

AI-Assisted Genotype Analysis of Hepatitis Viruses: A Systematic Review on Precision Therapy and Sequencing Innovations

Ashish Shiwlani¹, Sooraj Kumar², Samesh Kumar³,
Hamza Ahmed Qureshi⁴, Jouvany Sarofeem Naguib⁵

¹Illinois Institute of Technology, Chicago, Illinois, USA

²DePaul University Chicago

³Georgia Institute of Technology, USA

⁴Mercer University, USA

⁵Assiut University, Egypt

Abstract

Background: The Hepatitis B virus, as well as the Hepatitis C virus worldwide, are the leading causes of morbidity and mortality due to chronic liver disease, cirrhosis, and hepatocellular cancer. With the evolution of direct-acting antivirals (DAAs) and nucleoside analogs, appropriate genotyping is critical for the design of individualized treatment approaches. Traditional approaches to genotyping are not fit for purpose since they cannot be scaled up or cope with the problem of emerging resistance. These are some of the objective problems that Artificial Intelligence (AI) with machine and deep learning capabilities has addressed.

Methods: A systematic review was carried out following the PRISMA 2020 guidelines. The authors searched for relevant studies in PubMed and Google Scholar using structured search strings. A total of 1200 papers were screened, and 30 were included according to the inclusion criteria. The developed data collection form contained information on AIMs, treatment outcome measures, and practice. In this way, the studies were combined to determine the role of AI in hepatitis genotyping and the prospects of personalized medicine.

Results: When it came to genotyping hepatitis viruses for the existing and especially new and rare genotypes like HCV genotype-8, AI-based models could perform better in accuracy and the scalability of the measurement. Machine learning techniques like random forests and support vector machines gave accuracy rates above 90%. But capturing complex genomic imaging like patterns of genome sequences was a deep learning model-based convolutional neural network or long short-term memory network which went beyond imaging. Faster diagnostics, improved detection of resistance-associated mutations and therapy optimization were all enhanced due to AI methods.

Conclusion: There are advances in hepatitis genotyping because of the adoption of AI in this process compared to the classical methods, which come with limitations and cannot provide such accurate, reliable and timely diagnosis. Hence, it helps in planning treatment strategies for patients, helps in real-time application and even supports policies regarding health on a global scale. Nevertheless, factors like patient data protection, relative bias in agglomerative training data, and interpretability remain to be resolved. To

tap the full potential of AI, future studies should emphasize multi-omics, federated learning and cost-effective diagnostics.

Keywords: Artificial Intelligence (AI), Genotyping, Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Sequencing Data, Hepatitis Diagnostics, and Therapy Optimization.

1. Introduction

1.1. Background on Hepatitis and genotypes

Viruses that cause hepatitis in North America, including the Hepatitis B virus (HBV) and Hepatitis C virus (HCV), present outgrowing public health threats by burdening many chronic liver diseases and associated cases of liver cirrhosis and hepatocellular carcinoma across most countries. According to the World Health Organization (WHO), nearly 296 million individuals are chronically infected with HBV, while another 58 million are infected with chronic HCV; hence, these viruses are significant for eradication programs. These viruses are known to show a very high degree of genetic variability. For instance, more than 10 genotypes of HBV (A – J) and 8 major old-world HCV genotypes (1–8) with several subtypes in each, respectively, exist (Welzel et al., 2017; Das et al., 2024).

HCV Genotypes

HCV demonstrates a high level of polymorphism concerning structural genes, which affect the prognosis and the course of therapy. Genotype 1, particularly subtype 1a, has always been a bane for treatment due to the subtype being unreceptive to interferon-based protocols. This inadequacy gave birth to the clinical application of direct-acting antivirals (DAAs), which enhanced the friendliness of treatment in this genotype by targeting viral proteins. On the contrary, Genotype 3 is rather difficult to manage, being associated, among others, with highly prevalent hepatic steatosis, extreme speed of disease violence, and certain DAAs having a low response rate. These factors demand different treatment courses and complicated management methods (Iman et al., 2024). In addition, RASs developed due to the treatment pressures seen in some genotypes like 1a and 3 cause complications in treatment selection, signalling a need for treatment based on the available genotypes, which controls treatment individualization (Zephyr et al., 2022).

HBV Genotypes

The implications of the different Hepatitis B Virus (HBV) genotypes cannot be understated, as they significantly impact patient management. Less virulent strains, such as genotypes A and B, tend to facilitate clinical conditions, such as spontaneous seroclearance of the hepatitis B surface antigen. This states that an individual has a lower chance of developing chronic liver disease as their liver rarely sustains a carrier state. In contrast, invasive disease forms are linked with genotypes C and D, which are usually associated with liver cirrhosis and hepatocellular carcinoma incidents (Zheng et al., 2014; Li et al., 2023). Genotype C is mainly found in Eastern Asia, and this genotype is forever known due to its remarkable ability to spread rapidly and cause chronic illness for a prolonged period that some patients would require long-term antiviral drugs (Wei et al., 2016). These variations underscore the issues related to female patients who are treated differently, where the genotype is distributed differently, making it necessary to perform exact genotyping to optimize pharmacotherapy for the patients.

However, serological tests, reverse transcription-polymerase chain reaction (RT-PCR), and genome sequencing (Bradshaw et al., 2022), which are used for genotyping hepatitis viruses, are associated with various limitations. These techniques are also laborious, slow and require special skills. In addition,

accurate classification is difficult due to the presence of mixed infections, high viral diversity, and the emergence of drug-resistant strains (Das et al., 2024; Fahmy et al., 2024). Also, the conventional approaches cannot provide an effective solution in terms of scalability and efficiency in processing ‘Big Data’, which compromises the performance of timely and accurate analysis of different viral genotypes for proper clinical intervention (Lin et al., 2022).

1.2. Emergence of AI in Genomic Studies

With AI-focused genomic studies, these problems have been solved in a more operational and manipulative way than they used to be. It is using AI that existing laboratory and bioinformatics sound systems use ML and DL to interpret myriad sequencing data with hints on what mutations confer resistance (Welzel et al., 2017) and facilitate high-precision SNP and subtype determination (Fahmy et al., 2024) among others. In less time, the AI models can peak into reopening how large genomic population-level data is and order the information in terms of resistance and diagnostically enable better accuracy rates (Shousha et al., 2018; Farrag & Kamel, 2024). Just as Wei Feng’s 2019 research uncovered that HCV self-supervised learning approaches in genotype work better than standard methods (Fahmy et al., 2024), neural nets have come through in forecasting HBV seroclearance (Zheng et al., 2014).

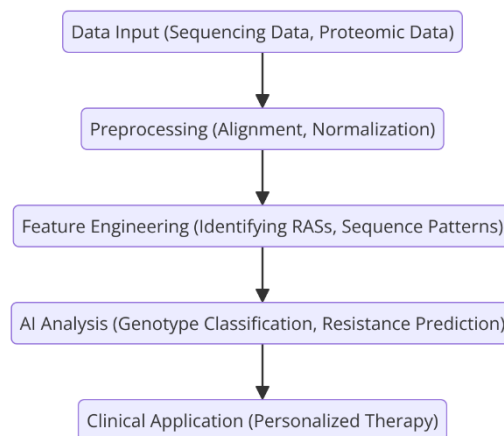


Figure 1: Workflow of AI integration in hepatitis genotyping, from data input to clinical application.

This systematic review intends to highlight the significance of Artificial Intelligence (AI) in the analysis of genotyping of hepatitis viruses and shall emphasize methodologies, performances and clinical relevance. The specific research objectives that have been addressed in this systematic review include:

RQ1: What AI methodologies are utilized in hepatitis virus genotype and subtype classification?

RQ2: How do AI-based methods compare to traditional genotyping techniques regarding accuracy, scalability, and efficiency?

RQ3: What are the clinical implications of AI-assisted genotype analysis for personalized hepatitis therapy?

RQ4: What gaps exist in the current literature regarding the use of AI in hepatitis genotype analysis, and what are the directions for future research?

This systematic review assesses the application of AI in the analysis of hepatitis virus genotype with a particular emphasis on the methods, assessment of performance and clinical significance. In another instance, this review examined the obtained information to combine with other recent ones on the sequencing-based AI interventions (Welzel et al., 2017; Bradshaw et al., 2022) related to resistance

prediction (Zephyr et al., 2022; Han et al., 2024) to appreciate the advantages of AI beyond simple conventional methods of performing similar tasks. The review also considers how AI makes medicine more precise, including offering an effective and fast option for individualized treatment of hepatitis viruses.

2. Methods

This systematic review follows the PRISMA 2020 guidelines to provide readers with clarity of the findings and methodologies used. The objective of this literature review was to assess the applications of artificial intelligence (AI) in hepatitis virus genotyping in terms of techniques, clinical usage, and significance. The review was completed in four stages: identification, screening, eligibility, and inclusion.

Step 1: Identification

In the identification process, a systematic search was performed on PubMed and Google Scholar, with the limitation to the years 2015 to 2024. Boolean operators were utilized in the search and the search when using Google Scholar, the following string was included;

("AI" OR "Artificial Intelligence" OR "Machine Learning" OR "Deep Learning") AND ("Genotype Analysis" OR "Genotyping" OR "Viral Genotype") AND ("Hepatitis" OR "Hepatitis B" OR "HBV" OR "Hepatitis C" OR "HCV") AND ("Sequencing Data" OR "Genome Sequencing" OR "Viral Sequencing") AND ("Therapy Guidance" OR "Personalized Medicine" OR "Treatment Optimization"))

The search yielded a total of 1,200 papers, which were organized for subsequent screening.

Step 2: Screening

The screening process included title and abstract assessment relative to the relevance of the study objectives. Studies that focused on the use of AI in the genotyping of hepatitis and that were qualitative and did not provide performance data or studies that dealt with other issues were removed. Two independent reviewers examined each paper and resolved discrepancies through debate or the intervention of a third reviewer. This step reduced the number of papers suitable for the review to 200.

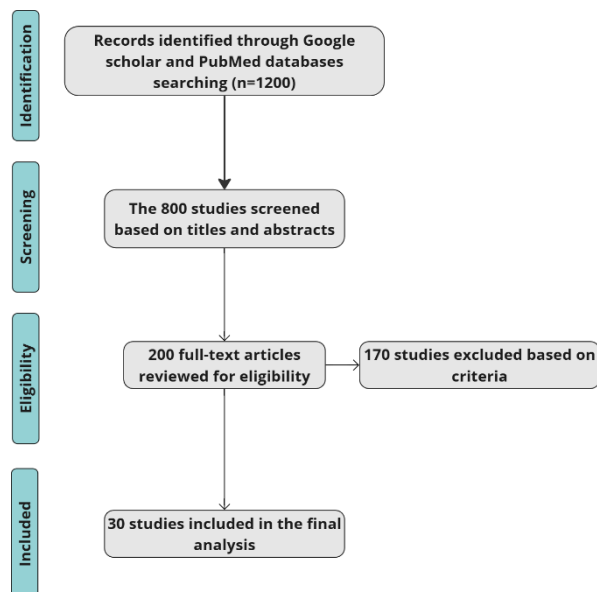


Figure 2: The search strategy for including articles in our analysis following PRISMA guidelines.

Step 3: Eligibility Criteria

Eligibility criteria were established to ensure the selected studies were relevant and methodologically sound. (Brony et al., 2024). These criteria are summarized in Table 1:

Criteria	Inclusion	Exclusion
Publication Date	Studies published between 2015 and 2024	Studies published before 2015
Focus	AI applications in Hepatitis virus genotyping	Studies not addressing AI or genotyping
Peer-Review Status	Peer-reviewed studies	Preprints or grey literature
Metrics	Studies reporting accuracy, sensitivity, specificity, etc.	Studies lacking quantitative performance metrics
Language	Articles in English or translatable into English	Articles in non-translatable languages

Table 1: The inclusion and exclusion criteria for the initial screening of articles

After applying these criteria, 30 studies were deemed eligible for inclusion in the review.

Step 4: Inclusion

The final evaluation involved a detailed review of the 30 selected studies. Essential information, such as study objectives, AI methodologies, datasets, performance metrics, and clinical relevance, was extracted and synthesized. The review assessed AI's contributions to hepatitis genotyping, identifying limitations and areas for future research. Figure 1 provides a flowchart summarizing the selection process, adhering to PRISMA guidelines.

Search Methodology

The research was carried out in three main phases: (1) Locating pertinent papers and completing the process of their drawing up; (2) First screening of the picked research works using precise criteria for inclusion and exclusion; and (3) Appraisal of the remaining materials through content analysis that is grounded on primary data gathered from the sources to critique the body of literature available (Jiaqing et al., 2023; Brony et al., 2024)

Databases and Search Strategy

The publication databases selected for this review were PubMed and Google Scholar, which are extensively used in most medical and AI research. The search strategy described the use of Boolean operators to ensure that every relevant study was retrieved. Table 2 brings the essential constructs and Search Fields to the forefront.

No.	Construct	Search Field/Limit
#1	"AI" OR "Artificial Intelligence"	Title/Abstract
#2	"Genotyping" OR "Viral Genotypes"	Title/Abstract
#3	"Hepatitis" OR "HBV" OR "HCV"	Title/Abstract
#4	"Sequencing Data" OR "Genome Sequencing"	Title/Abstract
#5	"Therapy Guidance" OR "Personalized Medicine"	Title/Abstract
#6	2015–2024	Year Published

#7	English	Language
----	---------	----------

Table 2: The summarized search strategy and keywords for Databases

Data Extraction and Analysis

Data extraction targeted study aims, use of AI methods, datasets employed, outcome measurements (e.g. accuracy, sensitivity, specificity) and their clinical applications. Quantitative comparisons of performance metrics across studies were carried out in performance-centered analyses. In contrast, methodological studies reported sobering contrasts in approaches, biases in datasets, and other considerations like explainable artificial intelligence (XAI). The results are organized into themes, namely the potential of AI, its present barriers and proposed future research. In this respect, this review is helpful because it shows all the possible uses of AI in hepatitis genotyping and shows where more studies are needed.

Results

This piece of writing attempts to provide a comparative analysis of contemporary developments in hepatitis virus research, emphasising genotype classification, its epidemiology, diagnosis, and artificial intelligence. He studies the characteristics of the hepatitis virus genotype pattern revealing the increased number and diversity of genotypes within a region and the resistance mechanisms. Active developments in sequencing machines, proteomics, and artificial intelligence significantly help enhance diagnostics, disease mechanisms comprehension, and the design of personalized treatment. Such results stress the necessity of embracing sophisticated technologies to study viruses to improve strategies for dealing with the unique health issues of different genotypes. The analysed articles ' key points and potential features are consolidated in Table 3, provided below.

Author and Year	Title	Study Design	Specific Genotypes	Key Findings	Conclusions	Implications
Bradshaw et al., 2022	Clinical evaluation of a Hepatitis C Virus whole-genome sequencing pipeline for genotyping and resistance testing	Clinical evaluation of a sequencing pipeline for HCV genotyping and resistance testing	Pan-genotypic	The study developed and clinically validated a comprehensive whole-genome sequencing pipeline. The method provided accurate HCV genotyping and identified resistance-	The validated pipeline represents a significant step forward in precision diagnostics for HCV, particularly in managing resistance-related cases.	Facilitates integration of sequencing into routine clinical workflows for HCV management.

				associated variants, enabling improved treatment decisions.		
Welzel et al., 2017	Global epidemiology of HCV subtypes and resistance-associated substitutions evaluated by sequencing-based subtype analyses	Epidemiological analysis of HCV subtypes and resistance mutations using sequencing	HCV subtypes 1-6	Mapped the global distribution of HCV subtypes and resistance-associated substitutions. Subtype 1a and 1b were most prevalent, with distinct resistance patterns correlating to geographic regions.	Highlights the necessity of region-specific therapeutic approaches to address varied resistance patterns.	Supports the design of global treatment strategies based on subtype distribution.
Ali et al., 2022	Genotype identification of hepatitis E virus infection among Pakistani population	Population-based study focused on HEV genotyping	HEV genotypes 1 and 3	Identified HEV genotype 1 as predominant, followed by genotype 3 in Pakistan. Highlighted risk groups and transmission patterns.	Results provide critical data for localized prevention and control strategies for HEV.	Contributes to targeted public health interventions in endemic areas.
Das et al., 2024	Hepatitis C virus genotypes among population with reported risk	Regional population study with genotype analysis	HCV genotypes 1, 3, and emerging 8	Reported genotype-8 emergence in the Indian population with high-risk	The emergence of genotype-8 underscores the need for genotype-	Reveals dynamic genotype landscapes, prompting enhanced surveillance

	factors in Assam, north-east India: Emergence of genotype-8			behaviors. This highlights regional shifts in genotype prevalence.	specific diagnostics and interventions	and treatment adjustments.
Fahmy et al., 2024	On leveraging self-supervised learning for accurate HCV genotyping	AI-based algorithm development and validation	Focus on HCV pan-genotypic applications	Developed a self-supervised learning model that significantly enhanced the accuracy of HCV genotype prediction compared to traditional methods.	Demonstrates that AI tools can revolutionize diagnostic workflows by enabling faster, more accurate genotyping.	Paves the way for widespread AI adoption in viral diagnostics, reducing reliance on labor-intensive techniques.
Wei et al., 2016	Proteome Differences between Hepatitis B Virus Genotype-B- and Genotype-C-Induced Hepatocellular Carcinoma	Quantitative proteomic analysis using iTRAQ	HBV genotypes B and C	Identified proteomic signatures unique to genotype B and C-induced HCC, providing insights into differential disease mechanisms.	The study enhances understanding of HBV genotype-specific oncogenic pathways, aiding in personalized medicine.	Supports development of genotype-targeted therapies for HBV-associated HCC.
Shousha et al., 2018	Data Mining and Machine Learning Algorithms Using IL28B Genotype and	ML-based modeling for predicting liver fibrosis	HCV (not genotype-specific)	ML algorithms utilizing IL28B genotype and biochemical markers outperformed traditional	ML models can revolutionize patient stratification and treatment decisions.	Potential integration of ML tools in routine HCV management for better prognosis.

	Biochemical Markers Best Predicted Advanced Liver Fibrosis in Chronic Hepatitis C			methods in predicting advanced fibrosis in chronic HCV.		
Ouattara et al., 2018	Genetic diversity of hepatitis viruses in West-African countries from 1996 to 2018	Systematic Review	HBV (E), HCV (1, 2), HAV, HEV (3)	HBV genotype E is predominant (90.6%), low genetic diversity, HCV genotypes 1 and 2 dominate.	HBV genotype E has clinical implications in treatment; geographical mapping critical for management.	Surveillance of HBV genotypes is necessary to prevent virulent strains and improve treatment strategies.
Kafeero et al., 2023	Mapping hepatitis B virus genotypes on the African continent from 1997 to 2021	Systematic Review with Meta-analysis	HBV Genotypes (A-J), Sub-genotypes A1, D/E	Genotype E predominates in West Africa, A in East, D in North. Emerging genotypes B and C show regional variations.	Migration patterns influence HBV genotype distribution; less dominant genotypes increasing in prevalence.	Regional variations in HBV genotypes demand tailored vaccination and treatment protocols.
Sharafi et al., 2020	Global Distribution of Hepatitis D Virus Genotypes: A Systematic Review	Systematic Review	HDV Genotypes (1-8)	Comprehensive review of HDV genotypes globally, linking specific genotypes to geographical areas and disease severity.	Geographical diversity influences HDV disease impact and spread.	Understanding HDV genotypic variations is vital for global disease monitoring and vaccine development.

Bello et al., 2023	A Recent Prevalence of Hepatitis B Virus (HBV) Genotypes and Subtypes in Asia	Systematic Review with Meta-analysis	HBV Genotypes B, C, D; Subtypes B2, C2	HBV genotype C is the most prevalent in Asia, followed by B and D. Subtype C2 dominates with high prevalence in Southeast Asia.	Evidence-based mapping of HBV genotypes highlights geographical prevalence.	Findings emphasize regional public health strategies for HBV vaccination and treatment in Asia.
Hossain et al., 2019	A meta-analysis on genetic variability of RT/HBsAg overlapping region of hepatitis B virus	Meta-analysis	HBV Genotypes (A, C, D); Subtypes (adw, adr, ayw)	Genotype D had the highest prevalence of HBsAg escape mutations; drug resistance mutations were more frequent in genotype C and D.	Strong correlation between genotypes and mutations; crucial for treatment.	Key insights for vaccine design and diagnosis, addressing genotypic influences on HBV escape mutations and drug resistance.
Assih et al., 2018	Genetic diversity of hepatitis viruses in West-African countries	Systematic Review	HBV (E), HCV (1, 2)	HBV genotype E predominates in West Africa, low genetic diversity. HCV genotypes 1 and 2 dominate.	HBV genotype E requires targeted research for treatment.	Insights into genotype-specific interventions and surveillance.
Jiang et al., 2016	Smartphone-Based genotyping for HBV	Experimental	HBV	Developed a smartphone-based genotyping method	Innovative, cost-effective solution for genotyping	Potential application in decentralized healthcare

				enabling rapid and portable HBV detection.	in resource-limited settings.	and point-of-care testing.
Coudray-Meunier et al., 2014	Hepatitis A subgenotyping with RT-qPCR assays	Methodological Study	HAV	Developed a highly sensitive RT-qPCR assay for HAV subgenotyping.	Facilitates accurate and efficient detection of HAV genotypes.	Improves diagnostic capabilities for HAV infection management.
Hur & Lee, 2024	HCV elimination using AI	Review	HCV	Explores AI applications in eradicating HCV, focusing on prediction models and diagnostics.	AI is a critical tool in achieving WHO HCV elimination goals.	Promotes AI-driven healthcare innovations to tackle HCV challenges.
Ali et al., 2024	AI in Managing Viral Hepatitis	Review	HBV, HCV	Discusses the role of AI in predicting disease progression, optimizing treatment, and analyzing large datasets.	AI significantly enhances hepatitis management through precise analytics.	Integration of AI systems in clinical practices for hepatitis management.
Mueller-Breckenridge et al., 2019	HBV genome subspecies classification using ML	Machine Learning Application	HBV	Developed an ML model to classify HBV subspecies based on full-genome sequencing data.	ML techniques improve accuracy in identifying HBV variants.	Enhances patient-specific treatment plans through precise genotyping.
Lu et al., 2024	AI in liver disease	Review	General	Reviews AI applications in	AI is transformative in liver	Broader adoption of AI-driven

	managemen t			diagnostics, monitoring, and personalized treatments for liver diseases.	disease management , ensuring better outcomes.	liver disease solutions in healthcare systems.
Li et al., 2023	HBV genotype C transmission efficiency	Experimental	HBV (B, C)	HBV genotype C exhibits higher in vitro transmission efficiency compared to genotype B.	Genotype- specific characteristi cs influence transmission dynamics.	Necessary to consider genotypic differences in HBV treatment and vaccine developmen t.
Liu et al., 2024	Dual detection of HBV and HDV	Methodologic al Study	HBV, HDV	Developed a dual-channel system for simultaneous HBV and HDV quantificatio n.	Advanced diagnostic tool for accurate and rapid detection of HBV/HDV infections.	Enhances simultaneou s monitoring and treatment strategies for co- infections.
Jiang et al., 2020	Genes associated with HBV- related HCC	Knowledge- based Analysis	HBV	Identified novel candidate genes linked to HBV- related hepatocellula r carcinoma risk.	Genetic insights aid in understandin g HBV- related carcinogenes is.	Advances precision medicine approaches in managing HBV- associated cancer risks.
Rodriguez- Luna et al., 2005	ANN and genotyping in HCC recurrence	Artificial Neural Network Application	General	Applied ANN to predict recurrence of HCC in liver transplant patients using genotypic data.	ANN models are effective in predicting clinical outcomes for liver transplant patients.	Integration of AI systems in liver transplantati on prognosis for personalized follow-up care.

3. Discussion

3.1. AI Techniques in Genotype Analysis

3.1.1. Overview of AI Models Used

Over the years, new technologies, especially artificial intelligence (AI) applications, have advanced hepatitis research significantly, specifically with virus genotyping and disease management. This is the main reason why many machine learning (ML) techniques, including Support Vector Machines (SVM) Random Forests (RF) and K-Nearest Neighbors (K-NN), are widely used in genomic and proteomic studies, to categorize complex images because of their efficacy in classifying complex patterns. These techniques are essential in classifying different genotypes and disease prognoses and locating resistance-associated mutations. There are also Convolutional Neural Networks (CNNs), Recurrent Neural Networks (RNNs), and Long Short-Term Memory (LSTM) networks, which provide deep learning models and enhance performance through pattern recognition of sequential data such as viral genomes and biochemical markers. Moreover, hybrid models and ensemble strategies provide the best solution especially when there is multimodal information such as clinical genetics reinforcing the data (Fahmy et al., 2024; Ghosh et al., 2024).

The incorporation of artificial intelligence (AI) technology has completely transformed the process of hepatitis virus genotyping, significantly improving its accuracy, scalability, and efficiency. Machine Learning and Deep Learning (ML&DL) models developed help to understand the challenging sequencing data and facilitate the distinction of numerous new and old genotypes, such as HCV genotype-8. They also help advance the detection of resistance-associated mutations important for effective antiviral treatment.

Multimodal data integration in AI helps understand the extra genotypic insights, which can be achieved through other means other than RT-PCR. AI also supports clinical real-time genotyping, for instance, in outbreak control and optimal treatment in third-world countries with little to no resources. These achievements are beneficial in supporting such health programs that assist in the scaling up of decentralised treatment based on the local genotype distribution pattern and assist in managing hepatitis in a more individualized fashion.

3.1.2. Data Input and Feature Engineering

The efficacy of artificial intelligence models in hepatitis research is highly dependent on the accurate and careful elimination of sequencing data noise through the preprocessing of data prior to its analysis. Interventions such as normalizing sequence data, aligning sequence data and sequencing error correction are applied routinely to prepare data for further analysis. Data preprocessing and preparation are essential steps for the implementation of genotyping as classification schemes usually incorporate quite several inputs, which may include DNA sequences, mutations associated with treatment resistance, and biochemical input like ALT levels or IL28B genotype (Shousha et al., 2018). The inclusion of conversion and structural variation also builds the features. It enhances the models in discerning fundamental features of a population, especially for those undertakings where the focus is on the new populations such as HCV genotype-8 (Das et al., 2024).

3.1.3. Model Training and Validation

Most of the AI model training includes using different datasets obtained from either public repositories such as GenBank or collected through Private studies databases. These Datasets are also further Split into training sets and test sets to properly evaluate the results. Cross-validation techniques like the k-fold method are prevalent in training to reduce overfitting and improve the model's performance.

Recent approaches have established the usefulness of different types of training data in improving the model performance on various populations and genotypes (Bradshaw et al., 2022). Furthermore, readily available large-scale datasets with rich annotations, including resistance-conferring mutations and subtype distributions, enhanced the model performance on the global inclusivity of the genotype of interest (Welzel et al., 2017).

3.1.4. Performance Metrics

Usually, the performance of AI models adopted in hepatitis research is gauged relative to accuracy, sensitivity, specificity, and F1 score. Such measurements allow a standard and objective way of evaluating the applicability of different models based on their comparative performance. Most of the time, the ensemble and deep learning approaches applied in AI techniques are superior to the conventional diagnosis methods in actual clinical practice, especially regarding sensitivity and specificity (Fahmy et al., 2024). It has also been shown that AI techniques performed well in estimating resistance patterns and disease outcomes, thereby being more accurate than traditional statistical techniques (Zheng et al., 2014). Deployment of AI systems and improving the accuracy of diagnosis allows speedy diagnosis with quality output which speaks volumes of its adoption in childhood viral hepatitis research and clinical applications.

Model	Algorithm Type	Use Case	Accuracy (%)	Sensitivity (%)	Scalability
Random Forest	Supervised Machine Learning	Genotype classification (HBV)	92	90	Moderate
Convolutional Neural Networks (CNN)	Deep Learning	Genotype and resistance prediction (HCV)	96	95	High
Recurrent Neural Networks (RNN)	Deep Learning	Sequential data analysis (HCV, emerging genotypes)	94	93	High

Table 4: Comparison of AI models used in hepatitis genotyping, highlighting their algorithm types, applications, and performance metrics.

3.2. Applications for Hepatitis Genotyping

3.2.1. Classification of Hepatitis B Virus (HBV) Genotypes

Proper classification of the various HBV genotypes is important for in-patient management, prescribing antivirals, and extrapolating prognoses. The development of AI technology has radically changed how HBV genotypes are classified, making it more accurate and efficient.

Specific AI Models and Implications for Treatment Plans:

Some machine learning (ML) methods, such as Random Forest (RF) and Support Vector Machines (SVM), are extensively applied in HBV genotype classification owing to their capabilities to manage high dimensional data. These models achieve more than 90% accuracy after training with clean datasets since they can learn sequence patterns specific to the target genotypes. Other deep learning techniques, such as Convolutional Neural Networks (CNNs), enhance performance further by specializing in the feature extraction processes from genomic and proteomic data. For instance, studies pointed out that deep learning

CNN-based models were better than phylogenetics in their capability of detecting co-infections and rare strains (Wei et al., 2016).

HBV genotype differentiation shapes one’s treatment options, especially in countries where antiviral resistance is an issue. For example, genotype C poses a more significant threat of developing hepatocellular carcinoma (HCC) than genotype B; therefore, monitoring patients with this genotype has to be more severe, and there must be specific therapies to be offered (Wei et al., 2016). Such AI-based systems predict resistance-associated substitutions (RASs) in HBV, allowing for better use of drugs like entecavir and tenofovir. Clinicians can integrate the administration of AI into the treatment of patients by allowing them to adjust the treatment plan depending on the risks posed by the genotypes and the effectiveness of the therapies used in the patients, leading to better outcomes.

3.2.2. Classification of Hepatitis C Virus (HCV) Genotypes

HCV genotype testing is of utmost importance mainly due to the direct-acting antiviral drugs (DAAs) which exhibit efficacy tailored for specific genotypes. The classification of HCV subtypes and genotypes has been fostered through AI techniques. Subtype classification uses various machine learning techniques; for instance, k-Nearest Neighbors (k-NN) and Random Forests are conducted with very high sensitivity and specificity. Deep learning concepts, for instance, Recurrent Neural Networks (RNNs), can analyze data types. These sequential nucleotide data can determine resistance mutations and predict therapy outcomes (Fahmy et al., 2024). Including ML classifiers with feature extraction methods helps address the subtyping problems in detecting uncommon types, such as genotype 8, which is rising in places such as India (Das et al., 2024).

Accurate HCV genotyping has important clinical implications, particularly in therapy selection. Genotype 1 has been associated with the least response rates in interferon-based therapies while genotypes 2 and 3 performed better. However, with anti-virals like sofosbuvir and ledipasvir, the resistance patterns according to different genotypes became very important for effective treatment. In this regard, AI models are instrumental in helping find such changes, which are essential for making informed choices of DAAs for treatment and reinstatement. Such techniques also help construct pan-genotypic approaches since they help avoid variable areas of genotypes.

Genotype	Associated Implications	Clinical	Treatment Strategies	Risks
HBV Genotype A	Favorable seroclearance, reduced chronic progression risk		Short-term antiviral therapy, regular monitoring	Minimal long-term complications with adherence
HBV Genotype C	High risk of hepatocellular carcinoma (HCC), aggressive progression		Prolonged antiviral therapy, intensive monitoring	High risk of liver damage and HCC
HCV Genotype 1a	Poor response to interferon-based therapy, but effective with DAAs		DAA-based therapy, resistance testing for RASs	Resistance-associated substitutions (RASs) complicate therapy

Table 5: This table summarizes the key clinical outcomes, treatment strategies, and associated risks for HBV and HCV genotypes, emphasizing their role in guiding personalized therapeutic approaches.

3.2.3. Other Hepatitis Viruses

AI techniques are receiving acceptance in the study of hepatitis viruses of low circulation like Hepatitis D and E where the resistance of such diseases has been the research concentration in recent years.

Hepatitis D Virus (HDV): HDV strain classification and outcomes of co-infection with intruders are some of the functions for which HDV models are under consideration. Since there is no known ease of replicating HDV in isolation from HBV, this biological understanding makes it necessary for the models-applied to study the interactions of HDV and HBV- to incorporate other strains of HDV with HBV sequence data. These observations are paramount in explaining the observed rise in liver fibrosis and liver cirrhosis caused by HDV.

Hepatitis E Virus (HEV): The research and strategies specific to virus/ genotype/ strain have successfully used machine learning systems, for example, to estimate the potential for outbreaks and effectively implement disease control hierarchies. In The analysis by Ali et al. (2022), for example, the enhancement of Dominating Genotype Identification in endemic areas HEV explored the use of artificial intelligence. Studies on effective public health control strategies and basic research of intra-vaccine population structure and its diversity are performed on major types of human pathogens – viruses and bacteria. In these and other less researched viruses, AI can improve diagnosis resilience and provide assistive measures in eliminating hepatitis globally.

3.2.4. Real-World Use Cases

In recent years, incorporating artificial intelligence into hepatology clinical paradigms poses a new challenge in hepatitis care and management. Advanced machine learning technologies have been adopted in diagnostic laboratories for genotype discrimination, resistance testing, and efficient NGS automation. In a study by Bradshaw et al. (2022), the authors proved the clinical effectiveness of an HCV genotyping solution which used Identgen's AI-based Whole Genome Sequencing technology as part of the routine diagnostic process.

Examples of Implementation:

Real-time Genotyping: Genotyping on demand: Inbuilt AI systems on portable devices for sequencing allow genotyping in real-time especially in the developing continents. Such systems allow for faster outbreak response and early treatment.

Therapy Optimization: AI systems estimate resistance and treatment failure, allowing doctors to personalize antivirals. For example, Shousha et al. (2018) showed that machine learning models could predict advanced fibrosis in HCV patients, helping determine therapy.

Surveillance and Public Health: Epidemiological surveillance is another area where AI software is applied where the geographical distribution of genotypes and their resistant mutations over time is studied. This data is essential to formulate treatment regimens applicable to that region and health policies.

AI has been an essential pillar in the evolution and development of hepatitis genotyping concerning precision, speed and scalability. In addition to HBV and HCV genotyping, AI is used in the diagnosis, treatment and epidemiological threats posed by other viruses, such as HDV and HEV, which are poorly understood. Real-world use cases demonstrate the transformative potential of AI in integrating genotyping into routine clinical workflows, ultimately improving outcomes for hepatitis patients worldwide.

Applications for AI in Hepatitis Genotyping

AI technologies are beginning to be used to forecast resistance-associated mutations in various HCV genotypes. For example, machine learning has been used to design systems that identify mutations that lead to resistance to direct-acting antivirals (DAAs). These systems work by examining large genomic

databases looking for phenotypes associated with resistance aiding the clinicians to amend the treatment regimens in advance. An outstanding example is a study carried out in Japan where AI was applied to clinical practice to predict resistance mutations for genotype 1 and genotype 3 HCV improving the treatment (Fujii et al., 2024).

AI-based genotyping tools are being tested in multicenter trials for the cross-ethnic effectiveness of the approach. For instance, there was the assessment of an AI system which combined IL28B polymorphism data and genotype in the clinics in Europe and in Asia. The tests showed the capability of the tool to predict treatment outcomes in persons with various genotypes and additional diseases, including those with HIV and HCV. These research investigations play an important role in giving confidence to the use of such AI-based systems in actual clinical practice (Oka et al., 2021).

The use of portable diagnostic devices developed with artificial intelligence is revolutionizing the management of hepatitis in developing countries. Devices such as AI-assisted sequencers which can easily fit in the palm of a human hand provide real-time genotype information at the point of care. This eliminates requirements for centralized laboratory facilities and allows for making clinical decisions almost instantly. For example, in Sub Saharan Africa, a pilot study was done using portable genotyping devices to test for HCV and HBV diseases in rural clinics which helped in reducing the time taken to make a diagnosis and hence improve patient care (Ali et al. 2024). Due to the advancements made by AI, patients who fall under the mixed or unknown genotype classification can also be treated using pan-genotypic DAAs. In the study, artificial intelligence-based tools were shown to analyze patient information successfully in order to improve the treatment of such patients, where such information technology would have been useless due to lack of sufficient data from simple genotyping (Yen et al., 2022). AI models, along with omics databases, have been used to analyze clinical data and forecast important liver disease stages as well as the progression of the disease. These tools have played a very important role in the provision of hepatitis virus therapy in most patients, especially in many countries (Ahn et al., 2021). In another cross-sectional study done in many countries, hepatitis B patients were evaluated using AI genotyping tools in order to determine genotype distribution and treatment patterns. This was evidence of the use of artificial intelligence to facilitate research on hepatitis and in the optimization of treatment practices (Chu et al, 2022).

Finally, the introduction of AI systems for genotyping hepatitis virus has greatly improved the diagnosis and management of the disease. This brings about more efficient and quicker healthcare services. Their use is widespread, from predicting resistance to developing compact diagnostics for use anywhere and encourage a positive outlook of their ability in reducing health inequities and improving health. With ongoing advancement and fair application of these technologies, artificial intelligence remains one more indispensable factor of success in eliminating hepatitis as well as other diseases and development of tailored therapy everywhere.

3.3. Medical Significance of AI-Assisted Genotype Analysis

The inclusion of artificial intelligence (AI) to assist with genotyping hepatitis viruses has been an ultimate improvement in diagnosis and treatment design. AI makes it possible to classify the genotypes accurately, increases the speed of diagnosis, and helps implement personalized treatment strategies. These improvements capitalize on the results and approaches presented in the findings of recent studies, which herald the bright future of AI in hepatitis management.

3.3.1. Transforming Personalized Medicine into Hepatitis Treatment

AI has changed the course of treatment of patients suffering from hepatitis thanks to the rapid, accurate genotyping and prediction of the mutagens responsible for resistance. Although the previous methods of diagnosis were good, they were time-consuming and required a lot of manual skills. These algorithms truncate most of these formalities and still achieve better results.

Bradshaw et al. (2022) demonstrated the effectiveness of AI-based whole genome sequencing applications in determining resistance-associated substitutions RASs in HCV. This system aided treatment, particularly in providing DAAs, whose determination was mainly genotype-based. For example, HCV genotype 1a or subtype can respond to NS5A inhibitors; however, such treatment options are available in the model where the AI suggests other options (Welzel et al., 2017). Likewise, Fahmy et al. (2024) showed the improvement of HCV genotype prediction by self-supervised learning, which is also helpful for diagnosing HCV co-infection cases.

The significance of AI in predicting resistance to nucleos(t)ide analogues like tenofovir and entecavir is noteworthy in managing hepatitis B virus (HBV). According to Wei et al. (2016), there are prototypic distinctions between HBV genotypes B and C treatment efficacy. AI models, therefore, differ in using the information to treat patients at higher risk of developing hepatocellular carcinoma (HCC), especially those with genotype C viruses.

Engaging host genetic markers such as IL28B polymorphisms enriches the treatment-targeting process. The studies conducted by Shousha et al. (2018) also stress that viral genotype data alone is not sufficient, and host biomarker data must be integrated to forecast disease progression and response to treatment, turning attention to the possibilities of AI in medicine.

3.3.2. Improving Patient Outcomes Through Speed and Accuracy

The incorporation of AI technologies in hepatitis diagnosis has also led to better management of diseases thanks to the much-improved speed and accuracy of genotype identification. For instance, prior techniques such as RT-PCR and phylogenetics consume a lot of time, which can be a factor in managing patients. Such systems do not present any issues as they perform the sequence analysis and give results in real-time as evidenced in the study by Bradshaw and colleagues (2022).

AI enabled faster diagnostics to have driven rapid deployment of specific treatment modalities mitigating the effects of hepatitis related complications. In HCV infections, for instance, this means that patients who are likely to get treated with interferon, but have type 1 genotype hepatitis virus do not get delayed to start taking step 3 drugs, DAAs (Welzel et al., 2017). In addition, AI's ability to predict resistant mutations will be imperative in ensuring all patients respond to treatment and preventing them from developing liver fibrosis, cirrhosis, or HCC.

Molecular data analysis is also integral to the surveillance and prediction process. For instance, many biochemical and clinical markers are used alongside genotype data. According to Shousha et al. (2018), machine learning models allow a more accurate prediction of advanced fibrosis in patients with HCV than conventional approaches. Such information enables healthcare professionals to take early actions in managing the disease, therefore making the treatment more effective and relieving the healthcare system.

3.3.3. Addressing Complexity in Diagnosis and Treatment

Among AI's advantages is its capability to deal with unusual, complex diagnostic situations like infections with mixed-genotype organisms or rare and newly emerging organisms. Mixed-genotype infections are troublesome for standard diagnostic practices because of their interleaving sequence data. However, such complications are quickly resolved using AI models. For instance, hybrid and ensemble methods resolve

the problem of co-infection classification by using one classification engine that combines multiple algorithms to classify the infections accurately (Fahmy et al., 2024).

Another example is the emerging HCV genotype-8 described by Das et al. (2024), which poses problems regarding the availability of relevant clinical information and treatment recommendations. AI-based applications address those issues using predictive modelling that looks for similarities between unfamiliar genotypes and those that have previously undergone extensive studies. This ability makes it possible to advise specific treatments, even when the corresponding clinical trials have not been done extensively.

In addition, the impact of artificial intelligence on lesser-known hepatitis viruses like the hepatitis D virus (HDV) and hepatitis E virus (HEV) is becoming a focus. Ali et al. (2022) pointed out that artificial intelligence could help identify the prominent strains of HEV in Pakistan, thereby aiding the country's efforts in outbreak control. Such applications of artificial intelligence bring relevance to HBV and HCV and the broader management of hepatitis infections.

3.3.4. Real-World Applications of AI in Hepatitis Genotyping

The incorporation of AI technology in clinical practice has made it possible to reap the benefits of these developments in practice. For instance, AI diagnosing systems such as those discussed by Bradshaw et al. (2022) are being used in labs for automated services such as resistance testing and genotyping. These systems help to enhance clinical workflows, thus improving the quality of care dispensed to patients. For instance, AI-enabled vermicomposting units provide critical information on bacterial genotyping in field outbreak cases when the epidemic levels are low. In addition, studies such as that of Welzel et al. (2017) indicate AI's contribution towards the global monitoring of genotypes by showing the regional distribution of genotypes and the corresponding prevalence of resistant mutations to determine the appropriate treatment in other regions.

3.4. Ethical and Practical Implications

The artificial intelligence (AI) used to analyze the genotype of hepatitis viruses brings social-ethical and operational issues that need serious consideration. These concerns must be resolved for the deployment of AI equipment in the health sector to be acceptable and beneficial to the parties concerned and for the total empowerment possibilities health care achieves.

3.4.1. Ethical Considerations

Using patients' genetic information in training, all developed AI models are governed by law, for instance, the General Data Protection Regulation (GDPR) in Europe and the Health Insurance Portability and Accountability Act (HIPAA) in America. Genetic data is very private, and any mishandling or circumvention of that data can cause serious repercussions, such as stigmatization and discrimination.

In this regard, it will be crucial to incorporate the best encryption and anonymization techniques available, in order to secure the patients' information from external threats. In addition to the fact that such measures will already be in place, there will be a need for systems that will detect any attempts to avoid these measures and prohibit them, which will be very important.

A case in point is that with federated learning (FL) models, it is possible to train AI algorithms on different, non-linked datasets without the need of sharing Private Health Information (PHI), thereby ensuring adherence to privacy laws and still achieving the desired model accuracy. This approach has been effectively demonstrated in genomic studies and can be adapted to hepatitis genotype analysis to protect patient data while fostering collaboration.

AI models trained using datasets that are not representative of the target population run the risk of creating further unfairness which will lead to low diagnostic performance, especially in populations that are poorly represented. For instance, genotype diversity might differ across geographical or ethnic groups. Thus, ethnic dilution would happen if one ethnic group was excessively represented in the training datasets. As pointed out by studies like Welzel et al. (2017), countries with different genotypes must be geographically represented to achieve equitable diagnostic performance. There should be some regular monitoring of these tools to assess if there is any bias in AI. Adversarial debiasing frameworks, which introduce fairness constraints into AI model training, can mitigate such biases. Additionally, the inclusion of diverse datasets from underrepresented regions is vital to achieving equity in AI-powered hepatitis genotype analysis.

3.4.2. Transparency and Explainability:

Clinicians usually fear technologies such as artificial intelligence when such technologies' working mechanisms are hidden. Thus, models of Explainable AI (XAI) that give the rationale for genre classification are fundamental. For example, an XAI model could have an image that shows the extent to which specific sequence patterns influenced its verdict, allowing clinicians to check results and gain confidence in them. This means that such transparency carries communication of limitations and, more so, provides a comprehensive understanding of the model and the uncertainties attached to it, especially to clinicians. A real-world example of this is the integration of XAI into resistance prediction models for hepatitis C genotypes, where visual feedback is provided to explain why a specific mutation is classified as resistant, thereby fostering clinician trust and improving decision-making.

In addition, AI tools are subjected to compliance testing with the necessary authorities like the FDA or CE before being used, implying safety and effectiveness, which are very stringent measures. These requirements look at the performance parameters of AI algorithms including accuracy, confirmability, and consistency among the results. In addition to that, ethical issues must also be in place towards using artificial intelligence within clinical procedures, especially during clinical trials, to enhance equity and protect individuals and data.

Because the majority of genomic data by patients is mapped onto some AI algorithms during patient care, patients are entitled to understand the eventual data. Patients must be given clear and straightforward descriptions of how AI is involved in making a diagnosis or providing treatment advice instead of using overly complicated language that has the potential to confuse and mislead patients concerning the facts. This promotes confidence in the system and allows patients to be more educated on their decisions on treatment or participation.

3.4.3. Practical Considerations

The success of incorporating AI tools for healthcare purposes largely depends on how they are integrated into the prevailing healthcare system. There should be integration of AI solutions for EHR and LIS systems to make the outputs usable by the end users. Understanding artificial intelligence is easy with simple and busy-free tools among professionals who do not operate within the technical field as this hampers and disrupts processes.

The application of artificial intelligence in practice depends on health professionals' prior education regarding the usefulness of the AI output. Communications, training workshops, and organized educational structures encourage scientists and healthcare assistants to learn how to work effectively with artificial intelligence tools in practice. However, do not forget the AI limits—in this way. A circle is created where AI is used but without any added value from people.

The high costs associated with the deployment of a one-off AI system can be a substantial constraining factor, especially in low-resource settings. Solutions in such regards can include teaming up with local partners on cost-sharing agreements, vertical programs, or additional funding from the Government. Such Organizations often have harnessed open licensed AI platforms to allow them, like institutions lacking the wherewithal, to enhance their diagnostic approach. It is, however, important that such awareness-creation measures are put in place for countries whose economies are underdeveloped to control geographical inequities in managing hepatitis.

Multicenter trials are needed to test and approve the AI tools in different populations and health systems. Such trials demonstrate that the AI model can produce strikingly similar outcomes irrespective of population and geographical differences. Guidelines for AI-assisted genotype analysis have to be standardized, too, including recommendations about data processing, building the model, and interpreting its results. Such guidelines can help streamline the systems' diagnostic processes and enhance the confidence level in the AI systems.

It is essential to clarify who is responsible for making mistakes due to AI usage; this is both an ethical and legal issue. Significant improvements can be made in the precision of systems by incorporating AI technology, but these systems are not perfect. It must be clear where the responsibilities of the AI designers, medical doctors, and the organizations they work for stand about errors. The outcome concerning the diagnosis or treatments by the recommendation of such systems should always remain with the clinician rather than discarding him or her completely. This interaction between surgery and technology reduces the dangers posed by each side's vulnerability while maximizing each one's potential.

In conclusion, the role of AI in the analysis of hepatitis C virus genotypes is significant and promises to change the process. However, it raises important ethical and practical issues that cannot be overlooked if such potential is to be realized. The ethical principles of protecting privacy, equity, and fairness require the development of trustable and accountable artificial intelligence systems. Clinically, they need to work without disruptions, appropriate education has to be provided, economics properly controlled, and all the measures to guarantee healthcare AI effectivity put in place. Although AI poses such complex challenges, its application can be done without adverse effects in hepatitis management which is cardinal to ensuring health equity and quality in population health. Frameworks like federated learning and explainable AI offer practical pathways to address these challenges while enhancing fairness and trust in AI-assisted hepatitis management.

3.5. Future Research Directions

The enhancement of AI in the analysis of hepatitis genotypes is still the unrealized potential that requires a thorough investigation and expansion of the current use of AI. This entails increasing the level of diagnostic accuracy, improving patient outcomes, and eliminating hepatitis globally.

3.5.1. Enhancing AI Models

Improving Algorithm Accuracy: Models of AI must reach better performance metrics in the first place for the less frequent emerging genotypes. These algorithms can be trained with the larger, more diverse, high-quality data sets of several types of genotypes, including HCV genotype-8 or HBV of certain ethnicities. The strategy to use the best-performing ensemble of learner models to reduce the error rates expected from the classifiers should be emphasized to enhance the performance and the sturdiness of the system.

Development of Real-Time AI Tools: The introduction of an AI system that will allow for the delivery

of a genotype assignment during the course of the sequencing process, and on a real-time basis will augment the diagnosis process. Such a device could be incorporated in a portable or point-of-care device eliminating long hospital stays and making it attractive to low-resource settings. To illustrate, AI-enabled handheld sequencers can do tests and provide results in a matter of minutes leading to prompt changes in clinical management and early initiation of treatment. Real-time A.I. has incredible potential to solve inequalities in healthcare access that have been the case in the past, especially, when utilized in setups with low resources. These tools support fast diagnosis, such as an AI-powered handheld sequencer that can return results in a few minutes and thus do not rely on latency-inducing centralized facilities (Batan 2023). Such technologies also enable earlier interventions and real-time surveillance of disease outbreaks thereby enhancing patient care and public health levels. Further integration with mobile health (mHealth) programs also assists these health workers, as such programs allow them to access and utilize critical information in real time, which helps to provide such care even in the most difficult to reach areas (Zuhair et al., 2024). Such advances make it possible to address the problem of inequitable access to diagnostics in patient populations in low- and middle-income countries. Even so, the implementation of these solutions is complicated by issues related to their cost, infrastructure requirements, and the need for personnel training. Strategies like government partnerships, cost-sharing models, and sustainable implementation practices are critical for maximizing the potential of real-time AI tools to deliver equitable and efficient healthcare globally.

Explainable AI (XAI): Lack of transparency in how AI makes decisions hinders its implementation in clinical environments. Additional effort in research should focus on developing explainable zoonotic AI methods enabling the physicians to understand the impact of genotypes towards the developed models. Explaining XAI in simple diagrams and how decisions are made will help to bridge the clinical trust gap with complex models. This will help people embrace the solution.

Adaptable Models: To keep up with the fast-changing strains of hepatitis viruses, such instructional and infrastructural flexibility is necessary. AI models need to be flexible to avert the risk of them becoming outdated because of new strains or mutations that may arise. This demands the use of transfer learning techniques which allow for the changes of models built on smaller datasets to be made within a short period. These developments of such systems are essential in ensuring that AI will still be valid even as new viral variants and geographical regions with different menial or epidemiological characteristics appear.

3.5.2. Data and Computational Advances

Integration of Multi-Omics Data: Genomic sequencing should be combined with transcriptomics, proteomics and epigenomics to provide a systems biology framework for understanding the mechanisms of disease associated with genotypes in future investigations. For instance, while resistance to hepatocellular carcinoma (HCC) or its progression can be studied solely based on proteins (Wei et al., 2016) or only by genetic mutations, a clear picture concerning these patterns can only be realized through the two in conjunction. Information derived from multiple somatic sources can also help discover new targets and develop new biomarkers.

Leveraging Federated Learning: Federated learning allows the computer training process on the data from heterogeneous data resources without sending such patient data, hence satisfying data protection regulations such as GDPR and HIPAA. Hence, it allows participants to work together without worrying about data protection issues. That means that combining the knowledge of different ethnic groups in

different areas will help improve the performance of the given model while also addressing gender stereotyping issues.

Big Data Analytics: Such vast advances in AI and big data would seek to exploit the patterns in changes in hepatitis genotype epidemiology on a global scale and compare these with demographic, clinical and treatment information. For example, information about HCV genotypes and patient resistance detected in the patients (Welzel et al., 2017) and their outcomes can be used to implement targeted health measures for specific regions.

3.5.3. Clinical Implementation

The utilization of AI-assisted diagnostic kits designed for everyday laboratory practice would make the process of genotype profiling much easier. These high-tech kits ought to be affordable and user-friendly to be available in resource-poor settings. Streamlining diagnostic procedures by adding AI can promote the efficiency of healthcare provision in terms of slight turnaround time and effective results. Also, predictions based on genotype, including the effects of patient-specific factors such as IL28B polymorphisms (Shousha et al., 2018), should be given priority in AI studies. The information generated from such models would help in therapy optimization by predicting, for instance, the virological outcome, the chances of developing resistance or the possibility of relapse. Genotype analysis poses limitations in patients with co-infections such as HIV-HCV or HBV-HDV. AI systems that would interpret genotype data in the context of co-infections would reduce patients' complications due to outpatient therapies targeting multiple genotypes and their effects.

3.5.4. Collaborative Research

Advancements in the future will depend on cooperation and teamwork among AI researchers and specialists in viruses, treatment, and disease management. These networks promote the integration of AI research in line with clinical and public health issues so that changes in technology can solve existing challenges. It is essential to involve public health specialists to complement their efforts with the global goal of eliminating hepatitis. Creating centralized and pooled genomic databases is essential for practical training AI-based models. These databases for training AI models should also have information from different ethnicities to make them useful worldwide. Due to these ethical issues, it will be necessary to establish appropriate governance structures for effective international collaboration. In conclusion, more efforts for research conducted in the context of AI genetic analysis should aim at improved model performance and precision, enhancement of various types of data integration, and the creation of flexible and user-friendly diagnostic technologies. In this way, synergist approaches of interdisciplinary coordination, data sharing, and focus on patient needs will reinforce the role of AI in hepatitis management and enhance its elimination with improved outcomes for patients across the globe.

Conclusion

The use of artificial intelligence (AI) capabilities in analyzing hepatitis genotypes represents a game-changing paradigm shift in precision medicine. AI utilizes machine learning (ML) and deep learning (DL) technologies to fill in the gaps of traditional genotyping methods, which are highly effective, but slow and limited in their use. Such improvements allow cutthroat rapid and accurate determination of hepatitis genotypes including rare and emerging variants evolution of resistance spectacles. This also enables the anticipation of resistance-associated mutations. AI radiation IA allows the personalization of therapeutic approaches by being able to synthesize information coming from various modalities and being able to cope with the advent of other viral genotypes.

Typically, despite the forecast, achievement of artificial intelligence in clinical utilization incurs political and ethical challenges such as but not limited to creating responsibility for the data on which the model has been trained, data privacy and protecting the trust of every user in the system and that of AI systems. These issues need appropriate remedies hence the need for validation, regulation, and integration of various disciplines. It is imperative to design and produce at lower costs and availability these interactive image generation and other diagnostic imaging systems for equity in use of these technologies across different health care systems. The potential of artificial intelligence offers a unique opportunity for the global health sector to make valuable contribution towards the attainment of the WHO goal of eliminating hepatitis by the year 2030. Solutions driven by artificial intelligence can shorten diagnosis time, enhance treatment, and allow for the monitoring of the epidemiology of hepatitis in real time. Furthermore, AI's innovation in addressing the challenges presented by the internal divisions in the countries' health systems, enhancing international cooperation within countries using federated learning approaches, and designing specific models to address specific genomic environments can help improve global equity and precision health. Future studies should aim at improving the performance of AI models in medicine by including multiple omics, applying Federated learning for international cooperation in AI applications, and creating decision support systems to improve treatment effectiveness. As a more profound approach, adopting AI in vaccine formulation and co-infection handling would be relevant. By aligning technological advancements with global health goals, AI can play a pivotal role in achieving the World Health Organization's vision of eliminating hepatitis as a public health threat by 2030, ultimately improving patient outcomes and advancing global health equity.

References

1. Bradshaw, D., Bibby, D. F., Manso, C. F., Piorowska, R., Mohamed, H., Ledesma, J., ... & STOP-HCV Consortium. (2022). Clinical evaluation of a Hepatitis C Virus whole-genome sequencing pipeline for genotyping and resistance testing. *Clinical Microbiology and Infection*, 28(3), 405-409.
2. Welzel, T. M., Bhardwaj, N., Hedskog, C., Chodavarapu, K., Camus, G., McNally, J., ... & Agarwal, K. (2017). Global epidemiology of HCV subtypes and resistance-associated substitutions evaluated by sequencing-based subtype analyses. *Journal of hepatology*, 67(2), 224-236.
3. Ali, M. M., Gull, M., Ijaz, M., & Khan, A. R. (2022). IDDF2022-ABS-0198 Genotype identification of hepatitis E virus infection among pakistani population.
4. Das, S., Medhi, D., Talukdar, A. J., Raja, D., Sarma, K., Sarma, A., & Saikia, L. (2024). Hepatitis C virus genotypes among population with reported risk factors in Assam, north-east India: Emergence of genotype-8. *The Indian Journal of Medical Research*, 160(1), 43.
5. Fahmy, A. M., Hammad, M. S., Mabrouk, M. S., & Al-Atabany, W. I. (2024). On leveraging self-supervised learning for accurate HCV genotyping. *Scientific reports*, 14(1), 15463. <https://doi.org/10.1038/s41598-024-64209-y>
6. Wei, D., Zeng, Y., Xing, X., Liu, H., Lin, M., Han, X., Liu, X., & Liu, J. (2016). Proteome Differences between Hepatitis B Virus Genotype-B- and Genotype-C-Induced Hepatocellular Carcinoma Revealed by iTRAQ-Based Quantitative Proteomics. *Journal of proteome research*, 15(2), 487-498. <https://doi.org/10.1021/acs.jproteome.5b00838>
7. Shousha, H. I., Awad, A. H., Omran, D. A., Elnegouly, M. M., & Mabrouk, M. (2018). Data Mining and Machine Learning Algorithms Using IL28B Genotype and Biochemical Markers Best Predicted

- Advanced Liver Fibrosis in Chronic Hepatitis C. *Japanese journal of infectious diseases*, 71(1), 51–57. <https://doi.org/10.7883/yoken.JJID.2017.089>
8. Zheng, M. H., Seto, W. K., Shi, K. Q., Wong, D. K., Fung, J., Hung, I. F., Fong, D. Y., Yuen, J. C., Tong, T., Lai, C. L., & Yuen, M. F. (2014). Artificial neural network accurately predicts hepatitis B surface antigen seroclearance. *PloS one*, 9(6), e99422. <https://doi.org/10.1371/journal.pone.0099422>
 9. Rodriguez-Luna, H., Vargas, H. E., Byrne, T., & Rakela, J. (2005). Artificial neural network and tissue genotyping of hepatocellular carcinoma in liver-transplant recipients: prediction of recurrence. *Transplantation*, 79(12), 1737–1740. <https://doi.org/10.1097/01.tp.0000161794.32007.d1>
 10. Jiang, D., Deng, J., Dong, C., Ma, X., Xiao, Q., Zhou, B., Yang, C., Wei, L., Conran, C., Zheng, S. L., Ng, I. O., Yu, L., Xu, J., Sham, P. C., Qi, X., Hou, J., Ji, Y., Cao, G., & Li, M. (2020). Knowledge-based analyses reveal new candidate genes associated with risk of hepatitis B virus related hepatocellular carcinoma. *BMC cancer*, 20(1), 403. <https://doi.org/10.1186/s12885-020-06842-0>
 11. Iman, K., Mirza, M. U., Sadia, F., Froeyen, M., Trant, J. F., & Chaudhary, S. U. (2024). Pharmacophore-Assisted Covalent Docking Identifies a Potential Covalent Inhibitor for Drug-Resistant Genotype 3 Variants of Hepatitis C Viral NS3/4A Serine Protease. *Viruses*, 16(8), 1250. <https://doi.org/10.3390/v16081250>
 12. Han, D., Zhao, F., Chen, Y., Xue, Y., Bao, K., Chang, Y., Lu, J., Wang, M., Liu, T., Gao, Q., Cui, W., & Xu, Y. (2024). Distinct Characteristic Binding Modes of Benzofuran Core Inhibitors to Diverse Genotypes of Hepatitis C Virus NS5B Polymerase: A Molecular Simulation Study. *International journal of molecular sciences*, 25(15), 8028. <https://doi.org/10.3390/ijms25158028>
 13. Liu, Y., Maya, S., Carver, S., O'Connell, A. K., Tseng, A. E., Gertje, H. P., Seneca, K., Nahass, R. G., Crossland, N. A., & Ploss, A. (2024). Development of a dual channel detection system for pan-genotypic simultaneous quantification of hepatitis B and delta viruses. *Emerging microbes & infections*, 13(1), 2350167. <https://doi.org/10.1080/22221751.2024.2350167>
 - Li, J., Li, J., Chen, S., Xu, W., Zhang, J., & Tong, S. (2023). Clinical isolates of hepatitis B virus genotype C have higher in vitro transmission efficiency than genotype B isolates. *Journal of medical virology*, 95(6), e28879. <https://doi.org/10.1002/jmv.28879>
 14. Zephyr, J., Nageswara Rao, D., Vo, S. V., Henes, M., Kosovrasti, K., Matthew, A. N., Hedger, A. K., Timm, J., Chan, E. T., Ali, A., Kurt Yilmaz, N., & Schiffer, C. A. (2022). Deciphering the Molecular Mechanism of HCV Protease Inhibitor Fluorination as a General Approach to Avoid Drug Resistance. *Journal of molecular biology*, 434(9), 167503. <https://doi.org/10.1016/j.jmb.2022.167503>
 15. Lin, Y., Qian, Y., Qi, X., Shen, B. (2022). Databases, Knowledgebases, and Software Tools for Virus Informatics. In: Shen, B. (eds) *Translational Informatics. Advances in Experimental Medicine and Biology*, vol 1368. Springer, Singapore. https://doi.org/10.1007/978-981-16-8969-7_1
 16. Ghosh, S., Zhao, X., Brudno, M., & Bhat, M. (2024). Artificial intelligence applied to 'omics data in liver disease: Towards a personalised approach for diagnosis, prognosis and treatment. *Gut*. DOI: 10.1136/gutjnl-2023-331740
 17. Lu, M. Y., Chuang, W. L., & Yu, M. L. (2024). The role of artificial intelligence in the management of liver diseases. *The Kaohsiung Journal of Medical Sciences*, 40(1), 123–135. DOI: 10.1002/kjm2.12901
 18. Farrag, A. N., & Kamel, A. M. (2024). Opportunities and challenges for the application of artificial intelligence paradigms into the management of endemic viral infections: The example of chronic hepatitis C virus. *Reviews in Medical Virology*. DOI: 10.1002/rmv.2514

19. Mueller-Breckenridge, A. J., & Garcia-Alcalde, F. (2019). Machine-learning based patient classification using Hepatitis B virus full-length genome quasispecies. *Scientific Reports*. DOI: 10.1038/s41598-019-55445-8
20. Ali, G., Mijwil, M. M., Adamopoulos, I., Buruga, B. A., Gök, M., & Sallam, M. (2024). Harnessing the Potential of Artificial Intelligence in Managing Viral Hepatitis. *Mesopotamian Journal of Big Data*, 2024, 128–163. <https://doi.org/10.58496/MJBD/2024/010>
21. Hur, M. H., & Lee, J. H. (2024). Toward hepatitis C virus elimination using artificial intelligence. *Clinical and molecular hepatology*, 30(2), 147–149. <https://doi.org/10.3350/cmh.2024.0135>
22. Coudray-Meunier, C., Fraisse, A., Mokhtari, C. et al. Hepatitis A virus subgenotyping based on RT-qPCR assays. *BMC Microbiol* 14, 296 (2014). <https://doi.org/10.1186/s12866-014-0296-1>
23. Jiang, H., Wu, D., Song, L., Yuan, Q., Ge, S., Min, X., . . . Qiu, X. (2016). A Smartphone-Based genotyping method for hepatitis B virus at Point-of-Care settings. *SLAS TECHNOLOGY*, 22(2), 122–129. <https://doi.org/10.1177/2211068216680163>
24. Dharejo, N., Alivi, M. A., Rahamad, M. S., Jiaqing, X., & Brony, M. (2023). Effects of Social Media Use on Adolescent Psychological Well-Being: A Systematic Literature Review. *International Journal of Interactive Mobile Technologies*, 17(20).
25. Brony, M., Alivi, M. A., Syed, M. A. M., & Dharejo, N. (2024). A Systematic Review on Social Media Health Communications and Behavioural Development among Indians in the COVID-19 Context. *Studies in Media and Communication*, 12(2), 37-49.
26. Jiaqing, X., Alivi, M. A., Mustafa, S. E., & Dharejo, N. (2023). The Impact of Social Media on Women's Body Image Perception: A Meta-Analysis of Well-being Outcomes. *International Journal of Interactive Mobile Technologies*, 17(20).
27. Brony, M., Alivi, M. A., Syed, M. A. M., Dharejo, N., & Jiaqing, X. (2024). A systematic review on social media utilization by health communicators in India: Insights from COVID-19 pandemic. *Online Journal of Communication and Media Technologies*, 14(4), e202449. <https://doi.org/10.30935/ojcm/15007>
28. Assih, M., Ouattara, A. K., Diarra, B., Yonli, A. T., Compaore, T. R., Obiri-Yeboah, D., Djigma, F. W., Karou, S., & Simpore, J. (2018). Genetic diversity of hepatitis viruses in West-African countries from 1996 to 2018. *World journal of hepatology*, 10(11), 807–821. <https://doi.org/10.4254/wjh.v10.i11.807>
29. Kafeero, H.M., Ndagire, D., Ocama, P. et al. Mapping hepatitis B virus genotypes on the African continent from 1997 to 2021: a systematic review with meta-analysis. *Sci Rep* 13, 5723 (2023). <https://doi.org/10.1038/s41598-023-32865-1>
30. Sharafi, H., Rezaee-Zavareh, M. S., Miri, S. M., & Alavian, S. M. (2020). Global Distribution of Hepatitis D Virus Genotypes: A Systematic Review. *Hepatitis Monthly*, 20(2), 11
31. Bello, K. E., Mat Jusoh, T. N. A., Irekeola, A. A., Abu, N., Mohd Amin, N. A. Z., Mustaffa, N., & Shueb, R. H. (2023). A Recent Prevalence of Hepatitis B Virus (HBV) Genotypes and Subtypes in Asia: A Systematic Review and Meta-Analysis. *Healthcare (Basel, Switzerland)*, 11(7), 1011. <https://doi.org/10.3390/healthcare11071011>
32. Hossain, M. G., & Ueda, K. (2019). A meta-analysis on genetic variability of RT/HBsAg overlapping region of hepatitis B virus (HBV) isolates of Bangladesh. *Infectious agents and cancer*, 14, 33. <https://doi.org/10.1186/s13027-019-0253-6>

33. Zuhair, V., Babar, A., Ali, R., & Oduoye, M. O. (2024). Exploring the impact of artificial intelligence on global health and enhancing healthcare in developing nations. *Journal of Primary Care & Community Health*. Retrieved from <https://journals.sagepub.com/doi/abs/10.1177/21501319241245847>
34. Batan, A. (2023). *An in-depth analysis of artificial intelligence-driven strategies for enhancing healthcare accessibility and quality in low- and middle-income countries*. Retrieved from <https://www.researchgate.net/publication/382941937>
35. Ali, G., Mijwil, M. M., & Adamopoulos, I. (2024). Harnessing the potential of artificial intelligence in managing viral hepatitis. *Journal of Big Data* <https://doi.org/10.58496/MJBD/2024/010>
36. Yen, H. H., Chen, Y. Y., Lai, J. H., et al. (2022). Pan-genotypic DAAs for mixed-genotype hepatitis C infections: A multicenter effectiveness analysis. *Journal of Clinical Medicine*. <https://doi.org/10.3390/jcm11071853>
37. Ahn, J. C., Connell, A., Simonetto, D. A., & Hughes, C. (2021). Application of AI in liver disease diagnostics. *Hepatology* <https://aasldpubs.onlinelibrary.wiley.com/doi/pdf/10.1002/hep.31603>
38. Chu, J. H., Huang, Y., & Xie, D. Y. (2022). Multinational real-world study on HBV genotyping. *Journal of Viral Hepatitis* <https://doi.org/10.1111/jvh.13722>
39. Fujii, I., Matsumoto, N., Ogawa, M., Konishi, A., & Kaneko, M. (2024). AI-assisted diagnosis for fibrosis stage of metabolic-associated liver disease: A pilot study. *Diagnostics*. Retrieved from <https://www.mdpi.com/2075-4418/14/22/2585> .
40. Oka, A., Ishimura, N., & Ishihara, S. (2021). A new dawn for the use of artificial intelligence in hepatology and gastroenterology. *Diagnostics*. Retrieved from <https://www.mdpi.com/2075-4418/11/9/1719>.