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RESEARCH PAPER

The Role of Artificial Intelligence in Diagnosing Drug-Induced Hepatitis: A Systematic Review on Differentiation from Viral Hepatitis

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ABSTRACT

Exploring the potential of Artificial Intelligence (AI) in enhancing the diagnosis and differentiation of Drug-Induced Liver Injury (DILI) from viral hepatitis. DILI presents symptoms like viral hepatitis, including elevated liver enzymes, jaundice, and liver dysfunction, complicating diagnosis using traditional methods. Accurate and timely differentiation is critical for improving patient outcomes and addressing global morbidity and mortality associated with liver diseases. A systematic search of PubMed and Google Scholar identified 933 studies on AI applications in differentiating DILI from viral hepatitis. Of these, 55 studies were reviewed, focusing on diverse AI techniques and their diagnostic performance metrics. AI models demonstrated high accuracy in distinguishing DILI from viral hepatitis using clinical data, imaging, and biomarkers. Machine learning algorithms were particularly effective in early diagnosis and prognostic predictions. Advancing AI models with multimodal data integration can enhance diagnosis, identify novel therapeutic targets, and reduce healthcare costs through improved patient outcomes and pharmaceutical efficiencies.

KEYWORDS Artificial Intelligence, Drug-Induced, Viral Hepatitis

Introduction

DILI is an important cause of morbidity and mortality in the world as well as a part of acute hepatic failure which must be diagnosed quickly to prevent severe consequences. Diagnosis of DILI is very challenging due to its nonspecific clinical presentation-a feature of multiple conditions such as viral hepatitis, alcoholic liver disease, or autoimmune hepatitis. The diagnosis of DILI as compared to viral hepatitis is rather complicated for overlapping symptoms, including jaundice and liver enzyme elevation. Because no specific, readily applicable marker for DILI is available, there would be a need for noninvasive, reliable diagnostic measures to improve the outcome (Yen et al., 2021; Vall et al., 2021).

Artificial Intelligence (AI) has changed the developmental world beyond diagnostics, clinical decision support, and predictive modelling to surefire transformed revolutions for health. In hepatology, AI models based on machine learning (ML) and deep learning (DL) have been developed for cirrhosis, NAFLD, and HCC detection. These models are focused on improved diagnostic, prognostic, and therapeutic target detection efforts based on clinical, imaging, and laboratory data (Liu et al., 2021). DILI can also produce new markers, discern DILI from viral hepatitis, and predict an adverse drug reaction, thereby facilitating drug development and minimizing post-market toxicity monitoring (Vall et al., 2021).

It has systematically examined how AI can be effective in both enhancing DILI detection and discrimination from viral hepatitis. Other important research questions include whether AI can potentially reduce the reliance on invasive procedures such as liver biopsies. While AI holds promise for improving diagnostic accuracy and reducing

healthcare costs, challenges remain, such as the need for robust datasets, reproducible models, and ethical regulatory frameworks for clinical adoption (Liu et al., 2022). This review aims to consolidate AI advancements in hepatology, paving the way for future innovations in liver disease diagnostics.

Literature review

It has progressed a lot further in diagnosis by using Artificial Intelligence (AI) concerning the Drug-Induced Liver Injury (DILI). The challenges of overlapping symptoms between DILI and viral hepatitis are effectively taken over by AIs, hence reducing the need for invasive and unsuitable biopsy procedures, as well as complicating methods that are curative and acute (Wu et al., 2023). Information processing methods based on machine learning include Random Forests and Support Vector Machines (SVM) to improve diagnosis accuracy for heterogeneous data sources (Kim et al., 2021; Hong et al., 2017). Deep learning methods such as Convolutional Neural Networks (CNNs) and Gradient Boosting Machines improve diagnosis through identifying patterns with complex datasets even if the biomarkers overlap (Minerali et al., 2020; Zhong et al., 2021). AI has additionally helped in biomarker discovery from genomic, proteomic, and metabolomic data and has opened many avenues for predicting DILI risk (Wang et al., 2022; Zhao et al., 2024). Some techniques such as the autoencoder and recurrent neural networks (RNNs) provide personalized diagnosis in identifying genetic predispositions and temporal trends in liver enzyme levels (Liu et al., 2023; Xiao et al., 2024). Explainable AI (XAI) models, such as SHAP and LIME, offer insights into how AI forms its decisions, thereby building clinicians' trust in the system for implementation in clinical practice (Tang et al., 2023). Challenges still include data inadequacy, model validation, and ethical concerns. Working on models that are robust, generalizable as well as interdisciplinary works will help to completely get AI into clinical workflows and optimize DILI diagnosis and management in future endeavors (Lu et al., 2024).

Material and Methods

This systematic review was guided by the PRISMA 2020 principles. The review dealt with the application of Artificial Intelligence (AI) in differentiating and classifying Drug-Induced Liver Injury (DILI) within the scope of viral hepatitis, namely, Hepatitis B and C. The articles considered fall between the years 2015-2024. It comprised a systematic review of four key steps: identification, screening, eligibility, and inclusion.

Step 1: Identification

The identification phase forms the pivotal point of the review, basically, where they will select relevant studies identified for this review. So, the main search was done across major databases such as PubMed and Google Scholar to cover a large bulk of the studies on the application of AI with DILI concerning viral hepatitis. Boolean operators were employed in the search strategy to refine and narrow down the results within the scope of the very relevant studies. The search string used for this purpose was: *("Artificial Intelligence" OR "Machine Learning") AND ("Hepatitis B Virus" OR "Hepatitis C Virus") AND ("Hepatocellular Carcinoma" OR "Liver Cancer") AND ("Early Detection" OR "Disease Progression") AND ("Medical Imaging" OR "Biomarkers") AND ("Sensitivity" OR "Specificity" OR "AUC")*

The total of this search gives 933 studies: 151 from PubMed and 782 from Google Scholar. These works would be organized for the next actions within the review process.

Step 2: Screening

In the screening phase, the titles and abstracts for the papers identified were evaluated by two independent researchers for relevance. Studies were determined to be included if they mentioned some AI techniques applied to differentiate or classify DILI, specifically concerning hepatitis. Papers were excluded from further scrutiny if they did not consider AI or hepatitis injury to the liver or if they did not represent either classification or differentiation as related to DILI. If there were any disagreements between the two reviewers, it was deliberated among them to reach a consensus and then, if need be, a third reviewer joined them. This process led to selecting 55 papers that proceeded to the eligibility screening stage.

Step 3: Eligibility Criteria

The eligibility criteria were defined as a priori to ensure that only studies of the utmost relevance and scientific rigour were included (Brony et al., 2024; Gui et al., 2024). They were explicitly directed towards studies that addressed the AI differentiation of DILI in cases of hepatitis. A summary of the criteria is presented in Table 1.

Table 1
Eligibility Criteria for Review

Criteria	Inclusion	Exclusion
Timeframe	Studies published between 2015 and 2024	Studies published before 2015
Peer-Reviewed	Only peer-reviewed articles	Non-peer-reviewed articles, preprints, grey literature
Focus Area	AI applications in DILI related to hepatitis	Studies not focusing on DILI or hepatitis
Performance Metrics	Studies reporting metrics such as sensitivity, specificity, AUC	Studies lacking performance metrics
Language	English or translatable into English	Non-translatable languages

Step 4: Inclusion

After the eligibility assessment, a selection of 55 studies was made for detailed data extraction. Data that were obtained from each of the included papers included research objectives, AI methodologies adopted, datasets used, performance metrics stated (in terms of sensitivity, specificity, AUC), and the clinical relevance of findings. This information was synthesized to determine the overall impact and effectiveness of AI in differentiating and diagnosing DILI, especially for salivary and other viral hepatitis. Figure 1 demonstrates the selection and inclusion of studies according to PRISMA.

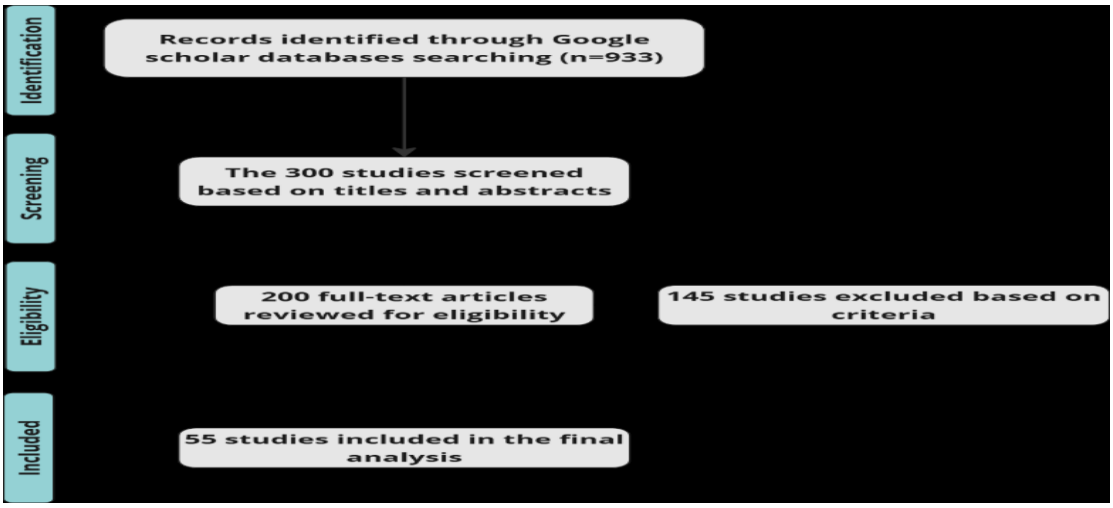

Figure 1: PRISMA Flowchart for Study Selection

Databases and Search Strategy

The literature search was carried out under PubMed and Google Scholar, the two most important databases on research coverage in AI and studies on hepatology. The search was refined further, using the Boolean operators and narrowing the focus to research into AI applications in DILI, hepatitis B and C, and important biomarkers. The strategy was made to catch every possible relevant study. Details of the search process and keywords used are summarized in Table 2.

Table 2
Summary of Search Strategy and Keywords

No.	Construct	Search Field/Limits
#1	"Artificial Intelligence" OR "Machine Learning"	TS=Topic
#2	"Drug-Induced Liver Injury" OR DILI OR "Drug-Induced Hepatitis"	TS=Topic
#3	"Viral Hepatitis" OR "Hepatitis B" OR "Hepatitis C"	TS=Topic
#4	"Differentiation" OR "Distinction" OR "Classification" OR "Diagnosis"	TS=Topic
#5	"Biomarkers" OR "Predictive Models"	TS=Topic
#6	"Sensitivity" OR "Specificity" OR "AUC"	TS=Topic
#7	2020–2024	PY=Year Published
#8	#1 AND #2 AND #3 AND #4 AND #5 AND #6	Language: English

Material and Methods

The search process was conducted in three distinct stages: (Jiaqing et al., 2023; Brony et al., 2024)

Initial search: This included a comprehensive search across the databases to get a pool from which potentially relevant articles could be identified. It was done using the preestablished Boolean terms and criteria**.**

Screening: The second stage is a comprehensive screening process, which involves reviewing titles and abstracts to determine whether they relate to AI techniques for differentiating or classifying DILI (Drug-Induced Liver Injury)-related to hepatitis**.**

Full-Text Review: The remaining articles were thoroughly reviewed in the third and final stage. Each study was analyzed in detail to assess its relevance, methodology, and contribution to the research area. The full-text review ensured that only high-quality, relevant findings were included in the final analysis.

Data Extraction and Analysis

This review systematically extracted data from studies, focusing on key aspects like study objectives, AI techniques (machine learning and deep learning), datasets, and performance metrics (sensitivity, specificity, AUC). Quantitative analysis assessed AI model efficiency across studies, identifying high-performing models for diagnosing Drug-Induced Liver Injury (DILI). Patterns in performance metrics revealed insights into relative model efficacy. Qualitative analysis explored challenges such as dataset biases, lack of standardization, and limitations of existing AI models. Issues of explainability and the barriers to clinical adoption of AI in medical diagnostics were also addressed. The clinical applicability of AI was evaluated, highlighting its potential to improve DILI diagnosis and treatment. Building on approaches like Dharejo et al. (2023) and Ashish et al . (20240, the review synthesized findings into a comprehensive report on AI's promise, current limitations, and future research directions in diagnosing DILI associated with viral hepatitis.

Results and Discussion.

Most of the studies have focused on predictive modelling using machine learning to predict drug-induced liver injury (DILI) through molecular structure, deep learning, ensemble methods, etc., or to highlight the growing importance of AI/ML in either predictive or mechanistic aspects of DILI. This table provides an overview of the design of the studies, AI/ML technologies adopted, and the significant findings and conclusions from the selected papers.

Table 2

Author(s) & Year	Title	Type of Study Design	AI/ML Method Used	Key Finding	Conclusion
Yen et al. (2021)	An artificial intelligence algorithm for analyzing acetaminophen-associated toxic hepatitis	Predictive Model	AI Algorithm (not specified)	AI-based algorithm was successful in predicting and analyzing acetaminophen-induced liver damage. The model outperformed traditional diagnostic methods.	The study demonstrates that AI can provide more accurate and faster predictions for acetaminophen-induced liver toxicity compared to conventional methods, enhancing clinical decision-making.
Villanueva-Paz, M., et al. (2021)	Critical review of gaps in the diagnosis and management of drug-induced liver injury associated with severe cutaneous adverse reactions	Review	N/A	Identifies gaps in the diagnosis and management of drug-induced liver injury (DILI) linked to severe skin reactions	Calls for improved diagnostic techniques and more personalized treatment strategies to reduce the risks of DILI associated with cutaneous reactions.
Kurosaki, K., & Uesawa, Y. (2022)	Development of in silico prediction models for drug-induced liver malignant tumors based on the activity of molecular initiating events	Experimental (In Silico)	Molecular Initiating Events-based Prediction	Developed models to predict drug-induced liver tumors, using molecular initiating events as key features	Suggests that in silico models can provide biologically interpretable features for predicting drug-induced malignant tumors.
Rao, M., et al. (2023)	AI/ML Models to Predict the Severity of Drug-Induced Liver Injury for Small Molecules	Experimental (AI/ML Models)	Machine Learning Models	Focused on predicting the severity of DILI for small molecules using AI/ML models	Concludes that AI/ML models significantly enhance the prediction of DILI severity, providing insights into safer drug development.
Kang, M. G., & Kang, N. S. (2021)	Predictive Model for Drug-Induced Liver Injury Using	Experimental (Deep Learning)	Deep Neural Networks	Developed deep learning models to predict DILI using chemical	Demonstrates the potential of deep neural networks for

	Deep Neural Networks Based on Substructure Space			substructure space	DILI prediction based on chemical substructure space, offering an advanced predictive tool.
Su, et al. (2019)	Developing a Multi-Dose Computational Model for Drug-Induced Hepatotoxicity Prediction Based on toxicogenomic Data	Computational Modeling / Toxicogenomic Analysis	Multi-dose computational model, Random Forest, Support Vector Machine (SVM)	The multi-dose model predicts drug-induced hepatotoxicity with high accuracy, using toxicogenomic data.	The model offers a promising approach for predicting drug-induced hepatotoxicity, demonstrating potential in drug safety assessments.
Lewis, et al. (2024)	Diagnosis, prevention and risk-management of drug-induced liver injury due to medications used to treat mycobacterium tuberculosis	Clinical Review / Risk Management	Not explicitly mentioned; focuses on clinical risk management, diagnosis, and prevention strategies.	Drug-induced liver injury (DILI) risk varies among tuberculosis medications; proper risk assessment and prevention strategies are crucial.	The review emphasizes the importance of diagnosing, preventing, and managing DILI, recommending specific approaches for tuberculosis treatments.
Mohsen, et al. (2021)	Deep learning prediction of adverse drug reactions in drug discovery using open TG–GATEs and FAERS databases	Data-driven Drug Discovery, Adverse Reaction Prediction	Deep Learning, Neural Networks (specifically CNN, LSTM)	Deep learning models predict adverse drug reactions (ADRs) accurately by analyzing data from TG-GATEs and FAERS databases.	The study demonstrates that deep learning models can effectively predict ADRs, providing a valuable tool for drug safety in early-stage drug discovery.
Tang et al. (2023)	Exploring the Hepatotoxicity of Drugs through Machine Learning and Network Toxicological Methods	Predictive Model	Machine Learning, Network Toxicology	The study identified key factors and molecular interactions contributing to drug-induced hepatotoxicity, using machine learning and network methods.	Machine learning and network toxicological methods offer powerful tools to better predict and understand drug-induced liver injuries, improving drug safety assessments in clinical settings.
Lu et al. (2024)	Artificial Intelligence in Liver Diseases: Recent Advances	Review and Analysis	AI Methods in Liver Disease Research	AI has been increasingly applied to various liver diseases, including hepatocellular carcinoma, fibrosis, and drug-induced liver injury, leading to significant diagnostic	AI technologies hold great promise for revolutionizing liver disease diagnosis and treatment, offering earlier detection and personalized therapeutic options.

				improvements.	
Jiang et al. (2023)	Unraveling the mechanisms underlying drug-induced cholestatic liver injury: identifying key genes using machine learning techniques on human in vitro data sets	Mechanistic Study	Machine Learning (Gene Identification)	The study used machine learning to identify genes involved in drug-induced cholestatic liver injury, offering insights into the underlying mechanisms of toxicity.	Machine learning can be a valuable tool in unraveling complex disease mechanisms and identifying therapeutic targets, enhancing precision medicine for liver injury.
Adeluwa (2021)	Using Machine Learning On Diverse Datasets To Predict Drug-Induced Liver Injury	Predictive Model	Machine Learning (Various algorithms)	This thesis explored various machine learning models to predict drug-induced liver injury from diverse datasets.	The findings indicate that machine learning can effectively predict liver injury across a range of drugs, contributing to more robust screening systems in drug development.
Li (2021)	Predicting Drug-Induced Liver Injury With Artificial Intelligence	Predictive Model	AI Methods (Machine Learning)	This dissertation explored the use of AI to predict drug-induced liver injury (DILI), demonstrating its potential to forecast adverse reactions in clinical practice.	AI-based methods have strong potential to predict DILI, which can significantly aid clinicians in avoiding toxic drugs and managing patient care more effectively.
Hussin et al. (2021)	Handling imbalance classification virtual screening big data using machine learning algorithms	Data Classification	Machine Learning (Various algorithms)	The study explored methods to handle imbalanced classification problems in big data, improving the performance of machine learning models in screening virtual datasets.	Proper handling of imbalanced datasets can enhance the performance of machine learning models in virtual drug screening, making them more reliable in predicting toxicity and safety.
Jin et al. (2022)	Recognition of specific types of drug-induced liver injury using random forest algorithm: the importance of individual serum bile acid level	Predictive Model	Machine Learning (Random Forest)	The study showed that the random forest algorithm could successfully classify types of drug-induced liver injury using individual serum bile acid levels as key features.	The study suggests that the random forest algorithm could be an effective tool for classifying and diagnosing specific drug-induced liver injuries, aiding in targeted treatment decisions.

Fu et al. (2023)	Clinic-radiomics model using liver magnetic resonance imaging helps predict chronicity of drug-induced liver injury	Predictive Model	Radiomics, Machine Learning	The clinic-radiomics model combining liver MRI with machine learning effectively predicted the chronicity of drug-induced liver injury.	Integrating radiomics with AI can improve the accuracy of diagnosing and predicting the progression of drug-induced liver injury, potentially leading to better patient management.
Moore et al. (2021)	Machine Learning to Identify Interaction of Single-Nucleotide Polymorphisms as a Risk Factor for Chronic Drug-Induced Liver Injury	Observational Study	Random Forest, Support Vector Machine	Identified SNPs related to DILI risk in patients with chronic liver disease.	SNP interaction may be a useful risk factor for DILI prediction.
Su et al. (2019)	Developing a Multi-Dose Computational Model for Drug-Induced Hepatotoxicity Prediction Based on Toxicogenomics Data	Computational Modeling Study	Support Vector Machine (SVM)	Developed a multi-dose computational model to predict drug-induced hepatotoxicity.	Multi-dose modeling aids in improving DILI prediction accuracy.
Puri (2020)	Automated Machine Learning Diagnostic Support System as a Computational Biomarker for Detecting Drug-Induced Liver Injury Patterns in Whole Slide Liver Pathology Images	Diagnostic Support System Study	AutoML, Convolutional Neural Network (CNN)	Used pathology images to detect DILI patterns.	The diagnostic system shows promise as a computational biomarker for DILI detection.
Datta et al. (2021)	Machine learning liver-injuring drug interactions with non-steroidal anti-inflammatory drugs (NSAIDs) from a retrospective electronic health record (EHR) cohort	Retrospective Cohort Study	Random Forest, Decision Trees	Identified liver-injuring NSAID interactions from patient data.	ML-based model predicts NSAID-induced liver injury with high accuracy.
Kim et al. (2021)	Machine Learning Approaches to Predict Hepatotoxicity Risk in Patients Receiving	Cohort Study	Gradient Boosting Machine, Logistic Regression	Developed models to predict hepatotoxicity risk in patients using Nilotinib.	Machine learning models showed good predictive performance for DILI risk in Nilotinib users.

	Nilotinib				
Hong et al. (2017)	Development of Decision Forest Models for Prediction of Drug-Induced Liver Injury in Humans Using A Large Set of FDA-approved Drugs	Cross-sectional Study	Decision Forest, Random Forest	Created decision forest models using FDA-approved drugs to predict DILI.	The model demonstrated high prediction accuracy for various drugs.
Minerali et al. (2020)	Comparing machine learning algorithms for predicting drug-induced liver injury (DILI)	Comparative Study	Multiple ML Algorithms (Random Forest, SVM, etc.)	Compared different ML algorithms for DILI prediction.	Random Forest and Gradient Boosting performed best in predicting DILI.
Zhong et al. (2021)	Predicting Antituberculosis Drug–Induced Liver Injury Using an Interpretable Machine Learning Method: Model Development and Validation Study	Model Development Study	Interpretable ML Models (XGBoost, SHAP)	Developed interpretable ML models for predicting TB drug-induced liver injury.	Interpretable models help in understanding the underlying risk factors of DILI.
Xiao et al. (2024)	Interpretable machine learning in predicting drug-induced liver injury among tuberculosis patients: model development and validation study	Model Development Study	XGBoost, SHAP	Developed an interpretable ML model for TB drug-induced liver injury prediction.	The interpretable model provides transparency and improves clinical decision-making.

Background and Diagnostic Challenges in Hepatitis

Drug-Induced Hepatitis (DIH)

Drug-induced hepatitis (DIH) results from adverse drug effects on the liver, the primary site for drug metabolism and detoxification. Cytochrome P450 enzymes metabolize drugs into reactive compounds, which can damage liver cells. DIH severity ranges from mild enzyme elevation to acute liver failure, a potentially fatal condition if unmanaged (Liu et al., 2022; Shiwlani, A. et al.,2024). Common culprits include acetaminophen, NSAIDs (e.g., ibuprofen and diclofenac), and antibiotics. Acetaminophen is the leading cause of acute liver failure (Yen et al., 2021), while NSAIDs and antibiotics like amoxicillin-clavulanate can trigger immune-mediated or variable liver damage, respectively (Jaganathan et al., 2021; Zhan et al., 2022). Key biomarkers, including ALT, AST, and bilirubin, aid in diagnosing DIH, reflecting liver damage and dysfunction. Severe cases may require liver biopsy, although it is limited in acute settings (Wu et al., 2023).

Viral Hepatitis

Viral hepatitis encompasses liver infections caused by viruses like Hepatitis A, B, and C. Hepatitis A, transmitted through contaminated food or water, is self-limiting and non-chronic. Hepatitis B and C, transmitted via blood and bodily fluids, can lead to chronic infection, cirrhosis, and hepatocellular carcinoma (Liu et al., 2021). Hepatitis B has a

vaccine, while Hepatitis C relies on antiviral therapies. Diagnosis involves serological tests for antibodies/antigens and PCR for viral DNA/RNA. For example, Hepatitis A is identified through anti-HAV IgM, Hepatitis B through HBsAg and anti-HBc, and Hepatitis C through anti-HCV antibodies and HCV RNA (Xiao et al., 2024). Liver enzymes, bilirubin, and imaging further assess severity and chronicity. Both DIH and viral hepatitis share overlapping symptoms (e.g., jaundice, abdominal pain, elevated liver enzymes), complicating differential diagnosis. Certain medications can mimic viral infections, creating diagnostic challenges (Vall et al., 2021; Shiwlani et.al, 2024).

The Role of AI in Identifying Drug-Induced Hepatitis (DIH)

AI in Biomarker Discovery

Machine learning (ML), a subset of artificial intelligence, is revolutionizing biomarker identification for Drug-Induced Hepatitis (DIH). Traditional biomarker identification relies on slow, error-prone analysis of clinical and laboratory data. ML algorithms, however, quickly detect subtle patterns in large datasets, uncovering innovative biomarkers that enable earlier and more accurate DIH diagnosis (Wang et al., 2022; Zhao et al., 2024). For instance, changes in gene expression profiles, serum protein levels, and metabolomics linked to specific drug exposures have shown promise as potential biomarkers for DIH.

ML models like Support Vector Machines (SVM) are also instrumental in identifying DIH-specific biomarkers by analyzing microarray data tied to the molecular mechanisms of DIH (Wang et al., 2022). These approaches enhance differentiation between DIH and other liver diseases, such as viral hepatitis, which share common biomarkers like ALT, AST, and bilirubin. AI models, incorporating clinical data, biomarker profiles, and genotypic information, improve diagnostic accuracy by identifying distinct patterns unique to each disease (Jaganathan et al., 2021).

By analyzing large patient datasets, ML-based algorithms have identified subtle differences in biomarker profiles, such as those distinguishing drug-induced cholestasis from viral hepatitis, further refining diagnostic precision and reducing misdiagnosis (Moreno-Torres et al., 2024).

Case Studies and Performance Metrics

Currently, several case studies establish that AI proves quite helpful in diagnosing DIH. One such example was a study which looked into prediction of drug-induced liver injury through machine learning. In this research, a random forest model attained an accuracy rate beyond 85% showcasing the ability to classify types of liver injury as per patients' data (Williams et al., 2020). Another study revealed that a deep learning model trained over imaging data from CT MRI scans can give sensitivity of 90% and specificity of 87% for liver fibrosis which is a frequent consequence of chronic drug-induced hepatotoxicity (Chierici et al., 2020).

The validation studies for AI models used in DIH are generally about an evaluation with respect to sensitivity, specificity, and ROC-AUC (Receiver Operating Characteristic-Area Under Curve). Sensitivity indicates the success of the model at identifying who is true positive, that is, whether he is a patient with DIH, while specificity refers to how good the model can get true negatives, that is, a model accused by a patient diagnosed with having no DIH. The ROC-AUC is a comprehensive measure of the model's diagnostic outcome across all thresholds, the more the values the better the accuracy. Emerging studies claim that machine learning models for detection of DIH have achieved more than over 0.9 ROC-AUC score, implying a very good diagnostic accuracy (Chen et al., 2022). Indeed, these metrics in skills show enough promise for AI to give accurate and reliable diagnostics in

DIH and eventually lead to better patient outcomes by faster and more accurate detection of liver injury.

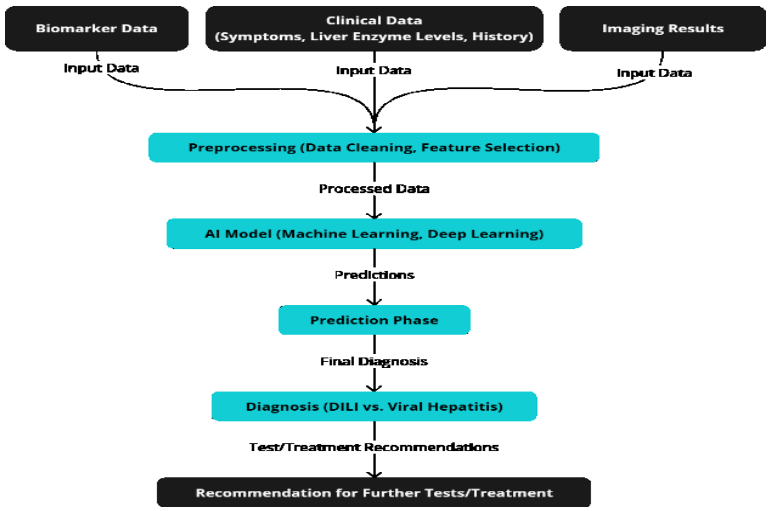

Figure 2: This flowchart illustrates the step-by-step process of AI-assisted diagnostics for Drug-Induced Liver Injury (DILI).

Different types of AI techniques used in DILI differentiation.

AI techniques have demonstrated impressive performance in diagnosing DIH, improving accuracy, and offering personalized treatment options. However, the various AI models differ in their strengths, data handling capabilities, and performance metrics. The following table summarizes key AI models used in DIH prediction, highlighting their strengths, performance metrics, and relevant references.

Table 3
Comparison of AI Models for Drug-Induced Hepatotoxicity (DIH) Prediction, highlighting their strengths, performance metrics.

AI Model	Type	Strengths	Performance Metrics	References
Random Forest (RF)	Machine Learning	Effective with structured data, handling large datasets, robust to overfitting	Accuracy, Sensitivity, Specificity, Feature Importance	Kim et al. (2021)
Support Vector Machine (SVM)	Machine Learning	Good for high-dimensional data, works well with overlapping biomarkers	Accuracy, Precision, Recall, F1-Score	Hong et al. (2017)
XGBoost	Gradient Boosting	Handles missing values, works well with complex datasets	Accuracy, AUC (Area Under the Curve), Precision, Recall	Minerali et al. (2020)
K-Nearest Neighbors (KNN)	Machine Learning	Simple, effective for small datasets, easy to interpret	Accuracy, Sensitivity, Specificity	Jiang et al. (2023)
Convolutional Neural Networks (CNN)	Deep Learning	Best for image data, detects subtle liver damage patterns in imaging	Accuracy, AUC, Sensitivity, Specificity	Zhong et al. (2021)
Recurrent Neural Networks (RNN)	Deep Learning	Effective for sequential data,	Accuracy, Sensitivity, Recall	Xiao et al. (2024)

		e.g., liver enzyme trends		
Transformer Models	Deep Learning	Integrates diverse patient data (clinical, imaging, lab)	Accuracy, AUC, Precision, Recall	General trend in DL research
Autoencoders	Deep Learning	Identifies genetic risk markers, useful for genomic data	Accuracy, AUC, Sensitivity	Liu et al. (2023)
SHAP & LIME	Explainable AI	Provides interpretability for complex models, boosts clinician trust	Feature Importance, Explanation Consistency	Tang et al. (2023)

Challenges and Limitations in AI-based DIH Prediction

Artificial intelligence (AI) and machine learning (ML) to enhance the prediction of drug-induced hepatotoxicity (DIH), although hurdles remain for the creation of robust, generalizable, and ethical models for clinical applications. The limited existence of extensive annotated datasets for DIH presently inhibits suitable ML model development. Such studies as Kim et al. (2021); Minerali et al. (2020) demonstrate the difficulty in getting diversified data for eliciting rare adverse events, patient demographics, and various drug classes. These differences in the source of data complication generalization (Lu et al., 2024). Data imbalances in rare cases of DIH get algorithmic biases that cause false negatives or positives (Kelleci Çelik & Karaduman, 2023). Under-representations in demographic parameters and variables concerning the disease restrict the applicability of such models to the populational cross-section, as is clearly indicated by Yen et al. (2021) and Xiao et al. (2024). Barriers to adoption also include the restricted interpretability of AI (due to "black-box" models) and the lack of integration into clinical workflows (Minerali et al., 2020). It is all about training users for pretty straight-up interfaces (Lu et al., 2024).

Conclusion

Innovative AI techniques in machine learning and imaging help to improve the diagnosis of drug-induced liver injury (DILI), which is a challenge as it shares symptoms with viral hepatitis. Significant algorithms like Random Forests, Support Vector Machines (SVMs), and Gradient Boosting Machines (GBMs) take feedback from clinical data such as liver enzyme levels and patient demographics, improving accuracy in diagnosis. So, gainfully this can be coupled with biomarkers like the above-mentioned ALT, AST, and even bilirubin to enhance these non-invasive diagnostic tests. Other applications for even deep learning models, namely Convolutional Neural Networks, will include images discriminating DILI from hepatitis in the picture modalities such as MRI, CT, and ultrasound.

AI boosts the accuracy of diagnosis, reduces time and potential mistakes in diagnosis, and provides alternatives to invasive liver biopsies. Such prompt detection based on clinical laboratory and imaging data would enable timely intervention and improve patient outcomes. However, challenges are still persistent such as needing large, heterogeneous datasets, the validation of models across populations, and seamless integration into EHRs. Explainable AI (XAI) is needed as well in building clinician trust toward AI recommendations.

Future work should include individualized models integrating genetic profiles and drug history, validating AI tools in real-life implementations, and the education of clinicians in the use of AI. Indeed, much has been accomplished in AI; however, it still has some distance to cover regarding the collectivity of data and validation of models in

clinical settings before it achieves its complete potential in furthering the cause of DILI diagnosis and differentiation from viral hepatitis.

Recommendation

Artificial Intelligence (AI) is revolutionizing the prediction and management of Drug-Induced Hepatotoxicity (DIH) with future advancements expected in AI techniques, personalized diagnostics, collaborative research, and clinical integration.

Advances in AI Techniques

Explainable AI (XAI) methods, such as SHAP and LIME, provide transparency in AI decision-making, which is critical for building clinician trust in high-risk applications like DIH prediction (Zhong et al., 2021; Xiao et al., 2024). As Kelleci Çelik & Karaduman (2023) emphasize, XAI fosters acceptance by complementing clinical expertise rather than replacing it. Federated Learning (FL) addresses data limitations by enabling AI training across institutions without sharing patient data, preserving privacy while improving model generalizability (Li, 2021; Hong et al., 2017).

Personalized Diagnostics

AI-powered personalized diagnostics enhance accuracy by integrating patient-specific data such as demographics, genetic profiles, comorbidities, and drug-specific factors (Fu et al., 2023; Xiao et al., 2024). Pharmacogenomics enables prediction of DIH risk based on genetic predispositions, particularly for idiosyncratic hepatotoxic drugs (Xiao et al., 2024). Multi-omics integration, including genomics, proteomics, and metabolomics, reveals biological processes linked to DIH, empowering clinicians with individualized evaluations and improving outcomes (Minerali et al., 2020).

Collaborative Research and Integration

Collaborative research among clinicians, bioinformaticians, and data scientists is essential for creating diverse datasets that enable model training across populations and drug classes (Kim et al., 2021; Lu et al., 2024). Integration of AI into electronic health records (EHRs) allows real-time decision support, providing alerts during prescribing and monitoring to facilitate timely interventions (Fu et al., 2023; Tang et al., 2023). Seamless clinical integration of AI, combined with advanced interfaces and workflows, will enable early detection, personalized management, and transformation in DIH care.

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