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ORIGINAL

Evaluation the relationship between serum levels of interleukin_37 and liver aminotransferase enzymes in acute and chronic stages of hepatitis B infection in Iraq

Evaluación de la relación entre los niveles séricos de interleucina_37 y las enzimas aminotransferasa hepáticas en las etapas aguda y crónica de la infección por hepatitis B en Irak

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Abstract

Background: Hepatitis B is liver inflammation that can be caused by viruses, medicines, or toxic substances. Inflammatory chemokines and cytokines, epithelial cells, PBMCs, and macrophages all produce interleukin IL-37, which has been associated with liver injury known as)IL-1 family member 7). The "AST and ALT" levels of aminotransferase enzymes "AST and ALT" are useful in the diagnosis of liver disease.
Methods: Interleukin-37, ALT, and AST concentrations in the blood serum of three distinct groups (anti- core (+), HB patients and healthy volunteers) were assessed using a variety of methodologies in this research.
Results: According to the findings of this research, The anti- core (+)group IL-37 serum levels differed significantly from those of the HB patients and healthy controls , While serum IL-37 levels did not differ significantly between HB patients and the healthy control group, "ALT" and "AST" serum levels were found to be significantly greater in the anti- core (+) group than in the other two groups, highly significant positive correlation between IL-37and "ALT" ($r=0.510$ and $P < 0.01$) and also with "AST" ($r=0.445$ and $P < 0.01$).
Conclusion: According to this study, which looked at three separate groups of patients, the anti- core (+) had the greatest levels of interleukines-37 and aminotransferase enzymes (ALT and AST), and the two appeared to be positively associated.

Key words: ALT, AST, IL-37, hepatitis B.

Resumen

Antecedentes: La hepatitis B es una inflamación del hígado que puede ser causada por virus, medicamentos o sustancias tóxicas. Las quimiocinas y citoquinas inflamatorias, las células epiteliales, las PBMC y los macrófagos producen la interleucina IL37, que se ha asociado a la lesión hepática conocida como (IL-1 family member 7). Los niveles de las enzimas aminotransferasas "GOT y GPT" son útiles en el diagnóstico de la enfermedad hepática.
Métodos: En esta investigación se evaluaron las concentraciones de interleucina-37, GOT y GPT en el suero sanguíneo de tres grupos distintos (anti-core (+) , pacientes con HB y voluntarios sanos) utilizando diversas metodologías.
Resultados: Según los resultados de esta investigación, los niveles séricos de IL-37 de los pacientes con core difieren significativamente de los de los pacientes con HB y de los controles sanos , Mientras que los niveles séricos de IL-37 no difieren significativamente entre los pacientes con HB y el grupo de controles sanos, los niveles séricos de "GOT" y "GPT" resultaron ser significativamente mayores en el grupo anti-core (+) que en los otros dos grupos, correlación positiva altamente significativa entre IL-37y "GOT" ($r=0.510$ y $P < 0,01$) y también con "AGPT" ($r= 0,445$ y $P < 0,01$).
Conclusiones: Según este estudio, en el que se analizaron tres grupos distintos de pacientes, los antinucleares (+) presentaban los mayores niveles de interleucinas-37 y de enzimas aminotransferasas (GOT y GPT), y ambos parecían estar positivamente asociados.

Palabras clave: GOT, GPT, IL-37, hepatitis B.

Introduction

As a result of exposure to blood and blood products as well as other bodily fluids and the use of sharps objects, people get hepatitis B, a liver inflammation[1]. Globally, 116 million people are chronically infected with hepatitis B, the WHO Western Pacific and African regions that number rises to 81 million. WHO A total of 60 million people in the WHO Eastern Mediterranean Region, 18 million in WHO south-east Asia, 14 million in WHO Europe, and 14 million in WHO Africa are ill. An estimated 5 million people in the Americas region have been affected[2]. Acute and chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC) can all be caused by the human (HBV). For a diagnosis of HBV infection and the disease it causes, a combination of clinical, biochemical and histological data is used. After HBV infection, a variety of viral antigens and antibodies can be found in the blood, and careful interpretation of the results is critical for the correct diagnosis of many clinical types of HBV infection[3,4.] AST and ALT, two enzymes found primarily in the liver but also in red blood cells, heart cells, muscle tissue, and other organs like the pancreas and kidneys, are involved in the metabolism of aspartate and alanine[5]. "Serum glutamic oxaloacetic transaminase (GOT) and serum glutamic pyruvic transaminase (GPT)" were previously referred to as "AST" and "ALT"[6]. AST and ALT readings can be used to diagnose liver disease. The normal range for AST and ALT blood levels is 5-40 u/l and 5-35 u/l, respectively. However, when tissues or organs such as the liver or heart are ill or injured, additional "AST" and "ALT" are released into the circulation, causing the enzyme levels to rise[7]. Serum alanine and aspartate aminotransferase "(ALT, AST)" levels begin to rise and jaundice may emerge within a few weeks of the appearance of viral indicators[8]. To put it another way, the degree of tissue damage is exactly proportional to blood levels of "AST" and "ALT". "AST" levels can rise by up to 20 times their normal value following serious injury, While it is possible for "ALT" levels to rise even further (up to 50 times greater than normal). Testing for the "AST/ALT" ratio (AST/ALT) can reveal whether or not someone's liver or another organ has been damaged[9,10]. ALT, inflammation, and/or fibrosis on liver biopsy may affect serum levels of certain of hepatic enzymes, bilirubin and albumin in patients with evidence of chronic hepatitis[11]. Hepatic function and disease severity can be evaluated and assessed using biomarkers[12]. "Natural killer (NK) cells", monocytes, and activated B cells all express "IL-37", an emerging member of the IL-1 family of cytokines[13,14]. Splice variants (a-e) are included in this set[15]. Pro-inflammatory cytokines and inflammation-inducing events can cause an increase in the IL-37 protein[16]. Macrophage or epithelial cell production of IL-37 effectively prevented the generation of pro-inflammatory and innate immunocytes[16,17]. In a variety of disorders, IL-37 inhibits inflammation and innate immunity[18]. There is still a lack of understanding of the role of IL-37 in the immunological response to chronic hepatitis B and C. In this research, the serum levels of IL-37, ALT, and AST were evaluated to see if there was a correlation between them at different phases of hepatitis B infection, as well as IL-37's role in hepatitis B virus pathogenesis.

Materials and methods

Blood samples collection

The anti –core (+) group consisted of 100 blood samples that tested negative for hepatitis B surface antigen (HBsAg(-)) using an immunoassay ELISA (HBsAg) (Imbian ELISA kit, Novosibirsk, Russia), but positive (+) anti-HBc by utilizing the anti-HBc II kit (Abbott Diagnostics, USA). Iraq's National Blood Transfusion Center was the source of this. Another 80 samples were taken from patients at Baghdad's gastrointestinal and hepatitis teaching hospital, while the third group acquired 20 samples from healthy people. Using centrifugation, the serum from each sample was divided into two 1.5-ml tubes and stored at a low temperature (-70°C) until testing.

Laboratory testing

Measured of the Interleukin -37, " (ALT)" and "(AST)"

An enzyme-linked immunosorbent assay (ELISA) kit from Cusabio was used to measure "IL-37" levels in the blood of each of the three study groups (the U.S.).Units per liter (U/L) is the most frequent way to measure ALT. (The U.S.A.: GenWay's ALT Assay Kit). Aspartate Aminotransferase is nearly commonly measured in units/ liter (U/L). Making Use of Activity Assay Kit (SIGMAALDRICH, US.A.).

Statistical analysis:

For both the descriptive and inferential analyses, SPSS software (version 20) was used. The average and standard deviation of the data were used to represent the findings. The statistical significance of the relationships between the variables was assessed through the application of one-way analysis of variance (ANOVA).

Results

Anti-inflammatory properties and the capacity to reduce the immune system's reaction to a number of ailments have made IL-37 a popular supplement (Akdis and others 2011). The relationship between HBV infection and IL-37 has not yet been investigated. Serum IL-37 concentrations in healthy individuals, HB patients, and core patients were all measured as part of this study. Results from this study show that IL-37 levels in the core group patients were significantly higher than those in HB patients and healthy groups, although there was no significant difference between patients and healthy groups in IL-37 serum levels, **table I**.

Table I: "IL-37" levels in three groups.

Groups	Mean + S.D	
Anti-Core (+)	404.49 + 166.8	a
HB Patients	245.87 + 84.73	b
Healthy	201.22 + 23.36	b
P value	< 0.01	

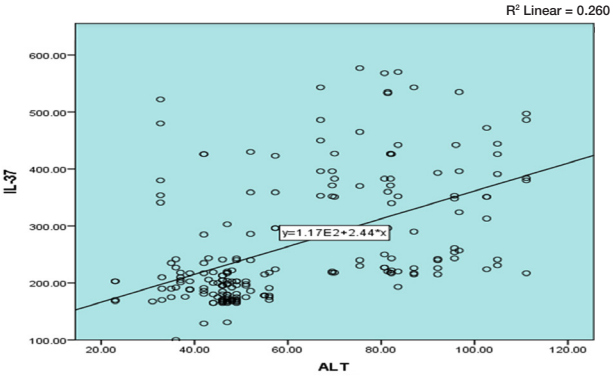
Serum "ALT" levels were also examined across three groups: core patients, patients with a diagnosis of hepatitis B, and healthy individuals. According to the results in the table, the ALT levels in serum were significantly higher in the Anti-core(+) group than in the other two, despite the fact that there were no differences between the HB patients and healthy groups, **table II**.

Table II: "ALT" levels in three groups.

Groups (ALT)	Mean + S.D	
Anti-Core (+)	78.15 + 20.27	a
HB Patients	45.36 + 7.46	b
Healthy	41.10 + 4.93	b
P value	< 0.01	

The correlation between IL-37 and ALT levels in three groups was studied according to the study, the serum levels of IL-37 (r = 0.510 and P: <0.001) were highly correlated with ALT (r = 0.510), **figure 1**.

Figure 1: The relationship between serum levels of interleukin-37 and aminotransferase (ALT).



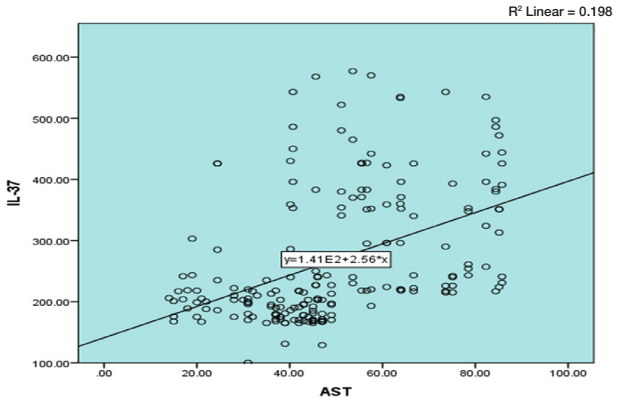
Anti-core (+) group had greater AST concentrations than patients and healthy people, whereas those in the HB group had higher AST concentrations than those in the healthy group but lower levels than those in the HB patients group (**Table III**).

Table III: "AST" levels in three groups.

Groups (AST)		
Anti-Core (+)	62.27 + 16.68	a
HB Patients	40.61 + 6.06	b
Healthy	19.35 + 4.10	c
P value	< 0.01	

It was revealed that serum levels of "IL-37" and "AST" were higher positively correlated (r =0.45) in three groups of samples, **figure 2**.

Figure 2: The relationship between serum levels of interleukin-37 and aspartate aminotransferase (AST).



Discussion

This inflammation is brought on by the hepatocyte and immune cell release of cytokines in response to the HBV core protein[19]. Donors who had (anti –HBc+) were shown to have considerably greater levels of serum IL-37 and their association to liver enzymes (ALT and AST) in this study compared to patients with HBV and healthy control groups. levels of IL-37, also were found to be positive correlated with ALT (r =0.510 and P:<0.01) and AST (r=0.445 and P<0.01) after using correlation analysis. Other researchers have discovered that the anti-inflammatory cytokine "IL-37" reduces the immune system's response to a variety of disorders because it is ability to inhibit both the natural and adaptive immune systems[20]. Study after study has shown that IL-37 inhibits a wide range of functions, such as antigen presentation and macrophage activation[21]. Previous studies have connected the "IL-37" to HB inflammation[22]. Proinflammatory and anti-inflammatory cytokines were found at significant concentrations in individuals with CAHB in the current study[22].

It is possible that patients with elevated levels of "IL-37" may have HB-specific immune responses. Increased "IL37" dramatically decreased expression of IFN-alpha (IL1beta) and TNF-alpha (IL-6) in PBMCs[23]. This shows that proinflammatory cytokines may increase the synthesis of "IL-37" in core patients, and that "IL-37" may initiate a negative feedback loop to reduce the excessive production of proinflammatory cytokines. Up regulation of antiinflammatory cytokines, such as "IL-37", could thus be a possible underlying mechanism for reducing inflammation and easing illness symptoms. However, the amounts of these anti-inflammatory cytokines may not be high enough to offset the negative effects of proinflammatory cytokines in individuals with progressive core disease[24,25].

Previous research discovered that individuals with achronic HB infection had much greater amounts of "IL-37" in their serum than healthy controls, and these higher levels of "IL-37" were found to be associated with higher levels of "(ALT)", which matched the findings of this study26. The aminotransferase enzymes "(ALT and AST)" are a sensitive marker for hepatocyte necrosis. Increased "ALT" levels are a better indicator of liver damage than decreased "ALT." The third zone of the liver acini contains a larger concentration of "AST", and injury to this zone can result in more severe alterations in "AST" levels[27]. Other investigations discovered that AST may be a more accurate predictor of liver parenchymal inflammation and necrosis, liver fibrosis and chronic hepatitis B consequences than "ALT". These findings are consistent with those of prior research[28] and contradict those of other studies that found a strong correlation between ALT levels and inflammatory grade[29].

Conclusion

This study measured the serum levels of interleukin-37 and liver aminotransferase enzymes (ALT and AST) this study found that serum levels of interleukin -37 in The anti –core (+) group was significantly higher than the other two groups (HB patients and healthy control)and there was a strong correlation between serum levels of interleukin-37 liver aminotransferase enzymes ("ALT" and "AST")in the donors who had the anti-HBc (+) / HBs Ag (-) or chronic HBV infection, which indicates the persistence of inflammation in the liver even when HBs Ag is not present.

Conflict of interest

Authors do not have any conflict of interest to declare.

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