Original Article

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The Outcome of Direct-Acting Antivirals in Treatment-Naïve Non-Cirrhotic, Chronic Hepatitis-C Infected Patients in a Tertiary Care Center

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Abstract

Background: To determine the outcome of Direct-Acting Antivirals in treatment-naïve Non-Cirrhotic, Chronic Hepatitis-C infected patients in a tertiary care Centre. **Subjects and Methods:** Hepatitis C positive non cirrhotics patients were included in the study. Treatment was given according to HCV Genotype and HCV Viral Load. 12 weeks after completion of treatment with Direct-acting antivirals patient were assessed for the Sustained Virological Response (SVR) ie.;SVR12. **Results:** The (Mean±SD) age was found to be 43.92±13.51 years. There are 11(44%) male whereas 14(56%) female. Out of total subjects, 3(12%) had diabetes mellitus whereas 5(20%) reported hypertension. Genotype 3 was found to be most common (72%). The mean±SD after treatment A.L.T U./L, A.S.T U/.L and I.N.R observed was 13.95±4.90, 14.97±5.03 and 1.40±0.54 respectively. The mean±SD Total Bilirubin mg/dL, Albumin g/dL and Hb g/dl observed was 0.72±0.32, 3.99±0.57 and 11.49±1.46 respectively. In 23 (92%) subjects S.V.R was achieved whereas in 2(8%) cases it was not achieved. **Conclusion:**Oral D.A.A accomplished higher SVR12 rates and were very much endured in this cohort based study associated with patients diagnosed with Chronic Hepatitis-C.

Keywords: Antiviral therapy, Non-Cirrhotic, Chronic Hepatitis-C

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Introduction

Hepatitis C virus (HCV) is a blood-borne viral disease that affects over 71 million individuals worldwide, representing a significant reason for liver cirrhosis and mortality.[1–4] The virus has six genotypes, genotype 1 is the most predominant all around the world, but in India genotype 3 is the most successive representing almost 66% of cases with persistent HCV infection.[5,6]

It has been assessed that the widespread of HCV in India is somewhere in the range of 0.5 and 1.5 percent,[7] however it very well may be assumed that this is only the visible part of the iceberg and a lot more HCV-infected patients remain undiagnosed.[8]

A sustained virologic response (S.V.R) is related with enhanced condition of life in addition to diminished fibrosis progression, cirrhosis-related difficulties, Hepatocellular Carcinoma, and all-cause mortality.[9,10]

Preceding the arrival of Direct-Acting-Antivirals (D.A.A) therapy, the pillar of HCV treatment included interferon (I.F.N)-based regimens that had regular contraindications, were ineffectively endured, and accomplished, a half S.V.R rate.

Presentation of D.A.A revolutionized the HCV treatment scenario. Direct Acting Antivirals (D.A.A) were first supported in the United States in May, 2011 and replaced the Pegylated-Interferon/Ribavarin as the norm of care for the therapy of Hepatitis C Virus.

S.V.R rates for D.A.A treatment surpass 90% in enrollment preliminaries and are better endured than I.F.N-based regimens.

There are various regimens accessible for the use of D.A.A. The American Association Study of Liver-Diseases (A.A.S.L.D) created HCV guidelines to help with choosing a specific D.A.A.

D.A.A are normally administered for eight or twelve weeks relying upon suggestions by A.A.S.L.D guidelines alongside the routine being given. Generally, S.V.R rates seem high with D.A.A regimens.[11]

Successful D.A.A treatment is characterized as a sustained virologic response at 12 weeks (S.V.R 12).

In the era of D.A.A, eradication of HCV infection has been extremely successful with most of the studies showing the achievement of S.V.R greater than 90%

Initially, protease inhibitors, telaprevir and boceprevir were introduced into the market to be used with Pegylated-Interferon/Ribavarin.

But due to multiple side effects, drug-drug interactions, complex regimen, high price and long duration of therapy, their production was discontinued and they were taken out of the market in 2014 and 2015 respectively.

Then 2^{nd} Generation Non-Structural Viral Protein3/4A & Non-Structural Viral Protein 5B inhibitors came to the market to be used with Pegylated-Interferon/Ribavarin. Subsequently, complete interferon-free regimen sofosbuvir plus simeprevir, sofosbuvir plus Ledipasvir and sofosbuvir plus daclatasvir and 4 fixed drug combinations dasabuvir, ombitasvir, paritaprevir and ritonavir with or without interferon got approved for the treatment of H.C.V.[12]

Over years multiple classes DAAs have been developed. These include Protease Inhibitors (P.Is), N.S.5.B(Nucleoside Polymerase Inhibitors 5 B), N.N.S.5.B(Non-Nucleoside Polymerase Inhibitors 5B) and N.S.5a inhibitors(Non-Structural Viral Protein 5A Inhibitor).[13,14]

In our country due to poor knowledge of health, hygiene and unethical practices by quacks especially in rural areas,Hepatitis-C prevalence rate is very high and contributes significantly to the global HCV burden. Now it has become easier to diagnose Hepatitis-C due to better diagnostic techniques in patients which were unreported, undiagnosed and remain infecting public at large.

Due to availability of specific Direct-acting antivirals (D.A.A) at much economical rate and also shorter course of therapy than earlier high priced medication of Hepatitis-C, better evaluation of such patients will be possible by this study. Further successful treatment of Chronic Hepatitis-C by D.A.A will stop progression to cirrhosis and its complications, thereby significantly reducing overall mortality and morbidity in such patients.

D.A.A. Regimens

Genotype	Drug	Treatment duration (weeks)
Genotype 1	Elbasvir/ Grazoprevir	12
	Glecaprevir/ Pilbrentasvir	12
	Ledipasvir/ Sofosbuvir	12
	Sofosbuvir/ Velpatasvir	12
Genotype 2	Glecaprevir/ Pilbrentasvir	12
	Sofosbuvir/ Velpatasvir	12
Genotype 3	Glecaprevir/ Pilbrentasvir	12
	Sofosbuvir/ Velpatasvir	12
Genotype 4	Elbasvir/ Grazoprevir	12
	Glecaprevir/ Pilbrentasvir	12
	Ledipasvir/ Sofosbuvir	12
	Sofosbuvir/ Velpatasvir	12
Genotype 5/6	Glecaprevir/ Pilbrentasvir	12
	Ledipasvir/ Sofosbuvir	12
	Sofosbuvir/ Velpatasvir	12

Subjects and Methods

The present prospective interventional study was conducted among 25 patients testing positive for H.C.V in the Dept. of General Medicine at Teerthanker Mahaveer Medical College & Research Centre from November 2019 to November 2020.

Inclusion Criteria

- Patient having age more than 18 years, testing positive for Hepatitis-C

Exclusion Criteria:

- Patients with any current or past cirrhosis,
- History of liver transplantation, prior history of intake of Direct-acting antivirals/Interferon therapy with or without Ribavarin.
- Female patients who are pregnant or breastfeeding
- Patients with any active malignancy. (Hepatic or Non-Hepatic).

Procedure

Treatment was given according to HCV Genotype and HCV Viral Load.

HCV Viral Load (By RT-PCR) was done twice i.e. just after completion of treatment and 12 weeks after completion of treatment with D.A.A.

SVR 12 and biochemical tests (Liver Function Test, PT/INR and Complete Blood Count) were done after the completion of treatment or at required intervals.

Results

Table 1: Gender and age distribution among the study subjects

Parameters	N=25	%
Gender		
Male	11	44
Female	14	56
Age in years (Mean±SD)	43.92±13.51	

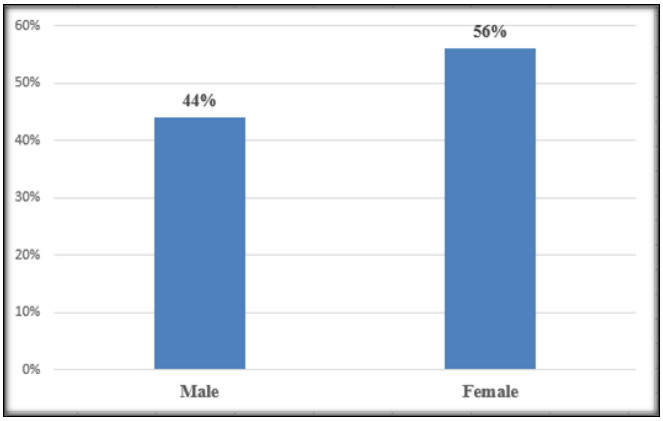

Figure 1: Gender and age distribution among the study subjects

Table 2: Genotype among the study subjects

Genotype	N=25	%
1B	2	8
1A	3	12
2	2	8
3	18	72

[Table 2 and Figure 2] describes the various genotype among the study subjects. Genotype 3 was found to be most common (72%), followed by genotype1A(12%) and genotype 2 and 1B (8%) among subjects.

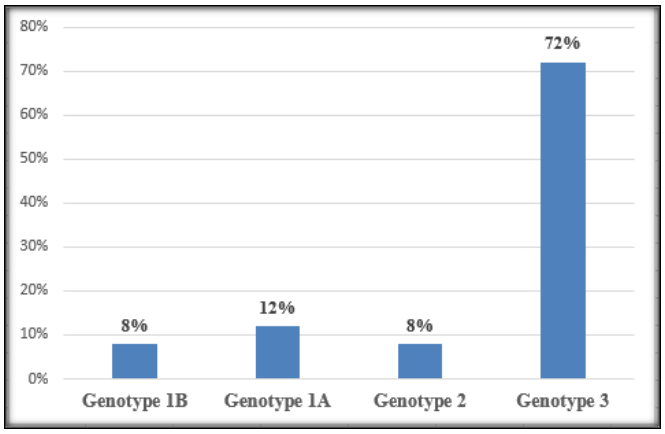

Figure 2: Genotype among the study subjects

Table 3: SVR among the study subjects after the treatment

SVR	N=25	%
Achieved	23	92
Not Achieved	2	8

[Table 3 and Figure 3] shows weather SVR was achieved among the study subjects after the treatment or not. It was reported that in 23(9%) subjects SVR was achieved whereas in 2(8%) cases it was not achieved.

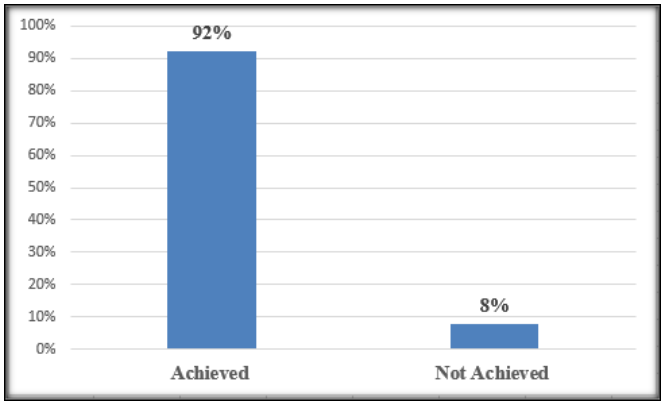

Figure 3: SVR among the study subjects after the treatment

The before and after treatment difference was found to be statistically significant for mean±SD ALT U/L, AST U/L and HCV RNA IU/mL ($p<0.01$) as shown in [Table 4, Figure 4].

[Table 5 and Figure 5] shows complications among the study subjects. The most common complication was asthenia (68%) followed by Muscle Cramps/Pain (56%), Pruritus (44%) and insomnia(24%).

Table 4: Impact of treatment on laboratory parameters

Parameters	Before the Treatment		After the Treatment		p value
	Mean	SD	Mean	SD	
ALT U/L	24.71	6.39	13.95	4.90	<0.01*
AST U/L	25.49	5.78	14.97	5.03	<0.01*
INR	1.49	0.38	1.40	0.54	0.79
Total Bilirubin mg/dL	0.72	0.32	0.63	0.29	0.58
Albumin g/dL	3.72	0.31	3.99	0.57	0.07
Hb g/dL	11.49	1.46	11.17	1.58	0.37
PLT Count lakh/cumm	2.07	0.67	2.06	0.51	0.72
HCV RNA IU/mL	$3.02*10^6$	$1.94*10^5$	864.44	2903.96	<0.01*

*: statistically significant

Table 5: Complications among the study subjects

Parameters	N	%
Asthenia	17	68
Pruritus	11	44
Hypo-hypertension	3	12
Muscle Cramps/Pain	14	56
Insomnia	6	24
Nausea/Vomiting	4	16

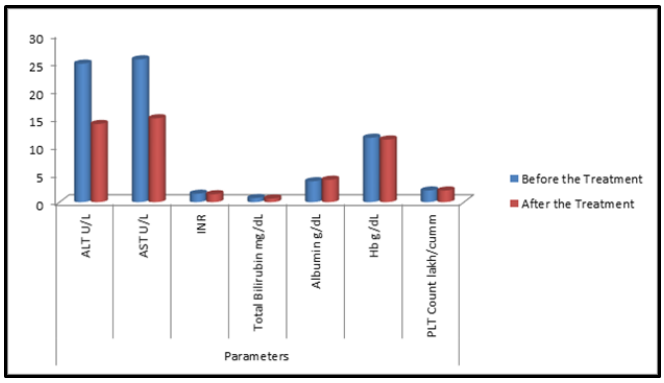

Figure 4: Impact of treatment on laboratory parameters

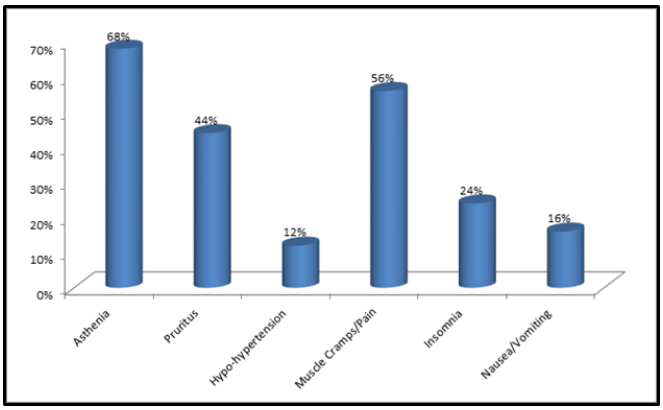

Figure 5: Complications among the study subjects

Discussion

The present prospective interventional study was conducted among 25 patients testing positive for H.C.V in the unit of GeneralMedicine at TeerthankerMahaveer Medical College & Research Centre from November 2019 to November 2021.

The (Mean±SD) age was found to be 43.92±13.51 years.There are 11(44%) male whereas 14(56%) female.Out of total subjects, 3(12%) had diabetes mellitus whereas 5(20%) reported hypertension.Genotype 3 was found to be most common (72%), followed by genotype1A (12%) and genotype 2 and 1B (8%) among subjects. The laboratory parameters at baseline among the study subjects. The mean±SD

A.L.T U/.L, A.S.T U/.L and I.N.R observed was 24.71±6.39, 25.49±5.78 and 1.49±0.38 respectively. The mean±SD Total Bilirubin mg/dL, Albumin g/dL and Hb g/dl observed was 0.63±0.29, 3.72±0.31 and 11.17±1.58 respectively. The mean±SD after treatment A.L.T U./L, A.S.T U/.L and I.N.R observed was 13.95±4.90, 14.97±5.03 and 1.40±0.54 respectively.Themean±SD Total Bilirubin mg/dL, Albumin g/dL and Hb g/dl observed was 0.72±0.32, 3.99±0.57 and 11.49±1.46 respectively. The before and after treatment difference was found to be statistically significant for mean±SD A.L.T U./L, A.S.T U./L and H.C.V R.N.A IU/mL ($p<0.01$). The patient was considered to have an S.V.R when the H.C.V-R.N.A (P.C.R) was negative 12 weeks after completion treatment. It was reported that in 23(92%) subjects S.V.R was achieved whereas in 2(8%) cases it was not achieved. The most common complication was asthenia (68%) followed by Muscle Cramps/Pain (56%), Pruritus (44%) and insomnia(24%).

Conclusion

Due to availability of specific Direct-acting antivirals (D.A.A) at much economical rate and also shorter course of therapy than earlier high priced medication of Hepatitis-C, better evaluation of such patients is possible. Further successful treatment of Chronic Hepatitis-C by D.A.A will stop progression to cirrhosis and its complications, thereby significantly reducing overall mortality and morbidity in such patients.

Oral D.A.A accomplished higher SVR12 rates and were very much endured in this cohort based study associated with patients diagnosed with Chronic Hepatitis-C. Thus compelling results with DAA-based treatment can be accomplished in resource-constrained safety health systems.

Limitations

This study had a few constraints. Limitations of the present study includes the follow up of only three months and recommendations according to multi centre study should be follow up of six months.

Because of its limited scale, its promising outcomes can't yet prompt a strategy change in H.C.V the board without being approved by a bigger proportion controlled clinical analysis. A multi-focus clinical preliminary intended to resolve these inquiries and for approving aftereffects of this pilotstudy, is as of now in it's introductory stage.

References

1. Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Lancet Gastroenterol Hepatol. 2017;2(3):161–176. Available from: https://doi.org/10.1016/s2468-1253(16)30181-9.
2. Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014;61(1):45–57. Available from: https://doi.org/10.1016/j.jhep.2014.07.027.
3. Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, 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):1081–1088. Available from: https://doi.org/10.1016/s0140-6736(16)30579-7.
4. Franco RA, Galbraith JW, Overton ET, Saag MS. Direct-acting antivirals and chronic hepatitis C: towards elimination. Hepatoma Res. 2018;4:74.
5. Narahari S, Juwle A, Basak S, Saranath D. Prevalence and geographic distribution of Hepatitis C Virus genotypes in Indian patient cohort. Infect Genet Evol. 2009;9(4):643–645. Available from: https://doi.org/10.1016/j.meegid.2009.04.001.
6. Garg G, Dixit VK, Shukla SK, Singh SK, Sachan S, Tiwari A, et al. Impact of Direct Acting Antiviral Drugs in Treatment Naïve HCV Cirrhosis on Fibrosis and Severity of Liver Disease: A Real Life Experience from a Tertiary Care Center of North India. J ClinExpHepatol. 2018;8(3):241–249. Available from: https://doi.org/10.1016/j.jceh.2017.11.011.
7. Puri P, Anand AC, Saraswat VA, Acharya SK, Dhiman RK, Aggarwal R. Consensus statement of HCV task force of the Indian National Association for Study of the Liver (INASL). Part I: Status report of HCV infection in India. J Clin Exp Hepatol. 2014;4(2):106–116. Available from: https://doi.org/10.1016/j.jceh.2014.05.006.
8. Gupta V, Kumar A, Sharma P, Arora A. Newer direct-acting antivirals for hepatitis C virus infection: Perspectives for India. Indian J Med Res. 2017;146(1):23–33. Available from: https://doi.org/10.4103/ijmr.ijmr_679_15.
9. Van Der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, et al. Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA. 2012;308(24):2584–93. Available from: https://doi.org/10.1001/jama.2012.144878.
10. Yek C, Flor CDL, Marshall J, Zoellner C, Thompson G, Quirk L, et al. Effectiveness of direct-acting antiviral therapy for hepatitis C in difficult-to-treat patients in a safety-net health system: a retrospective cohort study. BMC Med. 2017;15(1):1–8.
11. Itokawa N, Atsukawa M, Tsubota A, Ikegami T, Shimada N, Kato K, et al. Efficacy of directacting antiviral treatment in patients with compensated liver cirrhosis: A multicenter study. Hepatol Res. 2019;49(2):125–135. Available from: https://doi.org/10.1111/hepr.13256.
12. Ahmed M. Era of direct acting anti-viral agents for the treatment of hepatitis C. World J Hepatol. 2018;10(10):670–84. Available from: https://dx.doi.org/10.4254/wjh.v10.i10.670.
13. Das D, Pandya M. Recent advancement of direct-acting antiviral agents (DAAs) in hepatitis C therapy. Mini Rev Med Chem. 2018;18(7):584–596. Available from: https://doi.org/10.2174/1389557517666170913111930.

14. Chalikonda DM, Dhanekula RK, Miller A, Kistler CA, Javia A, Ahmed M. Mo1406-Hepatitis C Treatment Failure with Direct Acting Antiviral Therapy: Demographics and Clinical Management. Gastroenterol. 2018;154(6):1196.

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