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Original article

# Sleep disorders as presenting symptoms in positive COVID-19 patients in Aswan University Hospitals, Egypt

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**ABSTRACT**

**Background:** The coronavirus disease 2019 (COVID-19) is critically affecting not only the physical health but also mental health globally. This study aimed to define the frequency of sleep disorders in COVID-19 positive patients in Aswan University Hospitals, Aswan Governorate, Egypt to clarify the different clinical types of them and to identify factors associated with sleep changes during the COVID-19. **Methods**: Our study recruited 280 positive COVID-19 patients. Their sleep disorders were diagnosed by using Global Sleep Assessment questionnaire (GSAQ). Their socioeconomic status was determined by using Revised Kuppuswamy Socioeconomic Status Scale (RK SSS). The severity of anxiety symptoms and insomnia were determined by using Hamilton Anxiety Rating Scale (HARS) and Insomnia Severity Index (ISI) respectively. Diagnosis of Restless Leg Syndrome (RLS) was completed according to Restless Leg Syndrome Diagnostic Index (RLS-DI). **Results**: Sleep disorders were documented in 35.7% of our patients. They were categorized into insomnia (24.6%), RLS (15%) and poor sleep quality (17.4%). Younger age and female sex were the predominate age and sex. Most of them had severe anxiety. Upper class of socioeconomic status was the commonest SES. Most of patients had CORADS I and II respectively. **Conclusion**: The present study recognized that female gender, younger population, COVID- 19 related stressors were the major factors associated with sleep disorder. Further investigation is needed to understand the changes in sleep pattern among the patients of the COVID-19 pandemic.

## Introduction

Globally, the coronavirus disease 2019 (COVID-19) is having a serious negative impact on people's mental and physical health [1,2]. There is no information available on how common sleep disturbances are among those impacted by this pandemic. In order to maintain better physical and mental health as well as a higher quality of life; sleep is a physiological necessity [3, 4]. Sleep duration increases during the symptomatic phase of an influenza virus infection in humans, whereas it reduces during incubation. As of right present, the relationship between sleep problems and the COVID-19 pandemic remains unclear. By assessing the available data on the epidemiological

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impact on sleep disorders and related variables addressing the issues; this scoping research seeks to close this knowledge gap. We aim to draw attention to the sleep disturbances associated with the COVID-19 in Aswan Governorate through this pilot research. Encoded below are the exact questions that make up this scoping study:

• What is the proven COVID-19 patient population's epidemiological burden of sleep disorders?

• What are the contributing variables to sleep disturbances during COVID-19?

**Aim of study**

In this study, our aim was to: describe the prevalence of sleep disorders among COVID-19 positive patients in Aswan University Hospitals; Aswan Governorate, elucidate the many clinical subtypes of these disorders, and pinpoint the variables linked to altered sleep patterns during the COVID-19.

**Methods**

**Study settings**

This study was a single-center, observational, descriptive cross-sectional investigation that took place at Aswan University Hospitals (chest department, emergency room, and neuropsychiatry department) between March 2021 and May 2021.

**Study participants**

The Diagnostic and Statistical Manual of Mental Disorders [5] provided the definition of sleep disorders, which was the study's primary emphasis. Accordingly, between March 2021 and May 2021, the study sample comprised verified COVID-19 patients who experienced sleep disturbances. All patients who presented with sleep disruptions as symptoms of their condition were included in the research and recruited. Positive reverse transcription-polymerase chain reaction (RT-PCR) findings for SARS-CoV-2 were obtained for all patients, who were confirmed cases. Chinese Management Guidelines for COVID-19 were followed in the diagnosis and severity categorization of the condition. Depending on how serious their respiratory symptoms were, the patients were split into two groups: severe and non-severe.

The following were the inclusion criteria: a) be willing to participate in the survey and be at least 18 years old; b) not taking any medications that interfere with sleep.

Individuals who had any of the following conditions were excluded: a) history of neurological or mental problems in the past; b) history of medical conditions that interfere with sleep; c) history of medication use that interferes with sleep; d) history of sleep disruptions prior to COVID-19 infection and e) shift workers.

**Data collection procedure**

All patients with laboratory-confirmed SARS-CoV-2 infection were recruited. Their radiographic and laboratory evaluations, and information on age, sex, comorbidities, COVID-19 clinical symptoms, and illness severity were obtained. Demographic data, medical history, clinical findings, radiological results (chest computed tomography, or CT scan), and laboratory results (blood cell count, biochemical analysis, tests for liver and kidney function, D-dimer, ferritin level, and c-reactive protein) were gathered for each patient. At the time of admission, we classified the COVID-19 infection as severe or non-severe based on the American Thoracic Society's recommendations for community-acquired pneumonia. Every sleep disruption was examined and verified.

The Institutional Ethics Committee of our University's Faculty of Medicine gave its approval to the current investigation. The study received approval from our Medical Faculty's IRB committee. The goals, procedures, and risk/benefit analysis of the research were fully disclosed to each patient. Upon being accepted to participate in the study, each subject provided a written permission. The Declaration of Helsinki was followed in conducting the study. All patients were investigated for SARS COV-2 Virus as following:

**PCR for detection of SARS COV-2 virus blood samples**

● 2 mL of venous blood was collected aseptically in EDTA tubes for CBC.

● 2 mL blood was collected aseptically in sodium citrate tubes for D-dimer.

● 3 mL venous blood was collected in plain tube for serum collection; the serum of the patients will be used for detection of CRP and ferritin.

**Preparation of PCR**

Three crucial procedures were carried out in accordance with the manufacturer's instructions

for the QIAGEN (QIAamp-DSP virus spin kit, cat. no. 61,704) for the purification of viral nucleic acid from nasopharyngeal and oropharyngeal swabs. Sample gathering, RNA extraction, and viral RNA detection are the first three steps.

Sample collection was carried out by swabbing respiratory debris from the oropharynx and nasopharynx. A swab was a long, flexible stick with a soft tip that was placed into the nose to rapidly collect a sample. Within four hours of collection, the swab was collected, put in around 3 mL of viral transport medium, and sent to the clinical lab for testing. Following the sample's receipt, an extraction was carried out to separate the genetic material from it, including any potential viral DNA.

RNA extraction was carried out in compliance with the manufacturer's guidelines (AQUIGEN)

1. In a clean 1.5 mL RNase-free microcentrifuge tube, 10 µL proteinase K, 300µL lyses buffer DVN, and 4ul of poly A (lysis mix) were added. After that, we vortexed 200µL of the sample (a nasopharyngeal/oropharyngeal swab) for 15 seconds and allowed it to sit at room temperature for 5 minutes.

2. In a 2 mL collection tube, the lysate was gently placed onto the fine bind DNA spin columns. After closing the lid and centrifuging for one minute at 10,000 rpm, the filtrate was disposed of and the spin column was put into the same collecting tube.

3. Carefully opening the fine bind DNA spin columns, 700 µL of buffer DW1P was added. After closing the cap, the centrifuge ran for one minute at 10,000 rpm. The spin column was put in the same collecting tube as the filtrated, which was disposed of.

4. After cautiously opening the fine bind DNA spin columns, 700µL of buffer MWP was introduced. After closing the lid, the centrifuge ran for one minute at 10,000 rpm. The spin column was put in the same collecting tube as the filtrated, which was disposed of.

5. Centrifugation at full speed 12,000 rpm for 2 min to dry the membrane completely was performed.

6.The 1.5 mL RNase-free microcentrifuge tubes were filled with clean fine bind DNA spin columns, and the spin column lid was gently opened. The middle of the membrane was filled with 100µL of RNase-free dd$H_2O$. After the cover was shut, the mixture was centrifuged for one minute at 10,000 rpm.

7. Carrier RNA was diluted in buffer AVE to a level of 25 µL per sample for this procedure. In addition to the necessary number of samples, we also created carrier RNA for three extra samples (e.g., prepare carrier RNA for 10 samples if there are 7 samples).

25 µL carrier RNA was prepare as described below:

A. No internal control: carrier RNA: 5.6 µL and buffer AVE: 19.4 µL

B. With internal control: carrier RNA: 5.6 µL and Internal control: Up to 19.4 µL (if <19.4 µL internal control is used, final volume was adjusted to25µl with buffer AVE)

Viral RNA detection was carried out via real-time PCR, which results in a reaction that produces millions of copies of a tiny amount of the genetic material of the SARS-CoV-2 virus.

1. In each PCR tube, 15 ul of rehydration buffer was added.

2. Sample tubes were filled with 5 ul of elution buffer.

3. The tube closures were shut.

4. To create the positive control, 100 ul of nuclease-free water was mixed into the tube.

5. Instead of using the sample, 5 ul of the generated positive control reagent was utilized, together with the previously added rehydration buffer.

6. To prepare the negative control, 15 ul of rehydration buffer and 5 ul of negative control were combined.

**Data collection tools**

Every patient with a sleep disorder who tested positive for COVID-19 underwent:

1.Full neurological and medical evaluation, including clinical and demographic data collection on age, sex, marital status, employment status, and socioeconomic status.

2.The Global Sleep Assessment Questionnaire (GSAQ) is used to diagnose sleep problems [6]. It was a thorough screening technique to determine whether sleep problems were prevalent in the general public. There were eleven things total, and the answers were shown in a grid on a single page.

3.The Revised Kuppuswamy Socio-economic Status Scale (RK SSS) was used to assess

socioeconomic status [7]. The three primary socioeconomic status (SES) domains that were covered were education, total family income, and occupation. Families were categorized into five groups based on the Kuppuswamy SES total score, which varies from 3-29: "upper class (26-29), upper middle class (16-25), lower middle class (11-15), upper lower (lower middle, 5-10), and lower socio-economic class (< 5)."

4. Anxiety Rating Scale for Hamilton (HARS) [8]. The severity of anxiety symptoms was measured by HARS. It was composed of fourteen evaluations, each of which was defined by a set of symptoms. These claims were contradictory and consider both the somatic (physical symptoms associated with anxiety) and psychic (mental agitation and psychological anguish) elements of anxiety. Every item was rated on a scale from 0, which indicated no symptoms at all, to 4, which indicated the greatest degree of symptoms; the overall score can vary from 0 to 56. Less than 14 was regarded as normal, while a patient with mild anxiety was indicated by a score between 14 and 17. Additionally, a score of 18 to 24 denoted moderate anxiety, while a score of 25 or higher denoted severe anxiety.

5. The Index of Severity of Insomnia (ISI) [9]. This quick test was created to evaluate the type, degree, and effects of insomnia in people as well as track their response to therapy. Seven questions were on it. The sum of the seven responses determined the final score. The overall score was in the range of 0 to 28. Less than 7 was regarded as normal in the absence of insomnia, but scores between 8 and 14 indicated subthreshold insomnia in an individual. Additionally, a score of above 22 indicated severe insomnia, whereas a score between 15 and 21 denoted moderate insomnia.

6. The RLS-DI (Restless Leg Syndrome Diagnostic Index) [10]. The International Study Group's key diagnostic criteria, together with its supporting criteria and characteristics linked to RLS, were all related to the ten questions that made up the RLS-DI. RLS-DI states that a patient should be evaluated for RLS if they come with one of the following symptoms: 1. Insomnia or sleep issues brought on by an urge to move; or 2. Unpleasant feelings in the legs. The patient should be asked the essential criteria, which were questions 3 through 7. The patient was diagnosed with RLS if they provided a yes response to each of the five essential criteria questions. The questions from the associated and supportive criteria were be taken into consideration if the patient only provided a yes response to questions 3, 4, and 5. An RLS diagnosis was made if any one of the associated and supportive criteria has a yes response. Further considerations were be made if the patient responded negatively to any or all of the essential criteria questions, as well as to questions 3, 4, and 5. Likewise, alternative diagnoses should be taken into consideration as a potential cause of the patient's symptoms if the patient responded in the affirmative to questions 3, 4, and 5 and in the negative to questions 8, 9, and 10 on the diagnostic algorithm.

**Results**

In order to characterize the prevalence of sleep disturbances, we studied two hundred and eighty (280) positive COVID-19 patients who were presented to Aswan University Hospitals. 35.7% of our patients had documented sleep problems. The majority sex (55%) was female, with a mean age ±SD of 37.26 ± 7.5 years ($p$<0.001). Of these, 48% had extreme anxiety ($p$<0.001). Of them, 26% and 25% belonged to the upper middle class and upper class, respectively ($p$<0.001). CORADS I and II were present in 45 (61.6%) and 38 (55.1%) individuals, respectively (p<0.001) **(Table 1)**.

In this investigation, we identified three distinct categories of sleep disorders: poor sleep quality (17.4%), restless leg syndrome (RLS) (15%) and insomnia (69,24.6%) people **(Figure 1)**.

**Table (2)** demonstrated the inverse association between the incidence of sleep disorders and the CO-RADS categorization of the level of suspicion for COVID-19 infection. Patients with low levels of CO-RADS (I and II) were more likely to have all three forms of impaired sleep. Furthermore, we verified the inverse association between CO-RADS and the insomnia index (ISI) and anxiety level using the Spearman Rank Correlation Coefficient. Additionally, there was a negative correlation between the patients' socioeconomic status and the insomnia index **(Table 3)**.

Nevertheless, there was no discernible difference between the COVID-19 individuals who had sleep disturbances and those who did not in terms of related comorbidities (such as hypertension, ischemic heart disease, and diabetes mellitus) or laboratory tests (such as CRP, serum ferritin, and D-Dimer levels) **(Table 3).**

Using a multivariable logistic regression model, **Table (4)** revealed that among COVID-19 patients, smoking, female sex, CO-RADS I, and high anxiety levels were independent predictors of sleep disorders.

**Statistical analysis**

The researcher used IBM-SPSS 24.0 (IBM-SPSS Inc., Chicago, IL, USA) to verify, code, and analyze the data [11]. Characteristic statistics Calculations were made for means, standard deviations, medians, frequency, and interquartile ranges (IQR). Continuous variable normality was assessed using the relevant Kolmogorov-Smirnov or Shapiro-Wilk test. Test of significance: Monte Carlo/Chi-square To compare the variations in frequency distributions among the several groups, an exact test was employed. We looked at the relationships between sleep disorders and CO-RADS class using Spearman's Rank correlation. We employed multivariable logistic regression to find independent sleep disorder variables. When the p-value was less than 0.05, it was deemed significant.

**Table 1.** Basic characteristics of COVID-19 patients presented with sleep disorders

| Parameters | Patients had sleep disorders (N=100, 35.7%) | *p*-Value |
|---|---|---|
| Age /years (Mean± SD) | 37.26 ± 7.5 | = 0.307 |
| Sex (male/female) (NO/%) | 45/55 (45% / 55%) | 0.001* |
| Hamilton Anxiety Rating Scale (HARS) | | |
| No anxiety (No, %, P-value) | 7(7%) | |
| Mild anxiety (No, %, P-value) | 12 (12%) | |
| Moderate anxiety (No, %, P-value) | 33 (33%) | 0.001* |
| Severe anxiety (No, %, P-value) | 48 (48%) | |
| Revised Kuppuswamy socioeconomic status Scale (RK-SSC) | | |
| Upper class (No, %, P-value) | 26 (26%) | 0.001* |
| Upper middle class (No, %, P-value) | 25 (25%) | |
| Middle class (No, %, P-value) | 21 (21%) | |
| Lower middle class (No, %, P-value) | 19 (19%) | |
| Lower class (No, %, P-value) | 9 (9%) | |
| Insomnia Severity Index (ISI) | | |
| No Insomnia (No, %, P-value) | 9 (9%) | |
| Subthreshold Insomnia (No, %, P-value) | 22 (22%) | 0.001* |
| Moderate Insomnia (No, %, P-value) | 44 (44%) | |
| Severe Insomnia (No, %, P-value) | 25 (25%) | |
| Medical diseases | | |
| HT | 38 (38%) | 0.101 |
| IHD | 29 (29%) | 0.012* |
| DM | 40 (40%) | 0.277 |
| Smoking | 46 (46%) | 0.335 |
| CORAD | | |
| I | 45 (45%) | |
| 2 | 38 (38%) | 0.001* |
| 3 | 7 (7%) | |
| 4 | 4 (4%) | |
| 5 | 6 (6%) | |
| High ferritin levels | 44 (44%) | 0.201 |
| High D-Dimer levels | 24 (24%) | 0.294 |
| High CRP levels | 62 (62%) | 0.426 |
| Lymphocytes (mean ± SD) | 29.36±14.07 | 0.283 |

*Independent t-test was used to compare the means among groups, *Chi-square test was used to compare the frequency among groups

**Table 2.** Sleep disorder prevalence according to CO-RADS class

| | CO-RADS Class | | | | | p-value |
|---|---|---|---|---|---|---|
| | CO-RADS 1 (n = 73) | CO-RADS 2 (n = 69) | CO-RADS 3 (n = 43) | CO-RADS 4 (n = 54) | CO-RADS 5 (n = 41) | |
| Sleep Disorder | 45 (61.6%) | 38 (55.1%) | 7 (16.3%) | 4 (7.4%) | 6 (14.6%) | < 0.001* |
| Insomnia | 32 (43.8%) | 27 (39.1%) | 3 (7%) | 3 (5.6%) | 4 (9.8%) | < 0.001* |
| RLS | 17 (23.3%) | 17 (24.6%) | 5 (11.6%) | 1 (1.9%) | 2 (4.9%) | < 0.001* |
| Poor Sleep | 20 (27.4%) | 26 (37.7%) | 2 (4.7%) | 0 (0%) | 1 (2.4%) | < 0.001* |

*Chi-square test was used to compare the frequency among groups

**Table 3.** Correlations of CO-RADS class with sleep disorders

| | CO-RADS Class | ISI |
|---|---|---|
| | $r_s$* (p-value) | $r_s$* (p-value) |
| • CO-RADS Class | 1 | -0.441 (< 0.001) |
| • RK-SSC | 0.214 (< 0.001) | -0.322 (< 0.001) |
| • HARS | -0.321 (< 0.001) | 0.630 (< 0.001) |
| • Age/years | -0.003 (= 0.481) | 0.026 (= 0.331) |

*Spearman Rank Correlation Coefficient

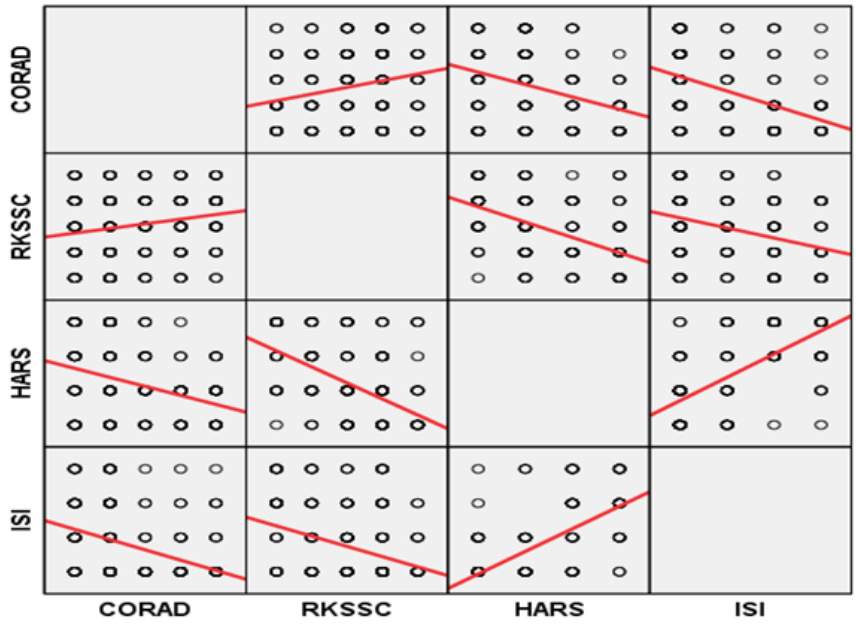
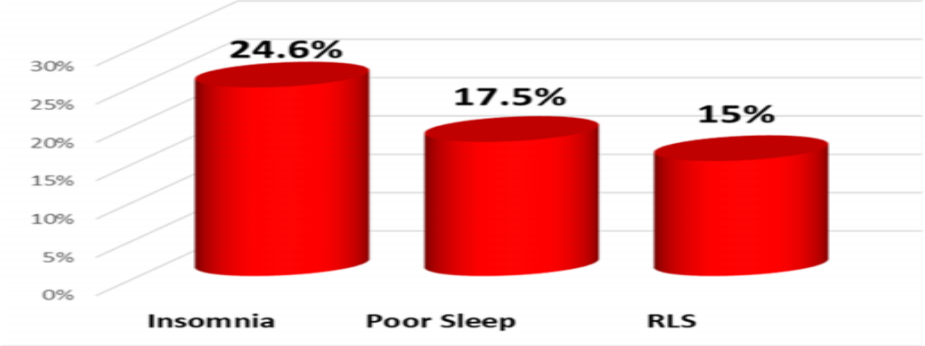



**Table 4.** Independent predictors of sleep disorders among COVID-19 patients: multivariable logistic regression model

| Variable | Multivariate | |
|---|---|---|
| | OR (95% CI) | p-value |
| • Age/years | 1.016 (0.991 – 1.042) | = 0.217 |
| • Sex (Female) | 6.699 (1.173 – 16.585) | < 0.001 |
| • Dyslipidaemia | 2.097 (1.069 – 4.116) | = 0.031 |
| • Smoking | 0.229 (0.079 – 0.660) | = 0.006 |
| • CO-RADS | 1 | < 0.001 |
| • CRP | 0.972 (0.843 – 0.989) | = 0.047 |
| • HARS | 9.105 (3.027 – 16.585) | < 0.001 |

OR= Odds Ratio; CI, Confidence Interval

**Figure 1**. Prevalence of Sleep disorders among the studied Cases



**Discussion**

The main conclusion of the current investigation, including sleep disturbances, was first covered. Next, a number of independent factors linked to sleep disruption were examined. In order to characterise the prevalence of sleep problems, our study, which covered 280 positive COVID-19 patients, was carried out at our university hospitals. 35.7% of our patients had documented sleep problems. They fell into three categories: poor sleep quality, RLS, and insomnia. The samples showed varying prevalences of sleep disturbances, ranging from 2.3% to 76.6%. 55.8% of COVID-19 positive individuals had sleep disturbances, according **to Li et al.** [12].

Geographically, there were differences in the prevalence rates of RLS and insomnia. For instance, 30% of Americans reported having insomnia in the USA [13]. Insomnia was only reported by 2.3% of Chinese workers [14]. **Casagrande et al.** reported that 57.1% of Italian participants experienced poor sleep quality and insomnia [15]. According to **Goldstein et al.**, 11% of the 572 patients hospitalised with COVID-19 had sleeplessness [16]. Notably, they also discovered that 3.9% of people had restless legs syndrome (RLS). A negative attitude towards control measures, fear of the negative impact on income, staying at home without employment, uncertainty about treatment and prevention measures, fear of contracting the infection, and worry about the disease are some of the factors that contribute to the occurrence of sleep disturbances during COVID-19 pandemics.

More sleep disturbances were seen in younger participants (37.26 ± 7.5 years) in our research. According to several research, younger people don't sleep as well as older people do **Beck et al.**[17]. However, **Wang et al.** also noted that elderly people had a greater probability of experiencing poor sleep [18]. This might be explained by the mental strain brought on by the epidemic as well as the existing and developing intellectual and procedural uncertainties. Multivariate logistic regression revealed that mild insomnia was independently predicted by younger age. During the COVID-19 epidemic, a recent study conducted in China also showed that younger participants had an increased risk of mental health conditions such general anxiety disorder [19].

The results of the current study indicated that women were more likely than men to experience sleep disturbances. This may be explained by women's greater vulnerability to anxiety and sadness. Our findings are in line with other research that found women to be the only ones experiencing increasing insomnia [20, 21]. But according to **Anzar et al.**, men were more likely to experience poor sleep quality and insomnia [22].

The current investigation discovered a substantial correlation between sleep disruption and a high degree of worry around COVID-19. Significant psychological strain might cause sleep disturbances in certain people. Furthermore, it has been noted that false material on COVID-19 is widely disseminated on social media [23, 24]. Further research is necessary to determine if false information on social media might increase people's fear about COVID-19, given the strong correlation found between sleep disruption and concerns about the virus. Our results are consistent with research indicating that those who suffer from sleeplessness are more likely to experience anxiety-related mental problems. There is a reciprocal association between anxiety, depression, and sleeplessness, according to several research [25].

The current investigation did not discover any connection between the incidence of sleep problems and the presence of comorbidities such as diabetes mellitus. Our findings disagreed with those of **Li et al.** [12], who found a strong correlation between sleep disruption and lower self-reported physical health. They proposed a number of aetiologies that might explain this correlation. Firstly, there is a clear correlation between psychological discomfort and worse physical health, such as chronic illnesses or reduced physical function. Secondly, individuals may cease seeing the physicians due to concerns about catching COVID-19. Furthermore, concomitant physical and mental disorders raised the likelihood of sleeplessness, according to **Tasnim et al.** [21].

Lastly, we would like to draw attention to two research limitations. First off, the tiny sample size meant that nonparametric, less statistically significant tests had to be performed to test the hypotheses because the data did not follow the normal distribution. Second, the study's cross-sectional design during the acute pandemic stage hampered the ability to draw conclusions about causality and the availability of adequate data at the follow-up.

**Conclusions**

Significant mental health issues, such as sleep difficulties, are linked to an increase in psychosocial stresses. During the COVID-19 pandemic, the current investigation found a number of COVID-19-related variables for sleep disruption in individuals. The primary variables linked to sleep disorders found in this research were female gender, younger population, and stresses connected to COVID-19.

**List of abbreviations**

COVID-19: The coronavirus disease 2019

GSAQ: Global Sleep Assessment questionnaire

RK SSS: Revised Kuppuswamy socioeconomic status Scale

HARS: Hamilton Anxiety Rating Scale

ISI: insomnia severity index

RLS: Restless Leg Syndrome

RLS-DI: Restless Leg Syndrome Diagnostic Index

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