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Pattern of Toxicity and Sampling for Detection of Acute Cannabis Toxicity Cases Admitted to Benha Poisoning Control Unit

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ABSTRACT

Tetrahydrocannabinol (Δ^9 -THC) is a psychoactive substance that is found in *Cannabis sativa L.*, which has been globally linked with acute toxicity cases. Finding the best biological sample for quick and accurate THC detection is essential for medical and forensic oversight. This study aimed to evaluate the most precise sample type for rapidly and accurately determining cannabis levels. We conducted a case-control study at Benha Poisoning Control Unit, Benha University Hospital, from December 1, 2023, to April 30, 2024. One hundred sixty-eight participants were recruited, comprising 84 with acute cannabis toxicity and 84 controls who matched in age and sex. Sociodemographic information, vital signs, clinical symptoms (neurological, gastrointestinal, and respiratory), and THC levels in blood, urine, and oral fluid using immunoassay (cutoff: 50 ng/mL) were all evaluated. The majority of cases were male (71.4%), aged 19-59; 52.4% were inhaled, while 83.3% were intentionally exposed. Common symptoms included tachycardia (47.5% when compared to controls), anxiety (40.8%), decreased consciousness (59.5%), vomiting (23.8%) and nausea (11.9%). THC levels (ng/mL) after 30 hours of exposure varied from 66 to 90 (blood), 59 to 77 (urine), and 400 to 700 (oral fluid/saliva). Three hours for blood and urine C_{max}, and five to nine hours for oral fluid. The maximum AUC (0–9h: 3977.08 mcg/mL.hr) and a positive correlation with blood ($r=0.9$, $p<0.01$) were observed in oral fluid. Conclusion, the most accurate sample for identifying recent cannabis use was oral fluid because of its high concentrations and extended detection window, which makes it perfect for emergencies.

INTRODUCTION

Cannabis is among the most common drugs that are abused. Globally, cannabis use and abuse are one of the most critical issues that have attracted the attention of health policymakers. However, different forms of cannabis with varying contents of active compounds, such as THC, as well as pharmaceutical products with varying contents of cannabinoids, have been produced and developed in recent years due to advances in cultivation and processing methods (Pattnaik *et al.*, 2022 & Suárez *et al.*, 2023).

There have been efforts to make policies to legalize the usage of cannabis for different health problems while controlling the abuse of cannabis, as it is still a matter of concern in most parts of the world because of the consequences, especially for different populations (Matheson *et al.*, 2020 & Alvaez *et al.*, 2023).

Concern about the abuse of cannabis and its derivatives has become a health concern, especially in recent years, due to its detrimental psychosocial effects in the youth population (Kroon *et al.*, 2020 & Gripe *et al.*, 2024). Several studies have suggested the consequences of cannabis abuse in the young population, including reduced academic performance and even expulsion from educational institutions (Pacheco *et al.*, 2019), dangerous sexual behaviors (Chandler *et al.*, 2021), high consumption of alcohol, other substance abuse (Hayaki *et al.*, 2016), and frequent car accidents due to driving under the influence of drugs (DUID) (Pearlson *et al.*, 2021 & Costales *et al.*, 2023). Cannabinoids in the resin of this plant are considered to be psychoactive and medicinally active chemical compounds. Cannabis contains over 460 active compounds, of which more than 70 are cannabinoid structures (Fordjour *et al.*, 2023). Δ 9-tetrahydrocannabinol is a primarily active cannabinoid that is responsible for most of the psychoactive properties of cannabis. However, it exists in a mixture with precursors that lack psychoactive properties, such as Δ 9-tetrahydrocannabinolic acids A and B (Sciences *et al.*, 2017). Due to the metabolism, 11-hydroxy-THC (THC-OH), 11-nor-9-carboxy-THC (THC-COOH), and acyl glucuronide Δ 9-THC-COOH were detected in blood and body samples. After exposure, Δ 9-tetrahydrocannabinol is promptly absorbed and distributed throughout the body tissues, such as adipose tissue, liver, lung, and spleen, as it is lipophilic. Afterwards, it is gradually redistributed into the blood and metabolized, with a relatively long half-life (Hanisch *et al.*, 2015).

Driving under the influence of cannabis (DUIC) has become a significant public safety problem due to the continuous changes being made to both medicinal and recreational cannabis regulations around the world. There are various methods for evaluating DUIC. Among is an effect-based approach in which a police officer or drug recognition expert (DRE) ought to demonstrate behavioural changes. However, there are concerns about the efficacy of this approach, as some cases can be challenging for prosecution. Therefore, some jurisdictions established a zero-tolerance policy toward DUIC. According to these laws, an abused driver will be considered a lawbreaker if delta-9-tetrahydrocannabinol (THC) is recognized at or above a specific concentration in a given biological sample, regardless of real impairment (Arkell *et al.*, 2019).

Blood, oral fluid (saliva), and urine are among the most common biological samples used for cannabis detection in epidemiological research. On the other hand, biological samples such as sweat, breast milk, or vitreous humour may be used depending on the study's purposes (Gjerde *et al.*, 2011).

Examination of oral fluids for cannabis derivatives can offer some distinct advantages compared to urine analysis. THC, as a main psychoactive compound of cannabis, is the analyte that is measured in oral fluids. The existence of THC in oral

fluids can be regarded as evidence for recent cannabis consumption. In contrast, urinal detection of THC can suggest either recent usage or a long-term accumulation (Niedbala *et al.*, 2001). The current study aims to evaluate the most accurate biological sample (blood, urine and oral fluids) to determine the cannabis level rapidly and precisely in acute cannabis toxicity cases at Benha Poison Control Unit, Benha University Hospital,, Egypt.

MATERIALS AND METHODS

1-Study Design and Population:

This case-control investigation was conducted at Benha Poisoning Control Unit, Benha University Hospital. One hundred sixty-eight participants were recruited from Benha Poisoning Control Unit. All cases are admitted to Benha Poisoning Control Unit during a period from December 1 2023, to April 30 2024, comprising 84 patients with acute cannabis toxicity (confirmed by medical history and immunoassay) and 84 matched (age and sex) healthy controls (recruited from the hospital visitors and screened via self-report and urine immunoassay).

2-Ethical Considerations:

Our study was conducted in accordance with the Helsinki Declaration. Also, it was approved ethically by the Medical Research Ethics Committee of Benha University under the ethical code of RC-18-12-2023. In accordance with ethical guidelines for human research, informed consent was taken from each participant before sample collection. Informed consent was obtained from the families of patients who were incapable of giving consent. Informed consent includes details about the study's purpose, methodology, location, and timing. Also, it was kept confidential to avoid potential bias. We adhered to the STROBE guidelines for the design and reporting of our research data.

3-Participants:

The study included two groups: Group A, which comprised 84 patients presenting with acute exposure to cannabis who were admitted to Benha poisoning control unit, and Group B included 84 healthy volunteers (with no history of drug use) matched for age and sex. We exclude patients presenting with no confirmatory history of cannabis intake, cases with other drug intake, patients with recent hemodialysis or false positive results due to drug intake like Proton Pump Inhibitors and NSAIDs.

4-All Participants Were Subjected to the Following:

4.1. Medical History:

We got the medical history from the conscious patients. When the patient was unconscious, we obtained it from the patient's relatives. The Sociodemographic characteristics (including age, sex, and education), route of exposure, intentionality, and marital status.

4.2. Examination:

General vital signs of the studied group: Neurological (CNS excitation and CNS depression); Gastrointestinal (nausea, vomiting, abdominal pain, and diarrhoea); and Respiratory (Respiratory depression, dyspnea, and cough).

2.4.3 Laboratory Investigations:

This included biological concentration of the following samples:

- Blood: 5ml of Peripheral venous blood samples were obtained from each case under complete aseptic conditions and collected in vacutainer tubes containing preservatives like potassium fluoride for further analysis.
- Oral Fluid: 0.1- 0.5 ml were collected using small plastic tubes. The liquid buffer in the transport vial is crucial. It stabilizes the oral fluid specimen, inhibits bacterial

growth, prevents drug degradation, and reduces the adsorption of drugs to the tube walls during transport. Short-term (Pre-analysis): Specimens should be kept refrigerated (around 4°C) when possible, though they are often stable at room temperature for a limited time

- Urine: Urine samples were obtained under the direct observation of medical personnel to prevent any potential manipulation and adulteration. Sampling performed in video camera surveillance-toilets. The urine samples were collected into dry, clean plastic cups with amounts of 10-20 ml.

5-Analytical Methods:

We used radioimmunoassay (RIA) for analysis. The instrument included a calibrated drug auto-analyzer (iCubio Biomedical Technology Company, Shenzhen, China). It was a fully automated random-access analyzer that detected drug levels using photometric methods, with a cutoff concentration of 50 ng/mL (Federal, 2004).

6-Management and Outcomes:

Management included symptom-specific treatments (such as antiemetics), observation, supportive care, and mechanical ventilation. Outcomes included being discharged from the hospital, being discharged against medical advice, being admitted to the ICU, and death.

7-Data Analysis:

Data analysis was performed using SPSS Statistics software version 28.0 for Windows (IBM Corp, Armonk, NY, USA, Released 2021). For qualitative data, we presented them as frequencies (numbers) and percentages (%). Quantitative data were shown as means \pm Standard deviation (SD) alongside the median, minimum, and maximum. Pearson's Chi-square (χ^2) was used to test the significance of the association between categorical variables. The Pearson correlation coefficient is used to measure the strength and the direction of the relationship between parametric quantitative variables. The area under the curve (AUC) was measured using the linear-log trapezoidal methodology. The level of significance for our data was set at 95%, and thus, a p-value $>$ 0.05 was considered non-statistically significant. Also, a p-value $<$ 0.05 was considered statistically significant, while a p-value $<$ 0.01 was considered highly statistically significant (Peacock and Peacock, 2020).

RESULTS

1- Distribution of Sociodemographic Characteristics of the Studied Groups, Cases of Acute Cannabis Exposure Versus Controls:

Table 1 shows the sociodemographic characteristics of the studied groups (84 cases of acute cannabis exposure versus 84 controls). The majority of our sample (59.5% of cases versus 50% of controls) were aged between 19 and 59 years, males were the most dominant sex category in the studied groups (71.4% in the case group versus 63.1% in control group), almost half of sample were married (47.6% in case group versus 53.6% in control group). The most prevalent education category was illiterate (40.5% in the case group versus 32.1% in the control group), followed by the highly educated category (35.7% of both groups). There was no significant difference in the distribution of age, sex, marital status, and education in the studied groups. Half of the case group had been exposed to cannabis by inhalation (52.4%), 35.7% by ingestion and only 11.9% by an unknown route of exposure. 83.3% cases were intentionally exposed to cannabis compared to only 16.7% by accident.

Table 1. Sociodemographic characteristics of the studied groups.

| Variables | Categories | Case group (n=84) | | Control group (n=84) | | Test of significance | P-value |
|-------------------|--------------|-------------------|------|----------------------|------|----------------------|---------|
| | | N | % | N | % | | |
| Age/years | <19 | 14 | 16.7 | 16 | 19 | X2= 1.612 | 0.434 |
| | 19-59 | 50 | 59.5 | 42 | 50 | | |
| | ≥60 | 20 | 23.8 | 26 | 31 | | |
| Sex | Male | 60 | 71.4 | 53 | 63.1 | X2=1.325 | 0.324 |
| | Female | 24 | 28.6 | 31 | 36.9 | | |
| Marital status | Unmarried | 44 | 52.4 | 39 | 46.4 | X2=0.595 | 0.537 |
| | Married | 40 | 47.6 | 45 | 53.6 | | |
| Education | Illiterate | 34 | 40.5 | 27 | 32.1 | X2=1.846 | 0.405 |
| | Intermediate | 20 | 23.8 | 27 | 32.1 | | |
| | High | 30 | 35.7 | 30 | 35.7 | | |
| Route of exposure | Ingestion | 30 | 35.7 | NA | NA | NA | NA |
| | Inhalation | 44 | 52.4 | NA | NA | | |
| | Unknown | 10 | 11.9 | NA | NA | | |
| Intentionality | Intentional | 70 | 83.3 | NA | NA | NA | NA |
| | Accidental | 14 | 16.7 | NA | NA | | |

X2: Chi-Square test, not significant at p>0.05, NA: not applicable

2- Vital Signs of the Studied Groups, The Case Group Following Acute Cannabis Exposure, Versus the Control Group:

Table 2 presents the vital signs of the studied groups. Notably, 47.5% of cases in the case group suffered from tachycardia, compared to 3.57% in the control group, indicating a highly significant difference between the two groups (p<0.001). 52.4% of cases had normal blood pressure in the case group, compared to 83.33% in the control group, with a highly significant difference between the groups (p<0.0001). There was a significant difference (p<0.00) between the two groups, with over half of the sample (64.3%) in the case group and 97.62% in the control group having normal oxygen saturation.

Table 2. The vital signs of the studied groups.

| Variables (Vital signs) | Categories | Case group (n=84) | | Control group (n=84) | | Test of significance | P-value |
|-------------------------|--------------|-------------------|------|----------------------|-------|----------------------|-----------|
| | | N | % | N | % | | |
| Heart Rate | Normal | 34 | 40.5 | 79 | 94.05 | X2= 55.091 | <0.0001** |
| | Tachycardia | 40 | 47.5 | 3 | 3.57 | | |
| | Bradycardia | 10 | 11.9 | 2 | 2.38 | | |
| Blood pressure | Normal | 44 | 52.4 | 70 | 83.33 | X2=19.667 | <0.0001** |
| | Hypertension | 30 | 35.7 | 8 | 9.52 | | |
| | Hypotension | 10 | 11.9 | 6 | 7.14 | | |
| Oxygen saturation | Normal | 54 | 64.3 | 82 | 97.62 | X2=30.265 | <0.0001** |
| | Hypoxemia | 30 | 35.7 | 2 | 2.38 | | |

3- Symptoms in the Cases (Patients) Acutely Exposed to Cannabis:

Table 3 presents the distributions of the symptoms, treatments, and outcomes following acute cannabis exposure in cases. Regarding neurological CNS excitation, 23.8% of the case group had paranoia, 17.9% had hallucination, 23.8% had visual disturbances, 11.9% had panic attack, tremors, and headache, 5.95% had myoclonus, and 7.1% had numbness and tingling, while 40.8% suffered from anxiety.

Regarding CNS depression, 23.8% had speech abnormalities, 35.7% had impaired coordination, 23.8% had visual disturbances, 11.9% had weakness, 5.95% had syncope, 59.5% suffered from reduced consciousness and 4.8% were comatose. Regarding gastrointestinal symptoms and side effects, 11.9% had nausea, 23.8% had vomiting, 3.6% had abdominal pain, and 4.8% had diarrhea. 59.5% suffered from reduced consciousness.

Regarding respiratory symptoms, 2.4% had respiratory depression, 1.2% had dyspnea, and no cases (0%) reported cough (this might be due to underreporting), with highly significant differences in their distributions ($p < 0.0001$).

Table 3. Symptoms, treatments, and outcomes of acutely exposed patients with cannabis.

| Variables | Categories | Cases (n=84) | |
|----------------------------------|------------|--------------|------|
| | | N | % |
| Neurologic CNS excitation | | | |
| Anxiety | Yes | 34 | 40.8 |
| Paranoia | Yes | 20 | 23.8 |
| Hallucinations | Yes | 15 | 17.9 |
| visual disturbances | Yes | 20 | 23.8 |
| panic attack | Yes | 10 | 11.9 |
| Tremors | Yes | 10 | 11.9 |
| myoclonus | Yes | 5 | 5.95 |
| Numbness, tingling | Yes | 6 | 7.1 |
| Headache | Yes | 10 | 11.9 |
| CNS depression | | | |
| Reduced consciousness | Yes | 50 | 59.5 |
| Speech abnormalities | Yes | 20 | 23.8 |
| impaired coordination | Yes | 30 | 35.7 |
| Weakness | Yes | 10 | 11.9 |
| Syncope | Yes | 5 | 5.95 |
| comatose | Yes | 4 | 4.8 |
| Gastrointestinal | | | |
| Nausea | Yes | 10 | 11.9 |
| Vomiting | Yes | 20 | 23.8 |
| Abdominal pain | Yes | 3 | 3.6 |
| Diarrhea | Yes | 4 | 4.8 |
| Respiratory | | | |
| Respiratory depression | Yes | 2 | 2.4 |
| Dyspnea | Yes | 1 | 1.2 |
| Cough | Yes | 0 | 0 |

4- Management and Outcomes Among the Case Group:

Regarding management, almost half of the cases (48.8%) received symptom-specific treatments, 47.6% received observation and supportive care, and only 3.6% received mechanical ventilation due to severe respiratory depression (Table 4). Considering outcomes, the majority of cases (71.4%) were discharged from the hospital, 23.8% were discharged against medical advice, 3.6% were admitted to the ICU, and 1.2% expired.

Table 4. Distribution of the outcomes in the patients.

| Variables | Categories | Total (n=84) | |
|------------|-----------------------------------|--------------|------|
| | | N | % |
| Management | Observation and supportive care | 40 | 47.6 |
| | Symptom-specific treatments | 41 | 48.8 |
| | Mechanical ventilation | 3 | 3.6 |
| outcomes | Improved and discharged | 60 | 71.4 |
| | Admission to the ICU | 3 | 3.6 |
| | Discharged against medical advice | 20 | 23.8 |
| | Expired | 1 | 1.2 |

5- Descriptive Distribution of THC Concentrations in Samples:

The descriptive results of the measured THC concentrations (ng/mL) in blood, urine, and saliva are presented in Table 5. Follow-up time ranged from 2 to 54 hours, with a mean of 20.821±17.314. Blood concentration ranged from 66 to 90, with a mean value of 82.50±8.663. Urine concentration ranged from 59 to 77, with a mean value of 68.167±7.332. Oral concentration ranged from 400 to 700 in the first thirty hours, with a mean value of 516.667±108.012.

Table 5. The THC concentrations measured in the blood, urine, and saliva (ng/ml).

| Variable | Mean± SD | Median (Min-Max) |
|-----------------------------|-----------------|--------------------|
| Time (hours) | 20.821±17.314 | 21.0 (2.0-54.0) |
| Blood Concentration (ng/mL) | 82.50±8.663 | 84.50 (66.0-90.0) |
| Urine Concentration (ng/mL) | 68.167±7.332 | 68.185 (59.0-77.0) |
| Oral Concentration (ng/mL) | 516.667±108.012 | 500.00 (400-700) |

SD: standard deviation, Min: Minimum, Max: Maximum

6- Pearson Correlation Coefficient Between the THC Concentration and the Time:

Table 6 revealed a moderate negative correlation between time and both blood and urine concentrations. Additionally, there was a strong positive correlation between blood, urine, and oral concentrations (Figs. 1-7).

Table 6. The Pearson correlation coefficient between the THC concentrations and times.

| Variable | Time | | Blood Concentration | | Urine Concentration | | Oral Concentration | |
|---------------------|--------|----------|---------------------|----------|---------------------|----------|--------------------|----------|
| | R | P value | R | P value | R | P value | R | P value |
| Time | | | -0.324 | 0.003** | -0.493 | <0.001** | 0.124 | 0.434 |
| Blood Concentration | -0.324 | 0.003** | | | 0.758 | <0.001** | 0.909 | <0.001** |
| Urine Concentration | -0.493 | <0.001** | 0.758 | <0.001** | | | 0.821 | <0.001** |
| Oral Concentration | 0.761 | 0.000 | 0.909 | <0.001** | 0.821 | <0.001** | | |

R: Pearson correlation coefficient, **: Highly significant (P<0.01)

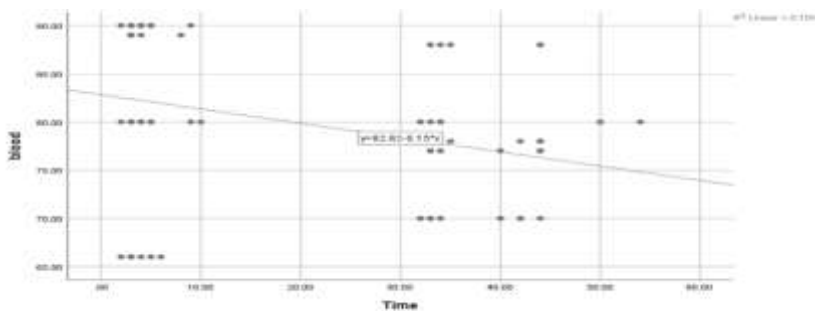


Fig. 1. Scattered plot representing the correlation between the time and THC concentrations in the blood of the studied groups

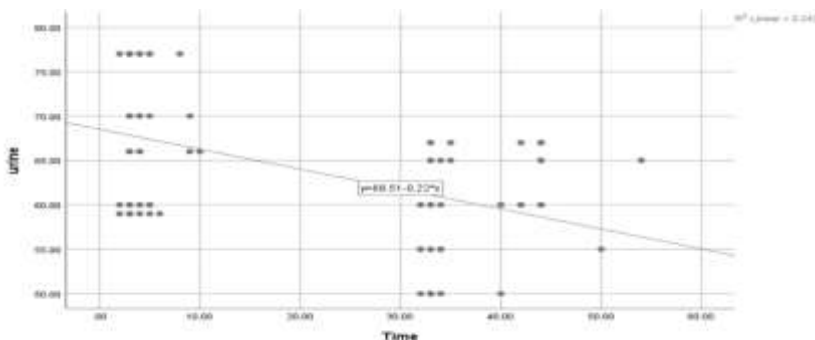


Fig. 2. Scattered plot represents the correlation between the time and THC concentrations in the urine of the studied groups

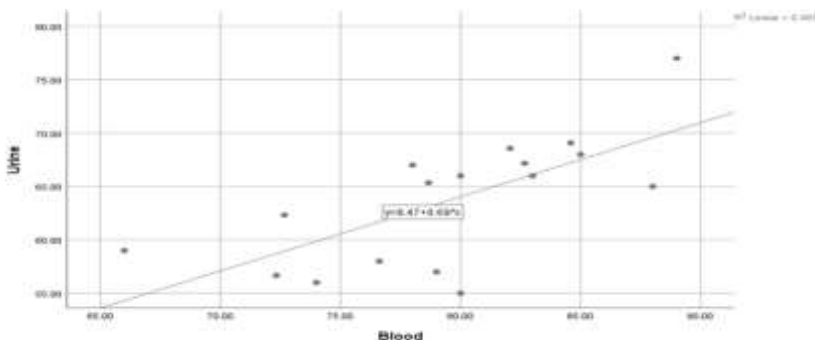


Fig. 3. Scattered plot represents the correlation between the THC concentrations in the urine and the blood of the studied groups

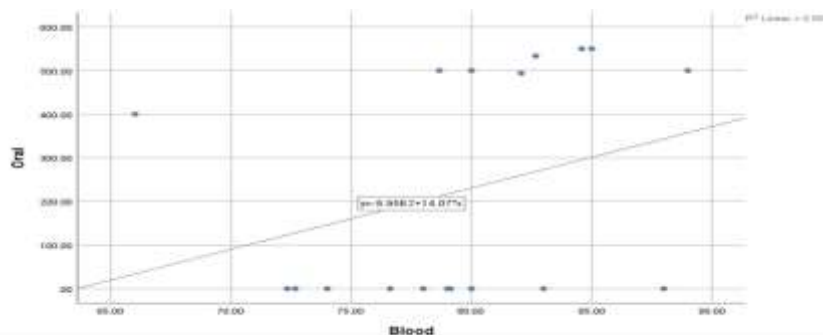


Fig. 4. Scattered plot represents the correlation between the THC concentrations in the oral fluid versus in the blood of the studied groups.

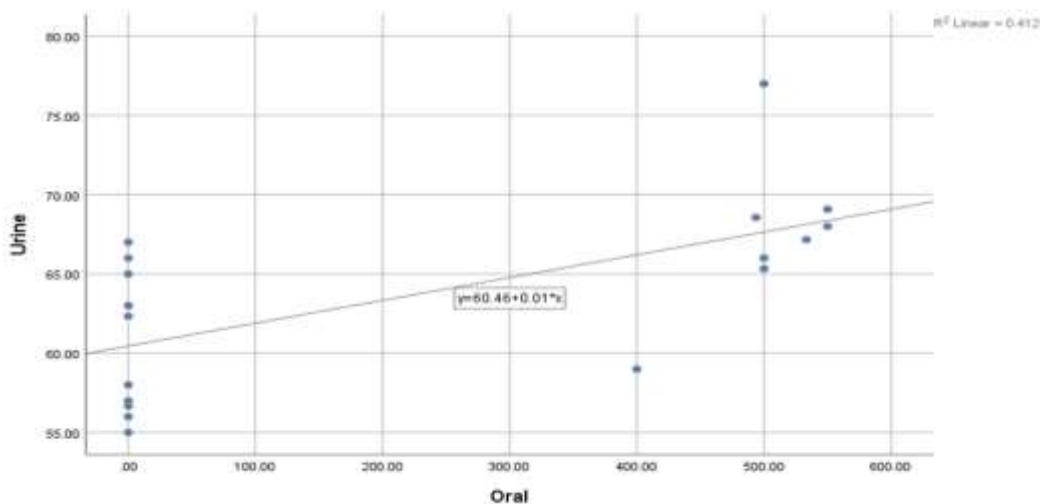


Fig. 5. Scattered plot represents the correlation between the THC concentrations in the urine and the oral fluid of the studied groups.

Table 7 presents THC concentrations in blood, urine, and saliva samples in different time intervals. The Cmax of blood and urine concentrations was observed at 3 hours after exposure, whereas the Cmax of oral concentration was at 5 and 9 hours.

Table 7. THC concentrations in different time intervals.

| Time intervals | Blood Concentration (Mean±SD) | Urine Concentration (Mean±SD) | Oral Concentration (Mean±SD) |
|----------------|-------------------------------|-------------------------------|------------------------------|
| 2.00 h | 78.67±12.06 | 65.33±10.12 | 500.00±173.21 |
| 3.00 h | 82.06±9.04 | 68.56±7.62 | 493.75±85.39 |
| 4.00 h | 84.58±7.54 | 69.08±6.99 | 550.00±116.77 |
| 5.00 h | 82.67±9.52 | 67.17±8.61 | 533.33±150.55 |
| 6.00 h | 66.00±0.0 | 59.00±0.0 | 400.00±0.0 |
| 8.00 h | 89.00±0.0 | 77.00±0.0 | 500.00±0.0 |
| 9.00 h | 85.00±7.07 | 68.00±2.83 | 550.00±70.71 |
| 10.00 h | 80.00±0.0 | 66.00±0.0 | 500.00±0.0 |
| 32.00 h | 74.00±5.48 | 56.00±4.18 | 0.00±0.0 |
| 33.00 h | 76.62±6.49 | 58.00±6.75 | 0.00±0.0 |
| 34.00 h | 79.0±6.48 | 57.00±5.7 | 0.00±0.0 |
| 35.00 h | 83.00±7.07 | 66.00±1.41 | 0.00±0.0 |
| 40.00 h | 72.33±4.04 | 56.67±5.77 | 0.00±0.0 |
| 42.00 h | 72.67±4.62 | 62.33±4.04 | 0.00±0.0 |
| 44.00 h | 79.0±5.679 | 63.44±3.358 | 0.00±0.0 |
| 50.00 h | 80.00±0.0 | 55.00±0.0 | 0.00±0.0 |
| 54.00 h | 88.00±0.0 | 65.00±0.0 | 0.00±0.0 |

SD: Standard Deviation

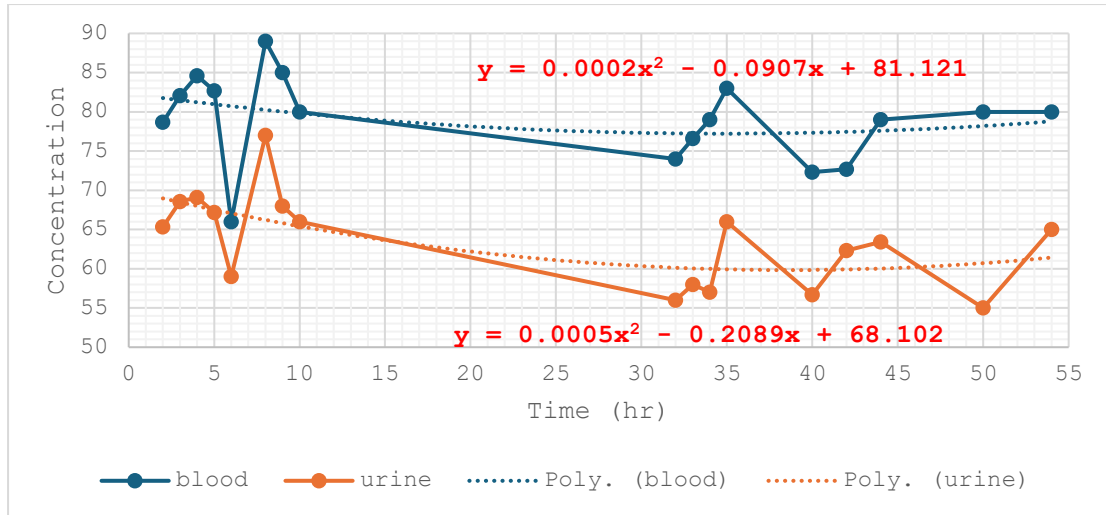


Fig. 6. Line Chart represents the average blood and urine THC concentrations in different time intervals of the studied groups

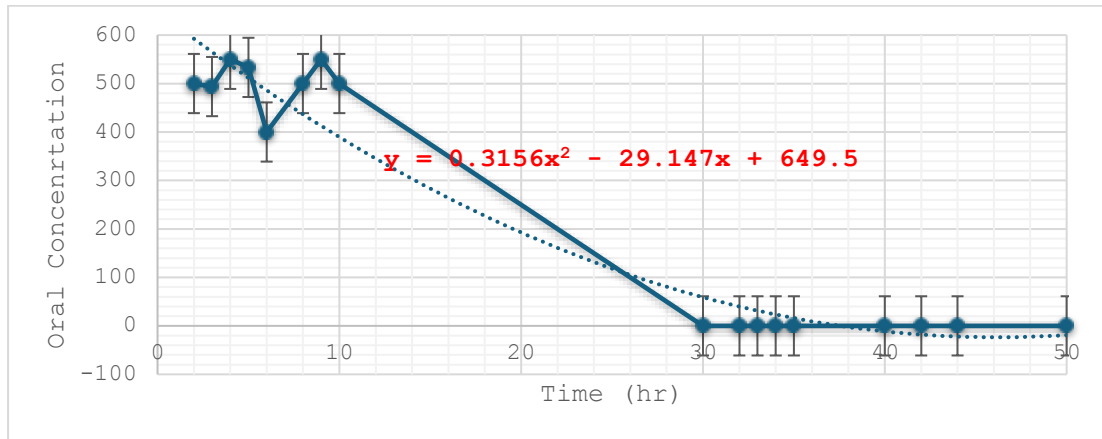


Fig. 7. Line Chart representing the average THC oral concentrations in different time intervals in the studied groups

Table 8 shows the cumulative AUC of each concentration across time intervals. AUC was measured using the linear-log trapezoidal rule. AUC (0-3h) of blood concentration was 163.69 (mcg/ml.hr), AUC (0-3h) of urine concentration was 135.77 (mcg/ml.hr), AUC (0-5h) of oral concentration was 2027.08 (mcg/ml.hr), AUC (0-9h) of oral concentration was 3977.08 (mcg/ml.hr).

Table 8. Area under the Curve (AUC) of THC concentrations in blood, urine, and saliva in different time intervals.

| Time | Blood concentration | | Urine Concentration | | Oral Concentration | |
|---------|---------------------|----------------------------|---------------------|----------------------------|--------------------|----------------------------|
| | AUC (mcg/ml.hr) | Cumulative AUC (mcg/ml.hr) | AUC (mcg/ml.hr) | Cumulative AUC (mcg/ml.hr) | AUC (mcg/ml.hr) | Cumulative AUC (mcg/ml.hr) |
| 2.00 h | 80.365 | 80.365 | 66.945 | 66.945 | 496.875 | 496.875 |
| 3.00 h | 83.32 | 163.685 | 68.82 | 135.765 | 521.875 | 1018.75 |
| 4.00 h | 83.625 | 247.31 | 68.125 | 203.89 | 541.665 | 1560.415 |
| 5.00 h | 74.335 | 321.645 | 63.085 | 266.975 | 466.665 | 2027.08 |
| 6.00 h | 155 | 476.645 | 136 | 402.975 | 900 | 2927.08 |
| 8.00 h | 87 | 563.645 | 72.5 | 475.475 | 525 | 3452.08 |
| 9.00 h | 82.5 | 646.145 | 67 | 542.475 | 525 | 3977.08 |
| 10.00 h | 1694 | 2340.145 | 1342 | 1884.475 | 5500 | 9477.08 |
| 32.00 h | 75.31 | 2415.455 | 57 | 1941.475 | 0 | 0 |
| 33.00 h | 77.81 | 2493.265 | 57.5 | 1998.975 | 0 | 0 |
| 34.00 h | 81 | 2574.265 | 61.5 | 2060.475 | 0 | 0 |
| 35.00 h | 388.325 | 2962.59 | 306.675 | 2367.15 | 0 | 0 |
| 40.00 h | 145 | 3107.59 | 119 | 2486.15 | 0 | 0 |
| 42.00 h | 151.67 | 3259.26 | 125.77 | 2611.92 | 0 | 0 |
| 44.00 h | 477 | 3736.26 | 355.32 | 2967.24 | 0 | 0 |
| 50.00 h | 320 | 4056.26 | 240 | 3207.24 | 0 | 0 |
| 54.00 h | 30731 | 34787.26 | 25674 | 28881.24 | 0 | 0 |

DISCUSSION

The current study aimed to determine the most accurate sample type for rapidly and precisely measuring cannabis levels. The results of the present study revealed that the majority of our patients (59.5%) were aged 19-59 years. Males were the most dominant sex category in the studied groups (71.4% in the case group). Almost half of the samples were married (47.6% in the case group). The most prevalent education category was illiterate (40.5% in the case group). There was a male predominance among patients, aligning with a result from a previous study by Onders *et al.*, (2016), who also reported that male children accounted for 50.7% of exposure to cannabis. The majority of the patients (88.3%) were from urban areas (El Masry and Tawfik, 2013). Regional patterns in Egypt, where cannabis usage is common among young males, are reflected in the male predominance (71.4%) and urban exposure (88.3%) (El Masry and Tawfik, 2013). Also, during the 17-month study period, a total of 127 adult exposures were recorded, comprising 102 in adults aged 19–59 and 25 in adults aged 60 years or older. The Majority of products were edibles and concentrates/oils, and most were ingested. A small percentage (11%) of cases were accidental exposures (Hendrickson *et al.*, 2020) . In this study, half of the case group had been exposed to cannabis by inhalation (52.4%), 35.7% by ingestion, and only 11.9% by an unknown route of exposure. Seventy cases (83.3%) were intentionally exposed to cannabis. Hospital admissions for inhaled cannabis exposure were more common than those for edibles, according to a retrospective observational study examining emergency visits related to cannabis exposure (Monte *et al.*, 2019). In this study, 47.5% of cases had tachycardia, while 52.4% had normal blood pressure in the case group. In the case group, more than half of the sample (64.3%) had normal oxygen saturation. The majority of older adults maintained a normal heart rate despite many having significant CNS toxicity. It is unclear why older adults may develop tachycardia less frequently. This might be due to

the physiologic effects of aging, medication effects from chronic antihypertensive or higher rates of edible use rather than smoked botanical material (Hendrickson *et al.*, 2020 & Richards *et al.*, 2020).

According to previous reports, sinus tachycardia is among the most common arrhythmia types in acute cannabis toxicity, which is due to the cannabis anti-cholinergic activities (Franz and Frishman 2016 & Paulraj *et al.*, 2025).

The stimulation of CB1 receptors by cannabis in the heart is responsible for its cardiovascular effects (Puhl, 2020 & Richards, 2020). Their stimulation can activate the sympathetic nervous system and block the parasympathetic nervous system (Cunha *et al.*, 2011 & Chinello *et al.*, 2017). Acute cannabis poisonings in the adolescent population manifested as various symptoms, including raised appetite, conjunctival injection, slurred speech, nystagmus, dry mouth, and ataxia. Vital instabilities following cannabis acute exposure include hypertension, tachycardia, and tachypnea. Also, highly potent cannabinoid products may cause hallucinations, anxiety, or dysphoria (Chen and Klig, 2019).

In the present study, 40.8% of the case group had CNS excitation, 23.8% had paranoia, 17.9% had hallucination, 23.8% had visual disturbances, 11.9% had panic attack, tremors, and headache, 5.95% had myoclonus, and 7.1% had numbness, tingling, while 40.8% suffered from anxiety. The fast absorption of THC, the primary psychoactive ingredient in cannabis, may account for the predominance of CNS excitement following inhalation (Felder and Glass, 1998). Monte *et al.* (2019) reported a predominance of neurological manifestations after synthetic cannabis exposure, including agitation, delirium, seizures and toxic psychosis. Regarding CNS depression, 23.8% had speech abnormalities, 35.7% had impaired coordination, 23.8% had visual disturbances, 11.9% had weakness, 5.95% had syncope, 4.8% had comatose, and 59.5% suffered from reduced consciousness. Following cannabis exposure, younger persons usually have CNS excitations, while older adults experienced sedation (Noble and Kusin, 2017 & Noble *et al.*, 2019). Regarding gastrointestinal symptoms and side effects, 11.9% had nausea, 23.8% had vomiting, 3.6% had abdominal pain, and 4.8% had diarrhea.

Fifty cases (59.5%) suffered from reduced consciousness. Patients with gastrointestinal symptoms are likely to receive antiemetics and anti-nausea medications, which usually control their symptoms (Shelton *et al.*, 2020). According to Noble and Kusin (2017), 11.9% of the patients in their study in the United States experienced vomiting.

Regarding respiratory symptoms, 2.4% had respiratory depression, and 1.2% had dyspnea. Another study reported respiratory failure in 1 patient (1.5%). In our study, considering management, almost half of the cases (48.8%) had symptom-specific treatments, 47.6% had observation and supportive care, and only 3.6% had mechanical ventilation. Considering outcomes, the majority of cases (71.4%) were discharged from the hospital, 23.8% were discharged against medical advice, 3.6% were admitted to the ICU, and 1.2% expired.

Cannabis toxicity symptoms, including neurobehavioral changes, panic attacks, cardiovascular stimulations, anxiety, depression, nausea, and vomiting, leading to severe complications such as coma and psychiatric disorders (Schmid *et al.*, 2020). In our study, THC concentrations (ng/mL) in blood, urine, and oral fluid ranged from 66 to 90, 59 to 77, and 400 to 700, respectively, within the first 30 hours. The C_{max} of blood and urine concentrations was observed 3 hours after exposure, whereas the C_{max} of oral concentration was observed at 5 and 9 hours.

Blood is the only biological sample, aside from cerebrospinal fluid, that reflects drug concentration in the brain. Urine is the most commonly used biological matrix for testing of abused substances (Tamama, 2020). It is easier to collect than blood, and easier to analyze. However, the urine sample will be positive for a drug for a significantly longer time than blood (Gjerde *et al.*, 2011). Oral fluid (mixed saliva) is a readily available medium that can be collected without intruding on privacy. Drug detection in oral fluid can reflect recent use and is thus a better option than urine or other samples (Kapur and Aleksa, 2020). Also, it is hardly adulterated. The application of oral fluid for drug abuse testing has increased over the last few decades. Oral fluid samples are routinely used for workplace drug testing as well (Bosker and Huestis, 2009).

The half-life of THC in the plasma following smoking is around 1.6 hours. However, it is usually extended to 27 hours in chronic abusers. After consuming cannabis products, the 11-COOH-THC metabolite is expelled from the bloodstream but also divides into adipose tissue, where it may be stored. The metabolite will gradually leach from adipocyte tissue into the blood and be ultimately eliminated in the urine. 11-COOH-THC will be detectable in urine and will persist longer in regular drug users (urinary half-life 10–19 days) than for occasional users (urinary half-life ~3 days (Hendrickson *et al.*, 2020) THC has a long terminal half-life of approximately 20–30 h; therefore, it may be detected for several days after the last administration of the drug. Oral fluid THC is a good indicator of very recent cannabis use. Oral fluid cannabis concentrations peaked at 10 minutes, the time point closest to vaporization, and then quickly decreased (Himes *et al.*, 2013). Urine analysis is now a low-cost method for determining past cannabis usage; it focuses mainly on THC metabolites, including the major metabolite THCCOOH. THCCOOH is not very indicative of recent consumption because it can remain in urine for up to 95 days (Kintz, 2020).

Toennes *et al.* (2008) reported that THC concentrations in the oral fluid peaked at 387 to 71 ng/mL, and in cannabis users reached 147 ng/mL after smoking 500 µg/kg of THC. On the other hand, Swortwood *et al.* (2017) observed that the peak of THC concentrations ranged from 68.6 to 7373 ng/mL at 0.17 hours following cannabis inhalation exposure with the products containing ~50.6 mg THC.

The accuracy of oral fluid (saliva) in assessing recent consumption is supported by its high AUC and correlation (Niedbala *et al.*, 2001), whereas blood correlates with impairment (Gjerde *et al.*, 2011). Dual peaks were explained by the faster C_{max} (3–5 hours) for inhalation (52.4%) compared to ingestion (9 hours). This shows the oral fluid superiority over urine, aligning with a previous study by Niedbala *et al.* (2001). This accuracy is essential, especially in light of the recent introduction of edible cannabis products (Spinle *et al.*, 2019 Matheson and le Foll, 2020). Nonetheless, our study had the following limitations. The generalizability of our research is hindered by the single-center design, small sample size (n=168), and potential immunoassay cross-reactivity.

Conclusion

Oral fluid is the best option for quickly and non-invasively detecting recent cannabis use, especially in emergencies, but blood is the ideal method for evaluating intoxication. These findings support the use of customized clinical and forensic procedures.

Recommendation

Future research should confirm these findings in a larger, multi-center population using Liquid Chromatography-Tandem Mass Spectrometry (LC-MS).

Declarations:

Ethical Approval: This study was conducted in accordance with the Helsinki Declaration. It was approved by the Medical Research Ethics Committee of Benha University under the ethical code of RC-18-12-2023.

Competing interests: The authors declare that there are no conflicts of /or competing interests.

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ARABIC SUMMARY

نمط السمية وأخذ العينات للكشف عن حالات التسمم الحاد بالقنب التي تم إدخالها إلى وحدة مكافحة التسمم بينها

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رباعي هيدروكانابينول (Δ^9 -THC) هو مادة ذات تأثير نفسي توجد في القنب الهندي، والتي تم ربطها عالميًا بحالات التسمم الحاد. يعد العثور على أفضل عينة بيولوجية للكشف السريع والدقيق عن رباعي هيدروكانابينول (THC) أمرًا ضروريًا للرقابة الطبية والطب الشرعي. تهدف هذه الدراسة إلى تقييم نوع العينة الأكثر دقة لتحديد مستويات القنب بسرعة ودقة. **طرق البحث:** أجرينا دراسة الحالات والشواهد في وحدة مكافحة التسمم بينها، مستشفى جامعة بنها، في الفترة من ١ ديسمبر ٢٠٢٣ إلى ٣٠ أبريل ٢٠٢٤. تم تجنيد مائة وثمانية وستين مشاركًا، من بينهم ٨٤ مصابًا بتسمم حاد بالقنب و ٨٤ ضابطًا متطابقين في العمر والجنس. تم تقييم المعلومات الاجتماعية والديموغرافية والعلامات الحيوية والأعراض السريرية (العصبية والجهاز الهضمي والجهاز التنفسي) ومستويات رباعي هيدروكانابينول (THC) في الدم والبول والسوائل القموية باستخدام المقاييس المناعية (القطع: ٥٠ نانوغرام/مل). **النتائج:** كانت غالبية الحالات من الذكور (٧١,٤%)، وتتراوح أعمارهم بين ١٩ و ٥٩ عامًا؛ ٥٢,٤% تم استنشاقهم، و ٨٣,٣% تعرضوا عمداً. وشملت الأعراض الشائعة عدم انتظام دقات القلب (٤٧,٥% بالمقارنة مع الضوابط)، والقلق (٤٠,٨%)، وانخفاض الوعي (٥٩,٥%)، والقيء (٢٣,٨%) والغثيان (١١,٩%). تراوحت مستويات رباعي هيدروكانابينول (نانوغرام/مل) بعد ٣٠ ساعة من التعرض من ٦٦ إلى ٩٠ (الدم)، ومن ٥٩ إلى ٧٧ (البول)، ومن ٤٠٠ إلى ٧٠٠ (سوائل الفم/اللعاب). ثلاث ساعات للدم والبول Cmax، وخمس إلى تسع ساعات للسوائل القموية. ولوحظ الحد الأقصى للمساحة تحت المنحنى (٠-٩ ساعات: ٣٩٧٧,٠٨ ميكروجرام/مل.ساعة) وارتباط إيجابي بالدم (ص = ٠,٧، ع > ٠,٠١) في السوائل القموية. تم إطلاق سراح غالبية المرضى (٧١,٤%) بعد العلاج الداعم. **الاستنتاج:** كانت العينة الأكثر دقة لتحديد استخدام القنب الحديث هي السائل القموي بسبب تركيزاته العالية ونافذة الكشف الممتدة، مما يجعله مثاليًا لحالات الطوارئ. لكن فحص الدم هو الطريقة المثلى لتقييم التسمم

