

Original Research Article

Estimation of serum levels of GM-CSF, IL-1 α , and Complement Components C3 and C4 in Patients with Chronic HCV

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ABSTRACT

Chronic hepatitis C virus (HCV) is a leading cause of liver-related morbidity and mortality throughout the world. The interactions between the virus and the components of immune systems plays an important role in the pathogenesis of the disease. The present study aimed to estimate serum levels of granulocyte-macrophage colony stimulating factor (GM-CSF), Interleukin-1 α (IL-1 α), and complement components C3 and C4 in patients infected with chronic hepatitis C virus. Forty-six patients with chronic HCV and 38 apparently healthy individuals were enrolled in this study. From each participant, 5ml of blood were taken, from which serum was obtained. ELISA was used to estimate serum levels of GM-CSF and IL-1 α , whereas single radial immunodiffusion assay was used to estimate serum levels of C3 and C4. Only GM-CSF had elevated non-significant mean value in HCV patients compared to control. The three other parameters had lower mean values in HCV patients (significant in case of C4) than control. Some factors of innate immune response represented by IL-1 α , and complement components C3 and C4 may have less prominent role against chronic HCV infection.

Keywords

Hepatitis C virus,
GM-CSF,
IL-1 α ,
Complement components
C3,
C4

Introduction

Hepatitis C virus infection is a frequent cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma. It is epidemic around the globe and is estimated to afflict 150-200 million people worldwide. It results in chronic disease in 85% of cases (1). The pathogenesis of HCV-induced hepatic injury could be attributed to either direct cytopathic damage by HCV and/or immune-mediated hepatic injury, especially via cellular immunity (2). However, it is likely that the interactions

between HCV and the host immune system have the major role in the pathogenesis (3).

GM-CSF is a cytokine that has a particular importance for its therapeutic use. It Primarily regulates myeloid cell production (4). The major role of this cytokine lies in its ability to govern the properties of mature myeloid cells of the granulocyte and macrophage lineages, particularly during host defense and

inflammatory reaction (5). Complement refers to a family of distinct proteins that play pivotal role in host defense against infection (6). It links the innate and adaptive immune responses by a variety of mechanisms, including enhancing humoral immunity, regulating antibody effector mechanisms, and modulating T cell function (7). The complement system is increasingly recognized as a mediator of protection or pathology in a variety of viral infections. Furthermore, the continued identification of novel mechanisms of viral antagonism of complement highlight the important role this system has in viral pathogenesis (8).

IL-1 is one of the most prominent pro-inflammatory cytokines involved in tissue inflammation (9). The key role of this cytokine appears to be related to its function concerning inflammatory cells, which is crucial for viral clearance and the host immune response (10). The mechanism of impaired immune activation in patients who develop chronic HCV infection is not well known (11). Therefore, this study aimed to investigate the serum levels of most important factors in innate immunity against hepatitis C virus infection.

Materials and Methods

The Study Population

A total of 46 outpatients (18-62 years old, 28 males and 18 females) with chronic hepatitis C virus infection attending Al-Kadhimiya Teaching Hospital and Al-Yarmook Hospital/ Baghdad were enrolled for this study. Other age matched 38 (31 males and 17 females) apparently healthy subjects were used as controls. Five ml of venous blood were collected from each participant in vacutainer tube. Serum was

obtained by allowing the blood to clot at room temperature for two hours and the tubes were then centrifuged.

Immunological assays

Enzyme-linked immunosorbent assay (Immunotech, France) was used to estimate serum levels of IL-1 α and GM-CSF, while single radial immunodiffusion assay (Biomeghreb, Tunisia) was used to estimate serum level of C3 and C4 according to the manufacturers' instructions.

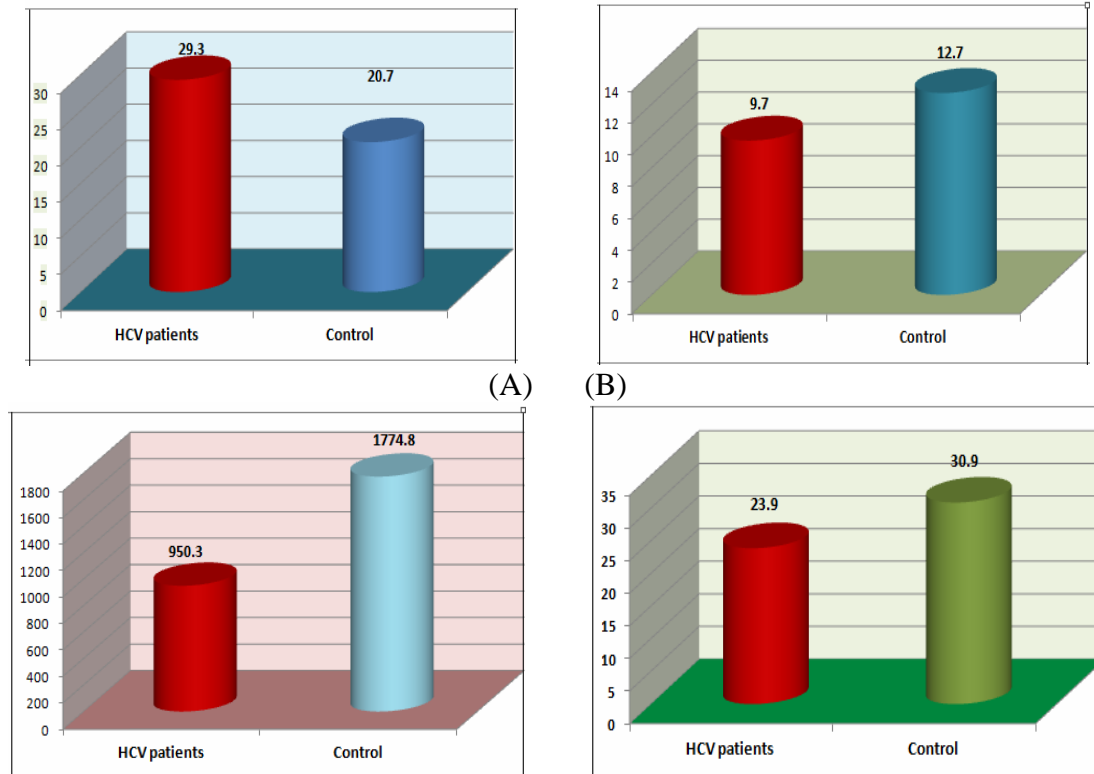
Statistical Analysis

Values were expressed as mean \pm SE. Statistical package for social sciences (SPSS) software was used to find out the least significant differences among means of groups. Statistical significance was set at a p value \leq 0.05.

Results and Discussion

Mean serum levels of GM-CSF, IL-1 α , C3, and C4 in HCV patients and control subjects are represented in Figure 1 (A, B, C, and D respectively). Except for GM-CSF, serum levels of the other three parameters in HCV patients have less mean values than corresponding values in controls. Mean serum level of GM-CSF in HCV patients was 29.3 ± 4.2 pg/ml compared to 22.7 ± 2.9 pg/ml in control with no significant difference (figure 1, A). Similarly, mean serum level of IL-1 α did not differ significantly between patients (9.7 ± 4.2 pg/ml) and control (12.7 ± 2.9 pg/ml) (figure 1, B), however, HCV patients have lower mean serum level of C3 (950.3 ± 92.9 pg/ml) than that of control (1774.8 ± 121.3 pg/ml) with significant difference (figure 1, C). Finally, Mean serum levels of C4 in

Figure.1 Mean serum levels of **A:** GM-CSF, **B:** IL-1 α , **C:** C3, and **D:** C4 HCV patients and control



patients and control were 23.9 ± 3.17 pg/ml and 30.9 ± 3.6 pg/ml respectively with no significant difference (figure 1, D). Interactions between HCV and the host immune system play an important role in HCV persistence and disease pathogenesis (3).

Widely produced in the body, GM-CSF plays an important role in the resistance to viral infections (8). This cytokine stimulates the production of neutrophil, monocyte, eosinophil, and erythroid and megakaryocytic cell growth (12). The current study revealed no significant increase in the GM-CSF in HCV patients, and this result is in accordance with that of Bahgat et al. (13), who found significant elevation in this cytokine among chronic HCV Egyptian patients.

Many studies have shown that patients with chronic hepatitis had somewhat lower levels of spontaneous and stimulated IL-1 expression by peripheral blood mononuclear cells (14), however, other studies have suggested increases serum levels of this cytokine in HCV patients (15).

Beside the immune cells, hepatocytes may participate in the production of some cytokines, a hypothesis which has been documented in the case of viral hepatitis (16). Among these cytokines are tumor necrosis factor-alpha (TNF- α) and IL-1 α which were shown to be secreted from HCV-infected hepatocytes (17). Despite this fact our study revealed no

significant decreased in IL-1 α in HCV patients compared with control subjects. This discrepancy may be explained by the ethnic variations between population and the possible presence of polymorphisms in IL-1 α gene among our patients that may cause reduction in the expression of this cytokine. However, this notion require further investigation to be documented or eliminated.

Complement is a non-cellular component of the immune system which causes cellular damage directly or through opsonization and chemotaxis-inducing effect (18). Decreased serum levels of complement components are expected results due to many factors the most important of which is that some of complement components are synthesized by the hepatic parenchymal cells. Thus, the synthesis rate of these components may be reduced as a direct consequence of injury and death of hepatic cells. Furthermore, there may be an increased in the consumption of complement by antigen-antibody complex with subsequent activation of complement by alternative pathway. These results are in accordance with many previous works (3,19,20) who reported a decline in serum levels of complement components in patients with hepatitis.

From the results of this study, it can be concluded that the innate immune response GM-CSF, IL-1 α , and complement components C3 and C4 has mild or undetectable effect.

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