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The Comparison of Serum Interleukin-8 Levels Based on Severity of Liver Cirrhosis

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ABSTRACT

Background: The molecule known as Interleukin-8 (IL-8), a chemotactic leukocyte, has been found to have a crucial role in the perpetuation of the inflammatory environment that is associated with hepatitis B virus (HBV) infection, as well as in the development of liver cirrhosis and cancer. **Objective:** The aim of this study was to carefully examine the role of IL-8 in the inflammatory reaction and to compare the levels based on the severity of liver cirrhosis. **Methods:** The study was conducted from February 2018 to September 2018 at the Gastroenterohepatology Division, Internal medicine Department, Faculty of Medicine, Universitas Sumatera Utara. The study was designed as an analytic comparative, cross-sectional study. The liver cirrhosis patients who participated in this study met the inclusion criteria and provided informed consent. **Results:** A total of 70 patients were included in the study, from which we identified 1 individual with child-pugh A, 28 individuals with child-pugh B, and 41 individuals with child-pugh C. The serum level of IL-8 was found to be 98 (11-320) (pg/ml). The IL-8 levels between child-pugh B and C patients did not exhibit any noteworthy differences during our analysis (p = 0.109, p>0.05). **Conclusion:** There is no notable inequality in the levels of IL-8 across different stages of liver cirrhosis.

Keywords: interleukin 8, IL-8, liver cirrhosis, severity.

1. BACKGROUND

Interleukin-8 (IL-8), a proinflammatory cytokine, has the capability to induce chemotaxis and degranulation of neutrophils, T-lymphocytes, and basophils, thereby playing a critical role in the pathogenesis of inflammatory responses caused by a variety of viruses and bacteria (1). Moreover, IL-8 has been identified as an important player in vitro in inhibiting IFN-α's antiviral effects (2). A major cause of liver disease worldwide, is frequently resistant to the antiviral alpha interferon (IFN). Host immune response plays crucial role in the pathogenesis of chronic hepatitis B virus (HBV) infection and other liver diseases such as cirrhosis and hepatocellular carcinoma (3). Cytokines, which are well-known for their crucial role in the organization of hepatic inflammation in different liver disorders, have been linked to the development of fibrosis and cirrhosis (4, 5). Prior investigations have recognized elevated amounts of IL-8 discharge in chronic or severe liver diseases, such as cirrhosis and alcoholic or autoimmune hepatitis when compared to normal control groups (3, 6). In this particular research, our aim was to examine the levels of serum IL-8 in a cross-sectional examination of consecutive patients with liver cirrhosis.

2. OBJECTIVE

The core aim of this research was to thoroughly assess the levels of IL-8 in the serum and analyze the complexities of its relationship with the severity of liver cirrhosis.

3. MATERIALS AND METHODS

This particular study was an analytical comparative research that employed a cross-sectional examination on patients diagnosed with liver cirrhosis and hepatitis B virus infection who were admitted to the Gastroenterohepatology Division, Internal Medicine Department, Faculty of Medicine, Universitas Sumatera Utara from February 2018 until September 2018. Consequently, the serum levels of IL-8 were measured in 70 patients who met the inclusion criteria and provided informed consent. These patients were diagnosed

Variable	n = 70
Gender [a]	
Male	43 (61.4%)
Female	27 (38.6%)
Age (years) [b]	51.24 ± 10.65
Viral marker [a]	
B	26 (37.1%)
C	9 (12.9%)
Others	35 (50%)
Ascites [a]	55 (78.6%)
Yes	15 (21.4%)
No	
Hepatic Encephalopathy[a]	
Yes	37 (52.9%)
No	33 (47.1%)
Child-Pugh[a]	
A+B	29 (41.4%)
C	41 (58.6%)

Table 1. Characteristic of Patients a Categorical data: n (%) b Numeric data, normal distribution: mean ± SD

with liver cirrhosis, which was confirmed by clinical findings, laboratory parameters, imaging, or histopathological examination. Patients with liver cancer, blood poisoning, long-term kidney problems, or those who declined to participate in the research were then excluded from the study.

The ethics committee of Universitas Sumatera Utara approved the protocol after obtaining written consent from all participants before the study commenced.

In this investigation, we gathered plasma from venous blood utilizing either EDTA or heparin as an anticoagulant. We then centrifuged the samples for 15 minutes at 1000 g within 30 minutes of collection, after which we assayed immediately or aliquot and stored the samples at <-20°C. It is worth noting that we assayed IL-8 with Quantikine HS ELISA Human CXCL8/IL-8 Immunoassay (R&D System). The diagnosis of HBV and HCV viral infections was based on the results of positive HBV serologic marker (HBsAg) and HCV serologic marker (Anti HCV). The classification of subjects into two groups was based on their test results for HBsAg and/or Anti HCV: the hepatitis group (positive cases) and the non-hepatitis group (negative cases for both tests). Moreover, we examined and compared the levels of serum interleukin-8 based on the severity of liver cirrhosis patients, the underlying disease type, and the clinical and laboratory parameters. Data analysis was conducted using the SPSS 22nd version (SPSS Inc., Chicago) through univariate analyses.

4. RESULTS

Of the entire cohort of 70 individuals, a majority of 43 (61.4%) were of the male gender. The Child-Pugh score distribution was distributed as follows: one patient witha Child-Pugh A classification, 28 patients with Child-Pugh B, and 41 patients with Child-Pugh C. Furthermore, hepatic encephalopathy was diagnosed in 37 (52.8%) patients, while 55 (78.5%) patients had ascites, as shown in Table 1. The mean serum level of IL-8 was recorded as 98 (11-320) (pg/ml). Table 2 exhibits the laboratory features of the study participants.

Laboratory	Child-Pugh A + B (n = 29)	Child-Pugh C (n = 41)	P
Age [a]	52.64 ± 9.91	50.10 ± 11.19	0.324
Total Bilirubin [b] (mg/dl)	2.33 (0.4-3.2)	3.47 (0.9-9.1)	<0.001
INR [a]	1.31 ± 0.29	2.30 ± 0.74	<0.001
Albumin [b] (g/dl)	2.9 (1.6-4.4)	2.0 (1.2-2.9)	<0.001*
Ureum [b] (g/dl)	33 (16-150)	34 (11-302)	0.912
Creatinine [b] (g/dl)	0.78 (0.42-9.51)	0.87 (0.26-8.25)	0.434
Hemoglobin [a] (g/dl)	9.34 ± 1.90	9.39 ± 1.47	0.565
Leukocytes [b] (/mm^3)	4945 (1029-16060)	7060 (1650-11670)	0.061
Platelet count [b] (/mm^3)	148500 (30000-415000)	81000(34000-677000)	0.046*
Interleukin-8 [b]	64.8 (11.7-320)	133.5 (11.0-320)	0.109

Table 2. Comparison of Laboratory Parameters between Child-Pugh of Liver Cirrhosis *p<0.05

5. DISCUSSION

IL-8 is a member of a different chemokine family and has limited biological functions. This chemokine is secreted by various cells, including hepatocytes, monocytes, epithelial cells, and fibroblasts, and it exerts a plethora of effects on the immune system, such as the recruitment of neutrophils, T lymphocytes, and basophils, as well as the induction of degranulation, oxidative bursts, and lysosomal-enzyme release (7-10).

Interestingly, high levels of serum IL-8 have been detected during hepatitis flares, suggesting a potential role of this chemokine in the pathogenesis of liver disease. Previous studies have demonstrated that the level of IL-8 in patients with chronic hepatitis B is significantly higher than that in healthy controls (11, 12). Moreover, IL-8 levels have been shown to increase with exacerbation of liver damage and decrease when conditions improve (13). In this context, Pollicino investigated whether hepatitis B virus (HBV) may directly induce IL-8 production and whether IL-8 may antagonize interferon-alpha (IFN-α) antiviral activity against HBV. The results showed that CHB patients had significantly higher levels of IL-8 both in serum and in liver tissue than controls (14). This finding is particularly relevant given that during the acute phase of hepatitis, inflammatory neutrophil infiltration of the liver is commonly observed (15). Notably, IL-8 is a neutrophil recruiting agent that is induced in hepatocytes after stimulation with IL-1 or TNF-α (16-18)·hepatocytes, and the host immune system, the natural course of chronic hepatitis B (CHB). The outcome of patients with cirrhosis was affected by serum IL-8 level. Even though the patient had undegone transjugular intahepatic portosystemic

shunt, high serum IL-8 level led to decompensation and mortality (19).

Another study showed that serum IL-8 level might be utilized in monitoring post-hepatitic cirrhosis patients. The level of serum IL-8 was still higher in post-hepatic cirrhosis patients compared to normal subjects. Further increase in serum IL-8 level was associated with poorer outcome and in line with previous diseas severity (20). The level of serum IL-8 was not only elevated in liver diseases associated with HBV infection. Swiatkowska-Stodulska, et al. in their found that serum IL-8 level was significantly higher in patients with alcoholic liver disease compared to normal subjects. Additionally, the serum IL-8 was in line with severity of alcoholic liver disease's clinical and laboratory parmeters (21).

Despite these compelling findings, our research failed to identify noteworthy variations in the serum level of IL-8 and the Child-Pugh score between the hepatitis and non-hepatitis groups, as shown in Table 2. This may be attributed to the fact that our subjects were liver cirrhosis patients who did not have an acute phase state or hepatitis flare during the research period. Nonetheless, our findings offer valuable insights into the intricate interplay between IL-8 and liver disease, which could potentially have significant implications for the advancement of innovative therapeutic approaches for individuals with liver disorders.

6. CONCLUSION

There was no significant difference in IL-8 among the severity of liver cirrhosis.

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