

Insomnia May Mediate the Relationship Between Stress and Anxiety: A Cross-Sectional Study in University Students

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Background: High perceived stress and anxiety disorders are usually comorbid with each other, with stress often sequentially preceding the development of anxiety. While prior findings showed a causal role of sleep problems in anxiety, no study has assessed the role of insomnia as a mediator in the relationship between stress and anxiety.

Methods: A cross-sectional study on university students (n = 475, age = 21.1±2.6 years) was conducted over 3 months. Participants completed self-report measures of Leeds Sleep Evaluation Questionnaire-Mizan (LSEQ-M), Perceived Stress Scale-10 (PSS-10), generalized anxiety disorder-7 scale (GAD-7), and a sociodemographic tool. The mediation effect model given by Baron and Kelly was used to determine the relationship.

Results: The prevalence of insomnia and anxiety disorder was 43.6% and 21.9%, respectively. Stress was significantly associated with LSEQ-M (insomnia measure) (b = -0.44, SE = 0.16, p<0.01), and high levels of anxiety (b = 0.25, SE = 0.03, p < 0.01). The indirect effect of stress on anxiety through LSEQ-M (insomnia measure) was significant (95% confidence interval [0.01, 0.04]). However, the indirect effect of anxiety on stress through LSEQ-M (insomnia measure) was non-significant (95% confidence interval [-0.01, 0.04]).

Conclusions: Students having higher perceived stress levels and comorbid insomnia were also likely to have a higher anxiety level.

Keywords: stress, anxiety, insomnia, mediator

Introduction

One-third of the population is reported to have anxiety disorders at some point in time during their lifespan.¹ Anxiety disorders have a high economic burden because they are associated with high utilization of healthcare services use and a substantial level of impairments. The situation is challenging because of the under-reporting of treatment, improper diagnoses, and non-use/availability of the proper treatment.¹ Stress and anxiety are major psychiatric health issues, both of which are highly prevalent in the university students' populations and most often coexist.² Studies using animal models of stress have shown that stress is involved in increasing or initiating anxiety.^{3,4} Social deprivation stress causes surfacing of anxiety, while chronic psychosocial stress increases anxiety-like behavior in mice.^{3,4}

A higher level of stress is associated with poor sleep quality in college/university students in different countries.⁵⁻⁷ Stress is associated with shorter sleep duration and longer sleep latency in adolescents.⁸ Some people have a trait-like reactivity to stress that may express in sleep problems (like insomnia-type symptoms) in response to

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stress.⁹ Such a sleep-reactivity is heritable susceptibility to sleep problems including insomnia.^{10,11} Such people are more prone to sleep disturbances when exposed to precipitating factors like caffeine consumption, circadian disruptions, etc.⁹ Stress-related sleep reactivity and anxiety symptoms may work as distinguishing features between insomniacs and good sleepers.¹² Estimates show that ~24–36% of the population with anxiety disorders were reported to have comorbid insomnia.¹³ In university students, clinical anxiety is more prevalent in those with insomnia, poor sleep quality, and excessive daytime sleepiness.¹⁴ All this evidence indicates that these three pairs, 1) stress and anxiety, 2) stress and insomnia, and 3) anxiety and insomnia, are often comorbid. However, a major shortcoming of existing studies is that they have not assessed insomnia, stress, and anxiety in one model, limiting the generalizability of the relationship between these three conditions. Thus, studies that account for the mediator and moderator relationship in a model are needed to understand these processes. Stress and anxiety disorders typically develop by late childhood and early adolescence, whereas sleep problems like insomnia increase during the transition from adolescence to adulthood, mostly driven by environmental and physiological changes.^{15–18} Thus, an examination of associations between insomnia, stress, and anxiety may be particularly useful in understanding their mediational role. Therefore, the research hypothesis was that stress and anxiety are associated and that the association is mediated by insomnia.

Materials and Methods

Participants and Procedure

A sample size of 507 students was determined based on 5% margin of error, 99% confidence level, population size (5553 students at Mizan campus of the Mizan-Tepi University (MTU) at the time of study in 2018), and 30% of the expected response distribution for anxiety.¹⁹ From a list of 650 enrolled students; 47 chose not to participate when approached, 78 did not provide responses or did not report for the interview, 28 were excluded after screening, and 22 responses were deleted from analysis because of missing responses for all (or most) of the items of all of the three questionnaires, ie, LSEQ-M, Gad-7, and PSS-10. Participants recorded their responses in hard copies of the survey questionnaire package during individual meetings with the researchers. Finally, 475 collegiate young adults (age: 21.1 ± 2.6 years) from MTU, Mizan-Aman, Ethiopia, were included in this cross-sectional

study. Students were enrolled in different courses at the university. The exclusion was based on the personal account of memory problems and those taking medicines for neuropsychiatric conditions. This was done to minimize the chances of memory-related bias affecting the quality of the study.

The study was reviewed and approved by the institutional ethical committee at the College of Health Sciences, Mizan-Tepi University, Ethiopia. All participants were given a brief explanation about the procedures to be followed before the commencement of the data collection. Participants were also informed that 1) participation was voluntary with the right to discontinue at any stage, 2) no direct benefits and risk(s) were associated, 3) standard procedures were in place to keep personal information confidential, 4) no fee to be paid, and 5) study results will be summarized using group properties using tables and figures without revealing individual's details. In compliance with the Helsinki declaration, informed written consent was given by the participants. Generalized anxiety disorder-7 scale (GAD-7), Leeds Sleep Evaluation Questionnaire-Mizan (LSEQ-M), and Perceived Stress Scale-10 (PSS-10) were used. As all participants were students of an Ethiopian government university with English as the medium of instruction; therefore, all questionnaire tools were used in English.

Measures

Generalized Anxiety Disorder-7 Scale (GAD-7)

GAD-7 measures respondents' anxiety-related symptoms over the last 2 weeks. It is a brief measure with seven items; each of these items is scored on an ordinal scale of 0–3, where '0' represents "not at all" and '3' represents "nearly every day".^{20,21} A total score for the scale henceforth is referred to as GAD total score; it is generated by adding scores for all the seven items. GAD total score may range from 0 to 21; a higher score implies increasing severity of anxiety complaints.²⁰ GAD-7 has been found to have adequate diagnostic validity for screening anxiety disorder at the cut-off score of 10 with sufficient accuracy.²²

Perceived Stress Scale-10 (PSS-10)

PSS-10 measures respondents' stress-related symptoms during the last month immediately preceding the screening. PSS-10 is a brief measure to assess the level of psychological stress with 10-items; each of these 10-items is scored on an ordinal scale of 0–3, where '0' represent "never" and '3' represents

“very often”.²³ A total score for the scale henceforth is referred to as the PSS-10 score; it is generated by adding scores for all the 10-items; scores for four of items are reversed before addition. The PSS-10 total score may range from 0 to 40; a higher score implies increasing severity of stress complaints.²³ The PSS-10 has been found to have adequate psychometric validation in the Ethiopian collegiate young adults.²⁴

Leeds Sleep Evaluation

Questionnaire-Mizan (LSEQ-M)

LSEQ-M is an adapted English version of the original LSEQ, which has been found to have adequate diagnostic validity for screening insomnia in collegiate young adults.²⁵⁻²⁷ LSEQ-M has 10-self reported items that are scored on a 100 mm visual analog scale (VAS).²⁶ A total score for the scale henceforth is referred to as the LSEQ-M total score; it is generated by adding scores for all the 10-items.²⁶ All the individual item scores are divided by 10 before addition to get the LSEQ-M total score.²⁶ Unlike, GAD-7 and PSS-10, lower scores for LSEQ-M are indicative of increasing severity of its measure, ie, insomnia.²⁶

Statistical Analysis

SPSS version 23.0, along with macros SPSS PROCESS, was used to perform the statistical analysis. Descriptive statistics, ie, mean \pm Standard deviation (SD), frequency, and percentage were used for presenting participants' characteristics. The mediation effect model given by Baron and Kelly was implemented to determine the relationship.²⁸ The mediating effect of a single mediator LSEQ-M (insomnia) on the relationship of psychological stress and anxiety was evaluated using SPSS PROCESS.^{29,30} Total scores of LSEQ-M, PSS-10, and GAD-7 were used as measures of insomnia, stress, and anxiety levels, respectively, in this study. Total scores of all these three measures were used as continuous measures. The Sobel test with criteria of absence of 0 in the bootstrapped confidence interval (CI) was used to indicate the significance of the indirect effect.

Results

Participants' Characteristics

The average age of the participating collegiate young adults in this study was 21.1 ± 2.6 years (Table 1). Most of the participants were males (80.0%) (Table 1). The mean GAD-7 total score, PSS-10 total score, and LSEQ-M total score were 7.3 ± 4.2 , 20.1 ± 5.5 , and 57.8 ± 20.0 , respectively

(Table 1). The prevalence of insomnia and anxiety disorders was 43.6% and 21.9%, respectively (Table 1).

Insomnia as a Mediator in the Effect of Stress on Anxiety

The results of the mediation analysis to assess the effect of stress on anxiety through LSEQ-M (insomnia measure) are shown in Figure 1. The overall model explained 15.94% of the variance in stress ($R^2 = 0.1594$, $F[1, 472] = 44.76$, $p < 0.001$). Stress was a negative and significant predictor of LSEQ-M ($b = -.44$, standard error (SE) = 0.16, $p < 0.01$), indicating that those with higher stress levels were likely to have a higher incidence of insomnia. LSEQ-M was also a negative predictor of anxiety ($b = -.04$, SE = 0.01, $p < 0.001$), indicating that those with insomnia were likely to have anxiety. The direct effect of stress on anxiety remained positive and significant after controlling for the effect of LSEQ-M ($b = 0.25$, SE = 0.03, $p < 0.001$). The indirect effect was statistically significant: 95% CI = (0.01-0.04), implying that insomnia was a significant mediator in the effect of stress on anxiety.

Insomnia Was Not a Mediator in the Effect of Anxiety on Stress

The results of the mediation analysis to assess the effect of anxiety on stress through LSEQ-M (insomnia measure) are shown in Figure 2. Insomnia did not mediate the reverse relation, ie, anxiety on stress: LSEQ-M was not a significant predictor of stress ($b = -0.01$, SE = 0.01,

Table 1 Participants' Characteristics

Characteristics	Mean \pm SD/Frequency (Percentage)
Age (yr)	21.1 \pm 2.6
Gender	
Female	95 (20.0)
Male	380 (80.0)
GAD-7 total score	7.3 \pm 4.2
PSS-10 total score	20.1 \pm 5.5
LSEQ-M total score	57.8 \pm 20.0
Insomnia	
Yes	207 (43.6)
No	268 (56.4)
Anxiety disorder	
Yes	104 (21.9)
No	371 (78.1)

Abbreviations: SD, standard deviation; GAD-7, generalized anxiety disorder-7 scale; PSS-10, Perceived Stress Scale-10; LSEQ-M, Leeds Sleep Evaluation Questionnaire-Mizan.

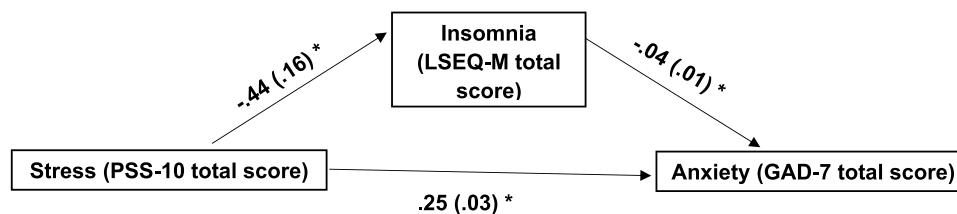


Figure 1 Model with LSEQ-M (insomnia measure) as a mediator in the effect of stress on anxiety.

Notes: First values are the unstandardized coefficients and second values within brackets are the standard errors; * $p < 0.01$. The indirect effect of stress on anxiety through LSEQ-M (insomnia measure) was significant (95% confidence interval [0.01, 0.04]).

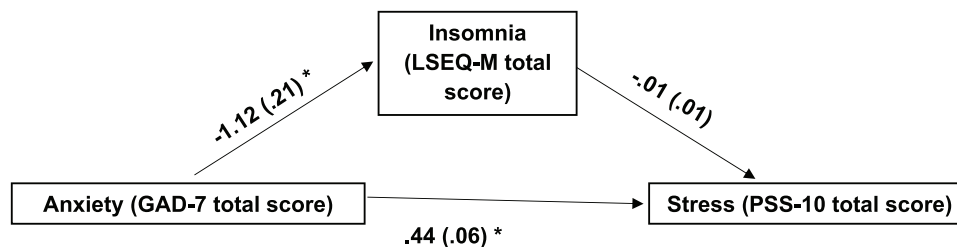


Figure 2 Model with LSEQ-M (insomnia measure) as a mediator in the effect of anxiety on stress.

Notes: First values are the unstandardized coefficients and second value within brackets are the standard errors; * $p < 0.01$. The indirect effect of anxiety on stress through LSEQ-M (insomnia measure) was non-significant (95% confidence interval [-0.01, 0.04]). And, LSEQ-M (insomnia measure) was not a significant predictor of stress ($b = -0.01$, $SE = 0.01$, $p = 0.35$).

$p = 0.35$), and the indirect effect of anxiety on stress through LSEQ-M was non-significant (95% confidence interval [-0.01, 0.04]).

Discussion

The current study examined insomnia as a mediator between stress and anxiety in university students. The bidirectional relationship between chronic stress and anxiety has already been established,^{30,31} with most of the previous studies emphasizing the underlying neurobiological mechanisms.³² However, there is a lack of studies on the underlying psychological mechanisms. To this end, we sought to examine the role of insomnia in mediating the relationship between stress and anxiety. Consistent with our hypothesis, the results provided evidence in support of insomnia as a mediator in the relationship between stress and anxiety symptoms. This implies that students having a higher perceived stress level, and insomnia were also likely to have anxiety. To the best of our knowledge, this is the first study to examine the mediator role of insomnia in the comorbidity of stress and anxiety.

To establish the mediating effect of a factor, it is desirable to use a longitudinal study design, this may provide more robust evidence. However, it is an accepted practice to employ Baron and Kelly's approach to build initial evidence about the mediating effect of a factor using

a cross-sectional design.²⁸ Moreover, longitudinal designs may raise ethical concerns as patient groups, ie, in this case, students with stress and/or anxiety and/or insomnia may have to be followed without allowing them to seek access to treatment for long periods. In such situations, Baron and Kelly's approach provides a more ethically viable approach to building initial evidence about mediating factors without the need to keep participants away from access to treatment.²⁸ Therefore, in this study, we used this method. The current study revealed that insomnia was not a significant mediator in the relationship of anxiety with stress. This implies that those with a higher level of anxiety and insomnia were not likely to have a higher level of perceived stress. The results suggest that there were possibly two types of insomniacs in this study population—one with stress-reactivity-related insomnia and another group with insomnia not related to stress.³³ Most or at least a major section of students with high stress in this study might have had a stress-reactivity to sleep. This seemingly explains the observation of high-stress score also predicting insomnia in the first model.^{9,12,33} However, the presence of insomnia did not predict high-stress scores in the second model. This is likely explained by the incidences of insomnia unrelated to stress as well. Furthermore, these data extend and support the notion that insomnia could be one pathway where psychological stress

may confer a high risk of anxiety. The findings of the present study are thematically similar to previous studies which showed that stressful life events often precede anxiety disorders.³⁴

There are several possible interpretations of the role that insomnia plays as a link between stress and anxiety. Firstly, poor sleep could affect an individual's ability to encode and consolidate emotional memory,³⁵ potentially leading to poor recall capacity of declarative memories during academic life.³⁶ Those students who are already dealing with increased perceived stress, the comorbid incidence of insomnia may further impair the memory encoding and recall during the exams, which may eventually lead to aggravated anxiety levels. Secondly, subjective poor sleep quality has been reported with increased amygdala activation, which is negatively associated with spatial and recall memory in students;³⁷ thus, impacting their academic performance, which also possibly increases anxiety levels. Indeed, subjective poor sleep quality predicted affective dysregulation involving anxiety and depression.^{37–39}

The present study supports the literature by suggesting the role of insomnia in the relationship between stress and anxiety development. This may be partially explained by the shared neuroendocrine mechanisms of stress reactivity and hypothalamic-pituitary and adrenal (HPA) stress axis activation.⁴⁰ Contrasting evidence shows that poor sleep^{41–44} and anxiety confer HPA dysregulation.^{45,46} Accordingly, good sleep quality may offer protection against stress and HPA axis activation.⁴⁷ On the contrary, poor sleep quality makes insomniacs vulnerable to stressful events in life and increases the probability of anxiety occurrence via activation of the HPA axis. Future studies should explore the role of clinical markers of insomnia and its role in mediating stressful events and anxiety.

The etiological basis of stress is multifactorial with most of the factors involved in the expression of psychological stress being external in nature such as a tight deadline or an argument with a friend that lasts for a brief period and may subside once the situation has been resolved.^{33,48} On the contrary, anxiety is a reaction to a stressful situation.^{34,48} Intriguingly, insomnia did not mediate the effects of anxiety on stress. A plausible explanation of our findings is that students with higher perceived stress and comorbid insomnia were likely to develop anxiety, possibly through the HPA axis pathway. However, the absence of opposite relationships, ie, a higher level of anxiety and comorbid insomnia in

students, was not associated with stress, possibly because of the absence of concomitant external stimuli for stress exhibition.

The role of insomnia in mediating the positive relationship between stress and anxiety has important clinical implications, one study suggested the worst clinical outcomes when stress was comorbid with anxiety in post-traumatic stress disorder (PTSD) patients.⁴⁹ Moreover, estimates may vary, but studies showed that patients having a diagnosis of mental health issues like stress had shown ~65% likelihood of having other comorbid mental health disorders.^{49,50} Consistently, each mental health disorder may exacerbate the other, impeding the patient's recovery cycle.⁵¹ Clinically, this finding supports the existing literature and optimizes the present clinical guidelines in the management of insomnia and prevent future predisposition of the patient to anxiety and other mental health disorders. Some of the commonly used behavioral interventional approaches for chronic insomnia are cognitive behavioral therapy, Mindfulness-Based Therapy in combination with behavioral techniques (MBT-I).⁵² Most of these treatment procedures for insomnia do help in the management of anxiety by prospective pathways, ie, by managing/decreasing the severity of insomnia, as well as stress.

Limitations

This study presents a novel role as a mediator of insomnia in the comorbidity of stress and anxiety. This study has some limitations. Firstly, the findings of this study should be interpreted based on the cross-sectional nature of the study. A cohort study with groups of participants with stress only, stress, and co-morbid insomnia, and anxiety with co-morbid stress may help to better establish the mediator role of insomnia for elicitation of anxiety in people with psychological stress. If such a mediator role of insomnia is further validated in cohort studies, then this would highlight the need for the treatments of stress and insomnia to manage anxiety and prevent the future risks for the development of comorbid anxiety and other mental health disorders. Secondly, the relationship in this study may have been slightly influenced by the biased gender ratio. It would be interesting to investigate the mediating role of insomnia in the relation of stress and anxiety among females. This is because sex/gender-related differences have been reported in anxiety disorders and their relationship with stress.⁵³ Additionally, not assessing

of physical activity levels and BMI and their consequent non-consideration in the model was a limitation.⁵⁴

Future studies should assess the potential differential relationship between insomnia, stress, and anxiety. However, regardless of the limitations of the present study, our findings contribute to the existing body of literature and could be potentially used to optimize clinical guidelines in the management of mental health complications in university students.

Conclusion

Students having higher perceived stress level and comorbid insomnia were also likely to have higher anxiety levels. Insomnia seemingly mediated the relationship between stress and anxiety in this cross-sectional study. However, further substantiation of this mediating role of insomnia needs to be established by longitudinal studies.

Data Sharing Statement

The de-identified dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The Human Institutional Ethics Review Committee, College of Medicine and Health Sciences, Mizan-Tepi University, Mizan, Ethiopia approved the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed written consent was obtained from all participants prior to the commencement of the study.

Consent for Publication

Not applicable.

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