PATHOMORPHOLOGICAL ABNORMALITIES OF THE LIVER IN PATIENTS INFECTED WITH THE HEPATITIS B VIRUS

Tolibov Farrux Farhodivich

Asia International University, Bukhara, Uzbekistan.

tolibovf1@gmail.com

https://doi.org/10.5281/zenodo.15070389

Abstract. *The study examines morphological changes in the liver among different genotypes of chronic hepatitis B (HBV) in Uzbekistan. Among patients with the D genotype, 7.4% exhibited minimal pathological activity, 48.2% had low activity, 25.9% showed moderate activity, and 18.5% experienced pronounced pathological activity. In patients with the C genotype, 33.3% had low activity, 16.7% showed moderate activity, and 50% exhibited pronounced activity. For those with the A genotype, 25% demonstrated minimal activity, 50% had low activity, 12.5% showed moderate activity, and 12.5% had marked activity. Notably, HBV infection with the C genotype presented with more severe disease progression and more pronounced pathomorphological changes compared to the D and A genotypes.*

Keywords: *Liver encephalopathy, chronic liver disease, Morphological, genotype, pathological process, chronic viral virus hepatitis B (HBV).*

ПАТОМОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ ПЕЧЕНИ У ПАЦИЕНТОВ, ИНФИЦИРОВАННЫХ ВИРУСОМ ГЕПАТИТА В

Аннотация. *В исследовании изучены морфологические изменения печени при различных генотипах хронического гепатита В (ХГВ) в Узбекистане. Среди пациентов с генотипом D у 7,4% наблюдалась минимальная патологическая активность, у 48,2% - низкая активность, у 25,9% - умеренная активность и у 18,5% - выраженная патологическая активность. У пациентов с генотипом С у 33,3% наблюдалась низкая активность, у 16,7% - умеренная активность и у 50% - выраженная активность. У пациентов с генотипом А у 25% наблюдалась минимальная активность, у 50% - низкая активность, у 12,5% - умеренная активность и у 12,5% - выраженная активность.*

Примечательно, что инфицирование вирусом гепатита В генотипом С сопровождалось более тяжелым течением заболевания и более выраженными патоморфологическими изменениями по сравнению с генотипами D и А.

Ключевые слова: *печеночная энцефалопатия, хроническое заболевание печени, морфологический, генотип, патологический процесс, хронический вирусный гепатит В (HBV).*

Introduction

Viral hepatitis remains a major global health concern due to its widespread prevalence and potential to cause severe complications, including fulminant hepatic cirrhosis, particularly in chronic forms of hepatitis B (HBV) (Aliev & Kushimov, 2002; Valiev et al., 2001; Khazanov et al., 2001).

Research on HBV is of particular significance in Uzbekistan, a region classified by the World Health Organization (WHO) as having a high prevalence of HBV markers (Zakirhodzhaev, 2003; Nepomnyashchikh, 1994). Given the burden of the disease, hepatologists in Uzbekistan emphasize the need for in-depth studies, along with preventive and anti-epidemic measures, to reduce both acute and chronic cases.

Significant advancements have been made in understanding various aspects of chronic HBV, including its etiology, pathogenesis, clinical manifestations, and diagnostic approaches, particularly with the use of modern molecular genetic techniques to identify mutational variants of the virus (Daminov et al., 2002; Podymova, 1996; Kidd-Ljunggren et al., 2002). However, despite these developments, several challenges remain unresolved, particularly in the clinical and morphological diagnosis of different HBV genotypes and their mutations.

Current clinical, serological, and instrumental diagnostic methods often fail to provide a sufficiently accurate diagnosis, which is essential for selecting optimal treatment strategies, monitoring disease progression, and predicting patient outcomes (Titov, 1996). Given these limitations, the use of **intravital liver biopsy**, followed by histological and immunomorphological examination of liver tissue samples, is becoming increasingly important.

This approach allows for the identification of chronic HBV, assessment of disease activity and progression, evaluation of antiviral therapy effectiveness, and early detection of cirrhosis (Serov et al., 1996).

Materials and Methods

The aim of this study was to analyze morphological changes in the liver across different HBV genotypes in Uzbekistan.

A total of **121 patients** (aged 15 to 70 years) diagnosed with chronic viral hepatitis B were examined. The **mean age** of the participants was **38.5 ± 9.1 years**. The diagnosis was established in accordance with the guidelines of the Ministry of Health of the Republic of Uzbekistan on viral hepatitis.

Materials and Methods

The study included **121 patients** diagnosed with chronic viral hepatitis B, comprising **78 men (64.4%)** and **43 women (35.6%)**, indicating a significantly higher prevalence in men (**$P < 0.001$**).

Many patients also had **concomitant conditions**, such as chronic cholecystitis and chronic pyelonephritis, which contributed to delayed diagnosis. All patients were hospitalized at the **Scientific Research Institute of Virology (SRIV) under the Public Health Ministry (PHM) of Uzbekistan**.

Diagnostic Procedures

The diagnosis was established using a **comprehensive assessment**, including clinical, epidemiological, anamnestic, biochemical, instrumental, and morphological examinations.

- **HBV markers** (HBsAg, anti-HBs, HBeAg, anti-HBe, anti-HBcor IgG, and anti-HBcor IgM) were detected in all 121 patients.
- Patients with markers of **HCV, HDV, and HAV** were excluded.
- **HBV genotyping** was performed using the **PCR method** in collaboration with the **Laboratory of Molecular Biology, Nagoya University (Japan), the Institute of Immunology (Uzbekistan Academy of Sciences), and the Health Reference Laboratory (PHM).**

It is noteworthy that most patients had received prior treatment for chronic viral hepatitis B but had **not undergone antiviral therapy** before admission to the SRIV clinic.

Clinical Examination

Patients exhibited a range of **clinical symptoms**, including:

- **Jaundice** (yellowing of the skin and sclera)
- **Dermatological signs** (skin rash, palmar erythema, telangiectasias)
- **Vascular abnormalities** (collateral veins on the anterior and lateral abdominal surface)

Physical examination assessed:

- **Liver and spleen size**, density, edge condition, and tenderness
- **Abdominal wall tension** and ascitic fluid presence
- **Urine characteristics**

Instrumental Studies

- **Ultrasound examination** assessed the gallbladder, pancreas, and intestines.
- **Esophagogastroduodenoscopy (EGD)** was used to evaluate esophageal varices, classified into three severity grades:
  - **Grade 1**: Mild varices (1-2 mm diameter), pale-pink esophageal mucosa.
  - **Grade 2**: Moderate varices (3-4 mm diameter), pale or hyperemic mucosa with swelling.
  - **Grade 3**: Severe varices (≥5 mm diameter), sluggish esophageal peristalsis, thin vascular bundles, and multiple erosions in the distal esophagus.

Biochemical and Laboratory Analysis

All patients underwent **serial biochemical testing** throughout the course of the disease, including:

- **Total bilirubin** (direct and indirect fractions)
- **Liver enzymes**: Aspartate aminotransferase (AST) and alanine aminotransferase (ALT)
- **Serum protein levels** (total protein, albumin, and globulin fractions)
- **Thymol test** and **coagulation studies** (prothrombin index, thrombotest, etc.)
- **Complete blood count (CBC)** and **urinalysis**

Liver Biopsy and Histological Examination

Intravital liver biopsy was performed on **41 patients** using the aspiration technique with a **Menghini needle**. Biopsy samples were analyzed at the **Virus Infections Morphology Laboratory of PHM**.

- **Tissue fixation** was done in **10% neutral formalin (2-4 hours)** and **Carnoy's solution**, followed by paraffin embedding.
- **Histological staining** methods included **hematoxylin and eosin (H&E)** and **Van Gieson staining**.
- The **Histological Activity Index (HAI)** was assessed using the **semiquantitative scoring system by Knodell et al. (1981)** to evaluate liver pathology severity.

CONCLUSION:

Analysis of morphological changes in relation to HBV genotype revealed the following findings:

- **D genotype**:
  - Minimal pathological activity: **7.4%**
  - Low activity: **48.2%**
  - Moderate activity: **25.9%**
  - Pronounced activity: **18.5%**
- **C genotype**:
  - Low activity: **33.3%**
  - Moderate activity: **16.7%**
  - Pronounced activity: **50%**
- **A genotype**:
  - Minimal activity: **25%**
  - Low activity: **50%**
  - Moderate activity: **12.5%**
  - Pronounced activity: **12.5%**

These findings indicate that **HBV D-genotype is the most prevalent** among the studied patients. However, it is important to note that **C-genotype HBV is associated with more severe pathological changes** compared to D and A genotypes.

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