

Clinical Profile and Drugs of Abuse Identified among People who Use Drugs Admitted to a Tertiary Hospital in the Philippines using a Validated LC-QTOF/MS Method

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ABSTRACT

Background. Drug use and abuse is a public health issue that has come into focus in the Philippines in the past years. Excluding the years of the COVID-19 pandemic, there has been a yearly increase in the number of admissions to treatment and rehabilitation centers. The census in the University of the Philippines-Philippine General Hospital (UP-PGH) National Poison Management and Control Center (NPMCC) shows a parallel increase in drug-positive patients consulting in the emergency room (ER).

Objective. The objective of this study was to describe the demographic, clinical, and drug use profiles of substance users admitted to the UP-PGH and referred to the NPMCC for drug testing.

Methods. This is a cross-sectional study where participants included patients aged 10 years and above who were referred to the NPMCC for drug testing within three days of the ER consult. Once consent or assent from children was obtained, patients were interviewed and examined. Urine samples were collected for drug screening using drugs of abuse screening test kits. A split sample was sent to the UP Drugs of Abuse Research Laboratory (UP DARL) for analysis using the liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF/MS). The data was encoded in the REDcap platform. The results were analyzed and summarized using descriptive statistics.

Results. Three hundred eighty-four (384) individuals participated in the study and submitted urine samples for testing from 1 January 2019 to 28 February 2020. One hundred thirty-four (134) samples were positive for sub-



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stances of abuse detected by drug screening test kits for methamphetamine (MAP), delta-9-tetrahydrocannabinol (THC), cocaine, 3,4-methylenedioxymethamphetamine (MDMA), benzodiazepines, and opioids, and by LC-QTOF/MS analysis. Majority of the patients were males with an average age of 34.54 ± 1.16 years old. Many complained of neurobehavioral changes necessitating consultation at the hospital emergency room. The neurologic and cardiovascular systems were frequently affected. By using the drugs of abuse test kit, methamphetamine was the most common substance of abuse detected and was seen in 40.3% of the samples. Amphetamine type stimulants were the most common group of drugs identified by LC-QTOF/MS analysis and was seen in 103 instances. New psychoactive substances detected more frequently than others include paramethoxymethamphetamine (PMMA), 3,4-methylenedioxy methamphetamine (MDMA) and 3,4-methylenedioxyamphetamine (MDA). A few cathinones like butylone and cathinone were also detected.

Conclusion. Methamphetamine was the most common substance of abuse detected in urine samples of the participants. New psychoactive substances were also detected in urine samples when LC-QTOF/MS analysis was utilized. Most persons who use drugs are unemployed young- to mid-adult males. The participants often had neurobehavioral and cardiovascular signs and symptoms.

Keywords: methamphetamine, LC-QTOF/MS, new psychoactive substances

INTRODUCTION

Substance use is prevalent in the Philippines. Over the last five years, the Dangerous Drugs Board (DDB) reports that there has been an increasing number of new admissions to drug treatment and rehabilitation centers. Before the pandemic in 2019, 5,119 new admissions were noted. This dropped to less than half (1,920) at the start of the COVID-19 pandemic in 2020 but this number has slowly risen since then to close to 90% of the pre-pandemic numbers.¹ In 2017, the Philippine Drug Enforcement Agency (PDEA) reported that only 5,072 out of 42,036 (12.07%) barangays in the country were drug-free.² The more recent report at the end of December 2023 found that close to 28,000 barangays were drug-free.³ The 2019 National Household Survey on the Patterns and Trends of Drug Abuse conducted by the Dangerous Drugs Board reported that 2 out of 100 Filipinos aged 10-69 years were current drug users. This translated to an estimated number of about 1.7 million Filipinos.⁴ A follow up survey conducted in 2023 reported a 16.6% drop in the number of current drug users translating to an estimated number of 1.479 million users.⁵

The University of the Philippines-Philippine General Hospital (UP-PGH) National Poison Management and Control Center (NPMCC) statistics reveals that referrals for substance use over the past years dipped by more than 50% mainly due to the COVID-19 pandemic but the referrals have been picking up again in the last two years for both stimulants and depressants (Figure 1). Methamphetamine (MAP) has been consistently the most frequently detected substance of abuse through the years.⁶

The detection of drugs of abuse in urine samples in the poison center has been carried out using drug screening test kits most often for MAP and THC only. If there is a strong

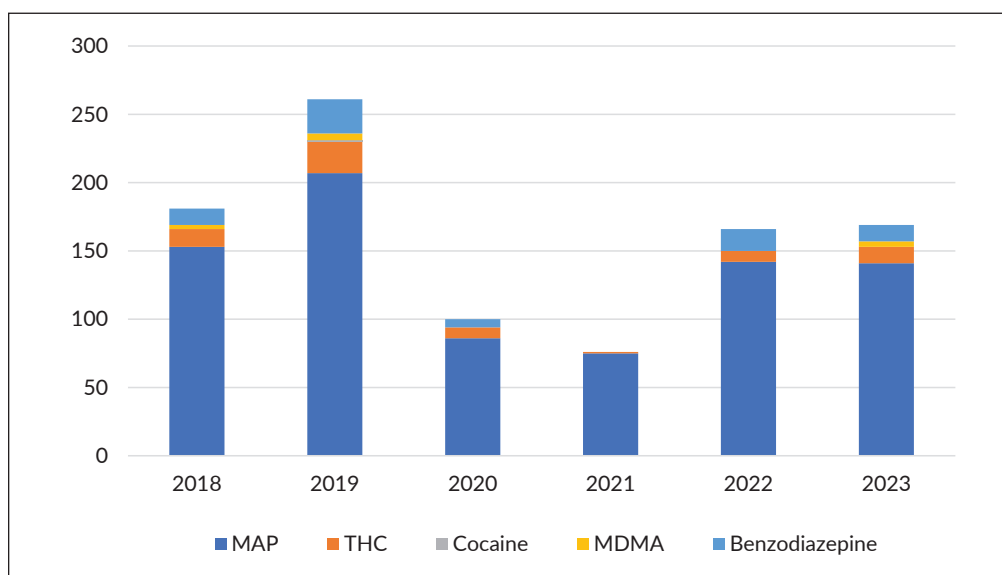


Figure 1. Number of patients consulting at the NPMCC for substance use (2018-2023).

suspicion of drug intoxication other than MAP or THC based on toxidrome analysis then screening of substances like cocaine, MDMA, benzodiazepines, and opioids is performed. Unfortunately, the results of these screening tests are not confirmed with more specific and sensitive tests. In rare instances, the clinical suspicion of drug intoxication is not validated at all by screening or confirmatory tests because of the lack of more sophisticated testing for drugs of abuse in urine samples.

New psychoactive substances (NPS) are substances of abuse that may have deleterious effects on human health but are not covered or identified by the schedule of drugs listed in international conventions on narcotics or psychotropic drugs.⁷ Most escape detection using standard drug screening kits or the usual targeted confirmatory testing procedures. These may be novel agents synthesized in clandestine laboratories by tweaking the chemical structure of substances known to have psychotropic effects or may be previously studied drug candidates that did not make it as approved prescription drugs. The United Nations Office of Drugs and Crime (UNODC) World Drug Report of 2022 revealed that from 2009-2018, there was a rapid increase in the introduction of NPS in the drug market. This has leveled off to 500 or so new drugs per year recently. The groups of drugs introduced were cathinones, phenethylamines, synthetic cannabinoids, tryptamines, new synthetic opioids and designer benzodiazepines. While the use of these substances shows a decline (except for ketamine) in high-income countries, the use in other parts of the world especially in middle- to low-income countries has yet to be evaluated.⁸

The current gold standard for targeted drug testing is liquid chromatography-tandem mass spectrometry (LC-MS/MS). Targeted testing facilitated by LC-MS/MS is not compatible with the rapid changes in the molecular composition of NPS drug products. Thus, the emergence of NPS has not only made legal highs possible but has allowed the use of such substances to escape detection. Advances in drug testing technology like liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) have made non-targeted detection of substances possible.⁸ This technology for drug testing was introduced to the Philippines through the creation of the University of the Philippines Manila Drugs of Abuse Research Laboratory (UP DARL), a project funded by the Philippine-California Advanced Research Institute (PCARI) under the Commission on Higher Education (CHED).

This study provides demographic and clinical data on people with confirmed use of traditional recreational substances and NPS for the first time in the Philippines. It will also describe the drug use profile of patients consulting in the ER of a tertiary hospital in the urban setting. The specific objectives of the study were as follows: 1) to describe the sociodemographic characteristics of people whose drug use is confirmed through urine tests and who have consulted at a tertiary hospital in the Philippines, 2) to describe the clinical profile and most common clinical presentation of

people whose drug use is confirmed through urine tests and who have consulted at a tertiary hospital in the Philippines, 3) to identify the drugs of abuse utilized by people whose use of drugs has been confirmed using drugs of abuse testing kits and LC-QTOF/MS analysis.

METHODS

This descriptive, cross-sectional study consecutively recruited patients referred for drug testing to the UP-PGH NPMCC aged 10 years and above from 1 January 2019 to 28 February 2020. Informed consent was obtained from the patient or legal guardian and a copy of the consent was retained by the subject. After consent was obtained, the participants were interviewed and examined. For minors, verbal assent from patients was taken, while the informed consent was signed by their parent or guardian. The interview focused on the sociodemographic and economic status of the patient. Symptoms were reviewed using a structured checklist. Physical, neurologic, and laboratory examination data were likewise recorded into a data sheet prepared for each patient. Patient data was entered into the Research Electronic Data capture (REDCap LTS Version 14.0.42) system based at the University of California San Francisco. Frequency analysis and generation of cross tabulations and charts were performed using Microsoft Excel.

Urine samples were collected within 72 hours of admission and analyzed using an immunoassay-based drug screening test kit (5 Panels Drug Test Kit MET/THC/MDMA/Cocaine/Opioid One Step Screening Test and Blue Screen BZO One Step Benzodiazepine Drug Test Device). A documented chain of custody procedure was also implemented in this study following the Department of Health Manual of Operations for Drug Testing Laboratories in the Philippines. Split samples were also analyzed by LC-QTOF/MS at the UP DARL using a reference library of 108 drugs mostly consisting of substances of abuse, prescription drugs, and NPS. For LC-QTOF/MS analysis, a non-targeted data acquisition method was developed in an Agilent LC1260- QTOF/MS 6550 operated through Automated MS/MS mode using an Agilent Turbo Jet spray electrospray ionization (ESI) source and a scan rate of 2 GHz in extended dynamic range, operated in the positive ionization mode. Chromatographic separation of analytes was done in an Agilent Poroshell 120 C-18 column (2.1 x 100 mm, 2.7 μ m) by gradient elution using LC-MS grade water with 0.05% formic acid and 5mM ammonium formate as mobile phase A and acetonitrile with 0.05% formic acid as mobile phase B. The total ion chromatogram that was generated from each sample run was analyzed using Agilent MassHunter Qualitative Analysis.

This study was reviewed and approved by UP Manila Research Ethics Board (UPMREB 2018-324-01) and registered in UP Manila Research and Grants Office (RGAO-2018-0296-01).

Table 1. Sociodemographic Characteristics of Participants

| Sociodemographic Characteristic | Frequency (n=134) |
|---------------------------------|-------------------|
| Age Mean (years) | 34.54±1.16 |
| Age Range (years) | 14-74 |
| Age Groups | |
| 11-15 | 5 |
| 16-20 | 15 |
| 21-25 | 25 |
| 26-30 | 15 |
| 31-35 | 14 |
| 36-40 | 13 |
| 41-45 | 21 |
| 46-50 | 9 |
| 51-55 | 7 |
| 56-60 | 5 |
| 61-65 | 3 |
| 66-70 | 0 |
| 71-75 | 2 |
| Sex | |
| Male | 101 |
| Female | 33 |
| Residence | |
| National Capital Region | |
| Manila | 32 |
| Parañaque | 21 |
| Makati | 10 |
| Las Piñas | 9 |
| Pasay | 4 |
| Taguig | 4 |
| Quezon City | 2 |
| Caloocan | 2 |
| Muntinlupa | 1 |
| Navotas | 1 |
| Pasig | 1 |
| Malabon | 1 |
| Region II | |
| Nueva Vizcaya | 1 |
| Region III | |
| Bulacan | 4 |
| Pampanga | 2 |
| Bataan | 1 |
| Region IVA | |
| Cavite | 30 |
| Laguna | 4 |
| Batangas | 1 |
| Rizal | 1 |
| Region V | |
| Masbate | 1 |
| Region VIII | |
| Samar | 1 |

| Sociodemographic Characteristic | Frequency (n=134) |
|---------------------------------------|-------------------|
| Highest Educational Attainment | |
| No formal education | 1 |
| Did not finish elementary | 14 |
| Elementary | 33 |
| Senior high school | 69 |
| College | 16 |
| Unknown | 1 |
| Employment | |
| Full time | 26 |
| Part time | 16 |
| Contractual | 10 |
| Unemployed | 77 |
| No data | 5 |
| Occupation | |
| Service provider | 39 |
| Laborer | 19 |
| Student | 13 |
| Business | 3 |
| Law enforcer | 1 |
| Housewife | 1 |
| None | 40 |
| No data | 18 |
| Income | |
| <10,000 per month | 39 |
| 10,000-19,999 per month | 18 |
| 20,000-34,999 per month | 1 |
| 35,000-64,999 per month | 1 |
| 65,000 and above per month | 0 |
| No income | 61 |
| No data | 14 |
| Smoking Status | |
| Never smoker | 56 |
| Former smoker | 14 |
| Current smoker | 64 |
| Ethanol Drinking Status | |
| Heavy drinking | 17 |
| Binge drinking | 10 |
| Less than once a month | 63 |
| Never | 42 |
| No data | 2 |

RESULTS

Three hundred eighty-four individuals consented to participate in the study. In 134 of the urine samples, drugs of abuse were detected by point of care testing and by LC-QTOF/MS analysis. The age range was between 14-74 years old with an average of 34.54 ± 1.16 years. Most participants (65.7%) belonged to the age range 21-25 up to 41-45. One hundred one were males and 33 were females where two of the females were pregnant. Table 1 shows the distribution of participants according to five-year age groups and biologic sex. Among

the females, the most common age group was from 21-25 years old. Majority of the patients reported residence in the Metro Manila area and from Cavite, a province immediately south of Manila (Table 1).

About half (69) of the participants were able to finish secondary school. Forty-seven (47) had some education. Sixteen (16) finished college and only one subject did not go to school. Majority of the participants (77, 57%) were unemployed but about 20% (26) were fully employed. Sixty-one patients declared no income. Of those with some source of income, the majority earned less than PhP 10000 per month.

Table 2. Number of Participants Reporting Specific Symptoms

| Symptoms | Number (n=134) |
|--------------------------------|----------------|
| Neurologic Symptoms | 65 |
| Depressed sensorium | 15 |
| Hallucinations | 12 |
| Agitation | 11 |
| Dizziness | 10 |
| Behavioral change | 10 |
| Headache | 9 |
| Delusions | 8 |
| Depression | 6 |
| Seizure | 6 |
| Lateralized weakness | 4 |
| Numbness | 3 |
| Confusion | 2 |
| Others | 11 |
| Cardiovascular Symptoms | 26 |
| Chest pain | 17 |
| Palpitations | 10 |
| Others | 3 |
| Respiratory Symptoms | 18 |
| Dyspnea | 18 |
| Cough | 3 |
| Orthopnea | 1 |
| Hemoptysis | 1 |
| Other Symptoms | 33 |
| Abdominal pain | 11 |
| Vomiting | 7 |
| Fever | 5 |
| Diaphoresis | 3 |
| Tremors | 2 |
| Others | 18 |

Major occupations reported included service providers (39) and laborers (19). Thirteen (13) were students. Table 1 lists the other details of the sociodemographic profile.

Clinical Characteristics

The common symptoms reported by the patients included the following symptoms grouped by the affected system found in Table 2. Many of the patients complained of neurologic symptoms like depressed sensorium and hallucinations. About 20% had cardiovascular symptoms like chest pain and palpitations. Difficulty of breathing and abdominal pain were also included in the list of symptoms.

The most common reasons for consultation in the hospital included behavioral change (18), stroke (18), substance ingestion (14), traumatic injuries (14), abdominal pain (8), and drug use/abuse (8). Forty percent (n=54) of the patients reported having co-morbid illnesses. These illnesses included hypertension, cardiac disease, psychiatric disease, tuberculosis, and other pulmonary diseases.

The average systolic blood pressure was 123.60 mmHg while the average diastolic blood pressure was 78.35. The highest systolic BP was 220 mmHg which was recorded from a patient who had used a stimulant. The average heart rate was 95.3 beats per minute. The highest HR was 180 beats per minute recorded from a patient who used a stimulant also. The average temperature was 36.76 degrees centigrade.

Table 3. Number of Participants who Tested Positive for Traditional Recreational Drugs and New Psychoactive Substances based on Immunoassay-based Drugs of Abuse Screening Kit and LC-QTOF/MS Analysis

| Substance | Screening Kit | LC-QTOF/MS |
|----------------------------------------------|---------------|------------|
| Amphetamines | | 103 |
| Methamphetamine | 54 | 67 |
| Methylphenidate | NA | 9 |
| Amphetamine | NA | 7 |
| Paramethoxymethamphetamine (PMMA) | NA | 6 |
| 3,4-methylenedioxyamphetamine (MDMA) | 4 | 5 |
| 3,4-methylenedioxyamphetamine (MDA) | NA | 4 |
| 3,4-methylenedioxy-N-ethylamphetamine (MDEA) | NA | 1 |
| Phenylpropanolamine | NA | 1 |
| Paramethoxyamphetamine (PMA) | NA | 1 |
| Pseudoephedrine | NA | 1 |
| Methylenedioxypropylamphetamine (MDPV) | NA | 1 |
| Cathinones | | 4 |
| Butylone | NA | 2 |
| Cathinone | NA | 2 |
| Cocaine | 0 | 3 |
| Benzodiazepines | 18 | 6 |
| Midazolam | NA | 3 |
| Alprazolam | NA | 1 |
| Clonazepam | NA | 1 |
| Temazepam | NA | 1 |
| Opioids | 1 | 30 |
| Tramadol | NA | 24 |
| Dextromethorphan | NA | 3 |
| Morphine | NA | 2 |
| Fentanyl | NA | 1 |
| Antihistamine | | 9 |
| Diphenhydramine | NA | 7 |
| Promethazine | NA | 1 |
| Hydroxyzine | NA | 1 |
| Antidepressants | | 3 |
| Citalopram | NA | 3 |
| Others | | 10 |
| Methoxetamine | NA | 6 |
| Scopolamine | NA | 1 |
| Tenofovir | NA | 1 |
| Naproxen | NA | 1 |
| Mefenamic acid | NA | 1 |
| Tetrahydrocannabinol | 6 | 0 |

*Some patients had more than one substance in the urine sample.

Drug Testing Results

Immunoassay-based drugs of abuse screening test kit showed that the following traditional recreational drugs were used: methamphetamine in 54 (40.30%), benzodiazepines in 18 (13.43%), THC in 6 (4.48%), MDMA in 4 (2.99%), and opioids in 1 (0.75%). The use of cocaine was not detected by point-of-care drug screening.

LC-QTOF/MS analysis of the urine samples revealed the presence of other substances. Table 3 shows the list of substances detected by group of substance.

In Table 3, 36 study participants had more than one substance of abuse detected either by drugs of abuse screening test kit or by LC-QTOF/MS analysis. The combinations of substances included either two or more traditional recreational drugs or traditional drug/s in combination with NPS or more than one NPS.

In some cases, the drugs of abuse screening test kit yielded a negative result but LC-QTOF/MS analysis was positive for a traditional recreational drug. For methamphetamine for example, the false negative rate for the drug screening kit was 27%.

Tetrahydrocannabinol (THC) was detected by the drug screening kit but was not detected by LC-QTOF/MS. At the time of the urine sample analysis, the negative mode runs on the analytical platform had not been optimized. THC can be detected only in negative mode runs of the LC-QTOF/MS.

In the physical examination of the study participants, most of the findings involved the neurologic and cardiovascular systems. For patients that used stimulants only (n=82), up to one third had cardiovascular system affectation, mainly tachycardia. Patients that used depressants (n=33) on the other hand, had predominantly neurologic system findings, such as depressed sensorium but also seizures in up to six patients. For eight patients in whom a stimulant and depressant were detected, both the neurologic and cardiovascular systems were affected. Table 4 shows the summary of the number of patients demonstrating a physical examination finding grouped by substance identified in the urine samples — stimulant, depressant, or both.

Ninety patients had an ECG with the most frequent finding was ST-T wave changes, followed by heart rate changes (mainly sinus tachycardia) and left ventricular hypertrophy. Rhythm changes (atrial fibrillation, sinus arrhythmias or premature ventricular contractions) were seen mainly in patients with stimulant use. An ECG reading of specific wall ischemia was reported in three patients with stimulant use. Troponin I level was requested in 11 patients, and was observed to be elevated in six patients. Total creatine kinase was performed in 53 patients and it was elevated in 29. Liver function tests were performed in 97 patients. The values were elevated in 26 patients.

Cranial CT scan was done on 26 out of 134 patients. In eleven cases, a hemorrhage was noted. Infarcts were seen in six and the study was normal in nine. No stark differences in the proportion of hemorrhages or infarcts were noted among those who took stimulants versus those who took depressants versus those who took both.

Clinicians were asked to identify a specific toxidrome if possible. A toxidrome was identified only in 32 out of the 134 subjects (sympathomimetic in 29 and one each for sedative hypnotic, cholinergic and anticholinergic, and cannabinoid).

Forty-eight hours from admission to the emergency room, there was one death from acute coronary syndrome, ninety-four patients (70%) were discharged or cleared by the

toxicology service while thirty-seven patients remained under the care of the toxicology service. One patient absconded and the other was transferred to another facility. The urine sample of the subject that died was found to have tramadol and methoxetamine, an NPS. The patient also ingested an herbal tea product.

DISCUSSION

Methamphetamine has been known to be the most common substance of abuse utilized by Filipino drug users based on the NPMCC statistics. This cross-sectional study confirms this observation. Southeast Asia is the second region in the world where amphetamine type stimulants are commonly seized. Methamphetamine accounts for most of these reported seizures. Among those seeking treatment for drug use in ASEAN countries, methamphetamine was identified as the most frequently used drug.⁸

The observation of the nervous system and cardiovascular system as the most affected organ systems is compatible with the known pharmacologic effects of stimulants like amphetamines, cathinones, and cocaine, and depressants like opioids and benzodiazepines. Methamphetamine, the most common stimulant identified in this study, stimulates the release of monoamines dopamine, noradrenaline, and serotonin in synapses and can block reuptake of the same. It causes stimulation of the central nervous system giving rise to arousal, euphoria, reduced fatigue, reduced appetite but also increased anxiety and sometimes psychosis. The action on the dopaminergic circuits in the brain is responsible for the problem of abuse.⁹ In the cardiovascular system, methamphetamine will raise both the heart rate and blood pressure. It causes vascular constriction and vasospasm. Chronic use leads to endothelial damage and pulmonary hypertension.¹⁰

Tramadol was the most common depressant identified in this study. It is considered to be an opioid analgesic but is also a serotonin and norepinephrine reuptake inhibitor. In this study, depression in sensorium was the most common manifestation of the use of the depressants but ironically seizures were also reported even more frequently than in those who used stimulants. The occurrence of seizures is a known manifestation of tramadol overdose. The seizures were regarded to be part of a serotonin syndrome however recent animal studies suggest that tramadol has a direct effect on GABA A receptors.¹¹

The new psychoactive substances identified in this study are predominantly stimulants (PMMA, MDA, MDEA, PMA, MDPV, butylone, cathinone, methoxetamine). None of the subjects identified these substances in their history suggesting that these may have been utilized unknowingly by the subjects or knowingly but without intent to disclose. The laboratory confirmed use of amphetamine type stimulants in the country is not surprising as Southeast Asia is reported to be the second region in the world known for the most drug seizures for this type of substance of abuse.⁸

Table 4. Physical Exam Findings of Patients according to Type of Drug Used

| Physical Exam Findings | Stimulants (n=82) | Depressants n=33) | Both (n=8) |
|-----------------------------------------|----------------------|----------------------|---------------|
| Neurological Manifestations | 48 | 31 | 10 |
| Depressed sensorium | 9 | 11 | 3 |
| Agitation | 7 | 1 | 5 |
| Hallucinations | 6 | 4 | 2 |
| Behavioral change | 5 | 1 | 1 |
| Delusions | 3 | 0 | 2 |
| Violent behavior | 2 | 2 | 3 |
| Coma | 1 | 1 | 0 |
| Confusion | 1 | 1 | 0 |
| Paranoia | 1 | 0 | 2 |
| Depressed affect | 1 | 2 | 0 |
| Flight of ideas | 1 | 0 | 0 |
| Depressed mood | 1 | 0 | 0 |
| Suicidal ideations | 0 | 0 | 1 |
| Lateralized weakness | 10 | 4 | 1 |
| Generalized weakness | 4 | 0 | 1 |
| Lateralized numbness | 3 | 0 | 0 |
| Seizures | 2 | 5 | 0 |
| Ataxia | 2 | 0 | 0 |
| Rigidity | 2 | 0 | 0 |
| Proximal weakness | 1 | 0 | 0 |
| Dysarthria | 1 | 0 | 0 |
| Facial asymmetry | 1 | 0 | 0 |
| Spasticity | 1 | 0 | 0 |
| Status epilepticus | 0 | 1 | 0 |
| Tremors | 0 | 1 | 0 |
| Aphasia | 0 | 1 | 0 |
| Decreased verbal output | 0 | 1 | 0 |
| Musculoskeletal Findings | 7 | 2 | 3 |
| Laceration | 1 | 0 | 0 |
| Gunshot wound | 1 | 0 | 0 |
| Multiple injuries | 1 | 0 | 0 |
| Edema | 1 | 1 | 0 |
| Abrasions | 1 | 0 | 0 |
| Fracture | 0 | 1 | 0 |
| Stab wound | 0 | 1 | 0 |
| Tremors | 0 | 0 | 1 |
| Calf pain | 0 | 0 | 1 |
| Head and Neck Findings | 12 | 2 | 2 |
| Mydriasis | 3 | 0 | 1 |
| Salivation | 1 | 1 | 0 |
| Otitis media | 1 | 0 | 0 |
| Lip swelling | 1 | 0 | 0 |
| Gunshot wound | 1 | 0 | 0 |
| Laceration | 1 | 0 | 0 |
| Hematoma | 1 | 0 | 0 |
| Throat pain | 1 | 0 | 0 |
| Conjunctival injection | 1 | 0 | 1 |
| Periorbital swelling | 0 | 1 | 0 |
| Facial bone fracture | 0 | 1 | 0 |
| Respiratory System Findings | 9 | 5 | 3 |
| Dyspnea | 5 | 2 | 2 |
| Tachypnea | 2 | 2 | 0 |
| Ventilatory support | 1 | 1 | 1 |
| Harsh breath sounds | 1 | 0 | 0 |
| Wheezing | 1 | 0 | 0 |
| Rales | 1 | 1 | 0 |
| Decreased breath sounds | 1 | 0 | 0 |
| Cough | 0 | 0 | 1 |
| Cardiovascular System Findings | 25 | 5 | 5 |
| Tachycardia | 17 | 3 | 5 |
| Chest tenderness | 3 | 1 | 0 |
| Bradycardia | 2 | 0 | 0 |
| Cardiomegaly | 2 | 0 | 0 |
| Irregular rhythm | 1 | 0 | 0 |
| Murmur | 1 | 1 | 0 |
| Neck vein engorgement | 1 | 0 | 0 |
| Gastrointestinal System Findings | 11 | 7 | 4 |
| Abdominal pain | 10 | 2 | 2 |
| Emesis | 2 | 1 | 3 |
| Diarrhea | 1 | 0 | 0 |
| Gunshot wound | 1 | 0 | 0 |
| Abdominal tenderness | 0 | 2 | 1 |
| Lower GI bleeding | 0 | 2 | 0 |
| Increased abdominal girth | 0 | 1 | 0 |
| Genitourinary System Findings | 0 | 1 | 1 |
| Hematuria | 0 | 1 | 0 |
| Flank tenderness | 0 | 0 | 1 |
| Dermatologic System Findings | 7 | 7 | 1 |
| Diaphoresis | 4 | 0 | 1 |
| Abrasions | 2 | 0 | 0 |
| Pallor | 1 | 0 | 0 |
| Burn | 0 | 2 | 0 |
| Fungal infection | 0 | 1 | 0 |
| Jaundice | 0 | 1 | 0 |
| Hematoma | 0 | 1 | 0 |
| Petechiae | 0 | 1 | 0 |
| Cuts | 0 | 1 | 0 |
| Flushing | 0 | 0 | 1 |
| Others | 6 | 0 | 0 |
| Fever | 2 | 0 | 0 |
| Edema | 2 | 0 | 0 |

Liquid chromatography tandem mass spectrometry (LC-MS/MS) is the current gold standard for drug testing globally. The introduction of NPS, however, in the drug market has unmasked the limitation of this technology. The rapid molecular evolution of the composition of NPS drug products does not allow LC-MS/MS and screening tests to cope with the ever-changing testing targets. LC-QTOF/MS analysis has a special advantage over LC-MS/MS in the ability for non-targeted testing of substances of abuse in

biological samples. The introduction of this technology in the country has allowed the identification of NPS in this group of patients. Such technology is particularly important when there is a strong suspicion of drug use as a cause of a patient's morbid state and yet the drug screening tests are negative. It will also be useful for drug use surveillance activities in the country in the future.¹²

It is noteworthy that stroke and traumatic injuries together comprised 34% of the referrals who had a positive

drug test result. This may suggest that substance use may be an important risk factor for these types of injuries that could be investigated among Filipinos in the future.

Limitations of the Study

This is a descriptive study on patients consulting at the emergency room with most patients coming from Metro Manila so it does not capture the extent of drug use in the country. There are many persons who use drugs who do not consult because they had no symptoms or the symptoms were perceived to be mild. Also, being a sensitive topic, not all patients who were screened for drug use agreed to be included in the study. The LC-QTOF/MS panel used only screens and confirms 23 NPS. By 2019, close to 1000 NPS have already been reported to UNODC. Although the analysis performed in this study is the most comprehensive done in the Philippines, it may still have missed a large number of NPS because of the limited reference library.

CONCLUSION

Methamphetamine is the most common substance of abuse detected in urine samples of people who use drugs. New psychoactive substances like PMMA, MDA, MDEA, PMA, MDPV, butylone, cathinone, methoxetamine can also be detected in urine samples when LC-QTOF/MS analysis is utilized. In this study population, neurobehavioral and cardiovascular signs and symptoms were most reported. Most persons who use drugs are unemployed young to mid adult males with behavioral disturbances, self-inflicted injuries, stroke, or traumatic injuries.

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Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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