

PATTERNS OF METHAMPHETAMINE USE AND ITS ASSOCIATIONS WITH PSYCHIATRIC SYMPTOMS IN PATIENTS UPON ADMISSION AT THE NATIONAL REHABILITATION CENTER LIDO BOGOR, INDONESIA

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ABSTRACT

Objective: Methamphetamine (MA) is a substance that is heavily abused worldwide. This present study aimed to investigate the association between the patterns of methamphetamine use and psychiatric symptoms in patients upon admission at The National Rehabilitation Center, Lido Bogor.

Methods: This was a cross-sectional study of MA abusers during the period of January 2016–December 2018 at The National Rehabilitation Center, Lido, Bogor. This study was done by assessing medical records. The inclusion criteria were MA abusers at the age of 18 y and above. Assessment of psychiatric symptoms was evaluated using Addiction Severity Index (ASI). Microsoft Excel and SPSS version 22.0 were used to process the data.

Results: The inclusion criteria were fulfilled by 1842 MA abusers. We found that 770 (41.8%) of MA abusers were assessed with psychiatric symptoms according to ASI. Depression was the most prevalent psychiatric symptom (31.9%), followed by anxiety (24.5%), and psychosis (8.9%). According to the results of multivariate analysis, the demographic profile and the mode of MA administration that are associated with the psychiatric symptoms were: female [odds ratio (OR): 1.95; 95% confidence interval (CI): 1.25–2.96, $p < 0.001$], 5-year duration of use [OR 1.43; 95% CI: 1.43 (1.19–1.73), $p < 0.001$], smoking as the route of administration [OR 1.3; 95% CI: 1.08–1.56, $p < 0.001$, $p = 0.006$], and concomitant use with other narcotics [OR 1.76; 95% CI: 1.46–2.13, $p < 0.001$].

Conclusion: Among MA abusers admitted to The National Rehabilitation Center, the main factors associated with psychiatric symptoms were: female, long duration of use, smoking as the route of administration, and concomitant use with other narcotics.

Keywords: Addiction severity index (ASI), Methamphetamine, Narcotics, Rehabilitation, Substance abuse

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INTRODUCTION

Substance abuse is a global problem that has invaded many facets of society. According to The United Nations Office on Drugs and Crime (UNODC), in 2018, around 269 million (5.4%) of the world's population aged 15-64 y had used narcotics and drugs at least once in their life [1]. While the Indonesian data, from The National Narcotics Agency (BNN) and the Indonesian Institute of Sciences (LIPI), showed that the national prevalence rate in 2019 was approximately 4.5 million or 2.4% of the population that were known to drug abusers. This data showed there were an increased prevalence rate in the last 2 y [2, 3].

Among the substances commonly abused, MA is the second most often used substance after marijuana. MA abusers were the most common patients admitted to rehabilitation facilities between 2015 and 2017 [2, 3]. MA is a substance belongs to the amphetamine-type stimulant (ATS) class, as well as the sympathomimetic amine phenethylamine class. It has a similar mechanism of action as an amphetamine; however, its penetration into the central nervous system is more significant, and its duration of effect is longer. Hence, MA has the potential to be abused more often, which leads to dependency. Changes in the brain's reward system caused by addiction can lead abusers to suffer mental symptoms like anxiety, sadness, and psychosis [4].

Along with the increase numbers of MA abusers, the emergence of its psychiatric symptoms, and the lack of data on the profiles of MA abusers, we aimed to investigate the pattern and the profiles of MA abusers and its association with psychiatric symptoms. The results of the patterns and profiles of the MA abusers can guide regulators

and health professionals in Indonesia in designing the most appropriate program for the prevention and treatment of MA abuse.

MATERIALS AND METHODS

Population and sample

This was cross-sectional data in MA abusers admitted to the national narcotics rehabilitation center in Lido Bogor from January 2016 to December 2018. The study was conducted by analyzing medical records obtained upon admission of the MA abusers. The inclusion criteria were all of MA abusers aged 18 y and above. Assessment of psychiatric symptoms was evaluated according to Addiction Severity Index (ASI). The ASI, a semi-structured interview used to evaluate substance used disorders (SUD) patients and assessed by physicians who have been trained to used ASI. The ASI was developed to provide an assessment of patient functioning across seven problem areas, commonly SUD, including medical status, employment, history of drug use, alcohol use, illegal activity, family/social relationships, and psychiatric status. The Ethical Committee of the Faculty of Medicine Universitas Indonesia approved this study with the No of KET-621/UN2. F1/ETIK/PPM.00.02/2019.

Data analysis

Microsoft Excel and SPSS version 22.0 were used to process the data. The description of MA abusers profiles and characteristics were provided in the descriptive data. The association with psychiatric symptoms were analyzed using bivariate and multivariate analysis. The difference in proportion was analyzed using the Chi-square of Fisher's exact test. The bivariate analysis findings that fulfilled the multivariate standards ($p < 0.25$) were then used in the multivariate

analysis (logistic regression). The p value cutoff of 0.05 is considered statistically significant for any significant differences.

RESULTS

Out of the total of 1900 MA abusers' medical records, 1842 abusers meets the inclusion criteria, while 58 abusers were eliminated due to incomplete data. MA abusers' demographic profile includes age, gender, employment, last education, and marital status (table 1). Most of MA abusers were males between the age of 18-40 y old. Most abusers used MA in conjunction with other addictive substances, including cannabis, opioids, tranquilizers, hallucinogens, alcohol, and other amphetamine-type stimulants. The majority of the abusers used MA at a dose of more than 0.2 g per usage for a duration of less than 5 y. MA was administered via smoking or inhaled (table 1).

Out of the 1842 MA abusers, 770 (41.8%) patients were found to have psychiatric symptoms upon admission. The types of psychiatric symptoms assessed were anxiety, depression, and psychosis. The proportion of abusers with psychiatric symptoms is reported in table 2.

We then analyzed the association between demographic characteristics and profiles of MA abusers with psychiatric

symptoms using bivariate analysis, followed by multivariate analysis. The profile and method of abuse that showed a statistically significant association with psychiatric symptoms were female gender (OR 1.95; 95% CI: 1.25-3.04), more than 5-years duration of use (OR 1.41; 95% CI: 1.16-1.71), smoking as the route of administration (OR 1.3; 95% CI: 1.07-1.57), and use with other narcotics (OR 1.48; 95% CI 1.17-1.87) (table 3).

Upon the bivariate and multivariate analysis of individual psychiatric symptoms (anxiety, depression, and psychosis), we found different factors of characteristics that were associated with each symptoms. Results from the multivariate analysis shows that the female gender (OR 1.6; 95% CI: 1.0-2.55), MA dose of more than 0.2 g (OR 1.26; 95% CI: 1.0-2.55), smoking as the route of administration (OR 1.37; 95% CI: 1.06-1.71), and concomitant use with other narcotics (OR 1.47; 95% CI: 1.13-1.91) were among the factors that increased anxiety symptoms (table 3). The factors found to be significantly associated with depression and psychosis were female gender, 5-year duration of use and smoking. Concomitant use of other narcotics increased the risk of depression (OR 1.3; 95% CI 1.01-1.65), however, it has a neutral effect on psychosis (OR 1.29; 95% CI: 0.92-1.82) (table 3).

Table 1: Demographic characteristics and profiles of MA abusers that were admitted to the national rehabilitation center, Lido Bogor

Characteristics	Number (N=1842)	n (%)
Age (years)	18-40	1702
	Over 40	140
Gender	Male	1753
	Female	89
Employment	Employed	1182
	Unemployed	660
Marital status	Single	1077
	Married	765
Concomitant addictive substances used	Cannabis	734
	Opioids	34
	Tranquilizer	66
	Hallucinogens	5
	Alcohols	831
	Other ATS*	273
Patterns of MA abuse:	<0.2	842
Dose (gram/each usage)	≥ 0.2	1000
Duration (year)	<5	1052
Route of administrations	≥ 5	790
	Smoked	937
	Inhaled	905

*ATS = Amphetamine-type stimulant

Table 2: Proportions of MA abusers with psychiatric symptoms based on the addiction severity index (ASI)

Psychiatric symptoms	N	%
At least one psychiatric symptoms	770	41.8
Anxiety	452	24.5
Depression	588	31.9
Psychosis	164	8.9
Psychosis and depression	96	5.2
Psychosis and anxiety	83	4.5
Anxiety and depression	319	17.3
Anxiety, depression and psychosis	65	3.5

Table 3: Multivariate analysis of the factors associated with psychiatric symptoms in MA abusers based on the Addiction Severity Index

Characteristics	Adjusted odds ratio (95% CI)	p-value
Association with Psychiatric symptoms		
Gender Female vs Male	1.95 (1.25–3.04)	0.003
Dose ≥ 0.2 grams vs <0.2 grams	1.15 (0.91–1.35)	0.27
Duration ≥ 5 y vs <5 y	1.41 (1.16–1.71)	<0.001
Route of administration smoked vs inhaled	1.3 (1.07–1.57)	0.006
Concomitant use with other narcotics Yes vs no	1.48 (1.17–1.87)	0.001
Use with other types of ATS Yes vs no	1.25 (-0.92–1.7)	0.14
Use with opioids Yes vs no	1.83 (0.83–4.0)	0.12
Use with tranquilizer Yes vs no	1.39 (0.83–2.42)	0.23

	Characteristics	Adjusted odds ratio (95% CI)	p-value
Association with anxiety	Gender female vs male	1.6 (1.0–2.55)	0.04
	Dose ≥ 0.2 grams vs <0.2 grams	1.26 (1.01–1.57)	0.006
	Duration ≥ 5 y vs <5 y	1.22 (0.98–1.52)	0.07
	Route of administration smoked vs inhaled	1.37 (1.06–1.71)	0.04
	Concomitant use with other narcotics Yes vs no	1.47 (1.13–1.91)	0.004
	Use with other types of ATS Yes vs no	1.2 (0.86–1.67)	0.28
	Use with opioids Yes vs no	1.66 (0.78–3.52)	0.18
	Use with tranquilizer Yes vs no	1.45 (0.82–2.56)	0.19
	History of prior rehabilitation Yes vs no	1.43 (0.93–2.19)	0.09
Association with depression	Gender Female vs Male	1.75 (1.12–2.72)	0.01
	Duration ≥ 5 y vs <5 y	1.35 (1.11–1.66)	0.003
	Route of administration smoked vs inhaled	1.34 (1.09–1.64)	0.004
	Concomitant use with other narcotics Yes vs no	1.3 (1.01–1.65)	0.03
	Use with other types of ATS Yes vs no	1.42 (1.04–1.95)	0.02
	Use with opioids Yes vs no	0.88 (0.41–1.88)	0.75
	Use with tranquilizer Yes vs no	1.88 (1.08–3.26)	0.02
	Alcohol use Yes vs no	1.07 (0.87–1.31)	0.4
	Association with psychosis	Gender Female vs Male	1.83 (0.98–3.4)
Duration ≥ 5 y vs <5 y	1.46 (1.05–2.02)	0.02	
Route of administration smoked vs inhaled	0.66 (0.47–0.91)	0.01	
Concomitant use with other narcotics Yes vs no	1.29 (0.92–1.82)	0.13	
Cannabis use Yes vs no	2.71 (1.07–6.83)	0.03	
Opioids use Yes vs no	2.71 (1.07–6.83)	0.03	
Tranquilizer use Yes vs no	1.2 (0.54–2.7)	0.64	

ATS = *ATS = Amphetamine-type stimulant

DISCUSSION

In the present study, we aimed to analyze the demographic profiles and characteristics of MA use associated with psychiatric symptoms, including anxiety, depression, and psychosis. We found several factors associated with the increased risk of psychiatric symptoms, such as gender, duration of use, route of administration and concomitant use with other narcotics.

Our study was done using a total sampling of patients admitted to the national rehabilitation center, Lido, Bogor, Indonesia from 2016 to 2018. This study's age range of MA abusers was dominated by the age group of 18-40 y. Our findings were in line with the studies from other regions in Asia that stated the average MA users were in their twenties to thirties [5, 6]. The majority of MA abusers also used other narcotics alongside MA. As reported by other studies, most abusers did so to replicate the effects they had when they initially started using opioids, primarily by combining MA with marijuana or alcohol [7–9]. In this study, similar proportions of MA abusers uses the high or low dose of MA (with the cut-off point of 0.2 g per usage). The need for different dose in each subject could be affected by the difference in metabolism and the longer duration of MA use [4, 10].

In the present study, we found a comparable proportion of smoking and inhalation as a method of MA administration. Other studies have shown that smoking is preferred because of the powerful euphoric impact that may be achieved as rapidly as intravenous treatment (approximately 2 min), while nasal delivery can takes about 5 min. Smoking also resulted in a higher bioavailability vs inhaled (90% vs 79%, respectively). The duration of MA use in our study was also like those found in other studies in Southeast Asian countries [12].

We found a high proportion of MA abusers with psychiatric symptoms (41.8%). The psychiatric symptoms assessed in this study were anxiety, depression, and psychosis. Psychiatric symptoms in MA abusers in this study were assessed from psychiatric addiction severity index domain. Psychiatric symptoms in MA users arise from prolonged duration of MA exposure, which has been demonstrated to cause neurotoxic and neuropathological effects. The most prevalent psychiatric symptom seen by MA users is depression [13, 14]. The proportion of psychiatric symptoms arising from MA use can differ in other populations. Different patterns of MA use and concomitant narcotic use may contribute to the differences between populations [13-15].

The multivariate analysis found that the demographic profile and method of MA abuse that had a statistically significant relationship

with psychiatric symptoms were gender, duration, route of administration and use with other narcotics. Psychiatric symptoms in MA abusers are more experienced by women than men. The increased risk in women might be attributed to the hormonal differences that resulted in different metabolism in women [4, 5]. It was reported that more psychiatric symptoms were found in MA abusers with a long duration of abuse. In this study, a duration of use of 5 y was more at risk of experiencing psychiatric symptoms than the duration of use <5 y. Our study agrees with other findings that the duration of MA use might predict the emergence of psychiatric symptoms [5, 16]. Smoking as the route of administration was more likely to increase psychiatric symptoms than the inhaled route. This is related to the difference in MA purity on the two routes. The form of MA in smoking is crystalline (ice meth), which has a purity of 60-80%. Even MA ice blue has a purity of almost 100%, while nasal powder (powder) with MA has a purity of 10% [17]. MA abusers often use MA with other narcotics (combinations) such as marijuana, opiates, different types of ATS, tranquilizers and hallucinogens. This combination is known to increase the risk of developing psychiatric symptoms because it will increase the toxicity of MA [18].

The results of multivariate analysis of the relationship between the demographic profile and the anxiety symptoms showed that the statistically significant variables were gender, dose, route of administration and use with other narcotics. In the previous study done by Glasner-Edward *et al.*, which examined the relationship between anxiety disorders, MA abuse and functional outcomes at a three-year follow-up, abusers who experienced anxiety had a significantly higher risk of being hospitalized for 12 mo [19]. The comorbidity of MA abuse and anxiety has implications for the course of the disease and treatment outcomes, so a comprehensive approach is needed to treat anxiety and co-occurring MA abuse. Symptoms of anxiety in women occurs twice as many (2:1) compared to men in MA abusers. These results were in line with the explanation above that there are differences in hormones and responding to stress between women and men. Different to the findings in the overall psychiatric symptoms, a higher dose of MA contributes to a higher risk of anxiety in MA abusers. The risk of Anxiety was also increased when smoking was used as a method of administration. As mentioned above, there were differences in the purity of MA crystalline forms. MA purity was linked to a higher risk of acquiring mental symptoms such as anxiety, sadness, and psychosis. MA abusers who used MA in conjunction with other opioids reported greater anxiety. The findings of this research are similar to those of a study by Hang Su *et al.*, which found that MA abusers who mix MA with other opioids are more likely to suffer

anxiety. These findings are corroborated by Jasmina Burdzovic *et al.*'s 10-year prospective analysis, which discovered that medication combinations were related to an increased prevalence of mental illnesses such as anxiety and depression [20, 21].

Gender, duration of use and the route of administration were the three main risks that increased the occurrence of depression and psychosis symptoms. According to the American Psychiatric Association, women are 1.5 to 2 times more likely than males to suffer from depression [5].

MA users often combine the use with other drugs such as tranquilizers and ATS. Anxiety, fear, tension, agitation, and memory disorder are all associated with tranquilizers usage. Another study discovered that the use of benzodiazepines might increase depression among MA users, with an OR of 2.1 [12]. The reason why abusers may take tranquilizers with MA is to lessen the effects of stimulants and dependency on MA. In contrast, the purpose of mixing with other ATS like ecstasy or methylenedioxymethamphetamine (MDMA) is to intensify the impact of MA. Stimulants are a kind of medicine that stimulates the central nervous system. Combining these medicines increases the chance of mental symptoms and increases the risk of cardiac issues and serotonin syndrome [16, 20].

According to previous research, MA may produce either long-term or short-term psychosis, often characterized by persecutory delusions, auditory and visual hallucinations, paranoia, and disordered speech. Unlike anxiety and depression, the inhaled administration route is more likely to trigger psychosis than smoking. This might be because the nasal route of administration can reach the brain directly through the olfactory and/or trigeminal nerve pathways [5]. MA increases the quantity of dopamine in the striatum, resulting in a large glutamate release in the cortex. This release will sometimes induce cortical interneuron injury, subsequently interfering with thalamocortical impulses, resulting in psychotic symptoms [5, 22, 23].

There are several limitations to this study. First, the data used is from secondary data, so it depends on the records in the Lido BNN medical records. The assessments of the way of abuse are based only on interviews, for example, on the duration, the first and last start of abusing the MA, which may result in recall bias. Another limitation of our study was that an accurate causality analysis could not be carried out between MA abusers and the onset of psychiatric symptoms. The nature of this study which was retrospective, might not eliminate other factors that influence the onset of psychiatric symptoms in MA abusers. The last limitation is the assessment of the psychiatric symptoms was based on ASI, not on DSM V.

The advantages of this study are the large number of samples and data taken from national rehabilitation center, Lido which is a national referral center from regions throughout Indonesia. Therefore, the findings in this study may be generalized to MA abusers in Indonesia. In addition, this study is the first to examine the profile and characteristics of MA abusers and its relationship to psychiatric symptoms.

CONCLUSION

Most psychiatric symptoms found in MA abusers were depression and anxiety. Female gender, longer duration of use, smoking as the route of administration and concomitant use with other narcotics are the factors that increase the risk of psychiatric symptoms among MA abusers. Our findings indicate that an early assessment of psychiatric symptoms and comprehensive management of MA abusers should be carried out. In addition, further prospective research is needed from the results obtained in this study.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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