ARTIKEL ASLI
Jurnal Penyakit Dalam Udayana
Udayana Journal of Internal Medicine
Volume 7, No. 2: 2023; 35-38

Print ISSN: 2580-2925
Online ISSN: 2580-2933

The efficacy of administering elbasvir/grazoprevir as hepatitis c therapy in hemodialysis patients with comorbid of hypertension and diabetes mellitus

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Crossref Crossmark
DOI : 10.36216/jpd.v7i2.228

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Received :18 October 2023
Accepted : 25 November 2023
Published : 01 December 2023

Background: Hepatitis C and chronic kidney disease (CKD) are significant global health burdens. Hemodialysis therapy can pose a risk of hepatitis C infection. Conditions related to Hepatitis C, such as hypertension and diabetes, have morbidity and mortality rates and can impact the outcomes of hepatitis C treatment.
Objective: This study aimed to assess the efficacy of Elbasvir/Grazoprevir as hepatitis C therapy in hemodialysis patients with comorbid hypertension and diabetes mellitus.
Methods: The target population for this study consists of hepatitis C-infected patients undergoing routine hemodialysis with comorbid hypertension and diabetes mellitus who were treated with Elbasvir/Grazoprevir. The data collected included demographic characteristics, comorbid conditions (hypertension and diabetes mellitus), cirrhosis status, and whether patients achieved Sustained Virologic Response (SVR). Multinomial logistic regression was used to calculate the odds ratio (OR).
Results: From the population profile of the study, a total of 164 individuals were included, with the majority being under 60 years old. Patients with comorbid hypertension or diabetes mellitus achieved SVR rates of 95% and 83.3%, respectively, while patients with both comorbid conditions, hypertension, and diabetes mellitus, had an SVR rate of 74.07%. The multinomial logistic regression analysis showed that patients with both comorbid conditions (HT and DM) had a higher risk of failing to achieve SVR compared to patients without comorbid conditions, with an OR of 22.4, $p = 0.005$.
Conclusion: Administering Elbasvir/Grazoprevir for hepatitis C therapy in hemodialysis patients with comorbid hypertension and/or diabetes mellitus carries a higher risk of SVR failure compared to those without comorbid conditions.

Keywords: *Hepatitis C, Hypertension, Diabetes, Hemodialysis, SVR.*

INTRODUCTION

Hepatitis C remains a global health burden with significant impacts on public well-being.[1] Hepatitis C virus (HCV) infections are common among hemodialysis (HD) patients and are associated with increased morbidity and mortality.[2] Patients with hypertension and diabetes undergoing chronic hemodialysis are at a higher risk of contracting hepatitis C (HCV) due to repeated vascular access use. In dialysis, three main risk factors affect HCV transmission; a history of blood transfusion, kidney transplantation, and the duration of hemodialysis.[3] Meanwhile, patients with hepatitis C who have comorbid conditions like Hypertension (HT), Diabetes Mellitus (DM), and other cardiovascular risks may worsen the prognosis and be at risk of a decreased response to hepatitis C treatment.[4] Research on the use of Elbasvir/Grazoprevir is becoming increasingly relevant because effective treatment should not only target the hepatitis C virus but also manage comorbid conditions that may contribute to the complexity of the disease. Antiviral agents (DAAs) are safe and effective in treating HCV infections in patients with Chronic Kidney Disease (CKD) on dialysis.[5] This study aimed to evaluate the efficacy of Elbasvir/Grazoprevir in the therapy of hepatitis C in hemodialysis patients who also suffer from comorbid conditions such as Hypertension and Diabetes Mellitus.

MATERIAL AND METHODS

We conducted a study on 233 patients diagnosed with hepatitis C based on hepatitis C serological laboratory testing who were receiving treatment with Elbasvir/Grazoprevir. The research employed a retrospective cohort study design. Data were collected from the medical records of patients diagnosed with Hepatitis C who were undergoing treatment at the outpatient clinic of Dr. Saiful Anwar Hospital in Malang

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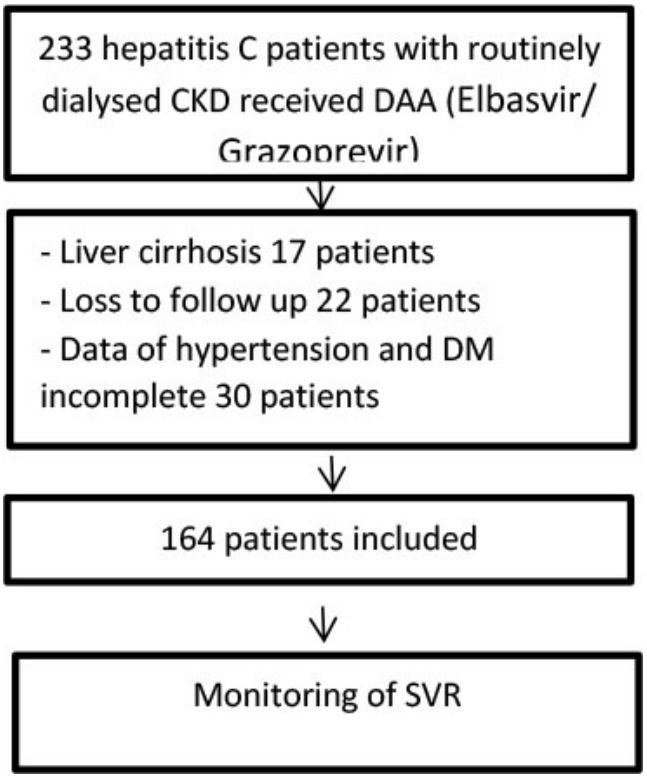

Figure 1. Research Flow.

from August 2020 to 2022. A total of 164 patients meeting the criteria were included in the study population. The research flow depicted in Figure 1.

Inclusion criteria for this study involved patients with hepatitis C based on a positive anti-HCV diagnosis with detectable HCV RNA who were undergoing hepatitis C treatment with the Elbasvir/Grazoprevir regimen. It also included patients with hepatitis C who were undergoing hemodialysis and had comorbid hypertension (HT) and/or diabetes mellitus (DM) at Dr. Saiful Anwar Hospital in Malang. The population excluded from the study comprised patients who did not attend follow-up appointments during the treatment and monitoring period (loss to follow up), as well as those with incomplete medical records. Additionally, patients receiving Interferon therapy, combination therapy, and patients with cirrhosis were also not part of the study population.

Fibrosis levels were assessed using transient elastography before initiating treatment. Demographic and virological characteristics, such as sustained virologic response (SVR) at 12 weeks after treatment with Elbasvir/Grazoprevir, were evaluated. Viral infection was assessed by measuring quantitative hepatitis C virus (HCV) ribonucleic acid (RNA) levels at the beginning of therapy, at the end of treatment (EOT), and at 12 weeks after EOT. Patients were considered to have achieved sustained virologic response (SVR) only if they had undetectable levels of HCV-RNA viral load at 12 weeks after the end of treatment (EOT).

An analysis was conducted to determine the influence of comorbid conditions (HT and/or DM) in hepatitis C patients undergoing hemodialysis on the achievement of SVR and non-SVR using the multinomial logistic regression method to calculate the odds ratio (OR) with a 95% confidence interval (CI). The reference value for statistical significance was set at a p-value of less than 0.05, indicating that results were considered significant.

RESULTS

From the population profile of this study, out of a total of 164 patients, the majority (75.6%) were aged 60 years or younger, which accounts for 124 individuals. The most common gender was male, with 102 patients (62.2%), while there were 62 female patients (37.8%). Among the patients, 65 had no comorbid conditions, 60 had hypertension (HT) as a comorbidity, 12 had diabetes mellitus (DM) as a comorbidity, and 27 had both comorbid conditions (as shown in Table 1).

In hepatitis C patients with CKD undergoing hemodialysis and comorbid hypertension (HT), the achievement of SVR was 95% (57 out of 60), while non-SVR was 5% (3 out of 60). Among patients with comorbid diabetes mellitus (DM), SVR was achieved by 83.3% (10 out of 12), and 16.6% (2 out of 12) did not achieve SVR. In patients with both comorbid conditions (DM and HT), SVR was achieved by 74.07% (20 out of 27), while 25.9% (7 out of 27) did not achieve SVR.

Based on the results of the multinomial logistic regression analysis, as shown in Table 2, hepatitis C patients undergoing routine hemodialysis with comorbid diabetes mellitus (DM) receiving Elbasvir/Grazoprevir therapy exhibited a higher likelihood of failing to achieve SVR compared to patients without comorbidities, with an odds ratio (OR) of 12.8, p 0.045, and a 95% confidence interval (CI) of (1.06-154.5). Similarly, in patients with both hypertension (HT) and DM comorbidities, the likelihood of failing to achieve SVR was significantly higher compared to patients without comorbidities, with an OR of 22.4, p 0.005, and a 95% CI of (2.6-193.1). Therefore, it can be concluded that comorbid DM and both comorbidities (HT and DM) significantly influence the achievement of SVR. However, in the case of comorbid HT, when compared to patients without comorbid HT and DM, the achievement of SVR did not show a significant difference, with an OR of 4.5, p 0.18, and a 95% CI of (0.5-42.1).

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DISCUSSION

Hepatitis C infection and CKD are major health burdens worldwide. Hepatitis C infection is associated with various extrahepatic manifestations in various organs, including the kidneys. The strong link between hepatitis C and chronic kidney disease is well-recognized. Hemodialysis, which is a life-supporting therapy for patients with end-stage renal disease (ESRD), can carry a risk of hepatitis C infection.[6]

Based on data from other studies, we found a significantly higher prevalence of systemic hypertension among patients with chronic HCV infection who have a history of DM. The increased prevalence of essential hypertension in HCV patients can occur in parallel with an increased prevalence of atherosclerosis (because DM and hypertension are important predisposing factors for atherosclerosis). Approximately 30% of adults are still unaware of their hypertension, and up to 40% of hypertensive patients do not receive treatment.[7]

The relationship between diabetes mellitus and the success of hepatitis C therapy has significant implications for disease management. Patients with hepatitis C and diabetes mellitus tend to face greater challenges in achieving sustained virologic response during antiviral therapy. Factors such as insulin resistance, higher chronic inflammation, and immune imbalances can influence the effectiveness of treatment. The presence of diabetes can also worsen liver damage caused by hepatitis C, accelerating disease progression.[4]

Table 1. Characteristics of subjects

variables	n= 164	Percentage (%)
Age		
≤60	124	75.6%
>60	40	24.4%
Gender		
Male	102	62.2%
Female	62	37.8%
Comorbid		
Without comorbid	65	39.6%
Hypertension (HT)	60	36.6%
Diabetes Mellitus (DM)	12	7.3%
Hypertension and Diabetes Mellitus	27	16.5%
Achievement of SVR		
No	14	8.5%
Yes	150	91.5%

A meta-analysis of patients receiving maintenance hemodialysis found that HCV-positive patients have a higher mortality rate compared to HCV-negative patients. This study indicates that liver-related deaths are higher than cardiovascular-related deaths among these groups [Adjusted RR 3.82 (95% CI: 1.92; 7.61) vs. 1.26 (95% CI: 1.10; 1.45)].[8] Based on these findings, this research provides information about the success of hepatitis C treatment in patients undergoing hemodialysis, which can prevent deaths due to hepatitis C. It also raises awareness that chronic Hepatitis C infection requires increased attention and treatment.

Diabetes mellitus, hypertension, and cardiovascular disease are some of the comorbidities that reduce the survival rates of CKD patients and make them poor candidates for current standard anti-HCV therapy. Managing HCV infection in kidney disease patients with multiple comorbid conditions remains a challenge.[9,10] Factors present in patients with hypertension, such as vascular damage, chronic inflammation, and negative effects of antihypertensive medications, can influence the efficacy of hepatitis C treatment. Additionally, hypertension can worsen liver conditions and increase the risk of disease progression.

This study indicates that patients with comorbidities have a higher risk of failing to achieve SVR compared to those without comorbidities. Patients with both comorbidities, DM and HT, have an even greater risk compared to those without comorbidities. Based on several pieces of literature we have gathered, chronic inflammation in comorbid conditions is one of the mechanisms behind the failure to achieve SVR in chronic Hepatitis C therapy. The more comorbidities found in patients, the higher the inflammatory response, which reduces the effectiveness of antiviral treatment.[11] This study also has limitations, including uneven distribution of the number of participants in each study group, a relatively small study population, and the potential influence of other comorbidities or chronic diseases that may not have been identified in the patients.

CONCLUSION

Elbasvir/Grazoprevir is effective in treating hepatitis C in patients undergoing hemodialysis with comorbid

Table 2. Result of multinomial logistic regression analysis

Groups	SVR, n (%)		OR (95% CI)	p
	Yes	No		
Without comorbid	64/65 (98.4%)	1/65 (1.53%)	-	-
HT	57/60 (95%)	3/60 (5%)	4.5 (0.5-42.1)	0.180
DM	10/12 (83.3%)	2/12 (16.6%)	12.8 (1.06-154.5)	0.045
HT and DM	20/27 (74.07%)	7/27 (25.9%)	22.4 (2.6-193.1)	0.005

DM: Diabetes mellitus; HT: Hypertension

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hypertension and/or diabetes mellitus. However, the risk of treatment failure increases with the presence of different types and numbers of comorbidities in patients. These findings offer new hope in the treatment of patients facing the dual challenges of hepatitis C and other health conditions. Nevertheless, further research is needed to gain a deeper understanding of the mechanisms at play and the long-term effects of using Elbasvir/Grazoprevir in patient populations with similar health profiles.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICS CONSIDERATION

This has been evaluated and received permission from Institutional Research Board of Faculty of Medicine, Brawijaya University / Dr. Saiful Anwar Hospital, Malang, East Java, Indonesia.

AUTHOR CONTRIBUTION

All authors shared equal contributions in this research, from conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, visualization, writing (original draft), and writing (review and editing).

FUNDING

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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