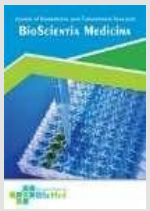
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

The Relationship between Neutrophil Lymphocyte Ratio and Hepatitis C Virus RNA in Hepatitis C Coinfected HIV Patients Receiving Direct-Acting Antiviral Therapy at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

Suyata[1], Prabjot Singh[1*], Harun Hudari[2], Taufik Indrajaya[3], Nurmalia Purnama Sari[4]

[1]Division of Gastroenterohepatology, Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

[2]Division of Tropical Disease and Infection, Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

[3]Division of Cardiovascular, Department of Internal Medicine, Faculty of Medicine, Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

[4]Department of Clinical Pathology, Faculty of Medicine, Universitas Sriwijaya/Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

ARTICLE INFO

Keywords:
Direct-acting antiviral
Hepatitis C virus
Human immunodeficiency virus
Neutrophil-lymphocyte ratio
Viral load

***Corresponding author:**
Prabjot Singh

E-mail address:
dr.sonnu@yahoo.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v7i1.761

A B S T R A C T

Background: Hepatitis C is an inflammatory disease of the liver caused by infection with the hepatitis C virus (HCV). Inflammatory markers are significant in assessing the course of an infectious or inflammatory disease. One of them is the neutrophil-lymphocyte ratio (NLR) and the amount of HCV RNA viral load, which combines neutrophils as an active inflammatory component and lymphocytes as a regulatory and protective component in a single parameter. Research on the relationship between NLR and HCV RNA in HIV patients coinfected with HCV is still limited. This study aimed to determine the relationship between NLR and HCV RNA in HIV-HCV coinfected patients who received DAA therapy and went to the outpatient polyclinic at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. **Methods:** Analytic observational study. A total of 38 research subjects participated in this study. Observation of NLR was carried out using hematology analyzer, and observation of HCV RNA levels was carried out using the PCR technique. Data analysis was carried out using SPSS univariate and bivariate. **Results:** There was a difference between pre-post therapy NLR and pre-post therapy HCV RNA viral load, $p<0.05$. NLR is in line with HCV RNA viral load as a prognostic tool for successful DAA therapy in HIV patients coinfected with hepatitis C. **Conclusion:** There is a relationship between HIV and HCV RNA in hepatitis C coinfected HIV patients receiving direct-acting antiviral therapy at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

1. Introduction

HIV (human immunodeficiency virus) is an RNA virus belonging to the family *Retroviridae*, subfamily *Lentivirinae* which attacks the immune system. The immunocompromised state of patients with HIV increases the risk of infection from other diseases. Hepatitis C infection is an infection of the liver parenchyma caused by the hepatitis C virus (HCV). Around 1.9 million Indonesians are infected with hepatitis C. In HIV-co-infected patients, the chances of curing HCV infection naturally are smaller. In addition, the rate of progression to fibrosis, liver decompensation, and hepatocellular carcinoma is higher. This makes HCV-induced liver disease the leading cause of non-AIDS death in people living with

HIV, even though clinically effective antiviral therapy for HCV infection is available.[1-5]

Initially, the sustained virologic response (SVR) rate as an indicator of a successful response to therapy to treatment in HCV infection with HIV coinfection was found to be lower overall than in HCV-infected patients without coinfection. However, with the advent of direct-acting antiviral (DAA) antiviral therapy, the treatment of HIV/HCV coinfected patients has dramatically improved SVR. DAA therapy offers an SVR of >95% for most HCV-infected patients, regardless of HIV-1 infection status. The DAA therapies currently available in Indonesia are sofosbuvir, ledipasvir/sofosbuvir, simeprevir, and daclatasvir. In addition to effective antiviral therapy, a fast and precise diagnosis is also needed so that therapy can be given as early as possible. The diagnosis of HCV infection can be made by history, physical examination, and supporting examinations. Investigations for HCV infection can be established by using anti-HCV and HCV RNA tests. HCV RNA testing is expensive, and not all health facilities in Indonesia are capable of testing HCV RNA. The neutrophil-lymphocyte ratio is a calculation of the absolute neutrophil count divided by the absolute lymphocyte count that can be used as a parameter to determine the loss of severe inflammatory status in the successful response to HCV infection therapy.[6-9] RNL is a promising prognostic therapy suggestion for HCV infection. This study aimed to determine the relationship between neutrophil-lymphocyte ratio (NLR) and HCV RNA in hepatitis C coinfected HIV (human immunodeficiency virus) patients receiving DAA (direct-acting antiviral) therapy at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

2. Methods

This study was an analytic observational study and used primary data from research subjects in the form of clinical data and supporting examinations. A total of 38 research subjects participated in this study, where the research subjects met the inclusion criteria. The inclusion criteria for research subjects were HIV patients with HCV coinfection who were treated at the internal medicine polyclinic at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia, aged 18-50 years, and willing to participate in the study by signing an informed consent form. This study was approved by the medical and health research ethics committee at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

This study observed the sociodemographic variables and clinical data of the research subjects. NLR measurements and HCV RNA levels before and after DAA therapy were measured. Neutrophil-Lymphocyte Ratio examination, which uses neutrophil and lymphocyte values, is carried out using a haemablood-analyzer. The quantitative examination of hepatitis C virus RNA in plasma or serum was carried out using the polymerase chain reaction (PCR) technique. Data analysis was carried out using SPSS software version 26. Univariate analysis was performed to present the frequency distribution of each test variable. Bivariate analysis was performed to determine NLR and HCV RNA levels before and after DAA therapy using the Wilcoxon test, with $p<0.05$.

3. Results

Table 1 shows the characteristics of the research subjects. The majority of research subjects were male, and the majority of research subjects had senior high school education. The majority of research subjects have self-employed jobs. The majority of research subjects have same-sex relationship risk factors.

Table 2 shows a comparison of NLR and HCV RNA pre and post-DAA therapy. The results of the study showed that there was a difference between the pre-therapy HCV RNA viral load and the post-therapy HCV RNA viral load, $p<0.001$. There was a difference between pre-therapy NLR and post-therapy NLR, $p<0.05$. Based on the Spearman correlation test, it was found that NLR with quantitative HCV RNA had a significant correlation with a p-value of 0.001 and $r=0.709$ before DAA therapy in HIV-HCV coinfected patients with a strong correlation. NLR with

quantitative HCV RNA had a positive correlation with a value of p<0.005 and r=0.603, which means that the higher the NLR value, the higher the HCV RNA viral load after DAA therapy in HIV patients coinfected with HCV with a strong correlation. The results of this study indicate that NLR is compatible with HCV RNA viral load as a prognostic means of successful DAA therapy in HIV patients co-infected with hepatitis C.

Table 1. Characteristics of research subjects.

Characteristics	N	%
Gender		
Male	30	78.9
Female	8	21.1
Education		
Primary school	2	5.3
Junior high school	2	5.3
Senior high school	27	71.0
Diploma	3	7.9
College	4	10.5
Occupation		
Not working	1	2.6
Housewives	4	10.5
Self-employed	17	44.7
Civil servant	5	13.2
Other	11	29.0
Viral load		
<400.000	19	50
>400.000	19	50
Risk factors		
Blood transfusion	2	5.3
Same-sex relationship	17	39.5
Cirrhosis status		
No cirrhosis	21	55.3
Cirrhosis compensation	8	21.0
Cirrhosis decompensation	9	23.7

Table 2. Comparison of NLR and HCV RNA pre and post-DAA therapy.

Characteristics	Median	Min – Max	p*
Viral load HCV RNA pretherapy	$43.1x10^4$	$10 – 60.04x10^6$	<0,001*
Viral load HCV RNA posttherapy	0	$0 - 48.8x10^3$	
NLR pretherapy	1.97	0.82 – 12.43	0,046*
NLR posttherapy	1,81	0,48 – 48	

*Wilcoxon test, before and after DAA therapy, p<0.05 significant.

4. Discussion

NLR is a calculation of the ratio of the absolute neutrophil count divided by the absolute lymphocyte count that can be used as a parameter to determine the loss of severe inflammatory status in the successful response to HCV infection therapy. A study shows that NLR can be used as a prognostic factor of liver fibrosis and hepatocellular carcinoma, especially in patients with HIV/HCV coinfection, and can help as an alternative to inflammatory biomarkers. In particular, individuals with higher NLRs appeared to have a greater relative risk of death in an age-adjusted analysis of HIV/HCV-negative patients compared with uninfected patients.[10-13]

The results of this study are in line with several studies. One study revealed that an increase in NLR may indicate a poor prognosis of chronic liver failure after a liver transplant. In another study investigating the relationship between postoperative changes in the value of NLR in Adult to adult living donor liver transplantation (AA-LDLT), it was found that higher NLR increases can be used as a predictor of

inflammatory changes to worsen the prognosis in AA-LDLT. In contrast to other studies which stated that an increase in NLR before getting therapy could indicate an unwanted virological response, the NLR value did not show a significant relationship with hepatitis C infection.[14-16]

These results are similar to studies where it was found that there was a significant relationship between RNL values and HCV RNA levels in patients with chronic hepatitis C and compensated liver cirrhosis after 12 weeks of DAA therapy. Based on other studies, it was revealed that the NLR value in liver cirrhosis was significantly lower than in chronic hepatitis C patients with a probability of liver cirrhosis and chronic hepatitis C without cirrhosis. In another study, it was shown that a high increase in NLR in patients with chronic hepatitis C showed a good virological response in patients with cirrhosis of the liver.[17-20]

5. Conclusion

There is a relationship between neutrophil-lymphocyte ratio (NLR) and HCV RNA in HIV (human immunodeficiency virus) Hepatitis C co-infected patients receiving DAA (direct-acting antiviral) therapy at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

6. References

1. Hanberg JS, Freiberg MS, Goetz MB, Rodriguez-Barradas MC, Gibert C, et al. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as prognostic inflammatory biomarkers in human immunodeficiency virus (HIV), hepatitis C virus (HCV), and HIV/HCV coinfection. Open Forum Infect Dis. 2019; 6(10): 1–9.
2. Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, et al. The global burden of viral hepatitis from 1990 to 2013: findings from the global burden of disease study 2013. Lancet. 2016; 388(10049): 1081–8.
3. Moosavy SH, Davoodian P, Nazarnezhad MA, Nejatizaheh A, Mahboobi H, et al. Epidemiology, transmission, diagnosis, and outcome of Hepatitis C virus infection. Electron physician. 2017; 9(10): 5646–56.
4. Morozov VA, Lagaye S. Hepatitis C virus: Morphogenesis, infection and therapy. World J Hepatol. 2018; 10(2): 186–212.
5. Migdal AL, Jagannathan R, Qayed E, et al. Association of obesity, diabetes, and alcohol use with liver fibrosis among US adults with hepatitis C virus infection. JAMA Netw Open. 2022; 5(3): e2142282.
6. Abdel-Razik A, Mousa N, Besheer TA, Eissa M, Elhelaly R, Arafa M, et al. Neutrophil to lymphocyte ratio as a reliable marker to predict insulin resistance and fibrosis stage in chronic hepatitis C virus infection. Acta Gastroenterol Belg. 2015; 78(4): 386-92.
7. Hayashi H, Takamura H, Ohbatake Y, Nakanuma S, Tajima H, et al. Postoperative changes in neutrophil-to-lymphocyte ratio and platelet count: A simple prognostic predictor for adult-to-adult living donor liver transplantation. Asian Journal of Surgery. 2018; 41(4): 341-8.
8. Meng X, Wei G, Chang Q, Peng R, Shi G, et al. The platelet-to-lymphocyte ratio, superior to the neutrophil-to-lymphocyte ratio, correlates with hepatitis C virus infection. International Journal of Infectious Diseases. 2016; 45: 72-7.
9. He Q, He Q, Qin X, Li S, Li T, et al. The relationship between inflammatory marker levels and hepatitis C virus severity. Gastroenterology Research and Practice. 2016; 2016.
10. Parekh BS, Ou C, Fonjungo PN, Kalou MB, Rottinghaus E, et al. Diagnosis of human immunodeficiency virus infection. Clin Microbiol Rev. 2019; 32(1): 1–55.
11. Zhao J, Chang L, Wang L. Nucleic acid testing and molecular characterization of HIV infections. 2019.
12. The Korean Society for AIDS. The 2018 clinical guidelines for the diagnosis and treatment of

HIV/AIDS in HIV-infected Koreans. Infect Chemother. 2019; 51(1): 77–88.
13. Ren L, Li J, Zhou S, Xia X, Xie Z, et al. Prognosis of HIV patients receiving antiretroviral therapy according to CD4 counts: A long-term follow-up study in Yunnan, China. Sci Rep. 2017; 7: 1–7.
14. Gobran ST, Ancuta P, Shoukry NH. A tale of two viruses: Immunological insights into HCV/HIV coinfection. Front Immunol. 2021; 12: 1–18.
15. Sherman KE, Peters MG, Thomas D. Human immunodeficiency virus and liver disease: A comprehensive update. Hepatol Commun. 2017; 1(10): 987–1001.
16. Schlabe S, Rockstroh JK. Advances in the treatment of HIV/HCV coinfection in adults. Expert Opin Pharmacother. 2018; 19(1): 49–64.
17. Chalouni M, Pol S, Sogni P, Fontaine H, Lacombe K, et al. Increased mortality in HIV/HCV-coinfected compared to HCV-monoinfected patients in the DAA era due to non-liver-related death. J Hepatol. 2021; 74(1): 37–47.
18. Soriano V, Vispo E, Fernandez-Montero JV, Labarga P, Barreiro P. Update on HIV/HCV coinfection. Curr HIV/AIDS Rep. 2013; 10(3): 226–34.
19. Region C protocol for the WE. Management of hepatitis C and HIV coinfection. 2013; 234–43
20. Nasta P, Cattelan AM, Maida I, Gatti F, Chiari E, et al. Antiretroviral therapy in HIV/HCV co-infection Italian consensus workshop. Adv Infect Dis. 2013; 03(02): 105–14.