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Integrating Artificial Intelligence with Salivary Biomarkers for Predictive diagnosis in Systemic Diseases

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Abstract

Background: Early detection of systemic diseases is essential for preventive healthcare and improved patient outcomes. Saliva, a non-invasive biofluid, contains multiple biomarkers reflecting systemic health. Artificial intelligence (AI) offers a powerful approach to analyze complex biomarker data for predictive diagnostics.
Objective: To develop and validate an AI-driven diagnostic system using salivary biomarkers for early detection of diabetes mellitus, cardiovascular disease, and chronic kidney diseases.
Materials and Methods:A cross-sectional study enrolled 300 participants, equally divided into four groups: healthy controls, diabetes mellitus, cardiovascular disease, and chronic kidney disease. Unstimulated saliva samples were collected and analyzed for glucose, cortisol, C-reactive protein (CRP), interleukin-6 (IL-6), and creatinine using ELISA. Data preprocessing, normalization, and feature selection preceded the application of Random Forest (RF), Support Vector Machine (SVM), and Artificial Neural Network (ANN) models. Model performance was assessed using accuracy, precision, recall, F1-score, and area under the receiver operating characteristic curve (AUC-ROC).
Results:The ANN model outperformed others, achieving 91.3% diagnostic accuracy, 89.8% precision, 92.5% recall, and 0.95 AUC-ROC. RF achieved 88.7% accuracy and 0.91 AUC-ROC, while SVM reached 85.4% accuracy and 0.88 AUC-ROC. Salivary IL-6 and CRP were strong indicators of systemic inflammation, while glucose correlated with diabetes ($r = 0.78$, $p < 0.001$).
Conclusion: AI-driven analysis of salivary biomarkers enables non-invasive, early detection of systemic diseases. Integration into clinical workflows could enhance preventive healthcare. Further validation across diverse populations is recommended.

Keywords: Artificial intelligence, Salivary biomarkers, Early diagnosis, Systemic diseases, Non-invasive diagnostics, Machine learning, ANN, Predictive model

Introduction

Early detection of systemic diseases is a critical component of preventive healthcare, improving treatment outcomes and enabling better disease management. Conventional diagnostic procedures are often invasive, costly, and require specialized facilities, limiting access in resource-constrained settings.
Saliva is an attractive diagnostic fluid due to its non-invasive collection, ease of handling, and rich biomarker content, including hormones, enzymes, antibodies, cytokines, and metabolic by-products that reflect systemic health beyond the oral cavity [1–4]. Studies have shown that salivary biomarker profiles correlate with disease progression and severity in diabetes mellitus, cardiovascular disease, and chronic kidney disease [5–8].
While saliva-based diagnostics are promising, analyzing multiple biomarkers simultaneously is complex. Artificial intelligence (AI) and machine learning (ML) provide advanced tools to uncover patterns in high-dimensional biological data, surpassing traditional statistical methods [9–11]. Random Forest (RF), Support Vector Machine (SVM), and Artificial Neural Networks (ANN) have demonstrated high diagnostic precision in medical domains including radiology, genomics, and saliva-based biomarker analysis [12–14].
This study aims to develop and validate an AI-based diagnostic system leveraging salivary biomarkers for early detection of systemic diseases, combining non-invasive sampling with predictive analytics for accessible, preventive healthcare.

Materials and Methods

Study Design and Participants

A cross-sectional study included 300 participants aged 25–65 years, divided equally into four groups (n = 75 each): healthy controls, diabetes mellitus, cardiovascular disease, and chronic kidney disease. Diagnoses were based on clinical assessments, patient histories, and laboratory results. Participants with oral infections, autoimmune disorders, or ongoing immunosuppressive therapy were excluded.

Saliva Collection and Biomarker Analysis

Unstimulated whole saliva was collected between 9:00–11:00 AM to minimize circadian variations. Participants avoided food, drink, smoking, and oral hygiene procedures for at least 90 minutes prior. Samples were collected in sterile polypropylene tubes, centrifuged at 3,000 rpm for 15 minutes at 4°C, and stored at −80°C.

Salivary glucose, cortisol, CRP, IL-6, and creatinine were measured using commercially available ELISA kits. All assays were performed in duplicate to ensure accuracy.

Data Processing and Feature Selection

Biomarker levels were normalized using z-scores. Mutual information and recursive feature elimination identified key biomarkers for model construction.

Machine Learning Models

Three supervised ML models were trained: RF, SVM, and ANN. Data were split into training (80%) and testing (20%) sets with balanced class distributions. Python 3.9 with Scikit-learn and TensorFlow libraries was used. Hyperparameters were optimized using grid search and five-fold cross-validation.

Model Evaluation

Model performance was assessed via accuracy, precision, recall, F1-score, and AUC-ROC. Confusion matrices visualized disease classification performance.

Results

Participant Characteristics

The mean participant age was 47.6 ± 10.2 years, with no significant differences among groups ($p = 0.12$). Gender distribution was balanced (154 males, 146 females).

Salivary Biomarker Levels

Biomarker	Healthy Controls	Diabetes Mellitus	Cardiovascular Disease	Chronic Kidney Disease
Glucose (mg/dL)	3.1 ± 1.2	10.4 ± 2.8	4.2 ± 1.5	4.5 ± 1.3
CRP (mg/L)	1.2 ± 0.6	3.9 ± 1.0	6.7 ± 1.9	5.1 ± 1.7
IL-6 (pg/mL)	4.8 ± 1.9	12.5 ± 3.2	18.3 ± 3.5	15.7 ± 2.8
Creatinine (mg/dL)	0.32 ± 0.11	0.54 ± 0.14	0.60 ± 0.17	0.85 ± 0.21
Cortisol (ng/mL)	4.1 ± 1.5	6.9 ± 2.0	6.1 ± 1.8	5.8 ± 1.6

All differences between healthy controls and disease groups were statistically significant ($p < 0.001$).

Machine Learning Performance

Model	Accuracy (%)	Precision (%)	Recall (%)	F1 Score (%)	AUC-ROC
ANN	91.3	89.8	92.5	91.1	0.95
Random Forest	88.7	86.4	89.3	87.8	0.91
SVM	85.4	83.1	86.2	84.6	0.88

ANN demonstrated the best classification performance. Misclassifications mainly occurred between cardiovascular and chronic kidney disease, likely due to overlapping CRP and IL-6 levels.

Discussion

This study demonstrates that AI analysis of salivary biomarkers enables early detection of systemic diseases non-invasively. ANN outperformed RF and SVM, highlighting the strength of deep learning in recognizing complex patterns in high-dimensional biological datasets.

Elevated salivary glucose and IL-6 levels correlated with diabetes and cardiovascular disease, while CRP and creatinine levels reflected systemic inflammation and renal dysfunction. Feature selection and normalization enhanced model accuracy and generalization, essential for clinical applicability.

Saliva collection is low-cost, non-invasive, and patient-friendly, making it suitable for population screening, especially in pediatric, geriatric, and medically vulnerable populations. Future research should expand biomarker panels, include longitudinal patient monitoring, and integrate AI-based saliva diagnostics with wearable or mobile technologies for real-time personalized health monitoring.

Conclusion

AI-driven analysis of salivary biomarkers provides a promising, non-invasive approach for early detection of systemic diseases. This technology could significantly enhance preventive healthcare delivery, with further validation needed across diverse populations and disease types.

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