Research article

The role of immune mediators in pathogenesis of hepatitis B virus infection

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(Received: July 2021 Revised: August 2021 Accepted: August 2021)

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ABSTRACT

Introduction and Aim: Viral hepatitis, is considered a major cause of cirrhosis and liver transplantation, both of which are life-threatening conditions. In comparison to Hepatitis C virus infection, Hepatitis B virus (HBV) infection has a lower rate of chronicity. The purpose of this study is to assess the immunological particles CD2 and CD4, as well as the cytokines IL-10, in HBV-infected patients.

Materials and Methods: Between April and June 2021, a case-control study was conducted on 180 female subjects with a mean age of 35 years who visited a private clinic in Mosul city. A (10 ml) sample of blood was collected from each subject by routine venipuncture technique, and the blood sample was centrifuged at 3,000 rpm for 10 minutes to separate the plasma, which was used for further investigations. The ELISA test was used to determine the sizes of cytokines in the serum (R&D Systems). A microplate reader was used to limit absorbance in copies (Beckman Coulter). The last concentration was measured in pg/ml.

Results: The findings of this study revealed that (15%) of cases had clinical symptoms of HBV, while (70%) of cases were asymptomatic, and (5%) of cases progressed to chronic liver disease. In compared to healthy control groups, HBV patients had highly significant variations in mean CD 2 and CD 4 expression (p<0.0001).

Conclusion: During the acute phase of hepatitis, the immune system successfully fights off the infection; however, differences in immune responses to different viruses may explain the tendency for acute infection to resolve rather than develop to chronic infection. Hepatitis viruses employ a variety of tactics to evade human immunity. To fully comprehend the complicated interplay between immunological mediators and HBV infection, more research is needed.

Keywords: Hepatitis B virus; cytokines; interleukin; interferons.

INTRODUCTION

Infection with the hepatitis B virus (HBV) is a common health issue. There are two billion people infected with HBV globally, with 257 million chronic carriers. Many persons afflicted with HBV, on the other hand, are completely unaware that they are infected (1). When they come into contact with a pathogen, their innate immune response is activated to prevent infection from spreading. Various cytokines are produced, as well as the activation of natural killer (NK) cells, during the early stages of viral infections (1,2).

Depending on the route and mode of infection, HBV infection can cause a variety of cytokine responses in liver cell types other than hepatocytes. Immune cells can regulate HBV in a non-cytolytic manner by releasing cytokines and other immune mediators (1). T cells can be inhibited by tolerogenic actions of hepatic ligands and cytokines as chronic infection progresses, which limiting their antiviral activity (2). Many studies at the time were based on immunological and serological methods. Following the discovery of the HBV element and the cloning of the HBV genome, molecular investigations advanced quickly (3). As seen by the high number of asymptomatic HBV carriers with minimal liver disease, HBV proliferation does not immediately cause cell damage (4). It is possible to detect the presence of T lymphocytes, when a virus infects a hepatocyte, it activates IFN, which causes macrophage inflammatory protein-1 (MIP–1) to be produced, which strengthens NK cells, which, in turn, discharge interferon, which causes straight hepatic penetrating lymphocytes to enter the liver parenchyma, allowing MHC-I peptide compounds to be distinguished over the exterior of the liver (5). The presence of vital CD2+ and CD4+ T responses in patients with acute illness appears to be linked to retrieval (6). In contrast, a decrease in response appears to predict the end of chronic disease. Ab-mediated decline, on the other hand, was linked to persistent disease, implying that CD4+ play a vital role in eradicating serious disease (7). A decrease in HBV variety is linked to the regulation of acute sickness, simulating a “enclosing” of HBV variety with a positive resistance reaction, whereas chronicity is linked to quasi-species extension (8). Cytokines function as the molecules of defense reaction that result in numerous physiological roles and adjust the defensive, provocative and repairing patient reactions, and mostly concealed by mono and lymph cells. cytokines from T cells act essentially in the host response. Stimulated T cells classified into two
subcategories rendering cytokines manufacturing (9). T helper-1 cytokines such as IL-2 and IFN-8 promote cell-mediated immunity (CMI), whereas T helper-2 cytokines such as IL-10 and IL-4 promote antibody-mediated immunity (AMI; 10).

**MATERIALS AND METHODS**

Between April and June 2021, a case-control study was conducted on 180 female subjects with an average age of 35 years who visited a private clinic in Mosul city. This study comprised 90 female hepatitis patients who were sent to a medical laboratory with HBV signs and symptoms and were anti-HBV antibody seropositive. They were included in the study once informed consent was obtained and all clinical information about them was properly recorded. Among the healthy controls where 90 participants in the study had no history of hepatitis and were found to be healthy following routine laboratory testing.

**Sample collection**

Each individual had a (10 ml) blood sample drawn using standard venipuncture techniques. The blood sample was centrifuged at 3,000 rpm for 10 minutes to extract the plasma, which was used for further research. The ELISA test was used to determine the sizes of cytokines in the serum (R and D Systems). A microplate reader was used to limit absorbance in copies (Beckman Coulter). The last concentration was measured in pg/ml.

**Statistical analysis**

Statistical analysis was showed by using Chi-square test to regulate the statistical changes among the groups by using a proposal statistical platform for social science (SPSS 19). The possibility of (P≤ 0.0001) was measured to be statistically significant.

**RESULTS**

1. **Medical remarks**

   In HBV patients, clinical manifestations included vomiting, fever, and loss of appetite, while some patients never showed any of these symptoms and were found to be asymptomatic carriers, as indicated in table (1).

The findings of this study revealed that 15% of cases had symptoms such as vomiting, fever, lack of appetite, and stomach aches, whereas 70% of cases were asymptomatic, and 5% developed into chronic liver disease. The majority of patients with acute HBV illness have clinically quiet symptoms, with about 15% to 20% of people developing medical signs and symptoms (11). The majority of individuals have clinically silent symptoms throughout the acute phase of HBV disease, with about 15% to 20% of people experiencing medical complaints (12). Fatigue, poor appetite, nausea, vomiting, abdominal pain, low-grade fever, jaundice, and dark urine are all symptoms of acute HBV infection. Tenderness in the liver, hepatomegaly, and splenomegaly are some of the clinical symptoms (13). While the majority of them (80–90%) have cirrhosis at the time of diagnosis, it is possible for HCC to develop without cirrhosis; this is especially true for HBV-related HCC (14).

2. **IL-10 in hepatitis patients**

   All individuals with HBV, whether those with acute or asymptomatic disease action, have a higher amount of IL-10 in their blood than healthy controls. Table 2 shows the results.

   Table 1: Symptoms of HBV infection in patients

<table>
<thead>
<tr>
<th>NO.</th>
<th>Clinical signs</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Acute signs</td>
<td>15</td>
<td>16.7%</td>
</tr>
<tr>
<td>2.</td>
<td>Chronic Liver disease</td>
<td>5</td>
<td>5.7%</td>
</tr>
<tr>
<td>3.</td>
<td>Chronic liver disease (asymptomatic signs)</td>
<td>70</td>
<td>77.6%</td>
</tr>
</tbody>
</table>

3. **CD2 and CD4 manifestation in HBV positive patients**

   As indicated in table (3), there were extremely significant changes in mean CD 2 expression between HBV patients and healthy control groups (p<0.0001). Also Results shown that there were highly significant differences in mean of CD 4 expression among HBV patients and healthy control groups (p<0.0001) as shown in table (4).

   Table 2: The concentration of IL-10 in patients and controls

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Serum level of IL-10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>70</td>
<td>1100.00</td>
</tr>
<tr>
<td>Acute</td>
<td>15</td>
<td>600.00</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>05</td>
<td>1700.00</td>
</tr>
<tr>
<td>Control</td>
<td>90</td>
<td>60.00</td>
</tr>
</tbody>
</table>
**DISCUSSION**

Although it is generally known that adaptive immunity plays a critical role in viral infection clearance (17), the pathogenesis of liver damage during acute and chronic HBV infection is still poorly understood (18). Because HBV is a noncytopathic virus, the pathogenesis of liver damage following HBV infection is mostly driven by immunological processes (19). T cells and other immunoregulatory cytokines play a critical role in the immune response to HCV infection (20). In this study, it was discovered that 15% of the cases had symptoms of liver illness, and 70% of cases were asymptomatic, 5% progressed to chronic liver disease, which is consistent with earlier research (21). Patients with HBV who have acute or asymptomatic illness have a higher amount of IL-10 in their blood than healthy controls (22).

According to the findings, there was a high mean of CD 2 expression among HBV patients and healthy control groups, which was consistent with previous research (23). On the other hand, the findings revealed that the mean CD 4 expression in HBV patients is higher than in healthy control groups, which is consistent with previous research (24, 25).

**CONCLUSION**

During the acute phase of hepatitis, the immune system successfully fights off the infection; differences in immune responses to various viruses may explain the tendency for acute infection to resolve rather than develop to chronic infection. Hepatitis viruses employ a variety of tactics to evade human immunity. The pathogenesis of hepatitis virus and several ways utilized by other related viruses are still being explored. The function of immune mediators and HBV's immunological pathogenesis will be fascinating to study, and it should lead to more accurate diagnosis of chronic viral hepatitis. To fully comprehend the complicated interplay between immunological mediators and HBV infection, more research is needed. These pathways, once elucidated, could contribute the development of new therapeutics for HBV patients who are developing liver disease.

**CONFLICT OF INTEREST**

Authors declare that there is no conflict of interest.

**REFERENCES**


**Table 3: Expression of CD2 in patients and controls**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Serum level of CD2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>70</td>
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<tr>
<td>Acute</td>
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<td>14.00</td>
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<tr>
<td>Chronic liver disease</td>
<td>05</td>
<td>06.00</td>
</tr>
<tr>
<td>Control</td>
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**Table 4: Expression of CD4 in patients and controls**

<table>
<thead>
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<th>Group</th>
<th>Number</th>
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</thead>
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<td>Mean</td>
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<tr>
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