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AN OBSERVATIONAL STUDY TO ASSESS SUSTAINED VIROLOGIC RESPONSE (SVR) AFTER THE TREATMENT WITH DACLATASVIR IN ADDITION WITH SOFOSBUVIR IN HCV GENOTYPE 3a DISEASE

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Abstract:
Study aim: *We held this study to conclude sustained virologic response (SVR) after the treatment with Daclatasvir in addition with sofosbuvir regardless of liver cirrhosis or any previous treatment history.*
Study design: *Open label observational study.*
Place and duration: *This study was conducted at mayo hospital, Lahore for the duration of one year starting from May, 2018 to March, 2019.*
Material and methodology: *We included a total number of 125 patients in our study who were having genotype 3a hepatitis C virus regardless of previous treatment history or presence of cirrhosis. Daclatasvir (60mg) in addition with sofosbuvir (400mg) on daily basis for the duration of 03 months were prescribed for treatment of those patients who were without cirrhosis. Whereas, daclatasvir (60mg) in addition with sofosbuvir (400mg) with ribavirin according to the weight of the patients were given to those patients who were either with treatment history or having cirrhosis. Dosage was prescribed on daily bases for the duration of 06 months. Use SPSS 21 for analysis of collected data.*
Results: *There were total 125 patients included in our study. Gender distribution as male and female was as 42 (33.60%) and 83 (66.40%) respectively. 124 (99.2%) patients achieved initial virological responses and end treatment responses. SVR24 (sustained virologic response at week 24) for 80.8% (101) patients among which there were 53 patients without cirrhosis and 48 patients were having cirrhosis. 95% (96) patients out of 101 achieved SVR24 (sustained virologic response at week 24). According to the findings of our study, compared to patients who underwent treatment before our study and those who were having cirrhosis, virological response was found much better in patients without cirrhosis and in treatment naive patients.*
Conclusion: *At the end of present study we concluded that in patients with chronic hepatitis C genotype 3a disease combination of daclatasvir with sofosbuvir is very effective.*
Key Words: *Sofosbuvir, Genotype 3a, Chronic hepatitis C, Daclatasvir, SVR24 (sustained virologic response at week 24).*

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INTRODUCTION:

According to the estimation of world health organization (WHO) 71 million population of the world is affected by chronic hepatitis C [1]. With an approximate prevalence of 6.70%, Pakistan is from the leading countries affected by hepatitis C virus [2]. Whereas, in a recently conducted study on Pakistani population, genotype 3a being most common prevalence of hepatitis C was approximated to be 8.64% while genotype 3a being most common one [3]. Much alarming situation was revealed in a very recent study conducted in Pakistan on a very large scale with an approximated prevalence of HCV to 4.90% [4]. Liver cirrhosis and HCV complications including mortality and hepatocellular carcinoma are caused by the chronicity of HCV infection [5]. Efforts for the treatment of chronic hepatitis C are boosted up in Pakistan due to the reduced prices of DAA and generics initiation. Globally for the treatment of chronic hepatitis C during 2016, half of the population of Pakistan and Egypt had started the DAAs which is rising in numbers day by day [6].

With sustained virological response of 91%, treatment via daclatasvir in addition with sofosbuvir once in a day for the duration of 3 months produced positive results in patients of HCV genotype 3 [7]. In phase III of ALLY3 study also noticed positive virological response in genotype 3 patients either they were treatment experienced or naive patients. SVR rate in comparison of naive to treatment experienced patients was observed higher in naïve patients as 96% to 86% respectively [8]. With weight-based ribavirin of sofosbuvir and daclatasvir, observed good SVR rate in advance liver disease patients [9]. Guidelines of AASLD 2017 showed strong proof and recommendation of sofosbuvir in addition with daclatasvir for genotype 3 patients. Patients without cirrhosis are recommended for treatment duration of 3 months and patients with cirrhosis are recommended for treatment duration of 6 months when weight-based ribavirin is adjoined to the treatment regardless of earlier pegylated interferon in addition with ribavirin treatment [10]. But this combination of treatment for genotype 3 HCV is not included in recently laid down EASL guidelines for treatment of HCV [11].

We didn't found studies related to efficiency of daclatasvir in addition with sofosbuvir for treatment of HCV in Pakistan. Therefore, the aim of our study was to find out the sustained virologic response (SVR) after the treatment with Daclatasvir in addition with sofosbuvir regardless of liver cirrhosis or any previous treatment history.

MATERIAL AND METHODOLOGY:

This study was conducted at mayo hospital, Lahore for the duration of one year starting from May, 2018 to March, 2019. We included a total number of 125 patients in our study who were having genotype 3a hepatitis C virus regardless of previous treatment history or presence of cirrhosis. This regimen was given to patients because free accessibility of DAAs in government organizations and included those patients who were not able to bear the expenses of this first line regimen. With a value of more than 15ng/ml as positive, baseline quantitative PCR testing was used to confirm persistence of chronic hepatitis C. Carried out genotype testing in laboratory of the hospital and selected those patients who were having genotype 3A by using non-probability purposive sampling. Carried out abdominal ultrasound by consultant radiologist for the confirmation of liver cirrhosis and existence of coarse echotexture of liver was cogitated as liver cirrhosis. Ultrasound was our compulsion because of non-availability of Fibroscan and Shear Wave Elastography which are recommended for presence of cirrhosis. Used Child Pugh Score for assessment of liver disease severity and patients were defined as in Child Class A, Child Class B and Child Class C according to the score as 5-6, 7-9 and 10-15 respectively. Included all those patients in our study who were having Child Class A and Child Class B and excluded those who fall in Child Class C. Those patients who had already experienced treatment were divided further into 02 groups as non-responders and relapsers. Non-responder were those patients who didn't responded to 6 months interferon in addition with ribavirin treatment. Relapsers were those patients who had a positive PCR after having ETR with 6 months treatment via interferon in addition with ribavirin.

Daclatasvir (60mg) in addition with sofosbuvir (400mg) on daily basis for the duration of 03 months were prescribed for treatment of those patients who were without cirrhosis. Whereas, daclatasvir (60mg) in addition with sofosbuvir (400mg) with ribavirin according to the weight of the patients were given to those patients who were either with treatment history or having cirrhosis. Dosage was prescribed on daily bases for the duration of 06 months. Carried out the PCR test after the one month of treatment to assess the EVR (Early Virological Response) and after the three months and 6 months treatment for assessment of ETR (End Treatment Response). Whereas, our prime goal of the study was to determine SVR24 (Sustained Virological Response) after the completion of treatment at 24th week. Use SPSS 21 for analysis of collected data. Categorical variables such as EVR,

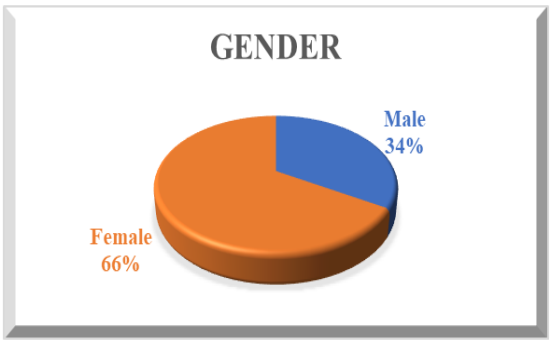
SVR or ETR were calculated and displayed as percentage and continuous variables like as age were showed and calculated in mean ± SD.

RESULTS:

There were total 125 patients included in our study. Gender distribution as male and female were as 42 (33.60%) and 83 (66.40%) respectively.

Table No 01: Gender distribution

Gender	Quantity	Percentage
Male	42	33.60%
Female	83	66.40%

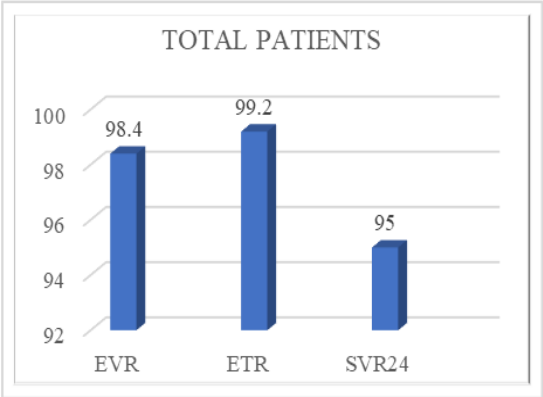


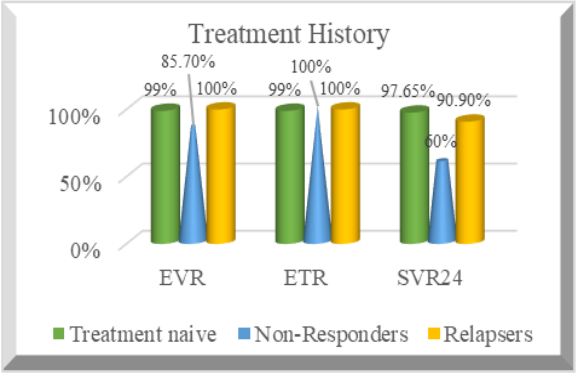
47.06±10.8 years was the mean age of the patients. Treatment naive, non-responder and relapsers patients were as 102(81.6%), 07(5.60% and 16(12.80%) respectively. Patients having cirrhosis were 58(46.40%) among which there were 43 treatment naive patients, 11 patients were relapsers and 4 patients were non-responder. Child Class A cirrhosis were there in 50 patients and Child Class B cirrhosis were there in 8 patients.

123(98.4%) patients achieved EVR (Early Virological Response) and 124(99.20%) patients achieved ETR (End Treatment Response). Among 123(98.4%) patients who achieved EVR (Early Virological Response) in accordance with treatment history there were 101(99%) treatment naive patients out of 102 patients, 06(85.70%) non-responder patients out of 07 patients and 16(100%) relapsers patients out of 16 patients. Among 124(99.20%) patients who achieved ETR (End Treatment Response) in accordance with treatment history there were 101(99%) treatment naive patients out of 102 patients, 07(100%) non-responder patients out of 07 patients and 16(100%) relapsers patients out of 16 patients. Despite of multiple reminders, 24 patients who were still alive but didn't reported for follow-up. 101(80.8%) patients were available for SVR24 among which there were 53 patients with out cirrhosis and 48 were having cirrhosis from which 96(95%) patients achieved SVR24. Percentage of SVR24 in patients without cirrhosis was 98.11% and in patients of cirrhosis was 91.66%. SVR24 (Sustained Virological Response) in accordance with treatment history there were 83(97.65%) treatment naive patients out of 85 patients, 03(60%) non-responder patients out of 05 patients and 10(90.9%) relapsers patients out of 11 patients. Results are shown below in table number 02.

Table No 02: Results of treatment with sofosbuvir in addition with daclatasvir with or without ribavirin

Statistics	EVR		ETR		SVR24	
	Qty	%	Qty	%	Qty	%
Total patients	123/125	98.4	124/125	99.2	96/101	95
Treatment History						
Treatment naive	101/102	99	101/102	99	83/85	97.65
Non-Responders	6/7	85.7	7/7	100	3/5	60
Relapsers	16/16	100	16/16	100	10/11	90.9
Cirrhosis						
Present	57/58	98.3	57/58	98.3	44/48	91.66
Absent	67/68	98.5	67/67	100	52/53	98.11
Child Pugh Class						
Class A	49/50	98	49/50	98	38/41	92.7
Class B	8/8	100	8/8	100	6/7	85.7





DISCUSSION:

The results of our study clearly show that sofosbuvir in addition with daclatasvir on daily bases is highly effective in patients of HCV genotype 3a of Pakistani population either cirrhosis exist or not. Rate of SVR24 was less in patients with cirrhosis as compared to patients without cirrhosis and in treatment experienced patients compared to treatment naïve patients. Good treatment response was observed in patients with compensated cirrhosis in our study. EVR and ETR was achieved in 98.30% patients having compensated cirrhosis.

A study was conducted about efficiency of sofosbuvir in addition with daclatasvir without or with ribavirin addition on hepatitis C patients b Welzel et al. In this study after one-month treatment HCV RNA was not detected in 73% patients, after 12-week treatment in 97% patients and after 24 weeks of treatment in more than 99% patients. But all genotype patients were included in this study. As compared to out study of genotype 3, 92% patients achieved SVR which was slightly less in patients who experienced treatment and having decompensated cirrhosis. Low SVR24 rates were observed in patients having cirrhosis and with treatment experience as compared to without cirrhosis and treatment naïve patients [12]. These results were like our study results.

In another study conducted by Alonso et al, high rated of SVR as 94% were observed in patients with HCV genotype 3 who were treated with daclatasvir in addition with sofosbuvir [13]. These results are also comparable with the results of our study as SVR 24 rate was 95%. In a study conducted in India by Mehta et al on HCV genotype 3 patients who were treated with daclatasvir in addition with sofosbuvir, SVR was achieved by 97.3% patients which clearly show high effectiveness of this regimen in genotype 3 patients [14]. On the other hand, lower SVR rates as 84.7% were observed in a study conducted by Ferrieria et al in patients having genotype 3 and treated with daclatasvir plus sofosbuvir regimen. But hence, he found no significant association of treatment experience or presence of cirrhosis with achieving SVR which represent similarity to our study results [15]. Even though, present EASL guidelines don't recommend the use of daclatasvir and sofosbuvir combination but due to the availability of only a few DAAs in Pakistan makes it an effective and affordable option to choose. As the sample size of our study was very low so, studies on larger scale are needed to determine other treatment options available in Pakistan.

CONCLUSION:

At the end of our study we concluded that in patients with chronic hepatitis C genotype 3a disease, combination of daclatasvir with sofosbuvir is very effective regardless of presence of cirrhosis and previous treatment history.

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