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RESEARCH ARTICLE

Prevalence of Hypochondriasis and its Association with Stress, Anxiety, and Depression caused by the Prevalence of COVID-19 among Pregnant Women Visiting Comprehensive Health Service Centers

Jalal Kavoosi¹, Kiavash Hushmandi², Sara Orouei³ and Rasoul Raesi^{4,*}

Abstract:

Background:

Stress, anxiety, and depression caused by potential COVID-19 infection can contribute to the spread of hypochondriasis disorder.

Aim:

This study aimed to determine the prevalence of hypochondriasis and its association with stress, anxiety, and depression caused by COVID-19 prevalence among pregnant women seeking care at the comprehensive health service centers in Khaf.

Methods:

A descriptive-analytical cross-sectional study was conducted using the census method to collect data from pregnant women in the second half of 2021. A web-based questionnaire was employed to collect data, which were analyzed using the Pearson correlation coefficient, multiple regression, independent t-test, one-way analysis of variance, and Tukey post hoc. The level of significance was set to p <0.05.

Results:

In this study, 87 pregnant women visiting comprehensive health service centers in the city of Khaf and ranging in age from 21 to 38 were examined. Hypochondriasis was characterized by an average mean score of 41.13 ± 18.06 among the women examined. In addition, the mean scores for depression, anxiety, and stress were moderate, amounting to 16.94 ± 5.18 , 13.26 ± 4.37 , and 20.57 ± 6.03 , respectively. There was a positive and statistically significant correlation between hypochondriasis and depression (r = 0.65), anxiety (r = 0.41), and stress (r = 0.42) (p < 0.001).

Conclusion

Pregnant women should be screened for and offered psychological interventions if they exhibit signs of depression, stress, or anxiety due to COVID-19, given the positive correlation between these conditions and hypochondriasis.

Keywords: Hypochondriasis, Stress, Anxiety, Depression, COVID-19, Pregnant women.

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1. INTRODUCTION

Pneumonia caused by the late 2019 coronavirus has both posed a threat to physical health and caused confusion and uncertainty among the general public due to the ambiguities

observed in the virus's behavior [1]. Individuals with COVID-19 report experiencing severe emotional distress, including but not limited to stress, anxiety, depression, unresolved grief, and the emergence of post-traumatic stress-related complications. A problem of particular clinical and health importance is the excessive emotional distress associated with being threatened with infection due to the spread of the disease from relatives, concerns caused by the

¹Department of Community Health Nursing, Shiraz University of Medical Sciences, Shiraz, Iran

²Department of Food Hygiene and Quality Control, Division of Epidemiology & Zoonosis, Faculty of Veterinary Medicine, University of Tehran, Tehran. Iran

³Department of General Psychology, North Tehran Branch, Islamic Azad University, Tehran, Iran

⁴Department of Health Services Management, Mashhad University of Medical Sciences, Mashhad, Iran

^{*} Address correspondence to this author at the Department of Health Services Management, Mashhad University of Medical Sciences, Mashhad, Iran; Tel: +98 (915) 7105007; E-mail: raesi.br881@gmail.com

suspicion of being involved with the real infectious agent, and hypochondriasis [2].

Someone with hypochondriasis is convinced that they are sick despite being in good physical health. The patient believes he is afflicted with a serious illness despite his clinical and laboratory examinations revealing no signs of illness [3]. Hypochondriasis can be triggered by a serious illness or the death of a patient's relative or by a childhood physical illness that has improved but left the individual in a state of hypochondriasis [4]. In an individual with hypochondriasis disease, natural bodily functions, such as sweating, bowel movement, and fluctuations in heart rate, can be perceived as signs of a serious illness. Minor abnormalities like a simple sore throat, mild swelling of a lymph node, or a runny nose are also considered significant issues [5, 6].

The prevalence of hypochondriasis in the general Canadian population was investigated by Looper (2001), who examined the people's social, medical, psychiatric, health, and disability characteristics. The prevalence of hypochondriasis in the general population of Canada was estimated to be between 1% and 2% [7]. In another study, Barsky *et al.* examined the prevalence of hypochondriasis in 136 patients, estimating that the prevalence was between 4.2% and 6.3%, which was lower than the general anxiety disorder rate [8].

Stress, persistent depression, anxiety, panic attacks, and even self-harm have been reported as early psychiatric symptoms of the COVID-19 outbreak. Furthermore, those who have been infected with the virus or had loved ones infected or suspected they were infected have reported higher levels of depression [9]. The results of a study by Karakose *et al.* (2021) reported a positive and significant relationship between the phobia of COVID-19 and the levels of work-family conflict, family-work, and psychological-social health dimensions of people [10]. Therefore, mental health support should be regarded as one of the essentials of health care for COVID-19 patients and those at risk, as well as pregnant women [11].

Pregnancy is an integral phase of a woman's life. This period is a pleasant time for women, although it may lead to a dire situation in certain cases. Women are more susceptible to mental disorders, such as stress, anxiety, and depression during pregnancy. In the course of pregnancy, women undergo physiological, psychological, and social changes. Depression, stress, and anxiety are among the most prevalent health issues in expectant women [12]. Fear and anxiety caused by a potential infection of COVID-19 are psychologically destructive factors that can lead to mental and psychological disorders and stress in the community [13].

The results of a study by Huang *et al.* (2022) showed that, in addition to causing physical damage, COVID-19 is also associated with causing a serious impact on mental health [14]. Therefore, these problems can lead to more prevalence of mental health disorders in societies and affect vulnerable groups, such as pregnant women [15, 16]. A review of studies indicates that increased feelings of loneliness, reduced social support, decreased life expectancy, fear and worry in response to stress, depression and clinical anxiety, and obsessive-compulsive obsessions associated with the disease can be

symptoms of serious clinical disorders [17, 18]. Other studies have reported that the COVID-19 pandemic can cause new psychiatric symptoms in individuals without a history of mental illness [19].

The COVID-19 pandemic quickly put the mental health of the world's people at risk. Due to the unknown nature of the coronavirus and also the existence of anxiety, stress, and depression as common symptoms, it can provide the ground for the occurrence of hypochondriasis disorders in different populations (especially for people at risk, such as pregnant women). Also, the disorder of hypochondriasis can make people more vulnerable to contagious diseases, including COVID-19 [20]. Studies conducted during the COVID-19 pandemic in the field of hypochondriasis involved providers of health services and medical students. This was during the time when the coronavirus pandemic put the mental and physical health of all the people in the society at risk.

To better diagnose these problems and provide targeted psychological interventions to improve mental health, professionals need an understanding of the mental state of those exposed to psychological disorders, such as pregnant women. Moreover, human societies will never be immune from similar diseases and pandemics. Therefore, the results of this research can help prepare society for the future to deal with and manage mental problems in similar diseases and pandemics. There has not been any research done to date on the correlation between hypochondriasis and the stress, anxiety, and depression experienced by pregnant women due to the spread of COVID-19. This study aims to determine the prevalence of hypochondriasis and its association with the stress, anxiety, and depression caused by the spread of COVID-19 among pregnant women referring to comprehensive health service centers in Khaf.

2. METHODOLOGY

This descriptive-analytical cross-sectional study aimed to determine the prevalence of hypochondriasis and its relationship with stress, anxiety, and depression among pregnant women during the second half of 2021. The statistical population consisted of pregnant women who sought care at comprehensive health service centers in Khaf.

There are three comprehensive health service centers in Khaf (comprehensive health service center number one, two, and three), and each of these three centers was selected as a cluster for sampling. Then, one of the clusters was selected as the research environment by simple random technique (Comprehensive Health Service Center number three). The total number of pregnant women covered by comprehensive health service center number three was 110. These people had health records and also had regular referrals for health services. Finally, using Cochran's formula for determining the sample size, taking into account the error level of 5%, 87 people were obtained as the final sample size, which was selected and studied using the available sampling method.

The following describes the data collection procedure: researchers visited each of the city's comprehensive health service centers and shared the study's goals with the healthcare personnel at the centers. When pregnant women visited to

receive services, healthcare providers were instructed to explain the objectives of the study and provide them with a link to the electronic questionnaire *via* SMS or WhatsApp if they met the criteria for participation in the study.

Inclusion criteria comprised access to a smartphone to receive the link to the electronic questionnaires, absence of chronic disease and pregnancy complications in the mother, informed consent to participate in the study, and absence of a history of mental illness. The absence of a definitive diagnosis of neurological and mental illnesses by a specialist doctor, as well as the non-use of drugs related to neurological and mental illnesses, were used to confirm the absence of a history of mental illness. The exclusion criterion included unwillingness to continue participating in the study.

The inability of some mothers to participate in the study due to a lack of access to smartphones or the Internet or to receive the electronic questionnaire was a significant barrier to collecting data. Regarding this issue, healthcare providers were requested to complete and register the electronic form for each mother individually by asking her about the questionnaire items. The researcher responded to all potential questions posed by pregnant women throughout the data collection process.

In order to collect data, a questionnaire was created on the Press Line website, and the link to the questionnaire was sent *via* WhatsApp and SMS to the participants. This online questionnaire contained three sections. The first section focused on demographic variables (age, occupation, number of children, trimester of pregnancy, level of education, family income, number of previous pregnancies, history of depression, history of depression in the family, history of abortion, intendedness of pregnancy, and history of COVID-19 infliction in relatives). The second section dealt with the Evans Hypochondriasis Questionnaire, whereas the third section concerned the Depression-Anxiety-Stress Scale (DASS-21).

The Evans Hypochondriasis Questionnaire consists of 36 multiple-choice questions, each with 5 options and, in some cases, 2 possible answers, yielding a total score from 0 to 60. The score 0-20 represents a person's health, the score 21-30 reflects borderline, the score 31-40 indicates mild hypochondriasis, the score 41-50 represents moderate hypochondriasis, and the score above 50 reflects severe hypochondriasis [21]. In previous studies, the content validity method and the calculation of Cronbach's alpha confirmed the validity and reliability of the questionnaire, respectively [22].

The DASS consists of 21 questions that measure anxiety (seven questions), depression (seven questions), and stress (seven questions), and is graded on a five-point Likert scale graded from zero to four (never = 0, almost never = 1, sometimes = 2, often = 3, and frequently = 4). The possible total score range is between 0 and 21. The DASS scores for anxiety, stress, and depression are classified into five categories (normal, mild, moderate, severe, and very severe) based on the scores obtained. The higher the score, the more severe the psychological disorder and the worse the mental health status. Sahebi *et al.* validated the DASS-21 for the

Iranian population [23].

The Evans Hypochondriasis Questionnaire was selected because it aligned with the objectives of the study, while the DASS scale was utilized because it had been employed in a previous, similar study [24]. It has been used to assess anxiety, depression, and stress in COVID-19 and is consistent with the objectives of this study.

Data were analyzed using SPSS-22 statistical software. First, the normal distribution of the data was checked using skewness and kurtosis coefficients, and according to the normal distribution of the data, appropriate statistical tests were used. Pearson's correlation coefficient test was used to investigate the relationship between variables, such as age, number of children, number of pregnancies, depression, anxiety, and stress with hypochondriasis. Multiple regression test was used to predict hypochondriasis based on depression, anxiety, and stress variables. The independent t-test was used to compare the mean of hypochondriasis according to the variables of education level, history of abortion, history of unwanted pregnancy, history of depression, family history of depression, and history of people close to COVID-19. One-way analysis of variance and Tukey's post hoc test were used to compare the mean of hypochondriasis according to job variables, monthly income level, and trimester of pregnancy. A significance level of 0.05 was considered.

3. RESULTS

The present research involved the examination of 87% of women who were referred to comprehensive health service centers in Khaf. The age range of the participants was between 21 to 38 years, with an average age of 28.69±4.62 years. The data indicated that the group with the highest frequency consisted of women who had attained a high school diploma or lower level of education (52.9%), individuals who identified as housewives (37.9%), and those with a monthly income ranging from 5-10 million tomans (51.7%). Nearly half of the women under investigation were found to be in their second trimester of pregnancy, accounting for 49.4% of the sample. The prevalence of abortion among the women under study was 14.9%, as was the incidence rate of unwanted pregnancy. The incidence rates of depression in the individual and family were noted to be 3.4% and 8%, respectively. Moreover, a significant proportion of the participants reported that their relatives had been inflicted with COVID-19, with a prevalence of 37.9% (Table 1).

The results indicated that the mean hypochondriasis score among the respondents did not differ significantly by level of education (p = 0.26). Still, it was significantly higher among healthcare personnel and those with a monthly income of less than 5 million tomans (p <0.01). It was found in a study that individuals with a history of abortion, unwanted pregnancy, depression, family history of depression, and COVID-19 in relatives, as well as those in their third trimester of pregnancy, had significantly higher mean scores of hypochondriasis compared to other individuals in the study (p <0.05). The study revealed a statistically significant and positive correlation between hypochondriasis and variables, such as age, number of children, and number of pregnancies (p <0.001).

Table 1. Distribution of pregnant women visiting comprehensive health service centers in Khaf in 2021 based on demographic characteristics and hypochondriasis score.

Variable	Frequency	Hypochondriasis	Danalara	
variable			Mean±SD	P-value
Education level	High diploma and lower university degree	46 (52.9) 41 (47.1)	43.22±15.15 38.78±20.80	0.26*
Occupation	Healthcare personnel Non-health care personnel Homemaker Self-employed	13 (14.9) 25 (28.7) 33 (37.9) 16 (18.4)	55.15±17.81 34.64±20.39 41.24±14.89 39.63±15.34	0.009**
Monthly income level (million tomans)	< 5 5-10 > 10	16 (18.4) 45 (51.7) 26 (29.9)	54.56±14.25 40.20±16.04 34.46±19.60	0.001**
Pregnancy trimester	1 st 2 nd 3 rd	23 (26.4) 43 (49.4) 21 (24.1)	23.43±4.75 41.53±15.21 59.67±13.07	<0.001**
History of abortion	No Yes	74 (85.1) 13 (14.9)	37.41±16.11 62.31±13.70	<0.001*
History of unwanted pregnancy	No Yes	74 (85.1) 13 (14.9)	38.20±16.81 57.77±16.32	<0.001*
History of depression	No Yes	84 (96.6) 3 (3.4)	40.17±17.51 70.00±3.46	0.004*
Family history of depression	No Yes	80 (92) 7 (8)	39.90±17.40 55.14±20.99	0.03*
History of COVID-19 infliction in relatives	No Yes	54 (62.1) 33 (37.9)	35.63±15.71 50.12±18.26	<0.001*
Age	Mean±SD	28.69±4.62	r=0.77	<0.001***
Number of children	Mean±SD	1.38±0.93	r=0.74	<0.001***
Pregnancy times	Mean±SD	2.83±1.10	r=0.74	<0.001***

Note: *: independent t **: one-way analysis of variance ***: Pearson's correlation coefficient.

Table 2. Descriptive indicators of research variables in pregnant women visiting comprehensive health service centers in Khaf in 2021.

Variable	Mean	Standard Deviation	Skewness	Kurtosis	Level
Hypochondriasis	41.13	18.06	0.42	-1.36	Moderate (41-60)
Depression	16.94	5.18	-0.26	-0.76	Moderate (14-20)
Anxiety	13.26	4.37	0.44	-0.06	Moderate (10-14)
Stress	20.57	6.03	0.47	0.69	Moderate (19-25)

Table 3. Regression coefficients related to the effect of depression, anxiety, and stress on hypochondriasis in pregnant women visiting comprehensive health service centers in Khaf in 2021.

Variable	Non-standard Coefficient		Standard Coefficient	T value Significanc	Significance	Correlation and	Coefficient of	
	B value	Standard Error	β value		Level	Dependence	Determination	
Constant	-11.71	6.43	-	1.82	0.07	0.70	0.47	
Depression	1.78	0.31	0.51	5.83	< 0.001			
Stress	0.63	0.25	0.21	2.53	0.01			
Anxiety	0.73	0.35	0.18	2.07	0.04			

Based on the obtained results, hypochondriasis was characterized by the average mean score of 41.13 ± 18.06 among the women examined. In addition, the mean scores for depression, anxiety, and stress were moderate, amounting to 16.94 ± 5.18 , 13.26 ± 4.37 , and 20.57 ± 6.03 , respectively. Based on the information presented in Table 2, it can be inferred that the research variables exhibited a normal distribution, as

evidenced by the coefficients of skewness and kurtosis falling within the range of -2-2.

Depression (r = 0.65), anxiety (r = 0.41), and stress (r = 0.42) were positively and significantly correlated with hypochondriasis in the women, as indicated by Pearson's correlation coefficient (p < 0.001). The present study employed a simultaneous multiple regression test to assess the degree to

which depression, anxiety, and stress variables could elucidate hypochondriasis in the female participants. The aforementioned test results indicated that the collective influence of depression, anxiety, and stress variables accounts for approximately 47% of the variance in hypochondriasis. Moreover, the results indicated that depression (β = 0.51) plays a larger role in explaining hypochondriasis in the women studied, followed by stress (β = 0.21) and anxiety (β = 0.18) (Table 3).

4. DISCUSSION

This study aimed to examine the prevalence of hypochondriasis among pregnant women seeking care at comprehensive health service centers in Khaf and explore its association with stress, anxiety, and depression induced by the COVID-19 pandemic. Hypochondriasis is a psychiatric condition characterized by an individual's persistent preoccupation with the belief that they are suffering from a severe medical condition despite the absence of any objective evidence of such an illness. The prevalence of hypochondriasis has surged significantly in light of the COVID-19 pandemic, affecting individuals who may not have previously exhibited symptoms of stress and anxiety.

This study involved the examination of 87 pregnant women who sought services at the comprehensive health centers located in Khaf during the second half of 2021. The present study collected data using the Evans Hypochondriasis Questionnaires and the DASS. The current investigation involved pregnant women within the age range of 21 to 38 years. Based on the collected data, the group with the greatest frequency consisted of females who had attained a high school diploma or lower educational qualifications (52.9%), individuals who identified as homemakers (37.9%), and those with a monthly income ranging from 5-10 million tomans (51.7%). The majority of the women under investigation were found to be in their second trimester of pregnancy, comprising 49.4% of the sample. Of the subjects under investigation, a proportion of 14.9% comprised expectant females employed within the healthcare industry.

The spread of COVID-19 is a contributing factor that can potentially elevate the levels of anxiety and stress experienced by expectant women [25]. Given the significant impact of maternal mental health on pregnancy outcomes, this study aimed to investigate the prevalence of hypochondriasis disorder among pregnant women as a potential strategy to enhance the mental well-being of pregnant women during the COVID-19 pandemic. This study's findings indicated no statistically significant variation in the incidence of hypochondriasis among the pregnant women examined based on their level of education. In line with this finding of the present study, the results of the study by Noghabi et al. (2014) demonstrated no significant relationship between the level of education and the prevalence of hypochondriasis [26]. However, in the study by Talaei et al. (2009), a significant relationship between the prevalence of hypochondriasis and the level of education was reported [22], which was inconsistent with the findings of the present study. This difference in the findings can be related to the different populations studied and also the different times examined in the studies.

The research conducted by Nasreen et al. (2011) involved the categorization of rural Bangladeshi mothers into two groups based on their literacy status. The study revealed a significant correlation between anxiety and literacy level, which aligned with the current investigation's outcomes [27]. The findings pertaining to employment and monthly income variables indicated a statistically significant increase in the prevalence of hypochondriasis among pregnant women employed in the healthcare sector and those with a monthly income below 5 million tomans. The incidence of this mental disorder in the occupational setting has been documented in various scholarly articles. This includes individuals with medical expertise, such as healthcare workers or medical students, who directly interact with patients. Approximately 3% of medical students have reported hypochondriasis, with onset typically occurring within the initial two years of their academic program. Nonetheless, it is worth noting that such complaints tend to be temporary [27].

The data acquired for other variables are presented below. In the sample of women analyzed, 14.9 percent had an abortion, 14.9 percent had an unwanted pregnancy, 3.4% had a personal or family history of depression, and 8.9% had a history of COVID-19 infliction in relatives. The present study found a statistically significant difference in the mean hypochondriasis scores between three groups of pregnant women, namely those in their first trimester (n=23), second trimester (n=43), and third trimester (n=21). Specifically, the average hypochondriasis score of the third-trimester group was higher than that of the second and first-trimester groups. According to some researchers, there exists a belief that the degree of anxiety experienced by expectant mothers during the first trimester of pregnancy is elevated. This level of anxiety is purported to decrease during the second trimester, only to resurge and return to its initial level during the third trimester as the delivery date approaches [28].

In line with this finding of the present study, the results of the study by Savron and colleagues showed that in every trimester of pregnancy, women experience hypochondriacal fears and beliefs in disease (phobia of disease). They also reported that these hypochondriacal beliefs and illness beliefs reach their maximum in the third trimester, so hypochondriacal fears and beliefs may affect the well-being, mental health, and health attitudes of pregnant women [29]. Also, in line with this finding of the present study, the results of the study by Shayganfard et al. demonstrated that health anxiety, that is, the fear of being infected with COVID-19, increases during pregnancy and especially in the last stages of pregnancy, this health anxiety and hypochondriacal behaviors can be associated with postponing routine medical examinations and screenings [30].

Only 13 of the 87 individuals studied had a history of abortion, while the remaining individuals had no abortion history. The findings indicated a statistically significant correlation between the occurrence of one or more abortions and the incidence of hypochondriasis. Furthermore, within the scope of this study, it was found that 13 individuals had a prior experience of unintended pregnancy. The study found a notable correlation between the intendedness of pregnancy and the

incidence of hypochondriasis, with a higher prevalence of the condition observed among individuals who reported a history of unwanted pregnancy. The absence of a comparable study precludes the ability to make comparisons between the findings of this research and those of other studies. The present research finding suggests that the occurrence of unwanted pregnancy may be indicative of inadequate preparation for pregnancy. Moreover, it is plausible to argue that the absence of sufficient preparation for pregnancy during the COVID-19 pandemic may result in the development of hypochondriasis disorder.

The findings of the present study showed that individuals with a personal history of depression, a family history of depression, and a familial history of COVID-19 infection exhibited significantly higher rates of these hypochondriacal conditions compared to others. In line with this finding of the current research, the results of the study by Zheng et al. showed that depression is the most common psychological response among pregnant women during the COVID-19 epidemic, which can be one of the main reasons for hypochondriacal behaviors in pregnant women [31]. Psychological issues during pregnancy can result in significant outcomes, including premature delivery, complications during pregnancy and delivery, delayed fetal development, and postpartum depression [32]. Limited knowledge is available from various regions of Iran, particularly smaller cities, regarding mental health care during pregnancy [33]. According to the World Health Organization (2008), the occurrence of anxiety during pregnancy has been linked to various risk factors. These include teenage pregnancy, unwanted pregnancy, previous history of stillbirth or repeated abortion, being nulliparous, pregnancy due to sexual assault, weak and inappropriate relationships with family members, and the unmarried state or separation of women [34].

A statistically significant and positive correlation was observed between hypochondriasis and variables, such as age, number of children, and number of pregnancies. It appears that the older age of the respondents increases the chances of contracting COVID-19, causing them to suffer from hypochondriasis disorder. In line with this finding of the present study, the results of a study by Mousavi et al. reported that the rate of hypochondriasis caused by COVID-19 disease increases with increasing age [35]. Also, the results of a study by Akhavan et al. showed that hypochondriasis increases with increasing age, and this increase in hypochondriasis is caused by increasing depression, anxiety, and fear of illness and death [36]. In contrast to the finding above, Fallon et al. did not yield a statistically significant correlation between hypochondriasis and age [37]. The potential explanation for the observed incongruity could be attributed to variations in sample size, distinct statistical populations, and the non-existence of the COVID-19 outbreak during their study.

CONCLUSION

This research was conducted to determine the prevalence of hypochondriasis and its relationship with the state of stress, anxiety, and depression caused by the spread of COVID-19 among pregnant women. The results showed that the prevalence of depression, stress, and anxiety caused by

COVID-19 has a positive and significant relationship with hypochondriasis disorder. Amidst the COVID-19 pandemic, there has been a noticeable decline in the mental well-being of individuals, with one of the consequential outcomes being the onset of hypochondriasis. This study revealed a moderate prevalence of the disorder in question compared to global studies. Hence, in the present scenario of elevated risk, it appears imperative to recognize individuals susceptible to psychological ailments so as to uphold their mental well-being through suitable measures, such as psychological therapies. However, further research should be conducted in larger communities, given the limitations of access to pregnant women and the significance of promoting the health of pregnant women.

LIMITATIONS OF THE STUDY

The study was subject to certain limitations, including a small sample size, uncertainty regarding the accuracy of respondents, psychological factors related to pregnancy during the COVID-19 pandemic, and personality differences. These limitations may have impacted the research findings. It is important to acknowledge that the researcher was unable to exercise control over all limitations. Among the study's other limitations was that a portion of the sample population lacked access to smartphones; for these individuals, the healthcare personnel completed the questionnaire as they received health services.

Given that the scope of this study was limited to a single urban area, it is advisable to exercise prudence when attempting to extrapolate the findings to other contexts. It is recommended that further investigations be conducted through the design of interventional and qualitative studies in various research environments and with larger statistical populations.

AUTHORS' CONTRIBUTION

KH and RR devised the main concept and took part in sampling. JJ and SS analysed the data and wrote the first draft. RR wrote the final draft.

ABBREVIATION

DASS-21 = Depression-Anxiety-Stress Scale

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Biomedical Research Ethics Committee of Mashhad University of Medical Sciences by issuing the code of ethics (IR.MUMS.REC.1400.118).

HUMAN AND ANIMAL RIGHTS

No animals were used in the studies that are the basis of this research. All human procedures followed were per the guidelines of the Helsinki Declaration of 1975.

CONSENT FOR PUBLICATION

Informed consent was obtained from the participants of this study.

STANDARDS OF REPORTING

STROBE guideline has been followed.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author [R.R] upon reasonable request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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