A Prospective Observational Study on Clinical Spectrum of Hepatitis C Patients in the Gastroenterology Department of a Tertiary Care Hospital

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Abstract:

Background: Among all hepatitis C(HCV) cases, 20-30% of patients develop chronic liver disease and require treatment to minimize further complications. Directly acting antiviral drugs for HCV treatment are now recommended widely for virological response. However, the drug selection depends on the extent of liver injury and existing comorbidities.

Methods:A prospective observational study was carried out in a tertiary care hospital in Andhra Pradesh. A total of 189 cases were collected during the study period for data on patient demographics and presence of comorbidities, and diagnostic and clinical characteristics. This study involves various antiviral drug combinations in patients suffering from HCV with other comorbidities.

Results: Among patients with hypertension, smoking and alcohol, and the presence of thyroid and cardiovascular diseases, the most widely prescribed drugs were Sofosbuvir+ Velpatasvir.

Conclusion: Patients suffering from chronic HCV with associated comorbidities are difficult to treat**.** Directly acting antiviral drug, sofosbuvir is the comment agent in all anti-HCV treatment regimens, and it is well tolerated in all patients.

Keywords: Viralhepatitis, Livercirrhosis, Fibroscan, Directly-acting antiviral drugs

1. Introduction

A single-stranded RNA virus, hepatitis C (HCV) belongs to the Flaviviridae familyand primarily affects the liver, leading to cirrhosis and cancer over many years. An acute infection

is non-serious, and most infected people may not show any initial symptoms. However, around 30% of HCV infection cases become chronic and cause severe damage to the liver. Chronic HCV infection is predominantly confined to the liver, causing fibrosis, cirrhosis and liver cancer.As per the recent WHO update, 5.8 crore people suffer from chronic HCV infection worldwide, and nearly 15 lakh new cases are detected yearly.[1] In India, approximately1.2crore people, live with hepatitis C infection, and the national viral hepatitis control programme aims to eliminatethe disease by 2030.[2]Hepatitis C virus exists in six major genotypes with varying degrees of global prevalence.[3] Among 6 genotypes, genotype 1 is predominantly confined to western countries, and the prevalence of genotypes1 and 3 are found in Southeast Asian countries like India.[4,5]The chronic form of HCVassociated with extrahepatic manifestations denotes its systemic involvement. Systemic events have mainly pertained to cardiovascular and endocrine-related, which may affect HCV treatment. It has been reported that the risk of diabetes mellitus (DM), hypothyroidism, hypertension (HTN)and cardiovascular complications is increased with chronic HCV infection.[6–8] In addition, personal habits like heavy alcohol intake and smoking posea greater hazardto hepatitis Cpatients.[9,10]Since an effective vaccine is not available, early diagnosis and treatment with antiviral drugs may achieve upto a 95% success rate.[11]However, understanding the extent of liver injury or fibrosis and associated comorbidities provides insights into treatment strategies. Treatment of hepatitis C is required to cure people with chronic infections. A sustained virologic response (SVR) is the primary goal of HCV treatment which can prevent relapse. In India, the standard therapy for HCV was oral ribavirin plus injectable PegINFα. However, with the introduction of pan-genotypic direct-acting antivirals (DAAs), the HCV treatment has taken a paradigm shift. The DAAs include sofosbuvir in combination with velpatasvir, daclatasvir, ledipasvir, or a combination of glecaprevir-pibrentasvir for all age groups.These antiviral agents target viral proteins that exhibit an SVR with reasonable safety and tolerability. Achieving SVR for morethan12 weeks post-treatment is the ultimate goal of HCV treatment that prevents relapse. However, host factors like treatment adherence and associated diseasescomplicate the treatment strategy. Also, choosing the right drug combination with sofosbuvir plays anessential role in chronic HCV infection. Keeping this in view, the current studyevaluated the treatment pattern in hepatitis C patients presenting various extrahepatic comorbidities. Additionally, monitoring the clinical and laboratory parameters in HCV patients provide an understanding ofthe treatment response that ultimately helps to achievea sustainable viral response.

2. Methodology

Ethical consideration: The study was conducted in a tertiary care hospital with prior approval from the Institutional Ethical Committee (IEC/AMRN/PP/H/03). Enrolment of patients into the

trial was based on inclusion/exclusion criteria. After obtaining written informed consent, we included all patients suffering from Hepatitis C irrespective of the comorbidities. We excluded all patients without Hepatitis C. We collected data on demographics (age and gender); comorbidities such as the presence of (Alcohol, smoking, hypertension, diabetes mellitus, thyroid and cardiovascular diseases); clinical characteristics such as (Fibro scan score (kPa) and USG abdomen (Grades); laboratory investigations such as (Liver function tests, total protein, albumin, globulin, calcium, sodium, potassium and complete blood counts). We also collected the therapeutic details of the patients.

Sample size: This is a prospective observational study carried out for 6 months in a tertiary care hospital in Andhra Pradesh. A total of 189 patients suffering from chronic hepatitis C infection were enrolled in the study.

Study Outcomes:The study outcomes were as follows: Prevention of future occurrence of the drug causing health problems; maintenance of patient comorbid conditions under the control of their levels along with the medication,and whether all patients received good medication adherence without any new suspected signs and symptoms.

Statistical Analysis:The normality of data for continuous variables was checked using the Kolmogorov-Smirnov test and summarized as mean ± standard deviation or median. Categorical variables were expressed as numbers and percentages (n, %). Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 16.0 (SPSS Inc., Chicago, IL, USA). All reported P-values were two-sided, with $P < 0.05$ indicating statistical significance.

3. Results:

A total of (n=189) patients were included in the study, and the median age was 58 (45-67) years. Most of the patients were male 115 (61%). The most common comorbidities present in the patients were diabetes, hypertension, cardiovascular diseases, and thyroid (Table 1). The laboratory investigations of the study patients have been represented in table 2. The median fibro scan score was 24 (9-50). The therapeutic details of the study participantshave been illustrated in table 3. Most of the patients received Sofosbuvir+ Velpatasvir and Sofosbuvir+ Ledipasvir. We also studied the drug prescription pattern among patients with different comorbid conditions (Table 4). Among patients with diabetes mellitus, the most commonly prescribed drugs were Sofosbuvir+ Velpatasvir and Sofosbuvir+ Ledipasvir. Among patients with hypertension, smoking and alcohol, and thyroid and cardiovascular diseases, the most widely prescribed drugs were Sofosbuvir+ Velpatasvir.

Table 1

Baseline characteristics of study participants (N=189).

No	Characteristics	N (%)
1	Age in years	
	Less than or equal to 58 years	96 (51)
	Greater than 58 years	93 (49)
2	Gender	
	Male	115 (61)
	Female	74 (39)
3	Alcoholic	93 (49)
4	Smoker	52 (28)
5	Diabetic	36 (19)
6	Hypertensive	167 (88)
7	Presence of thyroid diseases	123 (65)
8	Presence of Cardiovascular diseases	117 (62)
9	USG Abdomen Grades	
	Grade I	53 (28)
	Grade II	77 (41)
	Grade III	38 (20)
	Grade IV	21 (11)

Table 2

Laboratory investigations and clinical investigations of study participants (N=189):

No	Characteristics	Median (IQR)	
1	Fibro scan score	24	(9-50)
2	Serum bilirubin, **mg/dL**	10.8	(10.5-11.6)
3	Aspartate aminotransferase (AST)	243	(164-276.5)
4	Alanine transaminase (ALT)	472	(457-486)
5	Total protein, g/dL	7.4	(6.7-8.2)
6	Albumin, g/dL	3.9	(3.4-4.1)
7	Globulin, g/dL	2.6	(2.4-2.8)
8	Haemoglobin, g/dL	8.4	(7.6-9.1)
5	Total leukocyte count, per µL	6500	(5800-7500)
6	Platelets, per µL	2.1	(1.8-2.5)
7	Serum Creatinine, mg/dL	1.3	(1.1-1.5)
8	Sodium, mmol/L	137	(134-139)
9	Potassium, mmol/L	3.6	(3.4-3.8)
10	Calcium, mmol/L	9.3	(8.8-10.1)

Table 3

Therapeutic details of study participants (N=189)

No.	Characteristics	N (%)
1	Sofosbuvir+Velpatasvir	51 (27)
2	Sofosbuvir+Daclatasvir	47 (25)
3	Sofosbuvir+Ledipasvir	50 (27)
4	Sofasbuvir+Ribavarin	46 (25)

DM: Diabetes Mellitus; HTN: Hypertension; CVS: Cardiovascular Diseases

Table 4

Therapeutic details of study participants with comorbidities (N=189)

No	Drugs	DM N (%)	HTN N (%)	Smoking N (%)	Alcohol N (%)	Thyroid N (%)	CVS N (%)

1	Sofosbuvir+Velpatasvir	14 (39)	44 (26)	16 (31)	28 (30)	35 (29)	33 (28)
2	Sofosbuvir+Daclatasvir	5 (14)	43 (26)	14 (27)	24 (26)	32 (26)	29 (25)
3	Sofosbuvir+Ledipasvir	15 (42)	42 (25)	11 (21)	23 (25)	27 (22)	26 (22)
4	Sofasbuvir+Ribavarin	4 (11)	43 (26)	13 (25)	20 (21)	33 (27)	31 (27)

4. Discussion:

Hepatitis C primarily affects the liver, and chronic infection is challenging, especially with associated comorbidities. The interferon-based antiviral therapy was the backbone of HCV treatment till the introduction of directly acting antivirals (DAAs). Unlike injectable interferon-based therapy, orally active DAAs are convenient, with reliable safety and good patient compliance. Moreover, a sustainable viral response can be achieved in chronic HCV patients with DAA regimens. Considering the safety and tolerability data, WHO has recommended sofosbuvir-based regimens against pan-genotype HCV.The present study aimed to report the host factors involved in hepatitis C treatment with directly acting antiviral drugs.

In the present work, HCV-infected patients show concomitant diseases likehypertension, thyroid diseases, other cardiovascular diseases and diabetes. Also, few patients are chronic alcoholics and smokers. It has been reported that HCV patients show a high prevalence of extrahepatic comorbidities compared to the non-HCV-infected population.[12] This suggestsHCV infection is not localized to the liver and can be considered a systemic disease. The USG abdomen in this study showsmost patients have been diagnosedwith grade I, followed by grade II, III and IV.

Measuring liver stiffness is one of the good indicators to measure the extent of liver fibrosis and cirrhosis.Elastography, a non-invasive technique to detect liver stiffness by fibro scan,is widely used to identify the stage of liver fibrosis and cirrhosis.[13] The initiation of HCV treatment and prognosis depends on many factors, however, the ultrasound-based fibroscan is a good indicator. Liver stiffness is influenced by many factors, like inflammationand mast cell infiltration during hepatitis or carcinoma. Generally, in hepatitis, fibroscan grading of 2-7 kPa (F0-F1), 8-9 kPa (F2), 9-14 kPa (F3), and >14 kPa (F4) indicates normal, moderate, severe scarring and cirrhosis respectively.[14,15]. In the present study, the median fibroscanscore was 24, indicating the presence of liver cirrhosis in most patients. These patients require immediate treatment with antivirals to prevent further progression.

HCV patients in this study show elevated liver markers like bilirubin, AST, and ALT,indicating definitive liver injury in most patients. However, haemoglobin, total protein, albumin and globulin levels are within normal range. Also, we did not observe the abnormal concentration of serum electrolytes in study participants. The treatment strategies for HCV-induced liver

disease are associated with treatment failure and drug-related adverse effects. This could be becauseof a lack of pan-genotypic antiviral drugs, which can be administered orally for a long time to achieve better clinical outcomes. However, this could be overcome by introducing directly acting antiviral (DAA) drugs which can attain sustainable viral response (SVR).

In the present study, we observed that sofosbuvir antiviral drug is used for all patients along with other antiviral drug combinations.The antiviral activity of sofosbuvir is reported against all HCV genotypes. It acts as a chain terminator by inhibiting viral RNA polymerase called non-structural protein 5B (NS5B). It is proven to be efficacious against all HCV genotypes and is usually combined with other anti-HCV drugs. Its use with other antiviral drugs is recommended to produce maximum SVR in most patients. In the current investigation, sofosbuvir was combined with velpatasvir, daclatasvir, ledipasvir or ribavirin to treat HCV patients. All these drug combinations are prescribed equally in our study population. Combining sofosbuvir with NS5A inhibitorvelpatasvir is a fixed combination for all HCV genotypes. This combination is economical and has achieved a reasonable success rate(SVR) in 12 weeks of treatment. However, 24 weeks of combination therapy may be required in liver cirrhotic patients[16]. Prescriptions of sofosbuvir in combination with other DAAs are also observed in the study. All these drug combinations are proven beneficial in chronic HCV patients presenting other comorbidities. Treatment-responsive patients showed good adherence to DAAs-based treatment and demonstrated no adverse effects. However, following participants beyond the treatment period would have provided the data on relapse cases[17-19].

5. Conclusion:

Hepatitis C infection is left unnoticed until it becomes a chronic illness that damages the liver and quality of life. Mostpatientssuffer from chronic HCV with associated comorbidities and predisposed liver transfer. Directly acting antiviral drugshave proved efficacious in obtaining a sustained virologic response. Among available antiviral agents, the selection of a suitable regimen is vital.Therefore, understanding and assessingpatient factors before initiating therapy isessential, which helps in good patient adherence and expected clinical outcomes. In the present study,**a** directlyacting antiviral drug, sofosbuvir, is the comment agent in all anti-HCV treatment regimens and is well tolerated in all patients.

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