Review article

Association between perceived stress and depression among medical students during the outbreak of COVID-19: The mediating role of insomnia

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ABSTRACT

Background: The purpose of this study was to explore the association between perceived stress and depression among medical students and the mediating role of insomnia in this relationship during the COVID-19 pandemic in China.

Methods: A cross-sectional survey was conducted from March to April 2020 in medical university. Levels of perceived stress, insomnia and depression were measured using Perceived Stress Scale (PSS), Insomnia Severity Index (ISI) and Patient Health Questionnaire 9 (PHQ-9). The descriptive analyses of the demographic characteristics and correlation analyses of the three variables were calculated. The significance of the mediation effect was obtained using a bootstrap approach with SPSS PROCESS macro.

Results: The mean age of medical students was 21.46 years (SD=2.50). Of these medical students, 10,185 (34.3%) were male and 19,478 (65.7%) were female. Perceived stress was significantly associated with depression (β=0.513, $P < 0.001$). Insomnia mediated the association between perceived stress and depression (β=0.513, $P < 0.001$). The results of the non-parametric bootstrapping method confirmed the significance of the indirect effect of perceived stress through insomnia (95% bootstrap CI =0.137, 0.149). The indirect effect of insomnia accounted for 44.13% of the total variance in depression.

Conclusions: These findings contribute to a better understanding of the interactive mechanisms underlying perceived stress and depression, and elucidating the mediating effects of insomnia on the association. This research provides a useful theoretical and methodological approach for prevention of depression in medical students. Findings from this study indicated that it may be effective to reduce depression among medical students by improving sleep quality and easing perceived stress.

1. Introduction

In December 2019, a new type of coronavirus disease (COVID-19) broke out in Wuhan, which subsequently spread around the world (Zhu et al., 2019). The aftermath of such a pandemic disease not only harms physical but mental health as well, and the effects of mental harm are more widespread and more lasting than those of physical harm (Allsopp et al., 2019). Empirical studies have shown that during the SARS and MERS outbreaks, viral infections and the subsequent isolation and quarantine can quickly lead to sleep disorders, anxiety and depression

(Khan et al., 2020). As the number of COVID-19 cases is still increasing rapidly, psychological disorders may have affected and will continue to affect millions of people around the world. This suggests that more attention should be paid to the potential psychological problems caused by COVID-19, which can provide information for its intervention and prevention (Xiang et al., 2020).

During the COVID-19 epidemic, 35% of Chinese citizens suffered from psychological distress such as anxiety, depression and cognitive changes (Qiu et al., 2020). In battling the sudden emergence of COVID-19, the mental health of medical staff has been greatly challenged. A multicenter online survey of 1563 medical staff showed that the detection rates of depression and anxiety symptoms were 50.7% and 44.7%, respectively (Liu et al., 2020). As the reserve force of medical staff, the mental health of medical students deserves more attention. Medical students already have more medical knowledge and are the reserve force of health undertakings (Mullan et al., 2010). The prevalence of depressive symptoms among medical students was higher than that reported in the general population before the COVID-19 epidemic (Hope and Henderson, 2014; Puthran et al., 2016; Rotenstein et al., 2016; Voltmer et al., 2012). With the outbreak of COVID-19, medical students suspended classes and were unable to participate in social activities, which might not only affect academic performance but also aggravate depression (Abi-Rafeh et al., 2020; Tariq et al., Sah, 2020). The highly stressful experience of coping during the COVID epidemic may be associated negative emotional outcomes. Studies have found a high proportion of emotional disorders among medical students during the COVID epidemic (Cao et al., 2020; Lasheras et al., 2020; Nguyen et al., 2020). COVID related psychological distress in medical students puts them at great risk for a negative impact on their own health, academic performance, professional identity and the quality of future medical services (Bashir et al., 2020). Therefore, the mental health of medical students is worthy of attention during the epidemic.

Perceived stress is a person's appraisal of the level of threat from stressors, as well as their ability to cope with threat. Medical students typically experience a high perceived stress level, due to the stress of academic burden, lack of relaxation time, breadth of learning materials, and repeated examinations in a competitive environment (Bali et al., 2020; Iqbal et al., 2015). During the COVID-19 epidemic, medical students are experiencing increasing stress as the outbreak gradually affects their physical, emotional and mental health (Chandratre, 2020; Choi et al., 2020). Previous studies have found significantly high stress levels in medical students and has been reported from multiple countries worldwide even before the COVID epidemic (Bali et al., 2020; Garg et al., 2017; Gazzaz et al., 2018; Ludwig et al., 2015; Oura et al. 2020; Yusoff et al., 2010). These studies indicate that the high stress level of medical students is a phenomenon that transcends sociocultural factors, economic status, curriculum model.

Studies focusing on emotional distress caused by long-term exposure to stressors have found that compared with the general population, medical students have increased levels of depression (Azim and Baig, 2019; McGrady et al., 2012). Depression is a multifactorial emotional disorder, which is influenced by both genetic and environmental factors (Yu et al., 2019; Chiare, 2016). Studies on the etiology of depression have identified a moderate heritability of 40-50%, and several genes have been shown to be associated with depression, such as 5-HTTLPR, CYP2C9, and BDNF (Culverhouse et al., 2013; Kim and Sasaki, 2014). A meta-analysis showed that the interaction of 5-HTTLPR with stress had a small but significant effect on predicting depression (Bley et al., 2018). The relationship between perceived stress and depression is complex, and not thoroughly understood (Heinen et al., 2017).

In addition, increased levels of perceived stress have been reported in association with insomnia. Most people have experienced insomnia to some degree. It can manifest as difficulty falling asleep, or as difficulty maintaining sleep for more than 7 hours. In college students, insomnia may be significantly related to memory reduction and decreased learning abilities, which ultimately lead to a decline in academic performance (Haile et al., 2017). This has been shown to be a problem with medical students in particular (Bahammam et al., 2012; El Hangouche et al., 2018). According to recent studies, the rates of self-reported insomnia in college students ranged from 9.5 to 27% (Alqudah et al., 2019; Taylor et al., 2013). It has also been reported that insomnia is associated with an increased risk of depression (Cunnington et al., 2013; Grandner and Malhotra, 2017). In 2016, Li et al. performed a meta-analysis to examine the association between insomnia and the risk of depression, and the results showed pooled RR for insomnia to predict depression of 2.27 (Li et al., 2016). There is evidence that interventions such as cognitive behavioral therapy specially for insomnia may lead to improvements in depression (Gebara et al., 2018).

In our study, mediation analysis was performed to explore the relationships between perceived stress, insomnia and depression in medical students. Mediation analysis is a family of methods designed to extract information about the causal mechanisms by which a predictor affects an outcome (Mokhayeri and Mansournia, 2019; Preacher, 2015; Valente et al., 2017; Valeri and Vanderweele, 2013). It is expected that this method will help to better understand the occurrence of depression in medical students, the relationship between perceived stress and depression, and the mediating role of insomnia between the occurrence of perceived stress and depression. To our knowledge, no studies have examined the mediation model between perceived stress, insomnia and depression in medical students. This study will provide a better understanding of depression in medical students so that we can prevent future health problems, reduce academic stress, and improve sleeping habits for better academic achievement in medical students. The objective of the current study is to identify the association between perceived stress, insomnia and depression in medical students during the COVID-19 outbreak.

2. Methods

2.1. Participants

All the participants signed online informed consent before completing the online questionnaire, and the study was approved by the Biomedical Ethics Committee of Xinxiang Medical University and Hainan Medical University.

A cross-sectional survey on medical students was conducted from March to April 2020 during the COVID-19 epidemic in China. Three medical universities were selected for the survey, and the cluster stratified random sampling method was used. Given the severity of COVID-19 epidemic, the data was collected through online platforms rather than face-to-face interviews. All questionnaires were completed on WeChat official account platform. Finally, a total of 29,663 valid questionnaires were collected.

2.2. Measures

2.2.1. Basic information

Information regarding the participants' age, gender, education level, psychiatric history of individuals and family members, and COVID-19 related factors were asked to understand the characteristics of the participants.

2.2.2. Measurement of perceived stress

The Perceived Stress Scale 14 (PSS-14) is a measure of perceived stress and has shown good reliability and validity (Cohen et al., 1983). The scale includes 14 items that are scored on a 5-point rating scale ranging from 0 (never) to 4 (very often). The total score ranged from 0 to 56, which can be obtained by adding the scores of all the items. Higher scoring reflected higher levels of perceived stress (Meng et al., 2020). Cronbach's alpha in the present study was 0.808.

2.3. Measurement of insomnia

The Insomnia Severity Index (ISI) was used to assess the severity of insomnia, including 7 items. The participants answered questions on a 5-point scale ranging from 0 to 4 (0, not at all; 1, mild; 2, moderate; 3, severe; 4, extremely severe). The total score ranged from 0 to 28, with a higher score indicating a greater level of insomnia (Yu, 2010). The internal consistency of ISI in the present study was very good (α=0.873).

2.4. Measurement of depression

The Patient Health Questionnaire 9 (PHQ-9) is a self-report questionnaire that measures symptoms of major depressive disorder. The scale included 9 items that are scored on 4-point ranging from 0 to 3 (0, not at all; 1, several days; 2, more than half of all the days; 3, nearly every day). The total score ranged from 0 to 27, with a higher score indicating greater severity of depressive symptoms (Du et al., 2017). The internal consistency of the PHQ-9 in the present study was very good (α=0.886).

2.5. Statistical analysis

The descriptive analyses of the demographic characteristics and correlation analyses of the three variables were calculated. The mediation analysis was performed using one independent variable (perceived stress), one dependent variable (depression), and one mediator (insomnia). The mediation model was analyzed using Model 4 in the PROCESS Marco. For the best test of mediation effect, the bootstrapping procedure to measure indirect effect was carried out and 95% confidence intervals were estimated. The number of bootstrap samples was 5000. Control variables such as age, gender and education level were introduced in the model as covariates. If the confidence interval includes zero, it means that there is no significant mediating (indirect) effect at the significance level of 5%. All the analyses were performed using SPSS 25.0 for Windows.

3. Results

3.1. Demographic characteristics

A total of 29,663 medical students completed the surveys. Of these medical students included in the data analyses, 10,185 (34.3%) were male and 19,478 (65.7%) were female. The mean age of the medical students was 21.46 years (SD=2.50). The majority of the students have a bachelor's degree or above (93.4%). The percentage of students using tobacco was 5.3% and the percentage who consumed alcohol was 14.3%. Few students had a history of psychiatric disorder (1.1%) or family psychiatric disorder (1.1%).

3.2. Preliminary correlation analyses

The Pearson correlations for each of three variables were presented in Table 1. The results showed that depression was positively correlated with perceived stress (r=0.512, $P < 0.001$) and insomnia (r=0.679, $P < 0.001$). Insomnia was positively correlated with perceived stress

Table 1
Correlations between perceived stress, insomnia and depression.

Variables	Depression	Insomnia	Perceived stress
Depression	-		
Insomnia	0.679*	-	
Perceived stress	0.512*	0.399*	-
Mean	2.97	2.97	12.18
Standard deviation	3.88	3.63	6.15

* $P < 0.001$

(r=0.399, $P < 0.001$).

3.3. Mediation analyses

Following the correlation analyses results, we performed mediation analyses to further examine the association between perceived stress, insomnia and depression in medical students. The significance of the direct, indirect and total effects in the mediation model was identified after controlling for the sociodemographic variables (age, gender and education level). In Model 1, controlling for age, gender and education level, perceived stress was significantly associated with insomnia (β=0.400, $P < 0.001$). In Model 2, controlling for age, gender and education level, perceived stress had a significant relationship with depression (β=0.513, $P < 0.001$). In Model 3, controlling for age, gender and education level, both perceived stress and insomnia were included in the mediation model and showed significant relationship with depression. Simultaneously, the standardized regression coefficient (β) for perceived stress decreased from 0.513 to 0.287 (Table 2). Moreover, the results of the non-parametric bootstrapping method confirmed the significance of the indirect effect of perceived stress through insomnia (95% bootstrap CI=0.137, 0.149). A bootstrapped 95% confidence interval (CI) confirmed that the indirect effect of perceived stress had an impact of 0.143 that was produced by insomnia as a mediator on depression. The indirect effect of insomnia accounted for 44.13% of the total variance in depression (Table 3). These findings corroborate our hypothesis that insomnia may play a mediator role in the association between perceived stress and depression. Fig. 1 illustrated the mediation model, along with standardized path coefficients.

4. Discussion

This study examined the association between perceived stress and depression, and further examined the mediating effect of insomnia on this association among medical students during the COVID-19 pandemic. Our findings demonstrated that perceived stress was associated with depression, and insomnia played a mediating role when included in the association. The findings suggest that interventions or strategies ameliorating insomnia may be helpful to reduce the severity of depression both directly and indirectly in the medical students. College administrators and health policy makers need to recognize the importance of insomnia, and they should consider developing and providing interventions to encourage good sleeping habits among medical students with high level of perceived stress.

Perceived stress can be understood as the sense of imbalance between the stressors encountered in daily life and a person's coping capability. The phenomenon of perceived stress has received much

Table 2
Mediating effect of insomnia between perceived stress and depression.

	Perceived stress → Insomnia (Model 1)				
	B	SE	β	t	P
Age	-0.006	0.008	-0.004	-0.740	0.459
Gender	0.103	0.041	0.014	2.540	0.011
Education	0.011	0.065	0.001	0.168	0.867
Perceived stress	0.236	0.003	0.400	75.108	<0.001
	Perceived stress → Depression (Model 2)				
	B	SE	β	t	P
Age	-0.011	0.008	-0.007	-1.355	0.175
Gender	0.178	0.041	0.022	4.360	<0.001
Education	0.215	0.065	0.017	3.318	0.001
Perceived stress	0.324	0.003	0.513	102.828	<0.001
	Perceived stress, Insomnia → Depression (Model 3)				
	B	SE	β	t	P
Age	-0.007	0.006	-0.005	-1.139	0.255
Gender	0.115	0.033	0.014	3.545	<0.001
Education	0.208	0.052	0.017	4.031	<0.001
Perceived stress	0.181	0.003	0.287	66.111	<0.001
Insomnia	0.604	0.005	0.565	130.075	<0.001

Table 3
Mediating model examination by bootstrap

| | Perceived stress → Depression | | | |
	Effect	SE	LL 95%CI	UL 95%CI
Indirect effect	0.143	0.003	0.137	0.149
Direct effect	0.181	0.003	0.176	0.187

attention over the last two decades. Medical students may feel stressed when they feel course demands exceeds their resources. They have been reported to suffer from higher perceived stress and emotional distress compared to the general population and students in other academic fields (Heinen et al., 2017). Medical students are therefore a vulnerable group, and they are less likely to seek support. In this study, the correlation analysis revealed a positive relationship between perceived stress and depression, which indicated that high level of perceived stress was associated with depression. This correlation has been observed in medical students previously (Azim and Baig, 2019; Ludwig et al., 2015; McGrady et al., 2012; Romo-Nava et al., 2016; Silva and Figueiredo--Braga, 2018; Zeng et al., 2019). Romo-Nava et al. evaluated the association between stress and depression, and demonstrated that perceived academic stress was related factors of depression in medical students (Romo-Nava et al., 2016). Easing medical students' perceived stress is important not only for improving their ability to cope, but also for reducing the occurrence of depression.

In this study, perceived stress was also significantly associated with insomnia, consistent with previous studies (Alsaggaf et al., 2016; Backović et al., 2013; Herawati and Gayatri, 2019; Średniawa et al., 2019). Herawati et al. found that students with poor sleep quality were 4.7 times more likely to have higher stress than students who have good sleep quality (Herawati and Gayatri, 2019). Alsaggaf et al. showed that high levels of stress and the pressure of maintaining grade point averages can influence medical students' quality of sleep (Alsaggaf et al., 2016). According to the results of previous studies, there is a complicated two-way interaction between perceived stress and insomnia. Due to different intensities and durations of the stressors, the quality and quantity of sleep may vary, and may even affect the final result of sleep. In the psychological intervention for insomnia, we can focus on reducing the perceived stress level of medical students.

This study also found that insomnia was significantly correlated with depression. In other studies, medical students with persistent insomnia are developing depression compared to those without sleep difficulties (Marelli et al., 2020; Ramón-Arbués et al., 2020). With the outbreak of COVID-19, insomnia has become particularly prominent in students with the implementation of home confinement policy (Altena et al., 2020). There are several possible biological mechanisms through which

insomnia may increase the risk of depression. Experimental studies have shown that insomnia not only causes cognitive and emotional changes, but also disrupts emotional regulation and stability, which in turn leads to depression (Jackson et al., 2014; Novati et al., 2008). In a state of stress, people with sleep disorders have weakened anti-inflammatory and anti-infection ability and decreased immunity. The decrease of immune function can stimulate inflammatory reaction and lead to tissue damage. Tissue damage is in a state of chronic stress, which can easily lead to depression for a long time (Toda et al., 2019). Increased levels of inflammatory markers, such as C-reactive protein and interleukin-6, have been found to be associated with the risk of depression (Faraut et al., 2012; Gimeno et al., 2009; Okun et al., 2013). Moreover, as a chronic stress behavior, insomnia can promote the chronic activation of hypothalamic pituitary adrenal axis, which is considered to play an important role in the development of depression (Ehnvall et al., 2004; Balbo et al., 2010; Fernandez-Mendoza and Vgontzas, 2013). However, the role of insomnia treatment in regulating the risk of depression needs further study.

Our findings showed that insomnia had a mediating effect on the association between perceived stress and depression. This indicates that the impact of perceived stress on depression is partly mediated by insomnia, which means that students who are prone to insomnia are more likely to have severe symptoms of depression when exposed to stressors. We found that 44.13% of the relationship between perceived stress and depression was mediated by insomnia. This would indicate that improving the sleep quality of medical students can not only reduce the severity of depression directly, but also indirectly through mediating effects. Medical students are experiencing increasing depression as COVID-19 gradually affects their physical, emotional, and mental well-being. The current epidemic may aggravate existing mental health problems (Chandratre, 2020; O'Byrne et al., 2020; Tariq et al., 2020). Liu et al. conducted an online survey to investigate the mental health of medical students and found that universities need to take measures to prevent, identify, and deal with mental health problems among students during large-scale stressors (Liu et al., 2020). Li et al. suggested that COVID-19 related psychological distress is common among health profession students (Li et al., 2020). Specific intervention measures for the psychological problems of medical students still need to be explored in practice. Many studies, have focused on single aspects of the depression experienced by medical students, such as life stress, emotional distress, and attitude to frustration, but failed to investigate the relevant aspects in a general depression model (Gan and Yuen, 2019; Silva et al., 2017). We were interested in identifying approaches for interventions to reduce the occurrence of depression, taking into account perceived stress and insomnia. Therefore, counselling services focusing on improving sleep quality and easing perceived stress may be a useful option for reducing
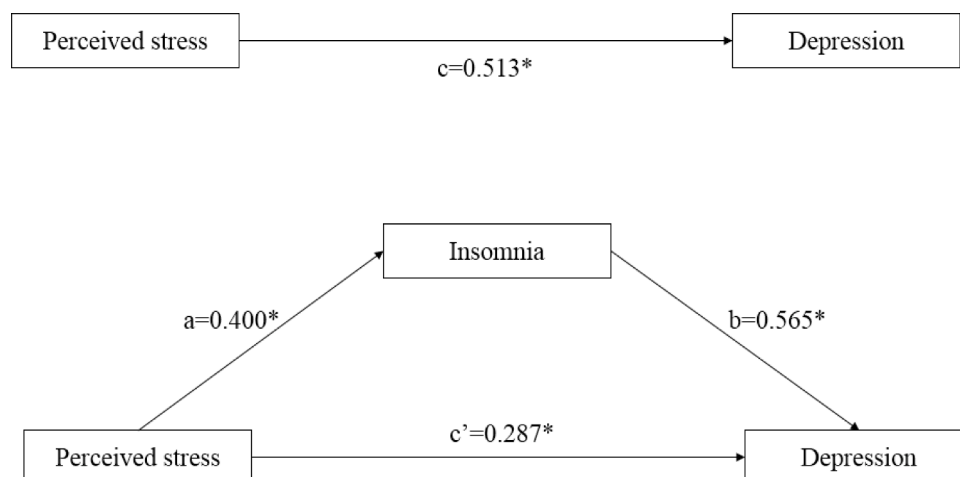

Fig. 1. Proposed models that investigate mediated effects. (*P < 0.001).

depression in medical students.

There are several limitations in the present study. First, the causality could not be established because of the cross-sectional study design. Longitudinal studies need to be conducted to confirm the findings obtained from this study. Second, the questionnaire used in our study to estimate medical students' perceived stress, insomnia and depression were all self-report. In future investigations, a combination of self-rating scales and clinically objective diagnosis can be used for the mental health evaluation. Third, the sample was drawn from only three medical universities, and may not be representative of medical students in China.

Although we cannot make a definitive conclusion on the causal links based on our cross-sectional investigation, our findings that perceived stress may confer a vulnerability to depression through increasing the occurrence of insomnia are in alignment with previous findings. It is the first study to estimate the mediating effect of insomnia on the association between perceived stress and depression in medical students during the COVID-19 epidemic. These findings contribute to a better understanding of the interactive mechanisms underlying perceived stress and depression. Importantly, this research provides a useful theoretical and methodological approach for prevention of depression in medical students.

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Notes on contributors

Fei Wang designed the study. Yang Wang and Yange Wei were responsible for literature searches and analyses. Rongxun Liu and Lijuan Liang participated in the data collection and administration. Ran Zhang and Rongxin Zhu extracted the data and assisted with the data analysis. Zhuang Liu and Yue Zhang carried out the statistical analysis and wrote the first draft of the manuscript. Zhuang Liu, Yue Zhang and Fei Wang participated in the revision of the manuscript. All authors contributed to and have approved the final manuscript.

Disclosure statement

No potential conflict of interest was reported by the authors.

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