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MACHINE-LEARNING CLASSIFIER FOR LIVER DISEASE AND PERIODONTITIS USING BIOCHEMICAL AND CLINICAL PARAMETERS

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ABSTRACT

Introduction: The liver is vital for various physiological functions, including bile and protein synthesis necessary for digestion, nutrient metabolism, and cholesterol regulation.

Volumen 15, N° 31. Julio-Diciembre 2025
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Periodontitis, an oral disease associated with systemic conditions like cardiovascular diseases and Alzheimer's disease, has recently been implicated in affecting liver health through systemic inflammation pathways. **Objective:** This study aims to investigate the use of machine-learning techniques, specifically light gradient-boosted trees, to diagnose liver disease in patients with periodontitis using biochemical and clinical parameters. **Methods:** From prior records, a Dental and Medical College obtained 325 data for preprocessing and exploratory analysis. Our research uses data preprocessing, feature selection, and model construction to predict liver disease risk in periodontitis patients. Gradient boosting, random forests, and Keras residual network are evaluated using accuracy and confusion matrix. **Results:** The study conducted extensive exploratory data analysis to assess key biochemical and clinical parameters indicative of liver health. The study evaluated the accuracy of machine-learning models—LGBM (Light Gradient Boosted Trees), Keras Slim, and Random Forest—for diagnosing liver disease in patients with periodontitis. Results indicated high accuracies of approximately 98%, 84%, and 96%, respectively, underscoring their potential for precise and non-invasive diagnostic applications in clinical settings. **Conclusions:** The study highlights the significant role of biochemical and clinical parameters in assessing liver health within the context of periodontitis. Elevated levels of these enzymes indicate potential liver damage or diseases, underscoring their utility as diagnostic markers.

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KEYWORDS: Liver diseases; Periodontitis; Diagnosis; Machine Learning; Biomarkers; Non-Invasive Diagnosis.

CLASIFICADOR DE APRENDIZAJE AUTOMÁTICO PARA LA ENFERMEDAD HEPÁTICA Y LA PERIODONTITIS UTILIZANDO PARÁMETROS BIOQUÍMICOS Y CLÍNICOS

RESUMEN

Introducción: El hígado desempeña un papel crucial en la digestión, el metabolismo y la regulación del colesterol. La periodontitis, una enfermedad oral, se ha relacionado con afecciones sistémicas y podría influir en la salud hepática mediante la inflamación. **Objetivo:** Este estudio tiene como objetivo investigar el uso de técnicas de aprendizaje automático, específicamente árboles de gradiente ligero potenciados (light gradient-boosted trees), para diagnosticar la enfermedad hepática en pacientes con periodontitis utilizando parámetros bioquímicos y clínicos. **Métodos:** Se analizaron 325 registros de un Colegio Dental y Médico. Se aplicaron técnicas de preprocesamiento de datos, selección de características y construcción de modelos para predecir el riesgo de enfermedad hepática. Se evaluaron los modelos LGBM, Keras Slim y Bosque Aleatorio mediante precisión y matrices de confusión. **Resultados:** El estudio realizó un extenso análisis exploratorio de

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
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datos para evaluar parámetros bioquímicos y clínicos clave indicativos de la salud hepática. El estudio evaluó la precisión de los modelos de aprendizaje automático—LGBM (Árboles de Gradiente Ligero Potenciados), Keras Slim y Bosque Aleatorio—para diagnosticar la enfermedad hepática en pacientes con periodontitis. Los resultados indicaron altas precisiones de aproximadamente 98%, 84% y 96%, respectivamente, subrayando su potencial para aplicaciones diagnósticas precisas y no invasivas en entornos clínicos. **Conclusiones:** El estudio destaca el papel significativo de los parámetros bioquímicos y clínicos en la evaluación de la salud hepática dentro del contexto de la periodontitis. Los niveles elevados de estas enzimas indican daño hepático potencial o enfermedades, subrayando su utilidad como marcadores diagnósticos.

PALABRAS CLAVE: Enfermedades hepáticas; Periodontitis; Diagnóstico; Aprendizaje automático; Biomarcadores; Diagnóstico no invasivo.

INTRODUCTION

The liver plays crucial roles in maintaining overall health (1–3). Among these functions, it processes food into bile and proteins essential for digestion, while eliminating potentially harmful substances. Additionally, it utilizes stored vitamins, carbohydrates, and minerals to metabolize nutrients absorbed from the gastrointestinal tract and regulates cholesterol synthesis. Periodontitis, a type of oral disease, has been linked to

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

systemic conditions such as cardiovascular diseases, preterm birth, low birth weight, and Alzheimer's disease (4–8). Recent studies have indicated that periodontal inflammation can impact liver health through systemic circulation.

Yoneda et al. demonstrated a significant association between *Porphyromonas gingivalis* infection and non-alcoholic fatty liver disease (NAFLD) in patients with periodontitis (9, 10). Even after adjusting for age, diabetes, and body mass index (BMI), regression analysis consistently showed a higher prevalence of *P. gingivalis* in NAFLD patients compared to healthy individuals. Patients with NAFLD and *P. gingivalis* infection exhibited lower blood albumin levels and elevated hyaluronic acid and type IV collagen levels, suggesting possible liver fibrosis (10, 11). These findings support the hypothesis that persistent *P. gingivalis* infection independently predicts NAFLD progression in untreated periodontitis, potentially accelerating liver fibrosis and impairing liver function (12).

Moreover, in mice fed a high-fat diet and infected with *P. gingivalis*, there was observed proliferation of hepatic stellate cells and increased collagen production (12, 13). Hepatocytes exhibited high expression of Toll-like receptor 2 (TLR2), and *P. gingivalis*-LPS stimulated mRNA production of proinflammatory cytokines. These results imply that untreated dental infections may expedite non-alcoholic steatohepatitis (NASH) progression to fibrosis via the *P.*

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

gingivalis-LPS-TLR2 pathway (14). Furthermore, presence of *Aggregatibacter actinomycetemcomitans* was associated with increased hepatic steatosis. Animals orally administered *A. actinomycetemcomitans* displayed altered cytokine profiles and liver lipid metabolism enzymes, suggesting that *A. actinomycetemcomitans* infection might pose a risk factor for NAFLD, possibly through modulation of intestinal flora rather than direct inflammatory processes (11).

In patients with liver cirrhosis (15), dysbiosis of the intestinal microbiome is often linked to elevated levels of oral bacteria, particularly in those with oral infections such as periodontitis, compared to healthy individuals. Salivary dysbiosis in these patients may contribute to systemic inflammation, creating a proinflammatory environment in the oral cavity and potentially increasing the risk of future liver-related hospitalizations. Women patients face significant barriers to timely diagnosis and referral, despite the critical importance of early detection in managing liver disease. While histologic biopsy remains the gold standard for diagnosing liver disease, it is an advanced and invasive procedure. Imaging techniques such as ultrasound, CT, and MRI are commonly used for diagnosis, but their widespread application in population screening is limited by cost. Various predictive algorithms have been developed to aid in diagnosis.

Volumen 15, N° 31. Julio-Diciembre 2025
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ISSN: 2244-8136

Treatment of periodontal disease, typically non-invasive and cost-effective, has shown promise in improving both oral and overall health. Recent clinical studies have highlighted potential benefits in patients with severe liver diseases like cirrhosis (10-14). Effective management of periodontal disease can reduce blood toxins and inflammation, potentially improving cognitive function, particularly in patients with hepatic encephalopathy. Periodontal care promotes favorable changes in gut and oral flora within a month, along with improvements in systemic inflammation, prognostic markers for cirrhosis, and cognitive function (10-15). Additionally, improvements in liver function markers (1) have been documented in patients with non-alcoholic fatty liver disease following nonsurgical periodontal therapy. Early referral of patients with various systemic conditions for dental evaluation, diagnosis, and treatment relies on the collaborative efforts of medical and dental specialists.

Despite advances in understanding these associations, gaps remain in comprehensively integrating dental care into the management of systemic diseases, particularly liver disorders. Integrating dental assessments and periodontal treatment early in the care continuum may mitigate disease progression and improve overall health outcomes.

By elucidating the intricate connections between oral health and liver disease, this

Volumen 15, N° 31. Julio-Diciembre 2025
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research seeks to underscore the importance of holistic healthcare approaches that address both dental and systemic health. Such insights are crucial for developing targeted interventions that can improve patient outcomes and reduce healthcare burdens associated with chronic liver diseases. Therefore, this study aims to evaluate and predict liver disease in patients with periodontitis using light gradient-boosted trees based on biochemical and clinical parameters.

Materials and Methods

This study was approved by the Ethical Committee of Saveetha Medical College and Hospital (Reference number IHEC/SDC/Faculty/23/perio/348). The methodology involved several steps: data collection, preprocessing, model selection, model training, model evaluation, hyperparameter tuning, cross-validation, and interpretability using the DataRobot tool (https://app.datarobot.com). A total of 325 records were obtained from Saveetha Institute of Dental College and Medical College, where informed consent was deemed unnecessary as the data were from previous records and anonymized. The collected data underwent preprocessing and exploratory analyses.

Light Gradient Boosted Tree Classifier

The Light Gradient Boosted Trees (LightGBM) classifier (16) is a machine learning model specifically designed for classification tasks. LightGBM is known for its efficiency and speed, making it a

preferred choice for both small and large datasets. Unlike traditional gradient boosting frameworks, LightGBM constructs trees in a leaf-wise manner, optimizing performance by splitting nodes based on maximum delta loss without the need for one-hot encoding of categorical features. Regularization techniques such as L1 and L2 are employed to prevent overfitting, while gradient descent optimization is utilized to find optimal tree splits using histograms.

Data were split into 80% for training and 20% for testing purposes , enabling the model to generalize well to new data. DataRobot applied LightGBM and Keras Slim Network for evaluation in clinical data analysis.

Keras Residual Neural Network

Residual Networks (ResNets) (18) are a type of convolutional neural network (CNN) architecture that excels in training deep networks by using skip connections to address the vanishing gradient problem. These connections allow gradients to flow directly through the network, facilitating the learning of residual mappings between input and output layers. Keras, a high-level deep learning framework (18), provides an API for building and training neural networks, including ResNets. Keras Slim utilizes the ResNet architecture previously proposed (18).

Data is split into categorical and numeric variables. Categorical variables are ordinally encoded, and missing values in

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

numeric variables are imputed. The processed data is then used to train a Light Gradient Boosted Trees Classifier (SchMix Loss, 16 leaves) to make predictions.

Results

Exploratory Data Analysis

Figure 1 along with Table 1, present the mean and standard deviation of biochemical and clinical parameters. Specifically, SGPT (Serum Glutamic Pyruvic Transaminase), SGOT (Serum Glutamic Oxaloacetic Transaminase), ALP (Alkaline Phosphatase), probing depth (PPD), and total bilirubin were analyzed. SGPT (ALT) is an enzyme primarily found in the liver, and elevated levels can indicate liver damage or disease, such as hepatitis or cirrhosis. SGOT (AST) is another enzyme found in various tissues, including the liver, heart, muscles, and kidneys, and elevated levels may indicate liver damage, heart issues, or muscle injury. ALP is an enzyme found in various tissues throughout the body, including the liver, bones, kidneys, and intestines. Elevated ALP levels can indicate liver disease, bone disorders, or bile duct obstruction.

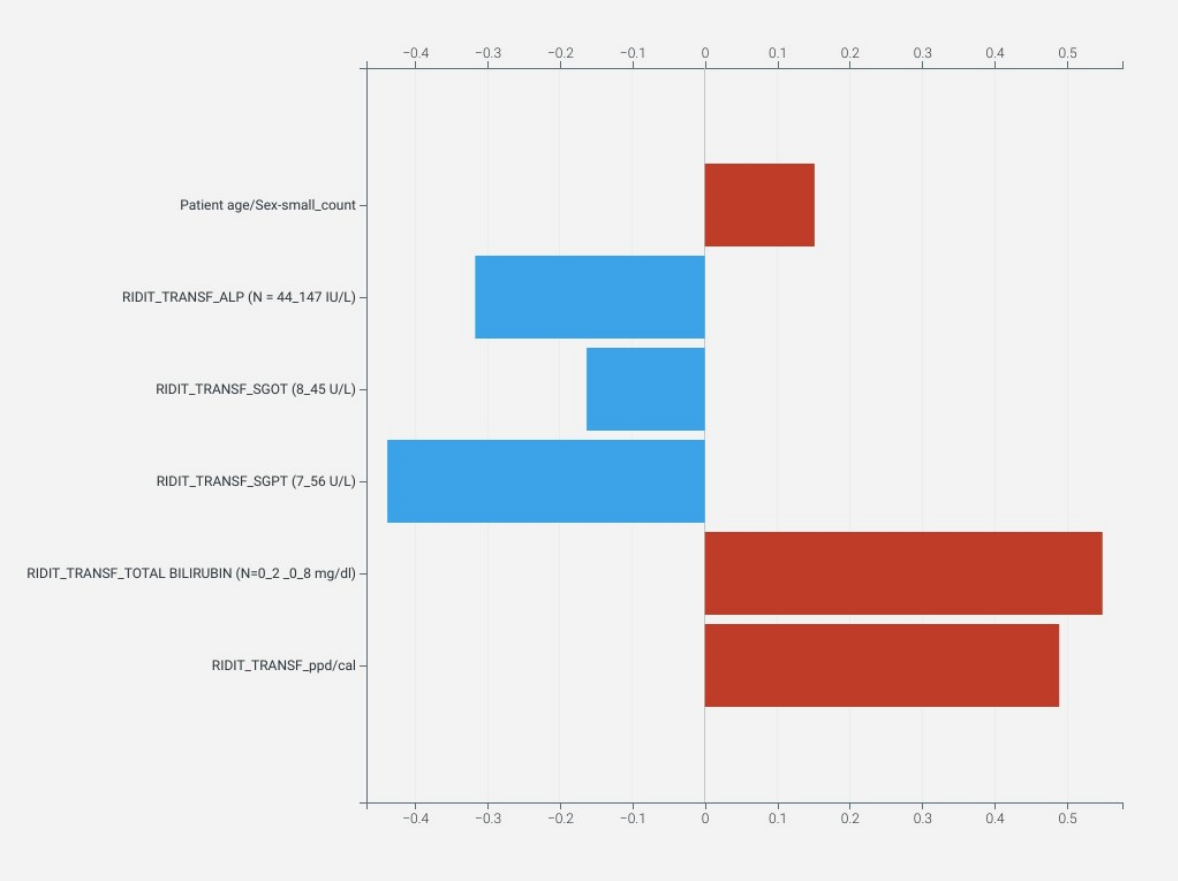

Figure 1. Data distribution across all classes.

Table 1 presents the mean and standard deviation for the following clinical and biochemical parameters: alkaline phosphatase (ALP), serum glutamic-pyruvic transaminase (SGPT), postprandial glucose (PPD), and serum glutamic-oxaloacetic transaminase (SGOT).

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

Table 1. Mean and standard deviation (SD) of all clinical and biochemical parameters.

Column1	Column2	ALP	SGPT	PPD	SGOT
Mean	1.963302752	213.164634	66.34756098	5.3109756	68.29268293
SD	2.95478173	154.729923	83.65281349	0.713094	82.34476457

Alkaline phosphatase (ALP), serum glutamic-pyruvic transaminase (SGPT), postprandial glucose (PPD), and serum glutamic-oxaloacetic transaminase (SGOT).

Figure 1 illustrates the distribution of data across various classes, highlighting the frequency or proportion of instances within each class. The visual representation provides insights into the class balance or imbalance within the dataset.

Figure 2a displays the lift diagram data generated by the Light Gradient Boosted Tree Classifier. The AdaBoost-based classifier demonstrates a robust model fit with both training and test data, exhibiting minimal overfitting. The lift diagram illustrates the effectiveness of the predictive model by comparing the proportion of positive responses identified by the model to a random selection. It highlights the model's ability to target the top segments of the dataset more effectively than random selection.

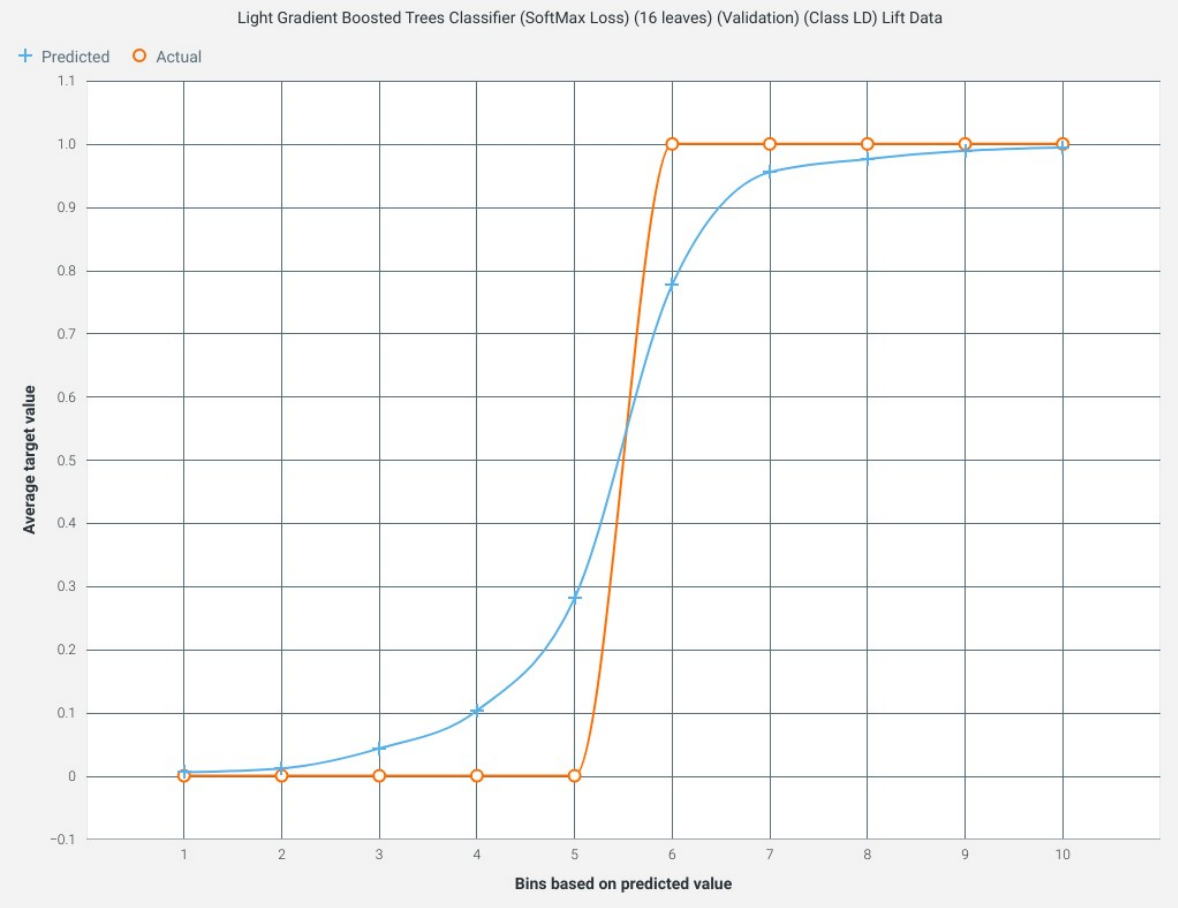

Figure 2. a. Lift diagram.

Figure 2b presents the line diagram data obtained from the Keras Slim Residual Neural Network layer, illustrating the model fit with actual and predicted data. The line diagram depicts the data trends over time or across different categories, highlighting changes, patterns, and relationships within the dataset. It provides a clear visualization of how the data points are connected and vary.

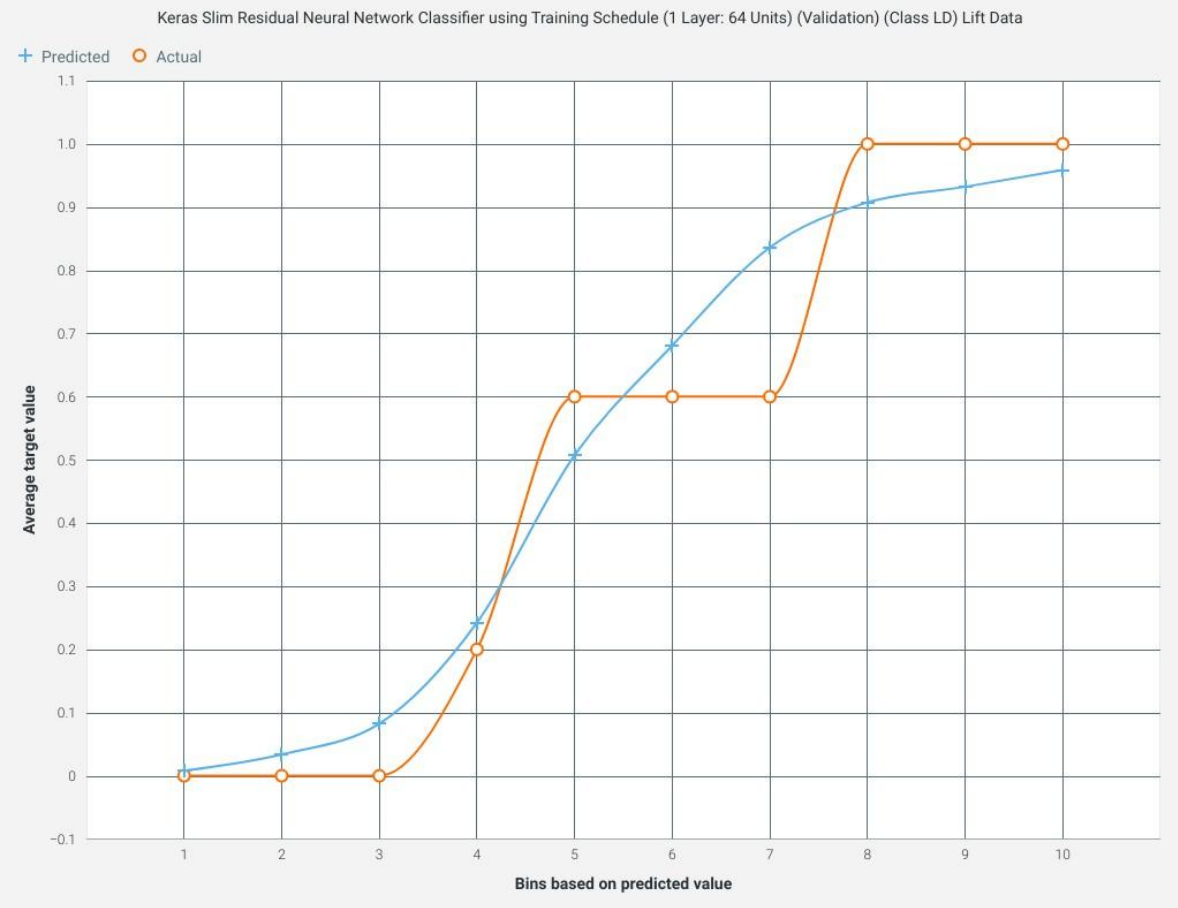

Figure 2. b. Line diagram data.

Figure 3a depicts the confusion matrix for all classes. The confusion matrix displays the performance of the classification model by showing the number of true positive, true negative, false positive, and false negative predictions for each class. This helps in evaluating the accuracy and errors of the model across different classes.

Figure 3. a. Confusion matrix for all classes

Figure 3b displays the confusion matrix for actual and predicted classes generated by the Keras Slim layer. The confusion matrix presents the performance of the classification model, displaying the counts of true positives, true negatives, false positives, and false negatives. It provides a detailed insight into the model's accuracy and the types of errors it makes.

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

Figure 3. b. Confusion matrix for actual and predicted classes generated by the Keras Slim layer.

Figure 3c presents the confusion matrix for actual and predicted classes generated by the Random Forest classifier. The confusion matrix illustrates the performance of the Random Forest classifier in predicting outcomes compared to actual results. It displays counts of true positive, true negative, false positive and false negative predictions, offering insights into the classifier's accuracy and error rates across different classes.

Figure 3. c. Confusion matrix generated by the Random Forest classifier.

Figure 4 illustrates the lift data from the Random Forest classifier, demonstrating a strong model fit. The lift chart shows the effectiveness of the Random Forest classifier by comparing the model's ability to identify positive responses against a baseline of random selection. It highlights the classifier's performance in ranking instances by their likelihood of being positive.

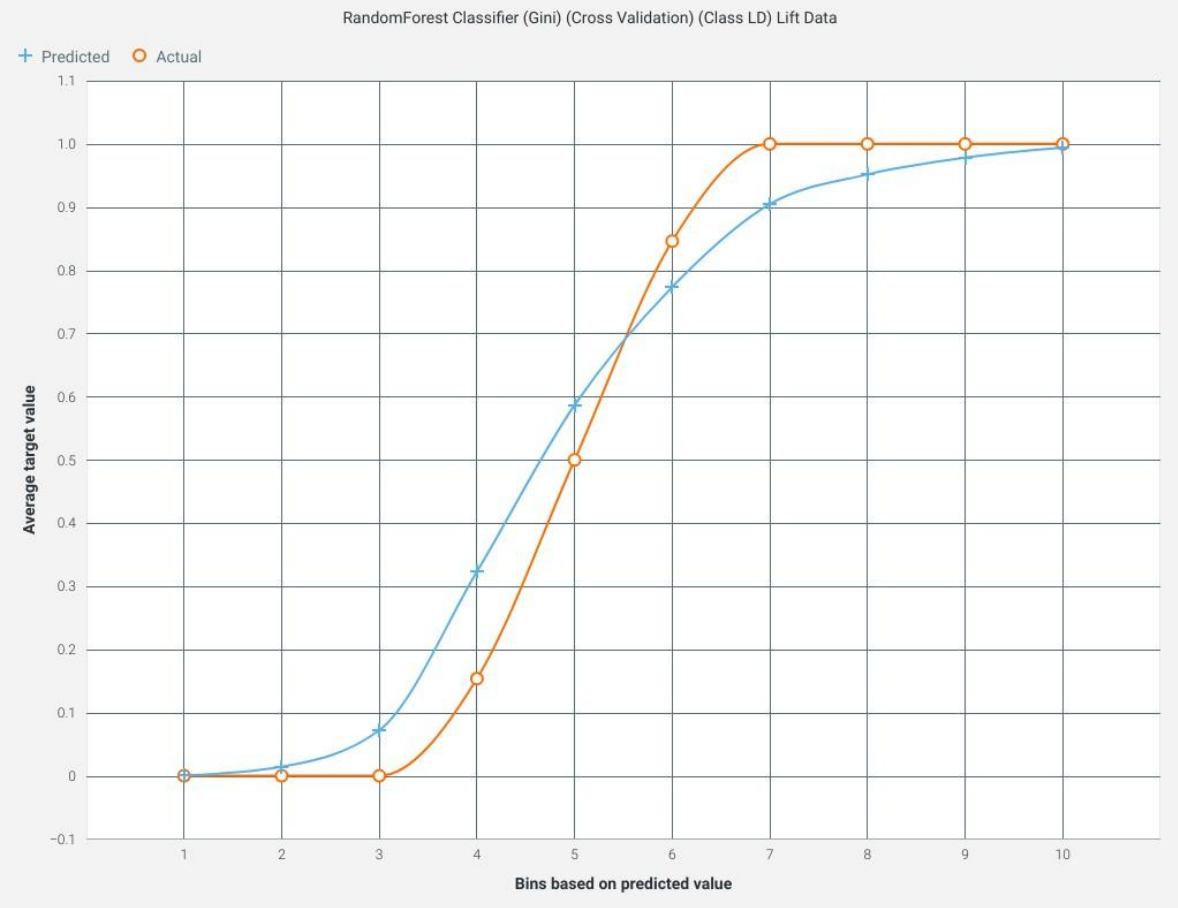

Table 2 presents the evaluation of the models along with their respective accuracies. This table compares the performance of different machine learning models based on their Area Under the Curve (AUC) scores. A higher AUC score indicates better discrimination ability of the model in distinguishing between positive and negative instances.

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

Table 2. Evaluation of the models.

Model	Area Under the Curve
LGBM	98
KERAS SLIM	84
RANDOM FOREST	96

The accuracy of the models varies depending on the characteristics utilized in the data. Specifically, LGBM, Keras Slim, and Random Forest achieved accuracies of approximately 98%, 84%, and 96%, respectively.

Discussion

The prevalence of liver disease is increasing due to conditions such as obesity, alcoholism, diabetes, and metabolic syndrome, which impose significant financial burdens. Traditional liver function tests (LFTs) primarily assess liver damage rather than overall function (19, 20). Machine learning techniques enhance diagnostic accuracy by categorizing patients into distinct disease groups. In this study, important biochemical markers including bilirubin, SGOT (AST), SGPT (ALT), and ALP, which are indicative of liver function, were utilized for machine learning (21, 22). ML algorithms such as Random

Volumen 15, N° 31. Julio-Diciembre 2025
Depósito Legal: PPI201102ME3815
ISSN: 2244-8136

Forest, SVM, and decision trees have demonstrated high accuracy rates in disease classification. Consistent with previous findings, clinical parameters related to periodontal health, such as probing depth, were found to correlate with parameters of liver disease (9, 10, 12, 14). Specifically, Random Forest and CART effectively classified 94% and 95% of patients with liver disease, respectively. Acute hepatitis was associated with higher levels of AST, ALT, and ALP compared to chronic hepatocellular carcinoma.

Liver parenchymal cells can be infected by bacteria like *P. gingivalis* found in periodontal infections, releasing enzymes such as alanine aminotransferase (ALT) and toxic byproducts like lipopolysaccharides (LPS) (23–26). The presence of bacterial LPS can lead to increased production of inflammatory cytokines, particularly TNF-α, which can damage both liver and periodontal tissues. Therefore, the interaction between liver and periodontal diseases largely involves bacterial LPS and TNF-α.

Studies in rats with experimentally induced periodontitis have shown significant ultrastructural changes in liver tissue and systemic effects (9,13). Liver histopathology revealed fatty accumulation indicative of steatosis and hepatocyte damage. Additionally, the periodontitis group exhibited higher serum levels of triglycerides, alkaline phosphatase, high-density lipoprotein, and total cholesterol compared to

controls. These findings underscore the potential for machine learning to predict and elucidate the connection between periodontitis and liver disease.

This study employed LightGBM, Keras Slim residual neural networks (27), and Random Forest to assess model accuracy (Figures 2-4). Accurately predicting and diagnosing liver disease in patients with periodontitis is crucial for medical and dental practitioners, given the life-threatening nature of liver disorders. Our LightGBM model demonstrated superior performance in classifying periodontal disease with liver disease compared to other models. Gradient boosting models (17) are favored for their ability to handle complex, nonlinear relationships in clinical data, leveraging ensemble learning to combine predictions from multiple weak models, typically decision trees, with softmax loss to enhance robustness and accuracy. In contrast, Keras Slim neural networks address the vanishing gradient problem effectively in clinical data. This study showed that LightGBM outperformed Keras Slim neural networks and Random Forest models (28–30).

While this study provides valuable insights into the relationship between periodontal disease and liver disorders, some limitations should be acknowledged. The use of machine learning models, while powerful in classification tasks, requires careful validation and interpretation of results to mitigate potential model overfitting or bias. Additionally, the study's focus on

biochemical markers and clinical parameters may overlook other important factors influencing disease progression, such as genetic predispositions or environmental exposures. Future research should address these limitations by employing prospective longitudinal studies, integrating comprehensive datasets, and incorporating diverse methodological approaches to provide a more nuanced understanding of the complex interplay between periodontal health and liver disease.

Moreover, it is recommended to further investigate the mechanistic pathways linking periodontal disease and liver disorders to elucidate the precise biological interactions involved. Future studies could explore longitudinal designs to establish causal relationships and assess how interventions targeting periodontal health impact liver disease progression. Additionally, integrating advanced omics technologies, such as genomics and metabolomics, could provide deeper insights into biomolecular signatures associated with disease comorbidities. Furthermore, considering the multifactorial nature of liver disease etiology, incorporating environmental and lifestyle factors into research methodologies may enhance our understanding of disease susceptibility and progression. Lastly, fostering interdisciplinary collaborations among clinicians, researchers, and data scientists will be crucial in translating research findings into clinical practice and developing personalized approaches for

managing patients with concurrent periodontal and liver diseases.

Conclusions

This research article utilized various machine-learning methods to diagnose liver disease in the presence of periodontitis, offering a non-invasive diagnostic approach. However, the challenge lies in the reliability of these methods, as not all liver diseases exhibit similar laboratory findings, posing difficulty for machines to accurately interpret. Enhancing classification strategies tailored to each specific liver disease could improve the machine's ability to discern nuanced diagnostic patterns. Future studies could focus on refining machine-learning algorithms to incorporate diverse clinical parameters and biomarkers, thereby advancing the accuracy and clinical applicability of non-invasive diagnostic tools for liver diseases associated with periodontitis. Additionally, exploring the integration of artificial intelligence with emerging diagnostic technologies may further enhance early detection and personalized management strategies in clinical practice.

Conflict of Interest: The authors have no conflicts of interest to declare

Ethics: The study was approved by the Ethical Committee of Saveetha Medical College and Hospital (Reference number IHEC/SDC/Faculty/23/perio/348). The study was conducted in accordance with the 1975 Helsinki Declaration, as revised in 2013.

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Author Contributions: PKY, JV and CMA: Conception, data analysis, interpretation, and manuscript drafting.

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