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Original Article

Evaluation of substance abuse and cigarette smoking in patients with COVID-19 and non-COVID-19 disease in Kashan-Iran

Amir Ghaderi[1]; Zahra Pilevar[2]; Zahra Rasoolian[2]; Shaghayegh Keyvandarian[2]; Kiomars Cheraghi[2]; Mohammd-JavadAzadchehr[3]; Fateme Padoei[2]; Peyman Mamsharifi[4]; Bahador Nemati[2]; Heshmatollah Moradpour Ghalerashidi[2]; Mohammad Hadi Farahzadi[5]; Hamid Reza Banafshe[1,6]; *Peyman Esmaili-Shahzade-Ali-Akbari[2,7]

[1]Department of Addiction Studies, School of Medical and Clinical Research Development Unit-Matini/Kargarnejad Hospital, Kashan University of Medical Sciences, Kashan, Iran.
[2]Student Research Committee, Kashan University of Medical Sciences, Kashan, Iran.
[3]Infectious Diseases Research Center, Kashan University of Medical Sciences, Kashan, Iran.
[4]Department of Psychology, Allameh Tabataba'i University, Tehran, Iran.
[5]Research Center of Addiction and Behavioral Sciences, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[6]Department of Pharmacology, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran.
[7]Department of Addiction Studies, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran.

Abstract

Introduction: Coronavirus is one of the biggest health problems in the world. The studies show that smokers or addicts are more vulnerable to the virus. The present study evaluated the frequency of smoking and substance abuse among patients with COVID-19 and other patients.

Materials and Methods: In this cross-sectional study in 2021, 1400 participants (Kashan, Iran) were included (700 patients in COVID-19 group and 700 people in non-COVID-19 group). Then, they fulfilled the Addiction Diagnosis Questionnaire (ASSIST), and their addiction was tested with a diagnostic kit. The data were analyzed through independent t-test, Chi-square, Fisher's exact test, and SPSS v.17.

Results: The prevalence of smoking and substance abuse in the COVID-19 group was 19.4% and 4.4%, respectively (23.0% and 9.2% in non-COVID-19 group, respectively). No significant differences in smoking frequency were observed between the two groups (P= 0.229). The results showed that the frequency of substance abusers was significantly lower in the COVID-19 group (P= 0.008).

Conclusion: The present results showed that the prevalence of smoking among patients with COVID-19 is not significantly different from other patients. Interestingly, the prevalence of substance abuse among participants with COVID-19 was significantly lower than other patients. Since the number of smokers or substance abusers was expected to be higher among patients with COVID-19, the cause of this paradox is unclear, and more studies are needed to clarify its various dimensions.

Keywords: Addiction, COVID-19, Smoking

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***Corresponding Author:**
Department of Addiction Studies, School of Medicine, Kashan University of Medical Sciences, Kashan, Iran.
peyman.esmaely@gmail.com
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Introduction

Coronaviruses are a large family of viruses that include the common cold virus to the causative agent of Severe Acute Respiratory Syndrome (SARS) (1). The virus now affects many people worldwide and, with high morbidity and significant mortality, is the world's biggest and most important health, political, and social challenge (2). The most common clinical symptoms are fever, fatigue, and having dry coughs. Some patients may complain from pain, nasal congestion, nasal discharge, sore throat, or diarrhea. These symptoms usually begin mild and start gradually (3). Some people become infected but have no symptoms and do not feel unwell. According to statistics, 1 out of every six infected people is seriously ill and has trouble breathing (4). Older people, substance users, and those treated with corticosteroids and chemotherapy are more vulnerable to COVID-19. About 2% of patients with this disease have died, unfortunately, often due to a weakened immune system (5).

COVID-19 virus attacks the lungs and respiratory system. Smoking, tobacco, opium, marijuana, alcohol, and other opiates and stimulants can increase the risk of coronavirus (6). Evidence has shown that methamphetamine can damage lung tissue and cause pulmonary hypertension. Therefore, experts warn of the possibility of worse consequences of COVID-19 among methamphetamine users (7). Alcohol consumption can lead to similar risks (8). Excessive opioid use can cause respiratory depression and hypoxemia and contribute to the worsening of the outcome of COVID-19 disease and the development of neurological and cardiopulmonary complications (9). Also, some evidence cites smoking as an indicator of poor prognosis associated with COVID-19 (10,11). Besides the damage smoking does to heart and lung health, the risk factor linked to COVID-19 is the expression of type-2 angiotensin-converting enzyme (ACE2) in smokers (12,13). Thus, there may be a link between the nicotinic pathway and increased virion entry due to overexpression of ACE-2 (potential SARS-CoV2 receptor) (12-15).

Although brief studies on the association of smoking and substance use with coronavirus infection since the onset of the coronavirus epidemic in the world have pointed to the destructive role of these substances, in most studies, the results have not been of statistical value (10). Therefore, due to the mortality rate in Iran and new mutations in this virus, information about the risks of this virus, especially in patients with a history of addiction, is still scarce. On the other hand, suffering from various diseases due to substance use increases the risk of developing COVID-19 and facing more serious psychological, social, and environmental complications. Therefore, the relationship between the mortality rate of the COVID-19 virus and the history of drug use cannot be ignored. The current study was designed to evaluate the status of smoking and substance use among patients with coronavirus infection and other patients in Kashan city-Iran.

Materials and Methods

In this cross-sectional study, 1400 (700 people in the COVID-19 group and 700 people in non-COVID-19 group) participants over 18 years old who were referred to Shahid Beheshti Hospital in Kashan- Iran were selected through simple random sampling method. We used the Cochran's formula to determine the sample size, calculated by considering 5% substance use in the normal population and a 4% difference with the patients. The required sample size for each group was 642 people. Due to possible dropout, 700 samples in each group were finally examined. Randomization was done using a regular (systematic) sampling method (K=N/n). Inclusion criteria were over 18 years of age, confirmation of COVID-19, and consent to participate in the study. Exclusion criteria were having underlying diseases (such as cardiovascular disease, diabetes, and hypertension), unwillingness to participate in the study, patients suspected of having COVID-19, and adverse health conditions to answer the questions. To confirm the lack of history of underlying diseases, the self-report method and the health information system of Kashan University of Medical Sciences were used. None of the participants had been vaccinated against COVID-19 (general vaccination was not carried out during the study period).

After receiving approval from the ethics committee of Kashan University of Medical Sciences (IR.KAUMS.MEDNT.REC.1399.228), the names and information of patients with definitive infection with COVID-19 (PCR test

and CT scan, March-August 2021) were extracted through the university Health Information System (HIS). After contacting the patients with the study description and receiving written consent to enter the study through a questionnaire, demographic information (gender, age, educational status, and employment status) was received. Then, the ASSIST (Alcohol, Smoking, and Substance Involvement Screening Test) was completed, and they were tested for addiction through a diagnostic kit. Finally, the information related to the frequency and duration of substance and cigarette consumption and the type of substance used were received and recorded. The control group included patients with a diagnosis other than COVID-19 infection who are randomly selected.

At the beginning of the session, the purpose of the study was explained to the patients, and they were assured about the anonymity and confidentiality of their responses. All patients signed the written informed consent forms.

Research instrument

A) Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST): It was developed by the World Health Organization and examined the use of various substances over the past three months, one year, and more than one year. ASSIST is relatively brief and has eight questions (or items) that include ten substances (tobacco, alcohol, cannabis, cocaine, Amphetamine-Type Stimulants (ATS), inhalants, sedatives, hallucinogens, opioids, and other substances). ASSIST examines the frequency of use of each substance and the problems associated with it (16). The different studies have been confirmed the validity and reliability of this instrument in different countries. Humeniuk et al. showed that ASSIST is a valid screening test for psychotropic substances (Cronbach's alpha= 0.89) (16). Hooshyari et al. also showed that ASSIST is valid and reliable in Iranian society (Cronbach's alpha= 0.68-0.93) (17).

We assessed the normality of data by the Shapiro-Wilk test, and all data had a normal distribution. In this study, quantitative data (age) were analyzed by independent t-test, and qualitative data were analyzed by independent t-test, Chi-square, and Fisher's exact test and SPSS version 17.

Results

In this study, 1400 patients were participated. Finally, the data of 880 cases were confirmed (432 COVID-19 patients and 448 other patients). Four hundred fifty-eight participants were male (422 were female). The mean age of participants was 43.99 ±16.13 years in COVID-19 group and 44.70±17.83 years in other patients. The educational level and professional status in two groups were not different significantly (*P*= 0.08 and *P*= 0.60, respectively) (Table 1).

Table 1. Demographic information of the participants

Variable		COVID-19 group	Non-COVID-19 group	P
Gender; N (%)	Male	238 (55.1%)	220 (49.1%)	0.087*
	Female	194 (44.9%)	228 (50.9%)	
Age (Year)		43.99±16.13	44.70±17.83	0.537**
Education; N (%)	Illiterate	24 (5.6%)	41 (9.2%)	0.080*
	Under diploma	143 (33.3%)	122 (27.2%)	
	Diploma	87 (20.3%)	98 (21.9%)	
	Higher education	175 (40.8%)	187 (41.7%)	
Having a job; N (%)		237 (55%)	249 (57%)	0.601*

P< 0.05. *Chi-squared test/ **Independent t-test

Among the participants, 84 (19.4%) in the COVID-19 group and 103 (23%) in the other patients had a smoking history. There was no significant difference between the two groups regarding the smoking frequency (*P*= 0.229). Regarding substance use, 19 (4.4%) people in the COVID-19 group and 41 (9.2%) people in other patients were substance users. In the COVID-19 group, the number of substance-using participants was significantly less (*P*= 0.008) than the number of substance-using participants in the group of other patients.

77.4% of smokers and 89.5% of substance users in the COVID-19 group have been using substances for more than a year. This rate was 85.4% and 97.6% in the group of other patients, respectively. The two groups were not different in terms of duration of substance use and smoking (Table 2).

Table 2. Frequency and duration of smoking and substance use of participants

Variable			COVID-19 group	Non-COVID-19 group	*P
Cigarette smoking (n (%))	Frequency of use		84 (19.4%)	103 (23%)	0.229
	Duration of use [a]	1≥ Years	19 (22.6%)	15 (14.6%)	0.219
		1< Years	65 (77.4%)	88 (85.4%)	
Substance use (n (%))	Frequency of use		19 (4.4%)	41 (9.2%)	0.008
	Duration of use [b]	1≥ Years	2 (10.5%)	1 (2.4%)	0.484
		1< Years	17 (89.5%)	40 (97.6%)	

a: n=84 in COVID-19 group and 103 in other patients, b: n=19 in COVID-19 group and 41 in other patients, $P< 0.05$. *Chi-squared test

The most abundant substances used in both groups were opium and its derivatives (52.6% in COVID-19 and 63.4% in other patients). 31% of substance users in the COVID-19 group and 24% in the other patients group used methadone.

The two groups was not different in frequency of types of substances (Table 3).

Table 3. Frequency of the type of drug used

Variable		COVID-19 group	Non-COVID-19 group	*P
Type of substance n (%) [a]	Naswar	0	3 (7.3%)	0.545
	Opium	8 (42.1%)	11 (26.8%)	0.376
	Opium syrup	2 (10.5%)	15 (36.6%)	0.076
	Heroin	1 (5.3%)	5 (12.2%)	0.654
	Codeine	1 (5.3%)	1 (2.4%)	0.537
	Tramadol	0	3 (7.3%)	0.545
	Crack cocaine	1 (5.3%)	1 (2.4%)	0.537
	Cannabis	6 (31.6%)	11 (26.8%)	0.796
	Cocaine	1 (5.3%)	4 (9.8%)	1.000
	Methadone	6 (31.6%)	10 (24.4%)	0.786
	Buprenorphine	1 (5.3%)	0	0.317
	Other substances	0	3 (7.3%)	0.545

a: study participants may have reported more than one type of substance, $P< 0.05$. *Chi-squared test or Fisher's exact test

Discussion

Coronavirus is one of the biggest health challenges in the world (2). Some factors, such as addiction, age, and the presence of the underlying disease, are known as risk factors for developing this disease (5,6). In this study, we examined the status of patients with COVID-19 and other patients regarding substance use and smoking.

The COVID-19 virus has had different mutations since it was identified as an epidemic, including alpha, beta, gamma, delta, and Omicron, which differ in the severity of the disease and the rate of transmission of this virus (18,19). According to the reports, the variants identified in Iran from March to August 2021 (the time of implementation of this study) include the alpha and delta variants (18). The results of studies suggest age is a risk factor for increased risk of developing COVID-19 (20). Interestingly, the results in Iran have shown that the highest prevalence of COVID-19 was in the age group of 50-59 years, and the lowest prevalence was in the age group of 0-9 years. Also, the highest death rate was in the age range of 70-79 years (21). Although the average age of the participants in this study was close to the age range that had the highest prevalence of COVID-19. The two groups was not different in the mean age. Therefore, age is not a confounding factor in this study. Also, although studies demonstrated the role of gender (female) in reducing the morbidity and mortality rate of COVID-19, there is no notable difference in the prevalence of COVID-19 between men and women (22). However, there was no significant difference in gender between two groups.

Previous studies have shown that smokers are generally more vulnerable to infections (especially respiratory infections). Smoking increases the risk of affecting by bacterial and viral infections such as colds, flu, and tuberculosis. Therefore, smoking is assumed to

be a potential risk factor for coronavirus infection (23). In addition, the data of some studies caused a paradox (smoker's paradox). The results of these studies indicated that smokers were less likely to be present in coronavirus-induced hospitalizations (24). In a meta-analysis study conducted in China, 5960 patients were examined. This study calculated the current smoking rate among those with COVID-19 as 6.5% (25). This number is significantly lower than the prevalence of active smoking in the general Chinese population (26.6%) (24,26). In another meta-analysis study, Farsalinos et al. examined 6515 patients. Their results showed an unexpectedly low prevalence of current smoking (6.8%) among hospitalized patients with COVID-19. According to their results, hospitalized current smokers had a higher chance of adverse outcomes due to COVID-19 compared to inactive smokers. However, compared to ex-smokers, they had a lower chance of adverse outcomes (27). Miyara et al., in a study in France that included inpatients (340 patients) and outpatients (139 patients) of COVID-19, calculated the daily smoking rate among them to be 6.1%. Meanwhile, the daily smoking rate in France in 2019 was reported as 24%. They concluded that the rate of daily smoking among COVID-19 patients compared to the general French population was significantly lower after standardization by age and sex. The results of their study suggest that smokers are less likely to be infected by COVID-19 (24,28).

In the current study, there were no significant differences between two groups in prevalence of smoking and duration of smoking. In justifying this paradox, there is evidence of the protective role of cigarettes against COVID-19. Nicotine is an agonist of the cholinergic anti-inflammatory pathway and can protect against COVID-19 (29). Also, Nicotine inhibits the production of pro-inflammatory cytokines (e.g., TNF, IL-1, and IL-6), thus possibly preventing cytokine-storm syndrome (29). In addition, Nitric Oxide (NO) produced during smoking helps maintain airway dilation. NO has been shown to inhibit the proliferation of SARS-CoV-2 and prevent it from entering the cell (30).

Since the coronavirus outbreak 2019 (31), there has been much debate about the impact of substance addiction on the likelihood of infection, prevalence, and complications of COVID-19. It has been stated that substance abusers are more at risk for coronavirus due to poor personal hygiene, sharing of personal belongings, and disregard for social distancing (32). A study of patient health records found that substance-abusing people were at higher risk for COVID-19 and adverse outcomes (33). In another study, Saeedi et al., showed that the mortality rate in the population of opium users is higher than the normal population (32).

However, there are perceptions of the protective effect of opium use against COVID-19 on social media that could lead people to use substances (31). In addition, some studies provide evidence of an immunomodulation role of morphine against cytokine storms, which could improve the clinical course of COVID-19. For example, in vivo and in vitro results have shown that morphine in the early stages (not late) of COVID-19 can relieve cytokine storms (34).

Another study found that suppression of levels of interleukins involved in COVID-19-induced hyperinflammatory syndrome was associated with short-term opium use due to competition with SARS-CoV-2 for binding to angiotensin-converting enzyme 2 (ACE-2) receptors (35). In the present study, the most common substance used was opium and its derivatives. Our results showed the frequency of substance users in the COVID-19 group than in the other patient group. In a prospective cohort study, Jamali et al. examined 4394 participants (in Iran). Their results showed that the prevalence of COVID-19 among participants with Opioid Use Disorder (OUD) is 4.17%, and among other participants, it is 6.22%. According to their conclusion, OUD is unrelated to COVID-19 (36). Interestingly, it has also been reported that out of 11,223 people receiving opioid substitution treatment in Ireland by the end of July 2020, just under 20 cases (~0.18%) of COVID-19 had been identified.

At that time, there were 26,000 confirmed cases of COVID-19 in Ireland. After the phased reopening in Ireland, despite the increase in the number of cases in the country, no significant increase was observed among people receiving opioid substitution treatment (37).

However, it has been demonstrated that the need for an Intensive Care Unit (ICU) in patients with COVID-19 with opioid abuse is significantly higher (38). Although studies provide various reasons to justify this paradox, the results seem more influenced by the fact that addicted people are often reluctant to seek

health care and, therefore, refer to a health center with more advanced disease (39).There were some limitations in this study. One of the most important limitations of this study is the lack of evaluation of the prevalence of COVID-19 in the population of addicts outside the hospital. Therefore, we suggested that in future studies, this study was performed on homeless and street addicts. According to the purpose of the study, another limitation is not investigating the role of the immune system status of the participants and their history of previous diseases. Therefore, it is suggested to consider these cases in further studies.

Conclusion

Overall, we showed no difference in the frequency of smoking among the COVID-19 group and other patients, indicating that smoking was not associated with the prevalence of COVID-19. Also, the frequency of substance use was lower than in other patients. Although there is evidence that cigarettes play a protective role against COVID-19, there is no convincing evidence on the role of substance use in reducing the risk of COVID-19. Therefore, further studies in this regard are recommended.

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