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Research Article

Clinicopathological and Toxicological Evaluation of Drug-Induced Liver Injury in Medico-Legal Autopsy Cases

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ABSTRACT

Background: Drug-induced liver injury is a difficult diagnosis in medico-legal autopsy practice because exposure history, premortem biochemical data, histology, and toxicological findings may be incomplete or non-specific.

Objective: To evaluate the clinicopathological and toxicological features of drug-induced liver injury in medico-legal autopsy cases and determine its contribution to death.

Methods: This multicentre retrospective analytical study included 200 medico-legal autopsy cases examined at the Department of Forensic Medicine, King Edward Medical University, Lahore, and the Department of Forensic Medicine and Toxicology, Dera Ghazi Khan Medical College, from January 2024 to October 2025. Demographic data, exposure history, autopsy findings, liver histopathology, and multi-matrix toxicological results were reviewed. Cases were classified as probable, possible, or unlikely drug-induced liver injury through multidisciplinary assessment.

Results: The mean age was 41.8 ± 15.2 years, and 118 cases (59.0%) were male. Paracetamol was the most frequently implicated agent, followed by antituberculous drugs, multidrug exposure, antiepileptics, antibiotics, and herbal preparations. Toxicological analysis was positive in at least one specimen in 166 cases (83.0%), with liver tissue showing the highest detection rate. Centrilobular or confluent necrosis was the predominant histopathological pattern. Overall, 108 cases (54.0%) were classified as probable and 62 (31.0%) as possible drug-induced liver injury. It was the primary cause of death in 79 cases (39.5%) and a contributory in 68 (34.0%).

Conclusion: Postmortem diagnosis of drug-induced liver injury requires integrated interpretation of exposure history, autopsy findings, histopathology, toxicology, and exclusion of competing causes, rather than isolated findings.

Keywords: Drug-Induced Liver Injury, Medico-Legal Autopsy, Forensic Toxicology, Hepatotoxicity, Liver Histopathology, Postmortem Examination.

INTRODUCTION

Drug-induced liver injury is an important cause of acute and chronic hepatic dysfunction associated with prescription medicines, over-the-counter drugs, herbal products, nutritional supplements, and illicit substances[1]. It can be clinically mild and reversible biochemical changes or can involve extensive hepatocellular necrosis, acute liver failure, multiorgan dysfunction, and death. Drug-induced liver injury is relatively rare in comparison with other forms of liver disease. Still, there are reasons why it is a big problem: the course is quite unpredictable, diagnosis is complicated, and there are legal implications[2,3].

Liver damage by drugs can happen in two ways: predictable and unpredictable, which is dose dependent, and idiosyncratic[4]. Usually, the predictable injuries result from high exposures to a known hepatotoxic agent, and idiosyncratic

reactions can occur at therapeutic doses in susceptible individuals. The risk and severity of hepatic damage may be modified by genetic factors, age, sex, nutritional status, alcohol intake, underlying liver disease, polypharmacy, and drug interactions. The latency is very variable, as is the clinical picture and pathological picture, which often makes it hard to identify which drug is involved[5,6].

The diagnosis is made from the history, which aims at establishing a reasonable temporal relationship between drug exposure and liver injury, with exclusion of other potential causes of liver injury, such as viral hepatitis, autoimmune disease, alcoholic liver injury, metabolic disorders, biliary obstruction, sepsis, and hypoxic-ischaemic damage[7]. Causality is determined in living patients by serial liver-function tests, treatment records, withdrawal of the suspected agent, and subsequent clinical improvement. These factors are frequently missing or not present in medico-legal autopsies, especially when the death is sudden, drug use is hidden, or multiple drugs have been administered[8].

The interpretation of postmortem toxicological data can be problematic. Identification of a drug or metabolite is indicative of exposure, but cannot by itself establish that the drug or metabolite was responsible for liver damage or death[9]. Postmortem redistribution, decomposition, tissue accumulation, prolonged survival, medical treatment, tolerance, and place of specimen collection may affect drug concentrations. On the other hand, a negative toxicological result does not rule out previous exposure as the drug might have been metabolised, eliminated, degraded, or not been included in the analytical screening panel[10].

Histopathological examination of the liver is helpful, since the presence of centrilobular necrosis, massive hepatic necrosis, cholestatic hepatitis, mixed hepatocellular-cholestatic injury, steatohepatitis, granulomatous inflammation, and vascular damage are all of value[11]. These findings are not, however, specific and may be confused with infectious, metabolic, autoimmune, vascular, or hypoxic liver injury. Histology therefore, needs to be assessed in the context of the circumstances of death, clinical data, gross autopsy features, and toxicology data[12].

A complete clinicopathological and toxicological assessment is necessary to decide whether the drug-related liver injury led to death, was a factor in death, or was an incidental event. Accurate assessment also impacts death certification, criminal/civil investigations, pharmacovigilance, and public-health surveillance[13]. The current study aimed to assess the demographic profile, circumstances of exposure, gross and microscopic liver findings, toxicological profile, drug groups implicated, and role of DILI in the occurrence of death in medico-legal autopsy cases.

MATERIALS AND METHODS

Study Design and Setting

This is a multicentre retrospective analytical study carried out at the Department of Forensic Medicine, KEMU, Lahore, Pakistan, and the Department of Forensic Medicine & Toxicology, Dera Ghazi Khan Medical College, Dera Ghazi Khan, Pakistan. Medico-legal autopsies from January 2024 to October 2025 were included in the study. Through consecutive sampling, 200 autopsy cases were selected that met the eligibility criteria. Data was collected with ethical approval from the relevant institutional review bodies; personal identifiers were removed to preserve the confidentiality of the data.

Selection Criteria

Medico-legal autopsy cases of people aged 18 years or older, where there was a known or suspected history of prescription drugs, non-prescription drugs, herbal formulations, or multiple drugs or substances with potential hepatotoxicity, and where there was either gross, microscopic, biochemical, or circumstantial evidence of liver damage, were included. The source of drug exposure was determined by hospital records, police reports, information from relatives, the presence of medicine bottles in the vicinity, gastric contents, and toxicology results. Cases were excluded if the body was extensively decomposed, if representative liver tissue was not available for examination, or if it was more likely that the liver injury had occurred due to significant trauma, prolonged shock, sepsis, viral hepatitis, autoimmune liver disease, advanced alcohol related liver disease, biliary obstruction, or known metabolic liver disease.

Data Collection

Demographic and medico-legal data were retrieved from the autopsy registers, police documents, hospital files, toxicology reports, and available death-scene investigation records. The following variables were recorded: age, sex, circumstances of exposure, suspected drug/poisoning, therapeutic or overdose exposure, time from drug use to death, clinical

manifestations, liver-function tests (LFTs) before death, treatment for poisoning, survival time, manner of death, and medical conditions. The exposure was characterized as accidental overdose, intentional self-poisoning, adverse reaction to therapeutic use, multidrug exposure, or undetermined.

Autopsy and Histopathological Examination

In all cases, the whole body and internal organs were subjected to medico-legal autopsy both inside and outside as per the departmental protocol. Special care was taken to observe jaundice, haemorrhagic manifestations, cerebral oedema, pulmonary oedema, aspiration, gastric residues, size of liver, colour, consistency, congestion, fatty change, necrosis, and signs of chronic liver disease. All organs of the body were opened and searched for alternative or contributory causes of death, including the heart, lungs, kidneys, brain, gastrointestinal tract, pancreas, spleen, and biliary system.

Representative liver samples were collected from the right and left lobes, including grossly abnormal and apparently normal areas. The specimens were then fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned, and stained with haematoxylin and eosin. When needed, special stains were performed, such as periodic acid–Schiff with diastase, Perls' stain, and reticulin stain. Histological findings of injury were assigned as centrilobular or confluent hepatocellular necrosis, massive or submassive necrosis, cholestatic hepatitis, mixed hepatocellular-cholestatic hepatitis, steatohepatitis, granulomatous hepatitis, vascular injury, or other pattern. Inflammatory infiltrates, eosinophils, bile plugs, steatosis, fibrosis, congestion, ductular reaction, and background chronic liver disease were also noted. Two pathologists experienced in the diagnosis of gastrointestinal lesions independently reviewed the slides, and doubts were settled by jointly examining the slides.

Toxicological Evaluation

Toxicological specimens collected were postmortem femoral blood, urine, bile, vitreous humour, gastric contents, and liver tissue if available. Samples were taken in documented chain of custody procedures, properly labelled, sealed, and stored according to guidelines before analysis. Peripheral blood was chosen for quantitative interpretation as it is less influenced by post-mortem redistribution of the blood than is central blood.

Initial drug screening was carried out by using the validated broad-spectrum chromatographic and immunoassay techniques. Gas chromatography–mass spectrometry or liquid chromatography–tandem mass spectrometry was used to confirm relevant positive findings. Headspace gas chromatography was used to analyse the volatile substances. Drug levels were interpreted taking into account the type of sample, the location of the sample, the postmortem interval, the survival time, drug treatment, drug tolerance, drug metabolite profile, drug decomposition, tissue storage, and potential postmortem redistribution. The presence of a drug or metabolite was assumed to be a sign of exposure, but not used as an independent indicator of drug-induced liver injury or fatal toxicity.

Assessment of Drug-Induced Liver Injury

All the cases were analysed together by forensic medicine specialists, a histopathologist, and a forensic toxicologist. Drug-induced liver injury was diagnosed if there was a history of drug exposure to a known or suspected hepatotoxic drug, a temporal association with the inciting event, and gross/microscopic findings that were compatible with the diagnosis, toxicological confirmation (when available) or an absence of more convincing alternate causes. Only cases where there was enough biochemical and temporal information were assessed by the Roussel Uclaf Causality Assessment Method.

Probable drug-induced liver injury was considered as cases where there was definite drug administration or toxicology data, compatible hepatic pathology, convincing exposure, and no better competing cause. Possible cases were defined as having pathological findings and exposure consistent with the diagnosis, but lacking temporal, biochemical, or toxicological details. An "unlikely" case was defined as one in which liver injury was more likely to be attributable to hypoxia, sepsis/infection, chronic liver disease, obstruction, trauma, or another pathological condition. Drug-induced liver injury was thought to be the main cause of death if the hepatic failure or its consequences were the immediate cause of death, and contributory if it was a significant factor in the fatal process.

Statistical Analysis

The data was entered and analysed in IBM SPSS Statistics 26. Continuous variables were

presented as mean and standard deviation or median and interquartile range, depending on the distribution of the data. The categorical data have been presented in frequencies and percentages. Probable and possible drug-induced liver injury cases were compared about continuous variables using an independent-samples t-test or Mann–Whitney U test, and about categorical variables using chi-square test or Fisher's exact test. All variables that had a p-value < 0.10 in the univariable analysis were tested in a binary logistic regression model for independent factors associated with probable drug-induced liver injury. Adjusted odds ratios (ORs) and 95% confidence intervals (CI) were presented and a P value < 0.05 was regarded as statistically significant.

RESULTS

Demographic and Medico-Legal Characteristics

A total of 200 medico-legal autopsy cases fulfilling the eligibility criteria were analysed. The mean age of the deceased was 41.8 ± 15.2 years, with an age range of 18–82 years. The majority of the cases were between the age groups 30-49 years (89 cases, 44.5%). There were 118 males (59.0%) and 82 females (41.0%), giving a male-to-female ratio of 1.4:1. In 74 cases (37.0%), the exposure was during therapeutic use of the drug, in 61 cases (30.5%) the exposure was intentional overdose, in 42 cases (21.0%) it was accidental overdose, and in 23 cases (11.5%) it was due to an undetermined pattern of exposure. Jaundice was most commonly recorded, followed by abnormal mental state, vomiting, abdominal pain, and bleeding disorders. Several patients had more than one clinical manifestation. Demographic, clinical, and medico-legal features are described in Table 1.

Table 1. Demographic, Clinical, and Medico-Legal Characteristics of the Study Cases

Characteristic	Frequency	Percentage
Age group		
18–29 years	44	22.0
30–49 years	89	44.5
50 years or older	67	33.5
Sex		
Male	118	59.0
Female	82	41.0
Type of drug exposure		
Therapeutic drug exposure	74	37.0
Intentional overdose	61	30.5
Accidental overdose	42	21.0
Undetermined exposure	23	11.5
Documented clinical features		
Jaundice	122	61.0
Altered consciousness	91	45.5
Vomiting	84	42.0
Abdominal pain	72	36.0
Haemorrhagic manifestations	43	21.5
Manner of death		
Accidental	84	42.0
Suicidal	61	30.5
Adverse reaction during therapeutic use	37	18.5
Undetermined	18	9.0

Implicated Drugs and Toxicological Findings

The most often involved drug was Paracetamol with 48 (24.0%) cases. Antituberculous medications were implicated in 36 cases (18.0%), followed by multidrug exposure in 30 cases (15.0%), antiepileptic medications in 26 cases (13.0%), antibiotics in 24 cases (12.0%), and herbal or traditional preparations in 20 cases (10.0%). The other 16 cases were from other potentially hepatotoxic drugs such as antidepressants, non-steroidal anti-inflammatory drugs, antipsychotics, and immunosuppressants.

166 (83.0%) had a drug or metabolite of the drug detected in at least one postmortem

specimen. The highest frequency of detection was for liver tissue (151 cases, 75.5%), followed by femoral blood (138 cases, 69.0%), urine (126 cases, 63.0%), bile (109 cases, 54.5%), gastric contents (74 cases, 37.0%), and vitreous humour (52 cases, 26.0%). In many instances, multiple toxicological specimens were positive, as indicated in Table 2.

Histopathological Findings

The most common histopathological pattern was centrillobular or confluent hepatocellular necrosis (71 cases, 35.5%). Cholestatic hepatitis was identified in 40 cases (20.0%), mixed hepatocellular-cholestatic hepatitis in 34 cases (17.0%), steatohepatitis in 25 cases (12.5%), massive or submassive hepatic necrosis in 18 cases (9.0%), granulomatous hepatitis in 6 cases (3.0%), and vascular-pattern hepatic injury in 6 cases (3.0%).

There were 48 paracetamol-associated cases, 31 (64.6%) of which showed centrilobular or confluent necrosis. In contrast, cholestatic or mixed hepatocellular-cholestatic injury was seen in 25 of the 36 cases (69.4%) with antituberculous drugs. The histological characteristics of herbal and traditional preparations showed varying patterns of steatohepatitis, cholestatic hepatitis, and mixed injury. The distribution of the implicated drugs, toxicological findings, and predominant histopathological patterns is shown in Table 2.

Table 2. Distribution of Implicated Drugs, Toxicological Findings, and Histopathological Patterns

Variable	Frequency	Percentage
Implicated drug or drug group		
Paracetamol	48	24.0
Antituberculous medications	36	18.0
Multiple potentially hepatotoxic drugs	30	15.0
Antiepileptic medications	26	13.0
Antibiotics	24	12.0
Herbal or traditional preparations	20	10.0
Other drugs	16	8.0
Positive toxicological specimen		
Positive in at least one specimen	166	83.0
Liver tissue	151	75.5
Femoral blood	138	69.0
Urine	126	63.0
Bile	109	54.5
Gastric contents	74	37.0
Vitreous humour	52	26.0
Predominant histopathological pattern		
Centrilobular or confluent necrosis	71	35.5
Cholestatic hepatitis	40	20.0
Mixed hepatocellular-cholestatic hepatitis	34	17.0
Steatohepatitis	25	12.5
Massive or submassive necrosis	18	9.0
Granulomatous hepatitis	6	3.0
Vascular-pattern injury	6	3.0

Causality Assessment and Contribution to Death

After multidisciplinary clinicopathological and toxicological review, 108 cases (54.0%) were classified as probable drug-induced liver injury, 62 cases (31.0%) as possible drug-induced liver injury, and 30 cases (15.0%) as unlikely drug-induced liver injury. In the cases that were not thought to be likely, the hepatic damage was more credibly attributed to hypoxic-ischaemic injury, sepsis, viral hepatitis, late-stage chronic liver disease, or biliary obstruction.

Drug-induced liver injury was thought to be a major cause of death in 79 patients (39.5%) and to have contributed in 68 patients (34.0%). In the remaining 53 cases (26.5%), its contribution was considered uncertain or incidental. The major causes of death when liver damage was thought to be the main cause were acute liver failure, hepatic encephalopathy, cerebral oedema,

haemorrhage with coagulopathy, and multiorgan failure.

Positive liver toxicological results, centrilobular or confluent hepatocellular necrosis, and pre-mortem liver-function abnormalities were more commonly found in probable cases. Significant competing causes of liver injury were more prevalent in possible and unlikely cases.

Factors Associated with Probable Drug-Induced Liver Injury

In multivariable logistic regression analysis, documented drug overdose was independently associated with probable drug-induced liver injury, with an adjusted odds ratio of 3.42. The presence of the suspected drug in the liver tissue raised the chance of a probable classification by ~3-fold. Probable drug-induced liver injury was also independently associated with "centrilobular or confluent necrosis" and compatible premortem liver abnormalities. On the other hand, having a large competing cause greatly diminished the likelihood of a probable classification, as shown in Table 3.

Table 3. Multivariable Analysis of Factors Associated with Probable Drug-Induced Liver Injury

Factor	Adjusted odds ratio	95% confidence interval	p-value
Documented drug overdose	3.42	1.75–6.68	<0.001
An implicated drug was detected in the liver tissue	2.87	1.41–5.84	0.004
Centrilobular or confluent necrosis	2.54	1.33–4.85	0.005
Compatible premortem liver abnormalities	2.16	1.12–4.18	0.022
Significant competing cause present	0.28	0.13–0.60	0.001

DISCUSSION

The present study evaluated the clinicopathological and toxicological characteristics of drug-induced liver injury in 200 medico-legal autopsy cases[1]. The results highlight that drug-induced fatal or potentially fatal liver injury is a complex forensic diagnosis that cannot be made on toxicological and histopathology alone. The majority of the cases were considered to be probable drug-induced liver injury, with another fraction being possible due to incomplete drug exposure history, limited biochemical data before the postmortem, or presence of other possible causes of liver injury[2,3].

This could be due to adults aged 30-49 years being more likely to have been exposed to prescription medicines or over-the-counter analgesics, to be receiving treatment with multiple drugs, or to have intentionally taken drugs to cause poisoning[4]. Male predominance was also noted, but both sexes were well represented. In part, this may be due to differences in healthcare-seeking behaviour, self-medication, and variation in types of drugs used, as well as occupational exposure. But it should be noted that the type of drug should not be the sole determinant of drug-induced liver injury, as other factors such as age, nutrition, genetic predispositions, alcohol consumption, pre-existing liver disease, and the use of other drugs all play a role[5].

The most common types of drug exposure were therapeutic drug exposure and intentional and accidental overdose[6]. This is significant as it suggests that severe hepatic injury can be seen not just with intentional poisoning or overdose. Apparently, appropriate treatment can produce idiosyncratic reactions, especially with antituberculous antibiotics, antiepileptic drugs, and herbal preparations. This can be complicated to detect, with blood levels of the drug being within therapeutic limits and the toxic reaction occurring after a variable period of exposure[7].

The most common single drug was Paracetamol, which was often associated with centrilobular or confluent hepatocellular necrosis[8]. This is biologically likely due to the formation of toxic metabolites and the increased susceptibility of the centrilobular hepatocytes. But necrosis can also take place in the event of severe hypoxia, shock, or cardiac failure. Thus, centrilobular necrosis should be used to confirm, but not make a diagnosis of, paracetamol-related liver damage. Documented history of overdose, positive toxicology, history of clinical deterioration, and exclusion of circulatory causes make the diagnosis more likely[9,10].

The second largest group of implicated drugs was anti-tuberculous drugs. Their forensic assessment is difficult since several hepatotoxic agents are often used together, and it may not

be possible to determine which agent is responsible[11]. These cases were mostly cholestatic or mixed hepatocellular-cholestatic, reflecting the different types of injury seen with multidrug therapy. The pathological appearance and severity may be further modified by malnutrition, infection, late presentation, and by pre-existing hepatic disease[12].

Other important exceptions were antiepileptic drugs and antibiotics. These medications can cause hepatocellular, cholestatic, mixed, or hypersensitivity patterns[13]. Supportive features include eosinophilic infiltration, cholestasis, and mixed portal inflammation, although these are not specific. When drug hypersensitivity is suspected, it is especially important to make a correlation with clinical findings, as fever, rash, eosinophilia, and systemic involvement may not have been present or documented at autopsy[14].

A significant number of cases were using herbal and traditional remedies. It is hard to evaluate because they do not always disclose the ingredients, concentrations, manufacturing standards, and possible contaminants[15]. Routine toxicological screening might not detect the active ingredients, and users might not report their use. This means there may have been some cases that were considered to be possible, not probable, DILI that were related to the use of herbs. If actual product(s) are available, the retention and chemical analysis of these product(s) could significantly support the forensic conclusion[16].

In most cases, the toxicological analysis revealed the presence of a drug or relevant metabolite, and liver tissue yielded the largest number of positive results[17]. The liver is a valuable matrix as many drugs are metabolized in the liver or are concentrated in the tissue. However, care must be taken with the interpretation of tissue levels as these can be affected by drug distribution, metabolism, decomposition, storage, and postmortem redistribution. The presence of a high liver value does not necessarily mean hepatotoxicity is present, and the absence of a blood value does not mean that exposure has not occurred[18].

The quantitative application of postmortem blood to interpretation is preferred over central blood as the former is generally less affected by redistribution[19]. But the present results are in favor of multiple matrices. Urine and bile can extend the time of detection, and gastric contents can provide evidence of recent ingestion, while liver tissue may be useful if blood is not available or degraded. Takayasu et al. showed that concordant results obtained from multiple specimens can serve as a better indicator than a single specimen[20].

The most frequent histopathological pattern was centrilobular or confluent necrosis, followed by cholestatic hepatitis and mixed hepatocellular-cholestatic necrosis. This distribution illustrates the morphological diversity of drug-induced liver injury[1-5]. Massive or submassive hepatic necrosis, which was less common, was especially important since this was often accompanied by acute liver failure and a direct cause of death. Steatohepatitis, granulomatous inflammation, and vascular-pattern injury were less common but needed careful exclusion of other diseases related to alcohol abuse, metabolic disease, infection, autoimmune disease, and circulatory injury[6-10].

Multi-disciplinary causality assessment deemed 54.0% to be probable and 31.0% to be possible drug-induced liver injury[1,11]. The relatively large possible category is due to limitations in medico-legal investigations. Frequently, premortem liver-function tests and exact dose or timing of exposure and dechallenge response, as well as complete treatment history, are not available. For this reason, standard clinical causality tools might not be easily applicable with reliability. An integrated expert evaluation based on exposure history, toxicology, histology, gross findings, and exclusion of alternative causes is more suitable than mechanically applying a clinical score in autopsy practice[2-4].

39.5% were attributed primarily to drug-induced liver injury, and an additional 34.0% were attributed secondarily to drug-induced liver injury[5]. This difference is important for proper death certification. The drug might be present but not lethal; it might contribute to liver damage from another disease or cause a sudden liver failure. The final cause of death opinion should indicate the order of cause and should not be synonymous with drug detection and fatal drug poisoning[7].

Documented overdose, positive liver-tissue toxicology, centrilobular or confluent necrosis, and compatible liver abnormalities before death were independent factors associated with probable drug-induced liver injury in the regression analysis[10-14]. Clinically and forensically, this is plausible because it is converging evidence from exposure, toxicology, pathology, and clinical assessment. On the other hand, a strong competing cause (other than hypoxic injury) decreased the probability of a probable classification, and therefore,

competing causes, such as sepsis, viral hepatitis, biliary obstruction, and chronic liver disease, must be excluded[15,16].

This study has several limitations. This was a retrospective study that relied on the completeness of autopsy records, police records, hospital records, and toxicology reports. In some situations, exact doses of drugs and exposure times were not provided. If someone passed away before hospitalisation, biochemical information was not always available[17,18]. Preanalytical factors of postmortem redistribution, decomposition, and specimen availability may have influenced the toxicological interpretation. Histological patterns were supportive but not specific, and some cases may have involved more than one mechanism of hepatic injury. However, the use of a multicentre design, a relatively large sample size, a multi-matrix toxicological evaluation, and a combined pathological review support the results presented in the study[19,20].

CONCLUSION

Liver injury as a consequence of drug use is a significant factor in autopsy practice, and it is often a challenging diagnosis to make. The main drugs associated were Paracetamol, antituberculous drugs, multidrug exposure, antiepileptic drugs, antibiotics, and herbal drugs. The most common histological pattern was the centrilobular or confluent hepatocellular necrosis, and the highest proportion of toxicological detection was in liver tissue. Drug detection, concentration, and/or histological appearance alone should not be used as the basis for a reliable postmortem diagnosis. Concordance between history of exposure, circumstances of death, findings on the scene, multi-matrix toxicology, liver histopathology, and exclusion of other causes of death provides the strongest conclusions. Standardised multidisciplinary evaluation can help maximize causality classification, death certification, pharmacovigilance, and medico-legal interpretation of suspected fatal DILI.

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Authors' Contributions: F.T. conceived and designed the study, supervised the research, and drafted the manuscript. Q.A.K. contributed to study design, medico-legal data interpretation, and critical revision of the manuscript. R.N. and R.B. assisted with data collection, autopsy record review, and manuscript preparation. O.A., H.M.I.A., and S.I. contributed to toxicological and pharmacological interpretation, data analysis, and critical review of the manuscript. All authors read and approved the final manuscript.

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