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Article received on:
01/11/2018

Accepted for publication:
12/10/2019

INTRODUCTION

Chronic hepatitis due to Hepatitis C Virus (HCV) is a worldwide disease. According to estimates about 185 million people are infected with HCV worldwide. Estimated prevalence is 2.8 % worldwide. HCV leads to acute hepatitis, chronic hepatitis, Cirrhosis of liver, Hepatocellular carcinoma and End stage liver disease.

Indications of treatment include chronic hepatitis, hepatic fibrosis, compensated and decompensated cirrhosis. Treatment is recommended for patients with high ALT, age more than 18 years, positive HCV RNA and compensated liver disease and DCLD not approaching MELD > 18.

SVR (Sustained Virological Response) is defined as negative HCV RNA 24 weeks after completion of antiviral therapy. The late relapse is very low after achievement of SVR (less than 1%). The

EFFICACY OF DACALTASVIR AND SOFOSBUVIR COMBINATION THERAPY IN CHRONIC HCV POPULATION IN PRIVATE CLINIC SET UP.

Hafiz Mughees Ather¹, Idrees Shani², Muhammad Aamer³, Arfan Mahmood⁴, Nazir Ahmad⁵

ABSTRACT... All- oral antiviral therapy for chronic hepatitis C is standard of care in 2018. Daclatasvir and Sofosbuvir combination therapy was approved in 2015 by EASL. Generics are also available since 2016. **Objectives:** We evaluated efficacy of Daclatasvir and Sofosbuvir based therapy in cirrhotic and non-cirrhotic patients. **Study Design:** Retrospective Observational Study. **Setting:** Athar Medical Center Muslim Town, Sargodha Road, Faisalabad. **Period:** One Year Dec 2017 to Dec 2018. **Material & Methods:** 151 patients were treated with Daclatasvir 60 mg daily and Sofosbuvir 400 mg daily combination therapy. Decompensated Cirrhotic patients were treated for 6 months along with ribavirin according to weight of patient. Treatment experienced patients were treated along with ribavirin. Naïve non-cirrhotic patients were treated for three months or 12 weeks. Primary end point was negative SVR 24 weeks after completing therapy. **Results:** Over all 151 patients were treated. 85 (56.29%) patients were male. 30(19.86%) patients were cirrhotics and remaining were non-cirrhotics. SVR was obtained in 149 patients. Treatment failure was seen in one cirrhotic and one non-cirrhotic patient. **Conclusion:** Daclatasvir and Sofosbuvir combination is highly effective in chronic hepatitis C patients in our population of Faisalabad division.

Key words: Daclatasvir, SVR (Sustained Virological Response), Sofosbuvir

Article Citation: Ather HM, Shani I, Aamer M, Mahmood A, Ahmad N. Efficacy of dacaltasvir and sofosbuvir combination therapy in chronic HCV population in private clinic set up. Professional Med J 2020; 27(7):1323-1327.
DOI: 10.29309/TPMJ/2020.27.07.486

patients who achieve SVR are found to have decreased inflammation, fibrosis and low liver related complications. There is low incidence of HCC and death rate. The HCV treatment also improves glucose tolerance.

There are six genotypes of HCV worldwide. HCV Genotype-3 is more prevalent in Pakistan. As compared to Genotype -1 and Genotype -4, GT-3 was considered easy to treat with PEG interferon and Ribavirin. With DAAs however SVR results of HCV GT-3 are inferior to GT-1 and GT-4. It is also considered aggressive genotype and the risk of decompensated liver disease and HCC are greater.

The safety and efficacy of direct acting antivirals has not been studied yet in our part of world and there is no study available from Faisalabad for efficacy of Daclatasvir.

On the basis of results of large trials, Sofosbuvir is recommended with Daclatasvir for treatment of HCV with or without ribavirin and treatment has been dramatically changed with advent of new antivirals.^{1,2}

The SVR rates were lower with PEG interferon and Ribavirin Therapy. But with inclusion of DAAs (Direct Acting Antivirals) SVR has increased upto 92-99%.

We conducted a study to evaluate the efficacy of Sofosbuvir and Ribavirin ±Daclatasvir in Cirrhotic and Non Cirrhotic, naive and treatment experienced patients.

MATERIAL & METHODS

A total of 151 patients were included in the study who received Sofosbuvir and Daclatasvir combination therapy. Cirrhotic and treatment experienced patients received Ribavirin as well. Cirrhotic patients received treatment for 6 months and Non Cirrhotic patients received treatment for 3 months.

The criteria used for labeling a patient Cirrhotic was, History suggestive of decompensation like upper GI bleeding, history of hepatic Encephalopathy, low platelets, high AST > ALT ratio, Low Albumin, High PT/INR, presence of Splenomegaly, dilated portal vein, nodular liver or Ascities on USG. The presence of portal hypertensive signs on EGD like esophageal, gastric or ectopic varices were considered as evidence of Portal HTN and Cirrhosis.

All patients who had treatment with Sofosbuvir and Daclatasvir therapy were included in the study. HCC patients, cirrhotics, ESLD with MELD score less than 18 were also included in the study.

Exclusion Criteria

- Those who did not complete treatment were excluded from study.
- Post liver transplant, HIV patients and those with end stage kidney disease were excluded from study.

It was retrospective analysis of the patients who were treated with Sofosbuvir and Daclatasvir. The study was conducted in DR Mughees Ather gastro liver and Endoscopy centre Sargodha road Faisalabad city where the patients received antiviral treatment and followed-up regularly. Genotype was not done because of economical issues and daclatasvir is effective in all genotypes. Fibro scan was also not done for patients because of non-availability to patients. Liver biopsy was also not done for any patient. SVR was compared among Cirrhotics and Non-Cirrhotics.

RESULTS

56.3 % were male and 43.7 % were female. Mean age was 55 years. 34% patients were Cirrhotics on the basis of the criteria mentioned above. Non-Cirrhotics had SVR 99%. Cirrhotics had SVR 96%. Treatment experienced patients had SVR 95%.

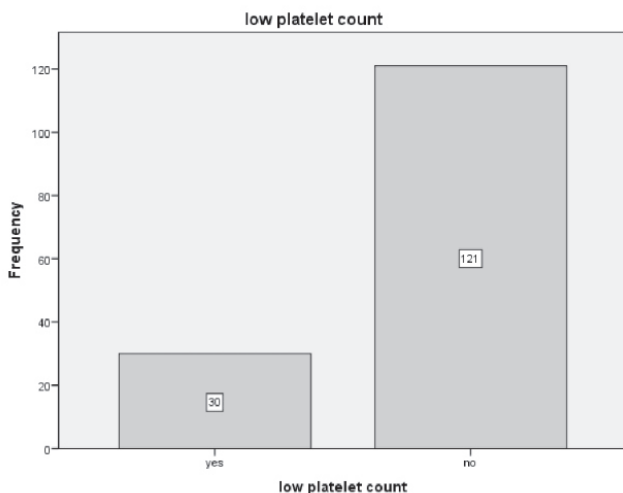
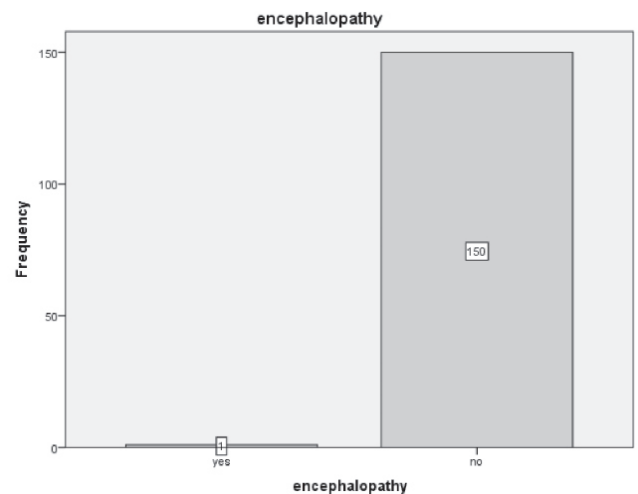
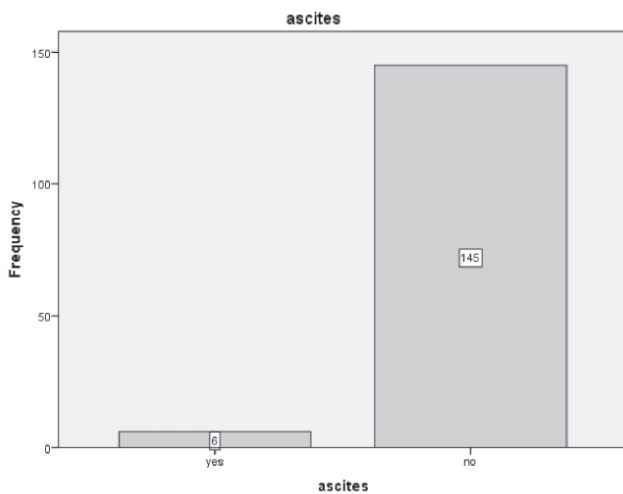
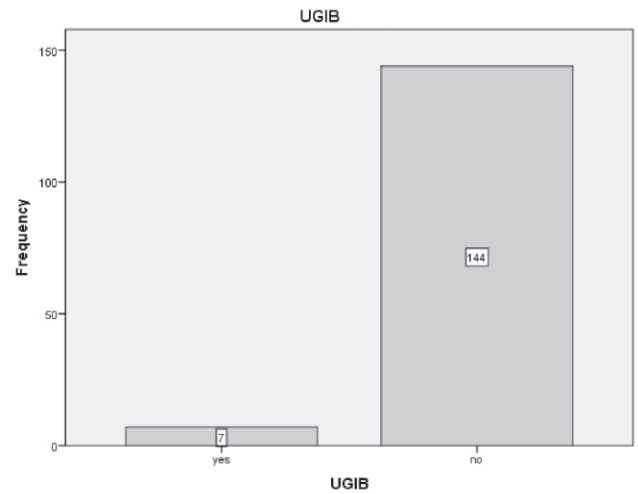
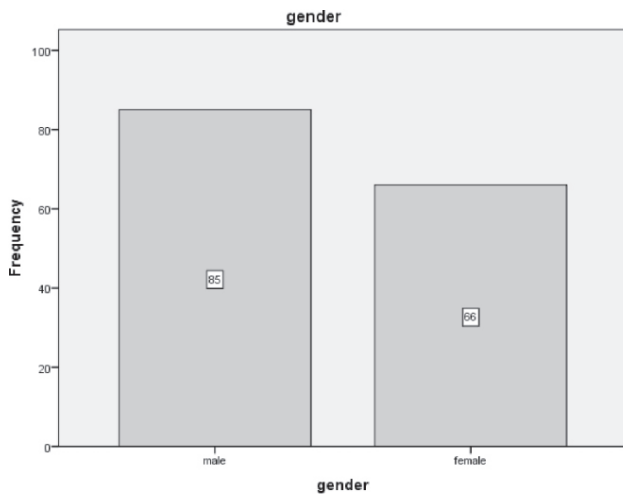
Gender		
	Frequency	Percent
Male	85	56.3
Female	66	43.7
Total	151	100.0

UGIB		
	Frequency	Percent
Yes	7	4.6
No	144	95.4
Total	151	100.0

ASCITES		
	Frequency	Percent
Yes	6	4.0
No	145	96.0
Total	151	100.0

Encephalopathy		
	Frequency	Percent
Yes	1	.7
No	150	99.3
Total	151	100.0

Low Platelet Count		
	Frequency	Percent
Yes	30	19.9
No	121	80.1
Total	151	100.0



In the study of JIM Young the estimated SVR at 12 weeks post treatment was 87% for previously treated G1 patients with decompensated cirrhosis.⁴

In the study of Poordad F et al⁵ post liver transplant and cirrhotic patients were treated with 12 weeks of SOF - dacla combination therapy. The SVR for HCV G3 patients was 83%.

In Ally 2 study⁶ 60 cirrhotic patients were included. Among them 67 % were male and median age was 59 years and range of age was 19 to 82 years. Different studies were done on Chronic HCV G-3 patients and G-1 to G-4 patients showing SVR ranging from 94 – 96%. ALLY-3⁷ study showed SVR 93 % among patients with F0 –F3 fibrosis score. It was 70 % for F4 fibrosis score patients. The overall SVR was 89% in

DISCUSSION

In study of JIM Young³ mean age was 56 years and 59 % patients were decompensated cirrhosis of liver. The overall SVR was 87 %.

different population of Chronic HCV patients. Our study showed that Sofosbuvir and Daclatasvir is an effective combination for Rx of Chronic HCV in our population. The study of Loui⁸ showed SVR 55% in G 3 patients but in our study it is about 98 %. The study of Hoelle Sette Jr⁹ showed SVR 95%. Our study showed PCR better than that study. The study of Sulkowski¹⁰ was on 211 naïve and treatment experienced patients showed SVR from 89% to 100% in different populations. The strength of our study is that patients were followed-up regularly. The weakness of the study is the small numbers of patients. Our data is in consistence with that study of ALLY-3 Study. It is not confirmed that addition of Ribavirin is beneficial in achieving high SVR.

CONCLUSIONS

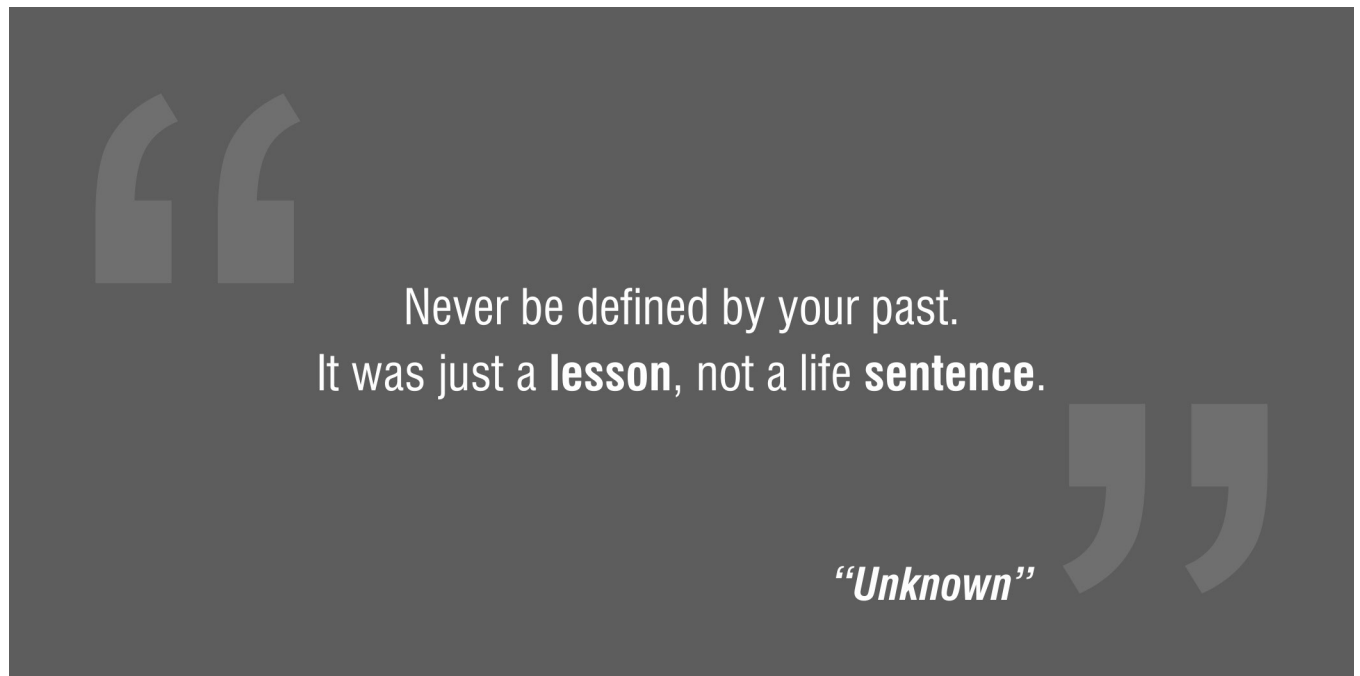
In Patients of chronic HCV having chronic hepatitis, compensated and decompensated cirrhosis of liver the Sofosbuvir and Daclatasvir combination is effective and safe for treatment of Hepatitis C Virus in predominantly Genotype-3 population of our area. Now we have new recommendations of drugs like Velpatasvir, Glecaprevir and Parbintasvir. Their efficacy still has to be evaluated in our area.

Our study showed that Daclatasvir and Sofosbuvir were associated with higher sustained Virological response. The Ribavirin is associated with adverse effects and naïve non-cirrhotic patients can be treated without Ribavirin.




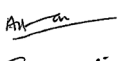
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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Hafiz Mughees Ather	Data collection, Data entry and analysis, Manuscript review.	
2	Idrees Shani	Results analysis and discussion.	
3	Muhammad Aamer	Study designed, Data interpretation.	
4	Arfan Mahmood	Data collection + Manuscript review.	
5	Nazir Ahmad	Proof reading, Manuscript review.	