

Role of Artificial Intelligence in Hepatitis B Virus-Associated Liver Injury Diagnosis Relationship

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ABSTRACT

HBV infection is one of the most significant health problems worldwide and the most frequent causes of chronic liver disease, cirrhosis and hepatocellular carcinoma. The mechanism of liver injury in HBV infection is a complicated process that is catalyzed by the viral replication, host immune response and progressive fibrotic alteration. Knowledge of the HBV life cycle since the entry of the hepatocytes and covalently closed circulation DNA to viral replication and maintenance is crucial to correlate molecular pathogenesis of HBV with clinical liver damage. The traditional methods of diagnosis, such as serological markers, biochemical parameters and image procedures such as ultrasonography, computed tomography are important in evaluation of the disease. Artificial intelligence (AI) has recently become the hepatological power tool that helps to improve the accuracy of non-invasive imaging based and assessing liver fibrosis, inflammation and early hepatocellular carcinoma. Machine learning and deep learning algorithm make it possible to interpret images automatically, predict risk and disease progression. This review focuses on the interrelation between HBV viral pathogenesis and liver injury pathogenesis and the rising presence of AI-based diagnostic, monitoring and clinical decision-making in HBV related liver disease. .

Keywords: Artificial Intelligence (AI), Hepatitis B virus (HBV), Liver, Fibrosis, cirrhosis, hepatocellular carcinoma (HCC)..

1. INTRODUCTION

Hepatitis B virus (HBV) infection is a serious global health issue in the face of the availability of vaccines and treatment medication. Globally, over 350 million individuals are chronically infected with HBV an annual mortality of approximately 1 million individuals due to HBV related complication[1]. HBV is a small partially dual stranded DNA virus belonging to the family of Hepadnaviridae. Hepatitis B virus (HBV) is an enveloped virus whose inner icosahedral nucleocapsid contains a partially double stranded relaxed circle of DNA (rcDNA) genome, which is replicated by reverse transcription of an.

intermediate RNA, the pregenomic RNA (pgRNA)[2]. Chronic HBV infection is linked to high chances of escalating liver fibrosis, cirrhosis, hepatocellular carcinoma (HCC) and eventually liver failure. Infection may be either acute or chronic and most of the HBV disease burden is associated with chronic disease. Globally, more than 240 million people are chronically infected with hepatitis B virus (HBV)[3]. The transmission of HBV is both vertical and horizontal, such as mother-to-child perinatal, contact with infected blood fluids, abuse of skin integrity and unprotected intercourse. Liver disease like cirrhosis and malignant liver tumors greatly affect the prognoses of a patient and thus early diagnosis and timely therapeutic intervention is important. The imaging diagnosis is usually non-invasive and essential for diagnosing and treating liver disease (e.g. screening to make an early diagnosis in a high-risk population and selection of the most appropriate treatment)[4]. Conventional methods of diagnostics are based on serological markers, viral loads measurement, liver function tests and histopathological analysis in the form of liver biopsy[5]. The recent trends within machine learning (ML) and deep learning (DL) under artificial intelligence (AI) have turned out to be the ground-breaking changes within the sector of hepatology. AI can handle large and complex volume of data (histopathology results, radiologic imaging, laboratory data and electronic health records) and may be applied to reach a diagnosis of the hepatic disease entities more precise and objective. AI-based models have shown good results in identifying liver fibrosis, suffering levels, clinical prognosis and early neoplastic alterations in patients with HBV. The combination of knowledge about the HBV viral pathogenesis and AI-based diagnostic imaging is a new and holistic way of comprehending the disease progression and providing the best way of managing patients[6]. The review paper will describe a comprehensive account of HBV viral pathogenesis and its contribution to liver damage, as well as the recent developments in AI-powered diagnostic imaging methods. This article highlights the possibilities of artificial intelligence to improve the early diagnosis and disease management, as well as individual treatment of HBV related liver disease by bringing together molecular virology with the latest advancements in computational tools

HBV Life Cycle

Hepatitis B virus (HBV) is an infectious virus that enters hepatocytes via a complex multistep life cycle that is central to liver disease development and progression[7]. The attachment to hepatocyte surface proteoglycans (HSPGs) is a low-affinity interaction after which the high-affinity interaction of the preS1 domain of a large hepatitis B surface protein to the sodium taurocholate co-solubilizing polypeptide (NTCP) proteins occurs resulting in viral entry. Once within the cell, the nucleocapsid is then transported to the nucleus where relaxed circular DNA (rcDNA) is converted to covalently closed circular DNA (cccDNA), which remains as a stable episomal minichromosomal and the transcriptional template of all viral RNAs and proteins[8].

Pregenomic RNA (pgRNA) is one of the viral transcripts that are necessary to replicate HBV and serve as the template to reverse transcription in newly formed nucleocapsids[9]. The viral polymerase enzyme facilitates production of negative and positive strand DNA, which lead to the production of progeny rcDNA. No matter what transpires to them, mature nucleocapsids recycle their rcDNA to the nucleus to sustain the intracellular cccDNA pool or are enveloped by surface proteins with the endoplasmic reticulum and Golgi apparatus and result in virion maturation and secretion. Though HBV in itself is not cytopathic, the presence of covalently closed circular DNA and the unremitting expression of viral antigens lead to immunopathic hepatocyte damage, chronic inflammation and progressive fibrosis. The process eventually led to the formation of liver cirrhosis and a great proneness to hepatocellular carcinoma[10].

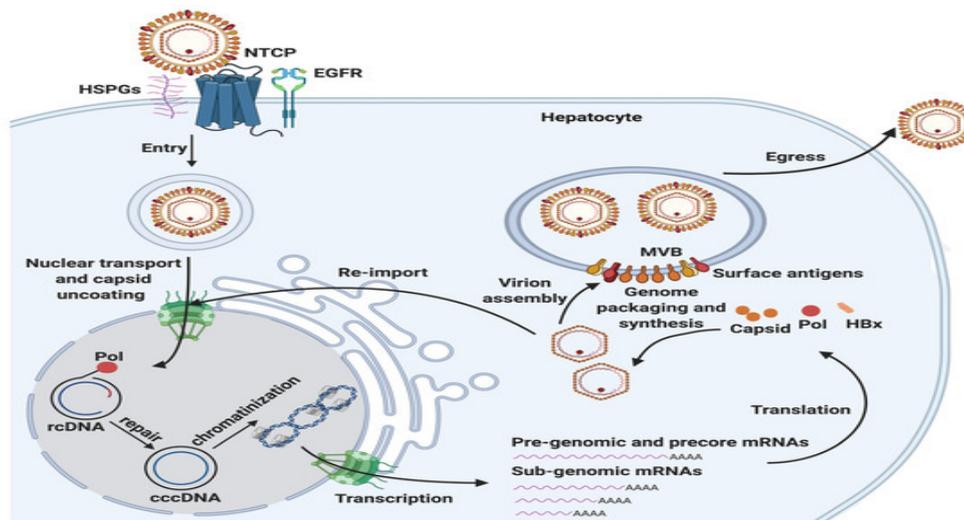


Fig.1: This figure depicts the Hepatitis B virus (HBV) life cycle in hepatocytes, and it can be seen that the virus attaches itself to HSPGs and enters hepatocytes through the NTCP, then nuclear delivery of the rcDNA and transformation into cccDNA, a stable transcription template. Pregenomic and subgenomic RNAs are transcribed, translated and put into nucleocapsid, which is reverse transcribed to give progeny DNA. Mature nucleocapsids either recycle to the nucleus to sustain cccDNA or obtain an envelope in the ER -Golgi pathway and are discharged

as infectious virions. Chronic liver disease is caused by persistent cccDNA and antigen expression[11]

Liver Injury and Progression of Disease in Chronic HBV infection

The Hepatitis B virus (HBV) infection causes liver damage mainly as a result of immune-mediated processes as opposed to direct cytopathic of viral replication[12]. After infection of hepatocytes, HBV DNA remains to form covalently closed circular DNA (cccDNA) in the nucleus used as a template of viral transcription and protein synthesis. Host immune recognition is included by viral antigens but in this case the HBsAg and HBeAg. The infection hepatocytes are targeted by HBV specific cytotoxic T lymphocytes (CTLs) and Natural killer (NK) cells which cause apoptosis and necrosis through the action of perforins, granzymes and pro-inflammatory cytokines like TNF and IFN- γ [13]. Although these immune responses are necessary in removing the virus, their continued existence results in chronic inflammation of the liver that stimulates hepatic stellate cells (HSCs) and includes the deposition of the extracellular matrix (ECM). The resultant fibrogenesis gradually interferes with the normal architecture of the liver and it ends in the fibrosis and cirrhosis[14].

Beside immunologically triggered damage the infection of the HBV helps to cause the hepatocellular damage in case of oxidative stress, dysfunction of mitochondria, endoplasmic reticulum stress, and cellular dysregulation of signaling processes, further enhancing the hepatocyte apoptosis and necrosis[15]. The recurring waves of liver injury and regeneration have to high likelihood of creating genomic instability which predisposes the hepatocytes to mutations. Direct interaction of HBV DNA into the host genome may facilitate oncogenesis through the modulation of gene expression, activation of oncogenes and interference effect on tumor suppressor pathways to enhance malignant change. Therefore, chronic HBV infection is a significant risk factor of hepatocellular carcinoma (HCC), which may occur without cirrhosis indicating the intrinsic oncogenic potential of the virus[16]. Such viral load, liver functioning, fibrosis process and early molecular indications of carcinogenesis monitoring are thus important in the prevention of advanced liver disease and better patient outcomes.

Applications of AI in HBV Liver Disease Diagnosis

Artificial Intelligence (AI) has evolved as a more important component of the hepatitis B virus (HBV) related liver injury diagnostics process as it offers greater skills in image interpretation, data combination and predictive modeling[17]. Because deep learning techniques, especially convolution neural networks, can automate liver segmentation, lesion detection and texture analysis they enhance the diagnostic accuracy of computed tomography, magnetic resonance imaging and ultrasound[18]. These techniques are used to detect liver fibrosis, cirrhosis and hepatocellular cancer which are typically difficult to diagnose by standard visual examination. AI has also improved non-invasive liver fibrosis evaluation by integrating elastography data with imaging feature and clinical factors[19]. Machine learning models reduce operator variation in fibrosis staging and tracking disease progression. Radiomic-based AI techniques go even further, providing diagnostic opportunities based on the extraction of quantitative imaging feature associated with histopathological changes, allowing for objective identification of disease severity and early malignant transformation.

In addition to imaging-based application, AI allows for the integration of multimodal clinical data, such as liver function tests, HBV DNA levels, serological markers, and demographic information. These comprehensive models provide specific risk identification, treatment response predicting and optimal surveillance approaches for HBV-related complication. AI is an effective addition to current diagnostic techniques in the treatment of chronic hepatitis B because it improves diagnosis accuracy, repeatability and clinical decision making.

Clinical Significance and Diagnostic Association

Serological Marker

Hepatitis B virus (HBV) infection is diagnosed and clinically using serological markers. Hepatitis B surface antigen (HBsAg) tests positive for active infection, while hepatitis B e antigen (HBeAg) and serum-specific antibodies test positive for viral replication condition giving a complete picture of the interaction between the host and the virus[20].

Biochemical Marker

Biochemical evaluation through liver function test provides essential information regarding HBV-associated liver injury. Elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels indicate hepatocellular damage caused by immune-mediated inflammation. Additional parameter such as bilirubin, alkaline phosphatase and albumin reflect functional status and disease severity in chronic HBV infection[21].

HBV Viral Load (Molecular Diagnosis)

Molecular methods of HBV DNA quantification like real-time polymerase chain reaction provide a direct quantitative determination of viral replication. Disease involvement and progression are closely associated with viral load levels which is one of the most critical factors in the assessment of chronic hepatitis B and clinical management approaches.

HBV RNA Assays

HBV RNA-detection is a new molecular method which is used as an indirect measure of covalently closed circular DNA (cccDNA) activity. Contrary to the HBV DNA, Serum HBV RNA can be retained even when antiviral suppression occurs which can provide more information regarding the continued viral transcription and persistent infection activity[22].

Liver Biopsy

Liver biopsy is the conventional gold standard of assessing liver injury associated with HBV, as it provides a direct opportunity to evaluate necroinflammation, fibrosis stage, and cirrhotic alteration via a traditional histopathological assessment technique[23]. Although it has been proven to be the most accurate method of diagnosis, its invasiveness, sampling variability as well as the risk of complication have restricted its daily application and more techniques that are not invasive have been used.

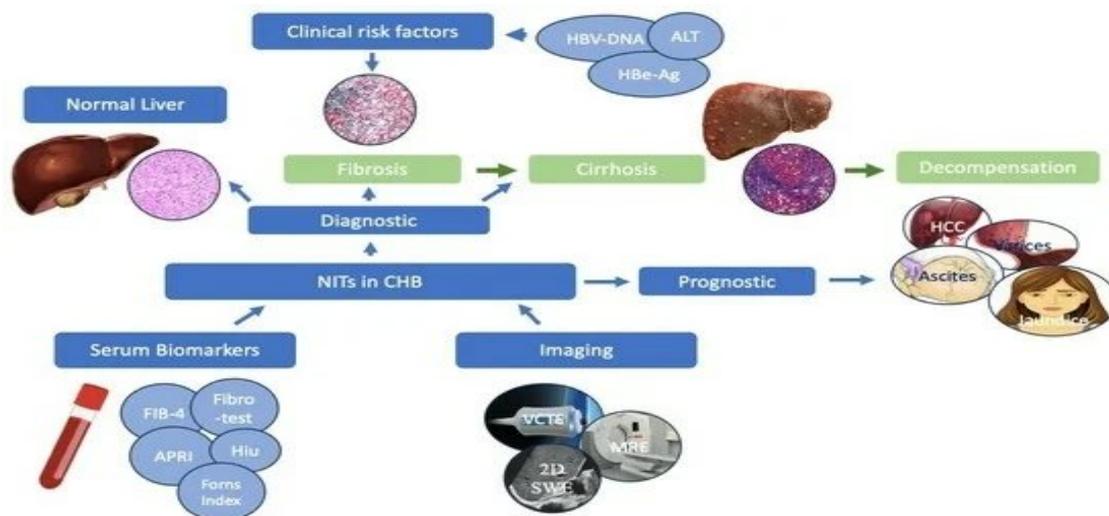


Fig.2: Chronic hepatitis B related liver disease progression and non-invasive evaluation. The figure represents the progression of a normal liver into fibrosis, cirrhosis, and decompensation with the progression being affected by virological factors, including HBV DNA, ALT, and HBeAg. Fibrosis staging and prognostic analysis in chronic hepatitis B are conducted by non-invasive tests, such as serum biomarkers and imaging based on elastography[24].

AI-based diagnostic and Imaging Techniques

AI-based Ultrasound Imaging

AI-assisted ultrasound imaging is an improvement of traditional sonography with automated evaluation of liver texture and structural patterns with machine learning and deep learning algorithms[25]. It enhances the recognition of minor parenchymal alterations and early liver damage and reduces the observer bias.

AI-Integrated Fibro Scan

The liver stiffness is assessed in Fibro scan as the substitute of Fibrosis. AI-powered analytical models enhance the accuracy of fibrosis staging; help add to reproducibility and allow distinguishing with a higher degree of reliability between mild and advanced fibrosis in chronic HBV infection[19].

AI-Assisted Magnetic Resonance Imaging (MRI)

MRI techniques especially the MR Elastography gives very sensitive results on liver stiffness and fibrosis. Image analysis with the help AI can also be used to enhance the characterization of tissues and identify lesions and has a better diagnostic level than ultrasound-based diagnostic options, particularly in the initial stages of the disease[26].

2. CHALLENGES AND LIMITATION

Despite substantial advances in artificial intelligence (AI) based diagnostic tools and biomarker-driven approaches to hepatitis B virus (HBV) associated liver disease, a number of hurdles and limitations to their widespread clinical usage remain[27]. A significant weakness is the diversity of datasets employed to build AI models. The majority of algorithms

have been trained on past, single center datasets that have small sample and may not sufficiently cover the type of populations, disease stages and comorbidities[28]. This makes the diagnostic results based on less generalizable and reproducible in various clinical environments.

The second difficulty is that there are no standardized protocols of data acquisition, imaging parameters and interpretation of biomarkers. The difference in ultrasound equipment, Fibro scan equipment, laboratory tests and experience of the operator can considerably affect the accuracy of the diagnosis and the work of the model resulting in a lack of consistency in the results[29]. Also, the implementation barriers like high cost, lack of sufficient computational infrastructure, privacy of data and untrained personnel limit adoption especially in resource constrained environments.

3. CONCLUSION

Hepatitis B virus infection is a complicated condition where viral persistence and immune response interact to play a role in the liver damage and clinical development. Long-term viability of ccDNA is facilitated by the maintenance of the virus and the chronic inflammation, fibroses, cirrhosis and hepatocellular carcinoma are mediated by immune-mediated mechanisms. The traditional techniques like serological markers, viral load analysis, liver profile and image do not cease to be of significance but some limitations exist particularly in early disease detection. Recent technology developments in artificial intelligence (AI) have contributed greatly to the assessment of HBV related liver injury through more precise, reliable and non-invasive analysis of imaging and clinical information. AI assist in the diagnosis of the disease earlier, enhancing the management and prognosis of chronic hepatitis B associated liver disease..

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