Medicine and BioHealth Journal

Journal homepage: https://ojs.omgfzc.com/index.php/MBJ

*(Original Article)*

# Tramadol addiction can be a killer for Covid-19 patients

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**Article Info**

***Article History:***
*Submitted/Received 16 December 2025*
*Received in revised format 27 July 2024*
*Accepted 28 July 2024*
*Available Online 10 August 2024*
*Publication Date 10 September 2024*

***Keyword:***
*Tramadol;Tramadol addiction;Covid-19, Mortality, Pathophysiology;Opioid abuse;Comorbidities,*

Cite this article: *Taha, E., Hamad, A. M., Soliman, O.S.E. (2025). Tramadol addiction can be a killer for Covid-19 patients. Med. Biohealth. J. 2(1), 1-9.*

DOI: Xxxxxxxxxxxxxxxxxxxxxxxxxx

**ISSN** 3007-6374



## ABSTRACT

**Background:** Tramadol abuse has emerged as a significant public health concern, with potential exacerbation during the COVID-19 pandemic due to increased stress, self-medication, and reduced healthcare access.

**Objectives:** This study examines the association between tramadol addiction, comorbidities, and COVID-19 outcomes.

**Methods:** A cross-sectional analysis was conducted on 60 participants aged 40–70 years, predominantly male (81.7%). Data on demographics, medical history (hypertension, diabetes, ischemic heart disease, COPD, smoking), COVID-19 diagnosis, tramadol abuse, and mortality were collected. Statistical correlations were assessed using chi-square and logistic regression.

**Results:** Most participants had hypertension (86.7%), diabetes (58.3%), and a COVID-19 diagnosis (90%). Tramadol addiction was present in 25% of cases and showed a highly significant association with mortality (P = 0.000), with 86% of addicted patients dying. No significant correlations were found between tramadol abuse and other variables, except for COVID-19, which demonstrated a strong interaction with tramadol-related deaths.

**Conclusion:** Tramadol addiction is strongly associated with increased mortality in COVID-19 patients, likely due to compounded respiratory risks. These findings highlight the need for increased public awareness about addiction, and further research to achieve patient tailored sedation doses.

## 1. INTRODUCTION

Tramadol, a synthetic opioid analgesic, is widely prescribed for moderate to severe pain due to its dual mechanism of action as a μ-opioid receptor agonist and serotonin-norepinephrine reuptake inhibitor (SNRI) [1,2]. Despite its therapeutic benefits, tramadol has a significant potential for misuse, dependence, and addiction, particularly in regions with lax prescription controls [3]. The COVID-19 pandemic exacerbated substance use disorders (SUDs) globally, as lockdowns, social isolation, economic stress, and disrupted healthcare services contributed to increased drug consumption and relapses [4]. The pandemic created a perfect storm for tramadol addiction, with many individuals self-medicating for pain, anxiety, or depression due to limited access to medical care [5]. Additionally, the rise in telemedicine and reduced in-person consultations may have led to overprescription or inadequate monitoring of tramadol use [6]. Studies indicate

that stress and psychological distress during COVID-19 were linked to higher opioid misuse, including tramadol [7]. This paper explores the intersection of tramadol addiction and risk mortality rate among COVID-19 patients during last pandemic. By understanding this risk, policymakers and healthcare providers can develop better strategies to mitigate tramadol misuse in future public health pandemics.

## 2. MATERIALS AND METHODS

### *2.1 Study design and setting*

This was a retrospective descriptive cross-sectional study to find correlation between addiction of tramadol and mortality rate.

### *2.2. Materials*

Materials were data that collected retrospectively from intensive care unit ICU record during the last pandemic of COVID-19 at the period between June 2020 to May2021.

### *2.3. Data analysis*

Descriptive statistics was used to describe data in form of mean and percentages. Also, Chi-square test was used to inspect associations between data. SPSS v. 26software was used to apply this statistical analysis.

### *2.4. Ethical consideration*

Anonymity of patients were and will be maintained, non-maleficence was observed for all patients as their information kept confidential. No data was collected from minors or vulnerable patients record. No discrimination was applied due to any patient background or whatsoever. Ethical approval from the relevant administration was secured.. The chi-square test showed a highly significant difference in age and a non-significant difference in gender. Figure 2 shows A CT image of an infarct in a patient 80 years old, while Figure 3 shows a CT scan of a 62-year-old patient with hemorrhage.

## 3. RESULTS

Minimum age was 40 and maximum was 70 years old while mean age was 55.12. This and age group distribution is shown in Table 1. There were 11(18.3%) female and 49(81.7%) male as shown in Figure 1. Most of the study population were hypertensive (86.7%), diabetic (58.3%), and smokers (71%), and positively diagnosed with Covid-19 (90%). However, most of them were free from ischemic heart disease (70%), also, free from COPD (70%), free from tramadol abuse/ addiction (75%), survived (78.3%), and none of them had previous stroke as appears in Table2, as well as Figure 2, Figure 3, and Figure 4. Furthermore, correlations of tramadol abuse (addiction) with age, sex, hypertension, diabetes millets, ischemic heart disease (IHD), previous stroke, covid 19 diagnosis, COPD, smoking, and death are shown in Table 3. By exploring correlation of tramadol addiction we found no significant relation except highly statistically significance with death as 13(86%) of the addicted patients died and P value was (0.000) as shown in Table3 and Table5. Also, we found COPD was not correlated with any parameters except near to correlate with diabetes P value was (0.09) as shown in Table 4. In addition, multilayer correlation of death and tramadol addiction with parameters under study revealed highly statistically significant correlation with positive diagnosis of Covid-19 as shown in Table 6.

Table 1: Ages and age groups distribution.

| Age group (Years old) | Frequency |
|---|---|
| 40-50 | 18(30%) |
| 51-60 | 27(45%) |
| 61-70 | 15(25%) |

DOI: https://doi.org/10.70274/medbiohealth.2024.1.1.17.
ISSN 3007-6374

Table 2. Distribution of study population by characteristics under study.

| Characteristics | Positive | Negative | Total |
|---|---|---|---|
| Hypertension | 52(86.7%) | 8(13.3%) | 60 (each) |
| Diabetes millets | 35(58.3%) | 25(41.7%) | |
| Ischemic heart disease (IHD) | 18(30%) | 42(70%) | |
| Previous stroke | 0(0%) | 60(100%) | |
| Covid 19 diagnosis | 54(90%) | 6(10%) | |
| COPD | 18(30%) | 42(70%) | |
| Smoking | 43(71.7%) | 17(28.3%) | |
| Tramadol abuse/addiction | 15(25%) | 45(75%) | |
| death | 13(21.7%) | 47(78.3%) | |

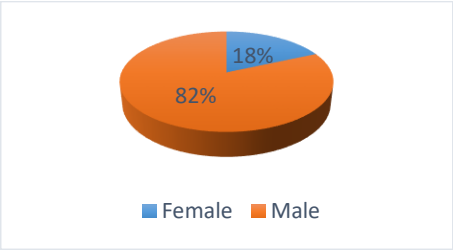


Figure 1. Gender distribution.

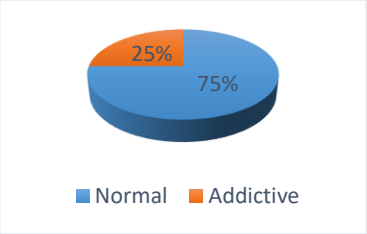


Figure 2. Tramadol abuse/addiction.

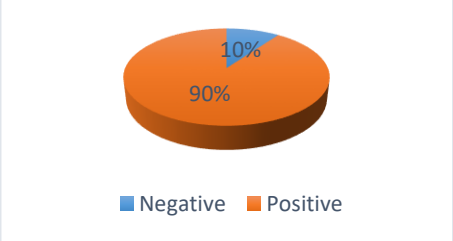


Figure 3. Covid-19 diagnosis.

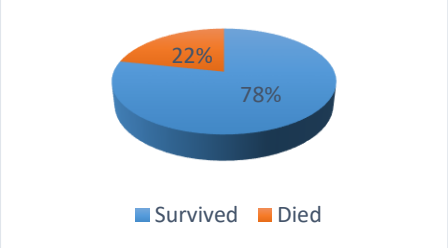


Figure 4. Death cases.

Table 3. Correlation of tramadol abuse/addiction with parameters under study?

| | | Tramadol addiction | | Total | P value |
|---|---|---|---|---|---|
| | | Positive | Negative | | |
| Age groups | 40-50 | 5 | 13 | 18 | 0.90 |
| | 51-60 | 6 | 21 | 27 | |
| | 61-70 | 4 | 11 | 15 | |
| | Total | 15 | 45 | 60 | |
| Sex | Female | 2 | 9 | 11 | 0.56 |
| | Male | 13 | 36 | 49 | |
| | Total | 15 | 45 | 60 | |
| Hypertension | Diseased | 14 | 38 | 52 | 0.38 |
| | Normal | 1 | 7 | 8 | |
| | Total | 15 | 45 | 60 | |
| Diabetes millets | Diseased | 6 | 29 | 35 | 0.09 |
| | Normal | 9 | 16 | 25 | |
| | Total | 15 | 45 | 60 | |
| IHD | Diseased | 5 | 13 | 18 | 0.74 |
| | Normal | 10 | 32 | 42 | |
| | Total | 15 | 45 | 60 | |
| Previous stroke | Diseased | 0 | 0 | 0 | ------ |
| | Normal | 15 | 45 | 60 | |
| | Total | 15 | 45 | 60 | |
| Covid 19 | Diseased | 13 | 41 | 54 | 0.61 |
| | Normal | 2 | 4 | 6 | |
| | Total | 15 | 45 | 60 | |
| COPD | Diseased | 5 | 13 | 18 | 0.74 |
| | Normal | 10 | 32 | 42 | |
| | Total | 15 | 45 | 60 | |
| Smoking | Smoker | 10 | 33 | 43 | 0.62 |
| | Non-smoker | 5 | 12 | 17 | |
| | Total | 15 | 45 | 60 | |
| Death | Died | 13 | 0 | 13 | 0.000 |
| | Lived | 2 | 45 | 47 | |
| | Total | 15 | 45 | 60 | |

Table 4. Correlation of COPD with parameters under study.

| | | COPD | | Total | P value |
|---|---|---|---|---|---|
| | | Positive | Negative | | |
| Age groups | 40-50 | 5 | 13 | 18 | 0.90 |
| | 51-60 | 9 | 18 | 27 | |
| | 61-70 | 4 | 11 | 15 | |
| | Total | 18 | 42 | 60 | |
| Sex | Female | 2 | 9 | 11 | 0.34 |
| | Male | 16 | 33 | 49 | |
| | Total | 18 | 42 | 60 | |
| Hypertension | Diseased | 16 | 36 | 52 | 0.74 |
| | Normal | 2 | 6 | 8 | |
| | Total | 18 | 42 | 60 | |
| Diabetes millets | Diseased | 13 | 22 | 35 | 0.09 |
| | Normal | 5 | 20 | 25 | |
| | Total | 18 | 42 | 60 | |
| IHD | Diseased | 6 | 12 | 18 | 0.71 |
| | Normal | 12 | 30 | 42 | |
| | Total | 18 | 42 | 60 | |
| | Diseased | 0 | 0 | 0 | |

DOI: https://doi.org/10.70274/medbiohealth.2024.1.1.17.
ISSN 3007-6374

| | | | | | |
|---|---|---|---|---|---|
| Previous stroke | Normal | 18 | 42 | 60 | ----- |
| | Total | 18 | 42 | 60 | -- |
| Covid 19 | Diseased | 16 | 38 | 54 | 0.85 |
| | Normal | 2 | 4 | 6 | |
| | Total | 18 | 42 | 60 | |
| Tramadol abuse/addiction | Addicted | 5 | 10 | 15 | 0.74 |
| | Non-Addicted | 13 | 32 | 45 | |
| | Total | 18 | 42 | 60 | |
| Smoking | Smoker | 14 | 29 | 43 | 0.49 |
| | Non-smoker | 4 | 13 | 17 | |
| | Total | 18 | 42 | 60 | |
| Death | Died | 4 | 9 | 13 | 0.94 |
| | Lived | 14 | 33 | 47 | |
| | Total | 18 | 42 | 60 | |

Table 5. Correlation of death with parameters under study

| | | Death | | Total | P value |
|---|---|---|---|---|---|
| | | Died | Lived | | |
| Age groups | 40-50 | 5 | 13 | 18 | 0.50 |
| | 51-60 | 4 | 23 | 27 | |
| | 61-70 | 4 | 11 | 15 | |
| | Total | 13 | 47 | 60 | |
| Sex | Female | 2 | 9 | 11 | 0.75 |
| | Male | 11 | 38 | 49 | |
| | Total | 13 | 47 | 60 | |
| Hypertension | Diseased | 12 | 40 | 52 | 0.49 |
| | Normal | 1 | 7 | 8 | |
| | Total | 13 | 47 | 60 | |
| Diabetes millets | Diseased | 5 | 30 | 35 | 0.10 |
| | Normal | 8 | 17 | 25 | |
| | Total | 13 | 47 | 60 | |
| IHD | Diseased | 4 | 14 | 18 | 0.94 |
| | Normal | 9 | 33 | 42 | |
| | Total | 13 | 47 | 60 | |
| Previous stroke | Diseased | 0 | 0 | 0 | ------- |
| | Normal | 13 | 47 | 60 | |
| | Total | 13 | 47 | 60 | |
| Covid 19 | Diseased | 13 | 41 | 54 | 0.17 |
| | Normal | 0 | 6 | 6 | |
| | Total | 13 | 47 | 60 | |
| Tramadol abuse/addiction | Addicted | 13 | 2 | 15 | 0.000 |
| | Non-Addicted | 0 | 45 | 45 | |
| | Total | 13 | 47 | 60 | |
| Smoking | Smoker | 9 | 34 | 43 | 0.82 |
| | Non-smoker | 4 | 13 | 17 | |
| | Total | 13 | 47 | 60 | |
| COPD | Diseased | 4 | 14 | 18 | 0.94 |
| | Normal | 9 | 33 | 47 | |
| | Total | 13 | 47 | 60 | |

Table 6. Correlation of death and tramadol addiction with parameters under study.

| | | Tramadol addiction | | | | Total | P value |
|---|---|---|---|---|---|---|---|
| | | Addicted | | Non-addicted | | | |
| | | Lived | Died | Lived | Died | | |
| Age groups | 40-50 | 0 | 5 | 13 | 0 | 18 | 0.17 |
| | 51-60 | 2 | 4 | 21 | 0 | 27 | |
| | 61-70 | 0 | 4 | 11 | 0 | 15 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| Sex | Female | 0 | 2 | 9 | 0 | 11 | 0.55 |
| | Male | 2 | 11 | 36 | 0 | 49 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| Hypertension | Diseased | 2 | 12 | 38 | 0 | 52 | 0.68 |
| | Normal | 0 | 1 | 7 | 0 | 8 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| Diabetes millets | Diseased | 1 | 5 | 29 | 0 | 35 | 0.75 |
| | Normal | 1 | 8 | 16 | 0 | 25 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| IHD | Diseased | 1 | 4 | 13 | 0 | 18 | 0.59 |
| | Normal | 1 | 9 | 32 | 0 | 42 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| Previous stroke | Diseased | 0 | 0 | 0 | 0 | 0 | ----- |
| | Normal | 2 | 13 | 45 | 0 | 60 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| Covid 19 | Diseased | 0 | 13 | 41 | 0 | 54 | 0.000 |
| | Normal | 2 | 0 | 4 | 0 | 6 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| Smoking | Smoker | 1 | 9 | 33 | 0 | 43 | 0.59 |
| | Non-smoker | 1 | 4 | 12 | 0 | 17 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |
| COPD | Diseased | 1 | 4 | 13 | 0 | 18 | 0.59 |
| | Normal | 1 | 9 | 32 | 0 | 42 | |
| | Total | 2 | 13 | 45 | 0 | 60 | |

## 4. DISCUSSION

The study population comprised individuals aged between 40 and 70 years, with a mean age of 55.12 years, reflecting a middle-aged to elderly cohort, which is consistent with populations at higher risk for chronic conditions such as hypertension, diabetes, and COVID-19

DOI: https://doi.org/10.70274/medbiohealth.2024.1.1.17.
ISSN 3007-6374

complications [8]. The predominance of males (81.7%) in the study aligns with previous research indicating higher rates of substance use disorders, including tramadol abuse, among men [9]. A significant proportion of participants had comorbidities, including hypertension (86.7%), diabetes (58.3%), and a history of smoking (71%). These findings are consistent with studies showing that chronic diseases and lifestyle factors such as smoking are prevalent among individuals with substance use disorders [10]. Notably, 90% of the study population had a positive COVID-19 diagnosis, suggesting a possible interaction between infection, chronic illness, and substance abuse. The pandemic has been associated with increased substance use due to stress, isolation, and self-medication [11]. The study found that 25% of participants had tramadol abuse/addiction, which is concerning given the drug's potential for dependence. Importantly, tramadol addiction showed a highly statistically significant correlation with mortality (P = 0.000), with 86% of addicted patients dying. This aligns with research indicating that opioid misuse, including tramadol, is associated with higher mortality, particularly in patients with respiratory conditions or COVID-19 [12]. The interaction between tramadol and COVID-19 may exacerbate respiratory depression, increasing the risk of fatal outcomes [13]. Interestingly, no significant correlation was found between tramadol addiction and other variables such as age, sex, or comorbidities, except for COVID-19 diagnosis. This suggests that while tramadol abuse itself is a critical risk factor for death, its association with COVID-19 may further worsen prognosis. A possible explanation is that tramadol's respiratory depressant effects could compound COVID-19-induced hypoxia, leading to higher mortality [14]. Chronic obstructive pulmonary disease (COPD) showed a near-significant correlation with diabetes (P = 0.09), which is consistent with studies linking metabolic disorders to pulmonary complications [15]. However, the lack of strong associations between COPD and other factors may be due to the relatively small sample size or confounding variables.

## 5. CONCLUSION

This study highlights a strong association between tramadol addiction and increased mortality, particularly in COVID-19 patients. The findings underscore the need for stricter monitoring of tramadol prescriptions, especially in high-risk populations with chronic diseases. Further research with larger cohorts is necessary to explore the mechanisms linking tramadol abuse, COVID-19, and fatal outcomes.

## 6. RECOMMENDATIONS

Based on this research, it is recommended to increase public health status by increase awareness about risk of obioid addiction including tramadol. In addition, future research direction can be to adjust dose used for sedation according to the each patient comorbidities especially lung diseases such as COVID-19

## ACKNOWLEDGEMENT:

Authors are thankful to all persons help during this research. Also, thanks to Al-Rayan National College of Health Sciences and Nursing for support.

## FUNDING:

This research received no external funding

## AUTHOR CONTRIBUTIONS:

All authors contributed equally to this work

## CONFLICTS OF INTEREST:

The authors declare no conflicts of interest.

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DOI: https://doi.org/10.70274/medbiohealth.2024.1.1.17.
ISSN 3007-6374