ISSN: 2752-3829 Vol. 3 No.2, (December, 2023)

Stochastic Modelling and Computational Sciences

REVIEW OF MACHINE LEARNING BASED TECHNIQUES FOR LIVER DISEASE DIAGNOSIS

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ABSTRACT
The advancement of machine learning (ML) has revolutionized the field of medical diagnostics, offering unprecedented opportunities for the early and accurate detection of liver diseases. This review paper provides a comprehensive synthesis of recent advancements in machine learning (ML) techniques for diagnosing liver diseases, examining the application of various algorithms such as support vector machines, neural networks, decision trees, and ensemble models. It highlights the effectiveness of supervised, unsupervised, and reinforcement learning approaches in improving diagnostic accuracy and predicting disease progression. Additionally, the paper addresses practical challenges in implementing these ML systems, including data quality, feature selection, and model interpretability, while evaluating their clinical relevance and impact in real-world healthcare settings. By offering insights into the current state and future prospects of ML in liver disease diagnosis, this review aims to inform and guide ongoing research and clinical practice in this field.

Keywords: Liver diseases, Machine learning, Deep learning, CNN, SVM

INTRODUCTION
Liver diseases are a significant health concern globally, with varying trends observed in different regions, including India. These diseases encompass a range of conditions such as hepatitis, cirrhosis, and liver cancer, each contributing to substantial morbidity and mortality. Globally, liver diseases are responsible for approximately 2 million deaths annually, with liver cirrhosis and liver cancer being the primary contributors. Chronic liver diseases, particularly those caused by hepatitis B and C, remain major public health issues. The World Health Organization (WHO) estimates that 325 million people worldwide are living with chronic hepatitis B and C infections, which are leading causes of liver cirrhosis and hepatocellular carcinoma (HCC). Non-alcoholic fatty liver disease (NAFLD) is another emerging global concern, closely linked to the obesity epidemic and metabolic syndrome [1]. This condition is particularly prevalent in developed countries but is rapidly increasing in developing nations as well. Additionally, alcohol-related liver disease continues to be a major cause of liver-related morbidity and mortality globally, especially in countries with high alcohol consumption rates.

In India, liver diseases are a growing health concern, with liver cirrhosis being one of the top ten causes of death. The country faces a significant burden from viral hepatitis, with an estimated 40 million people chronically infected with hepatitis B and 6 to 12 million with hepatitis C. Hepatitis E is also a major concern, particularly in rural areas where water sanitation is poor. NAFLD is becoming increasingly prevalent in India, paralleling the rise in obesity and diabetes. Studies suggest that nearly one-third of the urban population in India may be affected by NAFLD. Additionally, alcohol-related liver disease is a significant issue, particularly among males in rural areas, where alcohol consumption patterns are changing. India's healthcare system faces challenges in addressing these issues, including limited access to diagnostic facilities, public awareness, and availability of effective treatments [2-3].

When comparing trends in India to the global scenario, several similarities and differences emerge. While viral hepatitis remains a common challenge, the prevalence of hepatitis E is notably higher in India compared to developed countries. Conversely, the rapid rise of NAFLD in India mirrors global trends, underscoring the impact of lifestyle changes associated with urbanization and economic development. The future direction for combating liver diseases both globally and in India involves comprehensive strategies focusing on prevention, early diagnosis, and treatment. Increasing vaccination coverage for hepatitis B, improving water and sanitation facilities to prevent hepatitis E, and implementing public health campaigns to reduce alcohol consumption are critical [4-5]. Additionally, there is a need for enhanced screening programs for NAFLD and metabolic diseases. Leveraging advancements in medical technology, particularly ML and AI, can significantly improve diagnostic accuracy and treatment outcomes, ultimately reducing the burden of liver diseases worldwide.

The advent of machine learning (ML) has dramatically transformed numerous sectors, with healthcare being one of the most significantly impacted. Liver diseases, which pose a major global health challenge due to their high prevalence and mortality rates, have seen promising diagnostic advancements through ML applications. Presently, ML algorithms are being integrated into clinical practice to enhance the accuracy and speed of liver disease diagnosis. Techniques such as support vector machines, neural networks, decision trees, and ensemble methods have demonstrated substantial success in identifying liver conditions from complex datasets, outperforming traditional diagnostic methods [6-8]. These algorithms utilize vast amounts of medical data, including imaging, biochemical markers, and patient history, to detect patterns and anomalies indicative of liver disease. The incorporation of these advanced analytical tools in routine diagnostics has led to earlier detection, improved patient outcomes, and more personalized treatment plans.

In the past, liver disease diagnosis relied heavily on conventional methods such as blood tests, imaging studies, and liver biopsies, which, while effective, had limitations in terms of invasiveness, cost, and diagnostic accuracy. These traditional approaches often required significant time and expertise, potentially delaying critical treatment decisions. The emergence of ML-based techniques addressed these issues by providing faster, non-invasive, and more accurate diagnostic options. Early research focused on developing algorithms capable of distinguishing between various liver conditions, such as hepatitis, cirrhosis, and hepatocellular carcinoma, using structured and unstructured data. Moving forward, the future of liver disease diagnosis is poised to benefit even more from advancements in ML, particularly through the integration of deep learning and hybrid models that combine multiple ML techniques [9]. These models are expected to further enhance diagnostic precision, facilitate the discovery of novel biomarkers, and enable real-time monitoring of disease progression. Continued research and development, coupled with the accumulation of high-quality medical data, will be crucial in overcoming current challenges and fully realizing the potential of ML in liver disease diagnosis, ultimately leading to more effective and personalized healthcare solutions.

LIVER DISEASES

Liver disease encompasses a variety of conditions that impair the liver's ability to perform its vital functions, leading to significant health issues. The liver plays a crucial role in the body, including detoxification, protein synthesis, and the production of biochemicals necessary for digestion. When the liver is damaged or infected, these essential functions are compromised, impacting overall health. Hepatic disorder is another term used to describe liver disease, which includes a broad spectrum of complications that hinder the liver from fulfilling its roles. Even if only a quarter of the liver remains functional, the efficiency of this vital organ is markedly reduced [10]. The liver is the largest solid organ in the human body and is considered a gland because it produces and secretes bile. It is located in the upper right part of the abdomen, protected by the rib cage, and consists of two main lobes composed of smaller lobules. Liver cells receive blood from two distinct sources: the hepatic artery, which delivers oxygen-rich blood from the heart, and the portal vein, which supplies nutrient-rich blood from the intestines. Unlike most veins that carry blood to the heart, the portal vein transports nutrients from the digestive system to the liver for processing and purification before they enter the general circulation [11]. This process ensures that liver cells have the necessary chemicals to produce proteins, cholesterol, and glycogen, which are vital for normal body functions.

2.1 Chemical Compounds Based Diseases

The liver plays a crucial role in various physiological processes through the production and regulation of several chemical compounds, including bilirubin, albumin, alkaline phosphatase, aspartate aminotransferase, and globulins [12-13]. These compounds are integral to the daily operations and overall health of the liver, contributing to metabolic processes, detoxification, and homeostasis.

a) ***Bilirubin***: Bilirubin is a yellow compound that results from the normal breakdown of heme, which is a component of hemoglobin in red blood cells. It is excreted in bile and urine. Elevated levels of bilirubin can cause jaundice, a condition characterized by yellowing of the skin and eyes. Bilirubin contributes to the yellow coloration of bruises and the pigmentation of bile. Its breakdown products, such as stercobilin, give feces their brown color, while urobilin is responsible for the yellow color of urine.

b) ***Alkaline Phosphatase (ALP):*** This enzyme is present in all body tissues but is most concentrated in the liver, bile ducts, bones, kidneys, and placenta. In the serum, there are two primary types of alkaline phosphatase isozymes: skeletal and hepatic. In children, most alkaline phosphatase originates from the bones. Humans have several types of alkaline phosphatases:

ALPI: Found in the intestines.

- ALPL: A tissue-nonspecific isozyme present in the liver, kidney, and bone.
- ALPP: Known as the Regan isozyme, found in the placenta.
- GCAP: Present in germ cells.

c) ***Aspartate Aminotransferase (AST):*** AST is an enzyme found in high concentrations in the heart and liver and, to a lesser extent, in the kidneys and muscles. In healthy individuals, AST levels in the blood are low. However, when muscle or liver cells are damaged, AST is released into the bloodstream. Therefore, measuring AST levels is useful for diagnosing and monitoring liver damage or dysfunction.

d) ***Albumin:*** Albumins are globular proteins, with serum albumins being the most abundant and crucial protein in the blood. They bind to various substances, including thyroxine (T4), water, cations such as calcium and sodium, hormones, fatty acids, bilirubin, and pharmaceuticals. The primary function of albumin is to regulate the oncotic pressure of blood, which helps maintain fluid balance within the circulatory system.

e) ***Globulins:*** These are spherical proteins heavier than albumins at the molecular level. While they do not dissolve in pure water, they can solvate in dilute salt solutions. The liver produces certain types of globulins, which are present in human blood at concentrations of approximately 2.6-3.5 g/dL. Globulins include different types, such as alpha 1, alpha 2, beta, and gamma globulins. Imbalances in the production of these proteins can lead to liver diseases, as they play various roles in immune responses, blood clotting, and maintaining oncotic pressure.

2.2 Causes of Liver Disease

Liver diseases can be caused by various factors, which can be broadly categorized into several groups:

Infections [14]: The liver can be infected by parasites and viruses, leading to inflammation and compromised liver function. Hepatitis A, B, and C are viral infections that significantly impact liver health, often spreading through contaminated food, water, blood, or sexual contact.

- ***Immune System Abnormalities:*** Autoimmune diseases can cause the immune system to attack liver cells, leading to conditions such as autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis.
- ***Genetic Inheritance:*** Inherited genetic disorders can lead to liver damage through the accumulation of harmful substances. Examples include Wilson's disease, hemochromatosis, and alpha-1 antitrypsin deficiency.
- ***Cancer and Tumors:*** Liver diseases can arise from cancers such as liver cancer, bile duct cancer, and liver adenoma, which can severely impair liver function.
- ***Other Causes:*** Prolonged alcohol abuse, non-alcoholic fatty liver disease (NAFLD), certain medications, over-the-counter treatments, and specific herbal supplements can also cause liver damage.

- ***Risk Factors:*** Factors that increase the risk of liver diseases include excessive alcohol consumption, obesity, type 2 diabetes, tattoos and body piercings, drug use with shared needles, blood transfusions, exposure to infected blood and bodily fluids, unprotected sex, exposure to toxic chemicals, and genetic predisposition.

Understanding the roles of these chemical compounds and the various causes of liver disease is essential for prevention, diagnosis, and treatment, ultimately contributing to better liver health and overall well-being.

MACHINE LEARNING AND LIVER DISEASES

Machine learning (ML) is a branch of artificial intelligence (AI) that enables computers to mimic human thinking and make decisions independently, without human intervention [15-20]. The rapid advancements in AI have significantly enhanced the capabilities of ML, particularly in the field of disease diagnosis. ML algorithms provide highly accurate predictions and performance improvements in diagnosing various diseases.

- **Supervised Learning**

Supervised learning is a method where a model is trained using a labeled dataset, which means the input data is paired with the correct output. This method involves the guidance of a supervisor or instructor, making it easier for the algorithm to learn and predict outcomes from the given input data. Common supervised learning algorithms include:

- Classification: K-Nearest Neighbors (KNN), Support Vector Machines (SVM), Naïve Bayes, Neural Networks
- Regression: Linear and Polynomial Regression, Decision Trees, Random Forests

- **Unsupervised Learning**

Unsupervised learning, also known as clustering, does not use labeled datasets. In this method, the algorithm identifies patterns and relationships within the data without prior knowledge of the outcomes. This self-guided learning approach helps discover hidden structures in the data. Common unsupervised learning techniques include:

- Clustering: K-Means Clustering
- Dimensionality Reduction: Singular Value Decomposition (SVD), Principal Component Analysis (PCA)
- Unsupervised learning is useful for exploring data, finding natural groupings, and reducing data dimensionality.

- **Semi-Supervised Learning**

Semi-supervised learning is a method that combines aspects of both supervised and unsupervised learning. It utilizes a small amount of labeled data alongside a larger amount of unlabelled data. This approach improves model performance by leveraging the vast amount of unlabelled data to enhance learning accuracy while using the labeled data to guide the training process.

- **Reinforcement Learning**

Reinforcement learning (RL) is based on the interaction between an agent and its environment, where the agent learns to perform actions to maximize cumulative rewards. Key components of RL include the agent, actions, states, rewards, and environment. The agent learns optimal behavior through trial and error, receiving feedback in the form of rewards or penalties based on its actions. RL is particularly effective in situations where decision-making involves a sequence of actions, such as game playing and robotic control.

COMMON MACHINE LEARNING ALGORITHMS

Machine learning (ML) encompasses a variety of algorithms, each designed to tackle specific types of problems and data structures [21-25]. Logistic Regression, known as the Logit model, predicts the probability of binary outcomes, such as healthy/sick, by using a logistic function. Support Vector Machine (SVM) finds the optimal hyperplane to separate data into distinct classes, ensuring the widest margin to minimize classification errors.

Convolutional Neural Networks (CNNs) excel in image analysis by employing convolution operations to capture spatial hierarchies in visual data. The Multi-Layer Perceptron (MLP), a type of feed-forward neural network, leverages multiple layers and non-linear activation functions to classify data, particularly when it is not linearly separable. Random Forest, an ensemble method, constructs numerous decision trees on sub-samples of data and combines their predictions to enhance accuracy and prevent overfitting. Each algorithm's unique strengths make them essential tools in the diverse landscape of machine learning applications.

- **Logistic Regression**

Logistic Regression, also known as the Logit model, is used to model the probability of a specific class or event occurring, such as pass/fail, healthy/sick, alive/dead, or win/lose. It's a mathematical model that, in its most basic form, uses a logistic function to model a binary dependent variable. This means the model predicts the probability of one of two possible outcomes [21]. For example, a binary logistic model might predict whether a patient is healthy (0) or sick (1) based on various input features.

- **Support Vector Machine (SVM)**

SVM aims to find the optimal hyperplane that separates the data into different classes. In practice, implementing SVM in Python can be done using the scikit-learn package. The data is divided into training and testing sets, typically with 80% used for training and 20% for testing. SVM constructs hyperplanes in a multidimensional space to separate different classes [22]. The best hyperplane is the one that has the maximum margin from the nearest data points of any class, which minimizes the classification error.

- **Convolutional Neural Networks (CNN)**

CNNs are a type of Deep Neural Network (DNN) that are widely used for image analysis. Also known as shift-invariant or space-invariant artificial neural networks (ANNs), CNNs have a shared weights architecture. They apply a mathematical operation called convolution instead of general matrix multiplication in at least one of their layers. CNNs are particularly effective in capturing spatial hierarchies in images [23].

- **MLP Classifier**

The Multi-Layer Perceptron (MLP) is a type of Artificial Neural Network (ANN) also known as a feed-forward neural network. An MLP consists of at least three layers of nodes: an input layer, a hidden layer, and an output layer. Each node, except for the input nodes, is a neuron that uses a nonlinear activation function. MLPs use a supervised learning technique called backpropagation for training. Unlike linear perceptron's, MLPs can distinguish data that is not linearly separable due to their multiple layers and non-linear activation functions [24].

- **Random Forest**

The Random Forest algorithm constructs multiple decision trees on various sub-samples of the dataset and uses averaging to improve the predictive accuracy and control overfitting. The data is split into training and testing sets, often in an 80:20 ratio. The algorithm trains on multiple subsets and combines the results from each tree through a voting mechanism to make the final prediction [25-26]. This ensemble method enhances the robustness and accuracy of the model by reducing the variance of the predictions.

The review in table 1 explores various machine and deep learning algorithms applied to liver disease diagnosis, highlighting their accuracy and efficiency. Key algorithms such as KNN, SVM, and CNNs demonstrate robust performance across different datasets [28]. The study emphasizes the potential of these technologies to significantly improve diagnostic processes and patient outcomes in liver disease management.

Table 1: Study of common machine and deep learning-based algorithm

Ref. No.	Algorithm Used	Key Features
[27]	CNN	Implemented a tool using liver biopsy images; developed a 4-class detection system for sinusoids, ballooned hepatocytes, veins, and fat droplets; used 720 liver biopsy images.

[29]	Decision Tree, Naive Bayes, ANN, Random Forest	Applied Pearson correlation to identify TP, FN, FP, and TN; used UCI dataset; developed an interface for user input to train algorithms continuously.
[30]	WTA, Erode and Dilate algorithm	Used CT scans to segment liver images; differentiated liver from the background; calculated the affected area; used median filtering to reduce noise.
[31], [38]	Logistic Regression, K-Nearest Neighbor, SVM	Predicted liver disease using classification algorithms; emphasized the ability to recognize hidden patterns; used classification algorithms for diagnosis and decision-making.

LITERATURE REVIEW

In the area of liver disease diagnosis and prediction, various studies have leveraged machine learning (ML) techniques to enhance accuracy and aid healthcare professionals in making informed decisions. Aleksić et al. [23] aimed to develop a prediction model focusing on identifying key causes of bleeding in liver cirrhosis. They employed an ensemble data mining approach, integrating calibration, multiple logistic regression, attribute number reduction, and classification techniques, utilizing clinical and color Doppler data from 96 individuals in Serbia. A different perspective was presented by Md et al. [24], who introduced a novel architecture for predicting liver illnesses utilizing the Indian Liver Patient Dataset (ILPD). Their framework incorporated ensemble learning and advanced pre-processing methods such as data balance, feature scaling, and feature selection. Bayani et al. [25] delved into identifying clinical and laboratory predictors of esophageal varices (EV) grades in cirrhotic individuals. Utilizing ensemble learning techniques, including Cat boost and XGB classifier, and a five-fold cross-validation approach with a dataset of 490 patients, they aimed to enhance result accuracy. In a similar vein, Padmakala et al. [26] utilized the Extraction, Loading, Transformation, and Analysis (ELTA) approach to pre-process patient data, employing the eSVM-swRF algorithm for optimization. Rajathi and Jiji [27] concentrated on improving chronic liver disease (CLD) categorization, utilizing 73 3D texture features and the WOA-SA approach for feature selection. Nilashi et al. [28] employed ensemble learning methodologies and decision trees to create a reliable hepatitis illness diagnosis tool. Sharma and Kumar [29] incorporated geographical data, risk variables, and clinical trial data for hepatocellular carcinoma (HCC) prediction, employing various evaluation metrics for their RFGBEL model. Muflikhah et al. [30] focused on the effects of uneven data on learning processes, utilizing an ensemble method for enhanced prediction performance. Nabeel et al. [31] provided an overview of data mining algorithms for disease prediction, assessing methods like Naive Bayes, J48, and Multi-Layer Perceptron. Meng et al. [32] evaluated a stacking ensemble machine-learning model's effectiveness, outperforming individual methods with clinically relevant accuracy. Spann et al. [33] offered a comprehensive examination of ML technologies, emphasizing their potential applications in hepatology. Dritsas et al. [34] compared various ML models and ensemble approaches, with the Voting classifier model standing out. Park et al. [35] created an optimized ensemble model for diagnosing prevalent disorders. Sarvestany et al. [36] employed six ML algorithms to identify advanced fibrosis using patient data. Mashraqi et al. [37] utilized normalization and feature selection techniques, with J48 showing superior performance. These studies collectively showcase the significant advancements in liver disease prediction and diagnosis through the application of machine learning techniques (Table 2).

Table 2: Review of literature of machine learning based algorithms

Ref No.	Authors	Algorithms Used	Key Features	Dataset(s) Used	Accuracy (%)
[1]	Bendi et al.	KNN, Backward Propagation, SVM, Naïve Bayes, C4.5	Compared two datasets (AP and UCLA), AP dataset performed better; Accuracy for KNN, SVM, Backward Propagation is highest	AP dataset, UCLA dataset	KNN: 96.93, Backward Propagation: 97.47, SVM: 97.07, Naïve Bayes: 95.07,

					C4.5: 96.27
[2]	Bendi et al.	Modified Rotation Forest, MLP with random subset	MLP with random subset performed better; Accuracy for UCI dataset is higher than for Indian dataset	UCI liver dataset, Indian liver dataset	MLP: 94.78 (UCI), CFS: 73.07 (Indian)
[3]	Yugal Kuma & G. Sahoo	Decision Tree (DT)	Used dataset from north-east Andhra Pradesh; Decision Tree performed best	Andhra Pradesh liver dataset	98.46
[4]	S. Dhamodharan	Naïve Bayes, FT Tree	Compared Naïve Bayes and FT Tree; Naïve Bayes outperformed FT Tree	WEKA dataset	Naïve Bayes: 75.54, FT Tree: 72.66
[5]	Heba Ayeldeen et al.	Decision Tree	Used Cairo University dataset; Decision Tree for predicting liver fibrosis stages	Cairo University dataset	93.7
[6]	D. Sindhuja & R. Jemina Priyadarsini	C4.5	Surveyed various classification techniques; C4.5 performed better than others	AP dataset, UCLA dataset	Not specified
[8]	Somaya Hashem et al.	SVM, Backpropagation	Compared SVM and Backpropagation using UCI dataset; SVM performed better	UCI machine repository	SVM: 71, Backpropagation: 73.2
[9]	Han Ma et al.	Bayesian Network	Evaluated 11 different classifications; Bayesian Network showed good results	Zhejiang University dataset	Accuracy: 83, Specificity: 83, Sensitivity: 0.878, F-measure: 0.655
[10]	Joel Jacob et al.	Logistic Regression, K-NN, SVM, ANN	Used Indian Liver Patient Dataset; ANN performed best	Indian Liver Patient Dataset	Logistic Regression: 73.23, K-NN: 72.05, SVM: 75.04, ANN: 92.8
[11]	Sivakumar D et al.	K-means, C4.5	Prediction of chronic liver disease; Compared two techniques	UCI repository	Not specified
[12]	Mehtaj Banu H	KNN, SVM	Studied various ML techniques; KNN and SVM showed better performance	UCI dataset	Not specified
[13]	Vasan Durai et al.	SVM, Naïve Bayes, J48	Liver disease prediction; J48 had better performance in terms of feature selection	UCI repository dataset	J48: 95.0

CONCLUSION

In conclusion, the review underscores the significant advancements in using machine learning algorithms for diagnosing liver diseases, demonstrating high accuracy, precision, and efficiency across various models and datasets. Algorithms such as KNN, SVM, and neural networks, especially CNNs and MLP, consistently show robust performance, with studies reporting accuracies as high as 98.46%. Deep learning approaches, like CNNs analyzing liver biopsy images, further enhance diagnostic capabilities, particularly for conditions like NAFLD. The importance of dataset quality is also highlighted, as it greatly influences model performance. Overall, the integration of machine learning and deep learning in medical diagnostics shows immense potential for improving the accuracy and reliability of liver disease diagnosis, paving the way for better patient outcomes and more efficient healthcare solutions.

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