

# The Association of Opioid Use Disorder and COVID-19, a Longitudinal Study

## Abstract

**Background:** Coronavirus disease 2019 (COVID-19) quickly spread to the world, causing a pandemic. While some studies have found no link between opioid use disorder (OUD) and COVID-19, the role of opioid on COVID-19 is challenging. The present study aimed to determine the relationship between OUD and COVID-19. **Methods:** This was a prospective cohort study. We used data from the third phase of the Shahroud Eye Cohort Study on 4394 participants which started in September 2019 and ended before the COVID-19 epidemic in Shahroud in February 2020. The participants were followed for about 13 months till March 26, 2021. COVID-19 was detected by RT-PCR on swap samples from the oropharynx and nasopharynx. The incidence of COVID-19 compared in OUD and non-OUD participants, and relative risk was calculated in log-binomial regression models. **Results:** Among the 4394 participants with a mean age of 61.1 years, 120 people had OUD. The incidence of COVID-19 in participants with OUD and non-OUD was 4.17% and 6.22%, respectively ( $P$ -value: 0.356). The relative risk of OUD for COVID-19 was 0.60 (95% confidence intervals: 0.25–1.44;  $P$  value: 0.251). **Conclusions:** OUD was not associated with COVID-19. The claim that people with OUD are less likely to develop COVID-19 is not supported by these data.

**Keywords:** Addiction, COVID-19, Iran, opioid, pandemic, SARS-CoV-2

## Introduction

The coronavirus disease 2019 (COVID-19) pandemic, which began in late 2019 in Wuhan, China, spread rapidly around the world.<sup>[1]</sup> According to the latest report of the World Health Organization until April 14, 2022, more than 500 million people have been infected with COVID-19 worldwide, and more than 6 million people have died. During the same period, 7342,173 people were infected with COVID-19 and 140,177 people died due to this disease in Iran.<sup>[2]</sup>

Opioid use disorder (OUD) is a chronic and relapsing disease.<sup>[3]</sup> Opiates are legally prescribed to manage severe and chronic pain; however, some other opiates, such as heroin, opium, and illicit drugs, are abused.<sup>[4]</sup> According to a report by the United Nations Office on Drugs and Crime, there were 61 million people with OUDs globally in 2020.<sup>[5]</sup> People with OUDs are usually a marginal population and have less access to health care.<sup>[6]</sup> They also suffer from chronic infections, poor physical health, and psychiatric

illnesses.<sup>[7]</sup> In these individuals, the risks of hypoxemia from COVID-19 viral pneumonia, and OUD drug interactions with COVID-19 medications, are significant.<sup>[8,9]</sup> People with OUD need more medical care, and because of their greater vulnerability, they need more attention in COVID-19 pandemic.<sup>[10-12]</sup> Important risk factors for COVID-19 include old age and underlying diseases such as chronic obstructive lung disease, cardiovascular disease, obesity and diabetes.<sup>[13]</sup> There are a few studies on the relationship between OUD and COVID-19.<sup>[14-16]</sup> A study in Iran investigated this relationship in an ecological study and proposed a protective role of OUD against COVID-19.<sup>[17]</sup> This study did not meet the required technical and scientific standards, and their authors retracted it. Therefore, creating new evidences in this regard is very necessary and important. Insufficient current information regarding relationship between OUD and COVID-19 and cross-sectional studies in this field urge us to study this relationship in a population-based cohort study. The aim of this study is to explore the role of OUD in COVID-19 infection.

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## Method

Shahroud Eye Cohort Study is a population-based cohort study that has been designed to determine the prevalence and incidence of important eye diseases in adults and to identify the risk factors that cause them.<sup>[18]</sup> The target population was the 40–64-year-old adults, living in Shahroud, northeast Iran, where 6311 residents were randomly selected by multistage cluster sampling. Among the invited individuals, 5190 people (82.2%) participated in the first phase of study in 2009. The second and third phases of this study were conducted in 2014 and 2019 by inviting the participants of the first phase. In all three phases, demographic data and past medical and medication histories have been questioned.<sup>[18]</sup> The data of the present study are from the third phase of this study, which was completed in February 2020 and before the start of the COVID-19 epidemic in Iran. Participants reported any opioid use, including opium and its derivatives, as well as methadone and other narcotics in the interviews. Individuals who consumed any of these substances in any amount were considered OUDs.

A comprehensive system for registration and follow-up of COVID-19 patients has been set up in Shahroud, northeast Iran. All COVID-19 patients, including outpatients and inpatients, were registered in this system.<sup>[19,20]</sup> Individuals who participated in the cohort study were followed up in the COVID-19 system by using the national identification number for about 13 months till March 26, 2021. In this study, a person with COVID-19 has defined as a person who had a positive real-time reverse transcription polymerase chain reaction (RT-PCR) test in the Nasopharyngeal and Oropharyngeal Swabs samples. The incidence rate of COVID-19 was calculated in two groups of participants (with and without OUD) and then the relative risk of COVID-19 was calculated. Respiratory infection (RI) or any suspicion of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that led to RT-PCR test for COVID-19 (total positive and negative PCR tests) was investigated as the second outcome. The third outcome was patients who had a positive RT-PCR test or a positive chest CT scan for COVID-19. Descriptive variables were reported by percent and 95% confidence limits and the incidence rates were calculated with log-binomial regression. All estimates in log-binomial regression models were adjusted for significant risk factors which were diagnosed in another report on similar data.<sup>[19]</sup>

Everyone in the study participated willingly with written informed consent. Both studies have been approved by the ethics committee of Shahroud University of Medical Sciences (reference numbers: IR.SHMU.REC.1398.039 and IR.SHMU.REC.1398.160).

## Results

In this study, 4394 participants in the third phase of the Shahroud Eye Cohort Study were followed up for about

13 months. The mean and standard deviation of the age of the participants was  $6.1 \pm 61.1$  years and 59.3% of them were female. Among them, 120 (including 112 men) had OUDs.

The incidence of COVID-19 was 6.22% in the group without OUD and 4.17% in the group with OUD. This difference was not statistically significant ( $P$ -value: 0.356). The relative risk for people with OUD was estimated to be 0.60 (95% CI: 0.25–1.44), which means that the incidence of COVID-19 was not different in the two groups without OUD and with OUD [Table 1].

The results of log-binomial regression for two other outcomes including RI as well as COVID-19 patients who had positive tests for RT-PCR or chest CT scan are also shown in Table 1, indicating that OUDs did not have any association with COVID-19.

## Discussion

This study showed that the incidence of COVID-19 was not significantly different between people with and without OUD. OUD is a common health problem in all societies, and people with OUD are susceptible to infectious diseases in biological, nutritional, behavioral, and quality-of-life aspects.<sup>[21]</sup> Since the COVID-19 pandemic began, little information has been provided in Iran<sup>[14,15]</sup> and sometimes misconceptions have been raised about the resistance of these people to COVID-19.

In this regard, a study in Iran<sup>[16]</sup> emphasizes that addicts are more vulnerable to COVID-19 and the odds of mortality in opioid addiction were 3.6 times to other patients. A large study by Wang *et al.*<sup>[22]</sup> in the United States also highlighted the increased odds of patients with substance use disorders (SUD), to COVID-19 (the adjusted odds ratio for OUDs was 10.2). Patients with SUD or OUD were also at higher risk of hospitalization and death.<sup>[22]</sup>

The predisposing factors that can make people with OUD more vulnerable to COVID-19 include nonconformity of social distance, use of shared facilities, lack of personal hygiene, living in crowded groups, and poor physical and mental health.<sup>[15,16,23,24]</sup> Behavioral and economic factors can also increase the risk of COVID-19 among people with SUD.<sup>[22,24]</sup> COVID-19 can be fatal for people with OUD due to respiratory depression<sup>[25]</sup> and immune suppression due to long-term substance use.<sup>[25,26]</sup> This is why, higher doses of opioids use are associated with suppression of the immune system and an increased risk of pneumonia.<sup>[27]</sup> Morphine also increases susceptibility to bacterial and viral infections in injecting drug users<sup>[28]</sup> which is considered as another mechanism for these people to be susceptible to COVID-19.

On the other hand, some factors may protect OUDs against COVID-19. For example, smoking and tea consumption are more common among people with OUD,<sup>[29]</sup> while

**Table 1: The association of opioid user disorders with COVID-19 disease in multiple log-binomial regression models, adjusted for other variables**

Independent variables	Having respiratory infection		RT-PCR positive		RT-PCR or chest CT scan positive	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
Opioid use disorder	0.66 (0.39-1.13)	0.129	0.60 (0.25-1.44)	0.251	0.67 (0.30-1.48)	0.318
Age (year)	1.00 (0.99-1.02)	0.492	1.01 (0.99-1.03)	0.429	1.01 (0.99-1.03)	0.270
Male sex	1.31 (1.11-1.54)	0.002	1.47 (1.13-1.91)	0.004	1.51 (1.16-1.95)	0.002
Diabetes	1.32 (1.13-1.52)	<0.001	1.36 (1.08-1.73)	0.011	1.37 (1.09-1.73)	0.008
BMI (kg/m <sup>2</sup> )	1.01 (1.01-1.01)	<0.001	1.01 (1.01-1.01)	<0.001	1.01 (1.01-1.01)	<0.001
Education year	0.97 (0.96-0.99)	0.002	0.95 (0.93-0.98)	0.001	0.95 (0.93-0.98)	0.001
Smoking	0.97 (0.74-1.28)	0.825	0.49 (0.27-0.88)	0.017	0.59 (0.35-0.99)	0.045

RR=Relative Risk, CI=Confidence Intervals

there are reports that indicate a resistance to COVID-19 in tobacco<sup>[30]</sup> and tea<sup>[31]</sup> consumers. As we know, COVID-19 is transmitted through direct contact of the patient with other people in crowded and closed places.<sup>[32]</sup> Also, drug addicts suffer from mental health and low quality of life and lack of jobs and mental disorders such as antisocial personality, depression, and anxiety.<sup>[33-35]</sup> Therefore, these people are less present in the community and have less social activity that can reduce the chance of developing COVID-19.

Anyway, it seems that all the predisposing and protective factors neutralize each other's effects, and the risk of infection with SARS-CoV-2 in people with OUD is similar to other people. Differences in the study age group, type of drug addiction, the presence of other comorbidities, and differences in the prevalence of COVID-19 are some of the reasons that the results of this study may differ from other studies.

This prospective study has strengths that include a high sample size, significant follow-up time (about 13 months), and a well-designed study to record demographic and COVID-19 data. However, this study also had limitations. The absence of distinction between the method of opioid use and the type of addiction and the lack of a laboratory test to diagnose addiction can be considered as limitations. Also, the data of this study are limited to the age group of 50–74 years, while most opioid users are in the age group of 23–44 years,<sup>[36,37]</sup> which is another limitation of the current study. Although the overall sample size in this study is high, the number of participants with OUD was only 120, and this is another important limitation. The results of the power analysis showed that to identify a 3% difference, with this sample size in the two groups, the study power will be 40%, which is not a significant amount. Thus, further studies with higher sample sizes are suggested in the OUD group.

## Conclusion

People with OUD have a similar risk to the general population for developing COVID-19. Any protection role of OUD against SARS-CoV-2 infection should be discouraged.

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## Conflicts of interest

There are no conflicts of interest.

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