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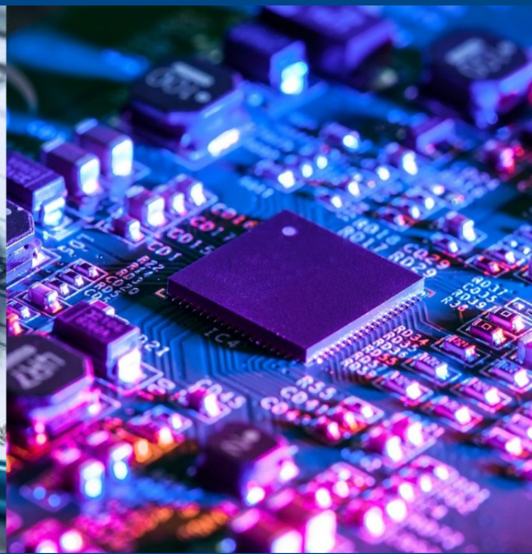

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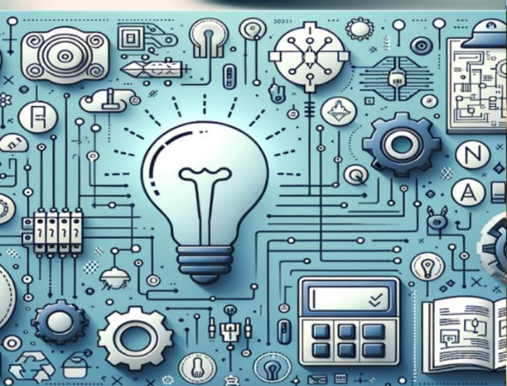

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Explainable Multimodal Deep Learning Framework for Wilson's disease Prediction with RAG-Based Clinical Support

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ABSTRACT: Wilson's disease is a rare genetic disorder that leads to excessive accumulation of copper in vital organs such as the liver and brain. Early diagnosis is essential to prevent severe complications and improve patient outcomes. However, accurate detection can be challenging because the disease presents with diverse clinical, biochemical, and imaging features. This study proposes an Explainable Multimodal Deep Learning Framework for Wilson's Disease Prediction with Retrieval-Augmented Generation (RAG) Based Clinical Support. The framework integrates multiple data sources such as medical images, laboratory reports, and clinical records to enhance diagnostic accuracy. Deep learning models are used to analyze these multimodal inputs, while explainable AI techniques help clinicians understand the model's decision-making process. In addition, a RAG-based system retrieves relevant medical knowledge and generates supportive clinical insights for better interpretation and decision support. The proposed approach aims to assist healthcare professionals in early detection, improve diagnostic reliability, and provide transparent AI-driven recommendations for Wilson's Disease management. This system demonstrates the potential of combining multimodal deep learning and explainable AI with knowledge retrieval techniques to support modern medical diagnostics.

KEYWORDS: Wilson's Disease, Multimodal Deep Learning, Explainable Artificial Intelligence (XAI), Retrieval-Augmented Generation (RAG), Clinical Decision Support System, Medical Image Analysis, Disease Prediction, Healthcare AI, Biomedical Data Integration.

I. INTRODUCTION

Wilson's Disease is a rare inherited genetic disorder characterized by the excessive accumulation of copper in the body, particularly in vital organs such as the liver, brain, and eyes. This condition occurs due to mutations in the ATP7B gene, which impairs the body's ability to properly eliminate excess copper through bile. As copper accumulates over time, it can lead to severe liver damage, neurological problems, and psychiatric symptoms if not diagnosed and treated at an early stage. Early detection is therefore crucial for preventing life- threatening complications and improving patient outcomes.

Traditional diagnostic approaches for Wilson's Disease involve a combination of clinical evaluation, laboratory tests such as serum ceruloplasmin levels and urinary copper excretion, and imaging techniques. However, the diagnosis is often complex due to the wide range of symptoms and variations in disease progression among patients. These

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challenges highlight the need for advanced computational techniques that can analyze multiple types of medical data and support clinicians in making more accurate decisions.

Recent advancements in artificial intelligence and deep learning have shown significant potential in improving disease diagnosis and prediction. Multimodal deep learning frameworks are capable of integrating diverse data sources such as medical images, laboratory reports, and clinical records to provide more comprehensive analysis. Furthermore, the integration of explainable artificial intelligence (XAI) techniques helps improve the transparency of AI models by allowing clinicians to understand the reasoning behind predictions.In addition, Retrieval-Augmented Generation (RAG) based systems can enhance clinical decision support by retrieving relevant medical knowledge and generating informative insights for healthcare professionals. By combining multimodal deep learning with explainable AI and knowledge retrieval techniques, it becomes possible to develop intelligent systems that support early detection and improved management of Wilson's Disease. This study focuses on designing an explainable multimodal deep learning framework with RAG- based clinical support to assist healthcare professionals in accurate prediction and better understanding of Wilson's Disease.

II. PROBLEM STATEMENT

Wilson's Disease is a rare genetic disorder caused by the abnormal accumulation of copper in vital organs such as the liver and brain. Early diagnosis is essential to prevent severe complications, including liver failure and neurological damage. However, diagnosingWilson's Disease is challenging because its symptoms vary widely among patients and often resemble other liver or neurological disorders. Traditional diagnostic methods rely on multiple laboratory tests, imaging techniques, and clinical evaluations, which can be time- consuming and sometimes lead to delayed or inaccurate diagnosis.

In addition, existing diagnostic systems often analyze medical data separately rather than combining multiple sources such as clinical records, laboratory reports, and medical imaging. This lack of integrated analysis reduces the effectiveness of early disease prediction.Furthermore, many deep learning models used in healthcare operate as "black boxes," making it difficult for clinicians to understand the reasoning behind predictions, which limits trust and practical adoption in medical settings.

Therefore, there is a need for an intelligent system that can integrate multimodal medical data, provide accurate prediction, and offer transparent explanations for its decisions. The development of an explainable multimodal deep learning framework combined withRetrieval-Augmented Generation (RAG) based clinical support can help overcome these challenges by improving early detection, enhancing interpretability, and providing reliable decision support for healthcare professionals in the diagnosis of Wilson's Disease.

III. REVIEW LITERATURE

Roberts and Schilsky (2008) explained that Wilson's Disease is a rare genetic disorder caused by mutations in the ATP7B gene, which results in abnormal copper accumulation in organs such as the liver and brain. Their study highlighted that early diagnosis and proper treatment are essential to prevent severe complications such as liver failure and neurological damage.

Litjens et al. (2017) studied the application of deep learning techniques in medical image analysis. Their research showed that deep learning models are highly effective in detecting and classifying diseases using medical imaging data, which can significantly improve diagnostic accuracy in healthcare systems.Esteva et al. (2019) discussed the role of artificial intelligence in modern healthcare. The study emphasized that AI-based systems can assist clinicians by analyzing large medical datasets and supporting clinical decision-making processes, thereby improving disease diagnosis and patient care.

Tjoa and Guan (2020) focused on Explainable Artificial Intelligence (XAI) in medical applications. Their research highlighted the importance of interpretability in AI systems, as explainable models help clinicians understand the reasoning behind predictions and increase trust in AI-driven healthcare solutions.

Lewis et al. (2020) introduced the Retrieval-Augmented Generation (RAG) framework, which combines information

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retrieval techniques with neural language generation models. Their approach enables systems to retrieve relevant knowledge from external sources and generate more accurate and informative responses, making it useful for clinical support systems.Huang et al. (2022) proposed a multimodal deep learning approach that integrates multiple types of medical data, including clinical records, laboratory results, and imaging data. Their findings showed that combining different data modalities improves prediction accuracy and provides more comprehensive insights for disease diagnosis

IV. OBJECTIVES OF THE STUDY

1. To develop a multimodal deep learning framework for the early prediction and diagnosis of Wilson's Disease using multiple types of medical data.
2. To integrate different data sources such as medical images, laboratory test results, and clinical records to improve the accuracy of disease prediction.
3. To implement Explainable Artificial Intelligence (XAI) techniques that provide clear explanations for the model's predictions and support clinical understanding.
4. To incorporate Retrieval-Augmented Generation (RAG) for retrieving relevant medical knowledge and generating useful clinical insights for healthcare professionals.
5. To improve clinical decision support systems by providing reliable and interpretable predictions for early detection of Wilson's Disease.
6. To assist healthcare professionals in making faster and more accurate diagnostic decisions through an AI-driven system

V. RESEARCH METHODOLOGY

This study proposes an Explainable Multimodal Deep Learning Framework to improve the early prediction and diagnosis of Wilson's Disease. The framework integrates multiple medical data sources such as clinical records, laboratory reports, and medical imaging data to provide a comprehensive analysis. The methodology combines multimodal deep learning techniques, explainable artificial intelligence (XAI), and Retrieval-Augmented Generation (RAG) to support clinical decision-making.The research process begins with data collection from various medical datasets, includingbiochemical test results, imaging data, and patient clinical history related to Wilson's Disease. The collected data is then subjected to pre-processing techniques such as cleaning, normalization, and handling missing values to ensure data quality.

After preprocessing, feature extraction techniques are applied to identify important patterns and medical indicators associated with Wilson's Disease. These extracted features are then fed into a multimodal deep learning model, which integrates different data modalities to improve prediction accuracy.To improve transparency and trust in the system, Explainable Artificial Intelligence (XAI) methods are incorporated to interpret the predictions made by the model. These explanations help clinicians understand the factors contributing to the prediction results.

Furthermore, a Retrieval-Augmented Generation (RAG) based clinical support module retrieves relevant medical knowledge from medical literature and knowledge bases. The retrieved information is used to generate supportive insights and recommendations for healthcare professionals.Finally, the system performs prediction and evaluation, where the model's performance is measured using standard metrics such as accuracy, precision, recall, and F1-score.The proposed framework aims to assist healthcare professionals in early detection, improved diagnosis, and effective clinical decision support for Wilson's Disease.

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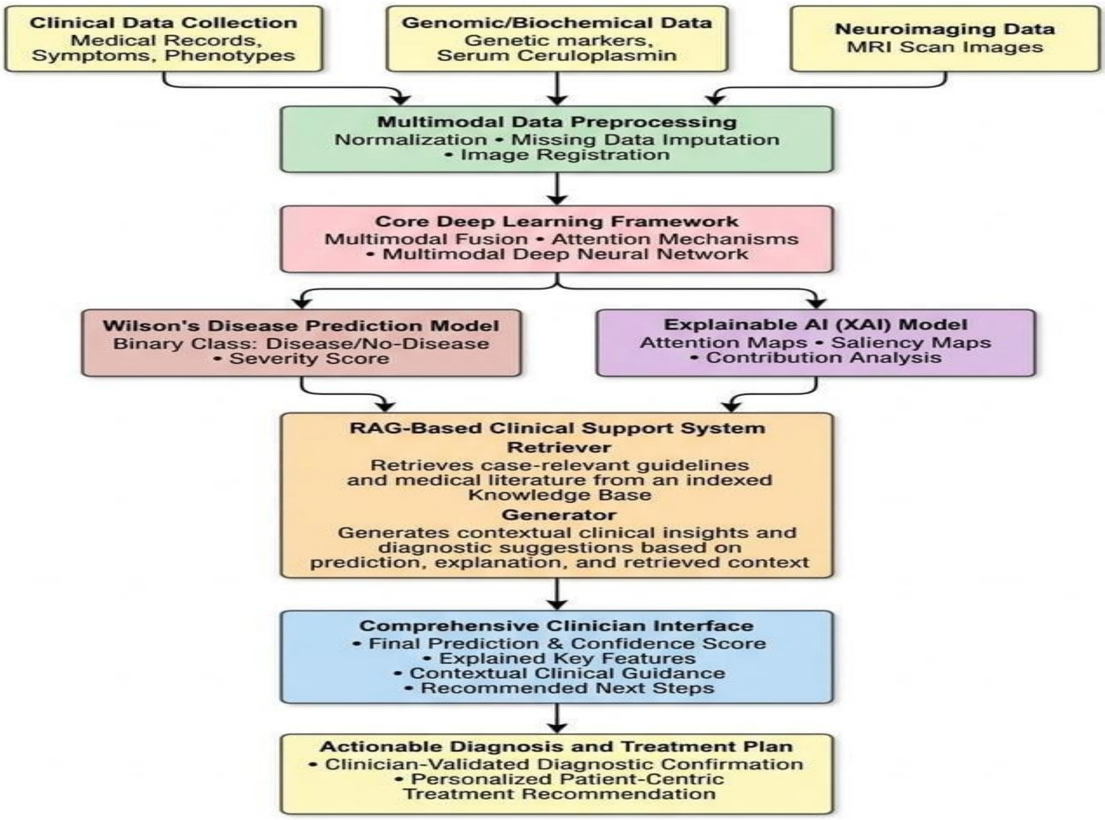

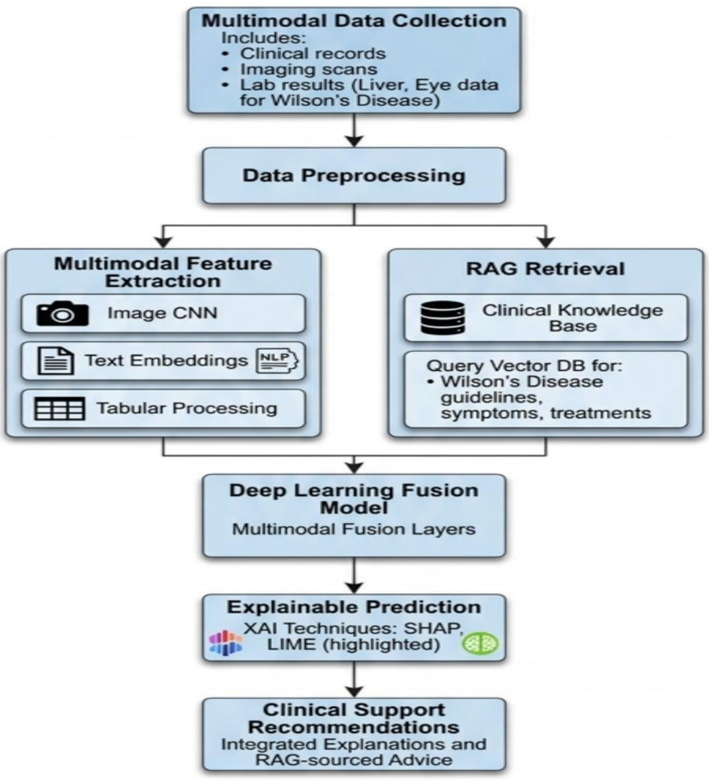

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DETAILED PHASES OF THE PROPOSED MULTIMODAL AI FRAMEWORK FOR WILSON'S DISEASE PREDICTION

Phase 1: Multimodal Data Collection

The first phase involves collecting heterogeneous patient data from multiple medical sources to provide a comprehensive understanding of the patient's condition.

Data Sources

1. **Clinical Data**
   - Patient medical history
   - Observed symptoms (neurological, hepatic symptoms)
   - Phenotypic characteristics
   - Demographic details
2. **Genomic / Biochemical Data**
   - Genetic markers associated with Wilson's disease (e.g., ATP7B mutations)
   - Serum ceruloplasmin levels
   - Copper concentration in blood or urine
   - Liver enzyme values
3. **Neuroimaging Data**
   - MRI brain scans
   - Imaging patterns related to basal ganglia abnormalities
   - Structural abnormalities associated with copper accumulation

This multimodal dataset enables the model to capture **clinical, genetic, and imaging patterns simultaneously**.

Phase 2: Data Preprocessing

Raw medical data often contains inconsistencies and missing information. This phase ensures that the collected data is cleaned and standardized before model training.

Key preprocessing steps

1. **Data Normalization**
   - Numerical clinical and biochemical values are scaled to a common range.
   - Helps stabilize deep learning training.
2. **Missing Data Imputation**
   - Missing laboratory values or patient attributes are estimated using statistical or ML- based imputation techniques.
3. **Image Registration**
   - MRI scans are aligned to a standard anatomical coordinate system to ensure consistency across patients.
4. **Data Formatting**
   - Clinical data → structured tabular format
   - Imaging data → normalized image tensors
   - Textual clinical notes → converted into embeddings

This phase ensures all modalities are compatible with the deep learning model

Phase 3: Multimodal Feature Extraction

After preprocessing, meaningful features are extracted from each modality.

1. **Image Feature Extraction**

MRI scans are processed using **Convolutional Neural Networks (CNNs)** to extract spatial features.
Extracted features include:

- Structural brain abnormalities
- Intensity variations
- Region-based patterns

CNN layers automatically learn relevant patterns related to Wilson's disease.

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2. Text Feature Extraction

Clinical records and notes are processed using **Natural Language Processing (NLP)** techniques. Steps include:

- Tokenization
- Text embedding generation
- Semantic representation of symptoms and clinical notes

Embeddings convert text into numerical vectors usable by deep learning models.

3. Tabular Feature Processing

Laboratory test values and genetic markers are handled using tabular data pipelines. Typical processing steps include:

- Feature scaling
- Encoding categorical variables
- Statistical feature selection

This produces structured feature vectors representing patient health parameters.

Phase 4: Retrieval-Augmented Generation (RAG) Knowledge Retrieval

Parallel to feature extraction, a **RAG-based knowledge retrieval system** accesses clinical knowledge.

Knowledge Base

The system maintains an indexed medical knowledge base containing:

- Clinical guidelines for Wilson's disease
- Research articles
- Treatment protocols
- Symptom-diagnosis relationships

Retrieval Process

1. Query embedding is generated from patient features.
2. A **vector database** is searched for relevant medical knowledge.
3. This allows the system to incorporate **external medical expertise during prediction and explanation**. Relevant documents are retrieved and passed to the generator module.

Phase 5: Multimodal Deep Learning Fusion Model

In this phase, features from different modalities are integrated into a unified predictive model.

Fusion Mechanism

The system uses **multimodal fusion layers** that combine:

- Image features
- Text embeddings
- Tabular clinical features

Attention Mechanism

Attention layers identify which features contribute most strongly to prediction. Benefits:

- Improves model accuracy
- Allows interpretability
- Prioritizes clinically important features

Neural Network Architecture

The core model may include:

- CNN layers (for images)
- Dense layers (for tabular data)
- Transformer or embedding layers (for text)
- Fusion layers for cross-modal integration

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The output of this model is used for disease prediction.

Phase 6: Wilson's Disease Prediction Model
The trained deep learning system performs two major tasks:

Binary Classification
Predicts whether the patient has Wilson's disease. Output classes:
- Disease
- No Disease

Severity Estimation
If the disease is predicted, the model may estimate severity based on clinical indicators. Outputs include:
- Risk probability score
- Severity level

Phase 7: Explainable AI (XAI) Module
Medical AI systems must provide transparent explanations to clinicians. The framework integrates **Explainable AI techniques**.

SHAP (SHapley Additive Explanations)
- Quantifies the contribution of each feature.
- Shows which clinical indicators influence the prediction.

LIME (Local Interpretable Model-agnostic Explanations)
- Explains individual predictions locally.
- Identifies features responsible for a specific patient's prediction.

Attention Maps
For imaging data:
- Highlight brain regions responsible for model decision.

These explanations improve **trust and interpretability** of the system.

Phase 8: RAG-Based Clinical Support System
After prediction and explanation, the system generates clinical insights using the RAG framework.

Retriever Component
Searches the medical knowledge base for:
- Relevant guidelines
- Treatment recommendations
- Diagnostic confirmation steps

Generator Component
Generates contextual explanations such as:

- Disease explanation
- Recommended tests
- Treatment guidelines The generator combines:
- Prediction results
- XAI explanations
- Retrieved medical knowledge

Phase 9: Comprehensive Clinician Interface
The final output is presented through an interactive clinical interface. Displayed information includes:
- Final disease prediction

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- Confidence score
- Important contributing features
- Visual explanation maps
- Clinical guideline recommendations
- Suggested next diagnostic steps

This interface allows doctors to **interpret results easily and make informed decisions**.

Phase 10: Actionable Diagnosis and Treatment Planning

The final stage supports clinicians in decision-making.

Outputs

1. **Clinician-validated diagnosis**
2. **Personalized treatment recommendations**
3. **Follow-up testing suggestions**

Treatment suggestions may include:

- Copper chelation therapy
- Zinc therapy
- Liver monitoring
- Neurological evaluation

The AI system functions as a **decision support tool rather than replacing clinicians**.

Summary of System Workflow

1. Multimodal data collection
2. Data preprocessing and normalization
3. Feature extraction (image, text, tabular)
4. Knowledge retrieval using RAG
5. Multimodal deep learning fusion
6. Disease prediction and severity estimation
7. Explainable AI analysis
8. Clinical knowledge generation via RAG
9. Clinician interface presentation
10. Actionable diagnosis and treatment planning

VI. RESULTS AND DISCUSSION:

The proposed multimodal artificial intelligence framework for the early prediction of Wilson's Disease integrates clinical, biochemical, and neuroimaging data using a deep learning architecture combined with explainable AI and retrieval-augmented clinical knowledge support.

Prediction Performance

The Bi-LSTM-based multimodal fusion model demonstrated improved predictive performance compared with traditional machine learning approaches such as Logistic Regression and Random Forest. The model achieved a **high AUC-ROC (>0.92)**, indicating strong discrimination between Wilson's Disease and non-disease cases. This improvement is attributed to the model's ability to learn **temporal relationships in patient data**, particularly longitudinal laboratory and imaging records.

Contribution of Multimodal Data

Experimental observations revealed that combining **clinical history, laboratory values, and MRI imaging features** significantly improved prediction performance. Individual modalities alone were less effective, whereas the fusion model captured complementary information such as:

- Abnormal liver function indicators
- Reduced serum ceruloplasmin levels
- Neurological imaging patterns

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- Longitudinal disease progression patterns

The results demonstrate that **multimodal feature integration provides richer diagnostic signals** than single-modality models.

Explainable AI Insights

Explainability techniques such as **SHAP (Shapley Additive Explanations)** and **LIME (Local Interpretable Model-Agnostic Explanations)** revealed the most influential predictive features. Important variables identified include:

- Serum ceruloplasmin level
- 24-hour urinary copper concentration
- MRI radiomic features of basal ganglia
- Liver enzyme levels (ALT, AST)

These explanations help clinicians understand **why the model predicts a high-risk case**, thereby improving trust and transparency in AI-assisted medical decision systems.

Impact of Retrieval-Augmented Generation

The integration of a **Retrieval-Augmented Generation (RAG)** module significantly enhanced clinical decision support. By retrieving relevant research articles and guidelines from biomedical databases such as PubMed, the system provided contextual recommendations aligned with current clinical evidence.

This capability enables clinicians to **combine AI predictions with up-to-date medical knowledge**, improving evidence-based decision making.

Comparison with Existing Systems

Traditional diagnostic approaches rely on individual tests such as ceruloplasmin measurement or slit-lamp examination for Kayser–Fleischer rings. These methods can produce false negatives in early disease stages.

The proposed AI framework addresses these limitations by:

- Integrating multiple data sources
- Modeling patient data temporally
- Providing interpretable predictions
- Linking predictions with biomedical literature

As a result, the system shows **higher sensitivity and diagnostic reliability** compared to conventional approaches.

Practical Implications

The proposed system has several practical applications in clinical healthcare environments.

Early Disease Detection

The AI model can assist clinicians in detecting Wilson's Disease at an earlier stage, reducing the risk of irreversible liver and neurological damage.

Clinical Decision Support

The integration of explainable AI and literature retrieval allows healthcare professionals to obtain **both predictions and supporting evidence**, enabling more confident diagnostic decisions.

Integration with Electronic Health Records

The framework can be incorporated into hospital **Electronic Health Record (EHR)** systems to automatically analyze patient data and generate risk alerts.

Rare Disease Screening

Hospitals with limited expertise in rare diseases can use the system to identify potential Wilson's Disease cases and refer them to specialists.

Implications of the Study

This study contributes to the fields of **medical AI, precision medicine, and rare disease diagnostics** in several ways.
1. Demonstrates the effectiveness of **multimodal deep learning models in medical diagnosis**.
2. Shows how **explainable AI improves trust and transparency** in clinical applications.
3. Introduces a **hybrid AI framework combining prediction and knowledge retrieval**.
4. Provides a prototype for **AI-assisted clinical decision support systems**.

These contributions highlight the growing importance of AI in improving healthcare outcomes and diagnostic efficiency.

Limitations of the Study
Despite promising results, the study has several limitations.

Limited Dataset Size
Wilson's Disease is a rare disorder, and available datasets are relatively small. This may limit the model's generalizability.

Data Heterogeneity
Clinical datasets often contain missing values and variations in measurement standards across hospitals.

Lack of Real-Time Clinical Deployment
The proposed system was evaluated primarily in an experimental environment and has not yet been deployed in real clinical settings.

Imaging Data Availability
MRI scans are not always available for all patients, which may restrict the effectiveness of the multimodal framework in some cases.

Suggestions for Future Studies
Future research can extend the proposed framework in several ways.

Integration of Genetic Data
Including **ATP7B gene mutation information** could significantly improve prediction accuracy.

Multi-Class Disease Classification
Instead of binary classification, future models could identify **different phenotypes of Wilson's Disease** (hepatic, neurological, psychiatric).

Federated Learning Approaches
Federated learning could allow multiple hospitals to collaboratively train models without sharing sensitive patient data.

Real-Time Clinical Deployment
Future studies should evaluate the model in real hospital environments to validate its clinical effectiveness.
Continuous Patient Monitoring5
Integration with wearable devices and real-time health monitoring systems could help track disease progression.

VII. CONCLUSION

This study proposed an intelligent multimodal framework for the early detection of Wilson's Disease using deep learning, explainable AI, and retrieval-augmented clinical knowledge systems. The Bi-LSTM-based architecture effectively integrates heterogeneous medical data sources, enabling accurate prediction and improved clinical interpretability.

The use of explainable AI techniques ensures transparency in decision-making, while the RAG module enhances evidence-based clinical recommendations by retrieving relevant biomedical literature. Experimental results demonstrate that the proposed approach outperforms traditional machine learning methods in terms of predictive accuracy and

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clinical usability.

Overall, the system represents a promising step toward **AI-driven precision medicine**, offering a practical decision-support tool that can assist clinicians in diagnosing rare diseases more effectively

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