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Albendazole-Induced Liver Injury: A Systematic Review of Clinical Presentations, Management, and Outcomes

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Abstract

Background. Albendazole, a commonly used anthelmintic, is linked to rare but potentially severe hepatotoxicity.
Purpose. This systematic review aimed to analyze reported cases to delineate patterns of presentation, identify risk factors, evaluate management strategies, and outline outcomes of albendazole-induced liver injury.
Materials and methods. Following PRISMA guidelines, we conducted a systematic review of case reports, case series, and observational studies. Data were extracted on patient demographics, albendazole exposure, clinical features, liver injury patterns, management strategies, and outcomes. Quality assessment was performed using the CARE 2013 checklist.
Results. We included 22 case reports (9 pediatric and 13 adult cases) and 2 observational studies. Pediatric cases predominantly involved hydatid cyst or prophylactic use, with a female predominance (67%). Liver injury onset ranged from 2 to 14 days, resolving with drug discontinuation and supportive care. Adult cases exhibited a wider latency (6 hours to 1 month), with severe instances requiring intensive care or liver transplantation. Observational studies indicated a higher frequency of severe hepatic events with albendazole compared to other anthelmintics, often linked to unsupervised use. All patients recovered following appropriate management, though some adult cases demonstrated prolonged recovery periods and risk of recurrent injury upon re-exposure.
Conclusions. Albendazole-induced liver injury is idiosyncratic, with significant variability in presentation and outcomes. Improved pharmacovigilance, patient education, and

research into predictive biomarkers are crucial to mitigate risks and enhance safety during albendazole therapy.
Keywords: albendazole, drug-induced liver injury, hepatotoxicity, pediatric hepatitis, pharmacovigilance

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Альбендазол-индуцированное поражение печени: систематический обзор клинических проявлений, методов лечения и исходов

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Резюме

Введение. Альбендазол – широко используемый антигельминтный препарат, который связан с редкой, но потенциально тяжелой гепатотоксичностью.
Цель. Анализ зарегистрированных случаев для описания характера проявлений, выявления факторов риска, оценки стратегий лечения и прогнозирования исходов поражения печени, вызванного альбендазолом.
Материалы и методы. В соответствии с рекомендациями PRISMA мы провели систематический обзор описаний случаев и наблюдательных исследований. Были получены данные о демографических характеристиках пациентов, воздействии альбендазола, клинических характеристиках, характере поражения печени, стратегиях лечения и исходах. Оценка качества проводилась с использованием контрольного списка CARE 2013.
Результаты. Мы включили 22 описания случаев (9 – у детей и 13 – у взрослых) и 2 наблюдательных исследования. Случаи у детей преимущественно были связаны с эхинококкозом или профилактическим применением, преобладали женщины (67%).

Начало поражения печени варьировалось от 2 до 14 дней и проходило после отмены препарата и поддерживающей терапии. У взрослых пациентов наблюдался более длительный латентный период (от 6 часов до 1 месяца), при этом в тяжелых случаях требовалась интенсивная терапия или трансплантация печени. Наблюдательные исследования показали более высокую частоту тяжелых печеночных осложнений при применении альбендазола по сравнению с другими антигельминтными препаратами, часто связанных с неконтролируемым применением. Все пациенты выздоровели после надлежащего лечения, хотя в некоторых случаях у взрослых наблюдались более длительные периоды восстановления и риск рецидива поражения при повторном применении.

Выводы. Поражение печени, вызванное альбендазолом, носит идиосинкразический характер и характеризуется значительной вариабельностью клинических проявлений и исходов. Улучшение фармаконадзора, информирование пациентов и исследования прогностических биомаркеров имеют решающее значение для снижения рисков и повышения безопасности терапии альбендазолом.

Ключевые слова: альбендазол, лекарственное поражение печени, гепатотоксичность, детский гепатит, фармаконадзор

■ INTRODUCTION

Albendazole is a broad-spectrum benzimidazole anthelmintic widely used in both clinical practice and public health programs for treating various parasitic infections [1]. Its effectiveness against both intestinal and tissue parasites, combined with its generally favourable safety profile, has made it a cornerstone of antiparasitic therapy worldwide. The drug is particularly valuable in treating conditions such as hydatid disease, neurocysticercosis, and various soil-transmitted helminth infections, serving both therapeutic and prophylactic purposes [1].

While albendazole is generally well-tolerated, there is growing recognition of its potential to cause drug-induced liver injury (DILI). This adverse effect, though rare, can range from mild elevation of liver enzymes to severe hepatotoxicity requiring intensive medical intervention [2]. The identification and characterization of albendazole-induced liver injury is particularly challenging due to several factors: the wide range of treatment indications, varying durations of therapy, and the potential for both immediate and delayed onset of hepatotoxicity [3].

Despite these concerns, there has been no comprehensive systematic review of albendazole-induced liver injury that synthesizes data from both case reports and observational studies. Understanding the patterns of liver injury, risk factors, and outcomes is crucial for several reasons. First, albendazole is frequently used in mass drug administration programs, making even rare adverse effects potentially significant from a public health perspective. Second, the drug is often available over-the-counter in many countries, leading to potential unsupervised use. Third, the increasing recognition of its effectiveness in treating various parasitic infections has led to more widespread and prolonged use in clinical practice [4, 5].

This systematic review aims to comprehensively analyse reported cases of albendazole-induced liver injury, examining patterns of presentation, risk factors, management

approaches, and outcomes. By synthesizing data from individual case reports and larger observational studies, we seek to provide clinicians with evidence-based insights for prevention, early recognition, and management of this serious adverse effect.

■ MATERIALS AND METHODS

Protocol and Registration

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6]. The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) under the registration ID: [CRD42025631629].

Eligibility Criteria

This review included case reports and case series describing liver injury or hepatitis attributed to albendazole therapy. The inclusion criteria were:

1. Population: Patients of any age or sex who developed liver injury associated with albendazole.
2. Exposure: Albendazole therapy, irrespective of dose or duration.
3. Outcomes: Documented cases of liver injury based on clinical, biochemical, or histopathological evidence.
4. Study Design: Published case reports and case series.
5. Language: Articles published in English.

Exclusion criteria included:

1. Studies where albendazole was not definitively implicated in liver injury.
2. Reports of liver injury resulting from other hepatotoxic drugs or conditions with no conclusive evidence for albendazole's involvement.
3. Reviews, editorials, and studies involving animal or in vitro experiments.

Information Sources

The following electronic databases were systematically searched:

- PubMed/MEDLINE.
- EMBASE.
- Web of Science.
- Scopus.
- Google Scholar.

Additionally, references cited in the included studies were screened manually for relevant articles.

Search Strategy

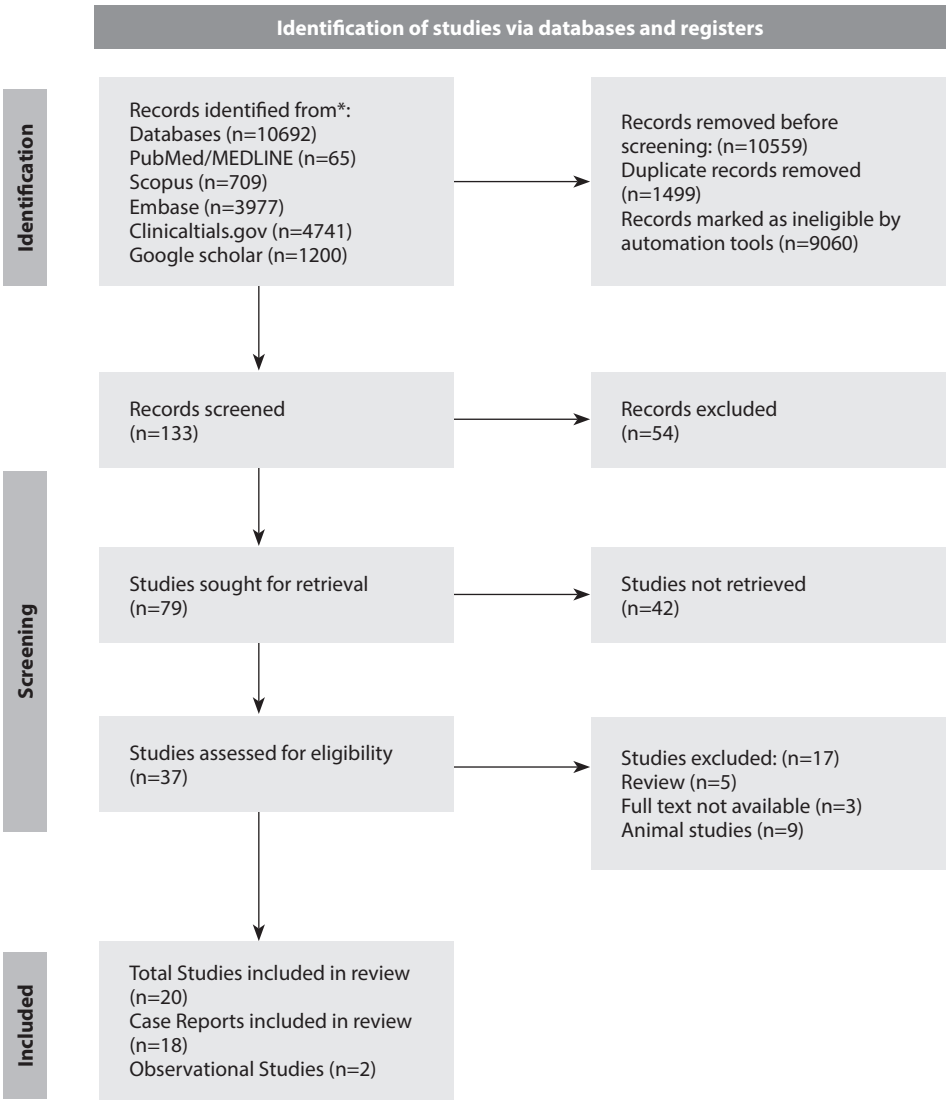
The search strategy was designed to identify all relevant case reports and case series. It combined keywords and Medical Subject Headings (MeSH) terms, including:

- "Albendazole".
- "Hepatitis".
- "Liver injury".
- "Hepatotoxicity".
- "Drug-induced liver injury (DILI)".

A detailed description of the search strategies for each database is provided in Supplementary File 1.

Study Selection

Titles and abstracts retrieved from the database searches were screened independently by two reviewers (MPS, MM). Full-text articles of potentially eligible studies were assessed against predefined inclusion and exclusion criteria. Disagreements were resolved through discussion or consultation with a third reviewer (SSK) (Figure).



Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Flowchart

Data Extraction

Data were extracted independently by two reviewers using a standardized data extraction form. The extracted data included:

1. Patient demographics (age, sex).
2. Albendazole details (indication, dose, duration).
3. Clinical features of liver injury (symptoms, time to onset).
4. Laboratory findings (liver enzymes, bilirubin, RUCAM score).
5. Management strategies (e.g., drug discontinuation, symptomatic treatment).
6. Outcomes (recovery, persistent liver dysfunction, or death).

Discrepancies in data extraction were resolved through discussion.

Risk of Bias Assessment

The quality of case reports and case series was assessed using the Case Report (CARE) 2013 checklist [7]. Each report was evaluated for clarity in patient demographics, exposure details, diagnostic criteria for liver injury, and outcome reporting.

Data Synthesis

A descriptive synthesis was performed to summarize the characteristics of reported cases in children, adolescents, and adults. Key findings were categorized and tabulated, including demographic details, patterns of liver injury (e.g., hepatocellular, cholestatic, or mixed), severity scores (e.g., RUCAM), management approaches, and outcomes [8].

The results were summarized in two categories: Albendazole-induced liver injury in children/adolescents and in adults. Subgroup analyses were conducted based on age groups, drug doses, and duration of therapy to identify trends in clinical presentation and outcomes.

■ RESULTS

Case Reports

Our systematic review identified 22 cases of albendazole-induced liver injury comprising 9 cases in children and adolescents (age 1–18 years) and 13 cases in adults (aged 18–50 years) from 18 published reports.

Observational Studies

Two significant observational studies provided additional epidemiological data on albendazole-induced liver injury:

1. WHO Pharmacovigilance Database Analysis.

A disproportionality analysis of the World Health Organization's pharmacovigilance database revealed that albendazole was associated with a higher proportion of serious adverse events compared to other benzimidazole derivatives and anthelmintic agents. Of 3,421 cases (67.0%) involving albendazole exposure:

- 336 cases were associated with hepatic disorders.
- 190 cases specifically involved hepatitis.
- Albendazole accounted for 67% of all serious cases reported.

2. Romanian Pediatric Cohort Study.

A six-year single-centre cohort study in Romania analyzing 2,533 children with acute liver disease found:

- 40 cases of drug-induced liver injury (DILI).
- 14 cases (38%) were attributed to albendazole.
- Latency period ranged from 3 to 89 days (mean: 21.6 days).
- 8 cases involved self-administration without medical supervision.
- 9 cases presented with jaundice.
- Pattern of liver injury was predominantly cholestatic (17%) or mixed (28%).

Pediatric and Adolescent Cases

Among the pediatric and adolescent cases, the age range was 1–18 years, with a female predominance (6/9 cases) (table 1). The most common indications for albendazole use were hydatid cyst (2 cases) and parasitic infections (1 case), while in the remaining cases, the indication was either prophylactic or not mentioned. The dosing regimen varied widely, with some patients receiving single doses while others underwent treatment for up to 3 weeks. In cases where the dose was specified, it ranged from 15 mg/kg/day to 400 mg twice daily.

The onset of liver injury typically occurred within 2–14 days after initiating treatment, with most cases presenting within the first week. The most frequent presenting symptoms included jaundice, yellowish discoloration of eyes, nausea, vomiting, and abdominal pain. The severity of liver injury was assessed using the CIOMS/RUCAM scale in most cases, with scores ranging from 7–13, indicating probable to highly probable causality.

Treatment primarily involved immediate discontinuation of albendazole (8/9 cases) and conservative management. Some cases required specific interventions such as prednisolone and ursodeoxycholic acid. All pediatric cases showed favourable outcomes with improvement in clinical symptoms and normalization of liver function tests.

Adult Cases

In the adult population (13 cases), ages ranged from 18–50 years, with a slight female predominance (7/13 cases) (table 2). Hydatid cyst was the most common indication (6 cases), followed by prophylactic use and parasitic infections. Treatment durations varied from single doses to 5 months of therapy, with doses ranging from 400 mg daily to 800 mg daily when specified.

The time to onset of liver injury varied considerably, ranging from 6 hours to 1 month after drug initiation. Clinical presentations included jaundice, fatigue, nausea, vomiting, and abdominal pain. Laboratory findings consistently showed elevated transaminases, with some cases presenting with significant hyperbilirubinemia. RUCAM scores ranged from 5–12, indicating probable to highly probable causality.

Management primarily involved drug discontinuation in all cases. While most patients improved with supportive care alone, one case required orthotopic liver transplantation. Of note, two cases reported recurrent liver injury with albendazole re-exposure, emphasizing the importance of avoiding re-challenge. All cases eventually achieved complete recovery, though recovery times varied from several weeks to months.

Table 1
Summary of case reports of albendazole induced liver injury in children and adolescents

Author/year	No. of patients	Case number	Age/Sex	Diagnosis	Dose of albendazole	Duration of treatment	Adverse drug reaction observed	Time to symptom	Severity of Drug-drug interaction	Drug discontinued due to adverse effect? Yes/No	Treatment of adverse drug reaction	Outcome
Negi et al. 2024 [9]	1	1	5 yr / female	Not mentioned	Not mentioned Prophylactic	Not mentioned	Yellowish discoloration of the eyes accompanied by clay-coloured stools for the 1 week	5 days	CIOMS RUCAM scale – 7 probable	Yes	Conservative management	Showed improvement during hospital stay
	1	2	7 yr / female	Not mentioned	Not mentioned Prophylactic	Not mentioned	Yellowish discoloration of the eyes along with vomiting persisting for the past 4 days	4 days	CIOMS RUCAM scale – 7 probable	Yes	Conservative management	Showed improvement during hospital stay
Nataša Dragutinović et al. 2022 [10]	1	1	8 yr / female	Enterobius vermicularis	Not mentioned	3 days	Nausea, vomiting, and fever, abdominal pian, dark urine	3 days	RUCAM score – 8	Yes	Prednisolone at a dose of 1 mg/kg and ursodeoxycholic acid at a dose of 20 mg/kg	Transaminases, gamma-glutamyl transferase (GGT), bilirubin, and total IgG levels were all within normal limits
Verdugo Thomas F, et al. 2016 [11]	1	1	15 yr / female	Eosinophilia associated with a positive Toxocara canis IgG result	400 mg BD	7 days	Presented with jaundice, choluria, anorexia, nausea, and epigastric pain, along with direct hyperbilirubinemia, elevated transaminases, coagulopathy, and hypokalemia	5 days	CIOMS score – 6	No [reaction developed after completion of drug therapy]	Supportive treatment and IV Vitamin K	Symptoms rapidly improved, and both liver profile and coagulation tests showed significant improvement.
Boceanu et al. 2015 [12]	1	1	15 yr / male	Not mentioned	Not mentioned	single dose	Biological picture of acute liver failure of unknown etiology	14 days	RUCAM score – 13	Yes	Not mentioned	Normalization of liver biochemical profile

Tugba Koca et al. 2015 [13]	1	1	6 yr / female	Hydatid cyst	15 mg/ kg/day	2 weeks	Patient experienced abdominal pain, with AST, ALT, and GGT levels at 663, 800, and 92 IU/L, respectively	~ 2 months	Not mentioned	Yes	None	Elevated transaminase levels quickly normalized after discontinuing albendazole
	1	1a	6 yr / female	Hydatid cyst	15 mg/ kg/day	3 weeks	Elevated transaminases levels	2 weeks	Not mentioned	Yes	Prednisolone and azathioprine	Normal laboratory findings and clinical features
Chirag Shah et al. 2013 [14]	1	1	7 yr / male	H/O 4 episodes of jaundice	400 mg single dose	–	jaundice with prodromal symptoms nausea, anorexia, vomiting	Within 7 days	Not mentioned	Yes	None	Symptoms resolved and enzyme levels normalized
Madhumita Nandi et al. 2013 [15]	1	1	5 yr / male	Not mentioned	Not mentioned	Not mentioned	Recurrent acute hepatitis – 4 episodes	2–3 days	RUCAM Score – 9	Yes	None	Condition improved with subsidence of jaundice and hepatomegaly

Notes: CIOMS – Council for International Organizations of Medical Sciences, RUCAM – Roussel Uclaf Causality Assessment Method, ALP – alkaline phosphatase, ALT – alanine transaminase, AST – aspartate aminotransferase, GGT – gamma-glutamyl transferase, IgG – Immunoglobulin G, BD – Twice a Day.

Table 2
Summary of case reports of albendazole induced liver injury in adults

Author/year	No. of patients	Case number	Age/Sex	Diagnosis	Dose of albendazole	Duration of treatment	Adverse drug reaction observed	Time to symptom	Severity of Drug-drug interaction	Drug discontinued due to adverse effect? Yes/No	Treatment of adverse drug reaction	Outcome
Sang Yi Moon et al. 2019 [16]	1	1	21 yr / female	Not mentioned		1 dose prophylactically	Nausea, fatigue, and jaundice	2 weeks	RUCAM score – 11	Yes	IV Fluid+ symptomatic therapy	Improvement in symptoms and Liver function.
Yavor Asenov et al. 2019 [17]	1	1	29 yr / female	hepatic hydatid cysts	10 mg/ kg/day	Not mentioned	Significant elevations in transaminase levels were observed, with ALT at 677 U/L and AST at 562 U/L	Not mentioned	RUCAM score >8	Yes	None	Undergone resection → recovery is uneventful

	1	2	50 yr / male	Hydatid cyst	Not mentioned	Not mentioned	Liver enzyme levels were elevated, with AST at 720 U/L, ALT at 642 U/L, total bilirubin at 0.93 mg/dL, direct bilirubin at 0.19 mg/dL, and an INR of 1.14	Not mentioned	RUCAM score – >8	Yes	None	Undergone resection → recovery is uneventful
	1	3	47 yr / male	Hydatid cyst	Not mentioned	Not mentioned	AST and ALT levels showed a rapid increase to 199 U/L and 482 U/L, respectively.	Not mentioned	RUCAM score – >8	Yes	Not mentioned	Undergone resection → recovery is uneventful
Yilmaz Bilgic et al. 2017 [18]	1	1	47 yr / female	Suspected gastrointestinal parasitosis with a probable history of albendazole-induced toxic hepatitis four years ago	400 mg	single dose	Presented with vomiting and anorexia for 4 days. On examination, jaundice was noted. Laboratory findings included ALT at 1332 IU/L, AST at 710 IU/L, ALP at 159 IU/L, GGT at 71 IU/L, total bilirubin at 4.3 mg/dL (direct: 2.8 mg/dL, indirect 1.5 mg/dL), and LDH at 542 IU/L	6 days	RUCAM score – 10	Yes	None	All abnormal laboratory results decreased by more than 50% within one month and normalized within two months.
Jose Fabio Freire et al. 2015 [19]	1	1	21 yr / female	intestinal helminths	400 mg BD	3 days	Fulminant acute hepatitis	3 days	RUCAM score – 7	Yes	Hospitalized in ICU (not mentioned details)	5 weeks after discharge, patient had excellent general condition with mild icterus in sclera
Tyler D. Aasen et al. 2015 [20]	1	1	38 yr / female	Hydatid cyst	Not mentioned	Not mentioned	Fatigue, malaise, and jaundice	Not mentioned	RUCAM score – 6	Yes	Orthotopic liver transplantation	Recovered
Nadia Ben Fredj et al. 2014 [21]	1	1	26 yr / male	Hydatid cyst	800 mg daily	1 month	Patient presented with right abdominal pain and jaundice. Laboratory results showed ALT at 2454 IU/L, AST at 1451 IU/L, alkaline phosphatase at 198 IU/L, total bilirubin at 341 mg/dL, and a prothrombin index of 77%.	1 month	Not mentioned	Yes	None	Clinical symptoms resolved and lab tests showed improvement

Gozu-kucuk R, et al. 2013 [22]	1	1	28 yr / male	Hydatid cyst	800 mg/ day	20 days	Laboratory results showed an AST level of 659 IU/L, ALT level of 968 IU/L, ALP level of 209 IU/L, GGT level of 108 U/L, LDH level of 667 IU/L, and a prothrombin time of 18.1 seconds	20 days	RUCAM score – 9	Yes	None	Liver enzyme levels decreased to within normal reference ranges.
Juan Ignacio Marin Zuluaga et al. 2013 [23]	1	1	25 yr / female	Non-specific gastrointestinal symptoms	Not mentioned	Not mentioned	Toxic granulomatous hepatitis.	2 weeks	RUCAM Score – 5	Yes	None	Resolution of toxic granulomatous hepatitis
David Ríos et al. 2012 [24]	1	1	47 yr / Male	hepatic hydatidosis	600 mg/ day	5 months	Jaundice syndrome Elevated transaminases	Not mentioned	RUCAM Score – 5	Yes	None	Asymptomatic and normal hepatic profile
Min Kwam Kim et al. 2008 [25]	1	1	25 yr / male	Prophylactically	400 mg	Single dose	Jaundice Had prev. h/o similar acute hepatitis d/t albendazole	~20 days	RUCAM Score – 12	Yes	None	Jaundice improved, transaminases levels normalized
Gi Young Choi et al. 2007 [26]	1	1	47 yr / Male	Not mentioned	Not mentioned	Single dose	Patient presented with fever, chills, myalgia, nausea, vomiting, and a skin rash on both forearms, accompanied by elevated serum transaminases	6 hours	RUCAM Score – 9	Yes	Not mentioned	Patient improved and discharged with no significant symptoms

Notes: IV – intravenous line, CIOMS – Council for International Organizations of Medical Sciences, RUCAM – Roussel Uclaf Causality Assessment Method, ALP – alkaline phosphatase, ALT – alanine transaminase, AST – aspartate aminotransferase, GGT – gamma-glutamyl transferase, LDH – lactate dehydrogenase, IgG – Immunoglobulin G, BD – Twice a Day.

Severity and Outcomes

Across both age groups, the severity of liver injury ranged from mild elevation of liver enzymes to severe cases requiring intensive care or transplantation. The pattern of liver injury was predominantly hepatocellular, characterized by marked elevations in transaminases. Despite the severity of some cases, complete recovery was achieved in all reported cases following drug discontinuation and appropriate supportive care.

Quality of Included Studies as per CARE Guidelines

The quality of the included case reports and series was assessed using the CARE (CAse REport) guidelines checklist, evaluating essential components such as keywords, abstract, introduction, patient information, clinical findings, timeline, diagnostic and therapeutic interventions, follow-up, discussion, patient perspective, and informed consent (Table 3):

- Keywords and Abstract: Most studies (72%) provided relevant keywords, and 61% included structured abstracts that adequately summarized the case details. Notable exceptions included Verdugo Thomas F. et al. (2016) and Juan Ignacio Marin Zuluaga et al. (2013), which lacked both elements.
- Introduction and Patient Information: Nearly all studies included an introduction and detailed patient information, ensuring clarity on the context and clinical background.
- Clinical Findings and Timeline: Clinical findings were consistently reported across the studies (94%), and 83% provided a clear timeline of events, facilitating chronological understanding of the diagnosis and treatment.
- Diagnostic and Therapeutic Interventions: Diagnostic interventions were reported in 94% of cases, and therapeutic details were outlined in 89%. However, some studies failed to mention either, particularly in older reports.
- Follow-Up and Outcomes: Follow-up data were available in 78% of studies, providing insights into patient recovery and treatment effectiveness. However, this critical component was missing in reports by Boceanu et al. (2015) and Gozukucuk R, et al. (2013).
- Discussion and Patient Perspective: While most studies included discussions contextualizing the case within existing literature (89%), none reported the patient's perspective on their illness or treatment experience.
- Informed Consent: Reporting of informed consent was universally absent, highlighting a critical gap in ethical reporting standards.

■ DISCUSSION

Drug-induced liver injury (DILI) remains a significant challenge in clinical practice, particularly with drugs like albendazole that are widely used for parasitic infections. This study highlights the clinical characteristics, risk factors, and management strategies of albendazole-induced DILI, focusing on practical aspects to guide clinicians in treatment and prevention.

Clinical Presentation and Diagnosis

The clinical manifestations of albendazole-induced DILI vary widely, ranging from asymptomatic elevations in liver enzymes to overt hepatic dysfunction characterized by jaundice, fatigue, abdominal discomfort, and, in rare cases, hepatic failure. Our findings align with published data that highlight albendazole as a hepatotoxic agent, particularly in individuals with underlying liver conditions [27, 28]. For clinicians, early recognition

Table 3
Reporting Quality Assessment of Included Case Reports using CARE guidelines

References	Keywords	Abstract	Introduction	Patient Info	Clinical Findings	Timeline	Diagnostic Intervention	Therapeutic Intervention	Follow-Up And Outcomes	Discussion	Patient Perspective	Informed Consent
Negi et al., 2024	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Nataša Dragutinović et al., 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Sang Yi Moon et al., 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Yavor Asenov et al., 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Yılmaz Bilgic et al., 2017	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Not mentioned
Verdugo Thomas F. et al., 2016	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Not mentioned
Boceanu et al., 2015	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	No	Not mentioned
Jose Fabio Freire et al., 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Tugba Koca et al., 2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Not mentioned
Tyler D. Aasen et al., 2015	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Nadia Ben Fredj et al., 2014	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Not mentioned
Chirag Shah et al., 2013	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Not mentioned
Gozukucuk R, et al., 2013	No	No	No	Yes	Yes	Yes	No	Yes	No	No	No	Not mentioned
Juan Ignacio Marin Zuluaga et al., 2013	No	No	No	Yes	Yes	No	No	Yes	No	No	No	Yes
Madhumita Nandi et al., 2013	No	No	No	Yes	Yes	Yes	No	Yes	No	No	No	Not mentioned
David Ríos et al., 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Not mentioned
Min Kwam Kim et al., 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned
Gi Young Choi et al., 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Not mentioned

of symptoms is crucial. Regular liver function monitoring is essential, as subclinical cases may progress to symptomatic hepatotoxicity if untreated.

Diagnostic approaches should include a thorough drug history, exclusion of alternative causes of liver dysfunction, and, when indicated, imaging or liver biopsy to rule out structural or immune-mediated conditions. Shen et al. emphasized that establishing a causal relationship using algorithms like RUCAM is critical for accurate diagnosis [28].

Risk Factors and High-Risk Populations

Our study identified self-medication and lack of medical supervision as major risk factors, particularly among pediatric populations. Children are more vulnerable to DILI due to developmental differences in liver enzyme systems and their smaller therapeutic windows, as noted in reviews of pediatric drug safety [29]. In adults, pre-existing liver disease, prolonged or repeated courses of albendazole, and the concomitant use of hepatotoxic medications are significant risk factors.

Clinicians must assess the risk profile of each patient before prescribing albendazole. Baseline liver function evaluation is particularly important in patients with chronic liver diseases, alcohol use disorder, or comorbidities that increase susceptibility to hepatic injury. Educating caregivers and patients on the importance of adhering to prescribed doses is paramount, especially in settings where over-the-counter access to albendazole is common.

Management Strategies

Acute Management. Early identification and discontinuation of albendazole are critical in managing DILI. Our study demonstrated that supportive care, including hydration, nutritional support, and symptomatic treatment, resulted in favourable outcomes in most cases. This aligns with Suk et al., who noted that prompt drug withdrawal often leads to complete recovery in mild-to-moderate cases [30].

For severe cases presenting with jaundice or coagulopathy, inpatient monitoring is recommended to manage complications such as hepatic encephalopathy or bleeding disorders. In rare instances of acute liver failure, advanced therapies, including corticosteroids or plasmapheresis, may be required, as documented in García-Cortés et al.'s analysis of severe DILI cases [31].

Re-exposure Considerations. Our findings reinforce the risks associated with re-exposure to albendazole, which can result in rapid and severe hepatotoxicity. Björnsson et al. emphasized that detailed drug histories and patient counselling are critical to preventing recurrence [32]. Patients must be educated about the potential risks and advised to avoid re-exposure unless no alternative treatments are available and benefits outweigh the risks.

Preventive Strategies

Monitoring Protocols. Establishing a robust monitoring protocol is essential to reduce the burden of albendazole-induced DILI. Andrade et al. recommend baseline and periodic liver function tests (LFTs) during therapy, particularly in high-risk populations such as children, the elderly, and patients with comorbidities [33]. In our study, periodic LFT monitoring allowed for early detection of subclinical hepatotoxicity, facilitating timely intervention.

Public Health Interventions. Public health campaigns focusing on the risks of self-medication and the importance of medical supervision are crucial, especially in regions with high albendazole use for mass drug administration programs. Incorporating community-based education programs can improve awareness among caregivers and patients, reducing the incidence of DILI.

Individualized Therapy. Tailoring albendazole therapy based on individual risk factors, including genetic predisposition, age, and comorbid conditions, can mitigate hepatotoxicity. Future research should aim to identify genetic markers of susceptibility to albendazole-induced DILI, as pharmacogenomic studies have shown promise in predicting adverse drug reactions [33].

Implications for Pediatric and Adult Care

Albendazole-induced DILI presents unique challenges in pediatric and adult populations. In children, the immature hepatic metabolism and smaller therapeutic windows necessitate cautious dosing and stringent monitoring. Conversely, in adults, comorbidities such as non-alcoholic fatty liver disease (NAFLD) and polypharmacy increase the risk of hepatotoxicity. Clinicians should adopt a holistic approach that includes patient education, routine monitoring, and multidisciplinary collaboration to manage complex cases.

Future Directions

While our study provides valuable insights, further research is needed to:

1. Explore the pathophysiology of albendazole-induced DILI at the molecular level.
2. Investigate the role of genetic predisposition in susceptibility to hepatotoxicity.
3. Develop evidence-based guidelines for monitoring and managing albendazole-induced DILI in specific populations.

Integrating these findings into clinical practice will enhance patient safety and outcomes, particularly in resource-limited settings where albendazole use is widespread.

■ CONCLUSION

This systematic review provides compelling evidence that albendazole-induced liver injury represents a significant clinical concern requiring careful consideration in both individual patient care and public health programs. The synthesis of case reports alongside pharmacovigilance data and cohort studies has revealed several critical insights: the idiosyncratic nature of the hepatotoxicity, the variable latency period, and the range of severity from mild enzyme elevations to acute liver failure. The disproportionate reporting of serious hepatic adverse events with albendazole compared to other anthelmintics, coupled with the significant proportion of cases involving unsupervised use, calls for a renewed approach to risk management. Future research efforts should focus on identifying genetic or environmental factors that may predispose individuals to albendazole-induced liver injury, developing biomarkers for early detection, and establishing evidence-based protocols for prevention and management. These advances will be crucial in optimizing the risk-benefit ratio of albendazole therapy while maintaining its vital role in global health programs.

The challenges highlighted in this review underscore the need for enhanced pharmacovigilance and international collaboration in monitoring drug safety. By

understanding and addressing these challenges, we can work toward maximizing the therapeutic benefits of albendazole while minimizing the risk of serious adverse events.

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