The relationship of serum level of interleukin-4 with the level of anti–hepatitis b antibodies

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Received 13 Mar 2023; Accepted 24 Apr 2023; Published 6 May 2023

Abstract

Hepatitis is a liver infection and inflammation that can be acute or chronic with a diverse etiology, including viruses, bacteria, medicines, and hazardous chemicals. Hepatitis B is the most common causes of chronic and acute hepatitis disorders worldwide. A cross-sectional study was carried out in Salahaldeen governorate from 15th of December 2021 to 25th of August 2022.The study included 90 hepatitis patients with hepatitis B, ranging in age from18 to 61 years. These individuals were hospitalized to general Sammarra hospital. The control group, which was matched to the patients analyzed, consisted of 40 people who appeared to be healthy. 5ml of blood was taken from each patient in this study for the purpose of ELISA testing to check HBs Ag, antibodies to both HBs, IL4.The result showed that all patient with hebatitis B had HBsAg and the number of people with HBV in males more than female. The mean serum level of IL-4 in HBV patients was (50.31±16.34) which was lower than that of control (82.97±21.63 pg/ml) with a significant difference. The mean serum level of anti-HBs IgG in HBV patients was (9.48 ±4.1 U/L) which was lower than that of control (14.77±7.22 U/L) with a significant difference.

Keywords: liver infection, antibodies, HBV patient, Iraq

1. Introduction

Viral hepatitis is a broad term for liver infection caused by viruses that are actively multiplying in the liver [1]. Jaundice is a common symptom of hepatitis induced by other causes, such as alcohol and drug addiction or metabolic diseases [2]. Acute hepatitis is a short-term inflammatory liver condition. During this six-month period, the disease may be clinically unnoticeable or may be accompanied by clinical features ranging from moderate symptoms like jaundice, nausea, and malaise to severe signs like liver failure or death [3]. Chronic hepatitis, in which disease signs can be found for more than six months, has the same clinical results as acute hepatitis [4]. Despite the availability of extremely powerful vaccinations and antiviral medications, an estimated 250 million people have chronic hepatitis B virus (HBV) infection [5]. HBV infection is one of the major cause of cancer-related death throughout the world. The majority of people generate a self-limiting acute infection that clears with a strong host immune response. The most essential protection against HBV infections is the hepatitis B vaccination, which is made with recombinant hepatitis B surface antigen (HBsAg) [6]. However, a small percentage of normal vaccine recipients (5-10%) fail to produce protective levels of hepatitis B antibodies (anti-HBs), increasing the risk of HBV infection, HBV vaccine is administered on a 0 month, 1 month, and 6 month [7, 8]. A non-responder (NR) is someone who has an anti-HBs antibody (Ab) titer of 10 mIU/mL 1-6 months after the three-dose protocol. Intrauterine infection, a high viral load in the maternal blood, vaccine escape mutants, viral reactivation, host genetic variables, an impaired immune system, and premature birth are all host factors that might lead to inadequate immunization. Other contributing variables include incorrect vaccine storage and shipping, as well as unsuitable immunization timing, interval, or place [9, 10]. Cytokines serve critical roles in antigen presentation regulation in both innate and adaptive immune response [11]. Chronic hepatitis B diagnosis has progressed from the simple detection of HBsAg to the complex antibody response against various viral proteins and finally to the detection and quantification of viral DNA Implementation of increasingly sensitive HBVDNA measurement technologies has substantially assisted illness diagnosis and management [12]. Viral load assessment is important during therapy since most guidelines recommend that HBV replication be suppressed as a main therapeutic goal [13]. HBV-specific CD8 T cells attack infected individuals directly hepatocytes and, as a result, recruit in additional immune system components, resulting immunopathogenesis and further liver injury [14]. However, in cases of chronic infection. HBV-specific CD8 T cells develop a comprehensive phenotype and generate less inflammatory cytokines [15], implying that HBV-specific CD8 T cells may not be a significant mediator of liver disease. Instead, liver damage is caused by the intrahepatic recruitment of other immune cells. Because persistent HBV infection is identified after several weeks or months. When the virus has already escaped and viremia is high, adaptive immune responses are evaluated for efficient viral control, whereas innate immune cells are ignored However, during HBV infection, both innate and adaptive immune responses play essential and diverse role. Different viral proteins and viral nucleic acids are recognized by antigen presenting cells (APCs) via pattern recognition receptors (PPRs), which include toll-like receptors (TLRs resulting in fast antiviral cytokine production and activation of other immune cells to the prevention of HBV infection [16-18]. Furthermore, activation of

innate immunity pathways promotes the recruitment of adaptive immune cells, which then execute HBV-specific tasks by precisely detecting and destroying virus-infected hepatocytes [19-21]. These cells then establish HBV-specific memory, which protects against future HBV infection. To suppress HBV infection, both CD4 and CD8 T cells collaborate. CD4 and CD8 T lymphocytes in HBV-infected chimps aided in infection resolution by generating interferon- (IFN-) and tumor necrosis factor- (TNF-) cytokines [22]. CD4 depletion reduced CD8 T cell response during acute infection, whereas CD8 T cell deficit led in HBV clearance failure during chronic infection, indicating a critical role in viral elimination.

2. Material and methods

A cross sectional study was carried out in Salahaldeen governorate from 15th of December 2021 to 25th of Augest2022. The study included collection of 100 samples, 60 patient who are infected with HBS and 40 healthy people as a control group ranging in age from 18to 60 years, as the samples were collected from auditors of the Samarra hospital. 5ml of blood was taken from each patient in this study via vein puncture using disposable syringes. Blood samples were collected deposited in plane tubes, let to clot for 30 minutes at 37 °C, then centrifuged for 15 minutes at 3000 rpm. Sera from the second tube were aspirated and transferred to Eppendorf tubes, which were then maintained at -20°C [23, 24]. For later serological testing for HBS IgG antibody, IL-4 assays using the ELISA technique. An interview was carried out with these patients using questionnaire form designed by the investigator and consisted of the following variables. age, sex, occupation, etc (Appendix I).

3. Results

Figure 1 shows that the mean serum level of IL-4 in HBV patients was 50.31±16.34 pg/ml which was lower than that of controls (82.97±21.63 pg/ml) with a significant difference.

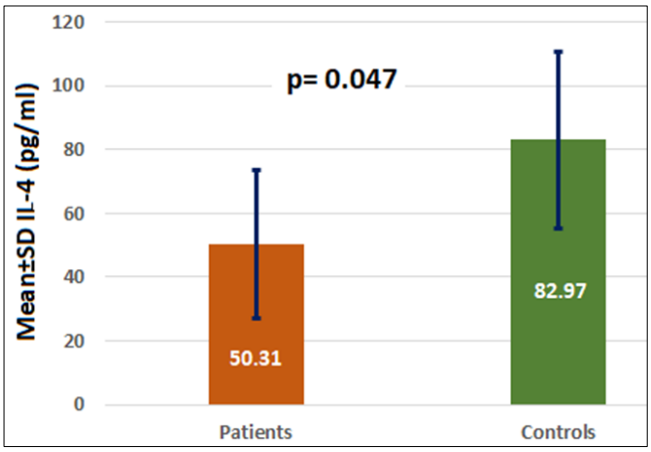

Fig 1: Mean serum level of IL-4 in HBV patients and controls

Figure 2 shows that Patients with HBV had lower serum level of anti-HBs IgG than controls (9.48±4.1 U/L versus 14.77±7.22 U/L) with a significant difference.

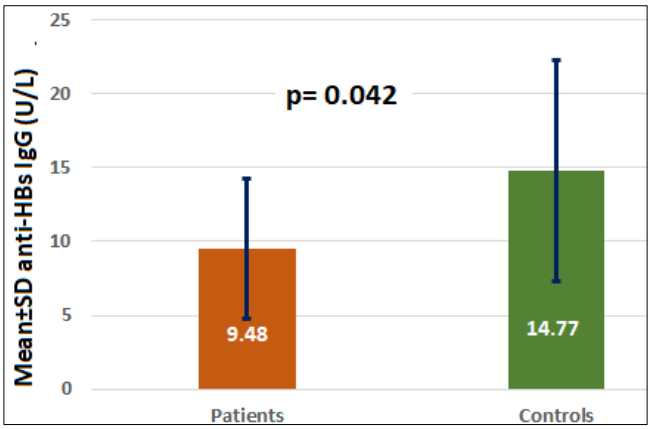

Fig 2: Mean serum level of anti-HBs IgG in HBV patients and controls

4. Discussion

Hepatitis B virus (HBV) infection is one of the primary causes of liver disease. with more than 2 billion persons worldwide infected. One third of those who have chronic HBV infection develop liver cirrhosis (LC), which in more than three quarters of instances progresses to hepatocellular carcinoma (HCC) [25]. Around 350 million of these people are thought to be persistent carriers of the HBV infection. Vertical transmission from infected mothers at or shortly after birth is the most common method of HBV transmission in this hyperendemic region [26], Despite the approximately 90% probability, only 5% to 10% of perinatally infected newborns become persistent carriers as adults; further, 10% to 30% of these persistent infectors advance to LC and HCC [27]. Differences in immunological, viral, or environmental variables cannot entirely explain such wildly varied illness outcomes. As a result, changes in host genetic variations may be crucial in these processes. IL-4, a pleiotropic Th2 cytokine [28], is well recognized for defining the Th2 phenotype of lymphocytes, as well as influencing cell proliferation, apoptosis, and the expression of multiple genes in lymphocytes, macrophages, and fibroblasts [29, 30]. During the peak time of the anti-HBs response, a receiver should respond to the vaccine within 1-6 months after the three-dose vaccine series. IL-4 is a cytokine that is released by activated Th2 lymphocytes, basophils, and mast cells. This cytokine is important in the T lymphocyte subset homeostasis. An imbalance between these T cell subsets has been linked to the human response to therapeutic vaccination [31]. Differences in the host immune response may be one of the causes of hepatitis B development and progression, with emerging evidence suggesting modulation of that cytokines and regulatory molecules should be considered key mediators in determining the host innate and adaptive immune response to HBV and viral clearance. The result showed that all patient with hebatitis B had HBsAg and the number of people with HBV in males more than female. As a result, cytokine levels may have an essential role in illness outcomes and effective antiviral immunity. In agreement with our finding, study by Seyed Hedayat Hosseini Khorami [32] who reveal significant decrease in IL4 in HBV patient, Monsalve–De Castillo F [33] find that the mean serum

level of IL4 in HBV patients was 4.1±0.2 while in control was 9.3±1.7. It has also been reported that the decrease in IL-4 levels could be a consequence of the auto-regulatory mechanism of IL-10. Anti-HBs Ab titers were considerably greater in the 6 months group than in the > 6 months group, as expected. In general, the 6 months subjects had more and stronger associations than the total or > 6 months subject, controls. These results agree with the study of (Tzu-Hsin Tsai [34] who reveal significant decrease in anti HBs IgG in HBV patient.

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