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Impact of different sofosbuvir based treatment regimens on the biochemical profile of chronic hepatitis C genotype 4 Patients

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Key words: Biochemical profile, CBC, Chronic hepatitis C virus, genotype IV, Direct acting antiviral (DAAs).

Abstract

Background: Huge efforts have been made to control chronic HCV in Egypt with introduction of Direct-Acting Antivirals (DAAs) with their anticipated excellent efficacy and tolerability.

Aim: To evaluate the effect of various DAA regimens on liver biochemical profile and hematological indices during treatment.

Methods: 272 patients chronically infected with HCV genotype 4 were treated by different DAA regimens (SOF/RBV, SOF/DAC ± RBV, SOF/SIM) for a duration of 12 or 24 weeks in Kasr Alainy Viral Hepatitis Center, Cairo University. Follow up was done for Serum Bilirubin(BIL), albumin(ALB), Alanine transaminase(ALT), Aspartate aminotransferase(AST), Prothrombin concentration, International normalized ratio (INR), and CBC at baseline, week 4, and end of treatment.

Results: The mean age was 54 years. 64.7% were male, 72.4% were treatment-naïve, 39% were cirrhotic. The overall SVR12 rate was 93.4%. With all treatment regimens, decline in ALT and AST occurred after treatment. In cirrhosis subgroup, there was a rise in BIL and INR; with no change in ALB and a decrease in white blood cells. Additionally, drop in hemoglobin and platelets in cirrhotic patients were noted with SOF/RBV, while SOF/SIM showed rise in BIL.

Conclusion: DAAs therapy is safe and effective in genotype 4 chronic HCV patients. It improves liver necro-inflammatory markers both in cirrhotics and non-cirrhotics. Cirrhotic

patients require careful observation being more vulnerable for treatment related complications.

1. INTRODUCTION

Egypt is known to be among the countries with highest Hepatitis C virus (HCV) prevalence [1], with HCV genotype-4 (GT-4) being the predominant genotype in Egypt [2].

HCV infection can progress to liver cirrhosis, that can lead to liver cell failure or hepatocellular carcinoma. The most important factor influencing progression is the extent of intrahepatic inflammation elicited by HCV [3]. Cure of HCV infection results in substantial reduction in liver-related morbidity and mortality [4].

For many years, the standard of care for treatment of chronic hepatitis C (CHC) had been a combination of pegylated interferon (Peg-IFN) and ribavirin (RBV) for 48 weeks. However, this combination had many drawbacks including its long course duration, severe side effects such as decrease in granulocytes, platelets and red blood cells or induction of autoimmune phenomena, in addition to its high cost which makes it not affordable for many patients in limited-resource countries [5].

The advent of direct-acting antiviral agents (DAAs) in the few recent years has revolutionized HCV treatment. PEG-IFN and RBV have largely been replaced by these highly effective, very well-tolerated DAAs of multiple classes. These new regimens provide higher SVR rates, in addition to higher probability of adherence to treatment, and much reduced side effects and impaired health-related quality of life during treatment [6].

Among these new drugs, sofosbuvir was the first approved DAA [7]. Sofosbuvir is an orally administered HCV nucleotide polymerase NS5B inhibitor, given once daily, and

has a good safety profile [8]. It has a pangenotypic activity and high efficacy when combined with other DAA classes, and is now primarily used as part of many interferon-free regimens [9]. Despite this, reports of possible hepatotoxicity have emerged in patients with decompensated cirrhosis [10] and also, it has been recognized that concomitant amiodarone intake might cause cardiotoxic effects through an unknown mechanism [11]. Other Nucleotide Inhibitors efficacy and safety remain in fairly early stages of clinical judgment [12].

The aim of the study is to evaluate the effect of different sofosbuvir based IFN-Free DAAs on liver biochemical profile, and blood picture in cirrhotic and non-cirrhotic CHC patients, reflecting the real-life cons and pros of these medications on the liver functions, as well as necroinflammatory changes and indirectly their reflection on patient quality of life.

2. PATIENTS AND METHODS

2.1. Patient Population

This retrospective study included 272 chronic HCV patients who received antiviral treatment in Kasr Al-Ainy viral hepatitis center, Cairo University, Cairo, Egypt, using different Sofosobuvir-based DAA treatment regimens. Patients were subjected to history taking, clinical examination and routine pretreatment laboratory work up. The diagnosis of CHC was established by the presence of HCV RNA using polymerase chain reaction assays. Liver cirrhosis was confirmed by fibroscan evaluation in all patients (with stiffness ≥12.5 kPa) [13] and ultrasonographic findings of liver cirrhosis ± laboratory tests (as low platelet count “<150,000/ml).

The choice of treatment regimen was following the treatment protocol of national committee for control viral hepatitis (NCCVH) and all patients were adherent to treatment and follow up.

2.2. Treatment regimens

Sixty-four patients received (Sofosbuvir/Daclatasvir +/- ribavirin) ***SOF/DAC +/- RBV*** for 12 weeks, 138 received (Sofosbuvir/simprevir) ***SOF/SIM*** for 12 weeks, while 40 patients were treated with (Sofosbuvir/ Ribavirin) ***SOF/RBV*** for 24 weeks.

2.3. Inclusion criteria comprised

Age 18-75 years and HCV RNA Positivity.

2.4. Exclusion criteria included total bilirubin >3 mg/dl, serum albumin ≤ 2.8 g/dl, INR ≥ 1.7, Platelets count <50,000/mm3, patient with untreated HCC, pregnancy, and uncontrolled diabetes; HbA1C > 9 %, decompensated cirrhotics (current or prior ascites, encephalopathy, or variceal bleeding).

Sustained virological response (SVR) was defined by undetectable HCV RNA by quantitative polymerase chain reaction assay (Cobas Amplicor, HCV Roche, Branchburg, NJ, USA, v 2.0, detection limit 15 IU/mL) at 12-week follow-up [14].

The study was approved by the institutional review board of faculty of medicine, Cairo university number (N-38-2016).

2.5. Laboratory Tests

Pretreatment laboratory tests in the form of complete blood cell counts (CBC), Serum creatinine, Prothrombin concentration (PC) , International normalized ratio (INR) , Alpha Feto protein (AFP) , Alanine aminotransferase (ALT) , Aspartate aminotransferase (AST) ,

Serum albumin (ALB) , Total bilirubin (BIL) , in addition to the HCV PCR were done. All these tests were repeated at week 4, end of treatment and 3 months after.

2.6. Statistical analysis

Data analysis was performed using STATA 13.1. For comparison of baseline characteristics between patients receiving different treatment regimens, differences in categorical variables were analyzed using the Chi-square test and differences in quantitative values were analyzed with the ANOVA test. The change in mean levels of different liver biochemical profiles and hematological indices after the start of therapy were compared using paired t-test or sign rank test according to the distribution of data.

3. Results

This study included 272 HCV genotype 4-infected patients, who received different sofosbuvir-based treatment regimens. 254 patients achieved SVR-12 (93.4%), and only 18 patients (6.6%) relapsed. Out of the 18 relapsers, 15 patients were in the SOF/RBV group, and 3 patients were given SOF/SIM. **Table 1** shows the baseline characteristics of the study patients. All patients were negative for HBsAg and HBcAb tests. The prevalence of liver cirrhosis was 39.7 %, and all cirrhotic patients in the study had Child A cirrhosis. About 27.6 % of patients enrolled in the study were treatment-experienced.

Comparison of the mean levels of different blood laboratory tests at baseline and at week-4 revealed significant reduction in both ALT & AST, with no significant change in albumin or blood picture **Table 2.** At end of treatment, there was also a significant decline in ALT, AST compared to pre-treatment levels. In addition, the WBCs count was reduced significantly as shown in **Table 3**. Significant reduction in APRI score results was noted in comparison between baseline and week 4 as well as baseline and end of treatment results **(Tables 2 and 3).**

To determine whether the changes in liver parameters or blood elements differed in different treatment regimens, we repeated the analysis for each treatment regimen separately **Table 4**. Liver transaminases showed significant decrease in all regimens, on the same time, At week 4, none of the patients had >3 fold elevation in ALT compared to baseline levels, and only one patient had AST elevation of 3.25 at week 4; this patient was non-cirrhotic, treatment-naïve, in the SOF/DAC group, whose baseline AST was 8, increased to 26 at week 4. This patient also had and end of treatment AST of 29; 3.6 folds higher than his baseline value. Another patient had >3folds elevation in ALT and AST at the end of treatment; this patient was a female, cirrhotic, treatment-naïve, who finally responded to the SIM/SOF treatment.

Serum bilirubin rose significantly in SOF/SIM regimen only. The drop of haemoglobin was only significant in SOF/RBV group, while the decline in WBCs count was only significant in SOF/SIM regimen.

Due to the vulnerable nature of the liver cirrhosis group, we aimed to study the changes in biochemical parameters in this subgroup separately. Cirrhotic patients had a significant rise in mean bilirubin & INR levels (*p* values, 0.04 & 0.01 respectively) and a mean negative change in prothrombin concentration (*p* value 0.02) representing probable worsening of liver functions. Also, WBCs count decline was only significant in liver cirrhosis group, **Table 5.**

When the change in biochemical tests in cirrhosis versus non-cirrhotic was studied separately in different regimens, we noticed the following; the rise in bilirubin in the SOF/SIM group was significant in non-cirrhotic, with only a trend towards significance in the cirrhosis group, no significant change in albumin levels post-treatment. Also, the drop in hemoglobin in the SOF/RBV group was significant in both cirrhosis and non-cirrhosis

groups; while the reduction in WBCs in the SOF/SIM group was only significant in those with cirrhosis **Table 6**.

4. Discussion

In this study, we evaluated the effect of various types of DAAs regimens (SOF/DAC ±RBV, SOF/SIM and SOF/RBV) on liver biochemical profile of 272 CHC patients who received treatment for 12 or 24 weeks. Follow up of liver biochemical profile and blood picture parameters among all treatment regimens revealed significant decline of ALT and AST. Cirrhotic patients showed rise in bilirubin and INR with no change in serum albumin, in addition to a decrease in White blood cells count.

Overall SVR 12 rate in the current study was (93.4%), This was comparable to that found by Eletreby and colleagues who evaluated the efficacy of simprevir/sofosbuvir combination therapy on 6211 Egyptian patients chronically infected with HCV genotype 4 and found overall SVR 12 rate of 94% [15]. However, was higher than found by Elsharkawy, et al, 2017 who studied the efficacy of dual therapy of sofosbuvir/ribavirin on 5667 patients with chronic HCV genotype 4 who were interferon ineligible and compared them to 8742 patients who were interferon eligible and received triple therapy of (SOF/IFN/RIB) . SVR rates were 78.7% and 94% for dual and triple therapy. selection of patients in the dual therapy group being more of the difficult to treat group (cirrhotic with higher FIB4 and lower Albumin levels) can explain the lower SVR results among this group [16].

Liver enzymes; AST and ALT, are known to have clinical significance in viral hepatitis and other forms of liver disease associated with hepatic necrosis [17]. In this study, the decline in ALT and AST among all treatment regimens and also among different subgroups, namely cirrhotic and non- cirrhotic, may indicate the significant role of DAAs in

improving hepatic necro-inflammatory changes induced by viral infection. This constitutes one of the goals of therapy of chronic HCV as stated in the EASL guidelines published in 2015 [14].

A meta-analysis performed by Akhtar et al in 2015 to study cirrhosis reversibility in hepatitis C patients with sustained virological response to antiviral therapy revealed fibrosis regression in 53% of cirrhotic patients who achieved SVR [18]. Results of the current study demonstrates significant decline of APRI score values (as simple serological marker for fibrosis assessment) between pretreatment and end of treatment results, this finding points to the predicted role of direct antivirals in fibrosis regression and warrants long term validated studies to assess and compare different DAAs combination therapies, and on the other hand this early reduction in fibrosis parameters should be taken with caution as it is mostly a reflection of the decline in necro-inflammation rather than the actual decline in fibrosis.

Among DAAs, simeprevir is a known inhibitor of bilirubin transporters OATP1B1and MRP2; with more potent inhibition of OATP1B1, which is responsible for influx of unconjugated bilirubin, than MRP2 that mediates efflux of conjugated bilirubin out of liver cell [19]. This results in increase in unconjugated rather than conjugated bilirubin with simprevir therapy [20]. In a randomized trial, the incidence of mildly increased bilirubin for simeprevir versus placebo in combination with peg-IFN and RBV treated patients was (22.8% vs. 10.0%) respectively [21]. In the current study, significant elevation of serum bilirubin occurred in simeprevir-containing regimen only, and the rise in bilirubin was significant in non-cirrhotics *(p = 0.02),* with a trend towards significance in the cirrhosis group *(p = 0.06),* larger number of cirrhotic patients treated with simprevir based therapy are needed to better validate the significance of bilirubin rise.

Safety and efficacy of SIM/SOF therapy in cirrhotic patients is of major concern. In the study done by Eletreby and colleagues in 2016 on 6211 patient with chronic HCV genotype 4, 41.2 % of them had child A cirrhosis, and none had child B or C cirrhosis, 97/6211 (1.6%) patients discontinued their treatment mainly due to hepatic decompensation, 48.5% (47/97) of them were cirrhotic, with 23/6211 (0.37%) cases had mortality due to liver failure [21]. In Phase IIb ASPIRE trial that compared simeprevir versus placebo in combination with pegylated interferon and ribavirin, neutropenia was reported more frequently in the simeprevir arm than in the placebo arm (25.8% versus 16.7%) [22]. In the current study, significant decline in WBCs count occurred in SOF/SIM regimen in cirrhotic patients only.

In this study, drop of haemoglobin was only significant in SOF/RBV group, and in both cirrhotic and non-cirrhotic groups. This was not surprising based on the well-known association between ribavirin therapy and haemolytic anaemia, even in the era of direct acting antivirals. NIAID SPARE trial investigated the use of sofosbuvir with either low-dose (600 mg daily) or weight-based (1000 or 1200 mg daily) ribavirin in genotype 1 patients for 24 weeks. This study revealed that 32% (8/25) of subjects in the weight-based dosing arm became anemic (haemoglobin ≤10.9 g/dL) and 6 subjects required dose reductions [23]. Similarly, Ruane and colleagues assessed treatment-naive and previously treated patients with genotype 4 HCV of Egyptian ancestry with sofosbuvir 400 mg and weight-based ribavirin therapy for 12 w (n = 31) or 24 weeks (n = 29). Four patients, all in the 24-week group (13.7%) had at least one hemoglobin level of <10 g/dl, but none had hemoglobin <8.5 g/dl [24].

Although therapy with DAAs is generally safe, adverse events are of particular concern in unstable patients with advanced cirrhosis [10], and issues of safety and tolerance should arise in patients with advanced disease [25]. In this study, we evaluated

the changes in biochemical parameters in cirrhotics versus non-cirrhotics. Cirrhotic patients had a significant rise in mean bilirubin & INR levels (*p* values, 0.04 & 0.01 respectively) and a mean negative change in prothrombin concentration (*p* value 0.02) representing probable worsening of liver functions. As regards liver enzymes elevation, only one cirrhotic patient had more than three folds' elevation of ALT and AST levels at the end of treatment, however achieved SVR for the received regimen (SIM/SOF therapy). None of patients in the current study discontinued treatment due to adverse events.

Moreover, studying the change in biochemical tests in cirrhotics versus non-cirrhotics separately in different regimens revealed that the rise in bilirubin in the SOF/SIM group was significant in non-cirrhotics, with a trend towards significance in the cirrhosis group. The drop in hemoglobin in the SOF/RBV group was significant in both cirrhosis and non-cirrhosis groups; while the reduction in WBCs in the SOF/SIM group was only significant in those with cirrhosis. This observation can point to the probable safer use of SOF/DAC combination than SOF/SIM or SOF/RIB combination in cirrhotic patients being associated with less adverse events; namely elevated bilirubin and decreased WBCs count and haemoglobin values.

5. Conclusions:

Based on liver biochemical profile analysis in our study, we can conclude that DAAs therapy is effective and tolerable in patients with chronic HCV genotype 4 patients. It improves liver necro-inflammatory changes both in cirrhotic and non-cirrhotic patients, evidenced by decreased liver enzymes' level, and that cirrhotic patients still require careful observation during DAAs therapy being the more susceptible for treatment related complications namely hyperbilirubinaemia, and cytopenias.

Key issues:

- Despite promising results of direct acting antivirals (DAAs), efficacy and safety of different DAAs combinations remain in fairly early stages of clinical judgment.
- Real life cons and pros of these medications and indirectly their reflection on patient quality of life are still debatable points.
- In the current study, overall SVR rate was 93.4%.
- In all patient's groups, a decline in ALT and AST was noted reflecting improvement of necroinflammatory activity.
- In cirrhotic subgroup, rise in BIL and INR was noticed with a decrease in White blood cells, while no change in ALB levels. Additionally, drop in Hemoglobin and platelets was noted with SOF/RBV combination, while BIL rise was noticed with SOF/SIM combination.
- DAAs therapy is safe and effective in genotype 4 chronic HCV patients, however careful observation should be payed to cirrhotic patients being more vulnerable for treatment related complications.

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Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Table 1. Baseline characteristics of participants across the studied treatment regimens

	SOF/DAC ±RBV (n= 64)	**SOF/SIM (n=138)**	**SOF/RBV (n=70)**	**Total (n=272)**	***P* value**
Age (years)	51.16 (11.27)	55.56 (10.69)	54.28 (9.91)	54.19 (10.74)	0.58
Gender Female (%)	30 (46.9%)	41 (29.7%)	25 (35.7%)	96 (35.3%)	0.06
Treatment status Experienced (%)	8 (12.5%)	30 (21.7%)	37 (52.9%)	75 (27.6%)	<0.001*
Liver condition Cirrhotic (%)	18 (28.1%)	45 (32.6%)	45 (64.3%)	108 (39.7%)	<0.001*
ALT IU/l {mean (SD)}	51.18 (35.26)	54.32 (37.36)	60.26 (40.69)	55.25 (37.85)	0.4
AST IU/l {mean (SD)}	45.15 (25.11)	52.61 (31.57)	67.80 (42.81)	55.11 (34.67)	0.0006*
Bilirubin mg/dl {mean (SD)}	0.78 (0.86)	0.84 (0.67)	0.92 (0.53)	0.85 (0.68)	0.5
Albumin g/dl {mean (SD)}	3.89 (0.65)	3.95 (0.54)	3.94 (0.46)	3.94 (0.54)	0.8
SVR 12	**64 (100%)**	**135 (97.8%)**	**55 (78.6%)**	**254 (93.4%)**	**<0.001**

*significant *p* value <0.05

Table2. Comparison of biochemical profile and blood elements at baseline and week-4 on treatment in the whole studied population (n=220)

	Baseline	**Week-4**	***P* value**
ALT IU/l	52.64 (38.05)	23.63 (13.52)	< 0.001*
AST IU/l	49.96 (32.05)	25.61 (14.41)	< 0.001*
Albumin g/dl	3.95 (0.57)	3.89 (0.74)	0.57
Haemoglobin g/dl	13.47 (2.20)	12.95 (2.42)	0.19
WBCs (x10^3/ml)	6.41 (2.29)	6.61 (2.39)	0.5
ANC (x10^3/ml)	3.52 (1.82)	3.47 (1.66)	0.8
Platelets (x10^3/ml)	174.78 (75.74)	177.89 (83.11)	0.7
APRI Median (IQR)	0.6 (0.7)	0.3 (0.4)	0.001*

Data are presented as mean and standard deviation unless otherwise stated

*significant *p* value < 0.05

Table3. Comparison of biochemical profile and blood elements at baseline and end of treatment in the whole studied population (n= 250)

	Baseline	End of treatment	*P* value
ALT IU/l	56.29 (36.53)	26.94(27.13)	<0.001*
AST IU/l	57.44(36.05)	31.29 (24.06)	<0.001*
Albumin g/dl	3.92 (0.52)	3.94 (0.48)	0.71
Bilirubin mg/dl	0.89 (0.67)	0.96 (0.57)	0.27
Haemoglobin g/dl	13.62 (2.09)	13.39 (1.88)	0.12
WBCs	6.11 (2.07)	5.81 (1.99)	0.03*
ANC	3.22 (1.50)	3.27 (1.45)	0.6
Platelets	175.87 (75.61)	180.46 (72.83)	0.39
APRI Median (IQR)	0.6 (0.6)	0.4 (0.4)	<0.001*
AFP ng/ml Median (IQR)	5.95 (9.4)	6.45 (6.23)	0.3

Data are presented as mean and standard deviation unless otherwise stated

*significant *p* value < 0.05

Table 4. Mean difference in biochemical profile values at end of treatment compared to baseline in different treatment groups

	Treatment group	Mean difference	*P* value
ALT IU/l	SOF/DAC ±RBV	- 30.64 (32.71)	<0.001*
	SOF/SIM	-26.61 (48.31)	<0.001*
	SOF/RBV	-31.99 (44.86)	<0.001*
AST IU/l	SOF/DAC ±RBV	-22.02 (22.65)	<0.001*
	SOF/SIM	-24 (41.83)	<0.001*
	SOF/RBV	-31.68 (41.70)	<0.001*
Albumin g/dl	SOF/DAC ±RBV	-0.01(0.74)	0.9
	SOF/SIM	0.02 (0.64)	0.76
	SOF/RBV	0.04 (0.49)	0.5
Bilirubin mg/dl	SOF/DAC ±RBV	0.04 (1.13)	0.8
	SOF/SIM	0.22 (0.38)	0.004*
	SOF/RBV	0.03 (0.53)	0.7
Haemoglobin g/dl	SOF/DAC ±RBV	-0.06 (2.85)	0.8
	SOF/SIM	-0.09 (1.80)	0.7
	SOF/RBV	-0.65 (1.49)	0.0006*
WBCs (x10^3/ml)	SOF/DAC ±RBV	-0.01 (2.05)	0.9
	SOF/SIM	-0.48 (2.20)	0.01*
	SOF/RBV	-0.09 (1.50)	0.7
Platelets (x10^3/ml)	SOF/DAC ±RBV	16.12 (93.67)	0.2
	SOF/SIM	7.23 (89.40)	0.4
	SOF/RBV	-7.43 (41.30)	0.14

Data are presented as mean and standard deviation

*significant *p* value < 0.05

Table 5. Change in liver biochemical profile and blood picture at the end of treatment in cirrhotic patients versus non-cirrhotic

		Mean difference (SD)	*P* value
Bilirubin mg/dl	Cirrhotic	0.14 (0.49)	0.04*

	Non-cirrhotic	0.02 (0.99)	0.8
INR	Cirrhotic	0.10 (0.23)	0.01*
	Non-cirrhotic	0.001(0.34)	0.9
PC (%)	Cirrhotic	-8.66 (20.48)	0.02*
	Non-cirrhotic	-4.669 (24.22)	0.12
Albumin g/dl	Cirrhotic	0.04 (0.56)	0.5
	Non-cirrhotic	-0.03 (0.69)	0.69
Hemoglobin g/dl	Cirrhotic	-0.44 (2.03)	0.06
	Non-cirrhotic	-0.25 (1.87)	0.2
WBCs	Cirrhotic	-0.69 (2.06)	0.007*
	Non-cirrhotic	-0.02 (2.02)	0.9
Platelets	Cirrhotic	1.28 (73.99)	0.9
	Non-cirrhotic	10.33 (80.14)	0.2

Data are presented in mean and standard deviation

*significant p value < 0.05

Table 6. Change in liver biochemical profile and blood picture at the end of treatment in cirrhotic patients versus non-cirrhotic by treatment regimens

			Mean difference	***P* value**
Bilirubin mg/dl	SOF/DAC ±RBV	Cirrhotic (no=12)	0.19 (0 .56)	0.2
		Non-cirrhotic (no= 32)	-0.03 (1.33)	0.9
	SOF/SIM	Cirrhotic (no= 8)	0.31 (0.39)	0.06
		Non-cirrhotic (no=19)	0.21 (0.36)	0.02*
	SOF/RBV	Cirrhotic (no=37)	0.08 (0.48)	0.3
		Non-cirrhotic (no=14)	-0.11 (0.63)	0.5
Albumin g/l	SOF/DAC ±RBV	Cirrhotic (n=14)	-0.03 (0.47)	0.8
		Non-cirrhotic (n= 29)	-0.06 (0.87)	0.7
	SOF/SIM	Cirrhotic (n=29)	0.09 (0.66)	0.4
		Non-cirrhotic (49)	-0.03 (0.62)	0.7
	SOF/RBV	Cirrhotic (no=31)	0.035 (0.49)	0.7
		Non-cirrhotic (no=12)	0.07 (0.50)	0.6
Haemoglobin g/l	SOF/DAC ±RBV	Cirrhotic (no=13)	0.42 (3.69)	0.7
		Non-cirrhotic (no=29)	-0.32 (2.46)	0.5
	SOF/SIM	Cirrhotic (no=18)	-0.65 (1.51)	0.08
		Non-cirrhotic (no=36)	0.14 (1.40)	0.5

	SOF/RBV	Cirrhotic (no=45)	-0.59 (1.46)	0.009*
		Non-cirrhotic (no= 24)	-0.75 (1.58)	0.03*
WBCs ($x10^3$/ml)	SOF/DAC ±RBV	Cirrhotic (no=17)	0.18 (2.03)	0.7
		Non-cirrhotic (no=41)	-0.09 (2.11)	0.77
	SOF/SIM	Cirrhotic (no=42)	-0.899 (2.03)	0.007*
		Non-cirrhotic (no=74)	-0.09 (2.21)	0.7
	SOF/RBV	Cirrhotic (no=8)	-1.48 (1.84)	0.06
		Non-cirrhotic (no=25)	0.35 (1.08)	0.11
Platelets ($x10^3$/ml)	SOF/DAC ±RBV	Cirrhotic (no=12)	34.47 (90.65)	0.21
		Non-cirrhotic (no=33)	11.04 (97.76)	0.5
	SOF/SIM	Cirrhotic (no=35)	6.80 (96.62)	0.7
		Non-cirrhotic (no=56)	13.97 (81.52)	0.2
	SOF/RBV	Cirrhotic (no=45)	-11.87 (39.39)	0.05*
		Non-cirrhotic (no=25)	0.87 (44.30)	0.9

Data are presented in mean and standard deviation

*significant p value ≤ 0.05