

## Original Article

## Prevalence of Commonly Abused Drugs Detected from Drug Testing in Unnatural Death Cases During 1-Year Period at Thammasat University Hospital

Aphinan Tangsermkijesakul, Tossanai Pipatchotitham\*

### Abstract

**Objective:** To determine the prevalence of commonly abused drugs (CAD) detected in unnatural death cases at Thammasat University Hospital (TUH) in 1 year and also evaluate drug prevalence data to propose appropriate toxicology panels used for autopsied deaths at TUH.

**Methods:** A descriptive cross-sectional study was conducted and unnatural death cases in 5 police stations sent to TUH for a medico-legal investigation from March 2020 to February 2021 were recruited in this study. All police records and autopsy reports were documented for demographic data. In this study, drug preliminary tests were performed with rapid chromatographic immunoassay test kits for 5 common drug classes including amphetamines, benzodiazepines (BZD), cannabinoids, opioids, and ketamine. Blood samples from cases with preliminary positive results were analyzed with the confirmatory tests.

**Results:** Two hundreds and sixty five autopsy cases were recruited in this study. Forty cases were positive for at least 1 substance and the prevalence of CAD detected at TUH in 1 year was 15.09%. The prevalence of all 5 drug classes among 4 police stations ranged from 13.56 to 16.26%. However, there was no positive cases for CAD in the highway station area. The highest prevalence by drug was amphetamine-type stimulants (ATS) (8.68%), followed by BZD (4.91%), delta 9-tetrahydrocannabinol (1.13%), morphine (0.75%), and ketamine (0.38%), respectively. The highest prevalence classified by manner of death that CAD were detected was suicide (25%), followed by accident (16.67%).

**Conclusions:** Five common drug classes could be detected in autopsy cases at TUH for 15.09%. ATS and BZD were presented with high prevalence throughout almost all areas of our responsibility and they should be in the routine toxicologic testing.

**Keywords:** Abused drugs, Prevalence, Unnatural death, Thailand

Received: 14 September 2021

Revised: 20 November 2021

Accepted: 26 November 2021

## Introduction

Drug abuse is an issue which concerns the global public health system. Abusers may encounter physical or psychiatric derangement and death may occur as direct result from drug intoxication or as an indirect result such as a motor vehicle accident.<sup>1,2</sup>

Toxicological investigation in postmortem examination is one of the standard procedures before cause and manner of death are concluded according to the Criminal Procedure Code of Thailand, Chapter 2 Postmortem Inquest, Section 148 - 156. Since forensic physicians assist the inquiry officials in death investigations, the prevalence of commonly abused drugs (CAD) in each area is important information for forensic physicians who collect and send biological specimens to laboratories for toxicological analysis. It's important because cost and effectiveness of toxicological tests are always a concern due to limited budget and medical resources. The prevalence of CAD detected in forensic autopsy cases is essential information for planning guidelines for toxicological analysis suitable for each forensic center. Moreover, the illicit drugs found in unnatural death cases reflect drug problems in the community.

There have been extensive studies of the prevalence of abused drugs and trends in drug abuse to provide toxicological data for death investigation systems. In Thailand, a conference paper of the Forensic Drug Addict Monitoring Network (FDAMN), supported by the Office of the Narcotics Control Board (ONCB), which reported information on substance abuse detection in unnatural death cases during 2007 - 2018, revealed that in 10.25% of unnatural death cases abused drugs were found. There were positive test results for amphetamines (4.39%), benzodiazepines (BZD) (4.27%), opioids (1.15%), kratom (0.85%), cannabinoids (0.30%), ketamine (0.12%), cocaine (0.06%), and MDMA/MDA (0.06%).<sup>3</sup> Previous studies in other countries showed a wide range of prevalence, from 3.2 to 60%, of CAD in unnatural death cases.<sup>4-7</sup>

This study aimed to discover the prevalence of CAD, based on the toxicological results in unnatural death cases, at Thammasat University Hospital (TUH) in 1 year. Our intention was to provide basic toxicology data for forensic physicians and to propose appropriate toxicology panels applying for the routine forensic autopsy at TUH.

## Methods

This was a descriptive cross-sectional study based on toxicologic data obtained from forensic autopsy cases at TUH in Pathum Thani province during the year from March 2020 to February 2021. Unnatural death cases from 5 police districts requiring further medico-legal postmortem examination were sent to the department of forensic medicine, TUH. All cases in which urine and blood specimens were available for toxicological analysis were included in this study. Decomposed bodies were excluded because blood hemolysis could lead to inconclusive or faulty analysis results. Urine specimens were collected by suprapubic aspiration for the preliminary investigation and femoral venous blood was obtained and prioritized for confirmatory analysis. Urine specimens were tested immediately with rapid lateral flow immunoassay test kits for the presumptive detection of 5 commonly abused drug classes relating to the statistical report of FDAMN including amphetamines, BZD, opiates, ketamine, and cannabinoids. When positive preliminary results appeared, a suitable confirmation test, either gas chromatography-tandem mass spectrometry or liquid chromatography-tandem mass spectrometry, was applied to exclude other structurally related compounds. These qualitative tests were comprehensive for drugs of interest in 5 common drug classes and globally standardized in forensic toxicology. In amphetamines and intoxication cases, quantitative measurement was also performed. Other information was gathered from inquest notes and autopsy reports. Gender, age, nationality, the police station which has authority over the case, cause of death, and manner of death were documented for this study.

The sample size was calculated from n4Studies on IOS. Data were recorded and analyzed with Microsoft Excel version 2013 and the results were analyzed through descriptive statistics. The prevalence of CAD, demographic data, and additional information obtained during medico-legal investigations are presented.

Calculated prevalence is shown as percentages. Continuous data are presented as mean  $\pm$  standard deviation (SD) or median and range. Numbers or percentages are used for categorical data.

The study protocols have been approved by The Human Research Ethics Committee of Thammasat University (Medicine) under the approval reference 051/2563.

### Results

A total of 265 death cases were included in this study. There were 229 males and 36 females with an average age of  $42.88 \pm 14.88$ , ranging from 16 to 79. Most of the cases were Thai (88.68%). The cause of death was a group of natural diseases (138 cases), followed by motor vehicle deaths

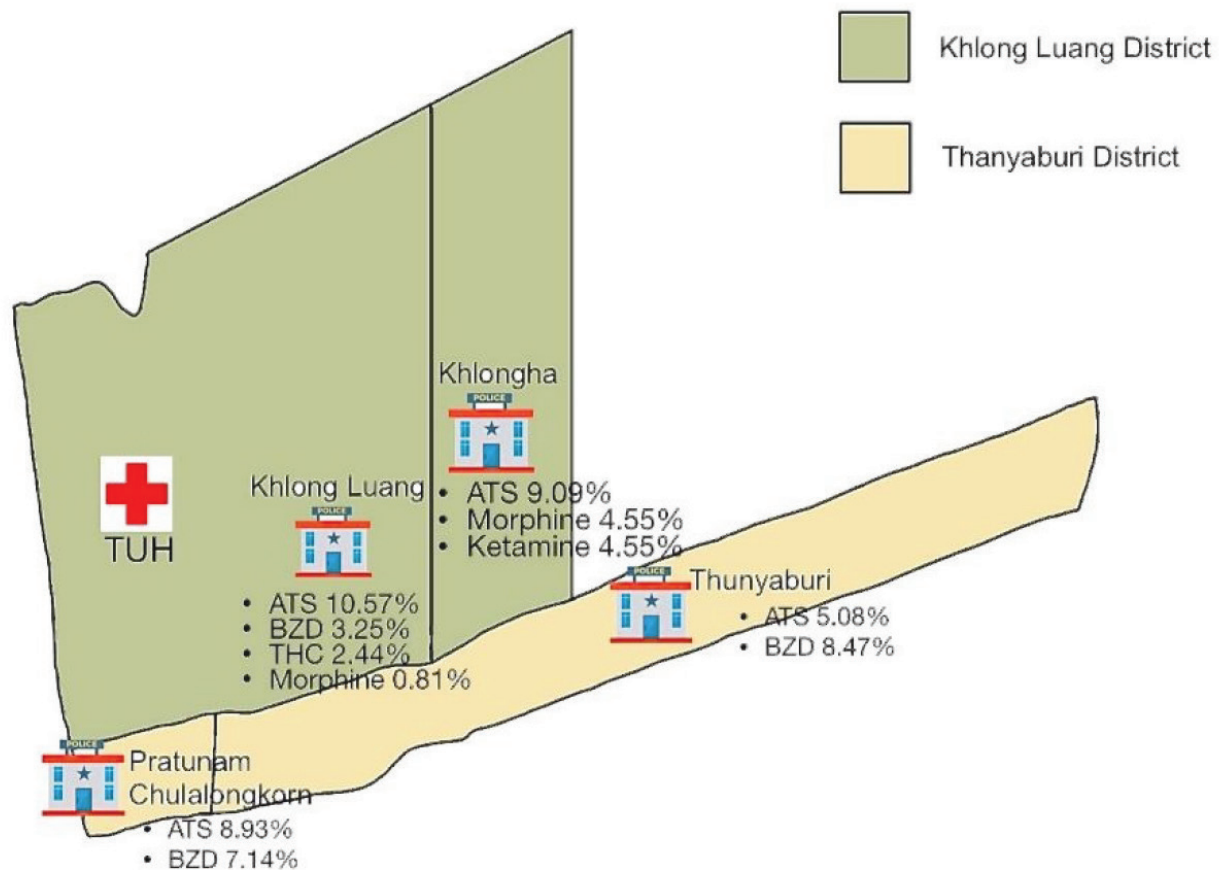
(68 cases), asphyxial deaths (28 cases), and the others (31 cases). The manners of death were natural (137 cases), accidental (84 cases), suicide (36 cases), homicide (7 cases), and undetermined (1 cases). Approximately half of the cases (46.42%) were sent from Khlong Luang police station. 64 of the 265 cases showed positive preliminary test results for at least 1 drug class, based on a band of visual immunoassay test kits. The preliminary results and positive predictive values for 5 drug classes are shown in Table 1.

**Table 1** The toxicological detection from preliminary and confirmatory results for 5 drug classes. The positive predictive value of each drug class is calculated while the other diagnostic test metrics were not studied

Drug Class	Preliminary test	Confirmation test	Positive predictive value (%)
Amphetamines	31	23	74.19
Benzodiazepines	24	13	54.16
Cannabinoids	8	3	37.5
Opioids	5	2	40
Ketamine	1	1	100

In 40 of the 64 cases at least one suspected substance was found from the confirmation test. The overall prevalence by case with at least one CAD detected by toxicological results in the 1-year study period at TUH was 15.09%. The highest prevalence among 5 common drug classes was amphetamine-type stimulants (ATS) (8.68%), followed by BZD (4.91%), Delta9-Tetrahydrocannabinol (THC) (1.13%), morphine (0.75%), and ketamine (0.38%). The prevalence was also calculated regarding the 5 police stations. At the highway police station there were no CAD cases. Among the other 4 police

stations, CAD prevalence by the number of cases for each police station ranged from 13.56 to 16.26%. ATS and BZD were the leading substances found. Four types of BZD were detected, including diazepam, clonazepam, lorazepam, and chlordiazepoxide. Khlong Luang Police Station had more variety of substance abuse cases than the other 3 stations. Ketamine was found only in 1 case, under Khlongha Police Station. The distribution of abused drugs is illustrated with a zoning map showing the jurisdictions of the 4 police stations (Figure 1).



**Figure 1** The prevalence for each abused drug detected in unnatural death cases at TUH is illustrated with a zoning map of the jurisdiction of 4 police stations near TUH, Pathum Thani Province.

The prevalence of CAD associated with each of 5 manners of death was also calculated. One-quarter of the suicide cases had evidence of abused drugs, followed by accident (16.67%), homicide (14.29%), and natural diseases (10.95%), as shown in Table 2. There was only one undetermined manner of death in this study and the toxicological confirmation test showed a positive result of diazepam. One case in the homicide group showed a positive result for THC.

The prevalence ratio of suicide between positive and negative groups of abused drugs was 1.88 and the prevalence ratio of an accident between positive and negative groups of abused drugs was 1.13.

Single drug use was characteristic of the abuse cases in our study. Polydrug abuse was found in only 2 cases. The first case was a 16-year-old male who died from combined drug intoxication. The toxicological test results showed diazepam (> 300 ng/mL) and THC (12.1 ng/mL). Further

investigation found mitragynine, tramadol, cetirizine, and diphenhydramine. The second case was a 33-year-old male who died from coronary artery stenosis. The toxicological results in postmortem examination showed positive morphine and ketamine. Mitragynine and tramadol were found in further investigation.

3 of 265 cases were diagnosed with death caused by drug intoxication. The first case was multi-drug intoxication as mentioned earlier. The other 2 cases were MA intoxication.

Quantitative measurement was done for the amphetamines panel and the analytical results reported the presence of methamphetamine (MA) and amphetamine (AM). After excluding 2 ATS intoxication cases and 1 case in which the blood specimen was not sufficient for quantitative measurement, concentrations of MA and AM and the concentration ratio between MA and AM were calculated, as shown in Table 3.

**Table 2** Prevalence of each drug was calculated and displayed in percentage through the cause and manner of death. Total percentage was calculated by the number of cases with at least one suspected drug present

Prevalence (N)	Drug	ATS	BZD	THC	Mophine	Ketamine	Total (Number of positive cases)
<b>Prevalence by CAD (265)</b>							
		8.68	4.91	1.13	0.75	0.38	15.09 (40)
<b>Prevalence by manner</b>							
• Natural (137)		5.11	3.65	0.73	1.45	0.73	10.95 (15)
• Accident (84)		13.09	3.57	1.19	-	-	16.67 (14)
• Suicide (36)		13.89	11.11	-	-	-	25 (9)
• Homicide (7)		-	-	14.29	-	-	4.29 (1)
• Undetermined (1)		-	100	-	-	-	100 (1)
<b>Prevalence by cause of death</b>							
• Natural disease (138)		5.07	4.35	0.72	1.45	0.72	11.59 (16)
• Motor vehicle injury (68)		13.23	2.94	-	-	-	16.18 (11)
• Asphyxia (28)		17.86	10.71	-	-	-	28.57 (8)
• Blunt trauma (14)		-	-	-	-	-	0 (0)
• Firearm injury (4)		-	-	5	-	-	25 (1)
• Sharp force injury (4)		-	-	-	-	-	0 (0)
• Drug intoxication (3)		66.67	33.33	33.33	-	-	100 (3)
• Fire death (3)		-	33.33	-	-	-	33.33 (1)
• Death due to physical agents (2)		-	-	-	-	-	0 (0)
• Ethanol intoxication (1)		-	-	-	-	-	0 (0)

**Table 3** The concentrations of MA and AM are demonstrated. Concentration ratios were calculated in cases that both MA and AM were detected (left side)

Case no.	MA (ng/mL)	AM (ng/mL)	MA to AM ratio
1	369	29.5	12.51
2	94.5	20.5	4.61
3	318	134	2.37
4	1051	104	10.11
5	89.9	44.5	2.02
6	89.1	39.2	2.27
7	797	29.9	26.66
8	214	31.5	6.79
9	392	35.8	10.95
10	60.6	15.1	4.01
11	83.6	10	8.36
12	568	26.7	21.27
<b>Mean (median)</b>	<b>343.89 (266)</b>	<b>43.39 (30.7)</b>	<b>9.33</b>

Case no.	MA (ng/mL)	AM (ng/mL)
1	55.6	0
2	242	0
3	237	0
4	59.4	0
5	189	0
6	204	0
7	41.5	0
8	177	0
<b>Mean (median)</b>	<b>150.69 (183)</b>	<b>0</b>

## Discussion

Toxicological testing is an important part of medico-legal postmortem examination. Forensic practitioners require toxicological test results to interpret cause and manner of death for their cases.<sup>1,2,4</sup> Substances of interest in medico-legal death cases depend on local laws.

In one year at TUH, there were 265 unnatural death cases, of which 15.09% involved illegal drug use under the Thai justice system. This is slightly more than the 10.25% from all regions of Thailand, reported by FDAMN, a subsidiary of ONCB.<sup>3</sup> In both studies, ATS and BZD were the drugs most encountered. These studies were in line with the study of Pan et al. in China which indicated ATS were the most frequently abused drugs, though the prevalence of drug abuse detected in China was as high as 60% of drug abuse cases including autopsied deaths.<sup>5</sup> Frost et al. reported the detection frequency in autopsy cases in Norway was 44% and the BZD group was the most detected, followed by opioids and ATS.<sup>6</sup> This was similar to the study of Lee et al. in Florida, United States of America, showing BZD, opioids, and THC were the most frequently found in autopsy cases, respectively, although the overall prevalence of detection in the Lee et al. study was only 3.2 - 4.7%.<sup>7</sup> Differences in drug use, in medico-legal death investigations, and in study designs in different parts of the world explain the large differences in drug abuse detection in different countries, as shown in Table 4.

The data for this study was collected from a period during the global coronavirus pandemic. Studies in Europe have shown new variations in patterns of drug use for people under lockdown.<sup>8,9</sup> Mariottini et al. observed an increase of drugs detected in postmortem cases, especially for AM, which rose two to threefold in some months compared to the previous 5-year average of the same month in Finland.<sup>9</sup> In Thailand, the government declaration of the state of emergency started on March 8, 2020 and covered all of the period of data compiled in this study. Circumstances of the pandemic may have affected our findings, so additional studies should be conducted for confirmation after the outbreak has been resolved.

Regarding the number of abused drugs detected per case, only 5% of the unnatural death cases in our study involved multidrug abuse. Simi-

larly, Pan et al. in China said that in 96% of drug abuse cases only 1 type of abused drug was present.<sup>5</sup> FDAMN, a subsidiary of ONCB, found that 15.84% of intoxication cases in Thailand were caused by multiple drugs use. In contrast, Lee et al. in the USA determined that 34.7 - 59.2% of drug abuse cases involved polydrug use.<sup>7</sup> In many European countries, the average number of substances found in unnatural death cases was also more than 1.<sup>6, 10-12</sup> Although toxicologic tests in most medico-legal death cases in Thailand revealed single-drug abuse, forensic physicians should be aware of the possibility of polydrug misuse.

The highway police station is the only one of the five police stations within our service area from which we detected no drug abuse. However, only 5 cases were sent to us for medico-legal postmortem examination, so additional cases from the highway station are still required to conclude that motor vehicle deaths on the expressway do not result from CAD. ATS and BZD were CAD at the other 4 police stations within our service area, so they should be listed in the toxicology screening test panel. However, the prevalence of BZD misuse might be overestimated. Many types of BZD are classified as Schedule II or Schedule IV of the Psychotropic Substances Act B.E. 2559 (2016) which can be used for medical treatment. Further history and quantitative measurement might differentiate licit use from illicit use.

THC was the third most prevalent of the five drug groups we tested for. Similar to the 2007-2018 study by FDAMN, we detected for less THC than ATS and BZD. THC is a major psychoactive component in the cannabis plant. In 2019, the year prior to this study, Thai law was amended to the Narcotics Act (No.7), B.E.2562 to allow cannabis extracts to be used for medical research and treatment.

Morphine and ketamine were also found in very small proportions. Morphine is the category II narcotics according to the Narcotics Act B.E.2522 (1979) and can be used legally as medication. Therefore, positive tests for morphine may include both legal and illegal use, as in the BZD group.

Manner of death in most of our cases were either suicide, accident, or natural death. ATS was detected in many of the suicide and accident cases. BZD was also detected in many of the suicide cases.

This finding is consistent with various other studies which identified drugs in the BZD group that were detected in suicide or self-inflicted deaths.<sup>11,12</sup> For example, the study of A. W. Jones et al. revealed the presence of diazepam in 5.4% and 12% of hanging suicides and poisoning suicides, respectively.<sup>11</sup>

Most of the accidental deaths were motor vehicle accidents. Nine of the 11 motor vehicle deaths tested positive for ATS. In 1994, interview research by Sriruecha et al. discovered that 80% of long-distance truck drivers in Thailand admitted to using ATS during work.<sup>13</sup> However, in northern Thailand, Narongchai et al., 2002 - 2003, discovered that of 13 cases of death with evidence of MA, two were accidental deaths and ten were homicides.<sup>14</sup>

The probabilities of suicide and accident in our study were 1.88 and 1.13 times higher for toxicological positive cases than for toxicological negative cases, respectively.

Approximately half of the cases were natural death cases. Except for ATS, we did not measure levels of concentration because the cause of death was obvious and our budget was limited. Further study should be performed on quantitative measurement of abused drugs in natural death cases.

We also compared qualitative and quantitative measurements of AM and MA in our autopsy cases. Our analytical results demonstrated that concentrations of MA and AM in blood and patterns of concentrations can be divided into 2 groups. In 60% of our cases, both MA and AM were detected in blood. Mean (median) concentrations (ng/mL)

and concentration ratios of MA to AM were 343.89 (266), 43.39 (30.7), and 9.33, respectively. In 40% of the cases, only MA was detected in the blood; the mean (median) concentration (ng/mL) was 150.69 (183). Due to the pharmacokinetics of MA and AM, 7% of MA administered dose is N-demethylated to AM, while the metabolism of AM itself does not produce MA.<sup>4</sup> MA detected in analytical result suggests the possibility of pure MA abuse or MA mixed AM and the concentration ratio of MA to AM might differentiate MA alone or MA mixed with AM. The concentration ratios of MA to AM in our study suggest mostly pure MA abuse in unnatural deaths rather than MA mixed with AM. Jones et al. suggested that concentration ratios of MA to AM between 3 to 10 are strongly correlated with pure MA abuse in driving under influence cases. In the Jones et al. study, mean (median) concentrations and the highest concentration (ng/mL) of MA were 720 (560) and 4200, respectively.<sup>15</sup> In some other countries, AM was more prevalent than MA.<sup>16,17</sup>

In conclusion, this study is the first report to disclose the prevalence of CAD found in unnatural death cases at TUH. CAD were detected in 15.09% of those cases. ATS and BZD were the CAD most frequently found in unnatural deaths, so they should be included in future routine toxicological testing. However, BZD is used for licit medical purposes as well as illicitly as a recreational drug. Further study is necessary to differentiate between licit and illicit BZD evidence in autopsies.



**Table 4** The prevalence of CAD detected from unnatural death cases in this study compared with those of studies

<b>Comparative data</b>	<b>This study</b>	<b>FDAMN by ONCB (Thailand)<sup>3</sup></b>	<b>Narongchai et al. (Thailand)</b>	<b>Pan et al. (China)<sup>5</sup></b>	<b>Frost et al. (Norway)<sup>6</sup></b>	<b>Lee et al. (USA)<sup>7</sup></b>
<b>Prevalence</b>	15.09%	10.25	-	60%*	44%	3.2 - 4.7%
<b>The first three commonly abused drugs</b>	1. ATS 2. BZD 3. THC	1. ATS 2. BZD 3. Opioids	1. MA 2. BZD 3. Toluene	1. ATS 2. Heroin 3. Ketamine	1. BZD 2. Opioids 3. AM	1. BZD 2. Opioids 3. THC
<b>Percentage of multidrug detection</b>	5%	15.84%**	-	4%	2.6%***	34.7 - 59.2%

\*Prevalence from all drug abuse cases including autopsy cases.

\*\*Percentage in intoxication deaths.

\*\*\*Percentage including ethanol.

### Acknowledgments

Financial support. None reported.

### Conflict of interest

All authors report no conflicts of interest relevant to this article.

### References

1. DIMAIO MD. Forensic Toxicology. In: *Handbook of FORENSIC PATHOLOGY, 2nd ed.* CRC Press; 2017:255-280.
2. Saukko PJ, Knight B. Poisoning and the Pathologist. In: *Knight's Forensic Pathology.* Boca Raton: CRC Press, Taylor & Francis Group; 2016:567-577.
3. Worasuwannarak W, Sribanditmongkol P, Aramrattana A, et al. Trends in Substance Abuse Detection in Unnatural Deaths in Thailand, 2007-2018. *ONCB Journal.* 35(3):44-51.
4. Levine BS, Kerrigan S, eds. *Principles of Forensic Toxicology. 5th ed.* Springer Nature; 2020.
5. Pan M, Wang X, Zhao Y, et al. A retrospective analysis of data from forensic toxicology at the Academy of Forensic Science in 2017. *Forensic Sci Int.* 2019;298:39-47.
6. Frost J, Slordal L, Vege A, et al. Forensic autopsies in a naturalistic setting in Norway: autopsy rates and toxicological findings. *Forensic Sci Int.* 2012;223(1-3):353-358.
7. Lee D, Delcher C, Maldonado-Molina MM, et al. Trends in licit and illicit drug-related deaths in Florida from 2001 to 2012. *Forensic Sci Int.* 2014;245:178-186.
8. Zaami S, Marinelli E, Vari MR. New trends of substance abuse during COVID-19 pandemic: An international perspective. *Front Psychiatry.* 2020;11:700.
9. Mariottini C, Ojanpera I, Kriikku P. Increase in drugs-of-abuse findings in post-mortem toxicology due to COVID-19 restrictions-First observations in Finland. *Drug Test Anal.* 2021;13(4):867-870.
10. Edvardsen HE, Tverborgvik T, Frost J, et al. Differences in combinations and concentrations of drugs of abuse in fatal intoxication and driving under the influence cases. *Forensic Science International.* 2017;281:127-133.
11. Jones AW, Holmgren A, Ahlner J. Toxicology findings in suicides: concentrations of ethanol and other drugs in femoral blood in victims of hanging and poisoning in relation to age and gender of the deceased. *J Forensic Leg Med.* 2013;20(7):842-847.
12. Bradvik L, Lowenhielm P, Frank A, et al. From substance use disorders in life to autopsy findings: A combined case-record and medico-legal study. *Int J Environ Res Public Health.* 2019;16(5):801.
13. Sriruecha P, Nansupawat W, Tanwatanakul J. The Amphetamine Abuse Among The Heavy Truck Drivers. *Srinagarind Medical Journal.* 1994;9(2).
14. Narongchai P, Narongchai S, Thampituk S. The incidence of drug abuse in unnatural deaths in northern Thailand. *J Med Assoc Thai.* 2007;90(1):137-142.
15. Jones AW, Holmgren A. Concentration ratios of methamphetamine to amphetamine in blood can help to distinguish use of methamphetamine from various mixtures of the two stimulants. *J Anal Toxicol.* 2012;36(9):634-637.
16. Jones AW, Holmgren A, Ahlner J. High prevalence of previous arrests for illicit drug use and/or impaired driving among drivers killed in motor vehicle crashes in Sweden with amphetamine in blood at autopsy. *Int J Drug Policy.* 2015;26(8):790-793.
17. Kankaanpaa A, Ariniemi K, Heinonen M, et al. Current trends in Finnish drug abuse: Waste-water based epidemiology combined with other national indicators. *Sci Total Environ.* 2016;568:864-874.