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Pregabalin and gabapentin abuse among university students in Jordan: A cross sectional study

Ahmad A Altarifi [1*], Omar Obeidat [2], Ahmad Guzu [2], Amr Said [2], Mahmoud Albakheet [2], Ahmad Makkawi [2], Zuheir Hasan [3], Mohammed Azab [4], Moureq R Alotaibi [5], Khalid Kheirallah [6], Tareq Saleh [2**]

[1] Department of Pharmacology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, JORDAN
[2] Department of Pharmacology and Public Health, Faculty of Medicine, The Hashemite University, Zarqa, JORDAN
[3] Department of Anatomy, Physiology, and Biochemistry, Faculty of Medicine, The Hashemite University, Zarqa, JORDAN
[4] Department of Microbiology, Pathology, and Forensic Medicine, Faculty of Medicine, The Hashemite University, Zarqa, JORDAN
[5] Department of Pharmacology and Toxicology, College of Pharmacy, King Saud University, Riyadh, SAUDI ARABIA
[6] Department of Public Health, Faculty of Medicine, Jordan University of Science and Technology, Irbid, JORDAN
*Corresponding Author: aaaltarifi@just.edu.jo
**Corresponding Author: tareq@hu.edu.jo

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ABSTRACT

Introduction: Pregabalin and gabapentin (or gabapentanoids) have been reported to be abused for potentially euphoric effects.

Objectives: In this work, we conducted a descriptive, cross-sectional study among university students from Jordan utilizing a structured online questionnaire.

Results: 96.1% of the participants indicated no previous or current use of gabapentanoids, while 53 (3.9%) self-reported previous or current use (ever-use) of any of both drugs. The rate of abuse was higher among males and older students' groups. 50.9% of drug users did not obtain a valid prescription. Most abusers indicated that their use of both drugs was for non-medical reasons (39.6%), and 69.8% students used both drugs despite being aware of their adverse effects. Hypersomnia was the most reported adverse effect. However, most participants (64.2%) did not report any withdrawal symptoms upon drug discontinuation. Marijuana/hashish was the most consumed substance with gabapentanoids.

Conclusions: Our results invite for further prescribed drug control and increasing the awareness against drug abuse among the youth in Jordan.

Keywords: pregabalin, gabapentin, abuse, dependence, withdrawal, DSM-V

INTRODUCTION

Drug misuse refers to the use of a prescribed drug for purposes other than those indicated, at doses greater (or for longer periods) than those indicated, for no legitimate medical complaint, or to experience euphoric effects [1]. Substance use disorder (SUD) is defined by the diagnostic and statistical manual of mental disorders (DSM-5) as a chronic, relapsing condition characterized by compulsive drug seeking and use despite adverse consequences [1]. SUD and controlled substance abuse are two problems that are widespread and detrimental to societies causing significant morbidity and mortality especially in vulnerable groups [2]. For example, illicit drug use increased significantly in young age groups in the United States, and was associated with increased risk of mental illnesses, which requires serious medical attention and mental health support [3]. Moreover, early drug abuse has been associated with overdose, hospitalizations, accidental injury, and suicide [2].

Pregabalin and gabapentin are anticonvulsant drugs that are used in the treatment of epilepsy [4]. Despite being an analogue of the inhibitory neurotransmitter γ-aminobutyric acid (GABA), pregabalin does not bind directly to GABA or benzodiazepines receptors [5]. Instead, pregabalin exerts an inhibitory effect through reducing the release of several central neurotransmitters such as glutamate, norepinephrine and substance P [6]. Pregabalin was initially used as a second-line treatment for epileptic patients with a suboptimal response to standard anticonvulsant therapy [7]. Currently, pregabalin is approved for the treatment of seizures, anxiety, neuropathic pain including diabetic neuropathy, fibromyalgia, and post-herpetic neuralgia [8]. Also, pregabalin is widely used off-label for alcohol withdrawal syndrome, restless legs syndrome, migraine, and vasomotor symptoms of menopause [8]. Gabapentin is a similar drug to pregabalin and is also an analogue of GABA [9]. Like pregabalin, gabapentin does not interact with GABA receptors, but rather, it exerts its action by

binding to a2d-1 subunit of voltage-gated calcium channels at the dorsal root ganglia, consequently leading to inhibitory postsynaptic potentials [10]. Currently, gabapentin is used as a first-line treatment of neuropathic pain [11].

Recently, several reports worldwide have highlighted the newly emerging potential for pregabalin abuse. A study by Zellner et al. indicated that the number of pregabalin abusers increased from zero to five in 2008-2011 to 105 in 2015 in Munich, Germany [12]. In the USA, there are increasing reports of pregabalin abuse as pregabalin-related visits in the USA ambulatory care quadrupled between the year 2003 and 2016 [13]. Of those, 50.0% co-abused an opioid and/or a benzodiazepine with no approved indication [13]. Around 45.8% of pregabalin was prescribed by primary care physicians, which raises concerns about physicians' and patients' knowledge about pregabalin abuse potential [13]. Evidently, patients developing pregabalin abuse following a valid prescription are not aware of the addictive potential of pregabalin and suggests the need for raising awareness about pregabalin and its abuse potential [14, 15]. Similar to pregabalin, recent evidence indicated that gabapentin have a comparable risk for abuse [16]. Gabapentin abuse can be easily overlooked in some countries since it is not a controlled substance, and thus, can be overprescribed or misused. When combined with opioids, gabapentin-related euphoria is potentiated [17].

In Jordan, pregabalin abuse was first reported in [18], which showed that pregabalin misuse/abuse was highest amongst patients with spinal disc herniation, followed by those with chronic pain and neuropathic pain. It was further demonstrated that pregabalin abuse was accompanied with a history of other drug abuse, which is consistent with previous observations in the literature [18]. The Jordan Food and Drug Administration issued a new decision in 2017 to include pregabalin formulas in the restricted list of drugs to tackle this issue. In 2017, a local media report claimed that pregabalin abuse was widespread among students at the University of Jordan, based mainly on testimonies from students [19]. Moreover, 400 packets of pregabalin from the university campus were confiscated [19]. Unfortunately, there is no clear evidence on the extent of pregabalin and gabapentin abuse amongst vulnerable groups such as university students in Jordan. Accordingly, in this work, we investigated self-reported evidence of both pregabalin and gabapentin abuse in public university students in Jordan.

MATERIALS & METHODS

Sample & Data Collection

Our sample consisted of university students from 6 public universities in Jordan. The study utilized a structured online questionnaire delivered to participants in the period between March 9th to April 8th, 2021. The online questionnaire was created via Google Forms and posted on several online platforms accessible to university students including official channels of communication between schools and students such as the official student online portals. The total population of the study was 1,456 university students representing the largest six universities in the country, namely: The University of Jordan, Jordan University of Science and Technology, The Hashemite University, Yarmouk University, Al Balqa Applied University, and Mutah University (https://www.mohe.gov.jo). The targeted population was all adult students above the age of 18, who are enrolled in one of the Jordanian universities at different levels (both undergraduate, postgraduate, and diploma), regardless of their gender, education, socioeconomic status, and other variables. All data was obtained by digital data collection.

Tools

The questionnaire was adopted, in part, from previous reports [20, 21], and modified to include questions related to the population of the study. The online questionnaire consisted of six main divisions: socio-demographics, drug use description, adverse effects, withdrawal symptoms, DSM-V criteria for substance use disorder and adjuncts. The socio-demographic section included questions on gender, age, marital status, level of education and current residence. The drug use description section consisted of questions investigating commercial names of pregabalin and related drugs, dose, availability of appropriate prescriptions (valid vs. invalid prescriptions), therapeutic indications, duration of drug intake, and source. Valid prescriptions indicate the availability of drug prescription from an authorized physician to an indicated patient. The adverse effects section was centered on inquiring about potential adverse effects of pregabalin use including pain, hypersomnia, poor concentration, hyperactivity, dry mouth, blurred vision, constipation, tremor and fatigue, while the section on withdrawal symptoms involved inquiries on depression-like symptoms, lack of concentration, anxiety, nightmares, suicidal ideation, insomnia, exhaustion, shivering, hallucinations, joint and muscle pain and convulsions. Participation in the study was voluntary and personal identifiers were not collected.

Statistical Analysis

Data was imported into EXCEL for data cleaning and recoding before being exported in SPSS version 26 for data analysis. Frequencies and percentages were presented. Chi-square test was used to assess the statistical association between categorical variables. Statistical significance was set at $p<0.05$.

RESULTS

Demographic Data

The total number of students who consented to participate in the study and completed the online questionnaire was 1,368 (n=1,368). Of those, 883 (64.5%) were females and 485 (35.5%) were males (**Table 1**). The majority of participants aged 18-19 years old (n=665, 48.6%), while 359 (26.2%) aged 20-21 years, 219 (16.0%) aged 22-23, and the remainder 125 (9.1%) participants were 24 or older (**Table 1**).

Regarding the participants' marital status, the vast majority of participants were single (n=1,304, 95.3%), 57 (4.2%) were married and seven (0.5%) were separated (**Table 1**). Around 1,115 (81.5%) lived in major cities, 201 (14.7%) lived in villages, and the remainder lived in refugee camps (n=31, 2.3%) or bedouin areas (n=21, 1.5%). The main fields of high school education in Jordan include the scientific and literary streams among other disciplines of study. In this work, 781 (57.1%) participants were holders of a scientific stream high school diploma, 432 (31.6%) were holders of a literary stream high school diplomas, while the rest (155, 11.3%) have high school

Table 1. Sociodemographic characteristics of study sample

Characteristics	n (%)
Age	
18-19	665 (48.6)
20-21	359 (26.2)
22-23	219 (16.0)
24 or above	125 (9.1)
Gender	
Male	485 (35.5)
Female	883 (64.5)
Marital status	
Single	1,304 (95.3)
Married	57 (4.2)
Divorced	7 (0.5)
Demography	
City	1,115 (81.5)
Village	201 (14.7)
Refugee camp	31(2.3)
Badia	21(1.5)
Field of study in high school	
Scientific stream	781 (57.1)
Literary stream	432 (31.6)
Management information systems	53 (3.9)
Industrial education	45 (3.3)
Domestic economics	22 (1.6)
Health education	13 (1.0)
Hospitality & tourism	10 (0.7)
Agricultural	9 (0.7)
Business	3 (0.2)
University	
Public	1,360(99.4)
Private	8 (0.6)
Current academic level	
Bachelor's	1,276 (93.3)
Master's	59 (4.3)
Diploma	21 (1.5)
Doctorate	2 (0.1)
Other	10 (0.7)

Note. Total number of participants who completed questionnaire is 1,368 student (n=1,368)

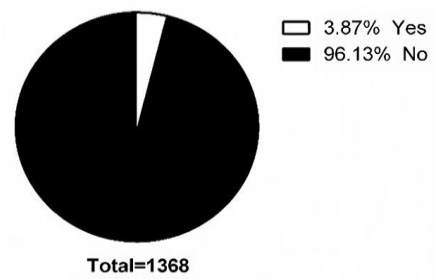

Figure 1. Self-reported rate of pregabalin or gabapentin use (Source: Authors' own elaboration)

diplomas in other fields of study. Almost all participants were enrolled in public universities (n=1,360, 99.4%) while only eight (0.6%) enrolled in private universities. Almost 1,276 (93.3%) were undergraduates studying towards a bachelor's degree, while 59 (4.3%) were enrolled in a Master of Science program, 21 (1.5%) were included in a diploma program, and only two (0.1%) were in a Doctor of Philosophy program (**Table 1**).

Extent of Pregabalin & Gabapentin Self-Reported Use

Overall, of the 1,368 participants, 1,315 (96.1%) indicated no previous or current use of pregabalin or gabapentin, while

Table 2. Association between sociodemographic factors & pregabalin or gabapentin abuse potential

Characteristics	Non-abusers	Abusers	p-value
Age			0.000
18-19	649 (97.6%)	16 (2.4%)	
20-21	350 (97.5%)	9 (2.5%)	
22-23	202 (92.2%)	17 (7.8%)	
24 or above	114 (91.2%)	11 (8.8%)	
Gender			0.003
Male	456 (94%)	29 (6.0%)	
Female	859 (97.3%)	24 (2.7%)	
Marital status			0.750
Ever married	62 (96.9%)	2 (3.1%)	
Never married	1,253 (96.1%)	51(3.9%)	
Area of residence			0.610
Urban	1,077 (96.6%)	38 (3.4%)	
Rural	238 (94.1%)	15 (5.9%)	
Field of high school study			0.217
Scientific	749 (95.9%)	32 (4.1%)	
Literary	420 (97.2%)	12 (2.8%)	
Others	146 (94.2%)	9 (5.8%)	
Education status			0.422
Bachelor's	1,228 (96.2%)	48 (3.8%)	
Others	87 (94.6%)	5 (5.4%)	

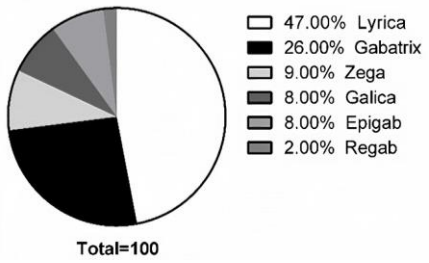

Figure 2. Distribution of commercially available preparations of pregabalin & gabapentin among participants (Source: Authors' own elaboration)

53 (3.9%) self-reported previous or current use (ever-use) of any of both drugs (**Figure 1**).

The rates of pregabalin and gabapentin use were higher among males in comparison to females as 29 (6.0%) of the male population were abusers compared to 24 (2.7%) out of the total female population (p=0.003) (**Table 2**). Moreover, the abuse rate was higher among older age groups (p=0.000) (**Table 2**). On the other hand, there was no significant association between the rates of abuse of both drugs and the marital status (p=0.750), demographics (p=0.610), field of high school study (p=0.217) and current educational status (p=0.422) (**Table 2**).

Regarding the commercially available formula of the drugs, the analysis revealed that the most frequently used drug by participants was lyrica (n=25, 47.0%) followed by gabatrix (n=14, 26.0%), zega (n=5, 9.0%), galica (n=4, 8.0%), epigab (n=4, 8.0%), and regab (n=1, 2.0%) (**Figure 2**).

26 (49.1%) of participants obtained a valid prescription prior to using the drug, while the remainder 27 (50.9%) stated that they have used the drug without obtaining a valid prescription (**Table 3**).

Self-Reported Daily Dosage & Duration of Use of Pregabalin & Gabapentin

For the dosage taken per day of both drugs, results showed that 22 (41.5%) of users abused any of the drugs at a dose of

Table 3. Discerption of drug dosage, frequency of use, duration of use, & source

Variable	n (%)
Prescribed use of the drug	
Prescribed	26 (49.1%)
Non-prescribed	27 (50.9%)
Dosage (per day)	
Less than 100 mg	22 (41.5%)
100-200 mg	11 (20.8%)
200-300 mg	4 (7.5%)
300-400 mg	8 (15.1%)
400-500 mg	3 (5.7%)
500-1,000 mg	4 (7.5%)
1000-1,500 mg	0 (0.0%)
More than 1,500	1 (1.9%)
Duration of use	
One time	17 (32.1%)
Two times or more	7 (13.2%)
One week-one month	11 (20.8%)
Two month-six month	6 (11.3%)
Six-12 month	2 (3.8%)
One year-two years	4 (7.5%)
Two year-five years	2 (3.8%)
More than five years	4 (7.5%)
Source*	
Pharmacy	29 (54.7%)
Without prescription	17 (32.1%)
Family member	11 (20.8%)
Friends	4 (7.5%)

Note. *An item in survey, where multiple answers were allowed

Table 4. Self-reported indications for use of pregabalin or gabapentin

Reported indications	n (%)
Non-medical use	21 (39.6%)
Mood & rest	13 (24.5%)
Chronic myelopathy	12 (22.6%)
Chronic low back pain	11 (20.8%)
Anxiety	11 (20.8%)
Daily life stress	9 (17.0%)
insomnia	6 (11.3%)
Peripheral neuropathy	5 (9.4%)
Fibromyalgia	5 (9.4%)
Shingles	3 (5.7%)
Migraine	3 (5.7%)
Seizures	2 (3.8%)
Diabetic neuropathy	2 (3.8%)
Restless leg syndrome	1 (1.9%)

Note. Multiple choices were allowed & total number of participants that reported pregabalin or gabapentin use was 53 (n=53) (for this component of survey, selection of multiple answers was allowed; thus, numbers & percentages might reflect multiple entries from a single participant)

100 mg/day or less, 11 (20.8%) used pregabalin at a dose of 100-200 mg/day, four (7.5%) at a dose of 200-300 mg/day, eight (15.1%) as a dose of 300-400 mg/day, three (5.7%) at a dose of 400-500 mg/day, four (7.5%) at a dose of 500-1,000 mg/day, and only one (1.9%) at a dose of >1,500 mg/day (**Table 3**). The drug that was consumed at doses higher than 1,000 mg/day was mainly lyrica. Then, participants were asked to determine the duration of use, and 17 (32.1%) of participants reported taking the drug once daily, seven (13.2%) took it twice or more, 11 (20.8%) for one week –one month period, six (11.3%) for two-six months period, two (3.8%) for six-12 months, four (7.5%) for one-two years, two (3.8%) for two-five years period, and lastly, only four (7.5%) participants reported consumption of any of the two drugs for more than five years. The drugs were obtained from local pharmacy as reported by 29 (54.7%) participants, 17 (32.1%) of them stated that they obtained the any of the drugs without a valid prescription from an illicit source, 11 (20.8%) got it from family members, and the remaining four (7.5%) obtained them from friends (**Table 3**).

Table 5. Parallel tobacco & other substances of abuse consumption

Variable	n (%)
Smoking alongside taking drug*	
No	25 (47.2%)
Cigarettes	23 (43.4%)
Electronic cigarettes	9 (17.0%)
Water pipe	8 (15.1%)
Chewable tobacco	4 (7.5%)
Use of other drugs*	
No	34 (64.2%)
Marijuana	15 (28.3%)
Alcohol	10 (18.9%)
Tramadol	6 (11.3%)
Captagon	4 (7.5%)
Opioids	3 (5.7%)
Benzodiazepine	3 (5.7%)
Joker	3 (5.7%)
Methamphetamine	3 (5.7%)
Xanax (alprazolam)	2 (3.8%)
Antidepressants	1 (1.9%)

Note. *Multiple choices were allowed

Self-Reported Indications of Use of Pregabalin & Gabapentin Among Participants

Of total participants' who reported the use of pregabalin or gabapentin, 21 (39.6%) indicated that their use of both drugs was for non-medical reasons. However, the remainder of participants who self-reported the use of both drugs reported at least one indication for which they sought drug consumption and as following: 13 (24.5%) participants used any of the drugs to elevate their mood, 12 (22.6%) participants used them for chronic myelopathy, whereas 11 (20.8%) participants used the drugs for chronic low back pain, 11 (20.8%) to relieve anxiety, nine (17.0%) to mitigate daily life stress, six (11.3%) for insomnia, five (9.4%) as part of the treatment of symptoms of fibromyalgia, three (5.7%) for neuropathic pain associated with shingles, three (5.7%) for migraine management, and lastly, one (1.9%) for restless leg syndrome (**Table 4**). Interestingly, five of participants used any of the drugs for the treatment of symptoms of peripheral neuropathy (9.4%), and two (3.8%) for neuropathic pain associated with diabetic neuropathy (**Table 4**). Finally, only two (3.8%) of participants reported the use of both drugs for the treatment of epilepsy.

Parallel Smoking & Other Consumed Substances

25 (47.2%) of participants denied tobacco smoking concomitantly with either pregabalin or gabapentin (**Table 5**). On the other hand, 23 (43.4%) of participants reported tobacco smoking alongside drug use, whereas nine (17.0%) used e-cigarettes, eight used water pipes (15.1%), and four (7.5%) used chewable tobacco. Lastly, 34 (64.2%) participants who self-reported pregabalin or gabapentin use denied the use of other substances of abuse. 15 participants used marijuana (29.0%) while 10 (18.9%) participants reported drinking alcohol, nine (17.0%) used opioids, and four (7.5%) used

Table 6. Self-reported adverse effects associated with use of pregabalin & gabapentin

Variable	n (%)
Awareness of adverse effects	
Yes	37 (69.8%)
No	16 (30.2%)
Adverse effects*	
Hypersomnia	23(43.4%)
Poor memory/concentration	14 (26.4%)
Fatigue	13 (24.5%)
Dry mouth	12 (22.6%)
Pain	7 (13.2%)
Hyperactivity	7 (13.2%)
Blurred vision	7 (13.2%)
Constipation	7 (13.2%)
Increased sociability	6 (11.3%)
Tremor	4 (7.5%)
None	16 (30.2%)

Note. *Multiple choices were allowed

fenethylline (captagon). Benzodiazepines, methamphetamine, and joker were all used by the same number of participants at a total of three (5.7%) for each substance, while only one (1.9%) participant reported the use of antidepressants (**Table 5**).

Adverse Effects & Withdrawal Symptoms

In the current study, 37 (69.8%) participants were aware of the adverse effects of both drugs whilst the remainder (n=16, 30.2%) were not (**Table 6**). In addition, our results revealed that the most common adverse effect experienced by participants was hypersomnia (n=23, 43.4%) followed by poor memory and concentration, which was reported by 14 (26.4%) participants (**Table 6**). Moreover, 13 (24.5%) of the participants reported the development of fatigue, 12 (22.6%) have had dry mouth, seven (13.2%) participants experienced painful episodes, seven (13.2%) suffered from hyperactivity, 7 (13.2%) reported blurred vision, seven (13.2%) had constipation, six (11.3%) thought they had increased sociability, while only four (7.5%) suffered from tremors.

Regarding the withdrawal symptoms, the majority of participants (n=34, 64.2%) did not experience any withdrawal symptoms, but those who did, reported depression-like symptoms as the main issue that developed following the cessation of drug use (n=14, 26.4%) (**Figure 3**). Other symptoms included difficulty concentrating, which was experienced by 13 (24.5%) participants; anxiety, experienced by 11 (20.8%) participants; nightmares, reported by nine (17%); suicidal thoughts, reported by nine (17.0%); insomnia, experienced by eight (15.1%); exhaustion, developed in eight (15.1%); shivering in six (11.3%); hallucinations in 6 (11.3%); joint and muscle pain in five (9.4%); and convulsions in only four (7.5%) of the participants (**Figure 3**).

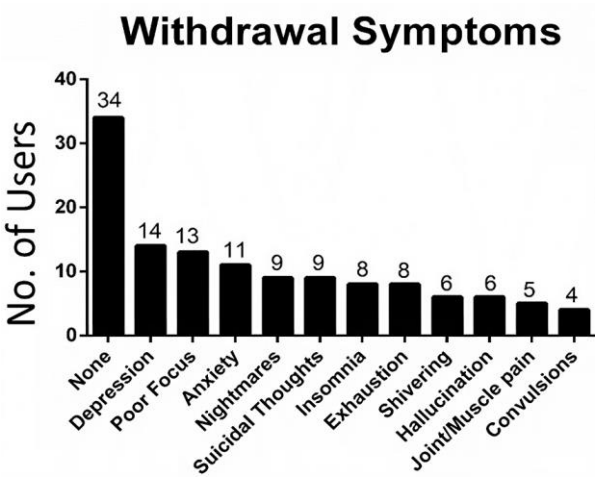

Figure 3. Self-reported adverse effects associated with discontinuation of pregabalin & gabapentin use (Source: Authors' own elaboration)

Finally, our analysis revealed that 24 (45.3%) of participants did not meet DSM-5 criteria of substance use disorder, six (11.3%) met criteria with mild severity, six (11.3%) met criteria with moderate severity and 17 (32.1%) met criteria with severe severity (**Table 7**).

DISCUSSION

This study examined the extent of pregabalin and gabapentin abuse amongst one of the vulnerable populations in Jordan. There were three major findings in this study. First, one in every 25 participants (3.9%) self-reported to have ever-used pregabalin or gabapentin with lyrica being the most used formula of pregabalin. Second, the most frequently experienced adverse effect of either drug was hypersomnia (43.4%). Although most candidates did not experience any withdrawal symptoms, yet in those who did, depression-like symptoms were the most reported among participants. Third, 29 of users met DSM-V criteria for substance use disorder for using pregabalin or gabapentin.

Pregabalin and gabapentin (or gabapentanoids) are commonly prescribed medications for the treatment of several medical conditions. Recent reports suggested that these drugs may be abused or misused by patients [22]. The illicit use of these drugs can be associated with tremendous morbidity and mortality especially if co-abused with other substances, such

Table 7. DSM-5 criteria for substance use & dependence among study participants who reported pregabalin or gabapentin use

DSM-5 criteria	Yes	No
Taking the substance in larger amounts or for longer than you're meant to	17 (32.08%)	36 (67.92%)
Wanting to cut down or stop using the substance but not managing to	19 (35.85%)	34 (64.15%)
Spending a lot of time getting, using, or recovering from use of the substance	19 (35.85%)	34 (64.15%)
Cravings and urges to use the substance	22 (41.51%)	31 (58.49%)
Not managing to do what you should at work, home, or school because of substance use	15 (28.30%)	38 (71.70%)
Continuing to use, even when it causes problems in relationships	18 (33.96%)	35 (66.04%)
Giving up important social, occupational, or recreational activities because of substance use	12 (22.64%)	41 (77.36%)
Using substances again and again, even when it puts you in danger	15 (28.30%)	38 (71.70%)
Continuing to use, even when you know you have a physical or psychological problem that could have been caused or made worse by the substance	12 (22.64%)	41 (77.36%)
Needing more of the substance to get the effect you want (tolerance)	19 (35.85%)	34 (64.15%)
Development of withdrawal symptoms, which can be relieved by taking more of the substance	21 (39.62%)	32 (60.38%)

as opioids [23]. Similar to other commonly abused drugs (such as heroin and cocaine), pregabalin increases the level of dopamine in the central nervous system, which is responsible, in part, for its reward effects [24].

Gabapetinoid abuse is a worldwide phenomenon with a prevalence of 1.6% based on a report conducted in 2017 [25]. In the UK, gabapentin and pregabalin abuse prevalence were 1.1% and 0.5%, respectively [26]. In the USA, gabapentin and pregabalin abuse prevalence were 2.1% and 1.5%, respectively, among an adult population aged 18-59 [22]. In countries in the region, a cross-sectional study of 370 was conducted in the Kingdom of Saudi Arabia found that gabapentin and pregabalin abuse prevalence was 4.6% and 23.6% among a population aged 16-30 years old, respectively [27]. Another cross-sectional study from Egypt found that the prevalence of pregabalin abuse was 30.0% among a population of 400 substance use disorder and psychiatric disorders patients [28]. In our study, the prevalence of gabapentoids abuse was 3.9% among university students in Jordan, which happens to be slightly higher than global rates and those in the USA and the UK but was somewhat lower than regional rates in Egypt and Saudi Arabia. These differences may be due to methodological differences in populations, timeframe, and assessment methods (online vs. live questionnaire).

In Jordan, the rates of gabapentinoid abuse in the general population are largely unknown. One study reported that 11.0% of total drug users abused gabapentoids according to the Jordanian Mental Health Care Clinics Database with increasing frequency of abuse overtime [29]. However, conclusions on the rate of use can be drawn partly from other evidence on the drug dispensation from local pharmacies. For example, a study involving 14 community pharmacies in Jordan for customers seeking pregabalin (n=77) revealed that 35 of them were suspected of abusing pregabalin. The most frequent complaint for which the customer asked for pregabalin was spinal disc herniation. The most frequent brand names of pregabalin was lyrica followed by zega [29]. Importantly, 94.3% of the population studied reported self-medication, reflecting the extent of illicit use of pregabalin, and the need to draw more attention towards the problem [18]. Lyrica was most abused drug in our study (47.0%) followed by gabatrix (26.0%), while in [18], lyrica and galica were the most abused drugs followed by zega. Almost half of abusers in our study did not have a prescription (50.9%), while in comparison, in [18], 94.3% did not have a valid prescription.

In our study, most abusers were males (29, 6.0%, p=0.003), which is consistent with previous findings, which indicated that males are more likely to abuse drug [18, 29]. However, issues of stigma among females in the Middle East regarding the reporting of their potential drug abuse remain a possible explanation of the observed gender difference. It is important to note that our study focused on university student populations aged 18-25, while other studies conducted in Jordan investigated rates of abuse among the general population, where most abusers were aged 21-40 [18]. However, we identified that abuse potential increased with increasing age. In our study, most abusers were smokers (52.8%), which goes in agreement with other reports from Jordan, where most pregabalin abusers are tobacco smokers [20]. On the other hand, in our study, only a minority of participants reported the consumption of other substances of abuse in contrast to previous studies in Jordan [20]. Again, this can be attributed to the nature of the sample in this work, which only included university students who might not have the financial ability or access to obtain other drugs of abuse. Most abusers continued taking gabapentinoids despite being aware of their adverse effects, with hypersomnia as the most reported, followed by poor memory and concentration, while in other literature in Jordan, abusers were not aware of its adverse effects [20]. The majority of abusers reported withdrawal symptoms when stopping the drug, which is consistent with previous data from Jordan, with depression being the most reported, followed by poor concentration [20]. Differences in pregabalin use observed above should be further investigated using qualitative studies especially when addressing tobacco use as a shared substance between users. This is specifically true when considering the high rates of waterpipe use among younger age groups in Jordan and the region [30, 31].

To our knowledge, this study is the first to examine gabapentoids abuse among university students in Jordan. The importance of this study is that it reports gabapentanoids abuse rates following the recent efforts of Jordanian health authorities to control their use. This indicates that pregabalin abuse still occurs despite being a prescription-only drug, suggesting the need for stricter laws and surveillance of pharmacies that dispense prescription-only drugs without a prescription. This is true considering the unfortunate low level of awareness among community pharmacists' regarding the potential for misuse and adverse effects of pregabalin [20]. In Saudi Arabia, despite being a controlled drug, gabapentin is still abused and usually in combination of opioids or alcohol [27]. Moreover, our analysis identified that one in every 10 users abused the drug for more than two years and one user indicated drug use at doses higher than 1,500 mg/day. While we have not investigated self-reported overdose symptoms, this evidence is somewhat alarming and suggests a potential for complications associated with drug overdose [32]. This invites further studies to measure the incidence of overdose among pregabalin and gabapentin abusers using qualitative designs. Finally, policy makers should recognize the risk of pregabalin abuse, especially among young adults, and increase the awareness of this potentially new risky behaviors of drug abuse.

CONCLUSIONS

Gabapentanoid use seems to be a serious public health problem than needs further investigation and public health interventions to increase awareness and combat use among both males and female students. However, this study has several limitations. First, data collection was through online forms, rather than direct interview-based surveying, mainly due to COVID-19 restrictions. This, however, is a suitable course of data collection for socially undesirable behaviors, especially among females. Second, our study sample consisted mostly of students from public universities. Despite that these universities enroll most college students in the country, data from students in private schools is missing, especially that those have different socioeconomic characteristics and might have different rates of pregabalin or gabapentin abuse. Third, social stigma and concerns regarding the consequences of use may have dampened the participation rates as well as the reporting of use.

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REFERENCES

1. National Institute on Drug Abuse. Misuse of prescription drugs research report. National Institute on Drug Abuse; 2020. Available at: https://nida.nih.gov/download/37630/misuse-prescription-drugs-research-report.pdf?v=add4ee202a1d1f88f8e1fdd2bb83a5ef (Accessed: 25 February 2023).
2. Schulte MT, Hser YI. Substance use and associated health conditions throughout the lifespan. Public Health Rev. 2014;35(2):1-27. https://doi.org/10.1007/BF03391702
3. McCance-Katz EF. The national survey on drug use and health: 2017. Substance abuse and mental health services administration 2019 May 7:7. Available at: https://www.samhsa.gov/data/sites/default/files/reports/rpt29392/Assistant-Secretary-nsduh2019_presentation/Assistant-Secretary-nsduh2019_presentation.pdf (Accessed: 25 February 2023).
4. French J, Glue P, Friedman D, et al. Adjunctive pregabalin vs gabapentin for focal seizures. Neurology. 2016;87(12):1242-9. https://doi.org/10.1212/WNL.0000000000003118
5. Gajraj NM. Pregabalin: Its pharmacology and use in pain management. Anesth Analg. 2007;105(6):1805-15. https://doi.org/10.1213/01.ane.0000287643.13410.5e
6. Stahl SM, Porreca F, Taylor CP, Cheung R, Thorpe AJ, Clair A. The diverse therapeutic actions of pregabalin: Is a single mechanism responsible for several pharmacological activities? Trends Pharmacol Sci. 2013;34(6):332-9. https://doi.org/10.1016/j.tips.2013.04.001
7. Silverman RB. From basic science to blockbuster drug: The discovery of lyrica. Angew Chem Int Ed Engl. 2008;47(19):3500-4. https://doi.org/10.1002/anie.200704280
8. FDA. Label: Pregabalin (LYRICA). FDA; 2018.
9. Taylor CP, Gee NS, Su TZ, et al. A summary of mechanistic hypotheses of gabapentin pharmacology. Epilepsy Res. 1998;29(3):233-49. https://doi.org/10.1016/S0920-1211(97)00084-3
10. Kukkar A, Bali A, Singh N, Jaggi AS. Implications and mechanism of action of gabapentin in neuropathic pain. Arch Pharm Res. 2013;36(3):237-51. https://doi.org/10.1007/s12272-013-0057-y
11. FDA. Label: Gabapentin (NEURONTIN). FDA; 2017.
12. Zellner N, Eyer F, Zellner T. Alarming pregabalin abuse in Munich: Prevalence, patterns of use and complications. Dtsch Med Wochenschr. 2017;142(19):e140-7. https://doi.org/10.1055/s-0043-104228
13. Zhou L, Bhattacharjee S, Kwoh CK, et al. Trends, patient and prescriber characteristics in gabapentinoid use in a sample of United States ambulatory care visits from 2003 to 2016. J Clin Med. 2019;9(1):83. https://doi.org/10.3390/jcm9010083
14. De Sousa A, Lodha P. Pregabalin misuse in a 75-year-old woman. J Geriatr Ment Heal. 2018;(1):94-8. https://doi.org/10.4103/jgmh.jgmh_35_18
15. Yazdi K, Hemetsberger U, Baier C. Pregabalin abuse of benzodiazepine and alcohol addicted patient. Psychiatr Danub. 2015;27(3):278-9. https://doi.org/10.1002/adaw.30237
16. Peckham AM, Fairman KA, Sclar DA. Prevalence of gabapentin abuse: Comparison with agents with known abuse potential in a commercially insured US population. Clin Drug Investig. 2017;37(8):763-73. https://doi.org/10.1007/s40261-017-0530-3 PMid:28451875
17. Nguyen TA. Gabapentin abuse. College of Pharmacy Student Research 2020:4. Available at: https://nsuworks.nova.edu/hpd_corx_stuarticles/4/ (Accessed: 25 February 2023).
18. Al-Husseini A, Abu-Farha R, Wazaify M, Van Hout MC. Pregabalin dispensing patterns in Amman-Jordan: An observational study from community pharmacies. Saudi Pharm J. 2018;26(3):306-10. https://doi.org/10.1016/j.jsps.2018.01.012 PMid:29556121
19. Akeed.com. "Lyrica… New addiction invades University of Jordan…" Akeed.com; 2017. Available at: https://akeed.jo/en/post/1394/_Lyrica_New_Addiction_Invades_University_of_Jordan_Press_Report_Based_on_Anonymous_Sources (Accessed: 25 February 2023).
20. Al-Husseini A, Wazaify M, Van Hout MC. Pregabalin misuse and abuse in Jordan: A qualitative study of user experiences. Int J Ment Health Addict. 2018;16(3):642-54. https://doi.org/10.1007/s11469-017-9813-4
21. Hashish RKH, Awad TE. Pregabalin abuse among patients with chronic pain syndrome. Pain Med. 2020;3(1):1009.
22. Evoy KE, Covvey JR, Peckham AM, Reveles KR. Gabapentinoid misuse, abuse and non-prescribed obtainment in a United States general population sample. Int J Clin Pharm. 2021 Jan;43(4):1055-64. https://doi.org/10.1007/s11096-020-01217-8
23. Kriikku P, Ojanperä I. Pregabalin and gabapentin in non-opioid poisoning deaths. Forensic Sci Int. 2021;324:110830. https://doi.org/10.1016/j.forsciint.2021.110830
24. Althobaiti YS, Almutairi FM, Alshehri FS, et al. Involvement of the dopaminergic system in the reward-related behavior of pregabalin. Sci Rep. 2021;11(1):1-9. https://doi.org/10.1038/s41598-021-88429-8
25. Evoy KE, Morrison MD, Saklad SR. Abuse and misuse of pregabalin and gabapentin. Drugs. 2017;77(4):403-26. https://doi.org/10.1007/s40265-017-0700-x
26. Kapil V, Green JL, Lait MC Le, Wood DM, Dargan PI. Misuse of the γ-aminobutyric acid analogues baclofen, gabapentin and pregabalin in the UK. Br J Clin Pharmacol. 2014;78(1):190. https://doi.org/10.1111/bcp.12277

27. Alkhalaf AA, Bukhari RA, Alshehri EA, Alshehri SO, Badr AF. Abuse liability of gabapentin in the Saudi population after the pregabalin restriction: A cross-sectional study. J Taibah Univ Med Sci. 2021;16(5):700-5. https://doi.org/10.1016/j.jtumed.2021.04.009
28. Gabr A. Prevalence and risk factors of pregabalin misuse among patients with substance use disorder. Al-Azhar Assiut Med J. 2019;17(4):393. https://doi.org/10.4103/AZMJ.AZMJ_126_19
29. A. Obiesat DM, Marashdeh DMF, K Al-Zoubi DA, M. Al-Alwan DM, Al-Odat DRT. Pregabalin abuse in between Jordanian youths need to concern. Int J Sci Res Manag. 2019;7(07):2011-3. https://doi.org/10.18535/ijsrm/v7i7.mp03
30. Kheirallah KA, Alsulaiman JW, Al-Sakran MH, Alzyoud S, Veeranki SP, Ward KD. Waterpipe tobacco smoking among Arab youth; a cross-country study. Ethn Dis. 2016;26(1):107-12. https://doi.org/10.18865/ed.26.1.107
31. Kheirallah KA, Veeranki SP, Alzyoud S, et al. Collision of waterpipe and cigarette smoking epidemics among youth in Arab countries. J Subst Abuse. 2016;21(5):530-6. https://doi.org/10.3109/14659891.2015.1082159
32. Evoy KE, Covvey JR, Peckham AM, Ochs L, Hultgren KE. Reports of gabapentin and pregabalin abuse, misuse, dependence, or overdose: An analysis of the food and drug administration adverse events reporting system (FAERS). Res Social Adm Pharm. 2019;15(8):953-8. https://doi.org/10.1016/j.sapharm.2018.06.018