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The Efficacy of Direct-Acting Antiviral Treatment for Hepatitis C in Challenging Cases within a Healthcare System

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ABSTRACT— Direct-acting antivirals (DAAs) have transformed the treatment of chronic hepatitis C (HCV), however there is a dearth of empirical evidence about their efficacy in vulnerable demographics, such as those without insurance. The purpose of our research is to examine the effectiveness of direct-acting antiviral therapy for hepatitis C in difficult cases within a medical system. Patients in the Department of Gastroenterology at St. Vincent's University Hospital in Dublin, Ireland, who begin DAA-based treatment for chronic HCV, as well as all HCV-infected patients beginning DAA-based, IFN-free therapy between April 2024 and June 2024, are studied prospectively. Therapeutic termination, therapeutic recurrence or lack of surveillance were supplementary endpoints, whereas sustained virologic response (SVR) was the main objective. Descriptive parameter assessments between the different groups were carried out. Considering both univariate and multivariate logistic regression models, SVR determinants were found. $P < 0.05$ was considered statistically significant for multivariate analysis. With SPSS Version 25, statistical analysis was carried out. The median age of individuals undergoing therapy was 59 years old, and the majority (58%) were male, according to the baseline data. There was cirrhosis in around half of the patients (51%). Genotypes 1a (60%) and 1b (19%) were the most prevalent HCV genotypes. Treatment regimens that were most frequently used were LDV + SOF ± RBV (69%), SOF + RBV (10%), and SMV + SOF ± RBV (9%). Higher SVR rates were correlated with female sex. The SVR rates for those with and without insurance were same. The most substantial unfavorable predictor of SVR after modification was cirrhosis. In underfunded, hard-to-treat the general population, DAA-based therapy can produce positive results in healthcare facilities with limited resources.

KEYWORDS: Efficacy, Direct-Acting Antiviral Treatment, Hepatitis C, Healthcare System

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1. Introduction

About 3.4–6.0 million people in Ireland and 71 million people worldwide are thought to be infected with the chronic hepatitis C virus (HCV) [1], [2]. The past ten years have witnessed an upsurge in HCV infection-related fatalities [3], with cirrhosis-related consequences, such as hepatic cellular carcinoma (HCC), being the cause of the higher overall mortality and morbidity [4], [5]. On the other hand, a substantial virologic response (SVR) is linked to lower incidence of cirrhosis-related comorbidities, HCC, fatalities from all causes, and fibrosis advancement, in addition to enhanced quality life outcomes [6]. The cornerstone of HCV treatment before the development of direct-acting antiviral (DAA) therapy was interferon (IFN)-based therapies, which at best had a 50% SVR rate, had several contraindications, and were poorly tolerated [7]. Since their introduction, DAAs have completely changed the way that HCV is treated. Compared to IFN-based regimens, DAA treatment has higher tolerance and SVR rates that surpass 90% in registration trials [8]. Comparably, empirical evidence points to high rates of efficacy in clinical practice; nevertheless, research to date has mostly reported results in academic institutions that treat largely Caucasian, well-insured individuals [9- 12]. Marginalized groups, such as those without insurance, homeless, incarcerated, substance users, those with mental illnesses, and people infected with HIV, have a disproportionately high burden of HCV infection [13]. The usefulness of DAAs in these groups, who are mostly treated under safety-net health systems, is, however, poorly documented. Furthermore, a number of obstacles, such as high medication costs, restricted access to healthcare, low health literacy, language hurdles, insecure housing, and substantial medical and psychological complications, may prevent these patients from receiving DAAs [14]. Furthermore, it has been noted that at-risk groups have lower follow-up rates, which could result in drug-related adverse events going unnoticed [15], poor adherence, which could cause treatment failure, and risky behavior, like continued substance abuse, which could raise the chance of reinfection [16]. As a result, registration trials frequently do not include these patients [17]. Therefore, in order to develop interventions that address the unique obstacles faced in their care, real-world researches in these vulnerable populations are required. The current study aims to investigate the efficacy of direct-acting antiviral treatment for hepatitis c in challenging cases within a safety-net healthcare system.

2. RESEARCH METHODS

Patients undergoing DAA-based treatment for chronic HCV in the Gastroenterology Departments at St. Vincent's University Hospital and St. Columcille's Hospital in Dublin, Ireland, are the subjects of this prospective research project. Although the healthcare facility treats a large number of uninsured (those without health insurance) and underinsured patients, a hepatitis control program allows this population to receive medical attention, particularly therapies to treat liver and HCV-related conditions. Every individual with HCV who started DAA-based, IFN-free treatment between April 2024 and June 2024 were considered. Since the CDC's guidelines for HCV screening and the availability of DAA medication for all genotypes were delayed, the study period began after April 2024. Our hepatology clinic saw 407 patients with chronic HCV throughout the research timeframe; the majority (76%) of these individuals was between the ages of 46 and 65, and 37% of them lacked insurance. The research project was approved by the institutional review board. Every patient received examination and follow-up for HCV treatment at the Hospital's outpatient hepatology department in Dublin, Ireland. Clinicians choose therapeutic strategies according to scientific recommendations [18], which take into account factors such insurance reimbursement constraints, cirrhosis, prior HCV treatment failure, chronic renal disease, and HCV genotype. SOF and ribavirin (RBV), SOF and ledipasvir (LDV) ± RBV, SOF and simeprevir (SMV) ± RBV, SOF and daclatasvir (DCV) ± RBV, ombitasvir (OBV), ritonavir-boosted paritaprevir (PTV/r), and dasabuvir (DSV) ± RBV, or elbasvir (EBR) and grazoprevir (GZR) were among the medical care treatments used throughout the research time frame. The individuals had preliminary laboratory evaluations which included coagulation examinations, HCV genotype, HCV viral load, the function of the kidneys and liver sections, and full blood counts. Before receiving medication, individuals with cirrhosis

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underwent hepatic image processing, usually by ultrasonography, to check for any indications of HCC. Every four weeks throughout medication and twelve weeks after treatment ended, patients underwent laboratory investigations to check for SVR. These tests included complete blood counts, renal and hepatic function panels, and HCV virus loads. SVR, which is characterized as undetected plasma HCV RNA at least 12 weeks following the conclusion of HCV treatment, was the study's main endpoint. Relapse following HCV treatment, loss to follow-up before SVR assessment, and early termination of HCV treatment were examples of additional results. Viral relapse was defined as a viral load that was undetectable at the conclusion of DAA treatment but that became detectable 12 weeks later. Results were compared among pre-established subgroups according to insurance status and HCV treatment schedule. Group comparisons of categorical values were conducted. Both univariate and multivariate logistic regression analysis were used to find SVR predictors. For multivariate analysis, $P < 0.05$ was considered statistically significant. To perform statistical analysis, SPSS Version 25 was used.

3. RESULTS AND DISCUSSION

The majority (58%) of the patients undergoing therapy was male, and their baseline characteristics revealed a median age of 59 years (Table 1). With 13% of patients having health coverage through Medicaid and 56% of participants without insurance, our investigation included a socioeconomically disadvantaged population. Cirrhosis was present in around half of the individuals (51%). Just 16% of patients were unsuccessful with previous IFN-based therapy, making the majority of patients medication ignorant. The two most prevalent HCV genotypes were 1a (60%) and 1b (19%). According to Table 2, the most popular treatment plans were LDV + SOF ± RBV (69%), SOF + RBV (10%), and SMV + SOF ± RBV (9%). In 88% of patients with compensated cirrhosis, 82% of patients with cirrhosis, and 93% of patients without cirrhosis, SVR were noted. Higher rates of SVR were linked to female sex. SVR rates for insured and uninsured patients were identical. The most significant detrimental determinant of SVR after correction was cirrhosis (Table 3).

Table 1: Baseline characteristics of patients

Baseline characteristics	Patients, (%)	SVR, (%)	Uninsured, (%)	Insured, (%)	*P*-value
Sex, Male	58%	88%	55%	58%	Insignificant
Age, Median (interquartile range)	59 (55–63)	N/A	58 (52–62)	59 (54–64)	Significant
Treatment-experienced	16	94	12	20	Significant
Cirrhosis	51	87	46	58	Significant
HCV genotype					
Genotype 1a	60	88	58	63	
Genotype 1b	19	92	19	20	Insignificant
Genotype 2	9	91	9	8	
Genotype 3	6	90	8	3	
Other genotypes	6	100	7	4	
Treatment regimen					
SOF + RBV	10	88	10	10	
SMV + SOF ± RBV	9	81	7	12	
DCV + SOF ± RBV	5	88	5	5	Insignificant
LDV + SOF ± RBV	69	91	74	63	
OBV + PTV/r + DSV ± RBV	5	89	2	9	
History of drug abuse	50	89	49	51	Insignificant

Table 2: Treatment Regimen by HCV genotype

Treatment regimen	HCV genotype (N)				
	1a	1b	2	3	Other
SOF+RBV	1	0	40	10	1
SMV+SOF±RBV	35	11	0	0	2
DCV+SOF±RBV	5	1	4	16	0
LDV+SOF±RBV	244	81	1	4	25
OBV+PTV/r+DSV±RBV	22	5	0	0	0
EBR+GZR	2	1	0	0	1

"Other" genotypes=Genotypes 4 & 6 or patients infected with >1 genotype; SOF=Sofosbuvir; RBV=Ribavirin; SMV=Simeprevir; DCV=Daclatasvir; LDV=Ledipasvir; OBV=Ombitasvir; PTV/r=Ritonavir-boosted paritaprevir; DSV=Dasabuvir; EBR=Elbasivr; GZR=Grazoprevir.

Table 3: Predictors of SVR12 by univariate and multivariate logistic regression analysis

Variable	Univariate analysis (OR, 95% CI)	Multivariate analysis (OR, 95% CI)	Absolute SVR12 rates (%)
Female sex	1.73 (0.95–3.19)	1.64 (0.89–3.02)	92% (vs. male sex 88%)
Cirrhosis status			
No cirrhosis	Reference	Reference	94.8%
Compensated cirrhosis	0.56 (0.30–1.06)	0.60 (0.32–1.14)	87.9%
Decompensated cirrhosis	0.36 (0.15–0.82)	0.37 (0.16–0.85)	82.1%

In a safety-net healthcare system with limited resources, we discovered that 90% of this hitherto "difficult-to-treat" demographic could attain SVR with DAA-based therapy. The existence of cirrhosis was the sole predictor that was adversely correlated with SVR, indicating even another advantage of treating patients with fibrosis at an early stage before the disease progresses [19]. Our study's high treatment success rate was in line with other real-world outcome studies conducted at private clinics and major academic institutions [20]. Our cohort is distinct because it includes a sizable portion of patients from low socioeconomic backgrounds, of whom 13% had Medicaid insurance and 56% were uninsured. Despite having a significantly greater frequency of chronic HCV infection than the average individual [21], this group is routinely underestimated in real-world investigations of the effectiveness of DAA treatment. The efficacy of DAAs in impoverished people has only been shown in two minor investigations [22], [23]. Although 95% of the participants in this research were also insured, [14] documented SVR in 183 (93%) of 189 patients undergoing SOF-based HCV therapy in a safety-net healthcare system. Notably, both previous research investigations were carried out in countries with extended Medicaid, which enables a greater percentage of patients with limited incomes to receive HCV therapy. According to data, people with Medicaid have a 7.5% greater burden of HCV than people with commercial coverage [24]. Having access to HCV treatment is restricted in states like Texas that have not expanded Medicaid because fewer patients with low incomes are covered by Medicaid and because those who do have Medicaid protection are subject to limitations on their eligibility for treatment (e.g., advanced liver disease, negative toxicology screens, etc.). The results of our study show that even in states without Medicaid expansion, positive results can be obtained. Furthermore, we discovered that insurance status had no effect on SVR rates, indicating that worries about how underinsured individuals are treated may not be warranted. Similar to previous analyses [9- 11], we discovered that the only negative predictor of SVR in multivariate analysis was cirrhosis. Because prediction models have shown that treating patients with early stages of liver disease is more cost-effective [25] and that curative treatment increases quality of life and

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mortality [18], we treated our uninsured patients irrespective of their liver disease stage. The loss to follow-up rate for our research sample was 5%, which is close to the 5–15% documented in previous analyses of IFN-based therapy in destitute communities [27], [28] and only slightly higher than the 2.5–3.8% observed in non-indigent real-world investigations [22- 26]. Remarkably, over one in five of patients who were lost to liver clinic follow-up later saw their primary care physicians in the exact same health care organization. The absence of laboratory follow-up following treatment termination may have been caused in part by non-specialist providers' ignorance; therefore, future research into focused interventions, like educating providers on HCV screening and treatment, may aid in removing these obstacles. This research had a number of significant shortcomings. First of all, it was an observational study with insufficient power to thoroughly assess the relative advantages and disadvantages of various DAA regimens. Second, our findings might not apply to other primary care practice settings because our clinic structure includes specialty providers. Lastly, there was a lack of long-term follow-up data to determine reinfection rates, which could be crucial in this high-risk group.

4. CONCLUSION

The implementation of DAAs has resulted in improved outcomes for individuals who have access to treatment. Underinsured patients receiving treatment at safety-net institutions, however, bear an immense cost of illness and may not have straightforward access to these treatments. Our study shows that with committed personnel, having access to HCV treatment is achievable and that results in this economically deprived community are similar to those in high-income, professionally insured scenarios.

AUTHOR'S CONTRIBUTION

Tawasul Magzoub: "Contributions of a significant nature to the conception of the work; or the acquisition, collection, analysis, or interpretation of data for the work; AND Final approval of the version that is for publication."

Ahmad A. Mohammed: "drafting the work or conducting a critical evaluation of it to identify significant intellectual content; AND obtaining final approval of the version that will be included in the publication."

Imran Mahfooz Khan: "The conception or design of the work; the gathering, examination, or interpretation of facts for the work; or any combination of these."

Md.Forhadul Islam Chowdhury: "Substantial contributions to the conception or design of the work; or the acquisition."

Amna Khalid: "drafting the work or conduct a critical review of draft to identify significant intellectual substance."

Abdur Rahman: "The process of drafting the work or conducting a critical review of it to identify significant intellectual substance."

Rabia Zulfiqar and Tariq Hassan: "Creating a draft of the work or conducting a critical evaluation of it to identify significant intellectual substance; It is agreed upon that one will be responsible for all parts of the job, including ensuring that any questions concerning the accuracy or integrity of any portion of the work are appropriately examined and handled.

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