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## Assessment of Concentration interleukins and liver function in patients infected with hepatitis type –B

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### ABSTRACT

**Back ground :** Hepatitis B virus (HBV) is one of the global problems that causes liver disease and thus leads to death. In 2019, the World Health Organization indicated that 296 million people worldwide suffer from hepatitis C virus infection. Hepatitis B virus primarily affects liver cells and replicates within them.

**Materials and Methods:** This study was conducted on patients attending and admitted to Balad General Hospital in Salah al-Din for the period (1/6/2024-25/11/2024), and the groups were classified into two groups, the first group, which included 40 healthy people (control group), and the second group, which included 50 patients infected with viral hepatitis B, and the ages of the samples targeted in the research ranged ( 25-60) years of age, a questionnaire was prepared that included information about age, patient history, blood receipt, and visit to the dentist. blood was then collected from patients and healthy people and separated using a centrifuge. Then immune and liver function variables were measured, which included (IL-2, IL-4, IL-8, AST,ALT,ALP)

**Results:** The current research showed a significant elevated in each of the levels (IL-2, IL-4, IL-8, AST, ALP, ALT). In the blood sera of patients infected with viral hepatitis B and healthy people, at its level, the probability of  $P \leq 0.05$ .

## INTRODUCTION:

It is a Latin term that indicates inflammation that affects the liver. The cause of this inflammation may be the result of infection with viruses, parasites, or bacteria, as well as other causes such as the use of alcohol, medicine, chemicals, and mycotoxins, and it may be the result of the interaction of antibodies with cells. The liver, as in the case of autoimmune hepatitis <sup>(1)</sup>.

Hepatitis B virus (HBV) is one of the global problems that causes liver disease and thus leads to death <sup>(2,3)</sup>. In 2019, the World Health Organization indicated that 296 million people worldwide suffer from hepatitis C virus infection <sup>(4)</sup>. Hepatitis B virus primarily affects liver cells and replicates within them <sup>(5,6)</sup>.

An early diagnosis of viral hepatitis provides the best opportunities to provide effective medical support to those infected and helps take the necessary steps to prevent transmission of the infection. The hepatitis B virus and HCV affect the cells of the infected liver and this leads to a defect in liver function, including a deficiency in the formation of blood clotting elements, and also causes a defect in the secretion of liver enzymes. The groups most susceptible to infection are thalassemia patients who need frequent blood transfusions <sup>(7,8)</sup>. Artificial kidney patients are more susceptible to infection with HBV and HCV because they need hemodialysis procedures in addition to receiving blood frequently. As for cancer patients treated with chemicals, their immune response is suppressed, which qualifies them for infection with both HCV and HBV, as these patients suffer from bone marrow failure, This results in anemia that requires frequent blood

transfusions. Most patients infected with the HBV virus recover completely without side complications. As for the rest, the infection continues for a period longer than six months and becomes chronic. The disease may develop into cirrhosis and liver cancer, and may cause death <sup>(9)</sup>.

Interleukins (IL) have an important and effective role in infections, especially viral hepatitis. Interleukins are considered a type of cytokines. It was initially thought that they are produced by white blood cells alone, but it was later discovered that they are also produced by many other cells in the body. These interleukins work together and create a series. One of the reactions that would arm the body's white leukocyte cells against disease, wounds, and the entry of bacteria the white cells detect the availability of bacteria at the site of infection, and then these cells release interleukin-2, which in turn gives a signal to other white blood cells called T-cells, which in turn release interleukin-2 and similar chemicals such as interleukin-4, which stimulate various cells. The immune system defends the body <sup>(10)</sup>.

Interleukins are proteins that stimulate the body's immune system to do its job. It consists of white blood cells in the body, which are the cells that work to destroy harmful objects that enter the body. It works on cell growth, differentiation, and movement, and is important in stimulating immune responses such as inflammation <sup>(11)</sup>.

IL8 is considered one of the cytokines that contribute to the inflammatory cellular response, which is a chemoattractant force for neutrophil blood cells to the site of inflammation, so it is called the neutrophil chemotactic factor and is secreted by

different types of immune and non-immune cells <sup>(12)</sup>. It was found that IL 8 levels are a predictive factor for many pathological conditions, as Tachibana et al <sup>(13)</sup> indicated. 2007 indicated that an increase in the level of IL 8 in the cytoplasm of hepatoma cells and in the vascular epithelial cells of the endothelium leads to an increase in angiogenetic activity, as IL 8 contributes to the growth of hepatic cancer cells , Through the increase in interleukins and liver enzymes in patients infected with viral hepatitis type, a study of the effect of the level of interleukins and liver enzymes in the blood serum of patients infected with viral hepatitis type B.

## **MATERIALS AND METHODS:**

This study was conducted on patients attending and admitted to Balad General Hospital in Salah al-Din for the period (1/6/2024-1/11/2024), and the groups were classified into two groups, the first group, which included 40 healthy people (control group), and the second group, which included 50 patients infected with viral hepatitis B, and the ages of the samples targeted in the research ranged ( 25-60) years of age, a questionnaire was prepared that included information about age, patient history, blood receipt, and visit to the dentist. blood was then collected from patients and healthy people and separated using a centrifuge. Then immune and liver function variables were measured, which included (IL-2, IL-4, IL-8, AST, ALT, ALP) .

### **Estimation of the level of immune variables in blood serum**

The levels of IL-2, IL-4, and IL-8 in the blood serum of patients infected with viral hepatitis B were estimated according to the manufacturer, Monobind Inc, USA.

### **Estimation of the levels of liver enzymes in blood serum:**

The activity of each enzyme (AST, ALT, ALP) was measured by adopting the ELISA technique (Sandwich) and by following the ready-made steps indicated in the custom analysis kit, and it differs from one device to another and according to its manufacturer.

## **Statistical Analysis**

The results were analyzed using the statistical program SPSS, and the average and standard deviation  $\pm$  SD were determined. The averages were also determined for a group of patients infected with viral hepatitis B and the control group using a T-test at the probability level ( $P \leq 0.05$ ).

## **RESULTS:**

The results of the current research showed a significant rise in each of the (IL-2, IL-4, IL-8, AST, ALP, and ALT). In the blood sera of patients infected with viral hepatitis B compared to healthy people, at its level, the probability of  $P \leq 0.05$ . as in Figures (1,2,3,4,5,6), respectively

## **DISCUSSION:**

Viral hepatitis is a condition of inflammatory development in the liver tissue as a result of a viral infection causing damage to the liver cells that may be temporary or permanent and is characterized by the presence of inflammatory cells within the liver tissue <sup>(14)</sup>. As the continuous rise in the level of interleukins and liver enzymes leads to a malfunction in cellular functions, the infection of several diseases, and the entry of viruses into the body, such as the viral hepatitis virus, interleukin-2 plays an important role in regulating the immune

system, as it participates in the differentiation of T cells. It regulates the immune response and internal balance, Interleukin-2 maintains regulatory T cells (Treg) and CD4<sup>+</sup> cell differentiation into effector T cell subsets after antigen-mediated activation <sup>(15)</sup>. that interleukin-2 can amplify CD8<sup>+</sup> T cell responses, while the application of interleukin-2-specific neutralizing antibodies stimulates the expansion of the T regulatory cell population, thus favoring either immunostimulation or suppression <sup>(16,17,18)</sup>. the result of increased interleukin-2 in the serum of patients with viral hepatitis B is consistent with the findings of Ozeki et al <sup>(19)</sup> and IL-2 is a therapeutic option for hepatitis B virus infection, due to its enhancement of antiviral CD8 responses <sup>(20)</sup>. Interleukin-4 is an anti-inflammatory cytokine that is secreted mainly by Th2 cells, which leads to proliferation and differentiation and thus acts as an immune response to many viruses, including hepatitis virus <sup>(21)</sup>. because interleukins regulate the immune system and play a role in cellular communication by generating and exerting their effects on a wide range of cell types and participating in the inflammatory response <sup>(22)</sup>.

Interleukin-8 is a protein belonging to the cytokine family, and it acts as a chemical agent that attracts white blood cells, especially neutrophils, to sites of inflammation. IL-8 is produced mainly by epithelial cells and immune cells such as macrophages and has an important role in many inflammatory and immune diseases, Such as rheumatoid arthritis, cardiovascular disease, viral hepatitis, and some types of cancer.

The reason for the high level of interleukin 8 is due to differences in genotypes. However, due to the small number of

samples, it was not possible to confirm this association between genotypes <sup>(23,24)</sup>.

As for liver enzymes, they are considered the standard for the internal organization of the liver - homeostasis. They are highly sensitive indicators in distinguishing acute liver diseases such as viral hepatitis, as high levels of liver enzymes help in diagnosing most liver diseases such as acute hepatocellular failure, in which ALT levels rise. Or equal to AST, The high levels of these enzymes inside the liver cells lead to their leakage into the circulatory system, which is evidence of cellular injury as it is the criterion for the internal organization of the liver (Hemeostasis) <sup>(25)</sup>. The activity of liver enzyme are elevated than the enzyme AST, as sources differ in their estimation. However, in alcoholic liver disease, the effectiveness of AST is higher than ALT <sup>(26)</sup>.

Hepatic cellular injury causes the release of ALT and AST, and ALT is more specific in indicating liver disease, while high AST may be due to damage to the liver, bones, kidneys, intestines, or white blood cells. Aminotransferases are sensitive indicators of hepatic cellular injury and help greatly in the Diagnosis of hepatocellular diseases. In most acute liver failure, ALT is higher or equal to AST <sup>(27)</sup>. Therefore, the activity of ALT and AST are higher in patients with viral hepatitis when compared to alcoholic liver disease and cirrhosis. Moreover, the levels of ALT and AST are higher in patients with alcoholic hepatitis than in patients with cirrhosis. These enzymes are located in the bile ducts. Therefore, biliary obstruction leads to an increase in the synthesis or formation of the alkaline phosphatase enzyme ALKP and its release into the circulatory system <sup>(28)</sup>. The increase in these

enzymes is consistent with the results of the study of both <sup>(29)</sup> and <sup>(30)</sup>, whose studies indicated an increase in liver enzymes in infected patients when compared to healthy people, and this indicates Hepatocyte injury.

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#### TABLES:

**Table (1):** shows the mean  $\pm$  S.D of the immunological and biochemical variables for the samples under study

| Groups<br>Parameter | Mean $\pm$ SD     |                    | P-Value        |
|---------------------|-------------------|--------------------|----------------|
|                     | Control<br>n=30   | Patients<br>n=50   |                |
| IL-2 (pg/ml)        | 0.95 $\pm$ 0.51   | 2.27 $\pm$ 3.08    | P $\leq$ 0.001 |
| IL-4 (pg/ml)        | 2.89 $\pm$ 1.77   | 5.35 $\pm$ 4.27    | P $\leq$ 0.001 |
| IL-8 (pg/ml)        | 7.2 $\pm$ 3.15    | 15.72 $\pm$ 13.87  | P $\leq$ 0.001 |
| AST (U/L)           | 9.67 $\pm$ 4.65   | 20.26 $\pm$ 37.36  | P $\leq$ 0.001 |
| ALP(U/L)            | 80.21 $\pm$ 27.76 | 110.36 $\pm$ 89.74 | P $\leq$ 0.001 |
| ALT (U/L)           | 15.5 $\pm$ 15.47  | 45.1 $\pm$ 130.61  | P $\leq$ 0.001 |

Figure (1) : IL-2 in the blood sera of the samples under study

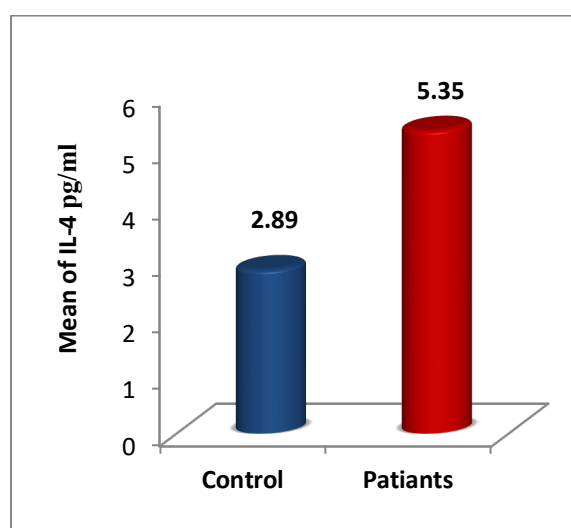


Figure (2) : IL-4 in the blood sera of the samples under study

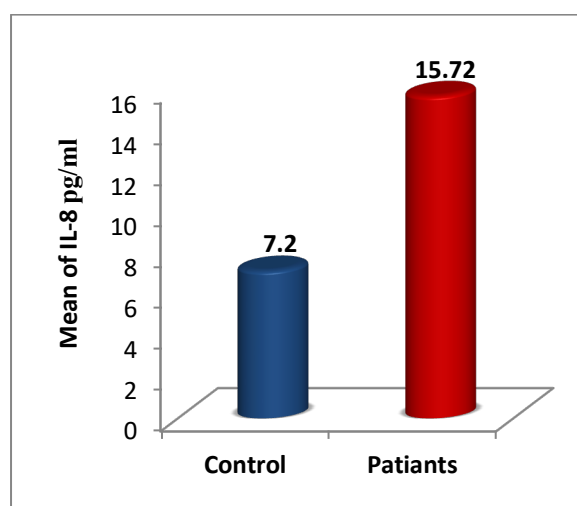


Figure (3) : IL-8 in the blood sera of the samples under study

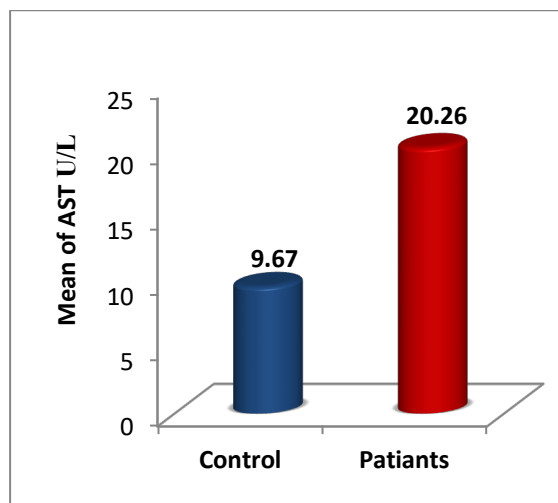


Figure (4) : AST in the blood sera of the samples under study

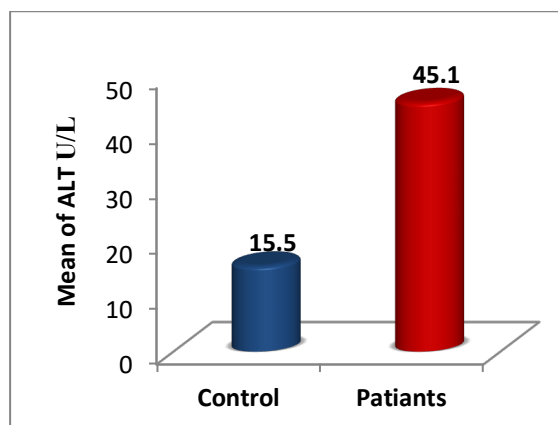


Figure (5) : ALT in the blood sera of the samples under study

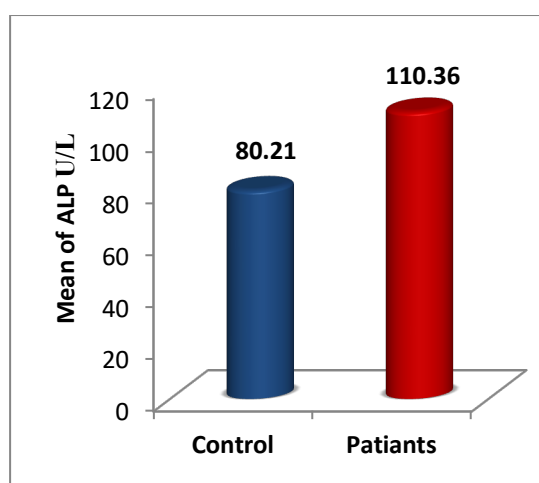


Figure (6) : ALP in the blood sera of the samples under study