Outcomes of Patients with COVID-19 in the Setting of Chronic Opioid Use Disorder

Heather F. Thiesset, PhD, MPH (heather.thiesset@hsc.utah.edu)
University of Utah  https://orcid.org/0000-0002-5484-5303

Michael Newman, MS
University of Utah

Joseph E. Tonna, MD, MS
University of Utah  https://orcid.org/0000-0001-8879-2628

Ray M. Merrill, PhD, MPH
Brigham Young University

Research Article

Keywords: opioid use disorder, COVID-19, admission rates

DOI: https://doi.org/10.21203/rs.3.rs-90857/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background: There are no known studies regarding the effects of COVID-19 in patients with a concurrent diagnosis of opioid use disorder (OUD). Due to the rapidly developing nature and consequences of this disease, it is important to identify patients at an increased risk for serious illness. The aim of this study was to understand the disease burden of COVID-19 on patients with OUD by looking at their rates of hospitalization, admission to the intensive care unit (ICU), and receipt of mechanical ventilator support.

Methods: This retrospective chart review compared clinical parameters from patients with positive COVID-19 status as identified by a positive SARS-CoV-2 PCR test and diagnosed OUD at the University of Utah Health. Descriptive statistics and prevalence ratios (PRs) were generated. Log binomial models generated PRs adjusted by age, sex, race, and comorbidities of asthma, pneumonia, and diabetes.

Results: COVID-19 patients with OUD were significantly more likely than patients without OUD to have asthma (p<0.01), diabetes (p<0.01), and chronic pneumonia (p<0.01), to be hospitalized (23% vs 4%; p<0.01), to be admitted to the ICU (11% vs 2%; p<0.01), and to receive mechanical ventilation (7% vs 1%; p<0.01). After adjusting for age, sex, race, asthma, pneumonia, and diabetes, patients with OUD continued to be at increased risk for inpatient hospitalization (aPR=5.65, 95% confidence interval [CI]=2.29-13.92), intensive care unit (ICU) admission (aPR=0.69, 95% CI = 0.19-2.45), and mechanical ventilation (aPR=1.25, 95% CI =0.27-5.75). Patients with OUD averaged longer stays in the hospital than those without OUD (9.53 days vs 0.70 days, p<.001).

Conclusion: Patients that have a diagnosis of OUD in the presence of COVID-19 are more likely to be hospitalized, admitted to the ICU, receive mechanical ventilation and have longer hospital inpatient stays compared to patients without OUD.

Background

The effects of the novel coronavirus COVID-19 (SARS-CoV-2) continue to be identified as it has reached pandemic proportions with 20,706,396 global cases and 751,033 global deaths as of August 14, 2020. Corresponding numbers in the United States are 5,215,958 and 166,483, respectively. COVID-19 is a virus affecting the respiratory system with main symptoms including fever, fatigue, shortness of breath/difficulty breathing, and cough. Preventive measures have been implemented to reduce the incidence of new cases throughout the United States. It has been estimated that approximately 25% of those infected with COVID-19 are asymptomatic. This creates a unique challenge in preventing the spread of transmission since asymptomatic carriers often remain unaware of their disease status and do not get tested. While generally those with comorbidities are at an advanced risk of increased morbidity and mortality from COVID-19, new evidence is emerging about select populations that are at increased risk from this disease including pregnant women, patients with cardiovascular conditions, and psychiatric patients.
Patients who misuse opioids are at greater risk for disease transmission during a pandemic because of increased stress, reliance on face-to-face medical care, a compromised immune system, not social distancing while procuring opioids, and reduced adherence to prescribed guidelines for Medication Assisted Treatment (MAT). The opioid epidemic has in recent years claimed 72,000 lives each year in fatal overdoses related to prescription pain relievers. Opioids act on pain receptors in the brain and can cause respiratory depression or other respiratory events. Respiratory depression brought on by OUD has a significant disease burden. However, adding the insult of COVID-19 has the potential of significantly increasing levels of morbidity and mortality in this population.

There are currently no known studies regarding the effects of COVID-19 in patients with a concurrent diagnosis of OUD. Because of the rapidly developing nature and consequences of this disorder it is important to identify patients at an increased risk for serious complications of COVID-19. The aim of this study was to identify whether COVID-19 patients with OUD are at increased risk of hospitalization, admission to the intensive care unit (ICU), and receipt of mechanical ventilator support.

**Methods**

This was a retrospective chart review examining outcomes of patients with opioid use disorder (OUD) who have a positive SARS-CoV-2 PCR test in both the inpatient and outpatient settings. Data were collected using patient data from the University of Utah Health system's electronic data warehouse. International classification of diagnosis (ICD-10) codes were utilized to extract data and identify patients with OUD (F11, T40, R78.1) diagnosed between October 2015 to June 22, 2020 and covid-19 (U07.1) from March 24, 2020 to June 22, 2020. Additionally, patients were considered to have COVID-19 if they had a positive SARS-CoV-2 PCR test recorded in their medical record. Approval for this study was obtained through the University of Utah Institutional Review Board.

**Analyses**

The primary outcome was probability of hospitalization, ICU admission, and mechanical ventilation. Prevalence ratios (PR) were generated using log-binomial models with OUD patients as the reference group for dichotomous variables. PRs were considered significant at the 1% level. Covariates were adjusted by age, race, sex, and diagnoses of comorbidities of chronic pneumonia, asthma, and diabetes. Univariate analyses were conducted using chi-square and relative risk ratios, as appropriate. Frequency statistics compared differences in demographics between patients with opioid use disorder (OUD) and without opioid use to determine the association for patients with OUD to be hospitalized, spend time in the (ICU) and be on a mechanical ventilator. Data analysis was completed using Stata 15.1 software (College Station, TX).

**Results**
Data consisted of 4633 individual patients with a diagnosis of COVID-19, of which 52% were males and 48% were females. Patients above the age of 60 years old only accounted for 12% of the total sample. Sixty-one patients also had a concurrent diagnosis of OUD as identified in the medical records. Patients with OUD were more likely to be male (61%), greater than 60 years of age (28%), and identified as white or Caucasian (70%) (Table).

Patients with COVID-19 and OUD were more likely than patients without OUD to have asthma (p<0.01), diabetes (p<0.01), and chronic pneumonia (p<0.01), to be hospitalized (23% vs 4%; p<0.01), to be admitted to the ICU (11% vs 2%; p<0.01), and to receive mechanical ventilator support (7% vs 1%; p<0.01) (Table). Furthermore, patients with OUD averaged longer stays in the hospital than those without OUD (9.53 days vs 0.70 days, p<.001).

Patients with OUD, after adjusting for age, sex, race, and the presence of underlying medical conditions including diabetes, asthma, and chronic pneumonia, were significantly more likely to be admitted to the hospital as an inpatient (aPR =5.65, 95% confidence interval [CI] = 2.29-13.92), be admitted to the intensive care unit (ICU) (aPR =0.69, 95% CI = 0.19-2.45), and receive mechanical ventilation (aPR =1.25, 95% CI = 0.27-5.75).

**Discussion**

Patients with COVID-19 and a concurrent diagnosis of OUD are at increased risk for hospitalization, ICU stay, and receipt of mechanical ventilation. They are also more likely to have comorbidities associated with the respiratory track such as asthma and chronic pneumonia. Like other patients with chronic diseases or other underlying conditions, patients with OUD represent a vulnerable population in the midst of an infectious disease pandemic. This is especially important given that upwards of 25% of COVID-19 cases do not exhibit symptoms,\(^6\) which can place OUD patients at a greater risk for contracting the disease because the procurement of opioids usually requires social contact.

While the opioid epidemic continues to be a major public health concern and has even increased during the COVID-19 pandemic, providers, treatment facilities, and patients should be aware of the additional risks associated with the disease for patients with OUD. Appropriate measures may include telehealth to deliver care and medication treatment for OUD patients.\(^{11}\) In addition, greater emphasis may be in order on the importance of social distancing and wearing masks and following other guidelines, as recommended by the Centers for Disease Control and Prevention (CDC).

This study is limited in that the results reflect information obtained from a single tertiary academic institution. Second, OUD classified by ICD-10 codes and medical records may not represent all patients since there is a lack of screening for opioid misuse in clinical settings.\(^{12}\) Third, with a small sample size there may not be enough power to detect significant differences in the population. Both mechanical ventilation and ICU admission rates were marginally insignificant, but we expect with a larger sample size this would not be the case. Finally, another potential limitation is that we are not able to assess socio-
economic status for individuals in this sample, which could be an underlying confounder in the hospitalization data$^{18}$.

**Conclusion**

Patients with OUD in the presence of COVID-19 are more likely to be hospitalized, be admitted to the ICU, receive mechanical ventilation, and have greater lengths of inpatient stay. In order to prevent the occurrence of severe illness and increased risk of morbidity and mortality from COVID-19, patients with OUD should receive counseling from health care workers regarding their increased risk. OUD patients should also strictly employ prevention measures of telehealth medication assisted treatment, mask wearing, and social distancing.

**List Of Abbreviations**

(in order of appearance in manuscript): OUD- opioid use disorder, ICU-intensive care unit- PRs-prevalence ratios, MAT-Medication Assisted Treatment, ICD-10-International classification of diagnosis codes, CDC-Centers for Disease Control and Prevention.

**Declarations**

*Ethics approval and consent to participate*- This study was approved in accordance with the guidelines and principles of the University of Utah Institutional Review Board. This study was deemed exempt from obtaining informed consent.

*Consent for publication*- Not applicable

*Availability of data and material*- Data and material are available upon request.

*Competing interests*- There are no competing interests associated with the research presented herein.

*Funding*- There are no funding sources to declare.

*Authors’ contributions*- HT, MN, JT, RM crafted the research question, hypothesis, and study design. HT, and MN collected the data. HT performed the data analysis while MN, JT, RM provided critical interpretation of the data. HT drafted the manuscript. MN, JT, RM provided essential revisions to the manuscript. All authors have read and approved the final manuscript.

*Acknowledgements*- Not applicable

**Table**

Bivariate Analyses of the Association between Selected Variables and Opioid Use Disorder (OUD).
|                     | OUD     | No OUD   | RR   | 95% LCL | 95% UCL | Chi-Square P Value |
|---------------------|---------|----------|------|---------|---------|-------------------|
| Sex                 | Male    | 37       | 60.7 | 2351    | 51.5    | 0.16              |
|                     | Female  | 24       | 39.3 | 2210    | 48.5    |                   |
| Age                 | ≥60     | 17       | 27.9 | 520     | 11.4    | 2.9               |
|                     | <60     | 44       | 72.1 | 4052    | 88.6    |                   |
| Race                | White or Caucasian | 43 | 70.5 | 1770 | 48.6 | 2.5 | 1.4 | 4.3 | <.001 |
|                     | Non-white | 18 | 29.5 | 1873 | 51.4 |                   |
| Diabetes            | Yes     | 14       | 23.0 | 258     | 5.6     | 4.8               |
|                     | No      | 47       | 77.0 | 4314    | 94.4    |                   |
| Asthma              | Yes     | 10       | 16.4 | 226     | 4.9     | 3.7               |
|                     | No      | 51       | 83.6 | 4346    | 95.1    |                   |
| Pneumonia           | Yes     | 13       | 21.3 | 170     | 3.7     | 6.6               |
|                     | No      | 48       | 78.7 | 4402    | 96.3    |                   |
| Hospital admission  | Yes     | 17       | 27.9 | 164     | 3.6     | 9.5               |
|                     | No      | 44       | 72.1 | 4408    | 96.4    |                   |
| ICU admission       | Yes     | 7        | 11.5 | 67      | 1.5     | 8.0               |
|                     | No      | 54       | 88.5 | 4505    | 98.5    |                   |
| Ventilator          | Yes     | 25       | 0.0  | 4       | 0.0     | 69.6              |
|                     | No      | 57       | 0.0  | 4547    | 0.0     |                   |

References

1. Ellington S SP, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status. *MMWR Morb Mortal Wkly Rep.* 2020;69:769–775.
2. Feng He YD, Weina Li. Coronavirus disease 2019: What we know? *J Med Virol.* 2020;92(7):719-725.
3. Yan Y, Shin WI, Pang YX, Meng Y, Lai J, You C, et al. The First 75 Days of Novel Coronavirus (SARS-CoV-2) Outbreak: Recent Advances, Prevention, and Treatment. *International journal of environmental research and public health*. 2020;17(7):2323.

4. Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, et al. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan. A Retrospective Observational Study. *American journal of respiratory and critical care medicine*. 2020;201(11):1372-1379.

5. Dennison Himmelfarb CR, Baptiste D. Coronavirus Disease (COVID-19): Implications for Cardiovascular and Socially At-risk Populations. *The Journal of cardiovascular nursing*. Jul/Aug 2020;35(4):318-321.

6. Hategan A, Abdurrahman M. Hidden in plain sight: Addressing the unique needs of high-risk psychiatric populations during the COVID-19 pandemic. *Psychiatry and clinical neurosciences*. 2020:10.1111/pcn.13022.

7. Williams JR, Cole V, Girdler S, Cromeens MG. Exploring stress, cognitive, and affective mechanisms of the relationship between interpersonal trauma and opioid misuse. *PloS one*. 2020;15(5):e0233185-e0233185.

8. Canan CE, Chander G, Monroe AK, Gebo KA, Moore RD, Agwu AL, et al. High-Risk Prescription Opioid Use Among People Living With HIV. *Journal of acquired immune deficiency syndromes (1999)*. 2018;78(3):283-290.

9. National Institute on Drug Abuse N. Overdose death rates. Available at: [https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates](https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates). Accessed January 19, 2019.

10. Tamhane AR, Westfall AO, Burkholder GA, Cutter GR. Prevalence odds ratio versus prevalence ratio: choice comes with consequences. *Statistics in medicine*. 2016;35(30):5730-5735.

11. Huskamp HA, Busch AB, Souza J, Uscher-Pines L, Rose S, Wilcock A, et al. How Is Telemedicine Being Used In Opioid And Other Substance Use Disorder Treatment? *Health affairs (Project Hope)*. 2018;37(12):1940-1947.

12. Thiesset HF, Schliep KC, Stokes SM, Valentin VL, Gren LH, Porucznik CA, et al. Opioid Misuse and Dependence Screening Practices Prior to Surgery. *The Journal of surgical research*. 2020;252:200-205.