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Differences in MPV (Mean Platelet Volume) / Lymphocytes Ratio In Chronic Hepatitis B with and without Cirrhosis Hepatic

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ABSTRACT

Introduction: The MPV/Lymphocyte Ratio is a simple inflammatory parameter that can be obtained from a complete blood count. Hepatitis patients with liver cirrhosis have a higher MPV causing thrombopoietin to decrease so that the platelet count decreases. The inflammatory response can cause a decrease in the number of lymphocytes and is closely related to a poor prognosis in patients with hepatitis B virus. This study aims to examine the differences in the MPV/Lymphocyte ratio in chronic hepatitis B patients with and without liver cirrhosis.

Methods: The samples for this study was chronic hepatitis B patients with and without liver cirrhosis who met he inclusion criteria. The research was carried out by taking blood samples from 94 patients treated in the internal medicine treatment room and Gastroenterohepatology polyclinic at Adam Malik Hospital, Medan. Samples were examined for MPV, absolute lymphocytes, then the MPV/lymphocyte ratio was calculated.

Results: The total number of subjects in this study was 94 and there were 62 men and 32 women. The results of the analysis showed that there was a significant difference between the cirrhotic and non-cirrhotic groups (p = 0.001).

Conclusion: There was a significant difference in the ratio of MPV/lymphocytes in the group of hepatitis B subjects with cirrhosis and in the group of hepatitis B subjects without liver cirrhosis. (p = 0.001).

Keywords

Chronic Hepatitis B with and without liver cirrhosis, MPV/Lymphocyte rasio, Liver cirrhosis

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INTRODUCTION

Chronic hepatitis is a series of liver disorders of varying causes and severity in which liver inflammation and necrosis persist for a minimum of 6 months. Hepatitis resulting from viral infections continues to be a global public health concern, affecting millions of people and causing thousands of deaths due to acute and chronic infections, cirrhosis, and liver cancer.[2] World Health Organization (WHO) estimates that around 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections occurring every year. In the same year, hepatitis B resulted in approximately 820,000 deaths, mostly due to cirrhosis and primary liver cancer.

Based on the 2013 Basic Health Research (Riskesdas), the prevalence of the hepatitis B virus (HBV) in Indonesia was around 7.1% (approximately 18 million individuals), and the prevalence of the hepatitis C virus was approximately 1.01% (around 2.5 million individuals).[4] Liver cirrhosis is a critical natural stage of HBV infection. Once the infection progresses to cirrhosis, the occurrence of hepatocellular carcinoma (HCC)

significantly increases, with an annual incidence ranging from 3% to 6%. Over the past two decades, many non-invasive examinations have been developed to assess the stage of liver fibrosis with good diagnostic accuracy.[6] MPV (Mean Platelet Volume) is an independent variable that determines the severity of inflammation and is associated with the severity of fibrosis, where heavier fibrosis is accompanied by higher MPV. Additionally, MPV examination, combined with the use of other non-invasive markers, can provide reliable data regarding the level of liver fibrosis severity in patients with chronic hepatitis B. In patients with cirrhosis, MPV is found to be higher compared to non-cirrhotic patients or healthy controls.

Furthermore, Ma et al (2018) found a positive correlation between MPV and the Model for End-Stage Liver Disease (MELD) score, reflecting the severity of liver disease. Moreover, MPV outperforms the MELD score in predicting short-term survival in patients with acute exacerbation of chronic liver failure.[8] In the study by Hu et al (2014) involving a total of 120 patients, including 17 patients with acute hepatitis B, 62 with chronic hepatitis B, and 41 with severe chronic hepatitis B, as well as 58 healthy controls, it was found that MPV significantly increased in patients with chronic Hepatitis B infection and was associated with the severity of the disease ($p < 0.05$).[9] A low lymphocyte count may indicate a high risk of infection. Lymphocytes play a crucial role in eliminating bacteria, viruses, toxins, and cancer cells in the human body. A decrease in the number of lymphocytes may signal a weakened immunity.

The immune system is correlated with inflammation, where a strong immune response can prevent Hepatitis B virus infection, while a weak immune response can lead to persistent or chronic infection. Inflammatory response can cause a reduction in lymphocyte count and is closely related to poor prognosis in Hepatitis B virus-infected patients.[11] Recently, the Mean Platelet Volume-To-Lymphocyte Ratio (MPVLR), a ratio of MPV to lymphocytes, has emerged as a new inflammation parameter. Several studies have indicated that this parameter holds predictive value for the diagnosis and prognosis of cardiovascular and cerebrovascular diseases, malignancies, diabetes, kidney and liver diseases, as well as appendicitis.[12] A study conducted by Wu et al in 2020, retrospectively involving 101 chronic HBV patients treated in the hospital from January 2018 to May 2019, examined MPVLR in all subjects. Multivariate analysis was conducted to identify independent factors associated with outcomes in HBV-DeCi patients. The study found that only MPVLR and MELD score (Model for End-Stage Liver Disease) were independent predictors of mortality ($p < 0.001$), compared to MPV ($p = 0.014$) and lymphocytes ($p = 0.001$). ROC curve analysis was performed to evaluate the relative efficiency of MPVLR and MELD score in predicting mortality. The MELD score had a cutoff value of 17.2, with a sensitivity of 50.0% and specificity of 81.0%. MPVLR had a cutoff value of 19.4 with a sensitivity of 60.5% and specificity of 81.0%. The study found that an increased MPVLR was associated with poor outcomes in chronic HBV patients and could potentially be a useful prognostic component in the future. Deceased patients had a higher MPVLR compared to surviving patients (median 22.1 vs 11.5 with $p < 0.001$).[13]

Further research is needed to determine the significance of MPVLR in chronic hepatitis patients with and without hepatitis cirrhosis.

METHODS

Research Design this study is an analytical study utilizing a cross-sectional data collection method to assess the difference in Mean Platelet Volume-to-Lymphocyte Ratio (MPVLR) between chronic Hepatitis B patients with and without liver cirrhosis.The research was conducted at the Department of Clinical Pathology, Faculty of Medicine, Universitas Sumatera Utara (FK USU), in collaboration with the Department of Internal Medicine, Gastroenterohepatology Subdivision, FK USU / RSUP H. Adam Malik Medan. The research took place from March 2023 to May 2023.

The population of this study comprised patients diagnosed with chronic Hepatitis B by the Department of Internal Medicine at RSUP Haji Adam Malik Medan who were admitted to the Internal Medicine Ward and the Internal Medicine Clinic at RSUP H. Adam Malik Medan. The total sample size was 94 patients. This

research was conducted at Haji Adam Malik Hospital Medan and at the Clinical Laboratory Installation of Haji Adam Malik Hospital Medan. The necessary material for this study was EDTA blood for a complete blood count examination. The MPV and absolute lymphocyte count values were obtained from the complete blood count examination. The complete blood count examination was promptly conducted using the Sysmex XN 1000 machine. To obtain the MPV/lymphocyte ratio, the MPV was divided by the absolute lymphocyte count.

The research was conducted after obtaining ethical clearance from the Health Research Committee of the Faculty of Medicine, Universitas Sumatera Utara, Medan, with No 263/KEPK/USU/2023, and research permission from the Research and Development Installation of RSUP H. Adam Malik Medan, with No LB.02.02/D.XXVIII.III.2.2.2/2190/2023.

RESULTS

In this study, a total of 94 patients were enrolled. Out of these, 62 patients (66%) were male, while the remaining 32 patients (34%) were female. A total of 44 patients (46.8%) were diagnosed with liver cirrhosis, whereas the rest, 50 patients (53.2%), did not have liver cirrhosis. The comprehensive characteristics of the study sample patients are presented in Table 1.

Table 1. Characteristics of Subjects

Characteristics	n (%)
Gender n (%)	
Male	62 (66%)
Female	32 (34%)
Cirrhosis	
Yes	44 (46,8%)
No	50 (53,2%)
Age (Years), Min-Max	52 (27 – 77)

Bivariate analysis was conducted on these patients. Numerical data will be analyzed based on their distribution. The Kolmogorov-Smirnov test indicated an abnormal distribution for the parameters of age, MPV (Mean Platelet Volume), absolute lymphocyte count, and the MPV ratio and MPV/lymphocyte ratio. Hence, these data were presented using the Mann-Whitney test. A comprehensive bivariate analysis is presented in Table 2.

Table 2. Bivariat Analysis

Clinical Parameter	Clinical Measurement		P value
	Cirrhosis	Non- Cirrhosis	
Age*	54 (29 -77)	50 (27-76)	0,151
MPV*	10,1 (7,7 – 14,0)	9,9 (7,8 – 13,2)	0,251
Absolute Limfosit*	1,03 (0,17 – 2,49)	1,29 (0,56 – 4,46)	0,001
MPV/Limphocyte Ratio	9,72 (4,51 – 53,33)	7,01 (2,29– 19,85)	0,001

**Mann-Whitney*

DISCUSSION

In this study, a significant difference in the mean MPV/Lymphocyte ratio was observed between the chronic Hepatitis B group with liver cirrhosis (9.72, 4.51 - 53.33) and the chronic Hepatitis B group without liver cirrhosis (7.01, 2.29 - 19.85), p = 0.001.

Consistent with the research conducted by Wu et al., 2020, a retrospective study involving 101 patients with decompensated chronic HBV-related liver cirrhosis, an increase in MPVLR was associated with poor outcomes in chronic HBV patients with decompensated liver cirrhosis, and it could potentially be a useful component of future prognostic scores.[14] This study contrasts with the research by Xu et al., where patients

with decompensated liver cirrhosis related to HBV with positive HBsAg had a lower MPV/Lymphocyte ratio compared to patients with negative HBsAg. One possible explanation for this discrepancy is that participants with positive HBsAg in Xu et al.'s study received antiviral treatment, thus improving their symptoms and physical condition.[6] Platelets are blood components crucial for the cessation of bleeding and the coagulation process. However, research findings indicate that platelets play a role in the inflammatory processes of both acute and chronic infectious diseases. Therefore, examining platelet parameters can provide insights into these diseases. One of the platelet parameters that can be evaluated is Mean Platelet Volume (MPV). In hepatic cirrhosis, platelet production is heightened in the bone marrow due to increased platelet utilization and destruction. This results in variations in platelet size, where younger platelets are larger and older platelets are smaller, thereby increasing the MPV value. MPV also provides valuable information regarding invasive infections caused by the HBV virus. The increase in MPV in hepatic cirrhosis is due to escalated production and consumption of platelets, where a higher MPV indicates a younger platelet age.[15]

In this study, a total of 94 patients participated. Among them, 62 patients (66%) were male, and the remaining 32 patients (34%) were female. The median age of the patients in this study was 52 years. Out of the total, 44 patients (46.8%) were diagnosed with liver cirrhosis, while the remaining 50 patients (53.2%) did not have liver cirrhosis. Consistent with the research conducted by Zhou et al 2019, they conducted a retrospective study involving 132 chronic hepatitis B patients with cirrhosis. From their study, it was found that there were 105 male subjects and 27 female subjects.[16] Our study shows that the median age of chronic hepatitis B patients is 52 years. In the study by Siregar J et al., 2021, the mean age of chronic hepatitis B patients with liver cirrhosis was 48.6 years, while for the chronic hepatitis B group without liver cirrhosis, it was 40.36 years.

Liver cirrhosis patients are increasingly prevalent with age. Liver cirrhosis is a chronic or long-term liver disease. The progression from liver cell damage to cirrhosis can occur within weeks to years. Symptoms and signs of this disease will only appear many years later after the patient has been exposed to risk factors for a long time.[18] In this study, there was no significant difference in MPV values with p = 0.151. This finding aligns with the research conducted by Wu et al., 2020, where MPV could not predict life expectancy outcomes (p= 0.008). In their study, they found that MPVLR (Mean Platelet Volume-to-Lymphocyte Ratio) was more accurate for prognostication in decompensated HBV patients compared to examining MPV or lymphocytes alone.[14]

This study contradicts the research by Kosekli, which showed that an increase in MPV can predict advanced fibrosis in patients with chronic hepatitis B. In that study, an MPV value > 7.52 fL had a sensitivity of 80% and specificity of 56% in determining advanced fibrosis (AUROC [area under the receiver operating characteristic curve]: 0.68, p = 0.002, confidence interval [CI] 95%, 0.58-0.77).[19]

This study demonstrates a significant difference in absolute lymphocyte values between the chronic Hepatitis B group with liver cirrhosis (1.03, 0.17 – 2.49) and the chronic Hepatitis B group without liver cirrhosis (1.29, 0.56 – 4.46), p = 0.001. A low lymphocyte count may be related to poor nutritional status and impaired immune response in patients with liver disease. Additionally, a lower lymphocyte count can be used as a predictor of mortality for liver transplant candidates.[14]

CONCLUSION

There is a significant difference in the Mean Platelet Volume (MPV)/Lymphocyte ratio between the chronic Hepatitis B groups with and without liver cirrhosis, p = 0.001, 2. The study involved a total sample of 94 individuals, with a higher number of male patients than female patients; 62 males and 32 females. The median age of the patients in this study was 52 years, There is no significant difference in Mean Platelet Volume (MPV) levels between the chronic Hepatitis B groups with and without liver cirrhosis, p = 0.251, There is a significant difference in absolute lymphocyte count between the chronic Hepatitis B groups with and without liver cirrhosis, p = 0.001.

DECLARATIONS
The research has received approval from Faculty of Medicine, Universita Sumatera Utara of Research and Ethics Committee. Participants were informed about this report.

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The Authors agree to publication in Journal of Society Medicine.

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The authors declare that there is no conflict of interest in this report.

AUTHORS' CONTRIBUTIONS
All authors significantly contribute to the work reported, whether in acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting and revising. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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