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A COMPARATIVE RESEARCH TO ASCERTAIN VIROLOGIC REACTION IN CHRONIC HEPATITIS C VIRUS (HCV) PATIENTS BY TWO DIFFERENT TREATMENT OPTIONS

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Abstract:

Objective: *This study was designed to ascertain the virologic reactions in patients of chronic hepatitis C, cured by means of sofosbuvir and daclatasvir versus sofosbuvir and ribavirin.*

Methodology: *It was a probable comparative research study which was administered in Allied Hospital, Faisalabad from February to October 2017. With either gender, chronic hepatitis C virus detected patients with age ranges from 18 to 60 years having detectable HCV RNA through PCR were select for study. Based on treatment, patients were divided into 2 categories; group A patients were handled with sofosbuvir + daclatasvir and group B with sofosbuvir + ribazole. For HCV RNA Quantitative, PCR had been carrying out to measure the viral RVR (at 4th week), EVR (at 12th week), ETR (at 24th week) and SVR after completion of 24 weeks treatment. The patients who failed to comply with treatment or having any impediment to investigations that caused to treatment cancellation were excluded from the study.*

Results: *Total 107 patients with average age of 36.46+11.34 years were select for study and majority (58.9%) of them were female. 19.6% patients treated with sofosbuvir + ribazole and remaining 80.4% with sofosbuvir + daclatasvir. In group A (sofosbuvir + daclatasvir) RVR, EVR, ETR & SVR* were significantly more with respect to group B (sofosbuvir + ribazole). In group B, 18 out of 21 patients achieved ETR. Post-treatment completion in both groups, no substantial variance founded in the viral load mean p-value 0.628.*

Conclusion: *Both treatments proved to have good effectiveness, however, sofosbuvir + declacavir treatment attained more important RVR, EVR, ETR and SVR with respect to sofosbuvir + ribazole.*

Keywords: *RVR: (Rapid Viral load Response), EVR: (Early Viral load Response), ETR: (End Treatment Response) and SVR: (Sustained Viral Response)*

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INTRODUCTION:

As per recent estimations, about 180 million of world populace are septic with HCV (hepatitis C virus) with the maximum occurrence in Asia and Africa [1, 2]. As per WHO (World Health Organization) and as an outcome of the previous studies, about 3 to 4 million new HCV cases take place per annum and because of HCV, 0.35 million people die per year [2]. Pakistan is the second most contributor to HCV [3, 4]. The disease antiquity evokes that around 85% of patients stay infected with HCV after the acquisition of acute hepatitis C disease [2] and because of that reason its treatment is developing till 1986 when interferon used for first-time [3]. Lately, ribavirin and pegylated interferon alfa combination was the typical Hepatitis C cure for genotype 1 for 48 weeks and for genotype 2 and 3 for 24 weeks [2]. Treatment development was a delay due to substandard constant viral reaction frequency and it's less usage because of contraindications and side effects [4, 5].

The standard care for treatment of chronic HCV infection has become the oral combinations of DAAs (direct-acting antivirals) [7, 8]. For many drug combinations in clinical trials, at post-treatment SVR 12 (week 12) frequency of sustained virologic response were more than 90%, with safety profiles excellent than peg-interferon based treatments. Nevertheless, concomitant medical conditions and advanced liver disease can undesirably move therapeutic reactions and confuse the clarification of outcomes. Therefore, such patients are typically exemplified in clinical trials, and disease condition may vary in significant means as compare to unsystematic trials. Communal-based platforms offer a significant balance to registration researches as more data collected regarding therapeutic advantages/disadvantage of new procedures in bigger populace [9]. All oral DAAs efficiently cure chronic HCV disease, however, snags and reaction of various treatments differ. Pathological consent attained through various treatment were statistically similar. However, SVR rates are better for sofosbuvir with a daclatasvir combination and treble drug usage and probabilities are more for decompensation as compare to ribavirin and sofosbuvir combination [10]. Sufficient documents do not exist in the literature for EVR and in patients treated through sofosbuvir+ declacavir including or excluding ribavirin. This study conducted because typically EVR and RVR are compared in peginterferon-based studies.

METHODOLOGY:

It was a probable comparative research study which was administered in Allied Hospital, Faisalabad from February to October 2017. Either gender of patients with chronic HCV (detectable HCV RNA through PCR) with age ranges from 18 to 60 years were select. Patients having co-infection with HBV, depressive illness not controlled on treatment, known allergies to sofosbuvir or ribavirin, eGFR < 30 ml/min, CTP score > 9, auto-immune hepatitis, pregnant or lactating females, haemochromatosis, alcoholic hepatitis, HCC and Wilson 's disease were excluded from the study. All patients consented before the study. Patients distributed in 2 groups as per applicable treatment; (group A treated with sofosbuvir + daclatasvir and group B with sofosbuvir + ribazole). LFT and CBC evaluated at week 2 and then subject to results, at every 4 weeks. Those patients were included who get through the definite treatment schedule and their whole data was collected from patients' individual records archived as a repetitive process and entered into specially designed proforma for studying each patient's variables. For HCV RNA Quantitative, PCR had been carrying out to measure the viral RVR (at 4^{th} week), EVR (at 12^{th} week), ETR (at 24^{th} week) and SVR on completion of 24 weeks treatment. The patients who failed to comply with treatment or having any impediment to investigations that caused treatment cancellation were excluded from the study. Complete data documented in proforma.

All the collected information entered in SPSS. Regular deviance and mean were considered for quantitative variables like age. Ratios and rates were considered for categorical data like gender, the recurrence rate of hepatitis d virus and educational status. Chi-square test was employed for comparison of HDV frequency using gender, age groups, and status of education, p-value below 0.05 was count as substantial.

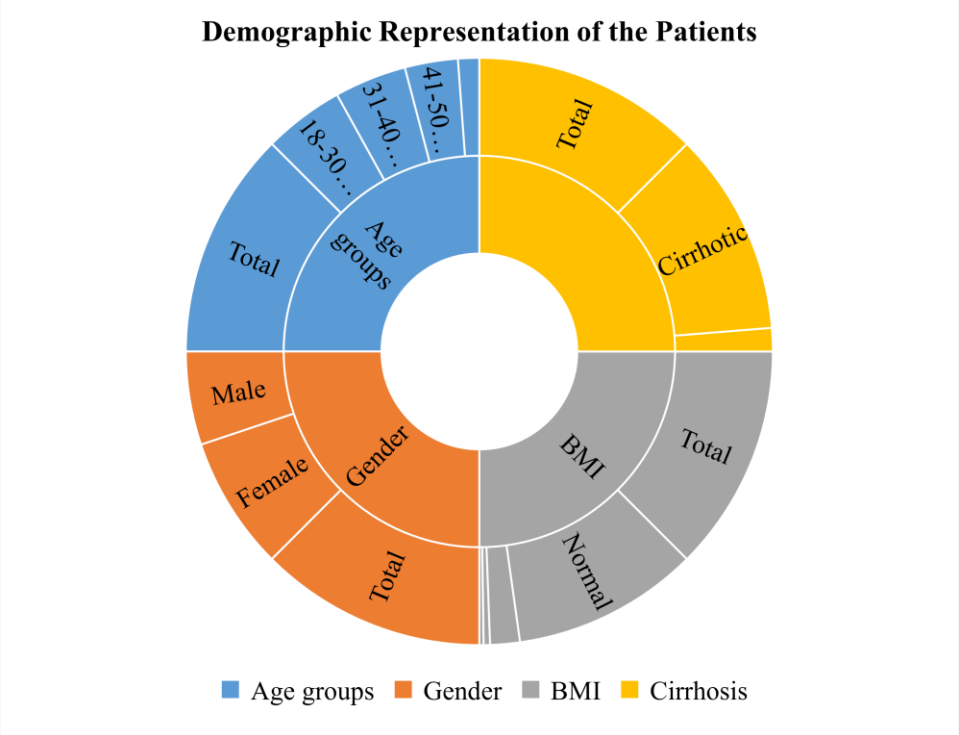
RESULTS:

Total 107 patients (with positive HCV RNA through PCR quantitative) selected for this study and get through sofosbuvir treatment in combination with 2 more treatments separately. The average age of the patient was 36.46+11.34 years with 58.9% female and 41.1 percent male. Age group 18-30 years and 31-40 years were most common with the percentage of 35.5% and 31.8%, whereas 41-50 years group patients were 23.4% and > 50 years were only 9.3% patients. Keeping in view the BMI, the majority of the patients (82.2%) were having regular BMI, whereas overweight patients were 13.1%, obese were 1.9% and underweight cases were 2.8%. Majority patients 89.7% were non-cirrhotic whereas 11 patients were cirrhotic.

Table – I: Demographic characteristics (n=107)

Basic characteristics		Frequency	Percentage
Age groups	18 to 30 years	38.0	35.50
	31 to 40 years	34.0	31.80
	41 to 50 years	25.0	23.40
	>50 years	10.0	9.30
	Total	107.0	100.00
Gender	Male	44.0	41.10
	Female	63.0	58.90
	Total	107.0	100.00
BMI	Normal	88.0	82.20
	Overweight	14.0	13.10
	Obese	2.0	1.90
	Underweight	3.0	2.80
	Total	107.0	100.00
Cirrhosis	Cirrhotic	96.0	89.70
	Non-cirrhotic	11.0	10.30
	Total	107.0	100.00

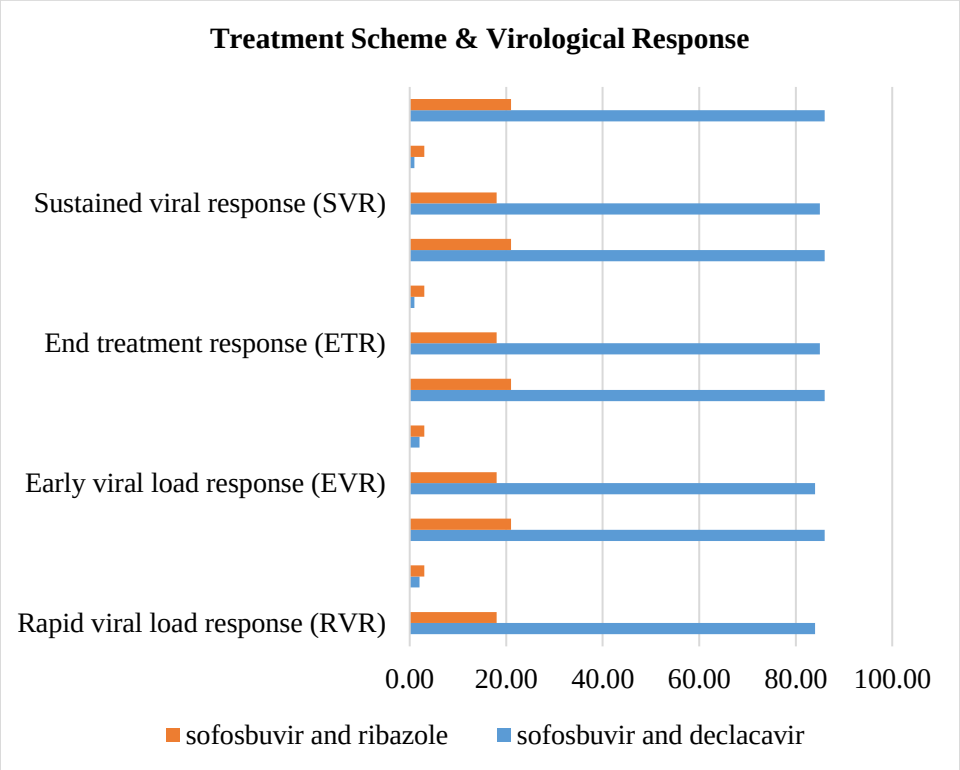
Mean age (Mean+SD = 36.460 + 11.340 years)



Patients treated with sofosbuvir + ribazole were 19.6% and remaining 80.4% with sofosbuvir + daclatasvir. During virologic response assessment per the treatment procedure, in group 'A' (sofosbuvir + daclatasvir), RVR was significantly more attained with respect to 'B' group (sofosbuvir + ribazole) with p-value 0.020. In group A, EVR was considerably more in comparison with group B with p-value 0.020. ETR was also significantly more attained in group 'A' (85 out of 86 cases achieved and only 1 didn't), whereas in group 'B', 18 out of 21 cases achieved, p-value 0.004. SVR in group 'A' was achieved by 85 patients out of 86 as compare to group 'B', in which 18 out of 21 patients achieved.

Table – II: Virologic response according to a regimen of treatment (n=107)

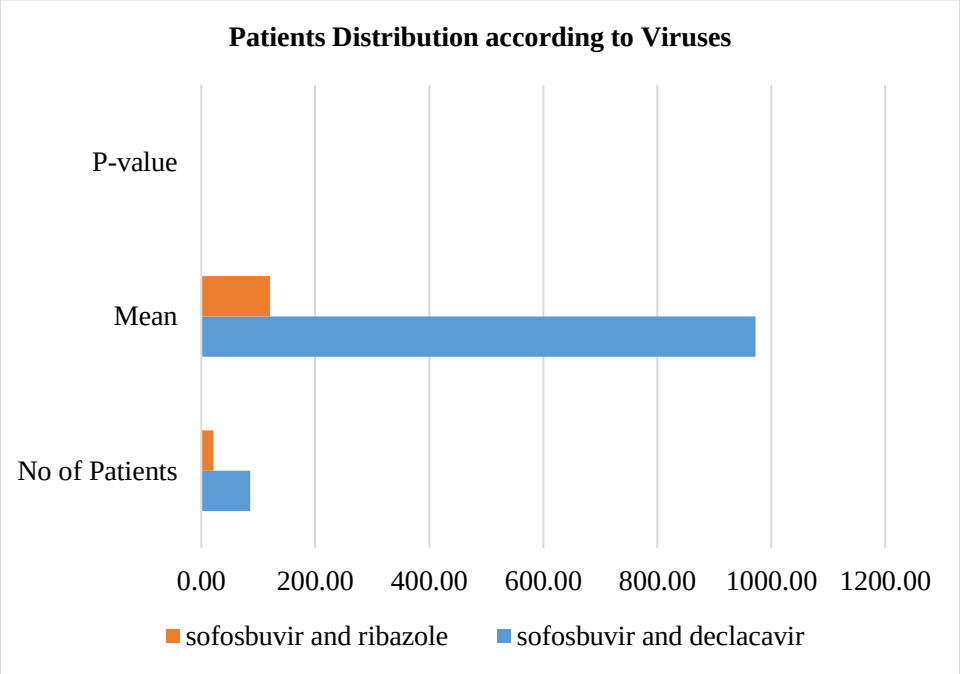
Viral response		Treatment regimen		P-value
		sofosbuvir and daclatasvir	sofosbuvir and ribazole	
Rapid viral load response (RVR)	Achieved	84.00	18.00	
	Not achieved	2.00	3.00	0.02
	Total	86.00	21.00	
Early viral load response (EVR)	Achieved	84.00	18.00	
	Not achieved	2.00	3.00	0.02
	Total	86.00	21.00	
End treatment response (ETR)	Achieved	85.00	18.00	
	Not achieved	1.00	3.00	0.00
	Total	86.00	21.00	
Sustained viral response (SVR)	Achieved	85.00	18.00	
	Not achieved	1.00	3.00	0.00
	Total	86.00	21.00	



Significantly no difference was come across in this study in both groups viral load means after treatment completion as in group A was 972.31±185 and in group, B was 120.40±135.6 with p-value 0.628.

Table – III: Patients distribution according to viral after complete treatment (n=107)

Treatment scheme	No of Patients	Mean + Standard Deviation	P-value
sofosbuvir and declacavir	86.00	972.310 + 185.20	0.6280
sofosbuvir and ribazole	21.00	120.400 + 135.60	



Treatment through Sofosbuvir epitomizes the first step to new treatment era of chronic hepatitis C patients because it is the first recommended directly enacting antiviral mediators with a huge genetic barricade and effective action versus all genotypes HCV [11, 12]. Moreover, its safety is admirable even with the higher risk of complications and advanced liver disease. It has relatively minimal risk of drug-drug reaction as it has an outstanding pharmacokinetic shape permitting its management as a single tablet per day [12]. 107 patients treated in this study with sofosbuvir + ribazole and sofosbuvir + daclatasvir. The efficacy of both groups was good, however, sofosbuvir + daclatasvir (group) patients revealed a noticeably better gain of RVR, EVR, ETR and SVR with a comparison to sofosbuvir + ribazole (group) p-value were 0.020, 0.020, 0.004 and 0.004 respectively. Similarly, Kutala BK et al [13] stated that SOF+DCV combination has better efficiency with respect to SOF+RBV (p=0.035).

Patients' mean age in the current study was (mean ± SD = 36.46 ± 11.34 years), and definitely 18-30 years and 31-40 years were the most common age groups with 35.5% and 31.8% share respectively. Umar M et al [14] stated in his study that among all, 50.9% (296) were males and 49.1% (286) were females (P-value 0.22). All participants mean age was 40.43 ± 9.622 years. Whereas comparatively in our study, 58.9% were females and 41.1% were male. Sarwar S et al [15] in another study stated the mean age as 49.4 ±12.1 years with 1.1 ratios between male and female (114/102).

Both RVR and EVR were achieved in the current study by both groups but group A achieves significantly more as compared to group B (p-value 0.020). Data in the literature does not exist where RVR and EVR were treated by sofosbuvir+ daclatasvir with or without ribavirin. RVR and EVR are commonly discussed in peg-interferon based researches, such as Mangia et al [16] and Delgard et al [17] presenting exalted RVR in general people ranging from 31–100%, and PPV from 69–100%.

Group A significantly achieved ETR more (85 out of 86 cases), while in group B 18 out of 21 cases achieved, (p-value 0.004). Comparatively, Siddique MS et al [18] in his study reported that Sofosbuvir treated patients have display

outstanding results with achievement in RVR was 99.5%, in ETR 99% and in SVR 98.5%. Higher rates of SVR were displayed in other studies wherein genotypes 1 and 2 patients treated with interferon-free combinations particularly with favourable outcomes, better safety profile and resistance free in cirrhotic and non-cirrhotic [19].

SVR in this study was also considerably attained more by group 'A' (85 out of 86 cases) and 18 patients achieved in group B out of 21. Likewise, El-Khayat H et al [20] in his study stated that SVR rate after 12 weeks treatment completion (SVR12) was 92% in non-cirrhotic patients and 87% in cirrhotic patients. As compared to other published studies, SVR was high as 98.7% in our study which may be due to not inclusion of decompensated cirrhotic patients. Similarly, Omar H et al [21] stated that overall 95.1% patients achieved SVR12 (94.7% for RBV treated patients and 95.4% for non-RBV treated patients, P = .32. Likewise, Welzel TM et [22] stated that 91% achieved SVR12) comprising of 92% patients cured with DCV+SOF and 89% with DCV+SOF+RBV. Shiha G et al stated that SVR12 achieved in 96.6% in patients treated with DCV + SOF, in 95.7% treated with DCV + SOF + RBV, in 93.3% with DCV + SOF and in 92.2% treated with DCV + SOF + RBV [23]. Also, the rate of SVR12 rate was noticeably more in non-cirrhotic patients treated for 12 or 24 weeks with DCV + SOF only.

CONCLUSION:

Both treatments revealed useful effectiveness, however, sofosbuvir + declacavir treatment attained more momentous RVR, EVR, ETR and SVR with respect to sofosbuvir + ribazole. Whereas in both groups, there was no substantial variance in the mean.

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