Malaysian Journal of Analytical Sciences (MJAS)
Published by Malaysian Analytical Sciences Society

ESTIMATION OF DRUG CONSUMPTION IN KUANTAN, PAHANG, MALAYSIA VIA WASTEWATER-BASED DRUG EPIDEMIOLOGY

(Anggaran Penggunaan Dadah di Kuantan, Pahang, Malaysia Melalui Epidemiologi Dadah Berasaskan Air Kumbahan)

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Received: 7 June 2024; Accepted: 24 July 2024; Published: 27 October 2024

Abstract

The wastewater-based drug epidemiology (WBDE) methodology has been extensively employed to estimate drug consumption in diverse communities worldwide, serving as a valuable supplement to conventional epidemiological approaches. However, such methodology has not been employed to study drug consumption rates in the East Coast of Peninsular Malaysia. In this study, we aimed to estimate drug consumption rates in Kuantan, Pahang utilizing the WBDE methodology. Untreated wastewater samples were collected from the 14 largest wastewater treatment plants (WWTPs) in Kuantan between August and November 2021. Excreted residues of amphetamine (AMP), methamphetamine (METH), 3,4-methylenedioxy methamphetamine (MDMA), 3,4-methylenedioxyamphetamine (MDA), and morphine (MOR) were analyzed using liquid chromatography coupled with triple quadrupole mass spectrometry. AMP, METH, MDMA and MDA were detected at mean concentrations ranging from below detection limit (<LOD) to 1890 ng/L, while MOR was not found in any of the samples. METH was the most prevalent illicit drug in Kuantan, with a total estimated mean consumption rate of 7.04 mg/day/1000 people. Although the estimated consumption rate may not be directly comparable to other research due to the decentralized design of WWTPs in the studied area, our findings have provided insights into hotspots and/or high-risk areas for drug usage in the serviced community and a deeper understanding of METH and MDMA consumption patterns across different WWTPs. This information would be valuable for local authorities in planning targeted solutions to address these issues.

Keywords: wastewater, illicit drugs, methamphetamine, Malaysia, liquid chromatography-tandem mass spectrometry

Abstrak

Metodologi epidemiologi dadah berasaskan air sisa (WBDE) telah digunakan secara meluas untuk menganggarkan penggunaan dadah dalam pelbagai komuniti di seluruh dunia, sebagai maklumat tambahan yang berharga kepada pendekatan epidemiologi secara konvensional. Walau bagaimanapun, kaedah sedemikian belum digunakan untuk mengkaji kadar penggunaan dadah di

Pantai Timur Semenanjung Malaysia. Dalam kajian ini, kami bertujuan untuk menganggarkan penggunaan dadah di Kuantan, Pahang dengan menggunakan kaedah WBDE. Sampel air sisa yang belum dirawat diambil daripada 14 loji rawatan air sisa kumbahan (WWTP) yang terbesar di Kuantan di antara Ogos dan November 2021. Sisa residu amfetamin (AMP), metamfetamin (METH), 3,4-metilenadioksimetamfetamin (MDMA), 3,4- metilenadioksimamfetamin (MDA), dan morfin (MOR) dalam sampel air sisa dianalisis menggunakan kromatografi cecair ditambah dengan spektrometri jisim gandaan tiga (LC-MS/MS). AMP, METH, MDMA dan MDA dikesan pada kepekatan di bawah had pengesanan (<LOD) hingga 1890 ng/L, manakala MOR tidak ditemui dalam mana-mana sampel. METH merupakan dadah berbahaya yang paling lazim ditemui di Kuantan, dengan jumlah anggaran kadar penggunaan purata sebanyak 7.04 mg/hari/1000 orang. Walaupun anggaran kadar penggunaan ini mungkin tidak boleh dibandingkan dengan penyelidikan yang lain disebabkan rekabentuk WWTP yang ternyahpusat di dalam kawasan kajian, penemuan kami telah memberikan pemahaman tentang kawasan titik panas dan/atau kawasan berisiko tinggi untuk penggunaan dadah dalam komuniti perkhidmatan dan pemahaman yang lebih mendalam bagi penggunaan METH dan MDMA di WWTP yang berbeza. Maklumat ini amat berguna untuk pihak berkuasa tempatan di dalam merancang penyelesaian yang disasarkan untuk menangani isu-isu ini.

Kata kunci: air sisa, dadah terlarang, metamfetamin, Malaysia, kromatografi cecair-spektrometri jisim tandem

Introduction

The trafficking and misuse of illicit drugs such as heroin, methamphetamine, and cannabis as well as the illegal use of prescription drugs have significant adverse effects on society and are recognized as global social issues. Recent statistics reveal that in 2021, a total of 123,139 individuals were identified as drug users and addicts in Malaysia [1]. This accounted for 377 drug abusers and addicts per 100,000 of the population with a ratio of 1 drug addict for every 265 individuals. In terms of age groups, youths (aged 19-39) constituted the largest segment of drug and substance users in Malaysia, accounting for 65.8%, followed by 32.5% adults (aged 40 years and older), and 1.6% teenagers (aged 13-18) [1]. Currently, official statistics of drug abuse and seizure rates in Malaysia are derived from drug sweep operations conducted by the Royal Malaysia Police (PDRM) in partnership with the National Anti-drug Agency (AADK). While this method offers a useful general overview of drug abuse in our society, it may result in underestimating consumption rates and drug use prevalence because the information is gathered from consumers themselves. Moreover, this approach lacks the ability to provide real-time updates and detect evolving patterns due to the time-consuming nature of data collection and analysis. Hence, there is a need for a systematic approach to monitor the extent of illicit drug use and its fluctuations over time, especially for effective planning and evaluating the success of law enforcement and health intervention strategies.

The concept of using wastewater treatment plants (WWTPs) to assess collective drug consumption was initially proposed by Daughton in 2001 and later implemented in Italy in 2005, focusing on cocaine as a model drug [2]. This technique is called the wastewater-based drug epidemiology (WBDE) which is based on the principle that after drug consumption, drugs or their metabolites are excreted and released into domestic wastewater. By collecting raw sewage samples from WWTPs and analyzing the concentrations of drug residues or their metabolites in these samples, the population-normalized total consumption for a specific drug within the sewage treatment service area's population can be back calculated. The WBDE approach has been widely used in estimating drug consumption within various communities across different countries. These studies have been conducted in countries such as Canada [3], the United States [4], Australia [5], South Africa [6], Europe [7], South Korea [8] and China [9, 10]. The results of these studies have shown close agreement with prevalence statistics from national epidemiological surveys, highlighting the approach's potential as a valuable complement to traditional epidemiological methodologies. This approach has only since recently been employed in Southeast Asian cities. For example, Nguyen et al. [11] applied it in Ho Chi Minh city, Vietnam. This was followed by Hue et al. [12] who assessed the prevalence of use of a range of illicit drugs in Hanoi, also in Vietnam. Meanwhile, in Malaysia, Du et al. [13] employed WBDE to monitor common illicit drugs in two WWTPs in Kuala Lumpur. Notably, there has been no report of the use of WBDE to estimate illicit drug use in the East Coast of Peninsular Malaysia prior to this study.

Kuantan (3.8168°N, 103.3317°E) is in the north-east of Pahang which is further divided into six sub-districts: Kuala Kuantan (downtown Kuantan), Beserah, Penor, Sungai Karang, Hulu Kuantan and Hulu Lepar. The Kuantan District has a population of 548,014 [14]. In 2021, the state of Pahang reported a total of 10,551 cases of drug misuse, constituting 8.6% of the national figures [1]. Due to the scarcity of community-level drug use statistics, the implementation of the WBDE approach could prove beneficial in facilitating future drug abuse monitoring and planning drug intervention strategies in Malaysia. The primary objective of this study was to investigate the concentrations of AMP, METH, MDMA, MDA, and MOR in influent wastewater samples obtained from Kuantan, Pahang, Malaysia. Additionally, the study aimed to assess the community-level consumption of these drugs within the area.

Materials and Methods

Sampling

The sampling campaign was conducted in the Kuantan, Pahang, Malaysia, covering the 11 largest WWTPs located within the Kuala Kuantan sub-district (designated as WWTP-A to WWTP-K). These WWTPs served several residential communities with a total population of approximately 149,000 inhabitants. Additionally, one largest WWTP from each of the Sungai Karang, Beserah, and Hulu Lepar sub-districts was selected, namely, WWTP-L, WWTP-M, and WWTP-N, serving approximately 14,600, 11,600, and 18,800 people, respectively. This sampling campaign took place during the post lockdown period (Phase 3 of National Recovery Plan [NRP]) from August to November 2021. In each WWTP, twenty-four-hour composite wastewater samples were collected at the inlets of these WWTPs over four consecutive working days using a peristatic pump (Watson-Marlow qdos 20) at a flowrate of 5 mL/min. The collected samples were acidified to pH 2 and stored at -20℃ until analysis. All 14 WWTPs primarily served residential areas with minimal commercial contributions.

Sample pre-treatment and analysis

The analytical standards (AMP, AMP-d6, METH, METH-d5, MDMA, MDMA-d5, MDA, MDA-d5, MOR and MOR-d3) were purchased from Lipomed AG (Switzerland). Sample pre-treatment and analysis were performed by using a previously validated analytical method [15]. In short, wastewater samples were filtered through a 0.7 µm glass fibre filter, spiked with internal standards (IS) and then loaded onto Oasis MCX SPE cartridges (Waters Corporation, USA). AMP, METH, MDMA, MDA and MOR were eluted with 2 mL Methanol (MeOH) and 2 mL of 5% ammonium hydroxide (NH4OH) in MeOH. The eluates were then evaporated to dryness under a gentle stream of nitrogen and later reconstituted in 100 µL of deionized water containing 5% acetonitrile and 0.1% formic acid. Concentrations of the five drug residues in the samples were identified and quantified by using an Agilent 6410 triple quadrupole mass spectrometer equipped with an electrospray interface and operating in positive ionization mode. A Zorbax Eclipse Plus C18 RRHD column (2.1 × 50mm, 1.8µm) was used for the separation of the analytes. A mobile phase comprising of solvent A: 0.1% formic acid in water, and solvent B: 0.1% formic acid in acetonitrile, was used at a flow rate of 0.35 mL/min. The mobile phase gradient was programmed as follows: 0-2 min: 92% A, 2-2.1 min: 75% A, 2.1-3 min: 100% B. The column temperature was maintained at 45℃, while the autosampler temperature was set at 4℃. Detailed analytical conditions are described by Izani et al. [15]. One procedural blank (i.e., solvent blank spiked with IS) and one duplicate sample were included in each analysis batch. No contamination of analytes was found in blank samples.

Estimation of illicit drug consumption

The daily illicit drug consumption per 1000 inhabitants was calculated using the formulas established by Zuccato, et al. [16], as shown in equations (1) and (2) below:

$$Load\ (\mu g/day/1000\ people) = \frac{C_i \times F}{\frac{P}{1000}} \times \frac{1}{10^3}\left(\frac{\mu g}{ng}\right) \quad (1)$$

$$Consumption = Load \times C_f \quad (2)$$

where C_i represents the concentration of drug residue in influent wastewater sample (ng/L), F denotes the total daily flow (L/day), P represents the population served by the WWTP, and C_f is the correction factor for each drug corresponding to daily consumption. The C_f used to convert the loads of influent wastewater to the drug consumption are 3.3 for AMP, 2.3 for METH and 1.5 for MDMA [16].

Statistical analysis

Statistical analyses were performed using OriginLab software. For statistical calculations, zero was assigned to no detections and concentrations below the detection limit (<LOD). Spearman rank correlation was employed to determine bivariate correlations, both between target analytes and between analytes and WWTP capacity. The Kruskal Wallis H test was used to compare composition of target analytes within the same WWTP and among different WWTPs. The significance level was set at $\alpha = 0.05$ in all the statistical analyses.

Results and Discussion

Occurrence and daily mass loads of illicit drugs in influent wastewater

The results from the wastewater analysis revealed the presence of four out of five target drug biomarkers (i.e., AMP, METH, MDA and MDMA) in the samples, with concentrations ranging from below detection limit (<LOD) to 1890 ng/L (Table 1). METH had the highest mean concentration, ranging from 2.03 to 1890 ng/L, with a high detection frequency (DF) of 96.4%. MDA followed, with mean concentrations ranging from <LOD to 21.6 ng/L and a DF of 58.9%. AMP exhibited mean concentration between <LOD and 78.2 ng/L, detected at a frequency of 26.8%. By contrast, MDMA was detected in eight of the WWTPs, with mean concentrations ranging from <LOD to 0.55 ng/L, while MOR was not detected in any of the samples, which could be related to its fast degradation in raw wastewater [17]. The presence of METH in relatively high concentrations across all WWTPs (Table 1) indicated the prevalence of this substance in the Kuantan region. Statistical analysis did not reveal any significant relationship between the capacity of WWTPs and the concentration of drug residues found in the wastewater samples, suggesting that the drug use patterns within the study catchments may have been different. MDA is known as an illicit drug in its own right and can also be a metabolite of MDMA consumption [18]. However, the absence of correlation between their concentrations in wastewater samples may be an indication that both drugs were taken independently within the served community.

In WWTP-A, WWTP-C, WWTP-E, WWTP-G, WWTP-H and WWTP-N, low ratios of AMP and METH concentrations were observed, with mean ratios of 0.02±0.01, 0.04±0.01, 0.01±0.01, 0.05±0.04, 0.01±0.03 and 0.01±0.01, respectively. These findings were consistent with previous studies conducted in Cyprus [19], Kuala Lumpur [13], and Guangzhou [10]. Moreover, concentrations of AMP and METH in these six WWTPs were moderately correlated (Spearman rank correlation, $r = 0.66$); however, these concentrations were not statistically significant as they exceeded the significance level set for all the analyses ($p > 0.05$). These observations suggest that the presence of AMP in these WWTPs could potentially be attributed to METH use, rather than AMP use itself [16]. By contrast, eight WWTPs (i.e., WWTP-B, WWTP-D, WWTP-F, WWTP-I, WWTP-J, WWTP-K, WWTP-L and WWTP-M) exhibited unusually high METH loads in the absence of AMP (see Table 1). This finding may indicate a higher level of METH use within the communities served by these WWTPs or possibly an intentional dumping incident [20].

Estimation of drug consumption

The estimates of population-normalized drug load varied across the studied locations, with values ranging from 0.05 to 508 µg/day/1000 people (see Table 2). Among the detected illicit drugs, METH demonstrated the highest mass in the current study, indicating its prominence as the principal misused substance in the samples taken from Kuantan examined in this study (Table 2). The daily mass loads of AMP, METH, and

MDA differed significantly among the various WWTPs (Kruskal Wallis H test, $p < 0.05$), suggesting distinct consumption patterns of these target drugs across the samples taken from different WWTPs. However, day-to-day fluctuations in mass loads within the same WWTP were not significantly different for any of the target drugs, implying relatively consistent drug consumption rates over the sampling period.

Table 1. Concentration (ng/L) of AMP, METH, MDA and MDMA measured in WWTPs

WWTP	**Mean (±SD) Concentration of Drug Residues, ng/L**			
	AMP	**METH**	**MDA**	**MDMA**
Kuala Kuantan				
A (n=4)	7.22±2.14	384±127	13.0±2.53	0.18±0.36
B (n=4)	<LOD	1520±225	7.65±8.83	<LOD
C (n=4)	2.92±5.84	459±388	5.27±9.84	<LOD
D (n=4)	<LOD	1540±296	1.99±3.99	<LOD
E (n=4)	4.30±3.01	82.2±7.24	18.7±12.6	0.20±0.41
F (n=4)	<LOD	1330±184	21.6±6.52	0.55±0.65
G (n=4)	78.2±156	1530±2890	0.08±0.15	<LOD
H (n=4)	0.42±0.52	49.5±8.57	17.6±7.68	0.11±0.23
I (n=4)	<LOD	590±52.1	15.8±11.0	0.19±0.22
J (n=4)	<LOD	2.03±2.09	9.33±11.3	0.34±0.67
K (n=4)	<LOD	370±10.3	2.82±5.63	0.55±1.10
Sungai Karang				
L (n=4)	<LOD	1890±199	0.07±0.14	<LOD
Beserah				
M (n=4)	<LOD	1180±185	<LOD	0.23±0.32
Hulu Lepar				
N (n=4)	16.7±4.83	456±143	15.0±3.66	<LOD

Table 2. Mean influent loads of drug residues

WWTP	**Population**	**Mean (±SD) Influent Loads of Drug Residues, µg/day/1000 People**			
		AMP	**METH**	**MDA**	**MDMA**
Kuala Kuantan					
A	26246	1.94±0.57	103±34.3	3.49±0.68	0.05±0.10
B	23567	-	408±60.4	2.06±2.38	-
C	18760	0.79±1.57	126±104	1.42±2.65	-
D	14508	-	415±79.6	0.54±1.07	-
E	14358	1.57±0.81	22.1±1.95	5.04±3.40	0.05±0.11
F	11353	-	358±49.6	5.81±0.18	0.15±0.18
G	10682	21.0±42.1	410±778	0.02±0.04	-
H	14575	0.11±0.14	13.3±2.31	4.73±2.07	0.03±0.06
I	11570	-	160±14.0	4.24±2.96	0.05±0.06
J	8873	-	0.55±0.56	2.51±3.03	0.09±0.18
K	9160	-	98.5±2.77	0.76±1.52	0.15±0.30
Sungai Karang					
L	11786	-	508±53.6	0.02±0.04	-
Beserah					
M	8943	-	317±49.9	-	0.06±0.09
Hulu Lepar					
N	23567	4.49±1.30	123±38.6	4.04±0.98	-

-: Not quantified as the compound was not detected in wastewater samples

Figure 1 illustrates the estimated METH and MDMA consumption rates across the 14 investigated WWTPs. In the calculation of these figures, the consumption was set to 0 when the consumption indicator was not detected in any sample. Notably, inter-WWTP variations were observed for both METH and MDMA. Samples from six WWTPs, namely, WWTP-B, WWTP-C, WWTP-D, WWTP-G, WWTP-L, and WWTP-N showed only METH consumption while the other WWTPs exhibited consumption of both METH and MDMA, with METH being dominant in all stations. The estimated mean METH consumption rates in the 14 examined WWTPs ranged from 1.25 to 1170 µg/day/1000 people, resulting in a total estimated mean consumption rate of 4860 µg/day/1000 people within the Kuala Kuantan sub-district, followed by Sungai Karang (1170 µg/day/1000 people), Beserah (729 µg/day/1000 people) and Hulu Lepar (282 µg/day/1000 people) sub-districts. For MDMA, the estimated consumption was relatively low with a total estimated mean of 0.95 µg/day/1000 people.

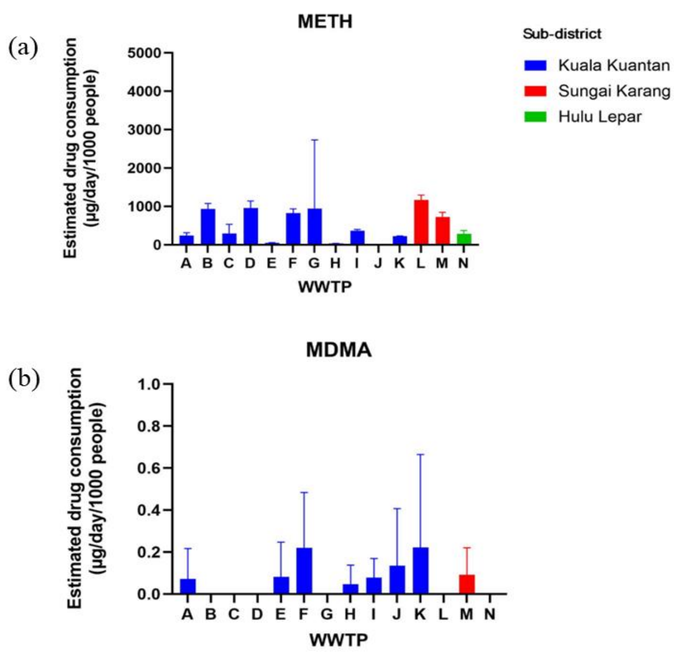

Figure 1. Estimated average community drug consumption (µg/day/1000 people) for (a) METH and (b) MDMA in Kuantan. Vertical bars indicate standard deviation of the average estimates for the WWTP

As illustrated in the hotspots map in Figure 2, higher METH consumption rates were observed near the Kuantan City center. This could be attributed to factors such as the availability of METH in urbanized areas and its potential association with locations where the trafficking of illicit drugs might occur as well as various socio-demographic aspects. The estimated consumption rates for MDMA, however, were relatively low with a total estimated mean of 0.95 µg/day/1000 people. A few areas of higher risk for MDMA consumption within the Kuala Kuantan and Beserah sub-districts could still be identified although the consumption rates were low as can be seen in Figure 2. Interestingly, no MDMA residue was detected at WWTP-L, despite having the highest individual estimated METH consumption rate (see Figure 1). This finding indicated a different source and usage pattern for both METH and MDMA in Kuantan. Overall, our findings were consistent with the Malaysian AADK report, which identified METH as the most frequently abused drug in 2021 (89.6%), followed by AMP (10.2%) and MDMA (0.2%) [1]. Data obtained from drug seizures in raids also confirmed this trend, with AADK reporting 10,228 kg of METH seizures and 1058 kg of MDMA seizures in the year 2021 [1].

Additionally, the 10% decrease in METH price in the market since 2020 in addition to the price of Ecstasy (MDMA) remaining unchanged [1] may have also be contributed to the high occurrence of METH concentration measured in wastewater samples.

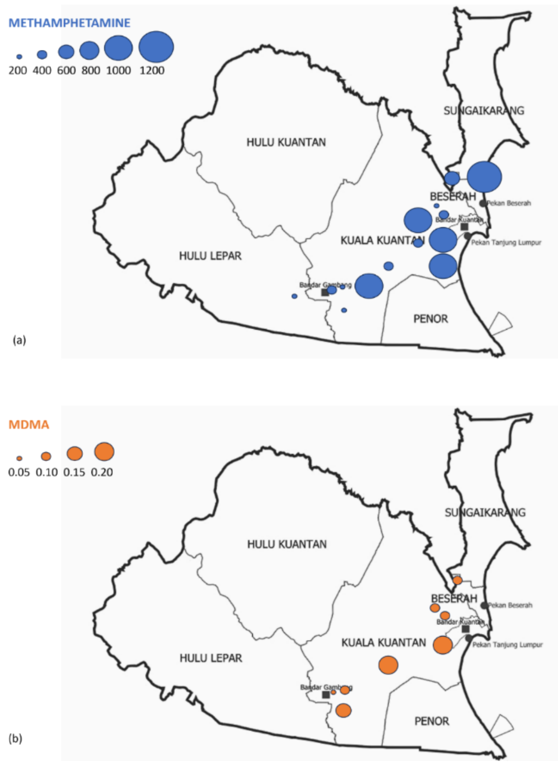

Figure 2. Hot spot areas (µg/day/1000 people) for (a) METH and (b) MDMA in Kuantan

The estimated METH and MDMA consumption rates in the current study in which samples were taken from Kuantan, Pahang located in the East Coast of Peninsular Malaysia were two and six orders of magnitude lower, respectively, compared to those reported in a past study in Kuala Lumpur, Malaysia by Du et al. [13], despite similar total population coverage in both studies (Table 3). In contrast to other WBDE studies in various Asian cities, METH consumption in Kuantan was estimated to be about three to 50 times lower than in Hong Kong, South Korea, Ho Chi Minh city, and Hanoi (Table 3), but similar to that reported in Qinghe, Beijing with a median consumption of 10.0 mg/day/1000 people [20]. Concerning MDMA, the estimated consumption in Kuantan District was low due to non-detection in several WWTPs. Similarly, this had been reported in studies conducted in Hong Kong [21] and several other megacities in China [20], suggesting a potential similarity in Amphetamine Type Stimulant (ATS) drug use patterns between Kuantan and these areas.

Conclusion

In this study, the WBDE approach was utilized to estimate illicit drug consumption in Kuantan, Pahang located in the East Coast of Peninsular Malaysia where the use of WBDE has not been reported. It has been evident that methamphetamine (METH) was found to be the most highly consumed narcotic drug in Kuantan, with a total estimated mean consumption rate of 7.04 mg/day/1000 people. Our estimated drug consumption rates were several orders of magnitude lower than those found in other cities and/or countries where similar studies had been conducted. Further studies monitoring the precursor biomarkers of other illicit drugs as well as sample collection at centralized WWTPs in other Malaysian cities over a longer period should consider

Table 3. Comparison of METH and MDMA consumption worldwide

Reference	Location	Population (Thousands)	Year of Sampling	Consumption (mg/1000 people/day)	
				METH	MDMA
This study	Kuantan, Malaysia	194	2021	7.04*	9.49E-04*
Du et al. [13]	Kuala Lumpur, Malaysia	220	2017	545	719
Lai et al. [21]	Hong Kong	3,500	2011	190	NA[a]
Kim et al. [8]	South Korea	108-3,700	2012-2013	22	NA
Nguyen et al. [11]	Ho Chi Minh City, Vietnam	450	2015	220	NA
Asicioglu et al. [22]	Istanbul	20,000	2019	120	94.8
Daglioglu et al. [23]	Adana, Turkey	784,625	2017-2018	3628	70
Lai et al. [24]	Auckland, New Zealand	1,300	2014	360	60.2
Mastroianni et al. [25]	Barcelona, Spain	1,162	2011-2015	157	188
Khan et al. [20]	Beijing, Guangzhou, Shenzhen, Shanghai	100-2,420	2012	10.0-109.5	<0.2-1.5
Oertel et al. [26]	Germany	3-1,420	2020-2021	0.67-354	2-127
Campo et al. [27]	Valencia, Spain	215-943	2011-2020	3.7-50.6	15.4-102.5
Moslah et al. [28]	Tunisia	195-1,000	2019	NA	35.8-1531.1
Hue et al. [12]	Hanoi, Vietnam	400-430	2018-2020	337.7	161.4

obtaining samples that would be more representative to provide more accurate data on illicit drug consumption in the country. The utilization of the WBDE approach in this study has enabled the identification of hotspots and/or high-risk areas, contributing toward a more comprehensive understanding of illicit drug use patterns within the study communities. This valuable information can aid relevant authorities in effectively targeting problematic areas for future prevention and awareness initiatives as well as in planning suitable strategies. It should be noted that, however, our study had several limitations. Firstly, our results should be interpreted with care as we obtained only a limited composite sample per WWTP (n = 4). Due to the decentralized design and relatively small capacity of WWTPs in Kuantan, our samples which had been collected within the Kuala Kuantan, Sungai Karang, Beserah, and Hulu Lepar sub-districts represented only 36.9%, 21.4%, 45.8%, and 89.4% of the entire population of each sub-district, respectively. All the 14 WWTPs that we selected for analysis in this study only served 35.4% of the entire population of Kuantan District; therefore, samples collected from these 14 plants might not be fully representative of other less populated areas in Kuantan District, for example, the Hulu Kuantan sub-district. Furthermore, this study only monitored drug use for four consecutive working days at different time periods of the year, leaving the temporal variations between drug consumption on weekdays and weekends unknown. During the estimation of consumption rates, the concentration of illicit drug residues was assumed to be consistent throughout the sampling period. Besides, employing a single excretion rate of the target drug for back calculation could introduce a certain level of uncertainty as metabolization varies among individuals [28]. Additionally, the measurements taken for COVID-19 management (e.g., lock down and contact restriction) may have altered leisure behavior and the absolute consumption volumes of drugs. Therefore, the results should not be generalized to patterns of drug use over long periods in Kuantan.

Acknowledgements

This study has received funding from the Ministry of Higher Education under Fundamental Research Grant Scheme (FRGS) [grant number FRGS/1/2019/STG01/UMP/02/5 (University's Reference No. RDU1901198)] and support from Universiti Malaysia Pahang Al-Sultan Abdullah in terms of laboratory facilities. Authors would also like to acknowledge Ms. Nasihah Musa (Monash University Malaysia) for her assistance with the LC-MS/MS analysis and Prof. Dr. Jochen Mueller (The University of Queensland, Australia) for his advice during this research. The authors would also like to express their gratitude to the staff of the Indah Water Konsortium Sdn Bhd (IWK) Kuantan for their cooperation in the sampling campaign and collection of samples.

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