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Association between Substance Use Disorders and Suicide Attempt: A Population-Based Case-Control Study

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Abstract

Background:

Suicide is an important global public health issue, with substance use disorders (SUDs) identified as one of the foremost contributors to suicide risk. With an increase in the evidence base and its evident associations, limited population-based data has existed from lower and middle income countries including Iran. The aim of this study was to investigate the independent association between SUD and suicide attempts in a large general population sample.

Methods:

We conducted a population based case control study utilizing integrated data from the Hospital Information System (HIS) and the Sina Electronic Health Record (SinaEHR) in Mashhad, Iran. We aimed to include all individuals who had evidence of a suicide attempt between 2017 and 2025 (n = 31214), alongside one control without any evidence of a suicide attempt captured in the same underlying population (n = 45871). Demographic, clinical and psychological variables were investigated through multivariable logistic regression, and adjusted odds ratios (AOR) with 95% CI were reported.

Results:

Substance use disorders appear as one of the strongest independent predictors of suicide attempt (AOR = 2.06, 95% CI: 1.91–2.21). Depression (AOR = 2.86), anxiety disorders (AOR = 2.83) and

bipolar disorder (AOR = 3.48) were also highly associated with elevated risk. Exposure to domestic violence nearly tripled the odds of suicide attempt (AOR = 2.96). Middle-aged adults (30 –59 years), unemployed individuals, students, males, and residents of metropolitan areas had significantly higher odds, whereas older age (≥ 60 years) showed a protective effect. Diabetes exhibited an unexpectedly strong association (AOR = 6.99).

Conclusion:

Our findings show that SUD is not just a secondary correlate but an important and independent driver of suicide attempts, which persist beyond what can be explained by mental disorders or socioeconomic considerations. To achieve effective prevention, suicide risk screening should be integrated in addiction services and interventions need to have a holistic approach targeting substance misuse, mental health problems as well as social adversity.

Keywords: Substance use disorders, Suicide attempt, Drug use disorders, Case control

1.Introduction

Suicide deaths exceed 720000 annually which makes it a major public health concern(1). The third leading cause of death among people aged 15 to 29 worldwide during 2021 was suicide(2). Suicide affects all regions of the world because it exists as a global health problem. The majority of worldwide suicide deaths occurred in low and middle income countries during 2021 because 73% of total suicides happened in these regions(3). The death of one person creates major social and emotional and economic consequences which affect families and friends and workplaces and entire communities throughout the world. The suicide death rate in Iran reaches 5.3 per 100,000 people with men experiencing twice the rate of women according to reports(4). The suicide attempt rates across Iran show significant differences between provinces because Hamadan and Kermanshah report 16.8 attempts per 100,000 people but Golestan Province has the highest rate at 117.8 per 100,000(5).

The diversity of prevalence rates, from 2 to 80 per 100000 people worldwide, illustrates that suicide mortality varies in its frequency and pattern as well as etiology by nation(6). Indeed, several interrelated biological, psychological, social and cultural factors are involved in suicide and their interactions can lead to suicidal behaviors in individuals(7). Mental disorders including depression, schizophrenia, substance-related disorders, personality disorder are chronic obstructive pulmonary disease (COPD), physical diseases such as hemodialysis cancer, AIDS anything malignant multiple sclerosis severe burns limb paralysis and congestive heart failure help in the risk of suicidal attempts and reattempts(8). Drug abuse, along with depression, is a significant risk factor for suicidal ideation and attempt as well as actual suicides. In addition,

chronic and heavy substance use can result in a substance use disorder (SUD), characterized by craving, impairment or distress, stable disruption of health and daily function, and an elevated risk for suicide(9, 10).

Multiple systematic reviews and meta analyses published recently demonstrate that SUD creates a direct connection with suicidal behaviors. Research shows that substance use including alcohol and tobacco and cannabis and cocaine and opioids and stimulants and inhalants and hallucinogens and sedative medications leads to higher suicide risk than staying substance-free(11, 12). Substance use increases the probability of developing or worsening mental health conditions including depression and anxiety and posttraumatic stress disorder and bipolar disorder and psychosis which results in elevated suicide risk. People who have mental health issues might use substances to manage their symptoms which makes their suicide risk even higher(13, 14).

In 2019, Mashhad University of Medical Sciences implemented a thorough registration system for suicide attempts within its Hospital Information System (HIS) for the first time. This system is directly connected to the existing electronic health record system at the primary care level known as SinaEHR(8). The HIS system tracks all suicide attempts through detailed records which include demographic data and attempt methods and mental health conditions and past attempt history. The system adds this information to SinaEHR health records to create a complete medical history for each patient. The system operates through all government hospitals and health centers to establish a wide network for data acquisition. The SinaEHR system implements standardized reporting protocols from WHO guidelines to enhance data consistency and enable better comparison between different regions of the country(4). The extensive nature of this new registration system has created remarkable opportunities for conducting in depth research in sociology in Iran. As a result, this population based case-control study has been developed to explore the relationship between substance use disorder and suicide attempts, while controlling for the impact of confounding variables in the general population.

2.Material and Methods

2.1. Study settings, design and data collection

We carried out a population based case control study with using the Sina Health Information System (SINAEHR) and the Hospital Information System (HIS) in Mashhad, Iran. The study included 31214 cases who attempt to suicide between March 1, 2017, to October 20, 2025. For each case, a control without any history of suicide attempt was randomly selected from the same population. the Sina Electronic Health Registration System (SinaEHR) database and the Hospital Information System (HIS), both operating under the supervision of Mashhad University of Medical

Sciences, Mashhad, Iarn. These sources provided comprehensive information about individuals referring to Mashhad's government hospitals for suicide attempts. Mashhad University of Medical Sciences, has 55 hospitals. Of these, 33 are government hospitals fully covered by our study, while 22 are private hospitals not included in our data collection. The 33 government hospitals account for approximately 70% of all hospital admissions. These two systems (SinaEHR and HIS) communicated with one another using the national code as a unique identifier for each individual. This study used a census approach to include all eligible cases, defined by documented suicide attempts among residents covered by Mashhad University of Medical Sciences. Cases were excluded if documentation was incomplete or inconsistent, the attempt occurred outside the designated timeframe or if nonresidents were admitted to Mashhad hospitals. We excluded fewer than 5% of total cases of suicide attempts based on these criteria.

2.2. Study variables:

Outcome variable: A suicide attempt was defined as a suicide attempt, and the diagnosis of Suicide attempt cases met the criteria of the ICD-10 code from "X60" to "X84". Data about substance abuse were gathered predominantly in the context of a medical examination during hospital admission. The information on substance abuse was recorded by the ICD-10 codes F10-F19. Demographic factors as gender, age, place of residence, marital status, occupation, education; Clinical factors as underlying diseases, focusing on high blood pressure and diabetes, mental disorders; Contextual factors as domestic violence experienced were determined in some variables. These variables were considered either as a risk of suicide attempt or protective factor on the basis of the literature. The Hurt, Insult, Threaten, Scream domestic violence, and screening tool HITS, were used gauged for the experience of domestic violence was assessed by using HITS. The HITS scale included four items that were measured on a five point Likert type scale from 1 to 5 points. Total HITS scores range from 4 to 20, with scores of 10 or higher implying a risk of domestic violence, a tool validated for research among Shiraz families(15). Psychological Disorder including depression (ICD-10: F32, F33), anxiety disorders (F41, F43), bipolar disorders ([F30, F31], F34), epilepsy disorder (G40, G41) and other disorders (F42, F44, F45, F50, F52, F40, F95, F84, F90, F91, F70-F73, T40, T51, F53, F20, F22, F23, F25). We used the International Classification of Diseases (ICD-10) codes registered in both the Sina and HIS systems to identify suicide attempts (X60-X84), completed suicides (X70-X84), high blood pressure (I10, I15), and diabetes (E10, E11). Suicide attempts were grouped using ICD-10 codes X60 to X84.

2.3. Measurement tool:

Three scales have been used in this study. The Kessler scale was used for psychological problems, the Edinburgh scale was used to measure depression, and the scale of Sherin et al. was used to estimate domestic violence (HITS test).

The brief HITS questionnaire was created by Sherin et al. (family doctor in America) to quickly screen for domestic violence. This tool includes 4 questions that address verbal and physical abuse. Each question provides 5 response options, where the lowest score possible is 1 and the highest score is 5, resulting in a total score range from 4 to 20. A score exceeding 10 indicates a positive result, confirming the presence of violence(16).

The Kessler emotional well-being scale included six items, capturing levels of restlessness, depressed affect, hopeless about the future, that everything is an effort and was worth it; difficulty concentrating on everything and anxiety. This instrument used a five-point scale (yhe options are: 0 “never” and 4 “very frequently”). The total score is obtained by summing the scores of individual items (range from 0 to 24). Scores of 12 or higher are considered positive.(17)

2.4. Sampling technique and procedure:

The sample size was determined by including all individuals who met the study’s inclusion criteria in the SINAEHR database during the defined period. All patients with a confirmed diagnosis Suicide attempt cases were classified according to the ICD-10 classification from codes X60 to X84 at university affiliated medical centers were included in the case group. For each case, a control was randomly selected from the same population base, ensuring they had no history of Suicide attempt.

2.5. Statistical analysis:

The data were coded and initially organized in Microsoft excel whilst the final data set for analysis was exported to Stata version 16. Baseline variables were summarized using descriptive statistics, that is, frequencies and percentages for categorical variables and means with standard deviations (SD) for continuous variables in the case-control groups.Bivariate associations between Substance use disorders and risk of suicide attempt were assessed using chi-square tests. Variables found to be statistically significant in bivariate analysis were subsequently included in a univariate logistic regression model. Those that remained significant were then entered into a multivariate logistic regression model to control for potential confounders. The final model reported adjusted odds ratios (ORs) with 95% confidence intervals (CIs), reflecting the independent Association between Substance use disorders and risk of suicide attempt.

3.Results

This investigation mainly centered around people among which 31214 cases of attempted suicide were traced and 45871 controls with no history of suicide attempts were identified. (figure1)

Table 1 shows that the distribution of demographic characteristics of the case and control groups varied significantly ($p < 0.001$ for all variables). The analysis points out that more than half of the suicide attempters were young people below 30 years that 54.4% were ≤18 years and 35.4% 18–29 years while the majority of the controls were 30 years or older. Females comprised a slightly higher proportion among cases (56.6%) compared with males (43.4%) whereas the control group included more females (62.9%) than males (37. 1%).Regarding marital status, 59.4% of cases were single and 28.7% were married, while 71.3% of controls were married. Occupation also varied significantly between groups. Students (66.4%) and unemployed individuals (52.4%) had higher representation in the case group, whereas housewives (75.5%), workers (83.3%) and employees (72.9%) were more frequent in the control group. Educational attainment showed a clear gradient. Participants with only primary education were predominant among cases (61.4%) compared with controls (38.6%), while those with a diploma (15.8% of cases vs. 84.2% of controls) or higher education (38.8% vs. 61.2%) were more common among controls. Place of residence also differed notably. Rural residents constituted 75.9% of cases compared to 24.1% of controls while urban/metropolitan residents were more prevalent in the control group ($p < 0.001$). (Table1)

And Clinical and behavioral variables also showed significant differences. Substance use disorder (SUD) was 13.8% vs 7.7% ($p < 0.001$). History of smoking was more in cases (47.7%) than controls (52.3%, $p < 0.001$). Among chronic conditions, diabetes mellitus (cases: 47.2% vs controls: 52.8%) and hypertension (cases: 7.8% vs controls: 92.2%) showed significant differences though the direction of association varied. Mental health related variables showed a big difference. Anxiety disorders was 17.5% in cases vs 11.0% in controls. Depression was 19.4% in cases vs 11.6% in controls. Bipolar disorder was 0.8% in cases and 0.2% in controls. Epilepsy was 1.0% in cases vs 0.6% in controls. Exposure to domestic violence was more in cases (56.0%) than controls (44.0%, $p < 0.001$). (Table1)

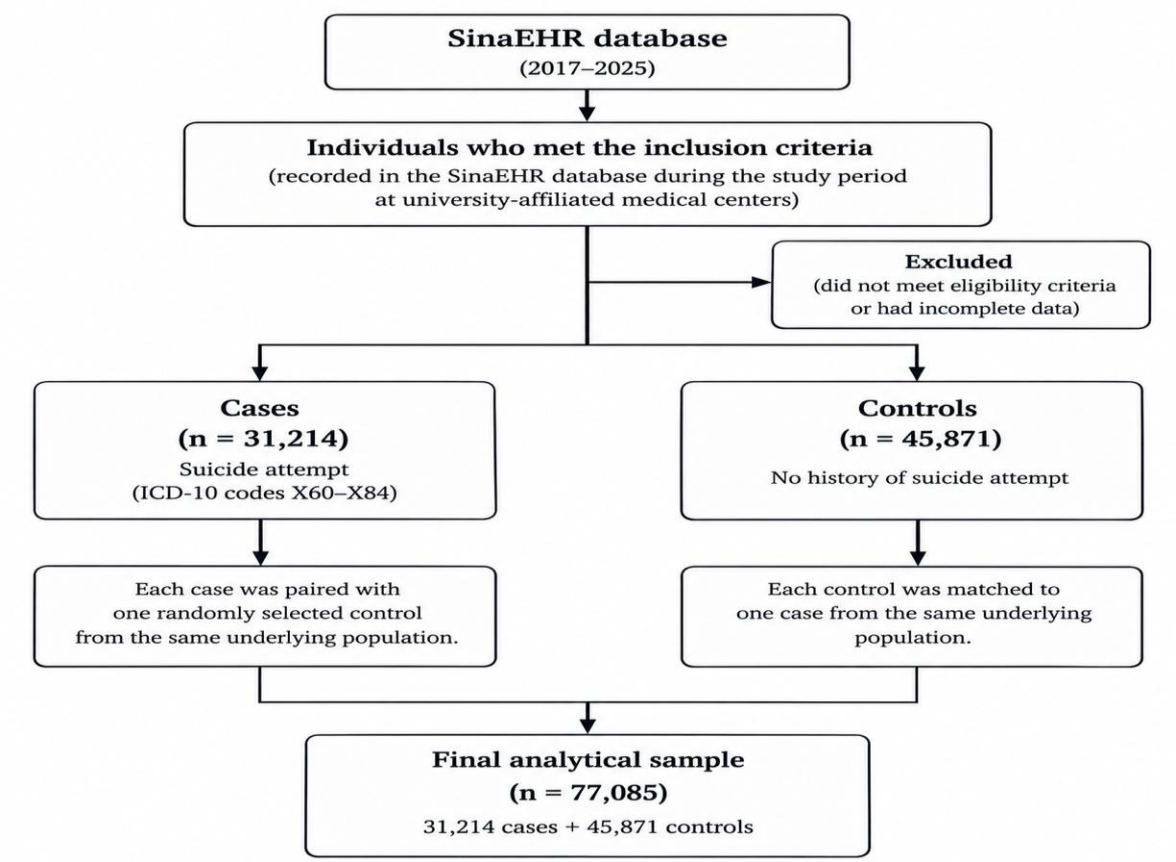


Figure 1. Flowchart of Participant Selection and Sampling Procedure

Table 1. Baseline demographic and clinical characteristics of participants by suicide attempt status (case–control groups)

Variables	**Case**(n=31214) **Freq(%)**	**Control**(n=45871) **Freq(%)**	**P value***
Age			
18≤	7893(54.4)	6627(45.6)	<0.001
18-29	10990(35.4)	20083(64.6)	
30-59	11197(52.00)	10352(48.00)	
60≤	1134(11.4)	8809(88.6)	
Gender<,			
Female	17682(38.00)	28809(62.00)	<0.001
Male	13532(44.2)	17062(55.8)	
Marital status			
Single	17589(59.4)	12003(40.6)	<0.001
Married	13625(28.7)	33868(71.3)	
Occupation			

Housewife	6069(24.5)	18719(75.5)	<0.001
Student	6976(66.4)	3532(33.6)	
Self-employed	2925(50.00)	2922(50.00)	
Unemployed	4179(52.4)	3793(47.6)	
Employee	799(27.1)	2153(72.9)	
Worker	1615(16.7)	8036(83.3)	
Other	8651(56.3)	6716(43.7)	
Level of Education			
Primary	8940(61.4)	5622(38.6)	<0.001
High school	12588(41.2)	17930(58.8)	
Diploma	1874(15.8)	10000(84.2)	
College graduate	7812(38.8)	12319(61.2)	
Place of Residence			
Rural	17461(75.9)	5548(24.1)	<0.001
Under 1 million inhabitants	6664(57.8)	4872(42.2)	
Suburb	13051(60.4)	8559(39.6)	
Metropolis	8695(41.5)	12235(58.5)	
History of Smoking			
No	24050(38.8)	38006(61.2)	<0.001
Yes	7164(47.7)	7865(52.3)	
History of Diabetes			
No	27254(39.7)	41441(60.3)	<0.001
Yes	3960(47.2)	4430(52.8)	
History of Hypertension			
No	30392(45.7)	36168(54.3)	<0.001
Yes	822(7.8)	9703(92.2)	
History of Hyperlipidemia			
No	30438(45.8)	36078(54.2)	<0.001
Yes	776(7.3)	9793(92.7)	
History of Substance use disorder			
No	26902(38.9)	42322(61.1)	<0.001
Yes	4312(54.9)	3549(45.1)	
History of Domestic violence			
No	30676(40.3)	45448(59.7)	<0.001
Yes	538(56.00)	423(44.00)	
History of Anxiety			
No	25749(38.7)	40842(61.3)	<0.001
Yes	5465(52.1)	5029(47.9)	
History of Depression			
No	25171(38.3)	40568(61.7)	<0.001
Yes	6043(53.3)	5303(46.7)	
History of Epilepsy			
No	30918(40.4)	45616(59.6)	<0.001
Yes	296(53.7)	255(46.3)	
History of Bipolar Disorder			

No	30968(40.4)	45767(59.6)	<0.001
Yes	246(70.3)	104(29.7)	
History of Other Mental Disorder			
No	30984(40.4)	45680(59.6)	<0.001
Yes	230(54.6)	191(45.4)	

* Chi-squared test

Table2: Logistic regression analysis of demographic factors associated with suicide attempt

Variable	**Categories**	**Univariate regression analysis**			**Multivariate logistic regression**		
		OR	95% Confidence interval	P-value	OR	95% Confidence interval	P-value
Age	18≤	1					
	18-29	0.45	0.44-0.47	<0.001	1.01	0.95-1.07	0.69
	30-59	0.90	0.87-0.94	<0.001	2.62	2.45-2.81	<0.001
	60≤	0.10	0.10-0.11	<0.001	0.20	0.17-0.22	<0.001
Gender	Female	1					
	Male	1.29	1.25-1.33	<0.001	2.50	2.37-2.64	<0.001
Marital status	Single	1					
	Married	0.27	0.26-0.28	<0.001	0.28	0.27-0.29	<0.001
Occupation	Housewife	1					
	Student	6.09	5.79-6.40	<0.001	3.30	3.07-3.55	<0.001
	Self-employed	3.08	2.91-3.27	<0.001	2.60	2.37-2.84	<0.001
	Unemployed	3.39	3.22-3.58	<0.001	2.68	2.48-2.89	<0.001
	Employee	1.14	1.05-1.24	0.002	1.00	0.89-1.12	0.97
	Worker	0.62	0.58-0.65	<0.001	0.36	0.32-0.39	<0.001
	Other	3.97	3.80-4.14	<0.001	3.75	3.53-4.00	<0.001
Level of Education	Primary	1					
	High school	0.44	0.42-0.46	<0.001	0.18	0.16-0.19	<0.001
	Diploma	0.11	0.11-0.12	<0.001	0.033	0.030-0.036	<0.001

	College graduate	0.39	0.38-0.41	<0.001	0.068	0.063-0.074	<0.001
Place of Residence	Rural	1					
	Under one million inhabitants	2.30	2.19-2.41	<0.001	2.22	2.06-2.38	<0.001
	Suburb	2.06	1.98-2.15	<0.001	2.07	1.95-2.20	<0.001
	Metropolis	4.42	4.25-4.61	<0.001	5.80	5.44-6.17	<0.001

The multivariate logistic regression showed that multiple demographic factors linked clearly to the chance of a suicide attempt. After control for confounding variables, age related to risk in a curved pattern. People aged 30 - 59 years had 2.6 times the odds of attempt when compared with those aged ≤18 years (AOR = 2.62; 95 % CI: 2.45 - 2.81; $p < 0.001$); therefore, middle aged adults form a high risk group. Adults aged ≥60 years had far lower odds (AOR = 0.20; 95 % CI: 0.17 - 0.22), which shows that risk falls sharply in later life. Males had higher odds of attempt than females (AOR = 2.50; 95 % CI: 2.37 - 2.64; $p < 0.001$). Although the raw data contained more female cases, the adjusted model showed that male sex acts as an independent risk factor - this points to gender related differences in behaviour and in psychosocial factors that shape suicide patterns. Employment status followed clear gradients. Students had more than three times the odds of attempt (AOR = 3.30; 95 % CI: 3.07 - 3.55); unemployed people had nearly three times the odds (AOR = 2.68; 95 % CI: 2.48 - 2.89). Employed workers had much lower odds (AOR = 0.36; 95 % CI: 0.32 - 0.39), which likely reflects the protective role of work and of stable income. Level of urbanization linked strongly to risk. People in metropolitan areas had almost six times the odds of attempt when compared with rural residents (AOR = 5.80; 95 % CI: 5.44 - 6.17; $p < 0.001$). People in suburban or small urban areas also faced higher odds. (Table 2) (Figure 2)

Table3: Univariate and Multivariate Logistic Regression Analysis of Substance Use Disorder and Other Clinical and Psychological Variables Associated with Suicide Attempt

Variable	Categories	Univariate regression analysis			Multivariate logistic regression		
		OR	95% Confidence interval	P-value	OR	95% Confidence interval	P-value
History of Substance use disorder	No	1					
	Yes	1.91	1.82-2.00	<0.001	2.06	1.91-2.21	<0.001
History of Anxiety	No	1					
	Yes	1.72	1.65-1.79	<0.001	2.83	2.67-3.01	<0.001
History of Depression	No	1					
	Yes	1.83	1.76-1.91	<0.001	2.86	2.69-3.04	<0.001
History of Domestic violence	No	1					
	Yes	1.88	1.65-2.14	<0.001	2.96	2.48-3.53	<0.001
History of Epilepsy	No	1					
	Yes	1.71	1.44-2.02	<0.001	1.73	1.35-2.21	<0.001
History of Bipolar Disorder	No	1					
	Yes	3.49	2.77-4.39	<0.001	3.48	2.57-4.73	<0.001
History of Other Mental Disorder	No	1					
	Yes	1.77	1.46-2.15	<0.001	1.01	0.76-1.33	0.92
History of hyperlipidemia	No	1					
	Yes	0.094	0.087-0.10	<0.001	0.10	0.09-0.11	<0.001
History of Smoking	No	1					
	Yes	1.43	1.38-1.49	<0.001	1.49	1.41-1.58	<0.001
History of Diabetes	No	1					
	Yes	1.35	1.29-1.42	<0.001	6.99	6.42-7.62	<0.001
History of Hypertension	No	1					
	Yes	0.10	0.09-0.10	<0.001	0.11	0.10-0.12	<0.001

Suicide attempts among those with a history of substance use disorder were 2.06-fold more likely than for other participants (95% CI: [1.91–2.21], $p < .001$). This demonstrates that there is arguably

no single other factor which can be more strongly and independently related with attempted suicides, except for substance misuse. This confirms that substance misuse remains one of the most powerful and independent predictors of suicidal attempt. Both anxiety and depression were strongly associated with suicide attempts. Individuals with depression had nearly threefold higher odds (AOR = 2.86; 95% CI: 2.69–3.04) and those with anxiety disorders had a comparable increase (AOR = 2.83; 95% CI: 2.67–3.01). Bipolar disorder emerged as one of the strongest psychiatric correlates, with affected individuals having more than three times higher odds of suicide attempt (AOR = 3.48; 95% CI: 2.57–4.73). Exposure to domestic violence substantially increased the odds of suicide attempt (AOR = 2.96; 95% CI: 2.48–3.53). Individuals with epilepsy showed moderately elevated risk (AOR = 1.73; 95% CI: 1.35–2.21) possibly due to neurobiological and psychosocial consequences of chronic neurological illness. Unexpectedly, diabetes mellitus demonstrated a strong positive association with suicide attempt (AOR = 6.99; 95% CI: 6.42–7.62). The magnitude of this effect may reflect the psychological burden treatment fatigue and comorbid depression common among individuals with chronic metabolic diseases. Smoking was independently associated with increased risk (AOR = 1.49; 95% CI: 1.41–1.58) consistent with its correlation with other maladaptive coping mechanisms. Interestingly, both hypertension and hyperlipidemia were inversely related to suicide attempt. This inverse relationship may be due to higher levels of medical monitoring or greater access to health care among these groups. (Table3) (Figure3) (Figure4)

In a separate multivariable logistic regression model including substance use disorder, depression, and anxiety, substance use disorder remained significantly associated with suicide attempt (AOR, 1.69; 95% CI, 1.61–1.78). Depression (AOR, 1.63; 95% CI, 1.56–1.70) and anxiety (AOR, 1.60; 95% CI, 1.53–1.67) were also independently associated with suicide attempt within this model. (Table4)

Table 4. Multivariable Logistic Regression Analysis of Substance Use Disorder, Depression, and Anxiety Associated with Suicide Attempt

variable	Adjusted odds ratio	95% Confidence interval	P-value
History of Substance use disorder	1.69	1.61-1.78	<0.001
History of Depression	1.63	1.56-1.70	<0.001
History of Anxiety	1.60	1.53-1.67	<0.001

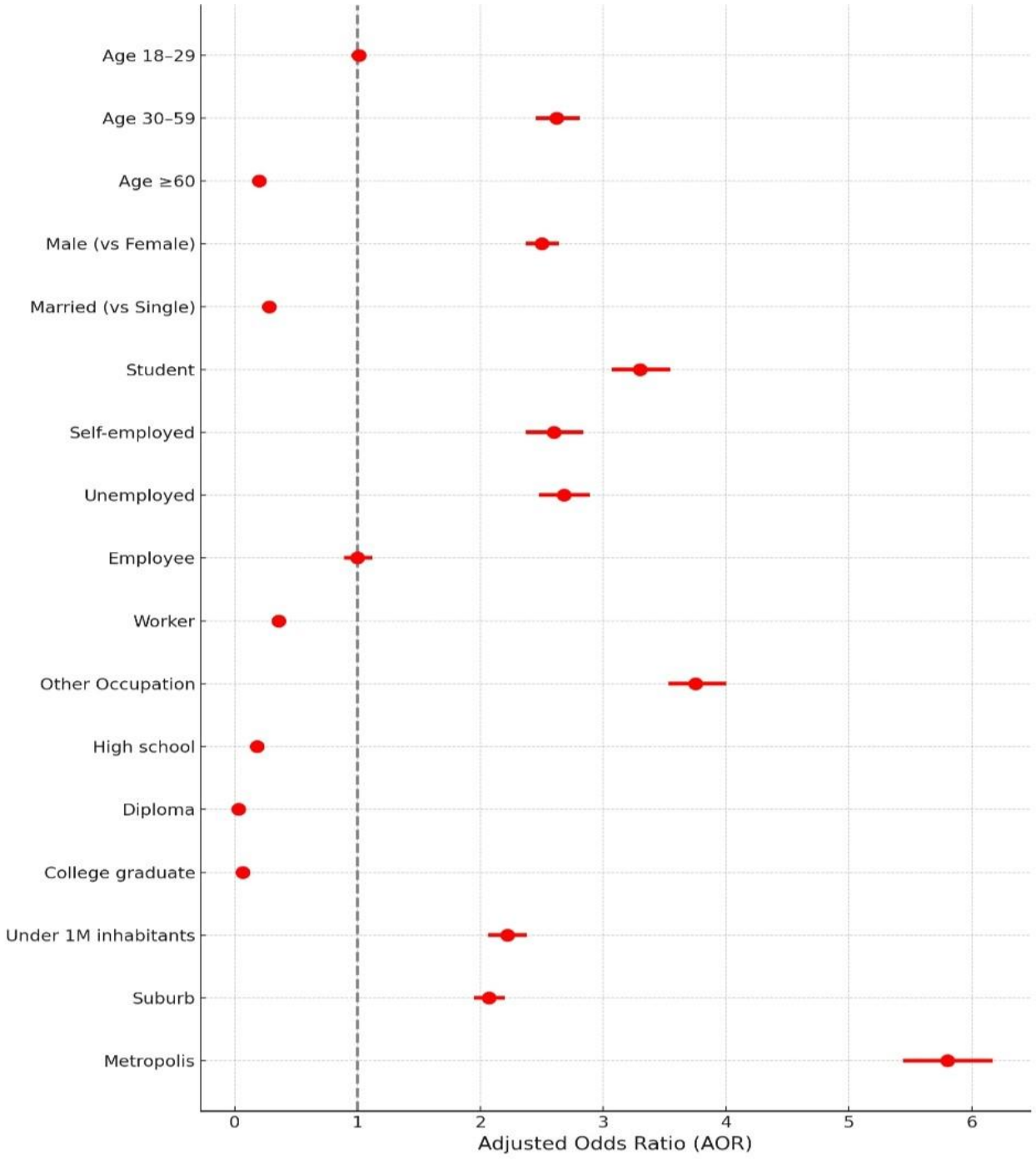


Figure2: Adjusted odds ratios for demographic factors associated with suicide attempt

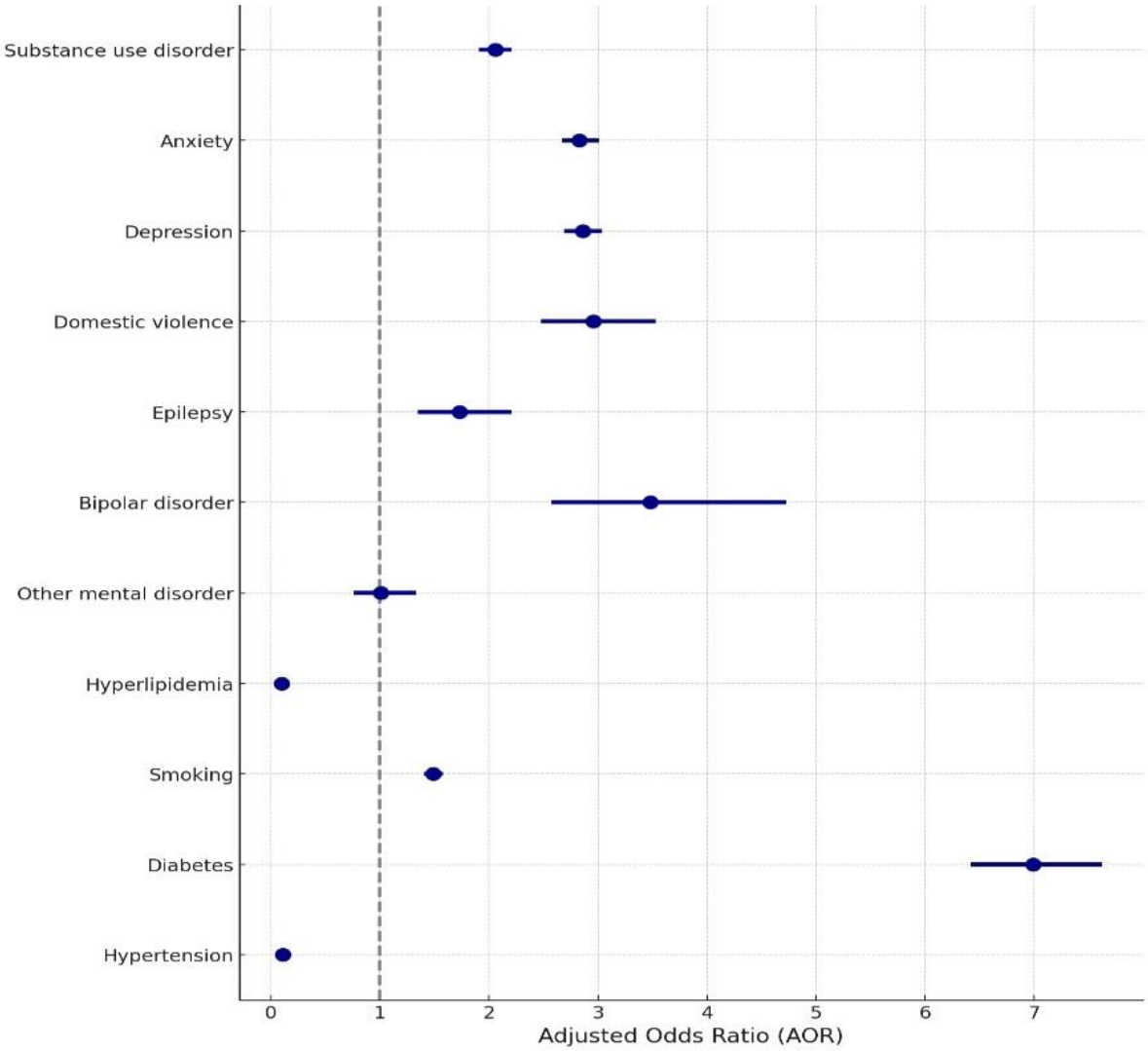


Figure3: Adjusted odds ratios for clinical and psychological factors associated with suicide attempt

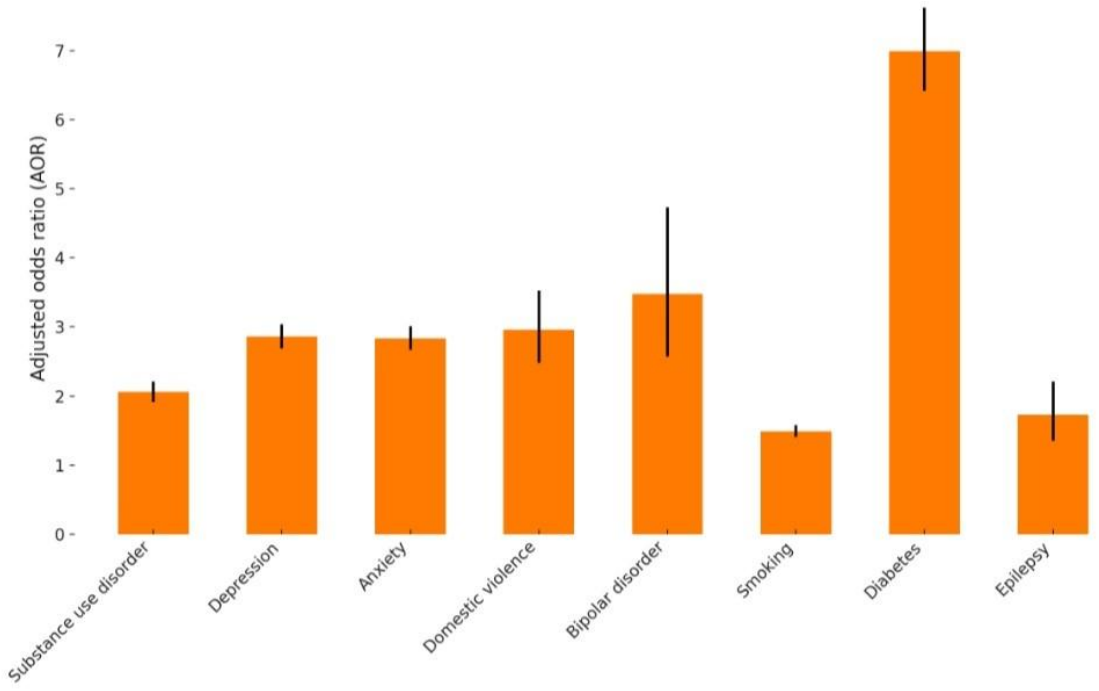


Figure4: Adjusted odds ratio for psychological and behavioral factors associated with suicide attempt

4.Discussion

This large population base case control investigation, comprising 31214 suicide attempters and 45871 controls, provides a comprehensive analysis of demographic, clinical and behavioral factors associated with suicidal behavior. Among these, substance use disorder (SUD) emerged as one of the most potent and independent predictors of suicide attempt even after adjusting for psychiatric comorbidities and sociodemographic confounders. The findings parallel and extend those of prior studies in various populations, including the Nova Scotia centralized-intake study of mental health and addiction clients , the US population-based case control analysis by Lynch et al (18)and the national 2020 survey analysis of Jones et al (19). Collectively, these data reinforce that substance misuse is not a mere correlate of suicidality but an independent, causally meaningful driver of suicide attempts.

Our finding that individuals with a history of SUD were approximately twice as likely to attempt suicide (AOR = 2.06; 95% CI 1.91–2.21) is consistent with multiple analyses showing a two to

four fold increase in suicidal behavior among people with alcohol, drug or polysubstance dependence (13, 18, 20). The Lynch et al study observed an eleven fold higher risk among adults with combined alcohol, drug and tobacco diagnoses compared with those without SUDs (18). Similarly, Jones et al confirmed that SUDs predicted elevated suicidal ideation and attempts across all age groups in US national data(19). Soboka et al reported parallel findings in Canada, with stimulant, hallucinogen and sedative misuse strongly associated with moderate or high suicide risk even after adjusting for depression, anxiety and trauma history (13).

These converging results point to shared biological and psychosocial mechanisms linking addiction and suicidality. Acute intoxication promotes impulsive behavior and cognitive constriction, while chronic substance use induces dysregulation of serotonergic and dopaminergic systems, impairing reward processing and impulse control(21, 22). On a psychosocial level, SUDs exacerbate social isolation, unemployment and domestic violence key interpersonal stressors that precipitate suicidal acts(23, 24). Importantly, our models persistence of SUD significance after adjustment for mood and anxiety disorders underscores that addictions influence on suicidality extends beyond psychiatric mediation. Depression, anxiety and bipolar disorder were each strongly associated with suicide attempts, consistent with meta analyses showing two to three fold risk elevations(25-27). In our study, depression and anxiety displayed near-identical effect sizes supporting the notion that negative affectivity and chronic distress are cross diagnostic pathways to suicidality(28). Bipolar disorder, though less prevalent (0.8% of cases) conferred one of the strongest associations (AOR =3.48) echoing reports that up to one third of individuals with bipolar disorder attempt suicide during their lifetime(29).The independent contribution of SUD, even after adjusting for these disorders, highlights complex interactional effects. Some individuals may self-medicate affective symptoms through substance use, while others develop substance-induced mood dysregulation that exacerbates suicidal ideation(30, 31).

Age, gender and socioeconomic status shaped suicide risk in a nonlinear manner. Compared with adolescents (≤ 18 years), adults aged 30–59 years had 2.6 times greater odds of attempting suicide whereas individuals aged ≥ 60 years showed markedly reduced risk (AOR = 0.20). This inverted U-shape mirrors the global midlife mortality phenomenon reported by Case and Deaton (32), who attributed rising midlife despair to economic strain, social disconnection and health deterioration. Middle aged adults often face converging pressures employment instability, caregiving responsibilities, and chronic disease that interact with psychiatric vulnerability to produce heightened suicide risk. Gender patterns followed the well established “gender paradox.” Although women comprised a slight majority among attempters (56.6%) men exhibited higher adjusted odds (AOR = 2.50). Prior epidemiologic work shows that women attempt suicide more frequently but men die by suicide more often due to method lethality and lower help-seeking behavior (33-35). These differences likely reflect gendered norms around emotional expression and coping, as well as variations in substance-use profiles; men are more prone to polysubstance misuse, which may amplify lethality (36). Employment status also demonstrated a strong gradient: students and unemployed participants had odds ratios exceeding 3, whereas employment was protective. These patterns align with systematic reviews linking job loss and financial hardship to suicidal behavior(37). Stable work may buffer against despair by providing structure, identity and social engagement.

Urbanicity was another powerful contextual factor. Metropolitan residents faced nearly six-fold higher odds of suicide attempt compared to rural dwellers. While rural suicide mortality often dominates Western data due to firearm access (38, 39), recent evidence suggests that in developing or rapidly urbanizing regions, urban residents may experience greater psychosocial strain, anonymity and economic inequality conditions fostering suicidal behavior(39, 40).

Chronic physical illnesses particularly diabetes mellitus displayed unexpectedly strong associations with suicide attempt. This finding is consist with multiple studies(41, 42).Conversely, hypertension was inversely related to suicide attempts that is consist with a study that low blood presure showed an association with suicidal ideation in the general Korean population(43). This protective surveillance effect suggests that ongoing therapeutic relationships may facilitate early detection of psychological distress. Additionally, in our study hyperlipidemia was inversely related to suicide attempts that is consist with a case-control study in this field(44). Epilepsy also conferred moderately elevated risk , consistent with prior meta-analyses reporting suicide risk ratios of 1.8–2.5 in epilepsy (45, 46). Neurobiological dysfunction, medication side effects, and social stigma may all contribute to this association. Exposure to domestic violence nearly tripled the odds of suicide attempt, underscoring the centrality of trauma in the etiology of suicidal behavior. Longitudinal studies confirm that interpersonal violence predicts subsequent depression, PTSD, and suicidality(47, 48). Substance misuse often co-occurs with domestic violence, creating a synergistic risk loop wherein disinhibition, guilt, and hopelessness reinforce each other(49). Smoking exhibited a smaller but independent association. While once attributed solely to confounding by psychiatric illness, recent evidence suggests nicotine's neuropharmacology effects particularly monoaminergic modulation may directly enhance suicide risk(50)

Clinically, our findings support universal suicide-risk screening among individuals with any SUD presentation, regardless of overt psychiatric symptoms. Screening tools should be embedded within addiction treatment and primary care workflows. Evidence-based interventions cognitive-behavioral therapy, dialectical behavior therapy, contingency management, and medication-assisted treatment have shown dual efficacy in reducing substance use and suicidal ideation.At the public-health level, preventive strategies must address upstream determinants: unemployment, poverty, gender-based violence, and educational disadvantage. Community-based programs fostering social support, as well as policy measures restricting lethal means and expanding crisis hotlines, remain vital components of comprehensive suicide prevention.

While the large sample and rigorous multivariate controls enhance confidence, several limitations warrant caution. The case control design precludes causal inference and may not capture temporal sequencing between SUD onset and suicidal behavior. Self-reported substance uses and psychiatric diagnoses are vulnerable to recall and social-desirability bias. Residual confounding by unmeasured variables such as impulsivity traits, trauma severity, or method availability may persist. Future longitudinal designs integrating ecological momentary assessment and biomarker data are needed to elucidate causal pathways.

Conclusion

The present findings reaffirm that substance use disorder stands among the most powerful and independent predictors of suicide attempt. Even after controlling for mood, anxiety and demographic variables, SUD retained a strong association, underscoring that addiction is not a secondary correlate but a central determinant of suicidality. The cooccurrence of SUD with depression, anxiety, trauma exposure, and socioeconomic disadvantage reflects an intricate biopsychosocial interplay requiring integrated prevention, treatment, and policy responses. Addressing substance misuse must thus be recognized as a cornerstone of suicide-prevention strategies worldwide.

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Authors' contributions

AM is the principal investigator and research leader. SA and EM designed the Study and drafted the manuscript and analyzed the data. SA contributed to the conception, design, data interpretation, and revising the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (2013 version) as adopted by the World Medical Association. Ethical approval was obtained from Mashhad University of Medical Sciences (Approval Code: IR.MUMS.FHMPM.REC.1403.071). Informed consent to participate was obtained from all participants prior to their inclusion in the study. For participants younger than 18 years, written informed consent was obtained from a parent or legal guardian prior to study participation.

Consent for publication

Not Applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number: not applicable

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