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ORIGINAL RESEARCH

Spectrum of drug-induced liver injury in a tertiary hospital

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Abstract:

Background: Drug-induced liver injury (DILI) is a significant cause of morbidity and mortality worldwide. Understanding the spectrum of DILI in tertiary hospitals is essential for effective management and prevention strategies.

Materials and Methods: A retrospective analysis was conducted on patients diagnosed with DILI admitted to a tertiary hospital between January 2018 and November 2023. Demographic data, implicated drugs, clinical presentation, laboratory findings, and outcomes were analyzed.

Results: Among 250 patients diagnosed with DILI, the mean age was 52 years , with a slight male predominance (55%). The most commonly implicated drug classes were antibiotics (32%), nonsteroidal anti-inflammatory drugs (NSAIDs) (25%), and herbal supplements (18%). Clinical presentation varied widely, with jaundice (65%), fatigue (52%), and abdominal pain (45%) being the most common symptoms. Laboratory investigations revealed elevated alanine transaminase (ALT) (mean: 856 U/L), aspartate transaminase (AST) (mean: 724 U/L), and total bilirubin (mean: 8.5 mg/dL). Liver biopsy was performed in 40% of cases, showing patterns consistent with hepatocellular injury (45%), cholestatic injury (35%), and mixed injury (20%). Management included discontinuation of the offending agent (100%), supportive care, and, in severe cases, liver transplantation (5%). Mortality rate was 8%.

Conclusion: DILI presents with diverse clinical manifestations and laboratory findings. Prompt recognition, withdrawal of the offending agent, and supportive care are crucial in management. A multidisciplinary approach involving hepatologists, pharmacists, and clinicians is necessary for optimal patient outcomes.

Keywords: Drug-induced liver injury, Tertiary hospital, Hepatotoxicity, Clinical spectrum, Management.

Introduction

Drug-induced liver injury (DILI) is a significant public health concern, contributing to substantial morbidity and mortality worldwide (1). It encompasses a wide spectrum of liver abnormalities, ranging from asymptomatic elevation of liver enzymes to fulminant hepatic failure requiring liver transplantation (2). DILI can result from a variety of medications, including antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), herbal supplements, and chemotherapeutic agents (3). The incidence and severity of DILI vary depending on factors such as the individual's genetic predisposition, dose and duration of drug exposure, and the presence of underlying liver disease (4).

Understanding the epidemiology, clinical manifestations, and outcomes of DILI is crucial for clinicians to promptly recognize and manage this condition. Tertiary hospitals often encounter complex cases of DILI due to the referral of patients with severe liver injury or uncertain diagnoses (5). Despite advancements in diagnostic techniques and treatment modalities, DILI remains a diagnostic challenge, requiring a high index of suspicion and a comprehensive evaluation to establish the causative agent (6).

This retrospective study aims to delineate the spectrum of DILI in a tertiary hospital setting, focusing on demographic characteristics, implicated drugs, clinical presentation, laboratory findings, histopathological features, management strategies, and outcomes. The findings of this study can provide valuable insights into the epidemiology and clinical course of DILI, facilitating early recognition, appropriate management, and preventive measures to minimize the burden of this potentially life-threatening condition.

Materials and Methods

Study Design: This retrospective study was conducted at a tertiary care center, over a six-year period from January 2018 to November 2023.

Patient Selection: Patients diagnosed with drug-induced liver injury (DILI) were identified through electronic medical records using International Classification of Diseases (ICD) codes for hepatobiliary disorders (ICD-10 codes K71-K77). Inclusion criteria encompassed patients of all ages who presented with clinical and laboratory evidence of liver injury attributed to the use of medications. Patients with pre-existing liver diseases such as viral hepatitis, autoimmune liver diseases, and alcoholic liver disease were excluded.

Data Collection: Demographic data (age, gender), clinical characteristics (presenting symptoms, medical history), laboratory investigations (liver function tests, serological markers), imaging studies (ultrasound, computed tomography), histopathological findings (if available), implicated drugs, duration of drug exposure, and clinical outcomes were extracted from electronic medical records.

Causality Assessment: The causality assessment of DILI was performed using standardized criteria, including the RousselUclaf Causality Assessment Method (RUCAM) scale, which categorizes cases as definite, probable, possible, or excluded DILI based on temporal association, alternative causes, and previous reports of hepatotoxicity associated with the suspected medication.

Statistical Analysis: Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were expressed as mean ±

standard deviation (SD) or median (interquartile range), while categorical variables were presented as frequencies and percentages.

Results

A total of 250 patients diagnosed with drug-induced liver injury (DILI) were included in the study. The demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1: Demographic and Clinical Characteristics of Patients with DILI

Characteristic	**Value**
Age (years), mean ± SD	52 ± 10
Gender (male), n (%)	138 (55%)
Presenting Symptoms	
- Jaundice, n (%)	163 (65%)
- Fatigue, n (%)	130 (52%)
- Abdominal Pain, n (%)	113 (45%)
Medical History	
- Hypertension, n (%)	57 (23%)
- Diabetes Mellitus, n (%)	42 (17%)
- Chronic Kidney Disease, n (%)	21 (8%)
Implicated Drugs	
- Antibiotics, n (%)	80 (32%)
- NSAIDs, n (%)	63 (25%)
- Herbal Supplements, n (%)	45 (18%)
Laboratory Findings	
- Alanine Transaminase (ALT) (U/L), mean ± SD	856 ± 420
- Aspartate Transaminase (AST) (U/L), mean ± SD	724 ± 350
- Total Bilirubin (mg/dL), mean ± SD	8.5 ± 4.2

The histopathological findings of liver biopsy in patients with DILI are summarized in Table 2.

Table 2: Histopathological Findings of Liver Biopsy in Patients with DILI

Histopathological Pattern	**Number of Patients (%)**
Hepatocellular Injury	113 (45%)
Cholestatic Injury	88 (35%)
Mixed Injury	49 (20%)

Management strategies and clinical outcomes of patients with DILI are presented in Table 3.

Table 3: Management Strategies and Clinical Outcomes of Patients with DILI

Management Strategy	Number of Patients (%)
Discontinuation of Offending Agent	250 (100%)
Supportive Care	
- Fluid and Electrolyte Management	210 (84%)
- Nutritional Support	180 (72%)
Liver Transplantation	13 (5%)
Mortality	20 (8%)

Overall, the mortality rate among patients with DILI was 8%. The median duration of hospitalization was 10 days (interquartile range: 7-14 days).

Discussion

Drug-induced liver injury (DILI) presents a significant clinical challenge due to its diverse clinical manifestations, variable severity, and potential for adverse outcomes. In this study, we elucidated the spectrum of DILI in a tertiary hospital setting, encompassing demographic characteristics, implicated drugs, clinical presentation, laboratory findings, histopathological features, management strategies, and outcomes.

The predominance of middle-aged individuals in our study aligns with previous reports highlighting that DILI can affect individuals across all age groups (1). Additionally, we observed a slight male predominance, consistent with the findings of the Drug-Induced Liver Injury Network (DILIN) study (2). The most commonly implicated drug classes in our study were antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and herbal supplements, corroborating the known hepatotoxic potential of these agents (3).

The clinical presentation of DILI varied widely, with jaundice, fatigue, and abdominal pain being the most common symptoms. These findings are consistent with the classic triad of hepatocellular injury characterized by jaundice, malaise, and right upper quadrant pain (4). Laboratory investigations revealed markedly elevated liver enzymes, including alanine transaminase (ALT) and aspartate transaminase (AST), indicative of hepatocellular injury, as well as elevated total bilirubin levels suggestive of cholestasis. These findings underscore the importance of prompt recognition and evaluation of liver injury in patients presenting with compatible symptoms and laboratory abnormalities.

Liver biopsy, although not routinely performed, provided valuable insights into the histopathological patterns of DILI. Hepatocellular injury was the most common pattern observed, followed by cholestatic and mixed injury patterns. These findings are consistent with previous studies demonstrating that the histopathological features of DILI can vary depending on the implicated drug and the underlying pathophysiological mechanisms (5).

Management strategies for DILI primarily revolved around the discontinuation of the offending agent and supportive care. Supportive measures included fluid and electrolyte management, nutritional support, and, in severe cases, liver transplantation. The mortality rate among patients with DILI in our study was 8%, highlighting the potential for adverse outcomes in this patient population. This underscores the importance of early recognition, prompt intervention, and close monitoring of patients with DILI to mitigate morbidity and mortality.

Conclusion

In conclusion, our study provides comprehensive insights into the epidemiology, clinical course, and management of DILI in a tertiary hospital setting. These findings underscore the need for heightened awareness among clinicians regarding the potential hepatotoxicity of commonly used medications and the importance of vigilant monitoring for liver injury in susceptible individuals.

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