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Effectiveness of SVR 12 in Hepatitis C Subjects Attending Tertiary Care Hospital in Lahore-Pakistan: an Observational Data

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ABSTRACT

Introduction: In Pakistan, for the patients of Hepatitis C virus (HCV), Direct-Acting Antiviral (DAA) therapy for 12 weeks and 24 weeks had been reported to be highly efficacious for genotype 3. We currently carried out an observational study to predict the rate of efficacy of sofosbuvir and ribavirin in hepatitis C patients to establish concrete or authentic data on this combination of DAA for long-term treatment.

Materials and Method: Among 2000 subjects who attended tertiary care unit in Lahore-Pakistan from November 2018 to February 2019, 1990 satisfied the criteria set for the present investigation i.e. SVR12 after being treated with sofosbuvir and ribavirin combination.

Results: It was noted that genotype 3a were more common among all the subjects under observation with 50.65 % (1008/1990) in females and 49.35% (982/1990) in males. Overall efficacy analysis was found to be 95.4% (1900/1990) in patients while the moderate response was noted in elderly subjects including both genders (61-90 years). DAA responders (male: female percentages) shown the following stats; 66.63 (42/66):36.36 (24/66) in 11-20 years, 56.6(240/424):43.39 (184/424) in 21-30 years and 44.73(272/608):55.27(336/608) in 31-40 years.

Conclusion: Collectively, this combinational drug therapy was observed to be successful among the Pakistani population. However, more comprehensive follow-up studies are needed on a larger pool of population nationwide to check only this combinational therapy (sofosbuvir and ribavirin) would be beneficial or not? Or next-generation DAA regimes would be the choice for the Pakistani population.

Keywords: *Direct-acting antivirals (DAA), Hepatitis C virus (HCV), Sustained viral response (SVR), Sofosbuvir, Ribavirin.*

INTRODUCTION

The global burden of the Hepatitis C virus (HCV) increases day by day whereas most people lost their lives if untreated or taken it casually. Poor hygienic control and liver metabolized medications are also reported to be responsible for the cause the Hepatitis C [1, 2]. Pakistan has one of the highest rates of this disease and more than 10 million population in this country is known to be infected with HCV. Among the

known genotypes (1 to 6), 3a being most prevalent in Pakistan and were difficult to treat [3, 4]. Most HCV patients have developed liver cirrhosis in the younger age group (25 to 35 years) accompanied with a severe complication like jaundice hepatocellular carcinoma (HCC), and if any other co-infection under treatment complication may lead to death.

It has been revealed that interferon alone is not efficient because of low efficacy rate while in some patients relapse, loss of appetite and muscle pain has also been reported. Till the end of 2011, HCV treated by interferon and in combination with ribavirin is considered to be the best. Due to reported side effects, a direct-acting antiviral (DAA) regimen represents a breakthrough and milestone that has completely changed the landscape of HCV treatment. Hence, sofosbuvir being the first DAA nucleotide inhibitor reported as being a choice of treatment for chronic hepatitis C. Concurrently, Sofosbuvir and ribavirin combination therapy for 12 and 24 weeks is highly efficacious for genotype 1and genotype 3 active against both genotype [4].

The current study was undertaken from a different region of Pakistan to predict the rate of efficacy of sofosbuvir (DAA) and ribavirin in hepatitis C patients due to the lack of concrete or authentic data to use this treatment option on a long term basis in this region.

MATERIALS AND METHODS

Ethical issues and settings

This potential cross-sectional study was conducted for four-month from November 2018 to February 2019. A total of 2000 patients were enrolled, informed about the study, and were explained that their record was kept safe and will be used for research purpose only. All the enrolled patients were categorized based on age (younger to older) into eight groups (A-H). A; 11 – 20, B; 21-30, C; 31-40, D; 41-50, E; 51-60, F; 61-70, G; 71-80, H; 81-90. A specially designed questioner was made to obtain the basic information regarding the patient lifestyle before collecting the subject's blood sample.

Exclusion and inclusion criteria

All the naïve, recurring HCV subjects and all HCV positive subjects who had received 12 weeks long therapy of DAA were included in the study while all HBV patients and HCV subjects up to 7 years of age though HCV positive were excluded from the study.

Statistical analysis

All the statistical analysis was performed on prism graph 5. The statistical significance of the difference among different groups was measured using the student t-test, the data were considered significant when the p-value was < 0.05(*), <0.01(**), and 0.001(***).

RESULTS

The current study included a total of two thousand patients among them six subjects were positive for HBV while four were positive for HCV under (1-10) year of age group (data not included). The rest of the 1990 subjects have been confirmed positive for HCV with genotype 3a. Among these subjects, 982 were males (49.35%) and the remaining were females 1008 (50.65%). Results had shown that little increase in the number of HCV in females as compared to males. Group-wise percentages of males and females in different age groups is presented as Group A: 66.63 (42/66) and 36.36 (24/66) in 11-20 years, group B: 56.61 (240/424) and 43.39 (184/424) in 21-30 years, group C: 44.73 (272/608) and 55.27 (336/608) in 31-40 years, group D: 45.94 (221/481) and 54.06 (260/481) in 41-50 years, group E: 52.41 (130/248) and 45.58 (118/248) in 51-60 years group F: 67.24(39/58) and 32.75(19/58) of 61-70 years, group G: 30.76(4/13) and 69.24(9/13) in (71-80) year, while group H represent: year of only 2 (100%) female subjects (81-90 years) (Figure **1**; Table **1**).

The overall response rate of 95.4% of total 1990 patients were successfully treated with the therapy of sofosbuvir and ribavirin, whereas 90 subjects (patients) did not show response towards (DAA) sofosbuvir and ribavirin therapy. The non-responding subjects and their respective percentages are shown in (Figure **2**; Table **1** & **2**) wherein the group-wise percentage of male; female with different age groups; Group A: 66.66(2/3); 33.34(1/3) in 11-20 years. Group B: 38.46(5/13), 61.34(8/13) in 21-30 years. Group C: 40 (12/30); 60(18/30) in 31 - 40 years. Group D: 39.13(9/23); 60.87(14/23) in 41-50 years. Group E: 30(3/10); 70(7/10) in 51-60 years. Group F: 22.22(2/9); 77.78(7/9) in 61-70 years. Group F & G single male and single female 71-90 years respectively.

Regarding gender-wise distribution in responders of various groups; group A-B has shown; male > females, group C-D has shown females > males, group E-F male > females, while group G-H has shown females > males (Figure **3**).

Table 1. Treatment response in enlisted patients (male & female) after receiving SVR12 week-long sofosbuvir-based regimen (n=1900).

Responders

Sr. No	Age group Years	Male	Female	Total
1	11-20	42 (63.63%)	24(36.36%)	66
2	21-30	240(56.60%)	184(43.39%)	424
3	31-40	272(44.73%)	336(55.27%)	608
4	41-50	221(45.94%)	260(54.06%)	481
5	51-60	130(52.41%)	118(45.58%)	248
6	61-70	39(67.24%)	19(32.75%)	58
7	71-80	4(30.76%)	9(69.24%)	13
8	81-90	0	2(100%)	2
Total		**948**	**952**	**1900**

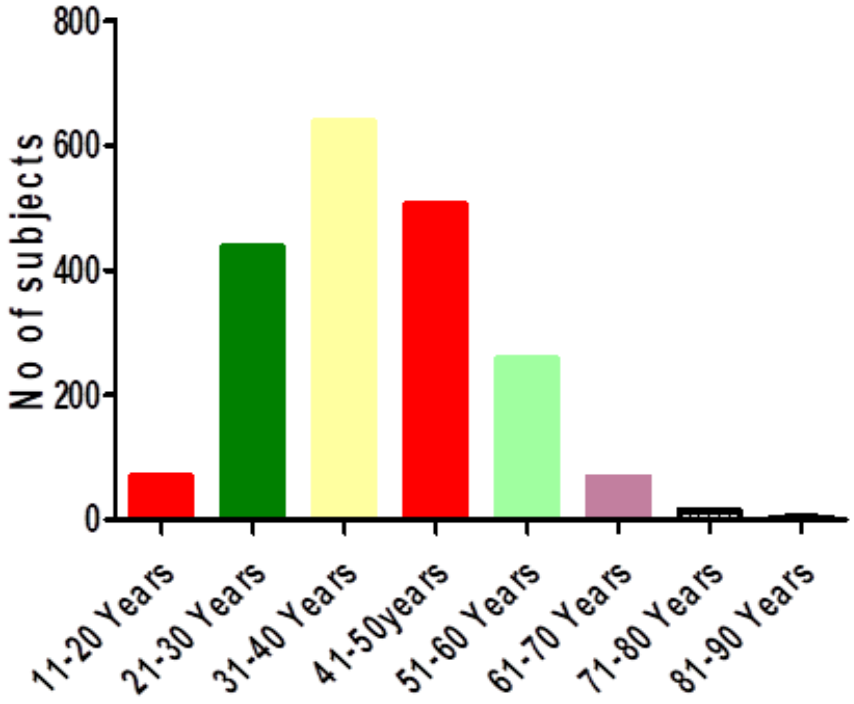

Figure 1. Age-wise distribution of HCV prevalence of all the enlisted subjects (n=1990) in the current study.

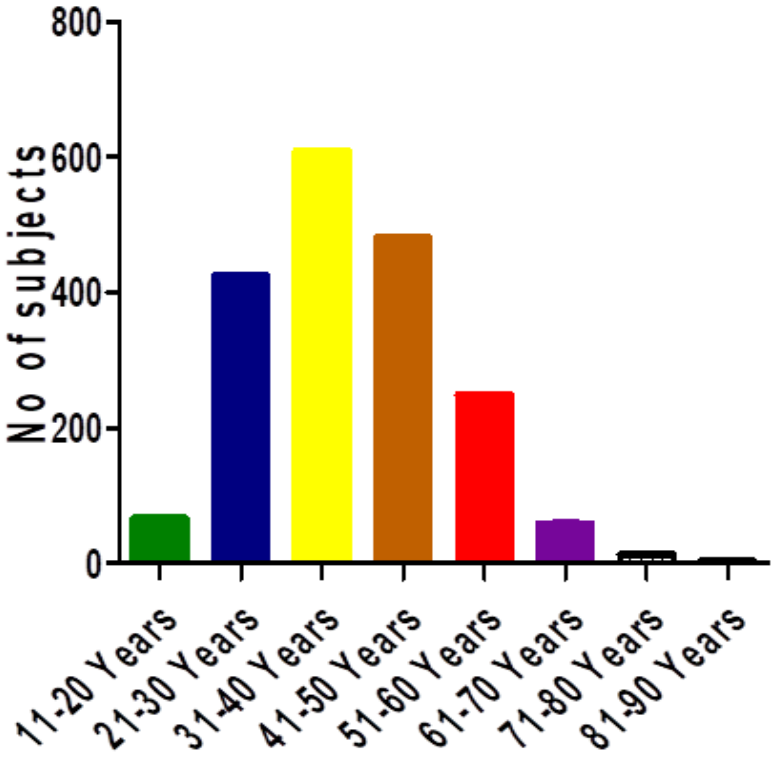

Figure 2. Prevalence of HCV in all the enlisted subjects of the current study 1900 patients A-H groups (11-90 years).

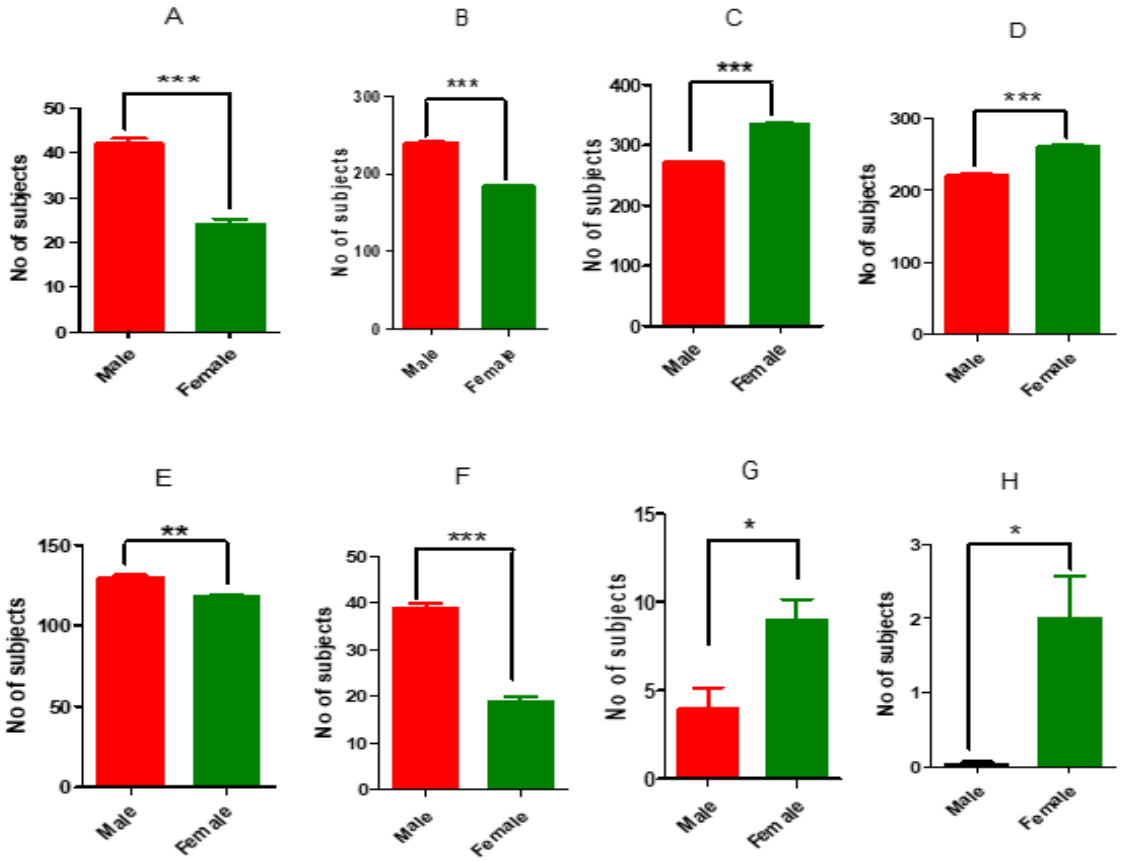

Figure 3. Gender-wise distribution of HCV responder against DAA from Pakistani population.

Table 2. Shows the HCV non-responders patient against the sofosbuvir.

NON RESPONDERS

Sr No	Age groups (Years)	Male	Female	Total
1	11-20	2(66.66%)	1(33.33%)	3
2	21-30	5(38.46%)	8(61.54%)	13
3	31-40	12(40%)	18(60%)	30
4	41-50	9(39.13%)	14(60.87%)	23
5	51-60	3(30%)	7(70%)	10
6	61-70	2(22.22%)	7(77.78%)	9
7	71-80	1(100%)	0	1
8	81-90	0	1(100%)	1
Total		**34**	**56**	**90**

DISCUSSION

This current observational study was performed to scrutinize the response rate of the sofosbuvir-based regime against HCV subjects attending tertiary care hospitals in Lahore Pakistan. Sofosbuvir is known to be a well-tolerated nucleotide polymerase inhibitor with activity against 3a genotypes with improved SVR rate. Sofosbuvir and ribavirin effectiveness in HCV patients infected with 3a genotype is also reported by various workers[6-8]. Our results have also shown a significantly high response rate in the Pakistani population while a small fraction of non-responders also noted. Other studies based on the Pakistani population have also exhibited an overall response rate of ≥ 90% [9-11]. The response rate 90% and 10% relapse rate during the treatment with sofosbuvir and ribavirin in 3a-HCV patients [12, 13]. SVR achieved about 97% in Japanese patients after being treated with sofosbuvir and ribavirin [14]. Moreover, a low incidence of late recurrence HCV had been observed by Sarrazin, *et al*. (2016) [15].

In previous studies, non-responsiveness is more common in cirrhotic as well as interferon-treated patients but our observations are not consistent with this finding because all the patients included in our study were non-cirrhotic and hadn't received any prior treatment [16]. The Nucleotide analog (Sofosbuvir) directly acts on the virus and inhibits the NS5B polymerase coding region of HCV and is held to be a more effective direct-acting antiviral drug. Rare side effects of Sofosbuvir have been observed as compared to interferon which makes it's a choice of treatment option [17]. In the current study, the overall SVR-12 rate in all the studied groups (A–H) was reported to be 95.6, 97, 95, 95, 96, 86.5, 92, and 66 percentages respectively. Sofosbuvir and ribavirin combination therapy for hepatitis C subjects infected with genotype 3a seems to be more effective in the current study.

The elimination of the hepatitis C disease from the Pakistani population is inspiring where most of the patients are infected with HCV genotype 3[18-20]. In the present study, a large number of population also reported to be non-responder, this might be due to resistant associated variants (RAVs) in which some specific amino acid substitutions and the different combination is effective for retreatment. It is also seen that elderly patients may be immune-compromised [21-23]. The possible treatment for non-responders after the failure of sofosbuvir+ ribavirin is the addition of daclatasvir [24].

Combination therapy of sofosbuvir and ribavirin for 24 weeks (SVR24) has shown a successful result ≥of 90%. According to our observation DAA therapy shown excellent results in HCV patients with genotype 3a. Collectively, this combinational drug therapy was observed to be successful among the Pakistani population. However, more comprehensive follow-up studies are needed on a larger pool of population nationwide to check only this combinational therapy (sofosbuvir and ribavirin) would be beneficial or not? Or next-generation DAA regimes would be the choice for the Pakistani population.

CONCLUSION

Collectively, this combinational drug therapy was quite successful among the Pakistani population. However, more comprehensive follow-up studies are needed on a larger pool of population nationwide to check only this combinational therapy (sofosbuvir and ribavirin) would be beneficial or not? Or next-generation DAA regimes would be the choice for the Pakistani population.

Conflict of interests

The authors declare no conflict of interests.

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