

Original Research



The prevalence of chronic fatigue syndrome and depression in Guilan medical students in 2020

Elahe Abdollahi^{ID}, Robabeh Soleimani^{ID}, Hamed Taherzadeh^{ID}, Fatemeh Eslamdoust-Siahestalkhi^{ID}

Kavosh Cognitive Behavior Sciences and Addiction Research Center, Department of Psychiatry, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

Article info

Article History:

Received: 11 July 2021
Accepted: 22 Sep. 2021
ePublished: 28 Nov. 2021

Keywords:

Chronic fatigue syndrome
Depression
Medical students

Abstract

Background: Chronic fatigue syndrome (CFS) and depression are specific mental disorders that can negatively affect college students' social, occupational, and academic performance, especially medical students. This study aimed to investigate the prevalence of CFS and depressive symptoms and their relationship with medical students.

Methods: This cross-sectional analytical study was conducted with 175 medical students at the Guilan University of Medical Sciences in 2020 in Guilan in the north of Iran. Three levels of medical students, including basic sciences and physiopathology, externship, and internship students, participated. A demographic information questionnaire, the Beck Depression Inventory-II (BDI-II), and the Chalder Fatigue Questionnaire (CFQ) were used to collect data. SPSS 22 was used to analyze the data, including Mann-Whitney, Kruskal-Wallis, and Spearman tests.

Results: The mean age of the participants was 23.92 ± 2.04 years. Of 175 participants, 50.9% were males. In all, 11.4% of subjects reported levels of CFS, and 38.8% of them showed levels of depression. The rates of CFS and depressions were not associated with age, gender, marital status, educational level, geographic area, or student habitation ($P > 0.05$). The use of cigarettes ($P = 0.002$), alcohol, and substances ($P < 0.0001$) showed a significant relationship with higher levels of CFS and depression scores. The relationship between the CFS score and depression was significant ($r = 0.523$, $P < 0.0001$).

Conclusion: The prevalence of CFS and depression among medical students were 11.4% and 38.8%, respectively. There was a positive association between CFS and depression. Implementing screening policies is recommended, along with programs to help promote mental and physical health among students.

Introduction

Chronic fatigue syndrome (CFS), or myalgic encephalomyelitis (ME), is a chronic and disabling illness that has various definitions.¹ It is commonly characterized by fatigue lasting for at least six months, worsened by exertion, and is not relieved by rest, leading to a reduction in daily activities.^{2,3} Other symptoms include sleep that does not refresh and neurocognitive problems characterized by slowness of thought or mental fog.³ Other fatiguing illnesses that can cause similar symptoms should be ruled out.⁴ The prevalence of CFS is estimated to be between 836 000 and 2.5 million Americans in the United States³ by the Institute of Medicine (IOM) and approximately 0.4%-2.5% around the world. Moreover, it is more common between 20 and 40 years old.⁵ Women are 1.5 to 2 times more likely than men to suffer from CFS.¹

On the other hand, depression is among the most common mental disorders, characterized by sadness, loss of interest or pleasure, feelings of guilt or worthlessness, disturbed sleep or appetite, feelings of tiredness, and poor concentration leading to impairments in daily activity.⁶ Between 1994 and 2014, the lifetime prevalence of depression was reported to be 10.8%.⁷ The prevalence of this disorder is more common among women (5.1%) than men (3.6%).⁶ In Iran, the rate of mental disorders was reported to be 23.4%, of which severe depression accounts for 10.4%.⁸ According to the results of a study, the range of any mental illness declines from 20 to 30-40 years old.⁹ A study in 2018 reported a significantly increased prevalence of depression in the United States between 2005 and 2015, increasing in young people more rapidly than in older people.¹⁰

*Corresponding author: Fatemeh Eslamdoust-Siahestalkhi, Email: fatemeh.eslamdoost@gmail.coms

© 2021 The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, as long as the original authors and source are cited. No permission is required from the authors or the publishers.

Although the general population is at risk for mental health illnesses, college students are highly vulnerable to psychiatric disorders.¹¹ In recent years, mental health has been widely studied among college students, and numerous studies show that mental health problems are very prevalent in this group.¹²⁻¹⁵ Investigation into 374 students between the ages of 18-24 years found that 33% of them had depressive symptoms.¹⁶ In both medical and non-medical students, the prevalence of depression is considerable, but no difference was found between the two groups in some studies.¹⁷⁻²⁰ In Iran, the rate of moderate to severe depression has been reported to be around 19.0% at the Kurdistan University of Medical Sciences.²¹ Findings of two meta-analysis studies have found that around 28% of medical students had depression or showed depressive symptoms.^{19,22} In another meta-analysis in China, the rate of depression was found to be 32.7% in medical students.²³ In other studies, the prevalence of depressive symptoms in medical students was reported to be 41.0% in Brazil²⁴ and 65.0% in Egypt.²⁵ In addition to academic pressures,²⁶ other factors such as long training,²⁷ workloads, financial difficulty, and sleep insufficiency²⁴ might all contribute to psychological problems, such as depression in medical students.

Fatigue is also a common problem in medical students, and it may affect not only their academic performance but severe fatigue is also associated with more stress.²⁸ Several factors can contribute to this problem, such as academic pressure, workload, family expectations,²⁷ and lifestyle factors like sleep quality²⁹ and smoking.³⁰ Based on a study by Pourmovahed et al., it seems that there may be a correlation between CFS and depression in medical students.³¹

Therefore, depression is of considerable importance in college students since it predicts a decrease in academic performance, especially in first-year students.³² In addition, considering the importance of CFS in the well-being of medical students and their academic performance,²⁸ we examined the prevalence of CFS and depression in Guilan medical students and their relationship with each other, due to the relatively high prevalence of depression in medical students in previous studies and the small number of studies on CFS and depression in Iran, especially among Guilan medical students. Timely recognition and diagnosis of psychological problems is an effective approach to improve medical students' mental and physical health and their performance.

Material and Methods

The current cross-sectional study consisted of a sample of 175 students at the Guilan University of Medical Sciences in the academic year 2019-2020. After obtaining ethical approval, participants were selected by convenience sampling. Inclusion criteria included studying at the Guilan Medical School and willingness to participate in the research; exclusion criteria included any history of

serious psychiatric or physical illnesses. After explaining the objectives of the study and obtaining informed consent, three questionnaires were completed by the participants. These included a demographic information questionnaire, the Chalder Fatigue Questionnaire (CFQ), and the Beck Depression Inventory-II (BDI-II). Due to COVID-19 conditions, the questionnaires were made available in two ways: printed and uploaded on the Internet.

Scales

Demographic information questionnaire

This questionnaire included demographic information, such as age, sex, marital status, educational level, substance use, and smoking.

Chalder Fatigue Questionnaire (CFQ)

Chalder, Berlowitz, and Hirsch, in 1993, developed a short 14-item instrument to measure the mental and physical symptoms of fatigue. The items of this tool are scored based on a 4-point Likert scale (0 = less than usual, 1 = no more than usual, 2 = more than usual, 3 = much more than usual). Overall scores range from 0 to 42, and the cut-off point is 22. This scale has been used in several studies in epidemiology and treatment outcomes in CFS patients. The validity and reliability of this scale were examined by Chalder et al. using the list of clinical interview symptoms, and the sensitivity and specificity were reported to be 75% and 74%, respectively. The internal consistency coefficient was 0.85 for physical fatigue and 0.82 for mental fatigue.³³ In Iran, in a study by Nasri et al., this scale was used as a screening tool, and the test-retest coefficient, internal consistency, and split-half coefficient were calculated at 0.85, 0.91, and 0.82, respectively, showing the high reliability and validity of this scale.³⁴

Beck Depression Inventory (BDI-II)

This questionnaire is one of the most suitable tools for measuring depression. It was created by Aaron T. Beck and has 21 items that measure the physical, behavioral and cognitive symptoms of depression. Each item has four options that are scored on a scale of 0 to 3 for a total score between 0 and 63. This scale indicates the severity of depression: no depression (0-13), mild depression (14-19), moderate depression (20-28), and severe depression (≥ 29). The BDI-II shows high reliability and can separate depressed from non-depressed subjects. The internal consistency of BDI-II has been reported at 0.9, and the test-retest reliability has been estimated to be between 0.73 and 0.96.³⁵ In Iran, internal consistency and test-retest reliability were reported at 0.87 and 0.74, respectively.³⁶

Statistical analysis

Based on Abedini et al.,³⁷ the sample size for the current study was calculated to be 175 people. SPSS 22 was used to analyze the data based on descriptive and analytical statistics. The Kolmogorov-Smirnov test showed that

distribution was not expected. Therefore, Mann-Whitney and Kruskal-Wallis nonparametric tests were used. Spearman's test was also used to determine the relationship between study variables. In this study, a *P* value of less than 0.05 is considered significant.

Results

The current study was conducted with 175 medical students from three-course areas, including basic sciences and physiopathology, externship courses, and internship courses, with a mean age of 23.92 ± 2.04. Table 1 shows the demographic characteristics of the participants.

The mean score for physical fatigue was 6.79 ± 4.89 and 5.04 ± 3.98 for mental fatigue, while the mean score for CFS was 11.83 ± 7.96. Figure 1 shows the frequency of CFS in participants.

The mean score of depression in the participants was 13.10 ± 10.52. The prevalence of depression in students is shown in Figure 2. Of 175 students, 69 (38.8%) reported levels of depression.

Table 2 shows a comparison of the mean scores for CFS and depression in the participants in terms of demographic variables using Mann-Whitney and Kruskal-Wallis tests. Among the variables studied, there was a significant relationship between CFS and depression scores among smokers (*P*=0.002), alcohol users (*P*=0.011, *P*<0.0001), and substance users (*P*=0.002, *P*<0.0001). Students who smoked drank alcohol, and used substances had higher mean CFS and depression scores.

Figure 3 shows that the positive relationship between the mean scores of CFS and depression in medical students is significant, using Spearman's test (*r* = 0.523, *P* < 0.0001).

Discussion

The current study examined the prevalence of CFS and

depression among medical students and the relationship between them. A total of 175 medical students, with a mean age of 23.92 ± 2.04 years, participated in the study. In all, 11.4% of students reported levels of CFS, with physical fatigue more prevalent than mental fatigue. The prevalence of depression in students was 38.8%, and approximately 18% had moderate to severe symptoms. Students who smoked drank alcohol, or used substances had significantly higher mean CFS and depression scores. There was no significant relationship between demographic characteristics, including age, gender, marital status, educational level, geographic area or accommodation, and rates of CFS and depression among the students. Mean scores of CFS and depression did show a significant relationship in medical students.

The rate of CFS in our study was found to be 11.4%, while the prevalence of CFS is estimated at between 0.4%-2.5 % around the world.⁵ In line with the current study, the prevalence of CFS in nurses was found to be 7.3% by Nasri.³⁴ The higher incidence of CFS may be due to stressful educational activities, study duration, fewer sports activities,³⁸ poor sleep quality,^{38,39} or other existing stressors.

In addition, the prevalence of depression is reported at 10.8% in the world⁷ and severe depression is estimated at 10.4% in Iran,⁸ but, similar to the current study, different studies have shown higher rates of depression in medical students. The results of a study in Yazd, Iran³¹ showed that

Table 1. Demographic variables of the participants (N = 175)

Variables	No. (%)
Gender	Female 86 (49.1)
	Male 89 (50.9)
Age	≤24 103 (53.9)
	>24 72 (41.1)
Marital status	Single 164 (93.7)
	Married 11 (6.3)
Educational level	Basic sciences and physiopathology 59 (33.7)
	Externship 57 (32.6)
	Internship 59 (33.7)
Geographic area	Native 125 (71.4)
	Nonnative 50 (28.6)
Residency	Dormitory resident 29 (16.6)
	Non-resident in the dormitory 126 (83.4)
Smoking	Yes 38 (21.7)
Substance use	Yes 15 (8.6)
Alcohol use	Yes 42 (24.0)

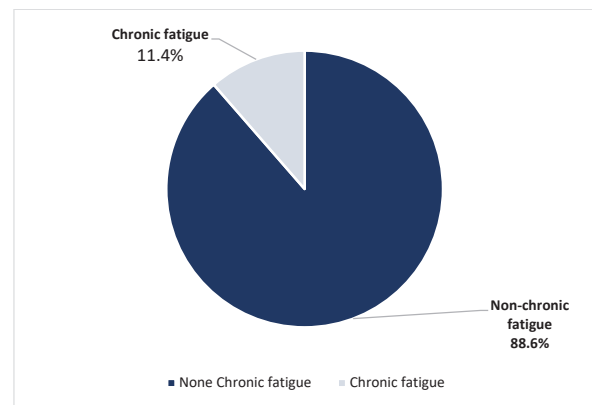


Figure 1. Frequency of CFS (N = 175).

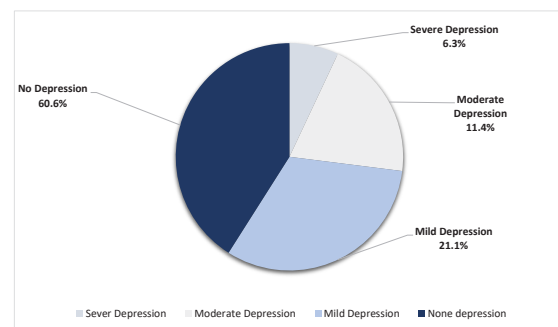
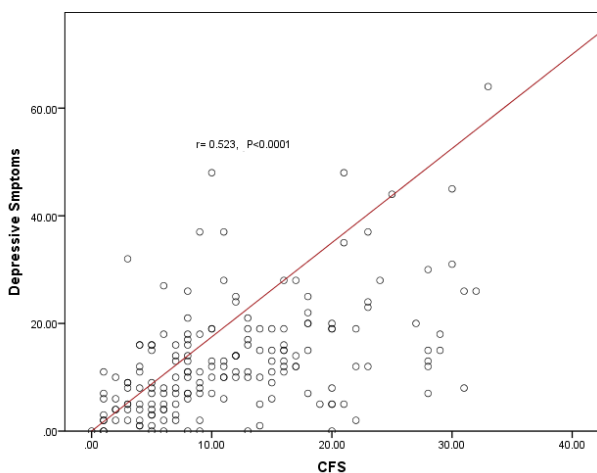


Figure 2. Frequency of depression (N=175).

Table 2. Comparison of the mean scores of CFS and depression with demographic variables (N=175)

Variables		CFS Mean \pm SD	Depression Mean \pm SD	CFS P value	Depression P value
Gender	Female	10.86 \pm 7.61	12.14 \pm 8.73	0.695*	0.454*
	Male	12.76 \pm 8.22	14.03 \pm 11.99		
Age	\leq 24	11.53 \pm 7.92	12.78 \pm 9.42	0.545*	0.911*
	$>$ 24	12.25 \pm 8.05	13.57 \pm 11.99		
Marital status	Single	11.60 \pm 7.87	12.88 \pm 10.42	0.161*	0.220*
	Married	15.27 \pm 8.86	16.45 \pm 12.14		
Educational level	Basic sciences and physiopathology	11.27 \pm 8.30	14.15 \pm 12.53	0.659**	0.709**
	Externship	11.81 \pm 7.40	11.61 \pm 8.28		
	Internship	12.41 \pm 8.22	13.49 \pm 10.29		
Geographic area	Native	11.60 \pm 7.67	12.98 \pm 10.60	0.231*	0.683*
	Nonnative	12.40 \pm 8.69	13.42 \pm 10.45		
Residency	Dormitory resident	11.62 \pm 8.93	12.83 \pm 7.52	0.662*	0.570*
	Non-resident in the dormitory	11.87 \pm 7.78	13.16 \pm 11.05		
Smoking	Yes	15.26 \pm 8.04	17.08 \pm 11.06	0.002*	0.002*
	No	10.88 \pm 7.70	12.00 \pm 10.14		
Substance use	Yes	18.80 \pm 8.90	26.87 \pm 16.84	0.002*	$<$ 0.0001*
	No	11.18 \pm 7.57	11.81 \pm 8.76		
Alcohol use	Yes	14.52 \pm 8.36	18.05 \pm 12.61	0.011*	$<$ 0.0001*
	No	10.98 \pm 7.66	11.54 \pm 9.30		

* Mann-Whitney test; **Kruskal-Wallis test.

**Figure 3.** Relationship between CFS mean scores and depressive symptoms.

around 27% of medical students in different medical fields reported moderate to severe symptoms of depression. In Hamedan, Iran, 37% of medical students experienced depression, with around 18% reporting moderate to severe depression.⁴⁰ In Birjand, Iran, the results of a study found depressive symptoms in 31.8% of medical students; about 20% of them had moderate to severe depression.⁴¹ A study among medical and nursing students in Jahrom found that 15% of students had moderate to severe symptoms of depression.⁴² The high rate of depression and CFS in medical students compared to the general population shows the importance of paying attention to the well-

being of college students, especially medical students, through screening policies along with counseling and treatment sessions, which ultimately play a crucial role in improving their academic and work performance and thus community health.

Consistent with the current study, there was a strong association between burnout and alcohol use in the United States⁴³ and Hong Kong³⁸ among medical students and between depression and tobacco and cannabis use among college students.^{44,45} The results of a study in Turkey showed that medical students who smoked cigarettes suffered from depressive symptoms 2.2 times more than nonsmokers.⁴⁶ The prevalence of alcohol use among medical students was reported at 58% in the U.S. medical students,⁴⁷ and in South Africa, the use of alcohol, drugs, and smoking was found to be considerable in medical students.⁴⁸ It seems that behaviors such as substance use may be maladaptive coping behaviors to help relieve stress among college students,⁴⁹ which has both personal and professional impacts on students' lives.^{50,51}

According to the results, the mean score of CFS and depression in male students were higher than in females. However, the difference between the two groups was not significant. This result is consistent with studies from Rezaei et al.⁴⁰ and Ershadi et al.⁵² on depression. According to a systematic review study in China, the rate of depression in medical students was significantly higher in males than in females.²³ In contrast, a higher rate of depression was reported for females in other studies.^{24,53}

Pourmovahed et al. reported that CFS in female students was significantly higher than in male students. The use of alcohol, substance use, and smoking might contribute to a higher rate of depression and CFS in males.³¹

The current study results showed that the rate of depression in basic sciences and physiopathology students was higher than in the externship and internship groups of students, while the CFS level in the internship group of students was higher than in the others. However, these differences were not significant. Al-Alawi et al.⁵⁴ found a higher rate of depression and burnout in the preclinical grade. More theoretical courses and a higher number of exams in the early years of medical education, as well as adaptation problems with this field's condition, might have led to a higher rate of psychological problems in this group of students. In the later years of medical education, a combination of practical and theoretical courses creates more interest, self-satisfaction, and self-efficiency in medical students.

Some studies have found a positive association between CFS and depression in line with the current study results.^{31,39} High numbers of medical students are exposed to stress, depression, and chronic fatigue due to unique problems, such as a high amount of course materials compared to other disciplines, severe stress due to dealing with critically ill patients, as well as other problems, including economic and family issues and even differences in cultures. Therefore, increasing awareness and improving students' mental health through counseling sessions, providing appropriate conditions to increase the health and welfare of college students, and increasing the number and types of recreational facilities and educational facilities might reduce psychological problems, such as depression and CFS.

The limitation of the study was that clinical interviews were not conducted to more accurately diagnose depression or CFS. The role of other factors, such as lack of interest in the field of study, socio-economic status of the family, and family history of mental disorders affecting the rate of depression and CFS, are indicated to obtain more precise results in future studies.

Conclusion

According to the results, the prevalence of CFS and depression among medical students at a university in northern Iran were found to be 11.4% and 38.8%, respectively. Around 18% of these students had moderate to severe symptoms of depression. The rates of CFS and depression were not associated with age, gender, marital status, educational level, geographic area, or student accommodation. The use of cigarettes, alcohol, and substances, on the other hand, showed significant relationships with higher levels of CFS and depression scores. There was also a positive association between CFS and depression.

Ethical approval

The ethical code was obtained from the Ethics Committee of the Guilan University of Medical Sciences (IR.GUMS.REC.1399.077). All participants signed an informed consent form before entering the study.

Competing interests

The authors declare no conflict of interest.

Authors' Contributions

All authors contributed to the design of the study, conceptualization, investigation, data interpretation, and final approval of the manuscript. Elaheh Abdollahi, Robabeh Soleimani, and Fatemeh Eslamdoust prepared the manuscript, which was approved by all authors. Hamed Taherzadeh performed data collection, and Fatemeh Eslamdoust analyzed the data.

Acknowledgments

The authors would appreciate all students who participated in this study.

References

1. Lim EJ, Ahn YC, Jang ES, Lee SW, Lee SH, Son CG. Systematic review and meta-analysis of the prevalence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). *J Transl Med.* 2020;18(1):100. doi: 10.1186/s12967-020-02269-0.
2. Johnston S, Brenu EW, Staines D, Marshall-Gradisnik S. The prevalence of chronic fatigue syndrome/ myalgic encephalomyelitis: a meta-analysis. *Clin Epidemiol.* 2013;5:105-10. doi: 10.2147/clep.s39876.
3. Committee on the Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Board on the Health of Select Populations; Institute of Medicine. The National Academies Collection: Reports funded by National Institutes of Health. *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness.* Washington, DC: National Academies Press (U.S.); 2015.
4. Rowe PC, Underhill RA, Friedman KJ, Gurwitt A, Medow MS, Schwartz MS, et al. Myalgic encephalomyelitis/chronic fatigue syndrome diagnosis and management in young people: a primer. *Front Pediatr.* 2017;5:121. doi: 10.3389/fped.2017.00121.
5. Słomko J, Newton JL, Kujawski S, Tafil-Klawe M, Klawe J, Staines D, et al. Prevalence and characteristics of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in Poland: a cross-sectional study. *BMJ Open.* 2019;9(3):e023955. doi: 10.1136/bmjopen-2018-023955.
6. World Health Organization (WHO). *Depression and Other Common Mental Disorders: Global Health Estimates.* WHO; 2017.
7. Lim GY, Tam WW, Lu Y, Ho CS, Zhang MW, Ho RC. Prevalence of depression in the community from 30 countries between 1994 and 2014. *Sci Rep.* 2018;8(1):2861. doi: 10.1038/s41598-018-21243-x.
8. Noorbala AA, Faghihzadeh S, Kamali K, Bagheri Yazdi SA, Hajebi A, Mousavi MT, et al. Mental health survey of the Iranian adult population in 2015. *Arch Iran Med.* 2017;20(3):128-34.
9. Gustavson K, Knudsen AK, Nesvåg R, Knudsen GP, Vollset SE, Reichborn-Kjennerud T. Prevalence and stability of mental disorders among young adults: findings from a longitudinal study. *BMC Psychiatry.* 2018;18(1):65. doi: 10.1186/s12888-018-1647-5.
10. Weinberger AH, Gbedemah M, Martinez AM, Nash D, Galea S, Goodwin RD. Trends in depression prevalence in the USA from 2005 to 2015: widening disparities in vulnerable groups. *Psychol Med.* 2018;48(8):1308-15. doi: 10.1017/

- s0033291717002781.
11. Tessema TT, Gebremariam TA, Abebe EA, Gebre RD. The prevalence and factors associated with mental distress among college students in Southern Ethiopia: a cross-sectional study. *Ethiop J Health Sci.* 2019;29(3):353-60. doi: 10.4314/ejhs.v29i3.7.
 12. Pedrelli P, Nyer M, Yeung A, Zulauf C, Wilens T. College students: mental health problems and treatment considerations. *Acad Psychiatry.* 2015;39(5):503-11. doi: 10.1007/s40596-014-0205-9.
 13. Blanco C, Okuda M, Wright C, Hasin DS, Grant BF, Liu SM, et al. Mental health of college students and their non-college-attending peers: results from the National Epidemiologic Study on Alcohol and Related Conditions. *Arch Gen Psychiatry.* 2008;65(12):1429-37. doi: 10.1001/archpsyc.65.12.1429.
 14. McLafferty M, Lapsley CR, Ennis E, Armour C, Murphy S, Bunting BP, et al. Mental health, behavioural problems and treatment seeking among students commencing university in Northern Ireland. *PLoS One.* 2017;12(12):e0188785. doi: 10.1371/journal.pone.0188785.
 15. Zeng W, Chen R, Wang X, Zhang Q, Deng W. Prevalence of mental health problems among medical students in China: A meta-analysis. *Medicine (Baltimore).* 2019;98(18):e15337. doi: 10.1097/md.00000000000015337.
 16. Beiter R, Nash R, McCrady M, Rhoades D, Linscomb M, Clarahan M, et al. The prevalence and correlates of depression, anxiety, and stress in a sample of college students. *J Affect Disord.* 2015;173:90-6. doi: 10.1016/j.jad.2014.10.054.
 17. Bacchi S, Licinio J. Qualitative literature review of the prevalence of depression in medical students compared to students in non-medical degrees. *Acad Psychiatry.* 2015;39(3):293-9. doi: 10.1007/s40596-014-0241-5.
 18. Honney K, Buszewicz M, Coppola W, Griffin M. Comparison of levels of depression in medical and non-medical students. *Clin Teach.* 2010;7(3):180-4. doi: 10.1111/j.1743-498X.2010.00384.x.
 19. Puthran R, Zhang MW, Tam WW, Ho RC. Prevalence of depression amongst medical students: a meta-analysis. *Med Educ.* 2016;50(4):456-68. doi: 10.1111/medu.12962.
 20. Alkot MM, Alnewirah AY, Bagasi AT, Alshehri AA, Bawazeer NA. Depression among medical versus non-medical students in Umm Al-Qura University, Makkah al-Mukaramah, Saudi Arabia. *Am J Psychiatry Neurosci.* 2017;5(1):1-5. doi: 10.11648/j.ajpn.20170501.11.
 21. Afkhamzadeh A, Rahmani K, Mojahed A, Molsaqi S. Prevalence of depression and its relation to risky behaviors in students of Kurdistan University of Medical Sciences, Iran, 2014. *Chronic Dis J.* 2018;6(3):136-42. doi: 10.22122/cdj.v6i3.285.
 22. Rotenstein LS, Ramos MA, Torre M, Segal JB, Peluso MJ, Guille C, et al. Prevalence of depression, depressive symptoms, and suicidal ideation among medical students: a systematic review and meta-analysis. *JAMA.* 2016;316(21):2214-36. doi: 10.1001/jama.2016.17324.
 23. Mao Y, Zhang N, Liu J, Zhu B, He R, Wang X. A systematic review of depression and anxiety in medical students in China. *BMC Med Educ.* 2019;19(1):327. doi: 10.1186/s12909-019-1744-2.
 24. Brenneisen Mayer F, Souza Santos I, Silveira PS, Itaquí Lopes MH, de Souza AR, Campos EP, et al. Factors associated to depression and anxiety in medical students: a multicenter study. *BMC Med Educ.* 2016;16(1):282. doi: 10.1186/s12909-016-0791-1.
 25. Fawzy M, Hamed SA. Prevalence of psychological stress, depression and anxiety among medical students in Egypt. *Psychiatry Res.* 2017;255:186-94. doi: 10.1016/j.psychres.2017.05.027.
 26. Yang F, Meng H, Chen H, Xu XH, Liu Z, Luo A, et al. Influencing factors of mental health of medical students in China. *J Huazhong Univ Sci Technolog Med Sci.* 2014;34(3):443-9. doi: 10.1007/s11596-014-1298-9.
 27. Pokhrel NB, Khadayat R, Tulachan P. Depression, anxiety, and burnout among medical students and residents of a medical school in Nepal: a cross-sectional study. *BMC Psychiatry.* 2020;20(1):298. doi: 10.1186/s12888-020-02645-6.
 28. Tanaka M, Fukuda S, Mizuno K, Kuratsune H, Watanabe Y. Stress and coping styles are associated with severe fatigue in medical students. *Behav Med.* 2009;35(3):87-92. doi: 10.1080/08964280903231979.
 29. Uyar K, Gündoğan R, Gürbüz Ö, Özçakar N. Status of fatigue and sleep quality in clinical medical students. *Marmara Med J.* 2016;29(3):164-9. doi: 10.5472/MMJoa.2903.05.
 30. Corwin EJ, Klein LC, Rickelman K. Predictors of fatigue in healthy young adults: moderating effects of cigarette smoking and gender. *Biol Res Nurs.* 2002;3(4):222-33. doi: 10.1177/109980040200300407.
 31. Pourmovahed Z, Yassini Ardekani S, Kalani Z, Alaghband M. The relationship between fatigue and depression in the students of Shahid Sadoughi University of Medical Sciences in Yazd 2014. *Community Health Journal.* 2017;9(3):63-73. [Persian].
 32. Mihăilescu AI, Diaconescu LV, Ciobanu AM, Donisan T, Mihailescu C. The impact of anxiety and depression on academic performance in undergraduate medical students. *Eur Psychiatry.* 2016;33(Suppl 1):S284. doi: 10.1016/j.eurpsy.2016.01.761.
 33. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. *J Psychosom Res.* 1993;37(2):147-53. doi: 10.1016/0022-3999(93)90081-p.
 34. Nasri S. Epidemiological Study of Chronic Fatigue Syndrome and its Relation to Psychiatric Difficulties in Nurses. *Iran J Psychiatry Clin Psychol.* 2004;9(4):25-33. [Persian].
 35. Wang YP, Gorenstein C. Psychometric properties of the Beck Depression Inventory-II: a comprehensive review. *Braz J Psychiatry.* 2013;35(4):416-31. doi: 10.1590/1516-4446-2012-1048.
 36. Ghassemzadeh H, Mojtabai R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory--Second edition: BDI-II-PERSIAN. *Depress Anxiety.* 2005;21(4):185-92. doi: 10.1002/da.20070.
 37. Abedini S, Davachi A, Sahbaei F, Mahmoudi M, Safa O. Depression in medical and nursing students, Bandar Abbas. *Hormozgan Med J.* 2007;11(2):139-45. [Persian].
 38. Lee KP, Yeung N, Wong C, Yip B, Luk LHF, Wong S. Prevalence of medical students' burnout and its associated demographics and lifestyle factors in Hong Kong. *PLoS One.* 2020;15(7):e0235154. doi: 10.1371/journal.pone.0235154.
 39. Wolf MR, Rosenstock JB. Inadequate sleep and exercise associated with burnout and depression among medical students. *Acad Psychiatry.* 2017;41(2):174-9. doi: 10.1007/s40596-016-0526-y.
 40. Rezaei T, Yazdi-Ravandi S, Ghaleiha A, Seif Rabiei MA. Depression among medical students of Hamadan University of Medical Sciences in 2014: the role of demographic variables. *Pajouhan Scientific Journal.* 2015;13(4):1-8. [Persian].
 41. Rahmani Bidokhti N, Sadeghi Khorashad M, Bijari B. Comparison of depression prevalence in medical students between the first and last years of Birjand University of Medical Sciences: brief article. *J Birjand Univ Med Sci.* 2014;21(2):246-52. [Persian].
 42. Najafipour S, Yektatalab S. The prevalence depression and relationships with academic failure on students of Jahrom

- University Medical Sciences. *J Jahrom Univ Med Sci*. 2008;6(3):27-37. doi: 10.29252/jmj.6.3.4.27. [Persian].
43. Jackson ER, Shanafelt TD, Hasan O, Satele DV, Dyrbye LN. Burnout and alcohol abuse/dependence among U.S medical students. *Acad Med*. 2016;91(9):1251-6. doi: 10.1097/acm.0000000000001138.
 44. Esmaeelzadeh S, Moraros J, Thorpe L, Bird Y. The association between depression, anxiety and substance use among Canadian post-secondary students. *Neuropsychiatr Dis Treat*. 2018;14:3241-51. doi: 10.2147/ndt.s187419.
 45. Walters KS, Bulmer SM, Troiano PF, Obiaka U, Bonhomme R. Substance use, anxiety, and depressive symptoms among college students. *J Child Adolesc Subst Abuse*. 2018;27(2):103-11. doi: 10.1080/1067828X.2017.1420507.
 46. Güleç M, Bakir B, Ozer M, Uçar M, Kiliç S, Hasde M. Association between cigarette smoking and depressive symptoms among military medical students in Turkey. *Psychiatry Res*. 2005;134(3):281-6. doi: 10.1016/j.psychres.2003.02.001.
 47. Trostler M, Li Y, Plankey MW. Prevalence of binge drinking and associated co-factors among medical students in a U.S. Jesuit University. *Am J Drug Alcohol Abuse*. 2014;40(4):336-41. doi: 10.3109/00952990.2014.907302.
 48. Vorster A, Gerber AM, van der Merwe LJ, van Zyl S. Second and third-year medical students' self-reported alcohol and substance use, smoking habits and academic performance at a South African medical school. *Health SA*. 2019;24:1041. doi: 10.4102/hsag.v24i0.1041.
 49. Metzger IW, Blevins C, Calhoun CD, Ritchwood TD, Gilmore AK, Stewart R, et al. An examination of the impact of maladaptive coping on the association between stressor type and alcohol use in college. *J Am Coll Health*. 2017;65(8):534-41. doi: 10.1080/07448481.2017.1351445.
 50. Ayala EE, Roseman D, Winseman JS, Mason HRC. Prevalence, perceptions, and consequences of substance use in medical students. *Med Educ Online*. 2017;22(1):1392824. doi: 10.1080/10872981.2017.1392824.
 51. Dumitrascu CI, Mannes PZ, Gamble LJ, Selzer JA. Substance use among physicians and medical students. *Medical Student Research Journal*. 2014;3:26-35.
 52. Ershadi Kia B, Shajari A, Tayebi F, Yaghoobifar MA. Identifying the prevalence and contributing factors of depression in students of health and health-related schools of Sabzevar University of Medical Sciences in the academic year 2009-2010. *Beyhagh*. 2015;16(1):33-43. [Persian].
 53. Pacheco JPG, Silveira JB, Ferreira RPC, Lo K, Schneider JR, Giacomini HTA, et al. Gender inequality and depression among medical students: A global meta-regression analysis. *J Psychiatr Res*. 2019;111:36-43. doi: 10.1016/j.jpsychires.2019.01.013.
 54. Al-Alawi M, Al-Sinawi H, Al-Qubtan A, Al-Lawati J, Al-Habsi A, Al-Shuraiqi M, et al. Prevalence and determinants of burnout syndrome and depression among medical students at Sultan Qaboos University: a cross-sectional analytical study from Oman. *Arch Environ Occup Health*. 2019;74(3):130-9. doi: 10.1080/19338244.2017.1400941.