Examination of Demographic Predictors, Risk factors and Utilization of Procedures in Stroke Inpatient Population with Cannabis Use Disorder

Rikinkumar S Patel1,2*

1Department of Psychiatry, Griffin Memorial Hospital, USA
2Department of Public Health, Arcadia University, USA

*Corresponding Author: Rikinkumar S Patel, Department of Psychiatry, Griffin Memorial Hospital, USA.

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Abstract

Objective: To evaluate the risk of comorbidities and adverse hospital outcomes in stroke patients with cannabis use disorder.

Method: We used Nationwide Inpatient Sample and identified 3636 young adults (18 - 35 years) with stroke using ICD-9-CM codes, 1807 cannabis users (CU) and 1819 non-CU. We used logistic regression model to generate odds ratios (OR).

Results: A higher proportion of CU were 26 - 35 years' age. African American male admitted for stroke had higher odds of comorbid cannabis use disorder. CU are more likely to have hypertension (OR 1.8) and psychiatric conditions like psychosis (OR 3.87) and alcohol abuse (OR 5.75). Thrombolytic therapy was utilized in 9% CU (vs 7% non-CU). There was about 148% higher use of endovascular/mechanical thrombectomy in CU compared to non-CU (P = .009).

Conclusion: We affirm that these findings indicate that CU had comparatively higher utilization of hospital resources due to a complex presentation at the time of inpatient admission for stroke. Further efforts to develop a collaborative care model for early diagnosis and treatment of cannabis use among the vulnerable population is necessary.

Keywords: Cannabis Abuse; Cannabis Dependence; Marijuana; Thrombolytic Therapy; Comorbidities

Abbreviations

CU: Cannabis Users; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; USG: Ultrasonography; OR: Odd Ratio; CI: Confidence Interval

Introduction

Stroke is the fifth leading cause of death in the United States after heart disease, cancer, chronic lower respiratory diseases and accidents. One out of every twenty deaths are due to stroke. Stroke is killing 140,000 Americans annually [1]. Every 40 seconds someone has a stroke and every four minutes a patient dies due to stroke in the United States. Stroke is a foremost cause of severe long-term disability in Americans and causes a financial burden of $34 billion annually [2].

In the United States, cannabis use is the second most commonly smoked substance after tobacco ranging from occasional recreational use to abuse. Marked increase of cannabis use was seen in teens aged 12 or older as the prevalence increased from 6.2% in 2002 to 8.3% in 2015. Cannabis use was most prevalent in young adults with 19.8% of persons aged 18 to 25, and only 6.5% of adults aged 26 or older were current cannabis users in 2015 [3]. As per the Drug Abuse Warning Network, the number of emergency department (ED) visits related to cannabis use have increased by 21%. There were 456,000 cannabis-related emergencies in the United States in 2011, which is much higher than the number of ED visits in 2009. During this ED visits, about 65% of the patients were male and 13% were in the age group of 12 - 17 years [4]. The total number of inpatient admissions with diagnosis of cannabis abuse or dependence over the period 2002 to 2011 was 2,833,567 (0.91% of total inpatient admissions) [3]. There exists an increasing trend of cannabis use with a prevalence of 0.52% in 2002 to 1.34% in 2011 (P < .001) [3].

The relationship between stroke and comorbid substance abuse has been often studied in detail. Despite the higher prevalence of cannabis use, research related to cannabis associated stroke is less studied. There exists a causal relationship between cannabis and stroke as cerebral ischemia develops within few hours of cannabis use, and also cannabis exposure provokes recurrent stroke and transient ischemic attack [5]. Some of the cerebrovascular effects induced by cannabis, like altered cerebral vasomotor function, cerebral vasospasm, and cerebral vasoconstriction may be the probable mechanisms for causing stroke in cannabis users [6]. Prior research studies have found that cannabis use increases the risk of stroke [4,7-9]. Furthermore, cannabis use increases risk for clinical symptoms and other negative outcomes [9-11].

No previous studies were conducted to the best of our knowledge to evaluate the demographic predictors of cannabis users in stroke inpatient population and the differences in health care utilization including diagnostic and treatment modalities. The purpose of this research is to study the relationship between cannabis use, demographic characteristics, comorbidities and healthcare utilization among hospitalized stroke patients.

Materials and Methods

Data Source

We conducted a nested case-control study, using the Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Study (NIS) database, sponsored by the Agency for Healthcare Research and Quality (AHRQ) [12]. NIS is the largest database of inpatient stays in the United States, and is known to be a valid and reliable data source for epidemiological estimates that involve inpatient care. The HCUP collects administrative data on hospital admissions and discharges in the form of the NIS.

We used the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to identify discharges with stroke as primary diagnosis and cannabis abuse/dependence as secondary diagnosis. Unique subject identifiers are used to conceal patient identity and prevent identification of multiple admissions for the same patient. Diagnostic and procedural information in the NIS are identified using the ICD-9-CM codes.

Inclusion Criteria

We analyzed the NIS database [12] from 2010 to 2014 to identify all patients (age 18 - 35 years) with a primary ICD-9-CM diagnosis code for ischemic stroke (433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.01, 434.11, 434.91, or 436) and secondary ICD-9-CM diagnosis code for cannabis abuse (304.30, 304.31, 304.32, 305.20, 305.21 or 305.22). Patients coded as "in remission" from cannabis abuse were excluded from our analysis to encourage the homogeneity of our sample. Cases were all patients (age, 18 - 35 years) with primary diagnosis for ischemic stroke and secondary diagnosis for cannabis abuse during the hospitalization. Comparison group included patients with primary diagnosis for ischemic stroke only and were matched upon severity of illness. We also performed a retrospective cohort analysis to derive a comparison cohort that had similar disease stage or morbidity as the cases.

Variables

Demographic variables examined in this study included age group (18 - 25 years, 26 - 35 years), gender (male or female) and race (Caucasian, African American, Hispanic and other). Based on existing literature, we identified suspected risk factors for stroke using ICD-9-CM diagnosis codes - alcohol abuse (291.0 - 291.3, 291.5, 291.8, 291.81, 291.89, 291.9 or 303.00 - 303.93, 305.00 - 305.03), depression (300.4, 301.12, 309.0, 309.1 or 311), diabetes (249.00 - 249.31, 250.00 - 250.33 or 648.00 - 648.04), hypertension (401.1, 401.9, 642.00 - 642.04, 401.0, 402.00 - 405.99, 437.2, 642.10 - 642.24 or 642.70 - 642.94), obesity (278.0, 278.00, 278.01, 278.03, 649.10 - 649.14, 793.91, V85.30 - V85.39, V85.41 - V85.45 or V85.54) and psychosis (295.00 - 298.9, 299.10 or 299.11).

The primary and secondary diagnoses had been identified at the date of admission whereas we recorded utilization of treatment modalities during the entire hospital stay. We identified treatment modalities for stroke using ICD-9-CM procedure codes - thrombolytic injection/infusion (99.10), endovascular/mechanical thrombectomy (39.50, 39.72 or 39.74), CT head (87.03), MRI brain (88.91), ultrasonography (USG) head/neck (88.71), USG heart/echocardiogram (88.72) and cerebral arteriogram (88.41).

**Statistical analysis**

All statistical analyses utilized Statistical Package for the Social Sciences version 23 (IBM, Armonk, NY, US) [13]. The incidence of stroke hospitalization among cannabis users and non-users was determined by searching all available primary diagnosis fields for the diagnosis of stroke. In these analyses, the Pearson Chi-square test was used for categorical data to compare characteristics of cannabis users (CU) versus non-cannabis users. Binomial logistic regression model was used to evaluate the demographic predictors and utilization of therapeutic procedures in CU versus non-CU (reference category). Separate models were run for each variable. We applied discharge weights in all regression models, and adjusted for medical and psychiatric risk factors as these disorders may account for some of the differences in hospital services utilization. As per the sample size and multiple comparisons of data, statistical significance was set a priori at < .01 for all analyses.

**Ethical approval**

Our database did not contain patients’ personally identifiable information. This study was exempted from Institutional Review Board of Arcadia University.

**Results and Discussion**

**Sample population characteristics**

Our study included 3636 inpatient admissions for stroke and consisted of patients between 18 and 35 years. About 80.1% patients were 26-35 years’ age and 54.6% males. In terms of racial distribution, the majority were Caucasian (47.1%) followed by African American (34%), and Hispanic (12.7%). The demographic characteristics of the study population per cannabis use is mentioned in table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-CU</th>
<th>CU</th>
<th>P value</th>
<th>Logistic Regression Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td><strong>Age at time of admission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 - 25 years</td>
<td>394</td>
<td>21.7</td>
<td>329</td>
<td>18.2</td>
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<td>26 - 35 years</td>
<td>1425</td>
<td>78.3</td>
<td>1478</td>
<td>81.8</td>
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<tr>
<td><strong>Gender</strong></td>
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<td></td>
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<td></td>
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<tr>
<td>Male</td>
<td>815</td>
<td>44.9</td>
<td>1163</td>
<td>64.4</td>
</tr>
<tr>
<td>Female</td>
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<td>55.1</td>
<td>644</td>
<td>35.6</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>956</td>
<td>54.2</td>
<td>684</td>
<td>39.8</td>
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<tr>
<td>African American</td>
<td>419</td>
<td>23.8</td>
<td>765</td>
<td>44.6</td>
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<tr>
<td>Hispanic</td>
<td>282</td>
<td>16.0</td>
<td>160</td>
<td>9.3</td>
</tr>
<tr>
<td>Other</td>
<td>107</td>
<td>6.1</td>
<td>108</td>
<td>6.3</td>
</tr>
</tbody>
</table>

**Table 1: Demographic characteristics of stroke patients by cannabis use.**

*The proportion between non-cannabis users and cannabis users was obtained using cross tabulation. Significant P value ≤ .01 at 95% Confidence Interval. The P values were obtained between non-cannabis users and cannabis users by using the Pearson Chi-Square (χ²) test. Odds Ratio and P values were generated using logistic regression model.*

*CU: Cannabis Users; OR: Odds Ratio; CI: Confidence Interval.*

**Demographic predictors of cannabis users in stroke inpatients**

About four-fifth of the stroke patients with cannabis use were young adults (26 - 35 years). When compared with non-CU, then age was not a significant predictor for CU among stroke patients. Majority of the CU were male (64.4%) and so males had higher odds for cannabis use compared to non-CU (OR 1.426). A higher proportion of CU were African American (44.6%) and they had two-fold higher likelihood of cannabis use compared to other races (OR 1.827).

Differences in risk factors

CU had higher mean number of chronic conditions compared to non-CU (6.06 vs 4.64; P < .001). Hypertension is the predominant risk factor in both the groups (40.5% CU and 32.1% non-CU), and CU had higher odds of hypertension compared to non-CU (OR 1.80). Also, obesity was seen in higher proportions of CU but diabetes was marginally higher in non-CU as shown in table 2. CU had higher odds of comorbid psychiatric conditions namely; psychosis (OR 3.869), alcohol abuse (OR 5.752) and depression (OR 1.266) compared to non-CU.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-CU</th>
<th>CU</th>
<th>P value</th>
<th>Logistic Regression Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N %</td>
<td>N %</td>
<td></td>
<td>OR 95% CI P value</td>
</tr>
<tr>
<td>Medical Risk factors</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>196 10.8</td>
<td>178 9.8</td>
<td>.357</td>
<td>.961 .556 - 1.661 .886</td>
</tr>
<tr>
<td>Hypertension</td>
<td>583 32.1</td>
<td>732 40.5</td>
<td>&lt; .001</td>
<td>1.800 1.073 - 3.021 .026</td>
</tr>
<tr>
<td>Obesity</td>
<td>180 9.9</td>
<td>230 12.7</td>
<td>.007</td>
<td>1.458 .858 - 2.479 .163</td>
</tr>
<tr>
<td>Psychiatric Risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>49 2.7</td>
<td>295 16.3</td>
<td>&lt; .001</td>
<td>5.752 3.269 - 10.120 &lt; .001</td>
</tr>
<tr>
<td>Depression</td>
<td>146 8.0</td>
<td>154 8.5</td>
<td>.588</td>
<td>1.266 .745 - 2.151 .382</td>
</tr>
<tr>
<td>Psychosis</td>
<td>51 2.8</td>
<td>146 8.1</td>
<td>&lt; .001</td>
<td>3.869 2.178 - 6.875 &lt; .001</td>
</tr>
</tbody>
</table>

*Table 2: Distribution of risk factors between cannabis users and non-users.*

The proportion between non-cannabis users and cannabis users was obtained using cross tabulation. Significant P value ≤ .01 at 95% Confidence Interval. The P values were obtained between non-cannabis users and cannabis users by using the Pearson Chi-Square (χ²) test. Odds Ratio and P values were generated using logistic regression model and were adjusted for age, gender and race.

CU: Cannabis Users; OR: Odds Ratio; CI: Confidence Interval.

Differences in utilization of therapeutic procedures

Cerebral arteriogram was utilized in higher proportion of non-CU, and also CU were less likely to be managed with cerebral arteriogram compared to non-CU, though the result was not statistically significant as shown in table 3. Thrombolytic therapy was utilized in 9% CU and 7% non-CU and after controlling the regression model for risk factors and demographics, CU were more likely to receive thrombolytic therapy as a part of inpatient management for stroke (OR 1.125; P = .671) but the result was not statistically significant. CU had more than two-fold higher odds of receiving endovascular/mechanical thrombectomy during hospitalization compared to non-CU (OR 2.477, P = .009).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-CU</th>
<th>CU</th>
<th>P value</th>
<th>Regression Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N %</td>
<td>N %</td>
<td></td>
<td>OR 95% CI P value</td>
</tr>
<tr>
<td>Utilization of procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT head</td>
<td>136 7.5</td>
<td>135 7.5</td>
<td>.991</td>
<td>.916 .528 - 1.592 .757</td>
</tr>
<tr>
<td>MRI brain</td>
<td>196 10.8</td>
<td>137 7.6</td>
<td>.001</td>
<td>.643 .377 - 1.099 .106</td>
</tr>
<tr>
<td>Cerebral arteriogram</td>
<td>340 18.7</td>
<td>221 12.2</td>
<td>&lt; .001</td>
<td>.710 .423 - 1.190 .194</td>
</tr>
<tr>
<td>USG head and neck</td>
<td>23 1.3</td>
<td>43 2.4</td>
<td>.012</td>
<td>1.372 .654 - 2.879 .403</td>
</tr>
<tr>
<td>Echocardiogram</td>
<td>613 33.7</td>
<td>663 36.7</td>
<td>.061</td>
<td>1.012 .612 - 1.674 .963</td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td>127 7.0</td>
<td>162 9.0</td>
<td>.027</td>
<td>1.125 .654 - 1.934 .671</td>
</tr>
<tr>
<td>Thrombectomy</td>
<td>21 1.2</td>
<td>55 3.0</td>
<td>&lt; .001</td>
<td>2.477 1.249 - 4.910 .009</td>
</tr>
</tbody>
</table>

*Table 3: Distribution of inpatient outcomes between cannabis users and non-users.*

The proportion between non-cannabis users and cannabis users was obtained using cross tabulation. Significant P value ≤ .01 at 95% Confidence Interval. The P values were obtained between non-cannabis users and cannabis users by using the Pearson Chi-Square (χ²) test. Odds Ratio and P values were generated using logistic regression model and were adjusted for age, gender and race, medical and psychiatric risk factors. CU: Cannabis Users; USG: Ultrasonography; OR: Odds Ratio; CI: Confidence Interval.

Discussion

This study analyzes the inpatient data from young adults admitted for stroke with versus without cannabis use disorder. The investigators disclose the demographic predictors of cannabis users among stroke inpatient population and the impact of comorbid cannabis use disorder on hospitalization outcomes and utilization of therapeutic procedures in stroke patients.

According to a study by Charilaou, et al. [3], the mean age of the hospitalized cannabis users was 35 years and 62% were male and Caucasian. Another study concluded that cannabis use was more prevalent among younger patients (25 - 34 years old), males and African Americans [14]. Our findings are consistent with this as majority of the CU in our study were in 26 - 35 years' age group and 64.4% were male. African Americans admitted for stroke have two-folds likelihood of comorbid cannabis use disorder.

Consistent with Wolff, et al. [15], cannabis-related strokes are seen in chronic or current cannabis users and in our study the admitted stroke patients had a secondary diagnosis of cannabis abuse or dependence. As per a Herning, et al. [16], chronic cannabis use is related to increased cerebrovascular resistance that is possibly due to pathologic changes in blood vessels or brain parenchyma. Thus, the cannabis users in this study had significant adverse inpatient outcomes. Few studies in the past had found that cardiovascular risk factors are prevalent in cannabis users. Jayanthi, et al. [17] conducted a study that showed increased levels of apolipoprotein C-III, which is a cardiovascular risk factor in cannabis users. In current study, medical risk factors like obesity and hypertension were seen in higher proportions of CU. Also, CU had higher odds of comorbid psychiatric conditions like alcohol abuse and psychosis compared to non-CU. CU had greater likelihood of comorbid depression but our results were not statistically significant and so partway support a previous study which concluded that cannabis use increases the risk of anxiety and depression [18].

Geller, et al. [11] recommended that an early diagnosis and immediate neurosurgical intervention of stroke based upon symptom complexity is very important to reduce morbidity and mortality rates in stroke. A key finding of this study is the differences in utilization of therapeutic procedures in stroke patients (CU versus non-CU). About 9% CU were managed by thrombolytic therapy for stroke admission compared to 7% non-CU. They had two-folds higher likelihood of being treated with invasive procedures like endovascular/mechanical thrombectomy compared to non-CU during hospitalization for stroke.

Limitations

The NIS is an administrative database and is short of a detailed clinical data necessary to make defined association between post-stroke outcomes in CU and non-CU. Furthermore, such studies are subject to selection bias due moderate sensitivity of diagnostic codes for stroke and cannabis use disorder. We could not validate for readmissions which add to the over-all sample inpatient population under study and there may have been underreporting of cannabis use as the ICD-9-CM codes entered in electronic health records may depend on insurance, billing and other external factors. Irrespective of these limitations, NIS provides an unparalleled population-based perspective on associations between stroke and cannabis use with methodical and temporal factors and provides a groundwork for future studies. NIS is subject to minimal reporting bias and potentially more reliable source as all patient information is coded autonomously of the physician. Nonetheless, this is the first study which systematically analyzes impact of cannabis use in the stroke inpatient population.

Conclusion

African American male admitted for stroke had higher likelihood of a co-diagnosis of cannabis use disorder. Among patients hospitalized for stroke, we observed CU differed significantly from non-CU in association of medical and psychiatric risk factors, and higher number of chronic comorbidities. The utilization of primary treatment modalities like thrombolytic therapy and thrombectomy was higher in CU. We affirm that these findings indicate that a co-diagnosis of cannabis use disorder may be a factor associated with higher utilization of hospital resources due to complex presentation at time of inpatient admission for stroke. Further efforts to develop a collaborative care model for targeting early diagnosis and treatment of cannabis use among young population is necessary.
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Bibliography


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