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# LATENT COURSE OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B: COMPARATIVE EVALUATION OF NONINVASIVE DIAGNOSTIC METHODS (APRI, FIB-4 AND FIBROSCAN)

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**Abstract:** Chronic hepatitis B (CHB) remains a significant global health burden, affecting approximately 296 million people worldwide. The progression of liver fibrosis in CHB patients often follows a latent course, making early detection crucial for preventing cirrhosis and hepatocellular carcinoma. While liver biopsy remains the gold standard for fibrosis assessment, its invasive nature has prompted the development of noninvasive diagnostic methods. This study aims to comparatively evaluate the diagnostic accuracy, clinical utility, and cost-effectiveness of three noninvasive methods—APRI (AST to Platelet Ratio Index), FIB-4 (Fibrosis-4 Index), and FibroScan (transient elastography)—in detecting and monitoring the latent progression of liver fibrosis in CHB patients.

**Keywords:** Chronic hepatitis B, liver fibrosis, noninvasive diagnosis, APRI, FIB-4, FibroScan, transient elastography

## Background and Significance

Chronic hepatitis B virus (HBV) infection represents one of the most prevalent chronic viral infections globally, with an estimated 296 million individuals living with chronic hepatitis B as of 2024. The disease burden is particularly pronounced in the Asia-Pacific region and sub-Saharan Africa, where prevalence rates exceed 5-10% of the general population. The natural history of CHB is characterized by a dynamic interplay between viral replication and host immune response, leading to varying degrees of hepatic inflammation and fibrosis progression.

The development of liver fibrosis in CHB patients typically follows an insidious, latent course spanning years to decades. This silent progression poses significant challenges for clinical management, as many patients remain asymptomatic until advanced stages of disease. The rate of fibrosis progression varies considerably among individuals, influenced by factors including viral load, HBeAg status, genotype, host genetic factors, concurrent infections, alcohol consumption, and metabolic comorbidities. Without timely intervention, approximately 20-30% of

The accurate assessment of liver fibrosis is crucial for several clinical decisions in CHB management. First, it determines the need for antiviral therapy initiation, as current guidelines recommend treatment for patients with significant fibrosis (≥F2) regardless of ALT levels. Second, it guides the intensity of surveillance for complications such as hepatocellular carcinoma and portal hypertension. Third, it provides prognostic information regarding disease trajectory and response to therapy. Fourth, it enables monitoring of fibrosis regression following successful antiviral treatment.

**Evolution of Fibrosis Assessment Methods**

Historically, liver biopsy has been considered the gold standard for fibrosis assessment, providing direct visualization of hepatic architecture and the extent of fibrosis deposition. The procedure allows for comprehensive evaluation using established scoring systems such as METAVIR, Ishak, or Knodell scores. However, liver biopsy has significant limitations that restrict its widespread application in routine clinical practice.

The invasive nature of liver biopsy carries inherent risks, including pain (reported in 20-30% of patients), bleeding (0.5%), and rare but serious complications such as pneumothorax or peritonitis. The procedure requires hospitalization or day-case admission, trained personnel, and imaging guidance, making it resource-intensive and costly. Furthermore, sampling error is a well-recognized limitation, as the biopsy specimen represents only 1/50,000th of the liver volume. Studies have demonstrated significant intra-observer and inter-observer variability in histological interpretation, with concordance rates of 70-80% even among experienced pathologists.

**Study Rationale and Objectives**

Despite the availability of multiple noninvasive fibrosis assessment methods, their comparative performance specifically in CHB patients with latent disease progression remains incompletely characterized. Previous studies have primarily focused on individual

methods or specific patient subgroups, with limited data on longitudinal performance in monitoring fibrosis evolution.

This thesis addresses several critical knowledge gaps in the field. First, it provides a comprehensive comparison of three widely available noninvasive methods in a large, well-characterized CHB cohort. Second, it evaluates the performance of these methods across different phases of CHB infection, recognizing the disease's heterogeneous nature. Third, it assesses the ability of each method to detect fibrosis progression over time, crucial for identifying patients requiring treatment escalation.

The primary objective is to determine the comparative diagnostic accuracy of APRI, FIB-4, and FibroScan in detecting significant fibrosis (≥F2) and cirrhosis (F4) in CHB patients, using liver biopsy as the reference standard. Secondary objectives include evaluating the performance of combined testing strategies, assessing the ability to monitor fibrosis progression over 36 months, identifying factors affecting diagnostic performance, determining cost-effectiveness in different healthcare settings, and developing evidence-based algorithms for noninvasive fibrosis assessment in CHB.

**Conclusion:** While FibroScan demonstrates superior diagnostic performance in detecting and monitoring liver fibrosis in CHB patients, the combination of methods enhances overall accuracy. APRI and FIB-4 remain valuable screening tools, particularly in resource-limited settings. A sequential diagnostic approach, utilizing serum markers for initial screening followed by FibroScan for confirmation, may optimize both diagnostic accuracy and resource utilization in managing the latent progression of liver fibrosis in CHB patients.

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