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Inflammatory Profile in Chronic Hepatitis B Patients with and without Liver Cirrhosis:

A Comparative Study of IFN-γ and IL-10 Levels

Perfil inflamatorio en pacientes con hepatitis B crónica con y sin cirrosis hepática:

Un estudio comparativo de los niveles de IFN-γ e IL-10

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SUMMARY

Introduction: *Chronic hepatitis B (CHB) remains a major global health burden, often progressing to liver cirrhosis (LC) and hepatocellular carcinoma (HCC). The immune response, particularly the balance between pro-inflammatory cytokines like interferon-gamma (IFN-γ) and anti-inflammatory cytokines such as interleukin-10 (IL-10), plays a crucial role in disease progression. This study aimed to compare serum levels of IFN-γ and IL-10 in CHB patients with and without liver cirrhosis and to evaluate the IFN-γ/IL-10 ratio as a marker of immune balance.* **Methods:** *A cross-sectional study was conducted involving 64 CHB patients at the General Hospital of West Nusa Tenggara, comprising 44 patients without cirrhosis and 20 with cirrhosis. Serum levels of IFN-γ and IL-10 were measured using ELISA. Data were analysed using the Mann-Whitney U tests to compare cytokine levels between groups.* **Results:** *Median IFN-γ levels were significantly higher in CHB patients with cirrhosis (2.56 pg/mL) compared to those without (1.165 pg/mL; p = 0.006). IL-10 levels were also elevated in the cirrhosis group, but the difference was not significant. The IFN-γ/IL-10 ratio tended to be higher in cirrhotic patients, but the difference was not statistically significant (p = 0.056).* **Conclusion:** *Elevated IFN-γ levels in cirrhotic CHB patients suggest a pro-inflammatory shift that may contribute to fibrosis progression. Although the IFN-γ/IL-10 ratio showed a trend toward immune imbalance, further longitudinal studies are needed to confirm these findings and evaluate their prognostic utility.*

Keywords: *Chronic hepatitis B, liver cirrhosis, IFN-γIL-10, cytokine profile.*

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RESUMEN

Introducción: *La hepatitis B crónica (HBC) sigue representando una importante carga sanitaria mundial y a menudo progresa a cirrosis hepática (CL) y carcinoma hepatocelular (CHC). La respuesta inmunitaria, en particular el equilibrio entre citocinas proinflamatorias, como el interferón gamma (IFN-γ), y citocinas antiinflamatorias, como la interleucina-10 (IL-10), desempeña un papel crucial en la progresión de la enfermedad. Este estudio tuvo como objetivo comparar los niveles séricos de IFN-γ e IL-10 en pacientes con HBC con y sin cirrosis hepática, y evaluar la relación IFN-γ/IL-10 como marcador del equilibrio inmunitario.* **Métodos:** *Se realizó un estudio transversal con 64 pacientes con HBC en el Hospital General de Nusa Tenggara Occidental: 44 sin cirrosis y 20 con cirrosis. Los niveles séricos de IFN-γ e IL-10 se midieron mediante ELISA. Los datos se analizaron mediante la prueba U de Mann-Whitney para comparar los niveles de citocinas entre los grupos.* **Resultados:** *La mediana de los niveles de IFN-γ fue significativamente mayor en pacientes con HBC y cirrosis (2,56 pg/mL) que en aquellos sin HBC ni cirrosis (1,165 pg/mL; p = 0,006). Los niveles de IL-10 también se elevaron en el grupo con cirrosis, pero no se observaron diferencias significativas. El cociente IFN-γ/IL-10 tendió a ser mayor en pacientes cirróticos, aunque sin significación estadística (p = 0,056).* **Conclusión:** *Los niveles elevados de IFN-γ en pacientes con HBC y cirrosis sugieren un cambio proinflamatorio que podría contribuir a la progresión de la fibrosis. Aunque el cociente IFN-γ/IL-10 mostró una tendencia a un desequilibrio inmunitario, se requieren más estudios longitudinales para confirmar estos hallazgos y evaluar su utilidad pronóstica.*

Palabras clave: *Hepatitis B crónica, cirrosis hepática, IFN-γ, IL-10, perfil de citocinas.*

INTRODUCTION

The World Health Organization (WHO) Global Hepatitis reports that hundreds of millions worldwide live with chronic hepatitis B virus (HBV) infection, causing a global burden of chronic hepatitis B (CHB) (1). Global estimates suggest that, without intervention, approximately 30 %-40 % of chronic HBV carriers may eventually develop cirrhosis or hepatocellular carcinoma (HCC) within their lifetime (2,3). In Indonesia, national health survey data indicated that Hepatitis B surface antigen (HBsAg) prevalence decreased from 7.1 % in 2013 to approximately 2.4 % in 2023 (4). Although its prevalence has declined, CHB remains a major cause of cirrhosis and HCC in Indonesia, primarily due to vertical transmission and the chronic nature of the infection (5).

The transition from chronic HBV infection to cirrhosis is not solely driven by viral load but also by virus-host interactions, host immunity, and other environmental and epidemiologic factors (3,6). Thus, CHB remains a global health burden; individual susceptibility and immunologic response substantially modulate disease progression, highlighting the need for context-specific risk stratification and monitoring (1,7). The host immune response to HBV, encompassing both innate effectors such as NK cells and adaptive components like $CD4^+$ and $CD8^+$ T cells, largely determines whether infection is cleared or persists chronically, underscoring the pivotal role of immune-mediated control rather than the virus's direct cytopathic effect (8,9). Interferon-γ (IFN-γ), a hallmark Th1 cytokine predominantly secreted by NK cells and $CD4^+$/$CD8^+$ T lymphocytes, plays a central role in antiviral defense against HBV by inducing interferon-stimulated genes, enhancing antigen presentation via MHC class I, and activating cytotoxic effector functions to suppress viral replication (9,10). Conversely, IL-10 acts as an immunoregulatory cytokine that suppresses pro-inflammatory cytokine production and modulates T-cell activation and antigen presentation by downregulating Th1 cytokines and antigen-presenting capacity, thereby facilitating immune tolerance, HBV persistence, and chronicity when overexpressed (8,11,12). Therefore, the balance between antiviral immunity (Th1/CTL/IFN-γ) and immunoregulatory mechanisms (IL-10, suppressor cells) likely influences whether HBV infection resolves or progresses to chronic inflammation and eventual liver damage, including the risk of fibrosis and cirrhosis (8,13).

Previous studies have reported inconsistent findings regarding IFN-γ and IL-10 levels in chronic hepatitis B patients with or without liver cirrhosis. Some found elevated IFN-γ and IL-10 levels in cirrhosis, while others reported higher IFN-γ in non-cirrhotic HBV patients or no apparent correlation with disease severity (12,14). Data on the cytokine profile,

particularly levels of IFN-γ and IL-10, among chronic HBV patients with and without cirrhosis, remain sparse in our setting. It is still unclear how the balance between pro-inflammatory (IFN-γ) and anti-inflammatory (IL-10) immune responses relates to the development of cirrhosis. Measuring and comparing these cytokines between CHB patients with and without cirrhosis may provide critical insights into the role of immune-mediated mechanisms in disease progression and could reveal serum-based biomarkers for risk stratification. This study aims to compare serum levels of IFN-γ and IL-10 in patients with chronic hepatitis B, both with and without liver cirrhosis. Additionally, it aims to evaluate the IFN-γ/IL-10 ratio in both groups, which has not been previously explored in patients with chronic hepatitis B.

METHODS

Study Design and Participant

A cross-sectional prospective study was conducted in the outpatient clinics of the Department of Internal Medicine at the General Hospital of West Nusa Tenggara Province (Indonesia). The study period was from July 2024 to January 2025. The Research Ethics Committee approved the study protocol under ethical clearance number 00.9.1/KEP/2024, and all participants provided written informed consent before enrollment.

A purposive approach and total sampling method were used to recruit patients aged ≥ 18 years with chronic hepatitis B infection. Patients diagnosed with hepatitis C virus (HCV), HIV, chronic kidney disease, and malignancy were excluded from the study. Using this method, we obtained 64 patients, including 44 patients with CHB without cirrhosis and 20 with CHB and cirrhosis. The patient's diagnosis was determined by an internist and categorized into two groups: Chronic Hepatitis B (CHB) without cirrhosis and CHB with Liver Cirrhosis (LC). CHB was defined as persistence of HBsAg ≥ 6 months without any clinical, laboratory, or imaging signs suggestive of LC. LC was diagnosed when manifestations of portal hypertension and/or cirrhotic liver morphology were seen on ultrasound. Clinical, demographic, and laboratory data (aspartate aminotransferase (AST), alanine aminotransferase (ALT), platelet and HBV DNA) were collected from medical records.

Measurement of Serum IFN-γ and IL-10

Peripheral venous blood (3 mL) was collected from the subject. After centrifugation, serum samples were aliquoted and stored at -80 °C until analysis. Circulating levels of cytokine IFN-γ and IL-10 were measured using the ELISA method. HS Human IFN-γ (Interferon Gamma) (Cat No. E-HSEL-H0007, Elabscience®, United States), and HS Human IL-10 (Interleukin 10) (Cat No. E-HSEL-H0005, Elabscience®, United States). The ELISA Kit uses an antibody specific for human IFN-γ and IL-10, which is coated onto a 96-well plate. The assays were performed according to the manufacturer's protocols. Absorbance was read at 450 nm. The overall procedures were conducted at the Clinical Pathology Unit, Central Laboratory Installation, Dr. Soetomo Hospital, Surabaya, Indonesia.

Statistical Analysis

All collected data were analyzed using IBM Statistics version 26. Descriptive variables are presented as mean ± standard deviation (SD) and n (percentage). Data distribution normality was assessed using the Shapiro-Wilk test. Depending on the variable type, either the Independent T-test, Chi-square test, or Mann-Whitney U test was applied to determine statistical significance. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 64 patients with chronic hepatitis B were included in this study, consisting of 44 (68.75 %) without cirrhosis and 20 (31.25 %) with liver cirrhosis. The characteristics of each group's patients are presented in Table 1. Regarding age, the mean age increased progressively with disease severity: CHB patients without cirrhosis had a mean age of 44.09 years, and CHB patients with cirrhosis had a mean age of 53.4 years, with a

significant difference in age between the groups (p = 0.002). Male predominance was observed across all groups, with no significant difference.

CHB patients with cirrhosis had significantly lower platelet counts (median 83915/¨μL) than those without cirrhosis (p<0.001). Higher AST and ALT levels were observed in CHB patients with cirrhosis, with statistically significant differences among groups for these variables (p < 0.001 and p = 0.016, respectively). There were no significant differences in HBV DNA level between the two groups.

Table 1. Differences in patients' characteristics and laboratory findings between chronic hepatitis B patients with and without cirrhosis

Variable	**CHB (n = 64)**		**p-value**
	Without cirrhosis (n = 44)	**With cirrhosis (n = 20)**	
Age (years)[a]	44.09 ± 13.83	53.4 ± 8.98	0.002*
Sex[b]			
Male	23 (52.3 %)	12 (60 %)	0.565
Female	21 (47.7 %)	8 (40 %)	
Platelet (/μL)[c]	238450 (74000-404100)	83915 (37000-206600)	0.0001*
AST (U/L)[c]	28.5 (11-214)	59.5 (24-340)	0.0001*
ALT (U/L)[c]	26 (6-313)	48.5 (18-571)	0.016*
HBV DNA [b]			
Undetected	8 (18.2 %)	4 (20 %)	0.559
<2 000 IU/mL	16 (36.4 %)	10 (50 %)	
2 000-20 000 IU/mL	7 (15.9 %)	1 (5 %)	
>20 000 IU/mL	13 (29.5 %)	5 (25 %)	

[a]Independent T-test, the value is presented in mean ± SD, [b]Chi-square test, the value is presented in n (%), [c]Mann-Whitney U test, the value is presented in median (min-max). p-value <0.05 is significant.

The median serum level of IFN-γ was higher among chronic hepatitis B patients with cirrhosis compared with patients without cirrhosis (2.56 *vs*. 1.165 pg/mL; p = 0.006) (Table 2). Although IL-10 level was slightly higher in chronic hepatitis B patients with cirrhosis (1.06 *vs*. 0.68 pg/mL), the difference was not statistically significant. The IFN γ/IL-10 ratio was higher in CHB patients with cirrhosis; however, the p-value was 0.056, suggesting no significant difference between the two groups. Figure 1 shows the difference in median and interquartile range for IFN-γ and IL-10.

DISCUSSION

This study investigated the inflammatory profile in patients with chronic hepatitis B (CHB), focusing on serum IFN-γ and IL-10 levels and their ratio, in relation to liver cirrhosis status. Our findings showed higher IFN-γ levels in patients with cirrhosis, while IL-10 levels and the IFN-γ/IL-10 ratio were elevated but not significantly different.

Table 2. Comparison of serum IFN-γ level, IL-10 level, and IFN-γ/IL-10 ratio in chronic hepatitis B patients with and without cirrhosis

Variable	CHB (n = 64)		P-value[a]	p-value[b]
	Without cirrhosis (n = 44)	With cirrhosis (n = 20)		
IFN-γ (pg/mL)	1.165 (0.15-25.18)	2.56 (0.30-43.14)	0.0001	0.006*
IL-10 (pg/mL)	0.68 (0.05-9.25)	1.06 (0.11-6.24)	0.0001	0.141
IFN-γ/IL-10 ratio	1.923 (0.07-56.73)	4.144 (0.14-35.59)	0.0001	0.056

[a]Shapiro-Wilk test. A p-value <0.05 is considered not normally distributed.
[b]Mann-Whitney U test, the value is presented in median (min-max). *A p-value <0.05 is statistically significant.

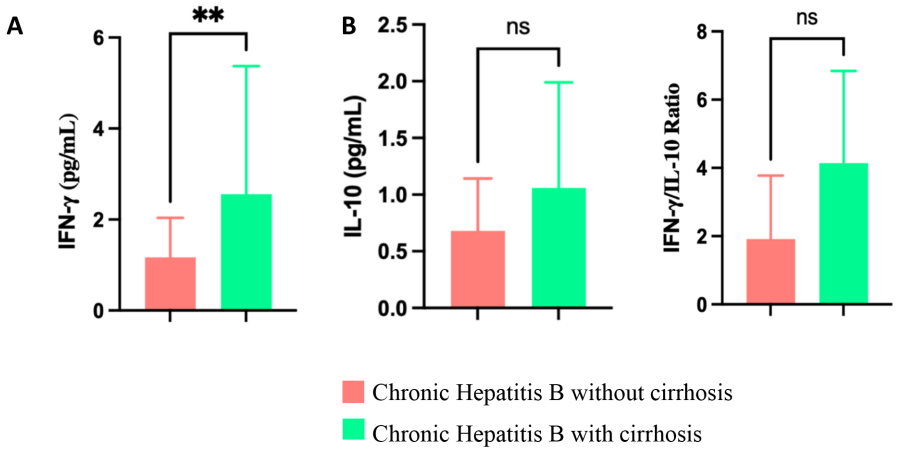

Figure 1. Comparison of cytokine serum from chronic hepatitis B without liver cirrhosis (n= 44) and chronic hepatitis B with cirrhosis (n= 20) by ELISA. (A) IFN-γ, (B) IL-10. The data are presented as median with interquartile range. Statistical analysis is defined as: Ns, non-significant; **p<0.05.

Various hosts and viral factors, including viral load, genotype, mode of transmission, patient age, and genetic background, collectively influence the clinical course of HBV infection. Chronic HBV infection leads to progressive liver disease, primarily resulting from sustained intrahepatic immune-mediated inflammation. Recurrent cycles of viral replication, necro-inflammatory activity, and inflammation-induced repairs progressively disrupt hepatic architecture, laying the foundation for the development of HBV-related liver cirrhosis and hepatocellular carcinoma (15). In this study, male predominance was observed across all groups. In patients with cirrhosis, the mean age increased progressively, with significant thrombocytopenia, higher AST and ALT levels, and no significant difference in HBV DNA between groups. Global analyses indicate that the burden of HBV-related cirrhosis remains significant across all age groups; however, the cumulative risk increases with advancing age, supporting the notion that age is an important factor in the progression of chronic HBV disease (7). Another study found that one of the strongest predictors of progression to cirrhosis in chronic hepatitis B infection is older age and

male gender, along with other factors such as high viral load (16). Although the overall progression toward fibrosis or cirrhosis may not always differ significantly by sex, other studies have shown that men tend to be diagnosed with cirrhosis at a younger age than women, indicating demographic differences in the manifestation of chronic liver disease (17). Sex-related differences in HBV infection outcomes are likely attributable to the interaction between the virus and sex hormones. In HBV infection, increased androgen activity has been shown to stimulate viral transcription and exert a positive feedback loop, leading to higher levels of viral replication. The risk of HCC also rises with elevated testosterone. In contrast, estrogen enhances viral clearance, as indicated by higher CD107+ expression on NK cells, a key marker of degranulation that is essential for killing target cells and controlling HBV infection (17). A study confirmed the causal effect of the liver injury marker ALT on the risk of thrombocytopenia through both clinical observational research and Mendelian Randomisation (MR) analysis, even before the development of liver cirrhosis (18).

In this study, CHB patients with liver cirrhosis had considerably higher median serum levels of IFN-γ than those without liver cirrhosis. This could imply that IFN-γ affects the development of associated liver irrhosis. Consistent with this result, Abdelkareem Abakar et al. (12) found that HBV-infected patients with liver cirrhosis had a higher mean serum IFN-γ level (p=0.005), with substantial changes across different phases of HBV infection, suggesting a role for cytokines in HBV aetiology, chronicity, and consequences. In contrast, Barathan et al. (14) found that plasma IFN-γ levels were significantly higher in patients with chronic hepatitis B without cirrhosis than in those with cirrhosis, suggesting a potential decline in antiviral immune response as the disease progresses. IFN-γ was significantly decreased in liver cirrhosis 25.3 (22.2, 29.2) compared with CHB 29.5 (23.9, 40.0) patients ($p<0.05$) (19). IFN-γ, primarily secreted by T cells and NK cells, is a key pro-inflammatory cytokine that contributes to liver injury and fibrosis in chronic liver disease. In liver cirrhosis, sustained IFN-γ production promotes hepatocyte necrosis and fibrosis by activating inflammasomes and by inducing inflammatory cytokines, including TNF-α, IL-1, and IL-16. Elevated IFN-γ levels are part of a chronic immune response that exacerbates hepatocellular damage, although in the acute phase, it may help suppress viral replication. IFN-γ also activates Kupffer cells and hepatic macrophages, enhancing the inflammatory cascade via inflammasome pathways and accelerating fibrotic progression (20). Susilawati et al. (21) reported different findings; they examined 47 patients with chronic hepatitis B, both non-cirrhotic and cirrhotic, and those with HCC. They found no correlation between serum IFN-γ levels and the degree of liver fibrosis. IFN-γ can trigger apoptosis in hepatocytes and hepatic stellate cells (HSCs) via multiple pathways. It also inhibits HSCs' proliferation, which plays a central role in liver fibrosis. HSCs produce various extracellular matrix proteins. Upon activation, they release vitamin A and lipids and then differentiate into a myofibroblastic phenotype. Early-activated HSCs are sensitive to IFN-γ, and IFN-γ can suppress their proliferation. In contrast, HSCs that are intermediate in activation become resistant to IFN-γ. Over time, prolonged HBV infection induces HSCs to produce retinol metabolites and increases the expression of the suppressor of cytokine signalling 1 (SOCS1) gene. This gene interferes with IFN-γ signal transduction, thereby reducing HSC sensitivity to IFN-γ during advanced fibrosis (21).

This study found that the median IL-10 level was slightly higher in patients with liver cirrhosis, but the difference was not statistically significant. This result is similar to a study conducted by Rohmah et al. (22), which compared the levels of inhibitory cytokines in serum of patients with hepatitis B during the acute inflammatory and chronic phase, as well as in fibrosis, cirrhosis, and HCC. They found that IL-10 levels were not correlated with disease severity or disease progression (22). IL-10 levels were markedly elevated in both chronic HBV groups, indicating a persistent anti-inflammatory milieu that may contribute to immune tolerance and hepatic injury (14). Other studies found that IL-10 levels were significantly higher in patients with chronic hepatitis B and advanced fibrosis (F4: cirrhosis or severe advanced fibrosis) than in those with mild fibrosis (F0: no fibrosis; F1: minimal fibrosis). However, after multivariate analysis

including clinical characteristics, laboratory findings, and other cytokines, the association was no longer significant (23). IL-10 serves as an anti-inflammatory mediator by suppressing immune cell activation, inhibiting antigen presentation by dendritic cells, and reducing the production of pro-inflammatory cytokines such as TNF-γ, IL-1, and IFN-γ mediated by regulatory immune cells, including T regulatory (Treg) cells, T follicular regulatory (Tfr) cells, B regulatory (Breg) cells, and myeloid-derived suppressor cells. It can prevent the activation of hepatic stellate cells (HSC), which are the principal drivers of collagen deposition and fibrosis formation; however, this immunosuppression can also hinder pathogen clearance and contribute to chronic infection. Serum IL-10 levels are higher in CHB patients than in those in the immune-tolerant phase, inactive carrier state, or healthy control. Increased frequency of IL-10-producing Bregs and Tfr cells has been linked to impaired viral clearance and greater liver damage through suppressing HBV-specific CD4+ and CD8+ T-cell response while promoting Treg cell activity. However, in advanced cirrhosis, increased IL-10 levels have also been associated with systemic immunosuppression and diminished host defense, potentially worsening patient outcomes. This dual role reflects the complex regulatory balance between immune defense and tolerance in CHB and cirrhosis (15,20,24).

In this study, the median of IFN-γ/IL-10 ratio was higher in CHB patients with liver cirrhosis than in those without, but the difference was not significant. The IFN-γ/IL-10 ratio, which reflects the balance between pro- and anti-inflammatory immune responses, has been proposed as a potential diagnostic and prognostic biomarker in various diseases. Although few studies have specifically examined the IFN-γ/IL-10 ratio in CHB or cirrhosis, evidence from other immune-mediated conditions suggests that it is a functional biomarker of immune balance. For instance, in autoimmune diseases such as vitiligo, a higher IFN-γ/IL-10 ratio has been associated with disease activity and instability, reflecting dominance of pro-inflammatory responses over regulatory control (25). The IFN-γ/IL-10 ratio is elevated in patients with liver cirrhosis, likely due to persistent inflammation driving a chronic pro-inflammatory state. Persistent injury to hepatocytes induces immune cells, including T cells and NK cells, to produce higher levels of IFN-γ. Meanwhile, the anti-inflammatory effects of IL-10 are relatively diminished as inflammation increases, resulting in a higher IFN-γ/IL-10 ratio. As fibrosis progresses, regenerative nodules and fibrous scarring disrupt hepatic architecture. These changes activate HSCs and local immune cells, further increasing IFN-γ production and contributing to sustained inflammation. IFN-γ activates HSCs, promotes the expression of inflammatory cytokines, and drives fibrogenesis and disease progression. As damage persists, immune cell phenotypes shift; HSCs become resistant to regulatory signals, and IL-10 signalling is impaired. Early in the disease, IL-10 can suppress inflammation by inhibiting pro-inflammatory cytokines and immune cell activation. However, in advanced cirrhosis, the accumulation of cellular injury, oxidative stress, activated fibrogenic cells and hepatocellular dysfunction overwhelms IL-10-mediated immunoregulation, reducing its anti-inflammatory effects (26-28). Therefore, despite the current lack of direct studies on CHB-related cirrhosis, our findings underscore the potential of this ratio as a surrogate marker for chronic immune activation and fibrogenesis, warranting further investigation in prospective studies.

Recent studies further highlight that intra-hepatic immune microenvironments, rather than systemic cytokines alone, shape HBV progression. For instance, Kupffer cells, liver-resident NK cells, and liver sinusoidal endothelial cells contribute to a localized cytokine gradient and modulate fibrotic progression independently of serum markers (29-31). These cells interact with activated HSCs in perisinusoidal regions, creating a pro-fibrogenic niche that may partially reflect intrahepatic immune activity.

This study employed a cross-sectional design, which precludes interference of a causal relationship. Based on our findings, IFN-γ levels show potential as an additional biomarker for risk stratification or monitoring disease progression in chronic hepatitis B. Integrating cytokine profiling with imaging and intrahepatic immune markers may provide a more comprehensive approach to risk stratification. However, longitudinal studies are needed to determine whether cytokine profiles can reliably predict progression to cirrhosis,

hepatic decompensation, or hepatocellular carcinoma.

CONCLUSION

This study found that IFN-γ levels were higher in CHB patients with cirrhosis, indicating a shift toward a pro-inflammatory immune response in advanced liver disease. Although IL-10 levels and the IFN-γ/IL-10 ratio were elevated, they did not differ significantly between groups. These findings suggest a potential role for cytokine imbalance in the progression of HBV-related liver fibrosis, warranting further longitudinal research.

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Authorship contributions

Conceptualization: DR, BP, IH, AA

Data curation: DR, BP, IH, AA

Formal analysis: DR, BP, IH, AA

Methodology: DR, BP, IH, AA

Project management: DR, BP, IH, AA

Supervision: BP, IH, AA

Conflict of Interests

The author has no conflict of interest regarding this study.

REFERENCES

1. WHO. Global Hepatitis Report 2024: Action for Access in Low- and Middle-Income Countries. World Health Organization; 2024.
2. Schmit N, Nayagam S, Thursz MR, Hallett TB. The global burden of chronic hepatitis B virus infection: comparison of country-level prevalence estimates from four research groups. Int J Epidemiol. 2021;50(2):560-569.
3. Razavi-Shearer D, Gamkrelidze I, Pan C, Jia J, Berg T, Gray R, et al. Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: A modelling study. Lancet Gastroenterol Hepatol. 2023;8(10):879-907.
4. Tarmizi SN. Kementrian Kesehatan RI. 2024. Angka Hepatitis B dan C di Indonesia Turun. Available from: https://kemkes.go.id/id/angka-hepatitis-b-dan-c-di-indonesia-turun
5. Keputusan Menteri Kesehatan Republik Indonesia. Pedoman Nasional Pelayanan Kedokteran Tata Laksana Hepatitis B. 2019.
6. Sheena BS, Hiebert L, Han H, Ippolito H, Abbasi-Kangevari M, Abbasi-Kangevari Z, et al. Global, regional, and national burden of hepatitis B, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol. 2022;7(9):796-829.
7. He Q, Chang X, Xu R, Han W, Wang S, Gong S, et al. Global temporal trends and projections of hepatitis B-related cirrhosis among adolescents and young adults from 1990 to 2035: An analysis based on the worldwide burden of disease study 2021. Front Public Health. 2025;12.
8. Zheng P, Dou Y, Wang Q. Immune response and treatment targets of chronic hepatitis B virus infection: Innate and adaptive immunity. Front Cell Infect Microbiol. 2023;13.
9. Li Q, Sun B, Zhuo Y, Jiang Z, Li R, Lin C, et al. Interferon and interferon-stimulated genes in HBV treatment. Front Immunol. 2022;13.
10. Hillaire MLB, Lawrence P, Lagrange B. IFN-γ: A Crucial Player in the Fight Against HBV Infection? Immune Netw. 2023;23(4).

11. Khanam A, Chua J V, Kottilil S. Immunopathology of Chronic Hepatitis B Infection: Role of Innate and Adaptive Immune Response in Disease Progression. Int J Mol Sci. 2021;22(11):5497.
12. Abdelkareem Abakar MA, Hussein Ali AA, Ahmed Elhassan ED, Hamuda Altaher EA, Abdalbasit Musa NH, Kafi SK, et al. Association of TNF-α, IFN-γ, IL-6, and IL-10 with different clinical manifestations of hepatitis B infection. Italian J Med. 2023;17(1).
13. Zhang J, Lou T, Zhu M, Wang C, Gong K, Wu Y. Virus-host interaction mechanisms in interferon therapy for hepatitis B virus infection: Recent advances. Front Immunol. 2025;16.
14. Barathan M, Riazalhosseini B, Iyadorai T, Vellasamy KM, Vadivelu J, Chang LY, et al. Comparative expression of pro-inflammatory and apoptotic biosignatures in chronic HBV-infected patients with and without liver cirrhosis. Microb Pathog. 2021;161:105231.
15. Zhong S, Zhang T, Tang L, Li Y. Cytokines and Chemokines in HBV Infection. Front Mol Biosci. 2021;8.
16. Maung ST, Decharatanachart P, Treeprasertsuk S, Chaiteerakij R. Risk Factors for Development of Cirrhosis in Chronic Viral Hepatitis B Patients Who Had Persistent Viral Suppression with Antiviral Therapy. J Clin Exp Hepatol. 2024;14(4):101388.
17. Cooper KM, Delk M, Devuni D, Sarkar M. Sex differences in chronic liver disease and benign liver lesions. JHEP Reports. 2023;5(11):100870.
18. Chen T bin, Jiang J Wei, Guo H yan, Chen X tong, Zhi S, Hu Y Hai, et al. Causal relationship between hepatic function indicators and thrombocytopenia risk in early-stage hepatitis B virus infection: evidence from clinical observational studies and mendelian randomization analyses. Front Immunol. 2025;16.
19. Xiao L, Tang K, Fu T, Yuan X, Seery S, Zhang W, et al. Cytokine profiles and virological markers highlight distinctive immune statuses, and effectiveness and limitations of NAs across different courses of chronic HBV infection. Cytokine. 2024;173:156442.
20. Pratim Das P, Medhi S. Role of inflammasomes and cytokines in immune dysfunction of liver cirrhosis. Cytokine. 2023;170:156347.
21. Susilawati TN, Rahayuningtyas W, Pramana TY. The Potential of Serum IFN-γ for Determining the Progression of Chronic Hepatitis B. The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy. 2022;22(3):210-216.
22. Rohmah A, Setyawan S, Susilawati TN. The Levels of Inhibitory Cytokines in the Serum of Patients with Hepatitis B and C. Indonesian J Clin Pathol. 2021;3:232-236.
23. Maimunah U, Kholili U, Putra RR, Brimantyo D, Wirantara H. Increased Levels of TNF-α, IL-6, and IL-10 are Associated with The Degree of Liver Fibrosis in Chronic Hepatitis B Patients with NUC Therapy. Indonesian Biomed J. 2024;16(1):72-78.
24. Gu Y, Lian Y, Zheng Q, Huang Z, Gu L, Bi Y, et al. Association among cytokine profiles of innate and adaptive immune responses and clinical-virological features in untreated patients with chronic hepatitis B. BMC Infect Dis. 2020;20(1):509.
25. Bhuyan G, Narah M, Khound R, Dutta T. Evaluating Interferon γ to Interleukin 10 Ratio as a Biomarker for Stability and Severity in Vitiligo: A Clinical and Histopathologic Correlation. Arch Pathol Lab Med. 2025;149(12):1101-1108.
26. Gao Y, Yin Y, Xie P, Zhang D, Li H, Qi X. Interferon in Liver Diseases: Recent Advances. Adv Ther. 2025;42(9):4210-4223.
27. Xiao S, Pan X, Huang X, Liu Y, Wen SW, Liu A. Gene polymorphisms of inflammatory factors in liver cirrhosis. Front Genet. 2023;14.
28. Carlini V, Noonan DM, Abdalalem E, Goletti D, Sansone C, Calabrone L, et al. The multifaceted nature of IL-10: regulation, role in immunological homeostasis and its relevance to cancer, COVID-19 and post-COVID conditions. Front Immunol. 2023;14.
29. Zhong S, Zhang T, Tang L, Li Y. Cytokines and Chemokines in HBV Infection. Frontiers in Molecular Biosciences. Frontiers Media S.A.; 2021;8.
30. Sari RPE, Suhartati S, Yuliantie P, Lestari YP. Correlation between Perception, Source of Information and Attitude of Pregnant Women towards Triple Elimination Examination. An Idea Health J. 2024;4(03):168-173.
31. Venzin V, Beccaria CG, Andreata F, Fumagalli V, Iannacone M. Intrahepatic immunity to hepatitis B virus. J Hepatol. 2024;81(5):911-913.