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Cannabis and Tramadol are Prevalent among the First Episode Drug-Induced Psychosis in the Egyptian Population: Single Center Experience

Mai Taha [1], Yasmeen M. Taalab [1,2,*], Warda F. Abo-Elez [3] and Sahar A. Eldakroory [1]

1 Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt; dr.nassz@ymail.com (M.T.); sam94267@hotmail.com (S.A.E.)
2 Institut für Rechtsmedizin und Verkehrsmedizin, UniversitätsKlinikum, 69120 Heidelberg, Germany
3 Psychiatry Department, Faculty of Medicine, Mansoura University, Mansoura 35516, Egypt; warda.aboelez@yahoo.com
* Correspondence: dryasmeen.taalab@gmail.com; Tel.: +49-17830-10680

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Abstract: (1) Background: Cannabis and tramadol are featuring prominently in Egypt; however, their prevalence in first episode psychosis is still uncertain. We aimed at determining the prevalence of cannabis and tramadol among the first-psychotic episode in Egyptian inpatients and to compare the demographic and psychopathological profiles of substance abusers versus patients with the comorbid diagnosis. (2) Methods: Patients presented with psychotic episode and admitted to Mansoura Psychiatric Department were recruited. Diagnosis of psychiatric illness and drug/substance use was carried out using the Diagnostic and Statistical Manual- Fourth Edition (DSM-IV) criteria. Standard urine tests and thin layer chromatography were performed to detect cannabis and tramadol. (3) Results: Of the 100 subjects in the study, the majority (55.6%) of patients were cannabis-only positive. Overall, cannabis-alone showed the highest frequency of substance used among the currently diagnosed psychotic disorders. According to urine tests, cannabis demonstrates the higher frequency of intake in both studied groups. 66.7% of the studied population had 1–5 years self-reported histories of substance abuse predating the first psychotic episode. (4) Conclusions: The percentage of cannabis and tramadol among the first episode psychotic patients has been unexpectedly high and the standard urine testing should be considered in emergency and mental health facilities.

Keywords: prevalence; drug abuse; psychosis; psychotic-spectrum disorders; cannabis; tramadol; first-psychotic episode; first episode drug-induced psychosis

1. Introduction

In Egypt, and regardless to the order of abuse, cannabis and tramadol are on the top list of the drug/substances used according to statistics of Fund for Drug Control and Treatment of Addiction (FDCTA). Half of the 129,850 people who entered drug rehabilitation in 2007 were addicted to cannabis, while 43% were dependent on opiates of various types. The majority of them are between 15 and 25 years of age. Rising rates of unemployment are said to contribute to the high addiction rates [1–3].

From 2007 to 2014, the Unit of Research in the General Secretariat of Mental Health and Addiction Treatment, Ministry Of Health, Egypt, conducted a cross-sectional community-based survey to study the substance abuse problem in the Egyptian governorates within the National Addiction Research Program [4]. A total number of 106,480 adult Egyptians were included in the survey, which revealed that about one fifth (19.1%) of the studied sample is regularly using the substance (tobacco smoking was excluded) [4]. Alongside, many of the outspread studies in different cities in Egypt have found

that 20% to 40% of adults with substance use disorders (SUD) use tramadol [5]. Furthermore, Egyptian adolescents with SUD showed a higher percentage of tramadol use 83% [6].

In 2018, the Egyptian Ministry of Social Solidarity reported on its official website that substance abuse rates in Egypt have hit 10%, or double the global average, and that tramadol is the most abused substance, followed by cannabis and heroin. More than 12% of Egyptian students are dependent on drugs/substances, 9% use "bango" and 3% are regularly using hashish. In a trial to explore the extent of the problem among students, a survey that was conducted in Mansoura University targeting 1564 medical students in 2017; 65.7% females and 34.3% males from almost 14 faculties including medicine, pharmacy, veterinary medicine, art, science, agriculture, law, and others showed the following: 618 (39.5%) are cannabis users and 63 (4%) are regularly using tramadol to improve their performance. These results are first to be published in the current article.

This recorded information make cannabis use disorders (CUDs) are among the most prevalent illicit/nonmedical drug use disorders, not only in Egypt, however, globally [7–17]. Essentially, CUD is well-documented for its various health risks, such as psychiatric disorders, motor vehicle injuries, and respiratory and cardiovascular diseases [11,17–19]. Nevertheless, a need to investigate CUD and related comorbidities in large clinical samples has become imperative [17]. Similarly, tramadol is associated with a wide range of disorders and, despite being a scheduled drug, the widespread illegal trafficking made it available, easily accessible, and cheap [20]. In 2012, the Egyptian Ministry of Health moved tramadol from schedule 3 to 1 as a highly addictive substance [21].

Opioid use disorders that are attributed to tramadol (OUD-T) have shown a significant association with psychiatric comorbidities. A study that was carried on 100 patients recruited from Zagazig University Hospital in Egypt and diagnosed with OUD-T has demonstrated that the prevalence of psychiatric disorders is significantly higher in the tramadol group when compared to the controls (45.8% vs 24%). Among the tramadol users, 45.4% had anxiety disorders, 36.4% had mood disorders, and 18.2% had psychotic disorders. The prevalence of psychiatric disorders among polysubstance abusers was compared to the pure tramadol users and was approximately likewise (50% vs 45.8%). Among the polysubstance users, 65.8% had mood disorders, 36.8% had anxiety disorders, and 28.9% had psychotic disorders [22].

Generally, psychosis is the defining feature of schizophrenia spectrum disorders, which is a common but variable feature of mood and substance use disorders (SUD), and a relatively common feature of many developmental, acquired, and degenerative neurologic and medical conditions. It also occurs in some people with bipolar disorder during either a manic or depressive episode, as well as in some individuals during a major depressive episode that is associated with major depressive disorder [23]. Across these conditions, psychosis is both a contributor to disability and a barrier to productivity and participation. Psychosis is, undoubtedly, a key target of evaluation and treatment among patients receiving care from neurologists and psychiatrists [23–26].

Noticeably, individuals with psychotic-spectrum disorders use cannabis at higher rates than the general population and individuals with other psychiatric disorders, which may contribute to increased rates of medical problems and mortality [27]. Mutually, crosstalk between illicit drug use, particularly cannabis use, and the onset of schizophrenia, has been demonstrated [28–30]. Comorbid drug/substance use has been profoundly encountered during the course and treatment of Psychotic-spectrum disorders, for example, the concomitant drug misuse in schizophrenia has been frequently encountered and further associated with an increased rate of hospital stay [31] and violence [32]. It is also well established that psychotic symptoms can occur following drug misuse, resulting in a diagnosis of drug-induced psychosis. However, unfortunately, little is known regarding first-episode drug-induced psychosis and only a few studies have examined drug-induced psychosis in detail. We hypothesize that there is an association between the occurrence of a first psychotic episode with cannabis and tramadol use. Therefore, we are investigating the prevalence of cannabis and tramadol use among Egyptian patients with first episode drug-induced psychosis versus patients with comorbid psychiatric

disorders. Additionally, we compare the demographic, diagnostic, and psychopathological profiles of substance users.

2. Experimental Section

2.1. Study Design and Patients Recruitment

The present study used a cohort design to describe a sample of patients who received a diagnosis of first-episode drug-induced psychosis as compared with comorbid psychiatric disorders. A hundred patients that presented with psychotic episode were recruited between the years 2016 and 2018 from the inpatient population admitted to Psychiatric Department at Mansoura University Hospitals. Two groups are characterized based on the DSM diagnostic criteria; first episode drug-induced psychosis and comorbid psychotic disorders. The former refers to those that experienced first time psychotic episode following drug abuse, whilst, the later displayed patients diagnosed with psychotic spectrum disorders with coexisting drug abuse.

2.2. Subjects

Data were collected for all included adult patients that were aged 18–65 years old, of both sexes who are examined by Mansoura consultant psychiatrists with a diagnosis of first episode psychosis, according to DSM-IV diagnostic criteria [33]. Each patient was given a clinical DSM-IV diagnosis by their consultant psychiatrist when they first presented to a secondary health care facility. This study was only concerned with patients that were diagnosed with a first episode drug-induced psychosis and psychotic illness co-existed with drug abuse where the participants provided a current or lifetime substance use, harmful use, and/or dependence. The only exclusion criteria were:

1. Patients with a medical illness known to cause psychiatric disorders or those with a past history of treated psychosis that is so-called presentation outside of the Trust area with a first-episode psychosis.
2. Patients on drugs that known to cause a false positive result in substance abuse analytical techniques.
3. Patients with mental impairment, dementia, delirium, and other cognitive impairment disorders.

2.3. Ethical Consideration

The consent form contains information regarding the purpose of the study, procedures, as well as the possible benefits and confidentiality of the results. The study protocol was approved by the Institutional Research Board (IRB) of Faculty of Medicine-Mansoura University with reference no.MS/16.10.57

2.4. Confidentiality

All patients were given unique identification numbers and confidentiality was strictly maintained.

2.5. Methodology

2.5.1. Clinical Diagnostic Procedures

All the participants were subjected to thorough history taking and full clinical examination, including sociodemographic data (age, occupation and residence), medication, past medical history, and family/social history. Initial survey study for selection of patients with SUD and psychotic illness was done using the Present State Examination 10th revision (PSE-10) of the WHO Schedules for Clinical Assessment in Neuropsychiatry (SCAN) version 2 [34], which constitutes the main instrument for clinical assessment. This is a standard semi-structured interview for eliciting signs and symptoms of mental disorders that is appropriate for use by psychiatrists. According to Hamdi and colleages (1995), PSE-10 has been translated into Egyptian colloquial Arabic, and an abridged form of the Arabic

version of the PSE-10 was employed in the survey based upon the short English form of the PSE-10. The short PSE- English-Arabic form adopted in this study covers all of the screening symptoms for psychiatric disorders in the domains of psychotic disorders, somatoform and dissociative disorders, and mood disorders [35].

For the diagnosis of Psychosis, the structured clinical interview for DSM-IV- clinician version (SCID-5-CV) is conveniently provided along each corresponding DSM-IV criterion, which aids in rating each as either present or absent. The SCID-5-CV is an abridged and reformatted version of the Research version of the SCID, the structured diagnostic interview that is most widely used by researchers for making DSM diagnoses for the past 30 years [36].

Clinical assessment was done for the diagnosis of substance use disorders: Structured Clinical Interviewing using DSM-IV (SCID-I). SCID-I is used to diagnose cannabis and Tramadol abuse or dependence and exclude other Axis I diagnosis according to DSM-IV TR classification. Its Arabic version was previously used and validated [33,36].

2.5.2. Sample Acquisition for Standard Urine Testing

Urine samples of 20 mL were obtained from all of the participants at the time of admission and before receiving any treatment in a clean, dry, sterilized, and labeled containers without any preservative and stored at −20 °C for urine analysis. Extraction was done for the detection of Cannabis and Tramadol using TLC using the standard protocol [37]. Active abuse of cannabis (during the last month prior to hospitalization) was registered according to urine tests and/or self-reports, and life-time abuse according to self-reports only. Psychiatric history and self-report were used to diagnose tramadol abuse and dependence (active and life-time).

2.6. Statistical Analysis

Data were entered and statistically analyzed while using the Statistical Package for Social Sciences (SPSS) version 16. Qualitative data were described as numbers and percentages. Chi square ($\chi 2$) test or Fisher's exact test or Monte Carlo test was used for a comparison between groups, as appropriate. Quantitative data were described as means (±SD) or medians, as appropriate. Data were tested for the normality by Kolmogorov-Smirnov test. For the normally distributed variables, the independent sample *t*-test was used for comparison between groups. While in the non-normally distributed variables, the Mann-Whitney test was used for comparison between groups. "*p*-value ≤0.05" was considered to be statistically significant.

3. Results

The one hundred patients that were included in the current study are admitted to the hospital following an attack of psychosis. All patients were followed-up to establish diagnosis. Based on the DSM diagnostic criteria, two groups are characterized; first episode drug-induced psychosis and comorbid psychotic disorders. The former refers to those experienced first-time psychotic episodes following drug/substance use, whilst the later displayed chronic psychiatric patients diagnosed with psychotic spectrum disorders who develop drug/substance use during the course and treatment of the disease.

Table 1 shows the sociodemographic data, including age, sex, marital status, residence, education, and occupation among the overall studied population (n = 100). Among the 100 patients that were included in the current study of the age range 18–55 years and a mean ± SD of 28.8 ± 8.3, 64 were male patients and 36 were females. Half are married (50%) and slightly more (54%) are living in rural areas. Regarding the educational level, 10% are illiterate, 22% showed the ability to read and write, 44% continued up to secondary level, and the university educated participants represents 24%. Among the studied group, 37% are unemployed, 19% are unskilled manual workers, 24% are skilled manual workers, and 12% are semi-professional workers, while only 8% are professional workers. Figure 1 demonstrates the age of first drug use among the overall studied patients (n = 100). The mean age of drug use onset was 25.4 ± 6.9, where the majority of cases (54%) started at the age range 20–30 years old.

Table 1. Sociodemographic data (Age, Sex, Marital status, Residence, Education, and Occupation) among the studied patients (n = 100).

Characteristic	Study Group (n = 100)
Age in years (Mean ± SD)	28.8 ± 8.3
Sociodemographic variable	**No. (%)**
Marital status	
Married	50 (50%)
Unmarried	50 (50%)
Gender	
Male	64 (64%)
Female	36 (36%)
Age of the first drug use (groups)	
10–20	27 (27%)
20–30	54 (54%)
30–40	14 (14%)
> 40	5 (5%)
Mean ± SD	25.4 ± 6.9
Residence	
Urban	46 (46%)
Rural	54 (54%)
Education	
Illiterate	10 (10%)
Read and write	22 (22%)
Secondary	44 (44%)
University	24 (24%)
Occupation	
Unemployed	37 (37%)
Unskilled manual worker	19 (19%)
Skilled manual worker	24 (24%)
Semi-professional worker	12 (12%)
Professional worker	8 (8%)

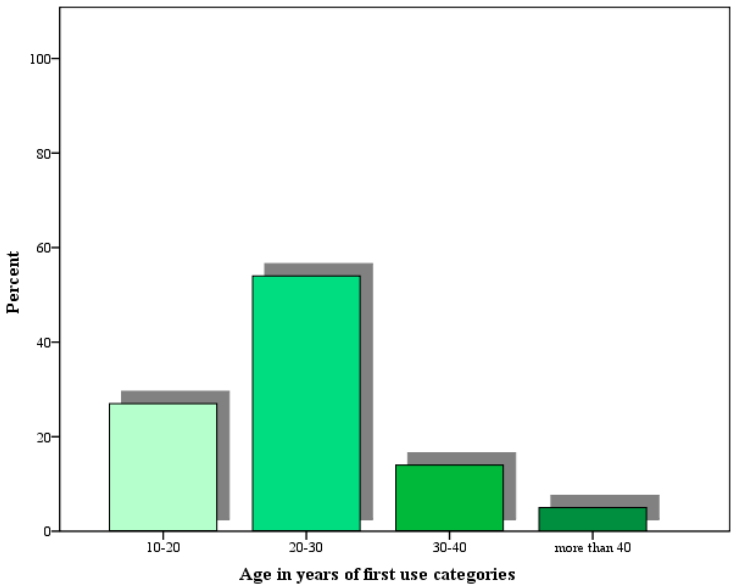

Figure 1. Age categories of first drug use.

Table 2 illustrates the comparison of the sociodemographic variables, including age, marital status, residence, education, and occupation between the two studied groups; first episode drug-induced psychosis and comorbid psychotic disorder. No statistically significant difference has been demonstrated regarding all of the studied characteristics, except when comparing the mean age between the two groups ($t = 6.3$, $p < 0.0001$). The mean age (in years) was significantly higher among the group of comorbid psychotic disorders (mean ± SD of 37.9 ± 8.5). As regarding patients diagnosed with drug induced psychosis ($n = 81$), the majority of cases are unmarried (54.3%), living in rural areas (56.8%), of secondary educational level (42%) and unemployed (38.3%). While, in patients with co-morbid drug abuse ($n = 19$), 13 cases of them (68.4%) are married, and 42.1% are living in rural areas. Further, 31.6% are unemployed, 21.1% are un-skilled manual workers, 21.1% are skilled manual workers, and 21.1% are semi-professional workers, while 5.3% are only professional workers.

Table 2. Comparison of the Sociodemographic characteristics (Age, Marital status, Residence, Education, and Occupation) between the two characterized groups; first episode drug-induced psychosis and comorbid psychotic disorders ($n = 100$).

Measure	First Episode Drug- Induced Psychosis ($n = 81$)	Comorbid Psychotic Disorders ($n = 19$)	Test of Significance	
Age in years (Mean ± SD)	26.6 ± 6.6	37.9 ± 8.5	$t = 6.3$, $p < 0.0001$	S [1]
Marital status	No. (%)	No. (%)	$\chi^2 = 3.2$, $p = 0.07$	N.S [2]
Married	37 (45.7%)	13 (68.4%)		
Unmarried	44 (54.3%)	6 (31.6%)		
Sex			$\chi^2 = 2.4$, $p = 0.06$	N.S
Male	51 (63%)	13 (68.4%)		
Female	30 (37%)	6 (31.6%)		
Residence			$\chi^2 = 1.3$, $p = 0.2$	N.S
Urban	35 (43.2)	11 (57.9)		
Rural	46 (56.8)	8 (42.1)		
Education			Monte Carlo test $p = 0.5$	N.S
Illiterate	7 (8.6)	3 (15.8)		
Read and write	19 (23.5)	3 (15.8)		
Secondary	34 (42.0)	10 (52.6)		
University	21 (25.9)	3 (15.8)		
Occupation			Monte Carlo test $p = 0.7$	N.S
Unemployed	31 (38.3)	6 (31.6)		
Unskilled manual worker	15 (18.5)	4 (21.1)		
Skilled manual worker	20 (24.7)	4 (21.1)		
Semi-professional worker	8 (9.9)	4 (21.1)		
Professional worker	7 (8.7)	1 (5.3)		

[1] Significance, [2] non-significance.

DSM diagnostic criteria, results of urine assay, and agreement between self-report and urine testing are shown in Table 3. The majority of patients with earlier onset drug/substance use displayed various psychiatric illnesses, in which the predominant disorder was the bipolar illness in 32 cases (39.5%), followed by schizophrenia in 27 cases (33.3%), then Schizo-affective disorder in 18 cases (22.2%), and finally delusional disorder only presented in 4 cases (4.9%). Comparatively, patients with co-morbid psychiatric disorders represent 19 patients of the whole studied cases with schizo-affective disorder appeared in 9 cases (47.4%), bipolar illness in 6 cases (31.6%), schizophrenia in 3 cases (15.8%), and delusional disorder appeared in only one case (5.2%).

Table 3. DSM diagnostic criteria, urine assay and agreement between urine testing and clinical diagnosis of drug use disorder among the studied patients (n = 100).

Characteristic	Study Group (n = 100)			
	First Episode Drug-Induced Psychosis (n = 81)	Comorbid Psychotic Disorder (n = 19)	Total (n = 100)	Test of Significance
Diagnosis according to DSM-V				
Bipolar illness	32 (39.5%)	6 (31.6%)	38 (38%)	Monte Carlo test p = 0.6
Schizophrenia	27 (33.3%)	3 (15.8%)	30 (30%)	
Schizo-effective disorders	18 (22.2%)	9 (47.4%)	27 (27%)	
Delusional disorders	4 (4.9%)	1 (5.2%)	5 (5%)	
Urine testing				
Cannabis and Tramadol	25 (30.9%)	5 (26.3%)	30 (30%)	Monte Carlo test p = 0.9
Cannabis	45 (55.6%)	11 (57.9%)	56 (56%)	
Tramadol	4 (4.9%)	1 (5.3%)	5 (5%)	
Negative	7 (8.6%)	2 (10.5%)	9 (9%)	
Duration of drug/substance use				
Below 1 year	13 (16.0%)	1 (5.3%)	14 (14%)	Monte Carlo test $p < 0.0001$
1–5 years	54 (66.7%)	3 (15.8%)	57 (57%)	
Above 5 years	14 (17.3%)	15 (78.9%)	29 (29%)	
Agreement of urine testing with history, self-report and clinical diagnosis of drug/substance use				
In agreement n = 88				
Non-agreement n = 12				

According to urine analysis tests, cannabis demonstrates the higher frequency of intake in both diagnosed groups. A total of 56 subjects were positive for cannabis only, 30 were positive for both cannabis and tramadol, and 5 individuals were positive for tramadol only, while 9 individuals were negative for any illegal substances (negative urine assay). In an analysis of agreement between drug/substance abuse and urine testing, a total of 88 patients showed positive urine testing, which is in agreement with diagnosis of drug abuse, whilst twelve subjects showed negative urine testing despite displayed drug/substance use diagnosis. A statistically significant difference has been demonstrated when comparing first episode drug induced psychosis and co-morbid psychotic disorder as regarding the duration of drug use ($p < 0.0001$).

The probability of distribution of the investigated drug/substance use among the population diagnosed with different psychotic disorders is shown in Table 4. Overall, cannabis-alone is the most frequently encountered substance throughout various psychiatric diagnosis. Cannabis use is demonstrated in 63.2% of the total population diagnosed with bipolar illness, 53.3% of the total schizophrenic patients, 51.8% of schizo-affective disorders and in 40% of the patients with delusional disorders. This is followed by concomitant use of cannabis and tramadol in which the frequency encountered are 26.3%, 36.7%, 29.6% and 20% among bipolar illness, schizophrenia, schizo-affective disorders and delusional disorders respectively. A statistically significant distribution has been detected for such association, with a p-value 0.03 in which cannabis generally showed the highest frequency of abuse among all psychotic disorders diagnosed in the current study.

Table 4. Association between the type of the drug used and the psychotic disorders diagnosed among the studied population (n = 100).

Drug Use Disorder	Psychotic Disorders				Test of Significance
	Bipolar Illness (n = 38)	Schizophrenia (n = 30)	Schizo-Effective Disorders (n = 27)	Delusional Disorders (n = 5)	
Cannabis and Tramadol	10 (26.3%)	11 (36.7%)	8 (29.6%)	1 (20%)	**Monte Carlo Test p = 0.03**
Cannabis	24 (63.2%)	16 (53.3%)	14 (51.8%)	2 (40%)	
Tramadol	1 (2.6%)	0	2 (7.4%)	2 (40%)	
Others	3 (7.8%)	3 (10%)	3 (11.1%)	0	

4. Discussion

Cannabis has been accused extensively and longley for psychiatric disorders. As early as 1235, numerous written quotes have directly linked cannabis to insanity [38]. Cannabis-induced psychosis has been reported in several studies with complete remission from psychotic symptoms following cannabis stoppage; however, no studies followed up patients for more than three months after the end of treatment [39]. Consequently, Verdoux concluded that any occurrence of psychotic symptoms after cannabis intake might be attributed to risk for subsequent schizophrenia-spectrum disorders [40]. Additionally, opioid use disorders that are attributed to tramadol (OUD-T) is a public health problem in Egypt and many studies have found a high prevalence of psychiatric comorbidities among patients with opioid use disorders [22].

Our approach was to recruit those patients that were admitted to psychiatric department with psychosis. Patients were diagnosed using DSM diagnostic criteria; self-report, medical history, and clinical interview. All the studied population were followed up to establish psychiatric diagnosis. Toxicological urine screening tests were also used, and the results were linked to the clinical diagnostic outcomes. Finally, two groups were characterized, the first episode drug-induced psychosis and the comorbid psychotic disorders with coexisting drug use.

Among the 100 patients that were included in the current study of the age range 18–55 years and a mean ± SD of 28.8 ± 8.3, 64 were male patients and 36 were females. Regarding sociodemographic characteristics, a statistically significant difference has been detected when comparing the age of onset of substance abuse between the two characterized groups, and no statistically significant difference could be detected throughout the comparison (marital status, residence, education, and occupation). The early onset of substance abuse might be attributed to a major risk for ultimate psychiatric illness and other related drug abuse consequences. Similarly, a study relating the symptoms of dependence to age of first use discovered that those who started using substance before age 15 (when compared with those who began use after age 18) were 2.45 times as likely to have problems with marijuana (63% vs. 41%) and 2.65 times more likely to have problems with other drugs (71% vs. 53%) [41].

Among the substances that were tested, cannabis has been solely shown to be the highly prevalent substance among the overall diagnosed psychotic disorders. Similarly, some other available population-based studies on the same issue have found that cannabis use is associated with later schizophrenia outcomes [28]. All of those studies support the concept of temporal priority by showing that cannabis use most probably preceded schizophrenia. These studies further deliver evidence that the association between adolescent cannabis use and adult psychosis persists after controlling for many potential confounding variables, such as disturbed behavior, low IQ, place, and level of education, cigarette smoking, poor socioeconomic standards, gender, age, ethnic group, unemployment, single marital status, and previous psychotic symptoms. Further evidence for a causal relationship is provided by the presence of a dose-response relationship between cannabis use and schizophrenia [42–44], specificity of exposure [43–46], and specificity of the outcome [45]. Overall, cannabis use appears to confer a twofold risk of later schizophrenia or schizophreniform disorder (pooled odds ratio= 2.34; 95% CI: 1.69–2.95) [28].

In the current study, among the variously diagnosed psychotic disorders, cannabis-alone use has been significantly more encountered: 24 out of 35 diagnosed with bipolar illness, 16 out of 27 diagnosed with schizophrenia, and 14 out of 24 diagnosed with schizo-affective disorders ($p = 0.03$). This association between DSM diagnosis and the type of substance used may indicate the preferential use of a specific substance per diagnosis, as Khantzian has proposed [47].

In accordance with these findings, Arendt, demonstrated that cannabis is often used as self-medication for controlling aggression, but there is no such evidence for the self-treatment of depression [48]. Individual's vulnerability to multiple substance/drug abuse has been extensively described in the literature and it might explain the correlation between cannabis and tramadol abuse. Such vulnerability was predicted by the interaction of the individual with criminal and substance abusing peers [49], the availability of substances abused, and the socioeconomic standards [50].

The coexistence of psychotic disorders with cannabis alone and/or cannabis + tramadol use is captivating and it raises the concern of whether there is a common liability to the use more than one substance/drug or a common psychological basis that might impedingly lead to this phenomenon [51]. One explanation relies on the "liability model", in which a common factor is responsible for the use of both licit and illicit drugs, regardless of their order. Genetic factors and peer pressure may put an individual at risk for using or abusing both legal and illegal substances, including tramadol and cannabis [52]. Further, the "gateway theory" states out that licit drug (for example; tramadol) may serve as a gateway to cannabis abuse [53], and oppositely, that cannabis is a "gateway drug" for the use of harder drugs [54], and that individuals who use cannabis heavily might also be using other substances, such as amphetamines, phencyclidine, and lysergic acid diethylamide, which are thought to be psychogenic [55].

Some findings come in support for this explanation, which showed that the use of other drugs among young adults is almost always preceded by cannabis use [56]. This is particularly applied for heavy cannabis users (50 times or more per year), who were 140 times more likely to move on to other illicit drugs than people who had not used cannabis before. However, in the Dunedin, Christchurch, Dutch, and Swedish studies, the association between cannabis and schizophrenia held, even when adjusting for the use of other drugs [43–46].

Another possible explanation is that individuals who start using cannabis early during the age of adolescence continue to use it in adulthood. As cannabis use intoxication can be associated with transient psychotic symptoms, this might account for the observed association. However, the diagnostic interview that was used in the Dunedin study explicitly ruled out a diagnosis of schizophreniform disorder if psychotic symptoms only occurred following substance use [28,40,57–60].

Thirdly, the early-onset cannabis use is a proxy measure for poor ultimate comorbidity, which is known to be associated with schizophrenia and other psychiatric outcomes [61]. Arseneault et al. found that cannabis use was specifically related to schizophrenia outcomes [45], as opposed to depression, suggesting specificity in longitudinal association, rather than general poor premorbid adjustment, although there is other evidence showing an association between cannabis use and depression [62].

However, the prevalence of cannabis and tramadol abuse among the studied Egyptian population might be commonly related to some environmental and economic factors, in which the most available substances/drugs are the most frequently encountered and that the drug preference is related in a larger extent to drug availability rather than the individual liking of the substance or the drug abused [50].

A remarkable finding in our research was that 66.7% of the study population had between 1–5 years self-reported histories of substance abuse predating the first psychotic episode. That is to say, drug abuse may share a common genetic predisposition along with psychotic disorders, in which an increased probability for an individual to abuse substances and concomitantly or eventually to develop psychosis [63,64]. However, the presence of such a significant percentage of the study population abused substances years prior to the first episode, is not conclusively explaining the direct causal effect of abuse on the occurrence of psychosis. Similarly, Katz et al. have demonstrated a closely high percentage of the population with a long history of drug abuse and the late onset of psychotic illness

presentation [52]. Despite the frequently encountered psychotic symptoms with cases of psychoactive substance intoxication and in cases of hallucinogen abuse, the symptoms that are found in our inpatient sample and in Katz et al. study cannot be conclusively explained by the abuse.

Our results neither prove that drugs of abuse should necessarily lead to drug-induced psychosis nor lead to schizophrenia or psychotic spectrum disorders otherwise, they indicate that both cannabis and tramadol are prevalent among population that presented with first episode psychosis and that first episode drug-induced psychosis is a risk factor for the development of a longer-term psychotic illness. We also highlight the importance of the standard urinary testing in emergency and mental health facilities. Further, our findings point out an underreporting of abuse that is perhaps due to nondisclosure of the abuse of illegal substances and an underdiagnosis of abuse in the presence of acute psychosis on the part of the admitting psychiatrist.

5. Conclusions

In conclusion, cannabis use is highly prevalent among the studied population presented clinically with psychosis. This is followed by the concomitant use of cannabis and tramadol. Cannabis-alone or cannabis + tramadol might induce psychosis; first-episode drug-induced psychosis, following a variable duration of drug/substance use. Additionally, drug use might develop during the course and treatment of psychotic-spectrum disorders; comorbid drug use. The exact relation is yet to be clarified and further studies are imperative to validate the results.

6. Limitations of the Study

The study sample was middle-sized. However, our emergency hospital and psychiatry department have a catchment area of the great delta region in Egypt, excluding Alexandria; we believe that the respondents in this study represent the general population. We propose that similar studies be replicated on a larger scale and in different venues to confirm our findings. Additionally, since the beginning of the study, there has been a remarkable increase in the use of synthetic cannabinoids, which were not included in the original toxicology screen. This might well serve to remind us that the significant percentage of substance users among the study population is probably an underestimate.

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