (p<0.001). PSQI score of patients without anxiety disorders has not differed from patients with low anxiety (p=0.928). Patients with mild and moderate anxiety had no differences in PSQI total scores(p=0.713).

It was measured that means of ISI was 20.0 (14.0–24.0) points in group 1, 12.0 (5.3–14.8) points in group 2, and 5.5 (2.0–9.8) points in group 3. There is a significant difference between groups (H=18.87, df=6, p<0.001). ISI was higher in group 1 (p<0.001) and in group 2 (p=0.047) compared to group 3, groups 1 and 2 had no significant difference (p=0.166). We have also performed analysis of distribution of ISI degrees in different groups (Table 2).

Table 2

Distribution of insomnia degree in patients with anxiety disorders after COVID-19, abs. (%)

Degree of insomnia	Groups			p-value
	Group 1 (n=20)	Group 2 (n=20)	Group 3 (n=20)	
Absence	2 (10 %)	6 (30 %)	12 (60 %)	0.003
Sub-threshold	4 (20 %)	9 (45 %)	5 (25 %)	
Moderate	9 (45 %)	4 (20 %)	2 (10 %)	
Severe	5 (25 %)	1 (5 %)	1 (5 %)	

We showed a statistically significant difference between the groups’ degree of insomnia ($\chi^2=19.71$, df=6, p=0.003) and a relatively strong link between the type of groups and ISI (Cramer’s V=0.405, p=0.002). It notices a tendency to more severity of insomnia in patients with anxiety disorders and COVID-19 in medical history during the last 6 months.

We have found a statistically significant impact on insomnia severity as anxiety disorders (p<0.001), as COVID-19 in medical history for the last 6 months (p=0.006). The contribution of anxiety was higher than COVID-19 because η^2 was 28.7 % and 13.4 % respectively. Furthermore, the relationship between these factors was significant (p=0.046) and conditioned 11.0 % of general dispersion. We have compared ISI means depending on level of anxiety and presence of COVID-19 during last 6 months in medical history (Fig.2).

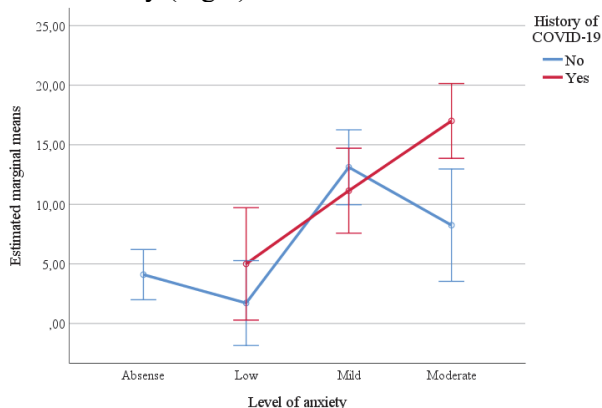


Fig. 1. Estimated marginals means of PSQI total score depends on level of anxiety and presence of COVID-19 during last 6 months in medical history

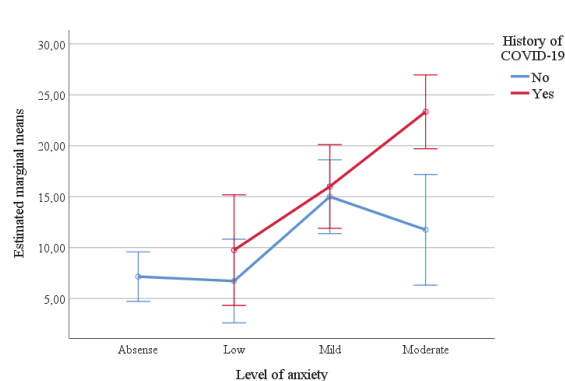


Fig. 2. Estimated marginals means of ISI depends on level of anxiety and presence of COVID-19 during last 6 months in medical history

Post hoc analysis of insomnia degree with considering anxiety level detected that patients with a low level of anxiety or its absence have lower ISI scores than those who have mild (p=0.001 and p=0.009 respectively) or moderate (p<0.001). The insomnia severity in patients without anxiety disorders has not

differed from patients with low anxiety ($p=0.991$). Patients with mild and moderate anxiety had no differences in the degree of insomnia ($p=0.218$).

During COVID-19, mental disorders have become more frequent, for example, anxiety and depression, sleep and circadian rhythms disorders, fatigue, etc [2]. Our research shows that anxiety level has a strong association with subjective sleep quality, sleep latency and habitual sleep efficiency. This correlation may be caused by chronotype and common disruption in serotonergic and γ -aminobutyric acid systems [1, 12]. It should be pointed out that anxiety in the post-COVID-19 period was associated with poorer sleep quality. It notices the importance of appropriate treatment for sleep disorders, especially insomnia, in a patient after COVID-19. Some researchers assume that it may reduce neuropsychiatric complications in the post-COVID period, namely anxiety and suicidality [10].

At the same time, it is intriguing that higher frequency of usage of sleeping medication and daytime dysfunction in patients with anxiety disorders and past COVID-19 may investigate in further studies. Recently it is also discussed the role of clock genes in COVID-19-related sleep disorders called “coronasomnia” [9]. This phenomenon can increase blood-brain barrier disruption which leads to neuroinvasion of SARS-CoV-2 and cause organic anxiety disorders.

On the other hand, the impacts of COVID-19 on sleep quality were different and can depend on sleep quality before this disease [7]. It is the first time that it has been discovered that anxiety disorder and past COVID-19 can potentially each other's affect sleep quality. These findings show the necessity for studying neuropsychiatric complications in post-COVID-19 and possible ways to improvement the rehabilitation of these patients.

It should be considered that our study was limited to a small number of patients. The authors assume that further complex study of relationships between neuropsychiatric complications in the post-COVID-19 period will improve the treatment strategy of these patients and their quality of life.

Conclusion

Anxiety disorders and COVID-19 in anamnesis of the last 6 months have links to poorer sleep quality ($p<0.001$ and $p=0.038$ respectively) and more severe insomnia ($p<0.001$ and $p=0.006$ accordingly). Their combined effect also significantly influences sleep quality ($p=0.019$) and degree of insomnia ($p=0.046$). These findings indicate a potential role of COVID-19 as an enhancer in relationships between anxiety and sleep disorders, which poses new challenges for finding a suitable therapy for mood and sleep disorders after COVID-19.

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