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Depression and its Association with Adverse Childhood Experiences in People with Substance Use Disorders and Comorbid Medical Illness Recruited during Medical Hospitalization

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Abstract

People who have experienced adverse childhood experiences (ACEs) are more susceptible to substance use disorder (SUD) and depression. The present study examined depression prevalence in hospitalized patients with SUD and examined the association of individual ACEs with major depression. Depression rates 3 months after discharge were also examined. Medical inpatients with SUD were recruited from Temple University Hospital. Depression was assessed using the

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Patient Health Questionnaire-9 (PHQ-9) at baseline and 3 months post-discharge. Participants were also assessed using an ACE scale at baseline. Of 79 baseline participants, 48% (38) had moderate to severe major depressive disorder (MDD) with PHQ-9 scores ≥ 15 . Among those with baseline MDD, 38% (9/24) continued to have MDD 3 months post discharge, and 42.9% (12/28) of those without MDD at baseline met criteria at 3 months. Sixty-three percent (50/79) of the participants reported 4+ ACEs at baseline. Two ACEs, Household Incarceration and Household Mental Illness, were significantly associated with having MDD at baseline and 3 months (adjusted mean PHQ-9 total score increase (SE) and p-value: 2.97(1.35), $p<.05$; 5.32 (1.37), $p<.005$, respectively). In this exploratory study, nearly half of medical inpatients with substance use disorder had moderate to severe major depression, with a similar percentage of participants having MDD as outpatients at 3 months. Approximately two thirds of participants reported four or more adverse childhood experiences at baseline. Inpatient medical hospitalization should be utilized as an opportunity to engage people with SUD in multidisciplinary treatment including psychiatric, trauma informed care, and substance abuse treatment.

Aims: People who have experienced adverse childhood experiences (ACEs) are more susceptible to substance use disorder (SUD) and depression. The present study examined depression prevalence in hospitalized patients with SUD and examined the association of individual ACEs with major depression. Depression rates 3 months after discharge were also examined.

Methods: Medical inpatients with SUD were recruited from Temple University Hospital. Depression was assessed using the Patient Health Questionnaire-9 (PHQ-9) at baseline and 3 months post-discharge. Participants were also assessed using an ACE scale at baseline.

Results: Of 79 baseline participants, 48% (38) had moderate to severe major depressive disorder (MDD) with PHQ-9 scores ≥ 15 . Among those with baseline MDD, 38% (9/24) continued to have MDD 3 months post discharge, and 42.9% (12/28) of those without MDD at baseline met criteria at 3 months. Sixty-three percent (50/79) of the participants reported 4+ ACEs at baseline. Two ACEs, Household Incarceration and Household Mental Illness, were significantly associated with having MDD at baseline and 3 months (adjusted mean PHQ-9 total score increase (SE) and p-value: 2.97(1.35), $p<.05$; 5.32 (1.37), $p<.005$, respectively).

Conclusions: In this exploratory study, nearly half of medical inpatients with substance use disorder had moderate to severe major depression, with a similar percentage of participants having MDD as outpatients at 3 months. Approximately two thirds of participants reported four or more adverse childhood experiences at baseline. Inpatient medical hospitalization should be utilized as an opportunity to engage people with SUD in multidisciplinary treatment including psychiatric, trauma informed care, and substance abuse treatment.

Keywords

Adverse Childhood Experience; Hospitalization; Major Depressive Disorder; Substance Use Disorder

1. Introduction

Substance use disorder (SUD) is estimated to affect 10.6% of individuals in the United States (Substance Abuse and Mental Health Services Administration, 2017) and patients

with SUDs experience both chronic and acute medical illness at a higher rate relative to the general population. SUDs are associated with complications in the cardiovascular, gastrointestinal, renal, pulmonary and the central nervous systems (Frishman et al., 2003a, 2003b; Stein, 1999). Individuals with SUD also tend to have limited access to medical care (Benjamin-Johnson et al., 2009; Heinzerling et al., 2006) frequently due to high rates of poverty, unemployment, and a lack of insurance (Wells et al., 2002). Patients with SUD use emergency services and are admitted to hospitals at disproportionately high rates (French et al., 2001; Rockett et al., 2005). In several studies, substance use disorders have been associated with elevated rates of medical hospital readmission. For example, a multicenter study of HIV-positive substance users found that 17.5% individuals had a hospital readmission within 30 days of initial hospital discharge (Nijhawan et al., 2019). The unique problems individuals with SUD experience make them a medically vulnerable and costly population, and finding methods to improve their care is an ethical and practical issue (Gelberg et al., 2000).

The comorbidity of depression and substance use contribute to readmission (Grant et al., 2004). Mental health disorders are common in the SUD population and major depressive disorder (MDD) affects approximately 24% of the SUD population (Miller et al., 1996) compared to approximately 6.6% among the general population (Kessler et al., 2003). Patients with affective disorders often have high rates of readmission that are heavily associated with substance use (Haywood et al., 1995). In a study of Florida Medicaid beneficiaries with a medical inpatient admission, individual risk factors for early readmission included drug and alcohol use disorder as well as major depression (Becker et al., 2017). Medical hospitalization and readmission are both frequent for patients with SUDs.

There are additional risks for individuals once they are hospitalized. MDD is endorsed at a disproportionate rate within the inpatient medical care population. A meta-analysis that included 10 inpatient studies and comprised 2592 patients indicated that 10 to 14% of inpatients met criteria for major depression (Katon & Schulberg, 1992). While these prevalence rates provide some insight into the complex relationship between depression and medical illness in medical inpatients, the prevalence rates for major depression in the substance abuse population with chronic medical illness has not been well studied, and there is limited data regarding this population. Further complicating the relationship between these factors is the inherent variability of prevalence rates within the hospitalized patient population, as different subgroups report differing rates of depression (Værøy et al., 2003). Individuals with SUD already have high rates of comorbid affective disorders, which make them particularly vulnerable to the reciprocal relationship between medical hospitalization and MDD. Analysis of this high-risk population will provide valuable data for the purposes of optimal patient care.

No studies have been performed as to whether there is a relationship between adverse childhood experiences and depression in the inpatient medical population with SUD, though existing literature suggests there is likely a strong association. Adverse childhood experiences (ACE) have been linked to increased health risks for alcoholism, drug abuse, depression, socioeconomic challenge, and chronic medical illness in adulthood (Corso et al.,

2008; Fuller-Thomson et al., 2016; Hughes et al., 2017; Lo & Cheng, 2007; Merrick et al., 2019). In their seminal study Felitti (et al.) found that 28.4% of individuals with 4+ ACEs used illicit drugs in their lifetime, compared with 6.4% of individuals who did not report ACEs (Felitti et al., 1998). Furthermore, people who experienced four or more ACEs had a 4- to 12- fold increased risks for alcoholism, drug abuse, depression, and suicide attempts, when compared to those with no ACEs (Felitti et al., 1998). Inpatients in a substance use treatment clinic who experienced childhood abuse had elevated risk of psychiatric disorders compared with individuals with no abuse history (Banducci et al., 2014).

The Specialized Community Disease Management (SCDM) study was designed to determine whether a specialized SUD transitional outpatient care intervention improved mental and physical health outcomes, compared to transitional care as usual for medical inpatients with SUDs. The current study is an exploratory sub-analysis of the SCDM project to determine the prevalence and persistence of major depression and relationship to adverse childhood experiences in this population. We hypothesize that there is a high prevalence of major depression in the medical inpatient population with SUD and that specific ACE indicators will predict increased risk of MDD in this population.

2. Methods

2.1 Participants and Procedures

The protocol was approved by the Treatment Research Institute (TRI, Philadelphia, PA) IRB. Temple University's IRB authorized TRI's IRB to serve as the IRB of record for this study.

Research participants were adult male and female inpatients who signed written informed consent and were recruited from the Temple University Hospital (TUH), an academic safety net hospital in Philadelphia, PA, who: 1) were diagnosed with congestive heart failure, pneumonia, acute myocardial infarction, chronic obstructive pulmonary disease, diabetes mellitus, end-stage renal disease, or had a previous medical hospitalization within the past six months regardless of medical condition, and 2) met criteria for a Substance Use Disorder by DSM-5 criteria. A total of 265 patients were screened, and 108 patients met eligibility criteria. One hundred patients then agreed to study participation. Of the 8 patients who were eligible but not enrolled, 2 patients were discharged from the hospital prior to enrollment consent, and 6 were not interested.

2.2 Treatment Groups

Participants were randomized to one of 2 groups, Treatment as Usual (TAU) (n=48) or Specialized Community Disease Management (SCDM) (n=49). The TAU group used Temple's standard "Advantage" transitional care program, in which a nurse navigator and a community health worker provided phone and in person support for 90 days post-discharge. Following discharge, the TAU team visited or called participants 1 to 2 times each week to help them problem-solve any adherence issues they had after their inpatient stay. These included medical issues, substance use disorder, access to psychiatric treatment, housing, nutrition, and other health supports. TAU participants were provided with referrals to mental

health and substance abuse treatment if requested but no treatment for these conditions were included as part of the TAU arm.

The intervention group consisted of participants randomized to the SCDM arm. The SCDM treatment arm incorporated three components; A) evidence-based continuing care strategy for risk monitoring and brief intervention, B) deployment of specialized peer community health workers, and C) novel health education communication tools developed through collaboration with patient and community stakeholders. The SCDM intervention lasted for 90 days and was administered by both (1) a clinical social worker functioning as a behavioral health consultant (BHC) trained in evidence-based brief intervention and brief treatment approaches, and (2) a certified peer recovery specialist (PRS). After enrollment the BHC conducted 1–2 brief intervention sessions (20–40 minutes) at bedside providing motivational enhancement treatment (MET) with targeted behavioral strategies, including providing various health communication materials. Following hospital discharge, the BHC conducted 15–20 minute follow-up phone calls with participants as a part of continuing care. Addressing medical care and deficits in housing and food was also provided by the SCDM arm. Mental health referrals were available, but mental health treatment was not part of the intervention. The research team was separate from the treatment team. Small incentives (\$10) were provided for participants who maintained contact with the research team to ensure adequate follow up.

2.3 Measures

2.3.1 Depression; Patient Health Questionnaire (PHQ-9).—Major depressive disorder (MDD) was assessed using the PHQ-9, a mood module from the Primary Care Evaluation of Mental Disorders (PRIME-MD) that is derived from DSM-IV criteria (Kroenke et al., 2001). The PHQ-9 has been shown to be valid in both clinical and general populations (Kroenke et al., 2001; Martin et al., 2006). The assessment yields a score ranging from 0 to 27, where higher scores are indicative of more severe depressive symptoms. The PHQ-9 was administered at baseline (i.e. during the inpatient hospitalization) and 3 months post discharge as an outpatient. PHQ scores 15 or greater were used to diagnose MDD. In the validation study by Kroenke and Spitzer, scores of 15 or greater had higher specificity for the diagnosis of MDD, and reflected moderate to severe MDD (Kroenke et al., 2001).

2.3.2 Adverse Childhood Experiences (ACE).—The ACE scale was administered at baseline, prior to any study intervention. The ACE was used to assess 10 types of childhood trauma: 1) physical abuse, 2) sexual abuse, 3) emotional abuse, 4) physical neglect, 5) emotional neglect, 6) witnessing domestic violence, 7) the presence of mental illness in the household, 8) the presence of substance abuse in household, 9) having an incarcerated family member, and 10) parental separation or divorce. These indicators were developed as a part of the Center for Disease Control- Kaiser Adverse Childhood Experiences Study, and have been shown to be related to negative physical and mental health outcomes (Felitti et al., 1998).

2.3.3. Covariates—Forced adjustments for age, gender and race were applied to all regression models.

2.4 Data Analysis

Data were expressed as frequencies and percentages for categorical variables, mean $\pm$ SD and/or median (interquartile range) for continuous variables by time points. Comparisons between TAU vs. SCDM were done using Student t test or Wilcoxon rank sum test for a continuous variable or Fisher's exact or Chi-square test for a categorical variable. Total/average PHQ score was independently analyzed to determine the prevalence of MDD at baseline and 3 months.

Mixed-effects linear regression or mixed-effects logistic regression/generalized estimating equation analysis was performed on the total PHQ score or its corresponding dichotomous indicator outcome version for MDD with post-hoc Tukey-Kramer multiple comparison adjustments to explore the relationship between adverse childhood experiences and depression while taking into account the longitudinal correlation in the outcome data. Regression models considered all 10 individual ACE variables, the total ACE score, and the dichotomized ACE Total (0–3 ACEs vs. ≥ 4 ACEs) as potential predictors. Whether an individual was African American or a different race as well as their education level was also considered. An insufficient sample of non-African American participants ($n=26$ at baseline) prevented individual analysis of other races. A stepwise variable selection procedure was utilized for determining a final mixed-effects regression model for the PHQ total score. These procedures selected only the most significant predictors for the relevant outcome variable into the final model while at the same time simultaneously adjusting for potential confounding variables such as treatment arm, time, arm*time, gender, and age since they were forced into the final regression model. The entry significance level was set at 0.25 while the stay significance level was generously set at 0.10 to make sure no important predictors would be missed in our model selection procedure. Treatment arm, time, and their interaction terms were forced into the final regression model, in addition to gender and age, for proper adjustments for potential confounding or effect modification. In case of missing items in either the PHQ or ACE data at baseline, a simple mean imputation was used to avoid having to drop such patients from data analysis using PHQ or ACE as long as at least 50% or more individual PHQ or ACE item scores were available from these patients. PHQ and ACE total scores were imputed this way for 8 and 7 patients at baseline, respectively. P-values less than 0.05 were considered statistically significant. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for all the data analyses.

3. Results

3.1 Participants

The analyses for the study focused on participants who had data at baseline for depression and adverse childhood experiences. One hundred participants provided informed consent, 97 participants were randomized to treatment arm. Participants that did not complete any portion of the ACE scale and the PHQ-9 were excluded ($n=21$). Of the remaining 79 participants, slightly over half (54%) were male and the mean (SD) age was 49.7 (10.8)

years (Table 1). Two thirds of participants primarily identified as African American (67%), while 19% identified as Hispanic, 16% as Caucasian, and 14% as either Multiracial/Other. One third endorsed alcohol use disorder and another third endorsed cocaine use disorder as their primary SUD.

At 3 months, 52 of the 79 participants were able to be located and were willing to continue study activities. Participants who dropped out of the study were not statistically different in regard to age, gender, race/ethnicity, depression, substance use disorder and study arm from the remaining participants at 3 months. Eight (10%) of the 79 participants who completed the PHQ at baseline had items missing from their responses, and on average completed 88% of the items. At 3 months, there were no missing responses from participants who completed the PHQ.

3.2 Prevalence of Depression at Baseline and 3 Months

At baseline, 38/79 participants (48%) had moderate to severe major depression with PHQ-9 scores 15 (Figure 1). Of the 52 participants who attended a 3 month follow-up (FU) visit, 9 (38%) of the 24 who had MDD at baseline continued to have MDD and 12 (42.9%) of the 28 who did not have MDD at baseline had MDD at follow-up. No significant differences in depression scores by treatment arm at baseline and 3-month follow-up were observed (Table 2).

3.3 Adverse Childhood Experiences

Almost all participants (91%) reported at least one ACE, and 63% reported four or more ACEs at baseline (Figure 2). Emotional abuse (66%), physical abuse (61%), and the presence of household substance use (67%) were the most commonly reported ACEs in our study population (Figure 3).

3.4 Association of Adverse Childhood Experiences and Depression.

Two ACEs, Household Incarceration and Household Mental Illness, were significantly associated with higher PHQ-9 depression scores at baseline and 3 months (adjusted mean PHQ-9 total score increase (SE) and p-value: 2.97 (1.35), $p=.03$; 5.32 (1.37), $p=.002$, respectively) (Table 2). The estimated increases were adjusted for treatment arm, time, gender, and age. No additional significant relationships were observed between depression and the other ACE indicators.

3.5 ACE total score and depression

ACE total score was also considered in the regression analyses but did not meet criteria for staying in the model to significantly predict total PHQ-9 score (i.e., $p>0.10$) and hence was dropped from the final regression model (Data not shown).

4. Discussion

This exploratory study analyzed the prevalence of moderate to severe major depression in an inpatient medical population with SUD. There are no prior studies that have examined the prevalence of major depression in medical inpatients with SUD. We found that nearly half

(48%) of our inpatient medical population with SUD had major depressive disorder at baseline and that more than one third (38%) of these individuals who participated in a 3-month study follow-up continued to meet MDD criteria. Although MDD prevalence abated among this group, nearly half (42.9%) of those without MDD at baseline had MDD at follow-up. These figures are higher than the figures are higher than the 24% prevalence in outpatients receiving SUD treatment (Miller et al., 1996). Our data also suggests that many inpatients with SUD and major depression meet MDD criteria months after hospital discharge, even with a transitional care intervention. The dual vulnerability from their medical illness requiring inpatient hospitalization and SUD puts them at high risk for continued MDD. Thus, it is important to screen for depression in patients with SUD and medical illness, both as inpatients, as well as during outpatient follow-up, given the high prevalence of depression in this population. Treatment for this population warrants further investigation for the purposes of learning more about the characteristics of depression over time and treatment response to optimize clinical care.

The most prevalent ACE in our medical inpatient SUD population was Household Substance Use (67%). The ACE of Household substance use in our study population was twice as prevalent as that reported in a study of incarcerated adults (32.7%) suggesting this is an extremely high risk population (Marotta, 2017). Preventive and treatment interventions targeted at the children living with adults with SUD could be a particularly cost effective intervention to prevent adult SUD and promote resilience and better decision making.

The high prevalence of adverse childhood experiences within our study population support prior literature which states individuals with SUD experience ACEs at a disproportionate frequency. Our results also align with prior data that indicate ACE scores are associated with an overall increase in major depression. Specifically, Household Incarceration and Household Mental Illness experienced as a child in this study were both significantly associated with the PHQ-9 total depression score and hence major depression during inpatient hospitalization and at 3 months. Interventions targeted at these two adverse experiences may be helpful in treating depression in this population. Individual and group psychotherapy targeted towards SUD populations with specific ACE experiences could be helpful in understanding past events associated with distress and changing coping methods and behaviors. Maladaptive stress mechanisms can be addressed before self-destructive behavior becomes chronic.

4.1 Limitations and Subpopulation:

Participants were recruited for a trial designed to determine whether SCDM could improve health outcomes for patients with SUD and chronic medical illness. The study had identified 588 inpatients with SUD, but a large number (169) refused to be screened for the study. Additionally, for others, medical complications prevented study participation (113) or there was a language barrier (112). Despite extensive efforts by study personnel, at the three-month follow-up one third of the participants were either unable to be located or did not want to continue study activities. The population with substance abuse and medical illness is an exceptionally challenging population to retain, and subsequent studies and interventions with this population will need to try novel methods to address retention.

The population in this current study was recruited from the Philadelphia area, predominately African American, and tended to have low levels of education. Gender differences were accounted for in the analyses, but no significant differences were found, likely due to a limited sample size. Race did not meet prespecified significance levels possibly due to insufficient sample size as well. The results of this study cannot be generalized to individuals of other racial backgrounds, individuals in dissimilar geographical regions, or highly educated populations with medical illness and SUD. Data on substance use, housing status, and services received during the three-month period between baseline and follow-up were not systematically collected. This would be valuable data to collect for a future study to determine how these factors may mitigate depressive symptoms in discharged inpatients.

Future studies could examine subgroups by primary SUD, as different subgroups may differ on which ACE is significant. These powered replicated studies could utilize the estimated regression coefficients and effect sizes (e.g., for subgroups on the significant ACEs) reported in the regression model table (Table 2).

5. Conclusion

The medical inpatient population with SUD has high rates of moderate to severe major depression when compared with other medical inpatients or those with SUD in the community or outpatients. Patients in this population with major depression in the hospital are likely to have major depression as outpatients three months later. Household Incarceration and household mental illness are adverse childhood experiences that are associated with an increased risk for moderate to severe major depression. Substance use, medical illness, adverse experiences in childhood and depression are interrelated variables that must be considered for comprehensive patient care. Integrating trauma informed care into ongoing SUD and medical treatment plans might be an effective strategy to treat depression and better address SUD in patients with chronic medical illness. Individualized efforts with a focus on harm reduction, not abstinence, and modest improvements in health care behavior with home-based combined behavioral and medical care might be an effective path to improved quality of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ACE PHQ Highlights

- Nearly half of medical inpatients with substance use disorder had moderate to severe major depressive disorder (MDD)
- Many participants with MDD at baseline continued to have MDD 3 months post discharge, and a large number of patients developed MDD between baseline and discharge
- Several Adverse Childhood Experiences (ACEs) were associated with higher PHQ-9 scores

Figure 1.

Prevalence of Depression by PHQ-9 category

Measure of major depression severity. Patient Health Questionnaire-9 (PHQ-9) scale was used to measure depression severity. High prevalence rates for moderate to severe depression were present among participants. At baseline, 48% of participants exhibited moderate to severe depression. At the 3 month follow-up, 40% of participants exhibited moderate to severe depression.

Figure 2.
Adverse Childhood Experience (ACE) Severity
ACE scores in hospitalized patients with comorbid SUD. At least one ACE was experienced by 91% of participants, and 63% experienced at least four or more.

Figure 3.

Percentage of participants who endorsed individual ACE indicators

Percentage ACE endorsement in hospitalized patients with comorbid SUD. Data is presented as percentage when an ACE is endorsed. (N=79)

Table 1.

Participant Demographics at Baseline and 3 months post discharge

	Baseline (N=79)	3 Months (N=52)
Gender		
Male	43 (54%)	28 (54%)
Female	36 (46%)	24 (46%)
Race		
African American	53 (67%)	35 (67%)
Caucasian	13 (16%)	7 (13%)
Race Other	11 (14%)	8 (15%)
Race Not Answered	1 (1%)	1 (2%)
More than One Race	1 (1%)	1 (2%)
Age		
Age, Mean (SD)	49.7 (10.8)	49.35 (10.0)
Age, Median (Range)	51.0 (23.0 – 76.0)	51.0 (26.0 – 76.0)
Ethnicity		
Hispanic	15 (19%)	11 (19%)
Not-Hispanic	63 (80%)	41 (79%)
Not Answered	1 (1%)	0 (0%)
Education		
No Degree	36 (46%)	25 (47%)
High School or GED	33 (42%)	21 (40%)
Associates/Bachelor's Degree	9 (11%)	5 (9%)
Refused	1 (1%)	1 (2%)
Primary Substance Use Disorder Attributed to Hospitalization		
Alcohol	33%	31%
Marijuana	9%	10%
Cocaine	32%	35%
Hallucinogens	1%	2%
Opiates	22%	19%
Others	3%	2%

Table 2:

Multiple Regression Mixed-Effects Model Results on The Total PHQ Using All Available Data (n=79 study subjects and 123 total observations at Baseline and 3 months at follow-up (FU))

Effects	β (SE)	p-value
Terms in Regression Model		
Arm (TAU vs. SCDM)	1.89 (1.49)	0.21
Time (3-month FU vs. Baseline)	-1.27 (1.84)	0.49
Arm*Time (TAU 3-month FU vs. Others)	-0.03 (2.47)	0.99
Gender (Male vs. Female)	0.43 (1.31)	0.74
Age	-0.12 (0.07)	0.08
Household Mental Illness: Yes vs. No	5.32 (1.37)	0.0002
Household Incarceration: Yes vs. No	2.97 (1.35)	0.03
Arm or Timepoint Comparisons of Interest		
Arm SCDM: 3-month FU vs. Baseline	-1.27 (1.84)	0.49
Arm TAU: 3-month FU vs. Baseline	-1.30 (1.64)	0.43
3-month FU: TAU vs. SCDM	1.86 (2.19)	0.40
Baseline: TAU vs. SCDM	1.89 (1.49)	0.21