Epidemiology, Burden, and Association of Substance Abuse Amongst Patients With Cardiovascular Disorders: National Cross-Sectional Survey Study

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Abstract

Background: Substance use disorders (SUDs) are considered to be a major risk factor for cardiovascular disorders (CVDs). In 2019, as per the National Drug Use and Health Survey (NSDUH), 20.4 million American adults suffered from a substance use disorder. The main purpose of this study is to determine the prevalence of several SUDs (cigarette smoking, cigar, smokeless tobacco, marijuana, cocaine/heroin/methamphetamine, and injectable illegal drug) amongst patients diagnosed with various CVDs (angina pectoris, myocardial infarction, and coronary heart disease).

Methods: This is a retrospective cross-sectional study carried out using the National Health and Nutrition Examination Survey (NHANES) database from 2013 to 2018, and respondents with CVDs were recognized using questionnaires. Different SUDs (active history) were identified amongst the adult population with a history of CVDs and without CVDs. Univariate analysis was performed using chi-square and unpaired t-test/Mann-Whitney test to identify characteristics of respondents with CVDs and mix effect multivariable logistic regression models were generated to find the prevalence of SUDs amongst the CVD population. Datasets were analyzed using Statistical Analysis System (SAS) software, and the p-value of < 0.05 was considered statistically significant.

Results: Of the 265465 respondents, 7.90% respondents were diagnosed with CVDs and were noted to be in older age group (median age: 69 years). CVDs were more prevalent amongst 66-years and above (19.36% vs. 45-64 years: 6.81% vs. 18-44 years: 1.17%), male (10.40% vs. female: 5.66%), Non-Hispanic White race (10.92%), and lower annual household income population (<$25000 vs. >$100,000:12.21% vs. 4.01%) (p<0.0001). When compared with respondents without a history of CVDs, respondents with a history of CVDs were noted to be more prevalent with a concurrent diagnosis of hypertension (85.98% vs. 79.53%), hypercholesterolemia (68.78% vs. 54.54%), diabetes (57.86% vs. 12.70%), stroke (17.4% vs. 2.71%), and congestive heart failure (28.80% vs. 13.1%) (p<0.0001). History of CVDs were more prevalent amongst those using marijuana (overall 53.14%; CVD vs. no-CVD 65.42% vs. 52.81%; p<0.0001), cigarette smoking (60.47% vs. 40.41%; p<0.0001), cigar-smoking (47.05% vs. 35.58%; p<0.0001), methamphetamine/cocaine/heroin (23.82% vs. 16.71%; p<0.0001), smokeless tobacco use (18.53% vs. 14.59%; p<0.0001), and injectable illegal drug use (4.67% vs. 2.43%; p<0.0001). Additionally, prevalence of history of CVDs was almost double in respondents using cigarettes without filters (2.28% vs. 1.10%; p<0.0001) when compared with respondents using cigarettes with filters.

Conclusion: Respondents who used marijuana or hashish, injectable illegal drugs, and e-cigarettes were at elevated risk for cardiovascular disorders. Providing situational awareness and offering a good support system can be a strategy to prevent the development of cardiovascular disorders among substance users.

Keywords: Cardiovascular disorders, marijuana, cocaine/heroin/methamphetamine, injectable illegal drug

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Introduction
The global burden of cardiovascular disorders (CVDs) has soared over the last few years. The year 2017 saw an increase in cardiovascular-related deaths by 21.1% as compared to that recorded in 2007 [1]. This increase is being attributed to lifestyle, food habits, and an increase in substance use disorders (SUDs), the most common being alcohol, tobacco smoking, e-cigarettes, stimulants, marijuana, steroids, and opioids. SUD is currently being regarded as major healthcare and social issue. According to the National Survey on Drug Use and Health (NSDUH), the prevalence of SUDs among individuals aged 12 or older has been escalating over the past decade, with 20.4 million cases reported in 2019 [2]. After relevant adjustment of other risk factors, studies suggest an increased incidence of acute cardiovascular emergencies like myocardial infarction with cocaine and/or marijuana use [3-5]. Overall mortality attributed to the consumption of tobacco in any form was as high as 8.7 million deaths in the year 2019, of which 36.7% were due to cardiovascular events [6]. Moderate alcohol consumption is considered to be cardioprotective; however cardiovascular mortality significantly increases in individuals who binge drink, i.e., >5 drinks per day in males and >4 drinks/day in females [7,8]. The impact of consumption of non-prescribed steroids on cardiovascular function is also being studied using modern-day technology. Many studies observed a significant change in left ventricular morphology along with a deranged lipid profile among individuals with frequent steroid use [9,10].

There is limited knowledge about the mechanism of how different substances impact cardiovascular health. However, few studies implicate multifactorial pathogenesis. Stimulants are associated with decreased catecholamine reuptake, thus causing sympathetic overdrive with increased myocardial oxygen demand and marked vasospasm along with abnormal platelet aggregation resulting in acute arterial hypertension, thrombosis, and accelerated atherosclerosis [11,12]. Similar to stimulants, marijuana also exerts its effect via increased sympathetic stimulation and depression of the parasympathetic system [13]. Analgesic properties of marijuana and opioids can lead to decreased awareness about cardiovascular symptoms, thus delaying the presentation of the patient to the hospital. Cigarette smoking has been acknowledged to generate oxidative stress on the arterial wall and also promote thrombus formation [14]. Researchers are also exploring the impact of advanced and effective nicotine delivery devices, popularly known as e-cigarettes, on cardiovascular health [15,16].

In the past decade, increased trends have been observed in the consumption of marijuana and methamphetamine, thus leading to increased mortality and morbidity among these substance users. Incidentally, a slight decrease in the use of cocaine was noted in the young patient population [2]. Complications of SUDs are preventable and reversible. Thus, American Heart Association (AHA) advises taking a detailed drug history in young patients presenting with cardiovascular events. This study is being conducted to see the point prevalence of various substance use in the population of age 12 years and older and with a positive history of cardiovascular events like myocardial infarction, angina, and coronary heart disease.

Materials And Methods
Study population
A retrospective cross-sectional study using the National Health and Nutrition Examination Survey (NHANES) database from 2013 to 2018 was performed. The datasets were downloaded from the NHANES website and combined using SAS software (Version 9.4). We included participants aged 12 years and older and identified respondents with a positive history of cardiovascular disease (CVD: myocardial infarction, angina, coronary heart disease, congestive heart failure). Sociodemographic variables such as age, gender, race, and annual household income were included. We excluded participants with missing information on age, race, cardiovascular disease, and smoking. We collected information on self-reported substance use (methamphetamine, cocaine, heroin, marijuana/hashish, injectable steroids, smoking [cigarette, cigar, smokeless tobacco, and e-cigarette]) from our study population. Patient characteristics of interest included: age (12-18, 19-45, 46-65, and 65 and older), gender (male and female), race (Mexican American, other Hispanics, Non-Hispanic White, Non-Hispanic Black, Non-Hispanic Asian, Other Race - Including Multi-Racial), concomitant diagnoses (hypertension, diabetes, hypercholesterolemia, obesity) and annual household income (AHI). Tables 4 and 5 in the appendix describe the definitions for the various concurrent conditions and the relevant questionnaire utilized for this study.

Details about the dataset
NHANES is a population-based, cross-sectional survey administered by the Centers for Disease Control and Prevention (CDC) to evaluate the health of children and adults in the USA. NHANES datasets are released in two-year cycles and utilize a multistage probability sampling design to create a national representative sample for each cycle. The sampling designs and protocols of NHANES are assessed by the US Department of Health and Human Services and approved by the National Centre for Health Statistics Research Ethics Review Board every year. The NHANES surveys comprise demographic, socioeconomic, dietary, laboratory, and health-related questions. The examination component includes medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel. The datasets are available on the CDC website https://www.cdc.gov/nchs/nhanes/about_nhanes.htm. The information on datasets and user guide resources are available on the NHANES website. Since the data is de-identified,
informed consent or IRB approval was not required.

Outcomes

The primary outcome of this study was to evaluate the prevalence of various SUDs amongst respondents diagnosed with CVDs in NHANES datasets between 2013 to 2018. The secondary aim was to find an association between the use of different substances and CVDs.

Statistical analysis

We analyzed the datasets using Statistical Analysis System (SAS) software (Version 9.4). We performed univariate analysis to find demographic characteristics of respondents with CVDs and the association between CVDs and substance use using an unpaired student’s t-test, Mann-Whitney test, and chi-square test. Mix effect multivariable logistic regression models were generated to predict the odds of the presence of different substances amongst respondents with CVDs. The sample size was not pre-decided, and a p-value of <0.05 (alpha criteria) was considered statistically significant. Models were adjusted with demographics (age, gender, race, AHI) and comorbidities (hypertension, diabetes, hypercholesterolemia, obesity). Areas under the receiver operating characteristic curve (ROC) (c-value) for individual models were calculated.

Results

Population and disease characteristics

From 2013 to 2018, we have identified 263465 respondents with mentioned details on CVDs. Out of these, 20821 (7.90%) respondents had a medical history of CVDs (angina [2.71%] and MI [4.51%]). History of CVDs were more prevalent amongst the population with age group of 66 and above (63.44% vs. 22.68%), male gender (62.23% vs. 45.98%), non-Hispanic White race (54.47% vs. 38.13%), and AHI less than $24,999 (41.80% vs. 25.94%) in comparison to respondents without a history of CVDs (p<0.0001). Respondents with a history of CVDs were found to be older (median age: 69 vs. 50-years old), 66-years and above (19.36% vs. 6.81% [46-65 years] vs. 1.17% [18-45 years]), male (10.40% vs. 5.66% [female]), non-Hispanic White (10.92% vs. 7.69% [other Hispanic] vs. 6.78% [Mexican American]), and with AHI less than $24,999 (12.21% vs. 4.01% [> $100,000]). (p<0.0001) Concurrent history of hypertension (85.98% vs. 79.53%), hypercholesterolemia (68.78% vs. 34.54%), diabetes (37.86% vs. 12.70%), stroke (17.4% vs. 2.71%), and congestive heart failure (28.80% vs. 1.31%) were more prevalent amongst respondents with a history of CVDs in comparison to respondents without a history of CVDs (p<0.0001) (Table 1).
TABLE 1: Demographic characteristics of respondents with cardiovascular disorders (NHANES years 2013-2018)

AHI: Annual Household Income; COPD: Chronic obstructive pulmonary disease; LDL: low-density lipoprotein

*Calculated by NIH equation 2 (mg/dl);

#Column percentage comparison from SAS output

Prevalence of substance abuse amongst respondents with CVDs

Using marijuana (CVD vs. no-CVD 65.42% vs. 52.81%; p<0.0001), cigarette smoking (60.47% vs. 40.41%; p<0.0001), cigar-smoking (47.05% vs. 35.58%; p<0.0001), methamphetamine/cocaine/heroin (23.82% vs. 16.71%; p<0.0001), smokeless tobacco use (18.53% vs. 14.59%; p<0.0001), injectable illegal drug use (4.67% vs. 2.43%; p<0.0001) cigarettes without filters (2.28% vs. 1.10%; <0.0001) were prevalent amongst the respondents with a history of CVDs when compared with respondents without a history of CVDs (Table 2).
| Substance                        | Cardiovascular Disorder n= 20821 (7.90%) # | No-Cardiovascular Disorder n= 242644 (92.10%) # | Total n=263465 (100%) | p - value |
|---------------------------------|---------------------------------------------|-----------------------------------------------|------------------------|-----------|
| Methamphetamine/Cocaine/Heroin (%) | 2304 (23.82)                                | 31914 (16.71)                                 | 34218 (17.05)          | < .0001   |
| Alcohol use disorders (%)       | 3427 (31.01)                                | 76207 (48.07)                                 | 79634 (46.96)          | < .0001   |
| Marijuana or hashish (%)        | 2673 (65.42)                                | 79458 (52.81)                                 | 82131 (53.14)          | < .0001   |
| Injectable illegal drug use (%) | 452 (4.67)                                  | 4647 (2.43)                                   | 5099 (2.54)            | < .0001   |
| Cigar smoking (%)               | 6620 (47.05)                                | 55688 (35.58)                                 | 62308 (36.53)          | < .0001   |
| Smokeless tobacco (%)           | 2607 (18.53)                                | 22835 (14.59)                                 | 25442 (14.91)          | < .0001   |
| E-cigarette (%)                 | 2177 (15.47)                                | 26731 (17.08)                                 | 28908 (16.95)          | < .0001   |
| Cigarette smoking (%)           | 12591 (60.47)                               | 98044 (40.41)                                 | 110635 (41.99)         | < .0001   |
| Cigarette Filter type - No (%)  | 81 (2.28)                                   | 405 (1.10)                                    | 486 (1.21)             | < .0001   |
| Cigarette Filter type - Yes (%) | 3476 (97.72)                                | 36320 (98.90)                                 | 39796 (98.79)          | < .0001   |
| Number of cigarettes smoked per day | 10 (5-20)                                   | 8 (4-15)                                      |                        | < .0001   |

TABLE 2: Prevalence of substance abuse amongst respondents with Cardiovascular Disorders
#Column percentage comparison from SAS output

Multivariable regression analysis showing the relationship between CVDs and substance abuse

After adjusting for socio-demographics (age, race, gender, and AHI) and concurrent comorbidities (hypertension, diabetes, hypercholesterolemia, obesity, and stroke), marijuana or hashish (aOR: 1.98; 95% CI: 1.98-1.98), injectable illegal drug use (aOR: 2.15; 95% CI: 2.14-2.15), cigarette smoking (aOR: 1.55; 95% CI: 1.55-1.55), were associated with higher odds of CVDs in comparison without substance abuse (Table 3).
| Substances                        | Odds ratio (OR) | 95% Confidence interval (95%CI) | p-value |
|----------------------------------|-----------------|---------------------------------|---------|
| Alcohol use disorders (1 vs. 0)  | 1.17            | 1.17-1.17                       | < .0001 |
| Marijuana or hashish (1 vs. 0)   | 1.98            | 1.98-1.98                       | < .0001 |
| Injectable illegal drug (1 vs. 0)| 2.15            | 2.14-2.15                       | < .0001 |
| Cigarette smoking (1 vs. 3)      | 1.55            | 1.55-1.55                       | < .0001 |
| E-cigarette (1 vs. 0)            | 2.61            | 2.61-2.61                       | < .0001 |
| **c - value**                    | **0.69**        |                                 |         |

**TABLE 3: Multivariable logistic regression analysis showing an association between substance abuse and cardiovascular disorders**

The model was adjusted for socio-demographics (age, race, gender, and annual household income) and concurrent comorbidities (hypertension, diabetes, hypercholesterolemia, obesity, and stroke).

**Discussion**

Multiple risk factors have been identified to be associated with CVDs. Our study has established an association with methamphetamine, cocaine, heroin, injectable illegal drug use, cigar-smoking, cigarette smoking, and cigarette smoking without filters. When compared to patients with non-premature atherosclerotic cardiovascular disease (ASCVD), patients with premature ASCVD had a higher prevalence of all recreational substance use, with female users having a greater risk of premature ASCVD compared with male counterparts. Among all illicit drugs, the use of amphetamines and cannabis were found to have the greatest odds of early-onset ASCVD [17]. In terms of gender, race, household income, and comorbidities, as shown in our study, there were various contributions indicative of a relative correlation amongst substance users.

As per the latest NSDUH compiled by the Substance Abuse and Mental Health Services Administration, among people aged 12 or older in 2019, 57.2 million people were reported to have used illicit drugs in the past year. Interestingly, marijuana was found to have been used by 48.2 million people in the year 2018. Per the same survey, in 2019, among people aged 12 years or older, 60.1% responded to having used a substance during the prior month, where alcohol was found to be more frequently consumed (50.8%), followed by use of tobacco (21.1%), and illicit drugs (15%) [2]. Across all age groups, prevalence rates of alcohol, tobacco, and marijuana use were noted to be higher when compared to other SUDs. While the prevalence rates of marijuana were higher than tobacco in the early adolescent population, it was noted to be reversed in the late adolescent population [18]. Overall, different age groups experienced different effects of SUDs concerning vascular events.

This retrospective cross-sectional study evaluated the prevalence of different SUDs amongst the population with a history of CVDs and the association of substance use with CVDs. We found that prevalence rates of CVD are higher in the cohort with a history of previous or current SUDs when compared to those who did not have any SUDs. A longitudinal record linkage study done by Thylstrup et al. stated that 828 individuals (4.53%) had a history of CVD at treatment entry out of the 17,642 patients seeking treatment for drug use disorder. And of the remaining 16,820 patients, 1535 were traced and found to be new incident cases of CVD during a mean follow-up time of 7.5 years [19].

With advancing age, the history of CVDs is more prevalent. Markedly the prevalence of CVDs is doubled in the age group 66 and above when compared to 45-65 years age group respondents (62.3% vs. 37.77%). Prevalence rates for CVD are higher among the non-Hispanic white population. This is contradictory to findings observed in a comprehensive examination of cardiovascular disease in Hispanics in the USA by Rodriguez CJ et al. [20]. In 2010, the American Heart Association declared 2020 health strategy goals to reduce deaths attributable to CVDs and stroke by 20% and to improve the cardiovascular health of all Americans by 20% by focusing on seven key risk factors: smoking, BMI, diet, physical activity, blood pressure, blood glucose, and total cholesterol [21]. Hispanics, especially female Hispanics, are significantly less aware of CVDs as the leading cause of death and their risk factors for CVDs compared to Non-Hispanic Whites [22]. Hispanic groups are more likely to be uninsured, have low socioeconomic status, and have poor education causing less access to health care and reporting [23]. Therefore, the above-mentioned factors could be the reason to have lesser prevalence rates of CVD in Hispanic Whites compared to non-Hispanic Whites. We also found hypertension to be the most common risk factor associated with CVD. Amongst the responders with CVDs, use of marijuana and cigarette smoking were more prevalent, followed by methamphetamine, cocaine, heroin, and injectable illegal drug use. According to a study done by Azofeifa et
al., between 2002 and 2014, there was a 455% increase in marijuana consumption among U.S. adults in the age group of 55-64 and a 333% increase in those older than 64 years, who are the utmost at-risk population for cardiovascular events [24]. A multi-center study done by Mittleman et al. showed that the risk of myocardial infarction onset was elevated 4.8-fold (95% CI, 2.9-9.5; p-value<0.001) within the first hour after smoking marijuana [25].

A retrospective study conducted by Jivanji et al. using the Behavioral Risk Factor Surveillance System (BRFSS) database of the year 2017 showed that odds of having CVDs were significantly high among the users of marijuana when compared to those who did not use marijuana. Furthermore, it was found that higher BMIs, lower income, no exercise, tobacco use, alcohol use, and depression all had a significantly higher prevalence of CVDs among marijuana users [26].

The incidence of cardiovascular disease was twice in the respondents with history of cigarette smoking without filters when compared to the patients with a history of cigarette smoking with filters (16.67% vs. 8.75%; p-value = <0.0001). Smoking is responsible for 14000 deaths annually from premature cardiovascular diseases. It has been established by previous studies that the introduction of filter use might have been associated with less cardiovascular event risk [27]. However, some studies have shown that there were no statistically significant results on the risk of CVDs and/or mortality among the population smoking cigarette with and without filters [26-30]. A cross-sectional survey reported a smoking prevalence of 77% among patients getting treatment for substance use problems [31]. Smoking can contribute to cardiovascular disease by the formation of atheromatous plaques and thrombosis [8,27]. A decline in the rate of recurrent myocardial infarction, recurrent congestive heart failure, and recurrent cardiac arrest after smoking cessation was evident in previous studies [32].

Our study is a large, nationwide population study covering from 2013 to 2018, which included the prevalence of various substance use and its association with cardiovascular disorders in a single study. However, our study has limitations corresponding to recall bias, no data on follow-up, or level of severity of the disease. The study also did not consider abuse details like duration and amount of intake. Hence, more research is required to identify the role of substance use in causing cardiovascular disorders.

**Conclusions**

Multiple risk factors have been identified with cardiovascular diseases. Our study has established an association with methamphetamine, cocaine, heroin, injectable illegal drug use, cigar-smoking, e-cigarette smoking, and cigarette smoking without filters. Hence, it is necessary to do further studies to access the risk of CVDs in the population using these substances. According to the American College of Cardiology and American Heart Association (ACC-AHA) guidelines, cigarette smoking is a vital independent risk factor for atherosclerotic cardiovascular disease and premature death. There is a need for further research to address the use of filters as a risk factor for CVDs in the high-risk population (i.e., in patients with a history of hypertension and diabetes).

Many complications of substance use disorders are preventable and reversible; it is very crucial to screen for these in patients with cardiovascular disease. All physicians must recognize the rise in cardiovascular events over the past decade and remain alert in counseling their patients accordingly. It is important to bring awareness among the general population as it is the first step toward the prevention of any disease. Strict guideline on the legalization of substance usage and accessibility is necessary.

**Appendices**

**Table 4**
| Demographic variables/Questionnaire | Description |
|-----------------------------------|-------------|
| RIDAGEYR                          | Age in years at screening |
| RIAGENDR                          | Gender |
| RIDRETH1                          | Race/Hispanic origin |
| INDHHIN2                          | Annual household income |
| WHQ030                            | How do you consider your weight |
| DIQ010                            | Doctor told you have diabetes |
| BPQ080                            | Doctor told you high cholesterol level |
| BPQ020                            | Ever told you had high blood pressure |
| ALQ111                            | Ever had a drink of any kind of alcohol |
| DUQ200                            | Ever used marijuana or hashish |
| DUQ250                            | Ever use any form of cocaine |
| DUQ290                            | Ever used heroin |
| DUQ330                            | Ever used methamphetamine |
| SMQ910                            | Ever used smokeless tobacco? |
| SMQ621                            | Cigarettes smoked in entire life |
| SMQ900                            | Ever used an e-cigarette? |
| DUQ370                            | Ever use a needle to inject illegal drug |
| DUQ380A                           | Drugs injected - Cocaine |
| DUQ380B                           | Drugs injected - Heroin |
| DUQ380C                           | Drugs injected - Methamphetamine |
| DUD380F                           | Drugs injected - Steroids or other drugs |
| MCQ160b                           | Ever told had congestive heart failure |
| MCQ160c                           | Ever told you had coronary heart disease |
| MCQ160d                           | Ever told you had angina/angina pectoris |
| MCQ160e                           | Ever told you had a heart attack |
| MCQ160f                           | Ever told you had a stroke |

**TABLE 4: NHANES variables/Questionnaire utilized for our study and their Descriptions**
## TABLE 5: NHANES Questionnaire utilized for our study in regards to Cardiovascular Disorders (CVD) and Substance Use disorder (SUD)

SP: Sample Participant

### Additional Information

**Disclosures**

*Human subjects:* Consent was obtained or waived by all participants in this study. *Animal subjects:* All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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