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EFFECTIVENESS OF SOFOSBUVIR IN THE TREATMENT OF PATIENTS HAVING HCV GENOTYPE III

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Abstract:
History: *Hepatitis C virus (HCV) infection rate is rising in the underdeveloped world and genotype III is the 2nd most common subtype to involve. Sofosbuvir has shown good results in the recent times.*
Objective: *The aim of our study is to determine the efficacy of sofosbuvir for the treatment of hepatitis c genotype III.*
Study Design: *This was a descriptive case series study*
Place and duration of Study: *The study was conducted in medical wards of Lady Reading Hospital, Peshawar from January 2019 to December 2019.*
Methodology: *The cases of HCV infection of genotype III assessed by PCR were included. These cases then were treated with oral sofosbuvir in a dose of 400 mg daily along with RBV with age appropriate doses. The efficacy was labelled as yes when there was negative result on PCR done at completion of 3 months.*
Results: *In the present study there were total 200 patients that had HCV PCR positive for genotype III, out of which 112 (56%) were males and 88 (44%) were females with mean age of 46.21±4.27 years. Efficacy of sofosbuvir was seen in 184 (92%) of the patients. This efficacy was better in those that had age 50 or less where it was seen in 118 (94.4%) of cases as compared to 66 (88%) with age more than this (p=0.07). The duration of HCV less than 1 year revealed success rate of 96.67% as compared to 90% with p value of 0.08. Conclusion: Sofosbuvir has shown a very high efficacy rate in cases with HCV infection due to genotype III and results were near significantly better in those that had age less than 50 years and infection for less than 1 year.*
Keywords: *HCV, Genotype III, Sofosbuvir.*

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INTRODUCTION:

Hepatitis especially due to viral disease is very common in developing countries like Pakistan. The hepatitis C virus (HCV) infection is the most leading one. It comprises six genotypes and multiple subtypes. HCV genotype III is the second most prevalent globally (54.3 million patients, 30.1%). [1-2]

The data has revealed that HCV genotype III has the highest chances to increase the risk of progression to cirrhosis or to hepatocellular carcinoma (HCC) and hence warrant urgent treatment. The Swiss Hepatitis C Cohort Study found that the most significant independent risk factors associated with accelerated liver fibrosis progression, in a multivariate model analysis, were histological activity [OR=2.03 (1.54–2.68), P<0.001], genotype III infection [OR=1.89 (1.37–2.61), P<0.001], male sex [OR=1.60 (95%CI=1.21–2.12), P<0.001] and age at infection [OR=1.08 (1.06–1.09), P<0.001].

Among patients with HCV infection and cirrhosis, genotype III infection is also the strongest predictor for the occurrence of HCC. [3,4] Until 2011, the only treatment options available for patients with HCV infection were interferon-based regimens, with pegylated interferon alfa 2a or 2b (PegIFN) and ribavirin (RBV). In 2011 the first direct-acting antiviral agents (DAAs), NS3/4A protease inhibitors (telaprevir and boceprevir) became available for HCV genotype 1 infection and but they had limited activity against HCV genotype III. In 2013, new DAAs became available for HCV infection treatment, though few are effective for HCV genotype III infection, such as daclatasvir (DCV) and sofosbuvir (SOF). SOF is a pyrimidine nucleotide analogue inhibitor of the HCV RNA-dependent RNA polymerase, with excellent antiviral activity against all HCV genotypes and a high genetic barrier to resistance. [5,6]

METHODOLOGY:

This descriptive case series study was conducted in medical wards of Lady Reading Hospital, Peshawar from January 2019 to December 2019. In this study 200 patients having HCV infection of genotype III assessed by PCR were included. All those patients of both genders having age ≥20 years and were diagnosed with HCV infection of genotype III through PCR were included in the study. All those patients suffering from ischemic heart disease, with end stage renal disease, with over cirrhosis and with HCC were not included in the study.
Detailed demographic and clinical data were taken. Data regarding co morbid conditions like DM and duration of

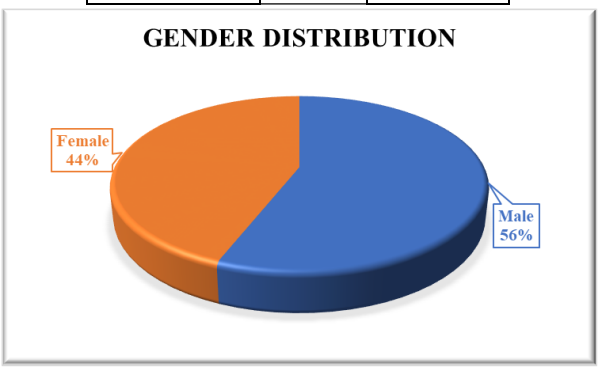
HCV infection (assessed by history and medical record) was also taken. These cases then were treated with oral sofosbuvir in a dose of 400 mg daily along with RBV with age appropriate doses. The efficacy was labelled as yes when there was negative result on PCR done at completion of 3 months. The data was entered in SPSS 23 version and then analyzed. Post stratification chi square test was applied taking p value < 0.05 as significant.

RESULTS:

In the present study there were total 200 patients that had HCV PCR positive for genotype III, out of which 112 (56%) were males and 88 (44%) were females with mean age of 46.21±4.27 years.

Table No 01: Gender Distribution

Gender	Qty	%age
Male	112	56%
Female	88	44%
Total	200	100%

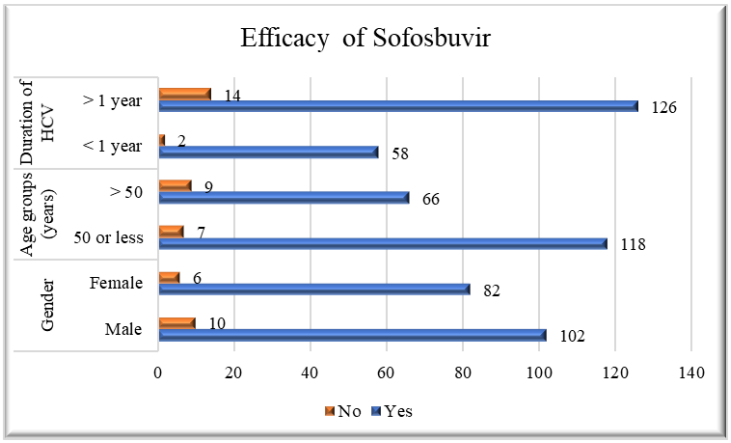


There were 32 (16%) cases that had co morbid of DM. Efficacy of sofosbuvir was seen in 184 (92%) of the patients. There was no significant difference in terms of gender with P=0.88. This efficacy was better in those that had age 50 or less where it was seen in 118 (94.4%) of cases as compared to 66 (88%) with age more than this

(P= 0.07). The duration of HCV less than 1 year revealed success rate of 96.67% as compared to 90% with p value of 0.08 as in table 01.

Table No 02: Efficacy of Sofosbuvir With Respect to Confounders

Efficacy	Gender		Total	P Value
	Male	Female		
Yes	102 (91.07%)	82 (93.18%)	184 (100%)	0.88
No	10 (8.83%)	6 (6.82%)	16 (100%)	
	Age groups (years)			
	50 or less	> 50		
Yes	118 (94.4%)	66 (88%)	184 (100%)	0.07
No	07 (5.60%)	09 (12%)	16 (100%)	
	Duration of HCV			
	< 1 year	> 1 year		
Yes	58 (96.67%)	126 (90%)	184 (100%)	0.08
No	02 (3.33%)	14 (10%)	16 (100%)	



DISCUSSION:

There is high burden of HCV infection and disease globally especially in the developing world and its number is continuously on the rise and is also posing a high burden over the health departments due to its various complications and poor outcome. With the advent of direct acting anti-virals, an era of all oral regimens has been introduced; Sofosbuvir being the first one to gain worldwide exposure is a non-nucleoside polymerase inhibitor (NS5B). Being the polymerase inhibitor, it has got pan genotypic effect. Several significant studies from west are available to evaluate the effectiveness of Sofosbuvir for different genotypes but data is relatively scarce for genotype III as it is more prevalent in eastern countries. Few clinical trials available in literature for genotype III, includes FISSION, FUSION, POSITRON, ALLY-3 and BOSON studies suggesting good acceptance of the drug but hints for a longer duration of therapy.

Efficacy of sofosbuvir was seen in 184 (92%) of the patients. There was no significant difference in terms of any study variable i.e gender, duration of HCV infection and age. However, the latter two had a near significance with p= 0.07 and 0.08. The treatment naïve group has shown the RVR of about 92% and SVR of 83.3% respectively. This response is irrespective of cirrhosis.[7] In VALENCE trial the SVR for treatment naïve non- cirrhotic patients was 93% and cirrhotic patients was 92% respectively and the results are quite comparable with our study. A multi-centre RESiP trial from Pakistan involving more than 5000 patients with 94% genotype III patients showed a SVR12 of 97% in non- cirrhotic and 89% cirrhotic treatment naïve patients respectively.[8]

As evident by the VALENCE trial the basic problem is to deal with the treatment experienced patients especially those who have already developed cirrhosis. The SVR in this group was only 60%.[9] Treatment experienced patients include both failures and relapsers to IFN/Peg-IFN along with Ribavirin in the past, however we did not study the cases with previous history of treatment.

Similarly, the results regarding decompensated cirrhosis are also very encouraging as compared to international data. HCV- TARGET study evaluated the Sofosbuvir based regimens for GT3 and only 39% SVR12 were observed.[10] Contrarily in our study 67% patients with decompensated cirrhosis have achieved RVR. Sofosbuvir and Ribavirin combination has shown a good safety profile in both cirrhotic and non- cirrhotic patients in our population. No serious side effects have been reported. Only complaints the patients come up with were fatigue, generalized weakness, myalgias, fever,

dry cough and headaches. All these side effects were easily manageable.

CONCLUSION:

Sofosbuvir has shown a very high efficacy rate in cases with HCV infection due to genotype III and results were near significantly better in those that had age less than 50 years and infection for less than 1 year.

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