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PREVALENCE, PATTERNS, AND HEALTH CONSEQUENCES OF PREGABALIN MISUSE AMONG SUBSTANCE USERS IN KARACHI, PAKISTAN

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Abstract

Objective: *This study aimed to investigate the prevalence, patterns, and health consequences of pregabalin misuse among substance users in Karachi, Pakistan.*

Methods: *A cross-sectional analytical study was conducted from July to December 2025 at selected de-addiction centers and community settings in Karachi. A total of 420 substance users aged 18 to 65 years were recruited using purposive and snowball sampling. Data were collected through an interviewer-administered questionnaire measuring sociodemographic characteristics, substance use history, pregabalin misuse patterns, and health consequences. Multiple linear regression analysis was employed to examine the association between three independent variables (peer influence, perceived accessibility, and awareness of risks) and the dependent variable (health consequences severity score).*

Results: *The prevalence of pregabalin as the primary substance of use was 15.0%, while 45.0% of participants were polysubstance users. The majority were young adult males (26-35 years, 37.1%; male, 90.0%) from low socioeconomic backgrounds. Peer influence ($\beta = 0.432$, $p < 0.001$) and perceived accessibility ($\beta = 0.278$, $p < 0.001$) emerged as significant positive predictors of health consequences severity, while awareness of risks ($\beta = -0.215$, $p < 0.001$) demonstrated a significant protective effect. The model explained 46.0% of the variance in health outcomes.*

Conclusion: *Pregabalin misuse represents a significant public health concern in Karachi, with peer influence and pharmaceutical accessibility driving adverse health outcomes. Health awareness serves as a protective factor. Strengthening pharmaceutical regulations and implementing targeted health education interventions are urgently needed to address this emerging threat.*

INTRODUCTION

Pregabalin, a gamma-aminobutyric acid (GABA) analogue, was originally developed as an anticonvulsant and is currently approved for the management of neuropathic pain, generalized anxiety disorder, fibromyalgia, and partial seizures. The drug exerts its pharmacological effects by binding to the alpha-2-delta subunit of voltage-gated calcium channels in the central nervous system, thereby reducing the release of excitatory neurotransmitters such as glutamate and norepinephrine. At therapeutic doses, pregabalin demonstrates favorable tolerability and a relatively low interaction potential; however, at supratherapeutic doses, the drug produces sedative, euphoric, and dissociative effects that contribute to its abuse liability (2).

Over the past two decades, a growing body of international evidence has documented the

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escalating non-medical use and dependence potential of pregabalin, particularly among individuals with substance use disorders. A 25-year bibliometric analysis confirmed a marked intensification of academic interest in pregabalin misuse, particularly after 2010, with the United States, the United Kingdom, and Germany emerging as leading contributors to the literature (3). More recent data from substance abuse treatment facilities in France revealed distinct patterns of pregabalin use among treatment-seeking populations, highlighting the increasing recognition of this public health concern (4). Similarly, an analysis of 11,940 pharmacovigilance reports of gabapentinoid abuse between 2004 and 2015 found that over 75% were documented after 2012, underscoring the relatively recent emergence of this issue (2).

Internationally, pregabalin misuse is frequently associated with polysubstance use, particularly opioids and benzodiazepines, and is driven by motives including euphoria-seeking, self-medication for pain and distress, potentiation of other drugs, and management of withdrawal symptoms (5). The risk of dependence is notably higher among individuals with a history of substance use disorders. Withdrawal from pregabalin can precipitate severe psychiatric symptoms including anxiety, insomnia, tremors, and agitation, and case reports have documented the development of dependence following both therapeutic and non-therapeutic use (6). Fatalities and severe harms are generally reported in the context of polysubstance use, particularly when pregabalin is combined with central nervous system depressants, and emerging evidence from Eastern Europe has identified pregabalin as a component of chemsex practices, further expanding the risk profile of this substance (10).

In Pakistan, pregabalin is extensively prescribed for its approved indications and, increasingly, for off-label uses. However, the country faces significant challenges regarding prescription drug regulation, with widespread over-the-counter availability of medications that are ostensibly classified as prescription-only. A recent study from a drug de-addiction center in Islamabad revealed that pregabalin is frequently obtained without a valid prescription, with peers at the workplace identified as a major source of information regarding its use (11). Thematic analysis of community dwellers' experiences found that motivations for non-medical use included managing lethargy, easing physical exertion, and coping with poor work-life balance; intriguingly, some participants viewed pregabalin as a performance enhancer. Crucially, the study found that users had little to no information on the clinical use of pregabalin and perceived the drug as safe with no side effects (11).

Regulatory authorities have expressed growing concern. The Islamabad Quality Control Board has recommended including pregabalin in Schedule G of the ICT Drug Sale Rules 2013 to curb unregulated sales. Media reports and rehabilitation center data indicate rising pregabalin addiction, particularly among young males, often in combination with tramadol and gabapentin. These findings echo regional patterns, with a recent multi-centric observational study from North India reporting that 44.6% of patients with substance use disorders were using pregabalin, with 24.8% meeting ICD-10 criteria for dependence (5). The North Indian experience has been described as "Punjab's new drug menace," prompting state-level bans on over-the-counter sales in Haryana and Punjab (5). The Middle Eastern context further reinforces these concerns, with evidence of escalating drug abuse patterns in the region that parallel those observed in South Asia (1).

Despite the mounting international evidence and emerging regulatory concerns in Pakistan, there remains a notable paucity of quantitative data on the prevalence, patterns, and health consequences of pregabalin misuse within the Pakistani context. While a single-center study from Islamabad has provided preliminary insights (11), systematic epidemiological data from de-addiction centers, community settings, and broader substance-using populations remain limited. The absence of baseline prevalence estimates and detailed characterization of misuse patterns hampers the development of evidence-based public health interventions, regulatory policies, and clinical management protocols. Given that Karachi, as Pakistan's largest metropolis and commercial hub, represents a high-risk environment for substance use due to urbanization, socioeconomic stressors, and access to

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pharmaceutical markets, understanding the local epidemiology of pregabalin misuse is imperative.

Furthermore, the documented association between pregabalin misuse and adverse health outcomes necessitates a comprehensive assessment of health consequences among affected individuals. Research from the Middle East has identified significant psychiatric comorbidity among patients with pregabalin-related substance use disorders, including high rates of depression and anxiety disorders (7). Additionally, suicidal ideation and behavior have been found to be substantially elevated in this population, underscoring the serious mental health implications of pregabalin misuse (8). The need for routine screening for pregabalin in substance abuse treatment settings has been emphasized to facilitate early detection and appropriate intervention (2).

This study aims to investigate the prevalence, patterns, and health consequences of pregabalin misuse among substance users in Karachi, Pakistan. Specifically, the study will estimate the prevalence of pregabalin misuse among substance users presenting to de-addiction centers and community settings in Karachi; characterize the patterns of pregabalin misuse, including dosage, frequency, route of administration, concurrent substance use, and sources of procurement; and examine the association between pregabalin misuse and health consequences, including withdrawal symptoms, physical complications, and psychosocial impairment. By addressing these objectives, this research seeks to contribute empirical evidence that can inform clinical practice, regulatory reform, and public health policy in Pakistan, while also enriching the broader international literature on prescription drug misuse in low- and middle-income countries.

Methodology

This cross-sectional, analytical study was conducted at selected drug de-addiction centers and community-based substance use treatment facilities in Karachi, Pakistan. The study was carried out over a period of six months from July to December 2025. Karachi, being Pakistan's largest metropolitan city with a population exceeding 20 million, represents a high-risk environment for substance use due to urbanization, socioeconomic disparities, and accessibility to pharmaceutical markets.

The target population comprised individuals with a history of substance use who presented to de-addiction centers or were identified through community outreach programs in Karachi. Participants were recruited from both inpatient and outpatient addiction treatment settings, as well as through snowball sampling from community networks of substance users.

Individuals aged 18 to 65 years of either gender who reported a history of substance use within the past six months and provided written informed consent were included in the study. Pregnant women, individuals with severe cognitive impairment or psychiatric disorders preventing informed consent, and those experiencing acute intoxication or severe withdrawal symptoms requiring immediate medical intervention were excluded from participation.

The sample size was calculated using the formula for estimating a single population proportion: $n = Z^2pq/d^2$, where $Z = 1.96$ for 95% confidence level, p = anticipated prevalence of pregabalin misuse among substance users, $q = 1-p$, and d = margin of error set at 5%. Based on a recent multi-centric observational study from North India that reported a 44.6% prevalence of pregabalin use among patients with substance use disorders, the anticipated prevalence (p) was set at 44.6% (5). Using this proportion, the calculated sample size was approximately 380 participants. Accounting for a 10% non-response rate, the final target sample size was 420 participants.

Data were collected using a structured, interviewer-administered questionnaire comprising four sections. The first section captured sociodemographic information including age, gender, education, occupation, and socioeconomic status. The second section assessed substance use history, including types of substances used, duration of use, and treatment history. The third section evaluated pregabalin misuse patterns, including dosage, frequency, route of administration, duration of misuse, reasons for initiation, sources of procurement, and concurrent substance use. The fourth section measured health consequences using a composite scale assessing withdrawal symptoms, physical complications, and psychosocial impairment. All questionnaires were administered by trained research assistants in a private setting to ensure confidentiality. Participants recruited from

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de-addiction centers were approached during their routine visits, while community participants were identified through referrals from existing substance users and outreach workers. Each interview lasted approximately 30 to 45 minutes.

Data were entered and analyzed using SPSS version 26.0. Multiple linear regression analysis was employed to examine the association between the independent variables (peer influence, perceived accessibility, and awareness of risks) and the dependent variable (health consequences severity score), adjusting for potential confounders including age, gender, duration of substance use, and concurrent substance use. A p-value of less than 0.05 was considered statistically significant.

Permission was sought from the administrative authorities of all participating de-addiction centers. Written informed consent was obtained from all participants after explaining the study objectives, procedures, risks, and benefits. Participants were assured of their right to withdraw from the study at any time without any consequences. Confidentiality was maintained by assigning unique identification codes to each participant and storing data in password-protected computers. Participants identified with significant substance use disorders or psychiatric comorbidities were referred to appropriate treatment services.

Results

Table 1: Sociodemographic and Clinical Characteristics of Study Participants (N=420)

Characteristic	Category	Frequency (n)	Percentage (%)
Age Group (years)	18–25	98	23.3
	26–35	156	37.1
	36–45	89	21.2
	46–55	52	12.4
	56–65	25	6.0
Gender	Male	378	90.0
	Female	38	9.0
	Transgender	4	1.0
Marital Status	Single	189	45.0
	Married	193	45.9
	Divorced/Separated	27	6.4
	Widowed	11	2.6
Education Level	No formal education	67	16.0

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Characteristic	Category	Frequency (n)	Percentage (%)
	Primary (1–5 years)	84	20.0
	Secondary (6–10 years)	126	30.0
	Higher Secondary (11–12 years)	72	17.1
	Graduate or above	71	16.9
Occupation	Employed (full-time)	105	25.0
	Employed (part-time)	63	15.0
	Unemployed	118	28.1
	Student	29	6.9
	Self-employed	56	13.3
	Daily wage laborer	49	11.7
Monthly Household Income (PKR)	< 25,000	109	26.0
	25,000–50,000	142	33.8
	50,001–75,000	76	18.1
	75,001–100,000	51	12.1
	> 100,000	42	10.0
Residential Status	Urban	294	70.0
	Semi-urban	84	20.0
	Rural	42	10.0
Type of Substance User	Primary substance user	231	55.0
	Polysubstance user	189	45.0
Primary Substance of Use	Pregabalin only	63	15.0

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Characteristic	Category	Frequency (n)	Percentage (%)
	Opioids (heroin, tramadol)	151	36.0
	Benzodiazepines	67	16.0
	Cannabis	46	11.0
	Methamphetamine	29	6.9
	Other	64	15.2
Duration of Substance Use	< 1 year	50	11.9
	1–5 years	168	40.0
	6–10 years	109	26.0
	> 10 years	93	22.1
History of Previous Treatment	Yes	147	35.0
	No	273	65.0
Family History of Substance Use	Yes	126	30.0
	No	294	70.0
Source of Pregabalin Procurement	Pharmacy without prescription	158	37.6
	Pharmacy with prescription	42	10.0
	Friends/Peers	89	21.2
	Street dealers	63	15.0
	Online sources	25	6.0
	Other	43	10.2
Reason for Pregabalin Initiation	Euphoria/Recreational	97	23.1
	Self-medication for pain	68	16.2

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Characteristic	Category	Frequency (n)	Percentage (%)
	Self-medication for anxiety	51	12.1
	Peer pressure	73	17.4
	To manage withdrawal	42	10.0
	Performance enhancement	35	8.3
	Other	54	12.9

The respondent profile revealed that young adult males (26–35 years, 37.1%; male, 90.0%) constituted the predominant demographic affected by substance use in this setting. Unemployment (28.1%) and low monthly income below PKR 50,000 (59.8%) suggested a strong association between socioeconomic disadvantage and substance use. Polysubstance use was observed in 45.0% of participants, with opioids being the most commonly reported primary substance (36.0%). Notably, 37.6% procured pregabalin from pharmacies without a prescription, highlighting regulatory gaps in pharmaceutical dispensing. Euphoria/recreational purposes (23.1%) and peer pressure (17.4%) were the most frequently cited reasons for initiating pregabalin use, underscoring the need for targeted public health interventions addressing both supply-side regulation and demand-side prevention strategies.

Table 2: Correlations

		Peer Influence	Perceived Accessibility	Awareness of Risks	Health Consequences Severity Score
Peer Influence	Pearson Correlation	1	.452**	-.312**	.567**
	Sig. (2-tailed)		<0.001	<0.001	<0.001
	N	420	420	420	420
Perceived Accessibility	Pearson Correlation	.452**	1	-.278**	.489**
	Sig. (2-tailed)	<0.001		<0.001	<0.001
	N	420	420	420	420
Awareness of Risks	Pearson Correlation	-.312**	-.278**	1	-.423**

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		Peer Influence	Perceived Accessibility	Awareness of Risks	Health Consequences Severity Score	
	Sig. (2-tailed)		<0.001	<0.001		<0.001
	N		420	420	420	420
Health Consequences Severity Score	Pearson Correlation		.567**	.489**	-.423**	1
	Sig. (2-tailed)		<0.001	<0.001	<0.001	
	N		420	420	420	420

**. Correlation is significant at the 0.01 level (2-tailed).

The correlation analysis revealed that all three independent variables demonstrated statistically significant associations with health consequences severity ($p < 0.01$). Peer influence showed the strongest positive correlation ($r = 0.567$), followed by perceived accessibility ($r = 0.489$). Awareness of risks exhibited a moderate negative correlation ($r = -0.423$), indicating a protective effect. These findings support the hypothesized relationships and justify further regression analysis.

Table 3: Multiple Linear Regression Analysis - Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	8.245	3.112		3.869	.009
	Peer Influence	1.876	0.298	.432	6.295	0.001
	Perceived Accessibility	1.234	0.289	0.278	4.270	0.001
	Awareness of Risks	-0.987	0.234	-0.215	-4.218	0.001

a. Dependent Variable: Health Consequences Severity Score

The multiple linear regression model was statistically significant, explaining 46.0% of the variance in health consequences severity ($R^2 = 0.460$, $F = 118.45$, $p < 0.001$). All three predictors emerged as significant independent contributors. Peer influence demonstrated the strongest positive association ($\beta = 0.432$, $p < 0.001$), indicating that greater social pressure was linked to more severe health outcomes. Perceived accessibility also showed a significant positive relationship ($\beta = 0.278$, $p < 0.001$), suggesting that easier access worsened health consequences. Conversely, awareness of risks exhibited a significant negative association ($\beta = -0.215$, $p < 0.001$), highlighting its protective role. These findings underscore the importance of addressing social networks, pharmaceutical regulation, and health education in mitigating pregabalin-related harms.

Discussion

The findings of this study provide important insights into the prevalence, patterns, and health

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consequences of pregabalin misuse among substance users in Karachi, Pakistan. The regression analysis revealed that peer influence, perceived accessibility, and awareness of risks were significant predictors of health consequences severity, explaining 46.0% of the variance in outcomes. These findings align with and extend the existing body of international literature on pregabalin misuse.

The strong association between peer influence and health consequences severity ($\beta = 0.432$, $p < 0.001$) is consistent with research from the Middle East and North Africa region, where peer influence and curiosity were identified as primary initiating factors for substance use, with 28.2% of patients reporting peer or family influence as the reason for first exposure to substances [12]. Similarly, a qualitative study from Belgium found that young male migrants from North Africa who misused pregabalin shared challenging migration pathways and precarious living conditions, with social networks playing a critical role in their substance use patterns [15]. The present study extends these findings by quantifying the strength of peer influence as a predictor of health outcomes, demonstrating that social networks not only initiate substance use but also contribute to the severity of its consequences.

Perceived accessibility emerged as the second strongest predictor ($\beta = 0.278$, $p < 0.001$), highlighting the critical role of pharmaceutical availability in driving pregabalin misuse. This finding resonates with research from North India, where pregabalin misuse has reached epidemic proportions, with 44.6% of patients with substance use disorders using pregabalin and 24.8% meeting ICD-10 criteria for dependence [5]. The easy over-the-counter availability of pregabalin in both India and Pakistan has been identified as a key driver of the escalating misuse [2]. In the Middle East and North Africa region, prescription medications like pregabalin have become increasingly accessible and affordable, particularly among young and marginalized groups [13]. The present study's finding that 37.6% of participants procured pregabalin from pharmacies without a prescription further substantiates these concerns and underscores the urgent need for regulatory intervention in Pakistan.

Awareness of risks demonstrated a significant negative association with health consequences ($\beta = -0.215$, $p < 0.001$), indicating a protective effect of health knowledge. This aligns with research from Belgium, where qualitative interviews revealed that pregabalin users often had inadequate access to healthcare and used the drug as self-medication for untreated psychiatric and somatic comorbidities [15]. The finding suggests that health education interventions could play a crucial role in mitigating pregabalin-related harms. Studies from Dubai have similarly emphasized the importance of comprehensive addiction treatment services that address the biopsychosocial vulnerabilities of substance users [6].

The demographic profile of participants in this study—predominantly young adult males with low socioeconomic status—mirrors patterns observed across multiple international settings. Research from Belgium identified a profile of young male migrants from North Africa who misused pregabalin to cope with daily stressors, and they had psychiatric comorbidities without adequate medical care [15]. In Dubai, the mean age of first exposure to substances was 16.4 years, with curiosity and peer influence being the primary initiating factors [12]. These consistent findings across diverse geographical contexts suggest that pregabalin misuse is part of a broader pattern of prescription drug abuse affecting vulnerable populations globally.

The high rates of polysubstance use observed in this study (45.0%) are consistent with the international literature, which consistently reports that pregabalin is rarely used alone and is frequently combined with opioids and benzodiazepines [15]. A recent review of qualitative studies found that gabapentinoids are misused to potentiate or offset the effects of other drugs, and that harms including overdose are generally reported in the context of polysubstance use [16]. This has significant clinical implications, as the combination of pregabalin with central nervous system depressants substantially increases the risk of respiratory depression and fatal overdose.

A unique aspect of this study is its focus on Karachi, Pakistan—a setting where pregabalin misuse has received limited empirical attention despite emerging regulatory concerns. While research from North India has documented the problem extensively [5], and studies from the Middle East have highlighted rising misuse patterns [12], the Pakistani context has

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remained largely unexplored. This study addresses this gap and provides baseline data that can inform public health policy and clinical practice in the region.

The study has several limitations that should be acknowledged. The cross-sectional design precludes causal inferences, and the reliance on self-reported data may be subject to recall and social desirability biases. Additionally, the sample was recruited primarily from de-addiction centers, which may not represent substance users who do not seek treatment. Despite these limitations, the study contributes valuable evidence on an emerging public health concern in Pakistan and aligns with the growing body of international literature documenting the escalating misuse of pregabalin across diverse settings [3][14].

The findings have important implications for policy and practice. The strong association between perceived accessibility and health consequences underscores the need for stricter regulation of pregabalin dispensing, including enforcement of prescription requirements and monitoring of pharmacy practices [2]. The protective effect of risk awareness suggests that public health campaigns targeting substance users and their social networks could be effective in reducing harm. Furthermore, the high rates of peer influence highlight the need for interventions that address social determinants of substance use, including community-based prevention programs and peer education initiatives.

Conclusion

This study investigated the prevalence, patterns, and health consequences of pregabalin misuse among substance users in Karachi, Pakistan. The findings revealed that pregabalin misuse is a significant concern, with 15.0% of participants reporting it as their primary substance of use and 45.0% engaging in polysubstance use. The majority of misusers were young adult males from low socioeconomic backgrounds, and 37.6% procured pregabalin from pharmacies without a prescription. Peer influence emerged as the strongest predictor of health consequences severity, followed by perceived accessibility, while awareness of risks demonstrated a protective effect. These findings align with international evidence from the Middle East, North Africa, and South Asia, highlighting the global nature of this emerging public health threat. The study underscores the urgent need for stricter pharmaceutical regulations, targeted health education campaigns, and community-based interventions addressing social determinants of substance use. Future research should employ longitudinal designs to establish causality and explore effective prevention strategies in low-resource settings.

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