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Research Article

Toxicological Patterns of Psychoactive Substance Use as Predictors of Violent Behavioral Outcomes in Medico-Legal Cases: A Retrospective Cohort Study

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ABSTRACT

Background: Psychoactive substance use is frequently encountered in medico-legal practice and may influence aggression through effects on judgment, behavioral inhibition, arousal, and impulse control. However, substance-specific toxicological predictors of violent behavior remain insufficiently characterized in local forensic populations.

Objective: To determine toxicological patterns of psychoactive substance exposure and identify independent predictors of violent behavioral outcomes among medico-legal cases.

Methods: This retrospective cohort study included 120 adult medico-legal cases evaluated at the Department of Forensic Medicine, King Edward Medical University, and Lahore Medical and Dental College, Lahore, Pakistan, between January 2025 and February 2026. Demographic, clinical, behavioral, and toxicological data were extracted from institutional records. The primary outcome was documented interpersonal violent behavior associated with the index medico-legal event. Associations were evaluated using univariable and multivariable binary logistic regression.

Results: Overall, 67 cases (55.8%) had violent outcomes and 92 (76.7%) had at least one psychoactive substance detected. Alcohol was identified in 45 (37.5%), cannabis in 34 (28.3%), stimulants in 24 (20.0%), opioids in 22 (18.3%), and benzodiazepines in 16 (13.3%) cases; 35 (29.2%) demonstrated polysubstance exposure. Violence occurred in 80.0% of polysubstance-positive, 79.2% of stimulant-positive, and 75.6% of alcohol-positive cases. Independent predictors were previous violent behavior (aOR 4.31, 95% CI 1.68–11.05), stimulant positivity (aOR 3.71, 95% CI 1.26–10.93), polysubstance exposure (aOR 3.39, 95% CI 1.30–8.87), alcohol positivity (aOR 2.88, 95% CI 1.23–6.74), and male sex (aOR 2.41, 95% CI 1.02–5.71).

Conclusion: Violent medico-legal outcomes were independently associated with stimulant exposure, alcohol positivity, polysubstance use, and previous violence. Integrating toxicological findings with behavioral history may improve early forensic risk stratification.

Keywords: Forensic Toxicology, Psychoactive Substances, Violence, Alcohol, Stimulants, Polysubstance Use, Medico-Legal Cases.

INTRODUCTION

Psychoactive substance use represents an important intersection between public health, clinical medicine, and forensic practice because its consequences extend beyond intoxication and dependence to accidental injury, interpersonal conflict, criminal behavior, and violence. Alcohol and other psychoactive drugs can alter perception, judgment, impulse control, emotional regulation, and responses to environmental threats, potentially influencing behavior during intoxication or withdrawal[1]. However, the association between substance exposure and violence is not uniform across

drug classes and is strongly modified by individual susceptibility, psychiatric comorbidity, previous violence, socioeconomic conditions, and the circumstances in which substance use occurs[2]. A small body of systematic evidence suggests that drug-use disorders are linked to greater risk of violence, with the strength of association differing widely based on the drug type and the population investigated[3].

Alcohol is especially important in the context of violent and medico-legal presentations, as acute intoxication can impair executive functioning, decrease behavioral inhibition, impair interpretation of social cues, and contribute to the escalation of interpersonal conflicts. Despite this, alcohol-related harm continues to be significant globally: In 2019, it was estimated that alcohol consumption was responsible for around 2.6 million deaths globally, of whom around 700,000 died as a result of alcohol-related injury[4]. Alcohol-related harm is important because it encompasses both unintentional and intentional injuries, and alcohol exposure is a particularly salient issue in emergency departments and at medico-legal services where assault, road-related trauma, domestic violence and other presentations of injuries are routinely assessed. However, the exposure to alcohol alone does not imply causation because aggressive behavior usually results from intoxication coupled with individual factors, past behavior, and provocation[5].

Stimulants may exhibit a different behavioral profile and are of particular forensic concern as acute exposures can be associated with increased levels of arousal, irritability, impulsivity, suspiciousness, agitation, and/or psychotic symptoms. In this regard, methamphetamine has gained a lot of attention[6]. A prospective longitudinal study found a dose-response effect of violent behaviors during methamphetamine use, independent of the presence of psychotic symptoms[4]. Likewise, evidence from longitudinal population-based studies has shown that methamphetamine use is an independent risk factor for perpetrating and being a victim of violence[5]. The results indicate that violent behavior induced by stimulants might be a combination of direct psychopharmacological effects and indirect factors like prolonged wakefulness, social instability, previous criminality, and the high-risk environment[7].

Other psychoactive drugs have a more varied association with violent behaviour. It has been reported that cannabis use is linked to aggression or violence in specific groups of people, including those with psychosis-spectrum disorders, but there is no straightforward causal link in the evidences[8]. A systematic review identified some correlations between cannabis use and violent or aggressive behavior among psychiatric populations, but noted limitations due to confounds and variation between the studies[6]. The relationship between opioids and benzodiazepines and aggression may shift during acute intoxication, as the effects of opioids and benzodiazepines may be mainly sedative, but may be affected by withdrawal, co-ingestion, drug-seeking behavior, or psychiatric or behavioral factors. Therefore, the forensic relevance of a positive toxicological finding is not only related to the detection of a substance, but also to its pharmacological class, the time of exposure, its concentration, the use of other drugs and the clinical context[9].

Violence-risk assessment becomes more complicated when Polysubstance use is involved. People can use multiple drugs at once or in different orders, and the pharmaceutical interactions can create behavioral responses that are distinct from those of any of its individual components[10]. Polysubstance exposure can also be an indicator of substance-use severity, impulsivity, social instability, frequent intoxication, and exposure to high-risk environments. A systematic review on the link between drug-use disorders and violent outcomes showed that there were increased risks of violent outcomes across the drug categories and that drug-use patterns that involved multiple drugs were of particular interest[1]. Therefore, identification of single-substance versus polysubstance exposure could be more clinically and forensically relevant than simply labeling someone as being substance-positive or substance-negative[11].

Forensic toxicology offers an independent method to determine the presence of alcohol and/or prescribed drugs, illicit drugs, and other toxic substances in biological samples and can be used in addition to clinical and medico-legal documentation. Toxicological evidence is especially useful when the drug history provided by the subject is incomplete, unreliable, or unavailable[12,13]. But the presence of a substance in a person should not be assumed as evidence of intoxication and a specific act of violence. Detection windows vary widely among substances and biologic matrices, and some substances or metabolites may be detectable after the acute behavioral

effects have subsided. Toxicological data thus need to be considered in the context of the circumstances of the incident, clinical examination, behaviour, drug history, history of violence and other medico-legal data. The application of various drug classes is relevant in Pakistani forensic practice, as a wide range of drugs such as cannabinoids, opioids, benzodiazepines and amphetamine type drugs are evaluated within the framework of forensic toxicology services[5].

There is considerable literature on the association between substance use and aggression and violent end points in the international literature, but there is little work that has been conducted on objectively documented patterns of toxicology and its association with violent outcomes in the Pakistani medico-legal population[14]. Prior toxicological investigations have focused on patterns of detection, intoxication, or the analytical aspects of forensic toxicology, but few have attempted to combine different classes of drugs, polysubstance use, demographic factors, psychiatric factors, and prior violent behavior in a predictive model. The relevance of this is that if specific toxicological patterns persist in association with violence even when other well-known behavioral and clinical factors are excluded, then perhaps this would facilitate interpretation of medico-legal cases and offer a more evidence-based strategy for early risk stratification[15].

Thus, the present retrospective cohort study was conducted to describe the toxicological profile of psychoactive substance use and assess their correlation with violent behavioral outcomes in medico-legal cases at two tertiary-care centres of Lahore, Pakistan. Multivariable analysis was also used to determine independent toxicological, demographic, psychiatric, and behavioral risk factors for violence. Alcohol positivity, stimulant exposure, polysubstance use, and prior history of violent behavior were hypothesized to be associated with an increased likelihood of violent medico-legal outcomes. These findings could aid in understanding the relative contribution of patterns of psychoactive substance use to violence, and in more formal incorporation of toxicological findings into clinical-forensic evaluations[16,17].

MATERIALS AND METHODS

Study Design and Setting

This retrospective cohort study was conducted at the Department of Forensic Medicine, King Edward Medical University, Lahore, Pakistan, and Lahore University of Biological & Applied Sciences, a project of Lahore Medical and Dental College, Lahore, Pakistan. Medico-legal cases evaluated between January 2025 and February 2026 were reviewed. Both institutions provide forensic and medico-legal services for individuals presenting with alleged assault, suspected intoxication or poisoning, interpersonal violence, road-traffic incidents, behavioral disturbance, suspected drug exposure, and other circumstances requiring formal medico-legal assessment. Data were obtained from clinical records, medico-legal documentation, emergency department notes, toxicology reports, and relevant laboratory records generated during the index presentation.

Study Population

The study population comprised adult patients who underwent formal medico-legal examination at either participating institution during the study period. Patients were eligible when sufficient clinical, behavioral, and toxicological information was available to determine both psychoactive substance exposure and the nature of the medico-legal event. A total of 120 eligible cases were included in the final analysis. Each patient contributed only one index medico-legal episode to avoid duplication of observations.

Sampling Technique and Sample Size

A consecutive non-probability sampling technique was used. All eligible medico-legal cases encountered during the defined study period were screened sequentially, and records fulfilling the eligibility criteria were included until the final sample of 120 cases was obtained. The sample was considered adequate for exploratory comparison of toxicological exposure patterns between violent and non-violent medico-legal presentations and for multivariable analysis of the principal predictors of violent behavioral outcomes.

Eligibility Criteria

Patients aged 18 years or older who underwent medico-legal examination and had available blood and/or urine toxicological testing during the index episode were considered eligible. Inclusion further required sufficient documentation of the circumstances surrounding the event to permit classification as a violent or non-violent behavioral outcome. Records also required adequate demographic

and clinical information regarding age, sex, previous violent behavior, psychiatric history, and substance-related findings.
Patients younger than 18 years were excluded. Records were also excluded when toxicological findings were unavailable, the biological specimen was considered inadequate or uninterpretable, documentation of the index event was substantially incomplete, or the behavioral outcome could not be classified reliably. Postmortem cases without adequate antemortem behavioral information were excluded. Where duplicate documentation represented the same event, only the most complete index record was retained.

Data Sources and Data Collection
Data were gathered using a pre-designed data extraction form on a retrospective basis. Data were gathered from medico-legal registers, patient records, emergency department records, forensic examination records, laboratory records, toxicology and police or legal records in the institutional record. The variables that were extracted were: age, sex, date of presentation, circumstances of the medico-legal event, alleged mechanism of injury or behavioral disturbance, previous documented violent behavior, previous medico-legal encounters, known psychiatric illness, suspected substance use, clinical features suggestive of intoxication, type of biological specimen collected, individual psychoactive substances detected, number of substances detected, and whether the index presentation involved violent interpersonal behavior. For each case included, a study identification code was used. Certainly, these data were not included in the analytical data set, including names, national identification numbers, police case identifiers, addresses, etc.

Assessment of Psychoactive Substance Exposure
The key exposure variable was the presence and pattern of the psychoactive substances found at toxicological examination. The drugs were grouped into clinically and forensically relevant categories including alcohol, cannabinoids, amphetamine-type stimulants, opioids, benzodiazepines and other psychoactive drugs reported in the toxicological report. Those in which only one class of psychoactive substance was found were defined as single-substance exposures. Two or more classes of psychoactive substances identified from the same medicolegal episode were considered polysubstance exposure. A dichotomous variable was also constructed to reflect the presence/absence of any psychoactive substance. Substance categories were not mutually exclusive, as patients with polysubstance exposure were included in multiple drug-specific categories. This method allowed assessment of the toxicological agents, as well as the added behavioral risk that might result from the combination of several agents being present simultaneously.

Toxicological Examination
Toxicological assessment was carried out by means of a blood and/or urine specimen taken as part of a routine medico-legal evaluation. Samples were obtained as near to the presentation as it was feasible based on the standard operating procedures (SOP) of the participating forensic and clinical services. Routine qualitative or semi-quantitative analytical methods commonly used in each of the laboratories were used for toxicological screening for common psychoactive substances. If confirmatory laboratory tests were done as part of the usual work of a medico-legal laboratory, the chromatographic or mass-spectrometric results were accepted as final. Alcohol exposure was estimated from the institutional procedure used to detect ethanol in the biological specimen available, and the presence of cannabinoids, opioids, benzodiazepines, and amphetamine-type stimulants was based on the relevant toxicological reports.
If medication administration records were available, drug administration that occurred after arrival in hospital was analysed separately to minimise the risk of misclassifying drugs administered for therapy as pre-presentation exposures. The toxicological data were correlated with the clinical signs, sample types, sample collection times and medication history. The specific analytical equipment, detection limits and confirmatory analyses should be stated in the final submitted manuscript based on laboratory practices which have been verified at participating institutions.

Primary Outcome
The primary outcome was the occurrence of an index medicine-legal violent behavior. Violence was defined as documented intentional physical violence towards another person, attempted physical violence towards another person, weapon or attempted weapon use, injury to a person, or a credible threat of injury to a person

during the medico-legal event. It may have happened just before the hospital presentation, during the circumstances that brought the person to the hospital, or during the early assessment in the hospital when obviously associated with the index episode. Classification was made using the combination of medico-legal documentation, clinical records, emergency notes and legal/police information if available.

The cases of accidental intoxication, accidental poisoning, non-violent road traffic incidents, accidental injuries, isolated substance use without aggressive behaviour and self-directed behaviour without interpersonal violence were considered as non-violent outcomes. An attempt was made to prevent circular classification, as toxicological positivity was not used to determine the behavioural outcome.

Secondary Outcomes

Secondary study outcomes comprised the overall prevalence of psychoactive substance exposure, prevalence of individual drug classes, prevalence of single substance and polysubstance exposure, sex-specific toxicological patterns, and differences between violent and non-violent medico-legal cases. The percentages of patients with violent behavior in each of the major toxicological categories were also assessed.

Predictor Variables

The characteristics that could potentially predict violent behavioral outcomes were: age, sex, any history of violent behavior documented, psychiatric co-morbidity, alcohol positivity, cannabis positivity, stimulant positivity, opioid positivity, benzodiazepine positivity, any psychoactive substance positivity, and polysubstance positivity. A history of assaultive, aggressive, or violent behavior was recorded in clinical, medico-legal, and/or accompanying legal records, which was considered previous violent behavior. Psychiatric co-morbidity was defined as having a pre-recorded psychiatric diagnosis before or during the index encounter. Age was treated as a continuous variable, and was also divided into appropriate sub-groups for selected sub-group analyses, where clinically relevant.

Data Quality Assurance

To enhance consistency, a standardized data extraction format was implemented, and operational definitions were agreed upon at both study sites. After data entry, the data set was checked for possible double entries, impossible data, differences in coding, missing data, and inconsistencies between clinical and toxicological data. If an exposure or outcome was not clearly defined in the case, the classification was reviewed again in relation to the source record before the final coding. A sub-sample of records was rechecked against the original documentation to check for consistency of data extraction by another group of people. Disagreements were resolved by consensus using all available source information.

Control of Bias and Confounding

Several methodological steps were taken to minimize potential bias. To minimize the investigator-driven selection of cases, consecutive inclusion of eligible cases was used. To minimize the variability of classification, the same definitions for substance exposure and violent behavior were used throughout both institutions. The behavioral outcome was based on clinical and medico-legal documents, and toxicological positivity was not used as a criterion for behavioral outcome. This was done to minimize observer and incorporation bias. A multivariable regression method was used to control for potential confounding demographic, psychiatric, and previous behavioral characteristics. Toxicological investigations were conducted as part of routine medico-legal practice, and there was unavoidable variation in specimen collection, timing, and analytical testing; this was recognized as a limitation of the retrospective study design.

Statistical Analysis

Data were entered and analyzed using IBM SPSS Statistics version 27.0. The distribution of continuous variables was examined using graphical assessment and appropriate tests of normality. Normally distributed continuous variables were summarized as mean ± standard deviation, whereas skewed variables were reported as median with interquartile range. Categorical variables were presented as frequencies and percentages. Baseline demographic, clinical, behavioral, and toxicological characteristics were compared between patients with violent and non-violent outcomes. The independent-samples t-test was used for normally distributed continuous variables, while the Mann–Whitney U test was used when continuous data were not normally distributed. Associations between categorical variables were examined using the Pearson chi-

square test or Fisher's exact test when expected cell frequencies were small.

Univariable binary logistic regression was initially performed to assess the association of each demographic, clinical, and toxicological variable with violent behavioral outcomes. Crude odds ratios with 95% confidence intervals were calculated. Variables considered clinically important and those demonstrating an association at $p<0.10$ in the univariable analysis were considered for entry into the multivariable model. A multivariable binary logistic regression analysis was subsequently performed to identify independent predictors of violent behavior. The principal exposure variables of interest were alcohol positivity, stimulant positivity, and polysubstance exposure, with adjustment for age, sex, previous violent behavior, psychiatric comorbidity, and other toxicological variables considered relevant to the final model. Results were expressed as adjusted odds ratios with 95% confidence intervals.

Multicollinearity between predictor variables was assessed before final model construction using tolerance statistics and variance inflation factors. Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, while model discrimination was assessed using the area under the receiver operating characteristic curve. A two-sided p-value <0.05 was considered statistically significant throughout the analysis.

Management of Missing Data

Records lacking sufficient information to determine either the principal toxicological exposure or the primary violent behavioral outcome were excluded before construction of the final analytical cohort. For secondary variables with occasional missing observations, analyses were performed using available data. Because the proportion of missing secondary data was expected to be limited and the study was retrospective, statistical imputation was not planned. The effective number of observations was reported for individual analyses whenever it differed from the total sample of 120.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki and institutional requirements governing retrospective clinical and medico-legal research. Ethical approval was obtained from the relevant institutional review board (approval no. ERC/2024/143A). Because the study involved retrospective analysis of existing records without direct patient contact or alteration of clinical management, the requirement for individual informed consent was waived by the approving ethics committee. All study data were de-identified before analysis, accessed only by authorized investigators, and reported in aggregate form to preserve participant confidentiality.

Confidentiality and Data Protection

Confidentiality was maintained throughout data collection, analysis, and reporting. Personally identifiable information was not entered into the research database, and each participant was represented only by a coded study number. Electronic research data were restricted to authorized members of the research team, while findings were reported only in aggregate form to prevent identification of individual medico-legal cases.

RESULTS

Study Population and Baseline Characteristics

A total of 120 medico-legal cases fulfilled the eligibility criteria and were included in the final analysis. The mean age of the study population was 33.3 ± 10.0 years, and 97 participants (80.8%) were male, while 23 (19.2%) were female. Overall, 67 cases (55.8%) were classified as having a violent behavioral outcome associated with the index medico-legal event, whereas 53 (44.2%) were categorized as non-violent.

Patients with violent behavioral outcomes were significantly younger than those with non-violent outcomes (31.4 ± 9.2 vs. 35.8 ± 10.6 years; p=0.019). Male participants constituted a greater proportion of the violent group compared with the non-violent group (88.1% vs. 71.7%; p=0.024). A previous history of violent behavior was also considerably more frequent among patients with a violent index event (41.8% vs. 15.1%; p=0.002). Although documented psychiatric comorbidity was more common among violent cases, the difference did not reach statistical significance (26.9% vs. 17.0%; p=0.198). The demographic, behavioral, and principal toxicological characteristics of the cohort are summarized in Table 1.

Table 1. Demographic, Clinical, and Toxicological Characteristics According To Violent Behavioral Outcome

Variable	Total (n=120)	Violent outcome (n=67)	Non-violent outcome (n=53)	p-value
Age, years, mean ± SD	33.3 ± 10.0	31.4 ± 9.2	35.8 ± 10.6	0.019
Male sex	97 (80.8)	59 (88.1)	38 (71.7)	0.024
Female sex	23 (19.2)	8 (11.9)	15 (28.3)	0.024
Previous violent behavior	36 (30.0)	28 (41.8)	8 (15.1)	0.002
Psychiatric comorbidity	27 (22.5)	18 (26.9)	9 (17.0)	0.198
Any psychoactive substance detected	92 (76.7)	58 (86.6)	34 (64.2)	0.004
Alcohol positive	45 (37.5)	34 (50.7)	11 (20.8)	<0.001
Cannabis positive	34 (28.3)	23 (34.3)	11 (20.8)	0.101
Stimulant positive	24 (20.0)	19 (28.4)	5 (9.4)	0.010
Opioid positive	22 (18.3)	9 (13.4)	13 (24.5)	0.119
Benzodiazepine positive	16 (13.3)	10 (14.9)	6 (11.3)	0.564
Polysubstance exposure	35 (29.2)	28 (41.8)	7 (13.2)	<0.001

Data are presented as n (%) unless otherwise indicated. SD, standard deviation. Continuous variables were compared using the independent-samples t-test, while categorical variables were compared using the Pearson chi-square test or Fisher's exact test where appropriate. A two-sided p-value <0.05 was considered statistically significant.

Overall Toxicological Profile

At least one psychoactive substance was detected in 92 of 120 cases (76.7%), while 28 cases (23.3%) had no investigated psychoactive substance detected. Among the total cohort, 57 patients (47.5%) demonstrated single-substance exposure, and 35 (29.2%) demonstrated polysubstance exposure involving two or more psychoactive substance classes.

Alcohol was the most frequently identified substance, occurring in 45 cases (37.5%), followed by cannabis in 34 (28.3%), stimulants in 24 (20.0%), opioids in 22 (18.3%), and benzodiazepines in 16 (13.3%). Because individual substances could coexist in polysubstance-positive cases, the percentages of specific drug classes were not mutually exclusive.

The presence of any psychoactive substance was significantly more frequent among violent than non-violent cases (86.6% vs. 64.2%; p=0.004). Alcohol positivity was identified in 50.7% of violent cases compared with only 20.8% of non-violent cases (p<0.001). Similarly, stimulant exposure occurred in 28.4% of violent cases compared with 9.4% of non-violent cases (p=0.010). Polysubstance exposure showed one of the largest between-group differences, occurring in 41.8% of violent cases compared with 13.2% of non-violent presentations (p<0.001), as shown in Table 1.

Substance Burden and Violent Behavioral Outcomes

A clear increase in the proportion of violent behavioral outcomes was observed with increasing toxicological complexity. Among patients with no detected psychoactive substance, 9 of 28 (32.1%) demonstrated violence. The corresponding proportion increased to 30 of 57 (52.6%) among patients with a single-substance exposure and to 28 of 35 (80.0%) among patients with polysubstance exposure. The overall difference across the three exposure categories was statistically significant (p<0.001).

When individual psychoactive substance classes were considered, stimulant-positive patients demonstrated the highest proportion of violent behavior at 79.2%, followed by alcohol-positive patients at 75.6% and cannabis-positive patients at 67.6%. In contrast, violence was recorded in 40.9% of opioid-positive cases. The relationship between toxicological exposure patterns and violent outcomes is presented in Table 2.

Table 2. Distribution of Violent Outcomes According To Toxicological Exposure Pattern

Toxicological exposure	Total cases, n	Violent cases, n	Non-violent cases, n	Violent outcome, %
No psychoactive substance detected	28	9	19	32.1
Single-substance exposure	57	30	27	52.6

Polysubstance exposure	35	28	7	80.0
Alcohol positive*	45	34	11	75.6
Cannabis positive*	34	23	11	67.6
Stimulant positive*	24	19	5	79.2
Opioid positive*	22	9	13	40.9
Benzodiazepine positive*	16	10	6	62.5

Individual drug categories were not mutually exclusive because patients with polysubstance exposure could be represented in more than one substance-specific category. The difference in violent outcomes across no exposure, single-substance exposure, and polysubstance exposure was significant ($p<0.001$).

Distribution of Specific Psychoactive Substances

Alcohol positivity was strongly associated with violent presentation on unadjusted analysis. Of the 45 alcohol-positive cases, 34 (75.6%) were associated with a violent outcome. In contrast, violence was documented in 33 of 75 alcohol-negative patients (44.0%). Alcohol positivity was therefore associated with approximately fourfold greater unadjusted odds of violence (crude odds ratio [OR] 3.93, 95% confidence interval [CI] 1.74–8.92). Stimulant exposure demonstrated a similarly strong relationship. Nineteen of the 24 stimulant-positive cases (79.2%) had violent outcomes compared with 48 of 96 stimulant-negative cases (50.0%), corresponding to a crude OR of 3.80 (95% CI 1.31–11.00). Polysubstance exposure demonstrated the largest toxicological crude effect estimate, with an OR of 4.72 (95% CI 1.86–11.98). Cannabis positivity was associated with a higher proportion of violence in descriptive analysis (67.6% vs. 51.2%), but the association did not achieve conventional statistical significance (OR 2.00, 95% CI 0.87–4.59; p=0.101). Opioid positivity showed no evidence of increased violence and was numerically more frequent among non-violent presentations. Benzodiazepine positivity was also not significantly associated with the primary outcome.

Behavioral Characteristics of Violent Cases

Among the 67 cases classified as violent, interpersonal physical assault represented the predominant behavioral manifestation. Weapon-associated aggression, severe threatening or assaultive agitation, and violence arising within domestic or interpersonal disputes were also documented. More than one behavioral characteristic could occur during the same medico-legal episode. Stimulant-positive violent cases showed a comparatively greater frequency of marked agitation, impulsive aggression, and threatening behavior, whereas alcohol-positive episodes more frequently occurred in the context of interpersonal disputes and physical assault. These behavioral patterns were treated as descriptive findings because the retrospective records did not provide sufficiently uniform quantitative information regarding severity of intoxication or temporal drug concentrations to support more detailed causal analyses.

Univariable Predictors of Violent Behavior

On univariable analysis, several demographic, behavioral, and toxicological characteristics were associated with the primary outcome. Previous violent behavior was associated with approximately fourfold greater odds of violence (OR 4.04, 95% CI 1.65–9.88). Male sex was associated with increased odds of a violent presentation (OR 2.91, 95% CI 1.13–7.53). Among toxicological factors, polysubstance exposure demonstrated the largest crude association (OR 4.72, 95% CI 1.86–11.98), followed by alcohol positivity (OR 3.93, 95% CI 1.74–8.92) and stimulant positivity (OR 3.80, 95% CI 1.31–11.00). Detection of any psychoactive substance was also associated with increased odds of violence (OR 3.60, 95% CI 1.47–8.85). Cannabis, opioids, benzodiazepines, and psychiatric comorbidity did not demonstrate statistically significant univariable associations.

Multivariable Predictors of Violent Behavioral Outcomes

Variables considered clinically relevant or demonstrating an association with violence in univariable analysis were evaluated in the multivariable binary logistic regression model. After adjustment for demographic, behavioral, psychiatric, and toxicological variables, previous violent behavior remained the strongest independent predictor, with an adjusted odds ratio (aOR) of 4.31 (95% CI 1.68–11.05; p=0.002). Among toxicological variables, stimulant positivity remained independently associated with violent behavior (aOR 3.71, 95% CI 1.26–10.93; p=0.017). Polysubstance

exposure was similarly an independent predictor (aOR 3.39, 95% CI 1.30–8.87; p=0.013), while alcohol positivity was associated with approximately threefold higher adjusted odds of violence (aOR 2.88, 95% CI 1.23–6.74; p=0.015). Male sex remained independently associated with violent outcomes (aOR 2.41, 95% CI 1.02–5.71; p=0.045). In contrast, younger age, psychiatric comorbidity, cannabis positivity, and opioid positivity did not independently predict violence after adjustment. Complete univariable and multivariable effect estimates are presented in Table 3.

Table 3. Univariable and Multivariable Logistic Regression Analysis of Predictors of Violent Behavioral Outcomes

Predictor	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Previous violent behavior	4.04 (1.65–9.88)	0.002	4.31 (1.68–11.05)	0.002
Stimulant positivity	3.80 (1.31–11.00)	0.010	3.71 (1.26–10.93)	0.017
Polysubstance exposure	4.72 (1.86–11.98)	<0.001	3.39 (1.30–8.87)	0.013
Alcohol positivity	3.93 (1.74–8.92)	<0.001	2.88 (1.23–6.74)	0.015
Male sex	2.91 (1.13–7.53)	0.024	2.41 (1.02–5.71)	0.045
Age ≤30 years	1.86 (0.88–3.93)	0.103	1.79 (0.80–4.01)	0.156
Psychiatric comorbidity	1.80 (0.73–4.41)	0.198	1.52 (0.59–3.94)	0.389
Cannabis positivity	2.00 (0.87–4.59)	0.101	1.46 (0.59–3.63)	0.412
Opioid positivity	0.48 (0.19–1.22)	0.119	0.72 (0.26–1.99)	0.528
Benzodiazepine positivity	1.37 (0.47–4.06)	0.564	—	—

OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval. Variables selected on clinical relevance and/or univariable p<0.10 were considered for multivariable modelling. A two-sided p-value <0.05 was considered statistically significant. Dashes indicate variables not retained in the final multivariable model.

Model Performance

The final multivariable logistic regression model showed good discriminatory ability, with an area under the receiver operating characteristic curve of 0.82 (95% CI 0.74–0.89). The Hosmer–Lemeshow goodness-of-fit test was non-significant (p=0.61), indicating no evidence of poor model calibration. Assessment of variance inflation factors did not identify problematic multicollinearity among the predictors retained in the final model.

Overall, the multivariable findings demonstrated that the probability of a violent medico-legal outcome was determined by a combination of previous behavioral history and acute toxicological pattern, rather than psychoactive substance positivity alone. Previous violence, stimulant exposure, polysubstance use, alcohol positivity, and male sex remained independently associated with violent outcomes, whereas cannabis, opioid exposure, and documented psychiatric comorbidity did not retain independent associations after adjustment.

DISCUSSION

The present study explored the association between psychoactive substance exposure and violent behavioural outcomes in medico-legal cases with toxicological evidence of substance exposure[1]. The overarching conclusion was that violent presentations did not occur evenly across various patterns of drug exposure. For violent cases, alcohol positivity, stimulant exposure and polysubstance use were significantly increased, and each was independently associated with violence, adjusting for demographic, psychiatric and prior behavioral factors. Toxicological results were most helpful when considered in the context of the individual's previous history of violence, which proved to be the strongest overall predictor[2].

A large proportion of the subjects were exposed to psychoactive substances, which emphasizes the role of toxicology in medico-legal practice. Over 75% of the study population were found to be multiexposed and nearly one-third were polysubstance exposed[3]. This shows that drug-related presentations are a significant part of the work of the medico-legal, and that a single drug suspected may underestimate the intoxication pattern. Finally, the increased prevalence of psychoactive substance positivity in violent cases also suggests a systematic toxicological evaluation in patients with assaultive behavior, altered mental status,

unexplained agitation, or circumstances consistent with intoxication[4].

Alcohol was the most common drug found, and also served as an independent predictor of violent behavior. This is in line with previous studies showing a high correlation between alcohol use, aggression, and violent injury[1,3]. Alcohol lowers behavioral inhibitions, can affect executive control, can affect how social signals are interpreted, and can enhance emotional reactivity. All these effects can contribute to the escalation of interpersonal conflicts, especially in people who are prone to impulsive or aggressive behavior. However, alcohol should not be viewed as a stand-alone causal factor. The causes of violence typically involve a mix of pharmacological, personality, past violence, provocation, and environmental factors[5].

One of the most toxicological associations with violent outcomes was stimulant exposure. Comparable to previous studies that have shown that stimulant-positive cases are at a significantly increased risk for violence, the adjusted odds of violence were considerably elevated in the stimulant-positive cases[6]. Acute stimulant intoxication can result in psychomotor activation, irritability, hypervigilance, diminished impulse control, persecutory thinking and, in some instances, stimulant-induced psychotic symptoms. Such effects can make the risk of aggression greater in times of perceived interpersonal threat or conflict. The diagnosis of stimulant exposure should therefore be a warning to consider agitation, psychosis, behavioural control and immediate risk to patients, staff and others in a forensic context [7,8].

Another significant independent predictor was polysubstance use. The percentage of violent outcomes was much higher for patients who had one substance detected than for those who had no substance detected, and highest for those who had more than one substance detected[9]. This pattern implies that the behavioural significance of cumulative toxicological complexity can be more important than the presence of one psychoactive agent. Polysubstance use might have additive or synergistic effects on cognition, inhibition, arousal and emotional regulation; it is also a marker of more severe substance use and more exposure to high-risk social environments. Previous systematic evidence has also shown that people with multiple drug-use disorders are at higher risk of violence[2].

The link between cannabis exposure and violence was less strong. In descriptive comparisons, cannabis positivity was more prevalent in the violent cases; however, this association was not observed following multivariable adjustment[10]. This is significant because cannabis is often found in toxicological screening, but may not reflect clinical intoxication at the time of an incident. Metabolites of Cannabinoids can be detectable for a long time, particularly in frequent users, which makes temporal interpretations difficult. Past studies have found a relationship between marijuana use and aggression in certain psychiatric groups, although it is unknown if marijuana use causes aggression or aggression causes marijuana use [6]. Consequently, caution should be exercised in interpreting cannabis positivity in medicolegal situations, and attention to co-ingestants, psychiatric signs, and behavioral history is highlighted[1].

In the adjusted model, there was no association between opioid positivity and increased violent behaviors. This is a pharmacologically plausible observation, as opioid intoxication is classically associated with sedation, decreased levels of consciousness, and psychomotor slowing, but not increased aggression [11]. But there can also be indirect medico-legal risk because of opioid dependence through withdrawal, drug-seeking behavior, economic stress, criminal behavior, or because of the concurrent use of stimulants and alcohol. The lack of an independent association in the current study should thus not be taken to mean that the use of opioids has no forensic value [12].

One significant finding was that there was a strong relationship between past violence and violence on the night of the index medico-legal event [13]. This was the strongest independent predictor even after controlling for toxicological exposure. Past violence is an important factor in violence risk assessment, as it may indicate ongoing patterns of behavior, environmental risk factors, impulsivity, antisocial traits, or recurrent substance-related aggression. The current results indicate that toxicology should not be used as a substitute for traditional behavioral evaluation, but rather should be used in conjunction with history of violence, psychiatric history, and the context of the violent event [14].

The other independent variable associated with violent outcomes was male sex. The violent group had more males, which is typical of many forensic groups. Sex alone, however, is not a very useful individual predictor and is not deterministically interpreted. This cohort also has a relatively small number of female cases,

and hence the strength of sex-specific conclusions is limited[15].

Interestingly, psychiatric conditions were not independent predictors of violence after adjustment. This finding confirms the difference between psychiatric diagnosis and true behavioral risk. Mental illness is not monolithic, and the majority of people with mental illness do not commit violence. Active symptoms, substance use, treatment attendance, prior history of aggression, personality characteristics, and context are more important influences on risk. Previous violence and toxicological exposure yielded more predictive information than simply the presence of a recorded psychiatric diagnosis in the present cohort[16].

The multivariable model showed good discrimination, indicating there might be practical utility in medico-legal risk stratifications by combining behavioral history with judiciously selected toxicological variables. Specifically, a profile of prior violent offenders, stimulant exposure, alcohol positivity, or polysubstance use may identify individuals who may benefit from more rigorous behavioral observations or more thorough psychiatric or addiction-related evaluations. This information can also be used to direct emergency and forensic staff in predicting agitation, enhancing staff safety, and focusing on early intervention [1,9].

Forensically, however, toxicological results need to be carefully examined. A positive test for a psychoactive drug proves only exposure and not impairment, culpability, or intent. The link between what is found and what actually happened in terms of a violent act will vary according to the type of specimen, concentration, pharmacokinetics, time of exposure, tolerance, co-ingested substances, and the behavioral context. Thus, toxicology should be regarded as one of a spectrum of techniques utilized during a multi-disciplinary medico-legal assessment and not as an autonomous factor for determining culpability or dangerousness[17,18].

The study has several merits. Objective toxicological results as opposed to self-reported substance use, which may be unreliable, especially in medico-legal situations. Each class of psychoactive substance was analyzed separately, and results for "single" and "polysubstance" exposure were differentiated. Additionally, all of the above-mentioned variables, such as previous violence, psychiatric comorbidities, demographic variables, and individual toxicological findings, were included in the same regression model, which allowed more clinically meaningful assessment of independent predictors[11,19].

However, there are a number of drawbacks that should be noted. The retrospective design relied on the completeness and accuracy of the previously recorded medico-legal and clinical information. Exposure time and dose were not consistently determined, and toxicological levels were not always available. In addition, urine positives could be a result of past exposure and not intoxication at the time of the violent event. Some residual confounding from socioeconomic status, personality characteristics, withdrawal states, severity of psychiatric symptoms, and environmental provocation could not be completely ruled out. The sample size was also relatively small, leading to larger confidence intervals for some estimates and a lack of detail with regard to some combinations of substances. Lastly, the study was carried out in two institutions in Lahore and may not be generalizable to other community or forensic populations [17-20].

Standardized behavioral assessment, quantitative toxicology, well-documented time from exposure to event, psychiatric symptom severity, and detailed polysubstance profile should be included in future prospective multicenter studies. These studies may help to elucidate whether substance-specific toxicological markers are useful in enhancing existing violence-risk prediction models and which combinations of behavioral and toxicological variables are most predictive [3].

CONCLUSION

Psychoactive substance exposure was common among the medico-legal cases examined, and distinct toxicological patterns were associated with violent behavioral outcomes. The toxicological predictors of violence were also independent variables: Alcohol positivity, stimulant exposure, and polysubstance use. However, neither cannabis use, opioid exposure, nor psychiatric comorbidities alone remained significant predictors of violence when adjusted for other factors. This information can be used to incorporate toxicological assessment into the medico-legal practice alongside behavioral history and clinical evaluation. Other areas where toxicology might enhance the early detection of persons at risk of aggression are the detection of stimulants, exposure to alcohol, or multiple substances. However, a positive toxicological

report does not necessarily mean that the substance caused or that it is dangerous to the individual. These associations warrant validation by larger, prospective multicenter studies for the purpose of improving substance-specific violence-risk assessment.

Author Contributions:

FT and QAK conceived and designed the study. AA and NN contributed to data collection and medico-legal assessment. AW and MT contributed to psychiatric evaluation and data interpretation. RB assisted with data collection and manuscript preparation. FT drafted the manuscript. All authors reviewed and approved the final version.

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Conflict of Interest

The authors declare no conflicts of interest.

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REFERENCES

1. Zhong S, Yu R, Fazel S: Drug use disorders and violence: associations with individual drug categories. Epidemiol Rev. 2020, 42:103-116. 10.1093/epirev/mxaa006.
2. Whiting D, Lichtenstein P, Fazel S: Violence and mental disorders: a structured review of associations by individual diagnoses, risk factors, and risk assessment. Lancet Psychiatry. 2021, 8:150-161. 10.1016/S2215-0366(20)30262-5.
3. Elbogen EB, Johnson SC: The intricate link between violence and mental disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2009, 66:152-161. 10.1001/archgenpsychiatry.2008.537.
4. Fazel S, Gulati G, Linsell L, Geddes JR, Grann M: Schizophrenia and violence: systematic review and meta-analysis. PLoS Med. 2009, 6:e1000120. 10.1371/journal.pmed.1000120.
5. Fazel S, Långström N, Hjern A, Grann M, Lichtenstein P: Schizophrenia, substance abuse, and violent crime. JAMA. 2009, 301:2016-2023. 10.1001/jama.2009.675.
6. Witt K, van Dorn R, Fazel S: Risk factors for violence in psychosis: systematic review and meta-regression analysis of 110 studies. PLoS One. 2013, 8:e55942. 10.1371/journal.pone.0055942.
7. McKetin R, Lubman DI, Najman JM, Dawe S, Butterworth P, Baker AL: Does methamphetamine use increase violent behaviour? Evidence from a prospective longitudinal study. Addiction. 2014, 109:798-806. 10.1111/add.12474.
8. Foulds JA, Boden JM, McKetin R, Newton-Howes G: Methamphetamine use and violence: findings from a longitudinal birth cohort. Drug Alcohol Depend. 2020, 207:107826. 10.1016/j.drugalcdep.2019.107826.
9. McKetin R, Boden JM, Foulds JA, Najman JM, Ali R, Degenhardt L, et al.: The contribution of methamphetamine use to crime: evidence from Australian longitudinal data. Drug Alcohol Depend. 2020, 216:108262. 10.1016/j.drugalcdep.2020.108262.
10. Sorkhou M, Johnstone S, Kivlichan AE, Castle DJ, George TP: Does cannabis use predict aggressive or violent behavior in psychiatric populations? A systematic review. Am J Drug Alcohol Abuse. 2022, 48:631-643. 10.1080/00952990.2022.2118060.
11. Håkansson A, Jesionowska V: Associations between substance use and type of crime in prisoners with substance use problems—a focus on violence and fatal violence. Subst Abuse Rehabil. 2018, 9:1-9. 10.2147/SAR.S143251.
12. Moore TM, Stuart GL, Meehan JC, Rhatigan DL, Hellmuth JC, Keen SM: Drug abuse and aggression between intimate partners: a meta-analytic review. Clin Psychol Rev. 2008, 28:247-274. 10.1016/j.cpr.2007.05.003.
13. Foran HM, O'Leary KD: Alcohol and intimate partner violence: a meta-analytic review. Clin Psychol Rev. 2008, 28:1222-1234. 10.1016/j.cpr.2008.05.001.
14. Borges G, Orozco R, Cremonte M, Buzi-Figlie N, Cherpitel CJ, Poznyak V: Alcohol and violence in the emergency department: a regional report from the WHO collaborative study on alcohol and injuries. Salud Pública Mex. 2008, 50 Suppl 1:S6-S11. 10.1590/S0036-36342008000700003.
15. Duke AA, Giancola PR, Morris DH, Holt JCD, Gunn RL: Alcohol dose and aggression: another reason why drinking more is a bad idea. J Stud Alcohol Drugs.

2011, 72:34-43. 10.15288/jsad.2011.72.34.

16. Huestis MA, Brandt SD, Rana S, Auwärter V, Baumann MH: Impact of novel psychoactive substances on clinical and forensic toxicology and global public health. Clin Chem. 2017, 63:1564-1569. 10.1373/clinchem.2017.274662.
17. Dinis-Oliveira RJ, Magalhães T: Abuse of licit and illicit psychoactive substances in the workplace: medical, toxicological, and forensic aspects. J Clin Med. 2020, 9:770. 10.3390/jcm9030770.
18. Boscolo-Berto R: Challenges and future trends of forensic toxicology to keep a cut above the rest. Adv Clin Exp Med. 2024, 33:423-425. 10.17219/acem/185730.
19. Nikathil S, Olaussen A, Gocentas RA, Symons E, Mitra B: Review article: workplace violence in the emergency department: a systematic review and meta-analysis. Emerg Med Australas. 2017, 29:265-275. 10.1111/1742-6723.12761.
20. Nikathil S, Olaussen A, Symons E, Gocentas R, O'Reilly G, Mitra B: Increasing workplace violence in an Australian adult emergency department. Emerg Med Australas. 2018, 30:181-186. 10.1111/1742-6723.12872.