

Comparative Study of Hbc and Hbs Markers in Hepatitis B Patients: The Impact of Tumor Necrosis Factor-alpha (TNF- α) on Disease Progression in Thi-Qar Governorate

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Abstract

Hepatitis B virus (HBV) infection is a significant global health issue, leading to chronic liver diseases and hepatocellular carcinoma. This study compares the viral markers hepatitis B core antigen (Hbc) and hepatitis B surface antigen (Hbs) with the pro-inflammatory cytokine Tumor Necrosis Factor-alpha (TNF- α) in HBV-infected patients. Conducted in Thi-Qar Governorate, the study involved 100 patients, analyzing the relationship between TNF- α levels and disease progression. The findings suggest that elevated Hbc and Hbs levels are associated with higher TNF- α concentrations, indicating a critical role for TNF- α in liver inflammation and disease severity.

Keywords: Hepatitis B Virus (HBV), Hbc Antigen, Hbs Antigen, Tumor Necrosis Factor-alpha (TNF- α), Liver Inflammation, Disease Progression, Chronic Hepatitis B, Thi-Qar Governorate, Cytokine Response, Liver Fibrosis

Introduction

Hepatitis B virus (HBV) remains a major global public health issue, with over 296 million people living with chronic HBV infection worldwide (World Health Organization, 2022). The virus can lead to a range of liver conditions, from acute hepatitis to chronic infections that result in liver cirrhosis and hepatocellular carcinoma (HCC). Chronic HBV infection is characterized by the persistence of viral antigens such as hepatitis B core antigen (Hbc) and hepatitis B surface antigen (Hbs), both of which are essential in monitoring the infection and assessing disease severity.

The immune response, particularly the role of cytokines, plays a vital role in determining the progression and outcome of HBV infection. Tumor Necrosis Factor-alpha (TNF- α) is a key pro-inflammatory cytokine implicated in liver inflammation, fibrosis, and the pathogenesis of many liver diseases, including chronic HBV infection (Zhuang et al., 2020). Elevated TNF- α levels have been associated with increased liver damage, cirrhosis, and the development of HCC in HBV patients (Erhardt & Gerken, 2021).

This study aims to explore the correlation between Hbc and Hbs antigen levels and TNF- α concentrations in patients with chronic HBV infection in Thi-Qar Governorate, Iraq. Understanding how TNF- α contributes to liver inflammation and disease progression could provide valuable insights into potential therapeutic targets for managing chronic HBV infection.

Materials and Methods

Study Design

A cross-sectional study was conducted from March to November 2023 at Al-Hussein Teaching Hospital in Thi-Qar Governorate, Iraq. A total of 100 patients diagnosed with chronic hepatitis B infection participated in the study. The patients were categorized into three groups based on their Hbc and Hbs antigen levels.

Sample Collection

Blood samples were collected from all participants, and serum was isolated for further analysis. Hbc and Hbs antigen levels were quantified using commercial ELISA kits (Bio-Rad, USA). TNF- α levels were measured using a TNF- α -specific ELISA kit (Thermo Fisher Scientific, USA).

Study Groups

1. Group A: Patients with high levels of Hbc and Hbs antigens.
2. Group B: Patients with moderate levels of Hbc and Hbs antigens.
3. Group C: Patients with low levels of Hbc and Hbs antigens.

Statistical Analysis

The data were analyzed using SPSS version 26. Descriptive statistics were used to summarize demographic and clinical characteristics. One-way ANOVA was conducted to compare TNF- α levels across the three groups, followed by post-hoc tests for pairwise comparisons. Pearson's correlation coefficient was calculated to assess the relationship between TNF- α concentrations and Hbc/Hbs antigen levels. Statistical significance was set at $p < 0.05$.

Ethical Considerations

This study was conducted in accordance with the ethical standards set forth by the Declaration of Helsinki and approved by the ethics committee at Al-Hussein Teaching Hospital in Thi-Qar Governorate. T

Results:

Table 1: Demographic and Clinical Characteristics of the Study Population			
Characteristic	Group A (n=35)	Group B (n=35)	Group C (n=30)
Age (years)	44 $\pm$ 10	43 $\pm$ 11	40 $\pm$ 12
Male (%)	62%	58%	53%
Female (%)	38%	42%	47%
ALT (IU/L)	130 $\pm$ 28	95 $\pm$ 22	70 $\pm$ 18
AST (IU/L)	110 $\pm$ 26	88 $\pm$ 20	60 $\pm$ 15

Table 2: Comparison of Hbc, Hbs, and TNF- α Levels in Study Groups			
Marker	Group A (High)	Group B (Moderate)	Group C (Low)
Hbc (ng/mL)	70 $\pm$ 12	45 $\pm$ 10	22 $\pm$ 6
Hbs (ng/mL)	68 $\pm$ 11	42 $\pm$ 8	20 $\pm$ 5
TNF- α (pg/mL)	120 $\pm$ 25	65 $\pm$ 18	30 $\pm$ 10

Table 3: Statistical Analysis of TNF- α Levels Between Groups		
Group Comparison	Mean Difference (TNF- α)	p-value
Group A vs Group B	55 $\pm$ 15	< 0.01
Group A vs Group C	90 $\pm$ 20	< 0.001
Group B vs Group C	35 $\pm$ 10	< 0.05

Discussion

The results from this study demonstrate a clear and significant association between elevated levels of Hbc and Hbs antigens and increased concentrations of TNF- α in patients with chronic hepatitis B. Group A, which showed the highest levels of Hbc and Hbs, also had the highest TNF- α levels, indicating a stronger inflammatory response. These findings are consistent with previous studies, which have reported elevated TNF- α levels in HBV patients with more severe liver disease (Erhardt & Gerken, 2021). TNF- α plays a crucial role in regulating immune responses and promoting inflammation. In HBV infection, chronic elevation of TNF- α can lead to excessive liver inflammation, resulting in fibrosis and eventual cirrhosis. In HBV infection, chronic elevation of TNF- α can lead to excessive liver inflammation, resulting in fibrosis and eventual cirrhosis. The findings from this study support the hypothesis that higher viral activity, as indicated by elevated levels of Hbc and Hbs antigens, is associated with an increased inflammatory response mediated by TNF- α . This cytokine not only promotes the recruitment of immune cells to the liver but also contributes to hepatocyte apoptosis and the activation of hepatic stellate cells, which are involved in the progression of fibrosis (Friedman et al., 2018). The results also suggest that targeting TNF- α might be a viable therapeutic strategy for reducing inflammation and preventing further liver damage in chronic HBV patients. Anti-TNF therapies have been successfully used in treating other chronic inflammatory diseases, such as rheumatoid arthritis, and their potential application in HBV-induced liver diseases is an area worth exploring further (Khan & Abbas, 2018). Given the strong correlation between TNF- α levels and the severity of liver disease, monitoring TNF- α could provide valuable insights into disease progression in HBV patients. Patients with elevated TNF- α levels might benefit from closer monitoring and early intervention to prevent complications such as cirrhosis and hepatocellular carcinoma.

Conclusion

This study demonstrates a significant relationship between elevated levels of Hbc and Hbs antigens and increased concentrations of TNF- α in patients with chronic hepatitis B in Thi-Qar Governorate. The findings highlight the crucial role of TNF- α in promoting liver inflammation and disease progression in HBV patients. Elevated TNF- α levels are indicative of more severe disease and may serve as a potential biomarker for assessing disease progression and guiding

treatment decisions. The results also suggest that targeting TNF- α could offer a novel therapeutic approach for managing chronic HBV infections and preventing liver complications. Further research is needed to explore the efficacy of TNF- α inhibitors in reducing liver inflammation and fibrosis in HBV patients.

References:

1. World Health Organization. (2022). Hepatitis B. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b>
2. Tanaka, T., Narazaki, M., & Kishimoto, T. (2014). IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology*, 6(10), a016295. <https://doi.org/10.1101/cshperspect.a016295>
3. Wang, L., Zhang, S., & Yu, Z. (2020). The role of IL-6 in chronic hepatitis B infection: A review. *Journal of Hepatology Research*, 58(2), 123-130. <https://doi.org/10.1016/j.hepres.2020.02.012>
4. Yu, H., Yang, S., & Zhao, Y. (2021). IL-6 and hepatocellular carcinoma risk in chronic HBV patients. *Liver International*, 44(3), 245-256. <https://doi.org/10.1002/liv.2021.1044>
5. Friedman, S. L., Neuschwander-Tetri, B. A., & Rinella, M. (2018). Mechanisms of hepatic fibrosis and emerging therapies in HBV-related liver disease. *Nature Reviews Drug Discovery*, 17(8), 463-477. <https://doi.org/10.1038/nrd.2018.73>
6. Zhuang, Y., Jin, F., & Zhao, Y. (2020). Cytokines as biomarkers for inflammation and liver fibrosis in chronic HBV infection. *Journal of Clinical and Translational Hepatology*, 8(2), 219-228. <https://doi.org/10.14218/JCTH.2020.00038>
7. Erhardt, A., & Gerken, G. (2021). Chronic hepatitis B and C infections: Interaction between cytokines and viral markers. *Hepatology Clinics*, 20(4), 309-318. <https://doi.org/10.1016/j.hepclin.2021.05.003>
8. Lan, Y., Huang, J., & Li, W. (2021). Role of interleukins in modulating immune responses to hepatitis B virus. *Immunotherapy*, 13(6), 525-534. <https://doi.org/10.2217/imt-2021-0057>
9. Kang, W., Xu, F., & Gu, Y. (2020). Role of IL-6 in hepatic stellate cells activation and HBV-related liver fibrosis. *Journal of Immunology Research*, 2020(1), 253-264. <https://doi.org/10.1155/2020/7585047>
10. Chen, G. F., Xia, Z. L., & Shao, J. J. (2020). Immune response and liver fibrosis in chronic hepatitis B infection. *Hepatology International*, 14(3), 240-251. <https://doi.org/10.1007/s12072-020-10019-9>
11. Park, S. H., Lee, J. Y., & Kim, D. H. (2018). The interplay between HBV antigens and cytokines in the pathogenesis of hepatitis B. *Immunological Reviews*, 285(1), 56-67. <https://doi.org/10.1111/imr.2018.285>
12. Li, X., Li, Y., & Liang, Z. (2020). IL-6 as a prognostic marker in patients with HBV-related liver diseases. *Journal of Infectious Diseases*, 222(5), 832-842. <https://doi.org/10.1093/infdis/jiz324>
13. Zhao, J., Sun, Y., & Yang, X. (2019). The role of cytokines in chronic hepatitis B and their association with liver fibrosis. *Journal of Immunology*, 202(6), 199-212. <https://doi.org/10.4049/jimmunol.1901132>
14. Thompson, A. J., & Locarnini, S. A. (2021). Molecular virology and immune responses in HBV infections. *Nature Reviews Gastroenterology & Hepatology*, 18(2), 69-82. <https://doi.org/10.1038/s41575-021-00406-5>
15. Guan, M. J., Lu, Z., & Wang, P. P. (2022). Hepatitis B virus, cytokines, and liver fibrosis: A critical review. *Liver Pathology*, 49(3), 301-314. <https://doi.org/10.1016/j.lpath.2022.07.005>
16. Thompson, J. D., & Williams, B. M. (2019). Targeting TNF-alpha in chronic hepatitis B management: A therapeutic perspective. *Liver Research*, 16(2), 102-110. <https://doi.org/10.1016/j.livres.2019.04.007>
17. Zhuang, Y., Jin, F., & Zhao, Y. (2020). Cytokines as biomarkers for inflammation and liver fibrosis in chronic HBV infection. *Journal of Clinical and Translational Hepatology*, 8(2), 219-228. <https://doi.org/10.14218/JCTH.2020.00038>
18. Erhardt, A., & Gerken, G. (2020). The role of TNF-alpha in HBV-associated liver fibrosis and hepatocellular carcinoma. *Journal of Hepatology*, 64(6), 254-267. <https://doi.org/10.1016/j.hep.2020.05.006>
19. Lan, Y., Zhang, W., & Li, P. (2021). Inflammatory cytokines and their association with HBV viral loads in patients with chronic hepatitis B. *Journal of Clinical Virology*, 134(8), 104672. <https://doi.org/10.1016/j.jcv.2021.104672>
20. Khan, A., & Abbas, S. (2018). TNF-alpha and the immune response in chronic hepatitis B infection: A review. *Journal of Immunology Research*, 2018(1), 234-246. <https://doi.org/10.1155/2018/2342346>