

Effect of sofosbuvir on some renal and cardiac functions in HCV patients in Egypt

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Abstract

Background: Chronic hepatitis C virus (HCV) infection is associated with many metabolic complications. Treatment of chronic HCV infection is transitioning from IFN-based to IFN-free regimens that composed of directly acting antiviral (DAA) agents. These DAAs therapy used for patients with a normal range of serum creatinine and glomerular filtration rate. Sofosbuvir (SOF) is one of the highly efficacious and well tolerated DAAs therapy that is primarily eliminated in the urine therefore, poses a challenge for its use in HCV patients with significant renal disease. This study was conducted to monitor the effect of oral treatment of pre-diagnosed HCV patients with 400 mg/d of sofosbuvir for 12 weeks on some kidney functions and cardiac enzymes in concomitant to lipid profile alterations.

Results: This study revealed a mild changes in the creatinine levels of both male and female groups, however serum uric acid showed a highly significant increase at male groups. A gradual elevation in the sodium levels were reported in all groups that accompanied with a non-significant increase in the potassium levels. Meanwhile, calcium level showed a significant decrease especially in the female group. A highly significant decrease in the phosphorus level noticed at all studied groups. The treatment-experienced patients with sofosbuvir showed many changes in lipid profile like highly significant increase at total cholesterol level, triglycerides, low-density lipoprotein-cholesterol (LDL-C) and very low-density lipoprotein-cholesterol (VLDL-C) while significant decrease in high-density lipoprotein-cholesterol(HDL-C) at all treated groups were reported. Both of creatine kinase (CK) and Lactate dehydrogenase (LDH) showed a significant decrease in the young female group (IV). On contrary, a significant increase in CK levels at old age male group (III) were revealed.

Conclusion: These results suggest that robust studies need to be conducted to confirm the efficacy and safety of sofosbuvir with dose adjustment in patients with renal or cardiac impairments.

Keywords: HCV, kidney diseases, sofosbuvir, lipids, antiviral therapy, egyptian patients

1. Introduction

Patients with chronic hepatitis C virus (HCV) infection and advanced liver disease have a poor and limited treatment options ^[1]. There is an urgent medical need for safe and effective treatments for patients with advanced liver disease. To date, few clinical trials have included patients with decompensated liver disease and the effect of sustained virologic response on liver-related function. Sofosbuvir Sofosbuvir (SOF) is a nucleotide analog inhibitor that approved recently for the treatment of HCV ^[2].

Sofosbuvir is a component of the first all-oral, interferon-free regimen approved by FDA for treatment of chronic hepatitis which inhibits the RNA polymerase that used by the hepatitis C virus replication ^[3]. SOF is initially activated in the liver and converted into an inactive metabolite that excreted by the kidney that poses a challenge for using in HCV patients with significant renal disease ^[4]. Many trials have assayed a wide range of sofosbuvir-based options on HCV-treatments, as a monotherapy or combined with ribavirin (RBV) with or without pegylated interferon alfa-2a ^[5]. However, the main drawback of the sofosbuvir- based treatment regimens is that their use has been studied only in patients with estimated normal glomerular filtration rate, and there is a concern about cardiac and hepatobiliary toxicity in patients with kidney diseases ^[6].

Overall, the use of SOF appears safe with few significant toxicities reported. However, potential cardiotoxicity has been reported in patients taking SOF along with amiodarone ^[7]. It is unclear if the increased exposure to SOF could lead

to increased cardiovascular toxicity ^[8]. Cardiac functional effects of DAA-based HCV elimination can be directly related to the infection since the new DAA drugs are devoid of the interferon unspecific side-effects upon cardiac function ^[9, 10]. The detection of cardiotoxic changes associated with many DAAs used for chronic HCV infection treatment were determined. The frequency of cardiac dysfunction after treatment suggests possible drug-related cardiotoxicity that exhibited recovery of cardiac function after ending of treatment period ^[11]. Many studies of HCV with cardiomyopathy are, by nature, unable to resolve the clinical key question if there is a true cause-effect relationship between HCV and cardiac dysfunction ^[12, 13 & 14]. In general, this study was carried out to evaluate the effect of drug combinations on some renal and cardiac functions.

2. Materials and Methods

2.1. Patients

Blood samples were obtained by venipuncture from peripheral blood of humans at Nasr city health insurance hospital, Nasr city, Cairo, Egypt. This study was performed after taking consent from all patients and the healthy volunteers with approval of the Ethical Committee of Nasr City Health Insurance. Fifty healthy control individuals and 200 patients with clinically diagnosed hepatitis C virus (HCV) were included in this study with age 21 to 60 years old. The HCV infection was clinically diagnosed or performed according to to Supreme Council and NCCVH.

Cases with other chronic diseases such as heart disease, kidney failure, cancer, and autoimmune diseases have been excluded.

2.2 Experimental design

The blood samples were divided into five groups as follows:

Group I (Control Group): Fifty blood samples were collected from normal humans.

Blood samples from pre-diagnosed patients with hepatitis C virus (HCV) were differentiated into:

Group II: Fifty male HCV patients with age from 21: 40 years old.

Group III: Fifty male HCV patients with age from 41: 60 years old.

Group IV: Fifty female HCV patients with age from 21: 40 years old.

Group V: Fifty female HCV patients with age from 41: 60 years old.

Blood samples were collected at standard time intervals from all groups: after one month (the first dose), two months (the second dose), three months (the third dose) of 400 mg/day of sofosbuvir administration and finally after 3-6 months of the end of treatment, the treatment regimen was consistent with the protocol of the Egyptian National Committee for Controlling HCV (NCCVH).

The samples were collected from patients and healthy volunteers into sterile tubes, centrifugated at 8000 rpm for 5 min and the sera were kept at sterile tubes until used for various biochemical analyses.

2.3 Physiological parameters

Serum creatinine, urea, and uric acid levels were detected according to the methods of *Schirmeister* [15], *Fawcett and Scott* [16], *Barham and Trinder* [17], respectively. However, sodium (Na), potassium (K⁺), calcium (Ca) and phosphorus levels were determined in the serum according to the methods of *Trinder* [18], *Sunderman and Sunderman* [19], *Gindler and king* [20] and *El-Merzabani et al* [21] respectively.

Meanwhile, lipid profile; cholesterol, high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C) and triglycerides, were detected by the methods of *Richmond* [22], *Fassati and Prencipe* [23], *Burstein et al.* [24] and *Wieland and Seidel* [25], respectively. However, very low-density lipoprotein-cholesterol (VLDL-C) was calculated according to Friedewald calculation *Friedewald* [26]. Creatine kinase (CK) and lactate dehydrogenase (LDH) levels were also detected using the method of *Young* [27] and *Meister et al.* [28].

2.4. Statistical Analysis

The results were statistically analyzed using SPSS® software (statistical package for Social Science, version 23, Illinois, USA). Tabulation and graphics of data were done using Microsoft Excel (2016). All data were expressed as means ± standard deviation. The differences between the control and treated groups assessed using one-way ANOVA followed by post-hoc test. The significance probability criterion for each statistical test was significant at $P \leq 0.05$, and highly significant at $P \leq 0.005$.

3. Results

A- Kidney function tests

Our study revealed mild changes in the kidney functions test. Young age groups showed a nonsignificant increase or decrease at groups II and IV during the study except after the administration of 2nd dose as compared to the control group (Table 1). However, groups (III & V) showed significant increase at all doses of administration as represented at the table (1). On the other hand, blood urea level revealed nonsignificant changes after different doses of SOF at all treated groups except group (IV) that showed a significant decrease as represented at the table (1).

Meanwhile, serum uric acid revealed a highly significant increase at male groups (II & III) after different doses in this study as compared to the control group. However, the female groups (IV & V) demonstrated a significant increase in serum uric acid after most of the doses administered during this study (Table 1).

Table1: Evaluation of the effect of 400 mg/day sofosbuvir on the kidney function testes at different time intervals of administration between in the different groups

Parameter	Group /Dose	1 st dose	2 nd dose	3 rd dose	After treatment
Creatinine	Control	0.72 ± 0.25			
	Group II	0.78 ± 0.17	0.79 ± 0.17*	0.77 ± 0.14	0.82 ± 0.15*
	Group III	0.84 ± 0.18*	0.85 ± 0.2*	0.83 ± 0.18*	0.84 ± 0.15*
	Group IV	0.66 ± 0.2	0.69 ± 0.13*	0.75 ± 0.18	0.69 ± 0.1
	Group V	0.84 ± 0.2*	0.86 ± 0.28*	0.83 ± 0.26*	0.83 ± 0.28*
Urea	Control	26.2 ± 7.1			
	Group II	27 ± 5.9	25.2 ± 4.5	26.7 ± 4.3	25.6 ± 4.1
	Group III	26.4 ± 5.7	25.1 ± 6.2	24.5 ± 6	25 ± 5.7
	Group IV	23.4 ± 4.3	23.2 ± 2.4*	22.2 ± 3.1*	23.2 ± 4*
	Group V	26.9 ± 14.2	25.2 ± 9.3	29 ± 16.8	29.1 ± 19.6
Uric acid	Control	3.8 ± 1.01			
	Group II	4.8 ± 0.9**	5.08 ± 1.04**	5.1 ± 0.9**	4.8 ± 0.8**
	Group III	4.8 ± 1.05**	5.5 ± 3.02**	6.4 ± 1.5**	6.8 ± 1.3**
	Group IV	4.02 ± 0.9	4.5 ± 1.03*	4.8 ± 1.4*	4.9 ± 1.4**
	Group V	4.2 ± 0.7	4.5 ± 0.8*	4.7 ± 0.9*	4.4 ± 0.7*

values are expressed as mean ± standard deviation (SD), n=30 sample in each group, * means significantly different as compared to the control group at $P \leq 0.05$. ** means highly significant difference as compared to the control group value of $P \leq 0.005$.

In the current study, serum electrolytes (Na, K⁺, Ca and Ph) were estimated at all studied groups, serum sodium (Na)

level showed nonsignificant decrease after the administration of 1st and 2nd doses of sofosbuvir (SOF) at all

studied groups except at group IV, showed highly significant decrease as compared to the control group as represented at fig (1), while after the administration of 3rd dose serum sodium level showed a nonsignificant increase at groups (II and V), a significant increase at group III and

highly significant increase at group IV. However, after the end of treatment Na showed a nonsignificant increase at male groups and showed a significant increase at female groups as represented at fig (1).

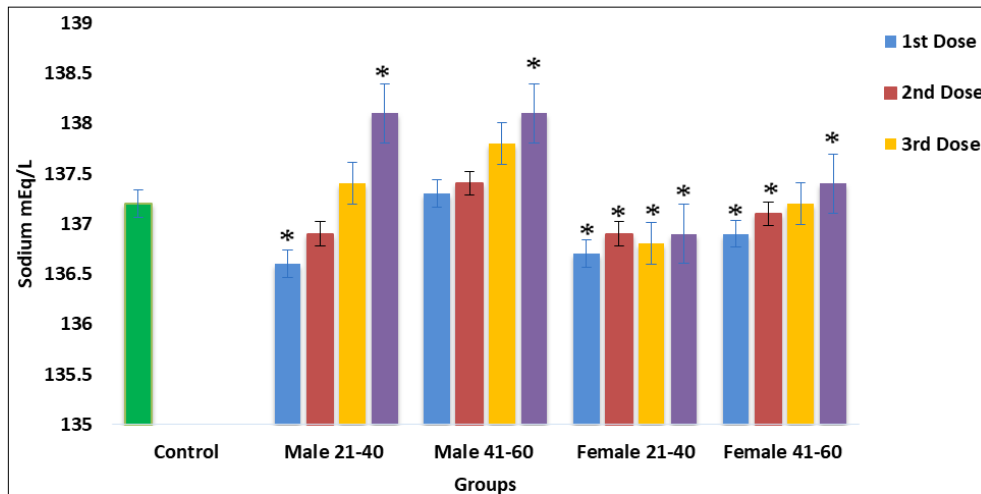


Fig 1: Evaluation of the effect of 400mg/ day sofosbuvir on sodium level at different time intervals of administrations (after one, two, three months and after the end of treatment) at the different groups.

Furthermore, Serum potassium (K⁺) level showed a nonsignificant decrease at group II & V during all doses as compared to the control group (Fig 2). However, at group III K⁺ demonstrated a significant increase after the administration of a 3rd dose of SOF and after the end of

treatment. Finally, group IV showed a significant decrease only after the administration of the 1st dose of SOF and nonsignificant decrease at the rest of times during the study as compared to the the control group (Fig 2).

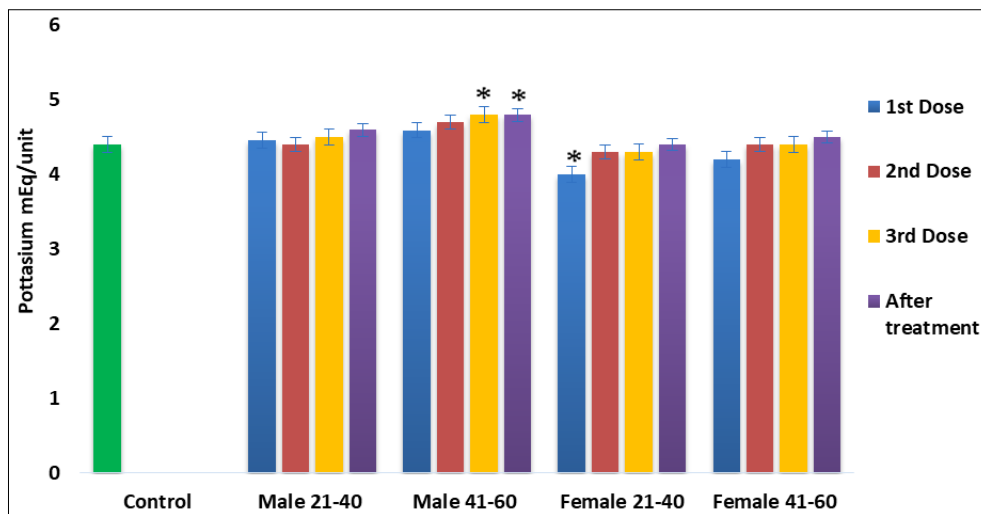


Fig 2: Evaluation of the effect of 400mg/ day sofosbuvir on potassium level at different time intervals of administrations (after one, two, three months and after the end of treatment) at the different groups.

Serum calcium (Ca) showed a nonsignificant decrease at male groups (II & III) during all times of the study as compared to the control group (Fig 3). While at the young female group (IV) it demonstrated significant decrease

during all times. Addition to highly significant decrease at the old female group (V) at all times during the study as represented at fig (3).

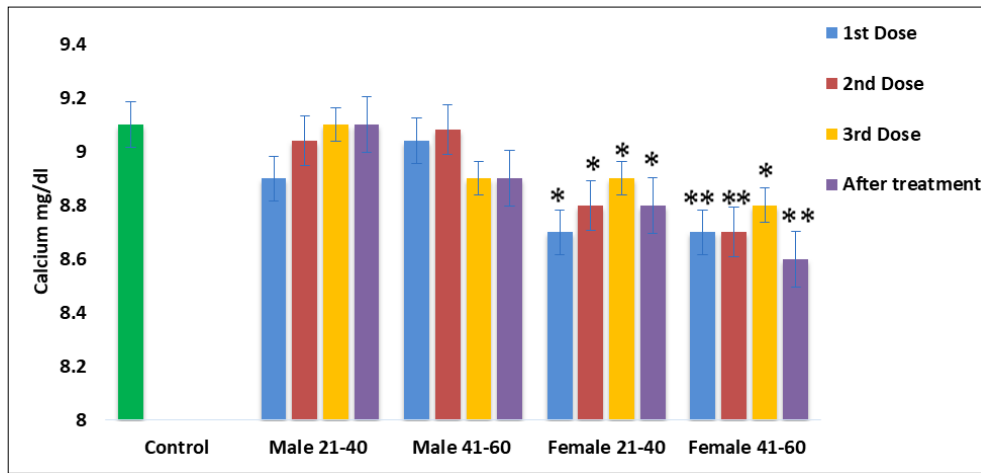


Fig 3: Evaluation of the effect of 400mg/ day sofosbuvir on calcium level at different time intervals of administrations (after one, two, three months and after the end of treatment) at the different groups

Serum phosphorus (Ph) level showed a highly significant decrease at groups (II, IV, and V) during all times of the study as compared to the control group (Fig 4). While it

showed a highly significant increase at group III after the administration of 2nd and 3rd doses of SOF as represented at fig (4).

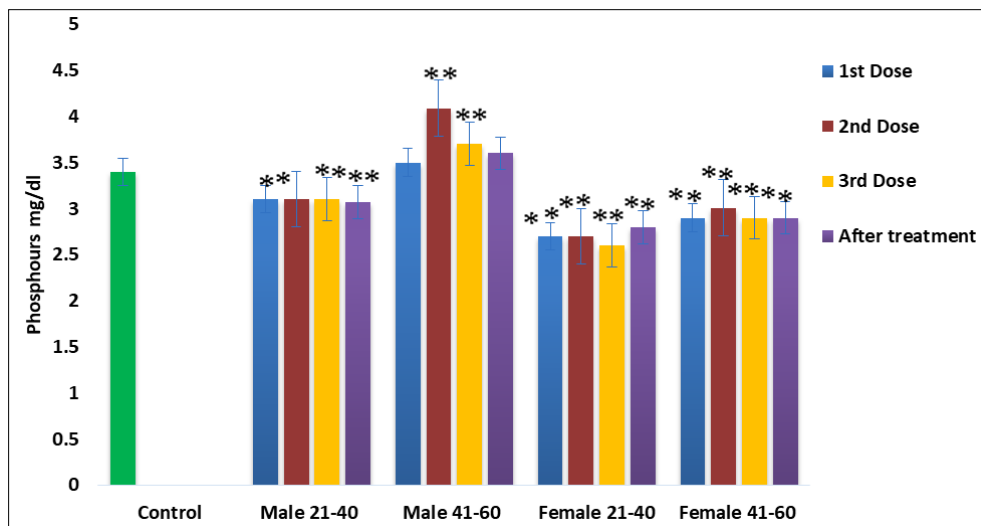


Fig 4: Evaluation of the effect of 400mg/ day sofosbuvir on phosphorus level at different time intervals of administrations (after one, two, three months and after the end of treatment) at the different groups.

On the other hand, our study also explained the effect of SOF administration on lipid profile; Serum total cholesterol (Chol) showed a highly significant increase during all times at studied groups as compared to the control group (Table 1). However, serum triglycerides (Trig) showed highly significant decrease after the administration of 1st and 2nd

doses of SOF at all studied groups except at group IV which showed a nonsignificant decrease at all times during the study. After the administration of the 3rd dose, Trig showed a significant decrease at groups II and V and also after the end of treatment at group V only as compared to the control group (Table 2).

Table 2: Evaluation of the effect of 400 mg/day sofosbuvir on the lipid profile at different time intervals of administration between in the different groups

Parameter	Dose/Group	1 st dose	2 nd dose	3 rd dose	After Treatment
Chol	Control	116.3 ± 33.03			
	Group II	180.8 ± 42.9**	197.3 ± 50.07**	197.8 ± 42.03**	181.4 ± 38.8**
	Group III	170.6 ± 39.2**	193.2 ± 38.9**	194.7 ± 41.8**	182.6 ± 31.7**
	Group IV	193.4 ± 28.3**	176.7 ± 21.1**	163.4 ± 19.9**	162.2 ± 20.8**
	Group V	177.6 ± 30.3**	197.1 ± 33.9**	192.0 ± 39.2**	177.1 ± 39.5**
Trig	Control	97.3 ± 25.3			
	Group II	143.3 ± 51.4**	123.9 ± 43.4*	116.7 ± 42.3*	114.3 ± 36.7
	Group III	146.9 ± 71.7**	126.5 ± 57.08**	113.06 ± 44.3	105.6 ± 41.9
	Group IV	108.06 ± 45.02	96.7 ± 28.9	89.9 ± 27.3	89.4 ± 26.4
	Group V	142.5 ± 62.1**	132.7 ± 50.5**	120.3 ± 44.2*	110.6 ± 41.7*

HDL-C	Control	48.4 ± 6.2			
	Group II	38.133 ± 7.4**	33.9 ± 6.8**	32.3 ± 6.2**	37.9 ± 5.07**
	Group III	42.9 ± 11.5**	40.9 ± 10.1**	38.8 ± 4.8**	37.3 ± 6.4**
	Group IV	46.2 ± 8.8	45.7 ± 6.5	42.4 ± 6.6**	43.8 ± 5.9**
	Group V	50.1 ± 12.9	47.7 ± 10.5	44.8 ± 9.3*	43.3 ± 7.6**
LDL-C	Control	83.9 ± 8.5			
	Group II	111.1 ± 40.02**	127.2 ± 38.6**	130.2 ± 35.7**	111.2 ± 28.4**
	Group III	103.06 ± 34.7*	119.5 ± 34.06**	125.9 ± 31.8**	117.6 ± 23.6**
	Group IV	124.2 ± 28.3**	108.2 ± 17.06**	99.2 ± 16.4**	97.6 ± 17.4**
	Group V	103.03 ± 32.5*	123.6 ± 34.3**	120.5 ± 34.6**	109.2 ± 36.7**
VLDL-C	Control	19.5 ± 4.3			
	Group II	33.8 ± 15.09**	36.5 ± 13.07**	38.5 ± 8.4**	33.8 ± 6.6**
	Group III	27.3 ± 10.9**	32.4 ± 9.5**	35.6 ± 8.8**	33.4 ± 5.9**
	Group IV	24.3 ± 7.3*	23.3 ± 4.6	23.2 ± 4.7*	22.2 ± 3.8*
	Group V	22.2 ± 6.5	26.06 ± 6.2**	27.4 ± 5.2*	24.01 ± 5.8**

Values are expressed as mean ± standard deviation (SD), n=30 sample in each group, * means significantly different as compared to the control group at P ≤ 0.05. ** means highly significant difference as compared to the control group value of P ≤ 0.005.

High-density lipoprotein cholesterol (HDL-C) showed highly significant decrease during all times at studied groups except at female groups (IV & V) showed nonsignificant decrease after the administration of 1st and 2nd doses of SOF when compared to control group as represented in table (1). On contrary, low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) showed a highly significant increase during all times at all studied groups when compared to control group as represented in table (2).

Creatine kinase (CK) showed highly significant increase at groups (III & IV) at all times during the study, while showed a nonsignificant decrease at group II and nonsignificant increase at group V when compared to control group as represented at the table (2). However, lactate dehydrogenase (LDH) showed highly significant decrease only at group IV at all times during the study and showed a nonsignificant decrease at the rest groups during the study V when compared to control group as represented at the table (3).

Table 3: Evaluation of the effect of 400 mg/day sofosbuvir on cardiac enzymes at different time intervals of administration between in the different groups

Parameter	Dose/Group	1 st dose	2 nd dose	3 rd dose	After Treatment
Ck	Control	89.1 ± 22.01			
	Group II	77.5 ± 17.4	80.1 ± 15.4	79.9 ± 15.06	81.5 ± 14.2
	Group III	106.7 ± 42.4**	110 ± 36.6**	112.3 ± 31.5**	112 ± 36.7**
	Group IV	70.8 ± 13.08**	76.3 ± 14.02**	76.8 ± 14.5*	76.2 ± 11.09**
	Group V	86.1 ± 29.5	87.5 ± 26.3	93.4 ± 29.2	91.3 ± 23.5
LDH	Control	268 ± 85.1			
	Group II	244.4 ± 65.3	262.3 ± 69.3	272.1 ± 74.9	277.6 ± 87.1
	Group III	264.6 ± 57.04	284.2 ± 64.6	299.8 ± 56.8*	289.4 ± 48.8
	Group IV	196.7 ± 32.9**	198.4 ± 29.6**	209.4 ± 35.3**	203.6 ± 32.8**
	Group V	274.9 ± 62.6	265.8 ± 53.4	283.2 ± 47.6	283.2 ± 47.7

Values are expressed as mean ± standard deviation (SD), n=30 sample in each group, * means significantly different as compared to the control group at P ≤ 0.05. ** means highly significant difference as compared to the control group value of P ≤ 0.005.

Discussion

HCV and its long-term resultant consequences is a major endemic medical health problem in Egypt. Having taken a representative sample of the country, from both urban and rural areas, an Egyptian demographic health survey conducted in 2008 concluded that 14.7% of the population has been infected, making this the highest prevalence in any population in the world [29].

Extra-hepatic manifestations (such as neoplastic, autoimmune and vascular diseases) occur in about 70% of patients infected by hepatitis C virus (HCV) [30] as well as HCV related inflammation, oxidative stress [31]. Among these manifestations, metabolic disorder, malnutrition and cardiovascular diseases (CVD) are more prevalent in HCV infected patients, but mechanisms are currently unknown [30]. It is well recognized previously that HCV infection can directly (glomerulonephritis and cryoglobulinemic vasculitis), or indirectly (via hepatic cirrhosis) cause renal dysfunction and increases the risk for incident chronic kidney disease (CKD) [32]. As SOF initially converted into

an inactive metabolite that undergoes renal excretion, the use of SOF in HCV patients with significant renal disease represents a particular challenge [33]. With the high need and limited alternatives, increasing the use of SOF in patients with renal dysfunction can be expected. This study was performed to assess the effect of SOF containing regimens in HCV infected patients on some baseline renal function and heart parameters.

Our study showed that serum creatinine demonstrated a significant elevation in old patients groups (III and V), however, no significant change was observed in both young groups (II and VI). This result was in agreement with [34] who reported an overall no significant change in kidney function by the new DAA therapy of HCV. However, serum urea showed non significant changes in all studied groups except for some fluctuations in the young female group. Differently serum uric acid showed a significant increase at the studied groups especially male groups (group II and group III). This come in accordance with Naggie *et al.* [35] who reported an elavation of urine biomarkers and patients

who had treatment-emergent worsening of renal function. *Kawaoka et al.* [36] demonstrated that sofosbuvir was metabolized in the kidney, therefore, the drug is contraindicated in patients with a renal impairment which may lead to renal cell injury, although renal function doesn't affect during the treatment period.

The present study also revealed significant increase at sodium level accompanied with a non-significant increase at potassium level this was in contrast with *Cox-North et al.* [37], who reported that the treatment of sofosbuvir was associated with no significant change in serum electrolytes at patients with renal dysfunctions. It is possible that these changes could be related to increased exposure to SOF metabolites, highlighting the need for prospective pharmacokinetic studies evaluating different doses and dosing regimens.

At female groups, persistent hyponatremia developed with time was obviously observed this may be related with high prevalence of extrahepatic clinical and biological manifestations, lack of blood products, duration of the infection, this hypothesis most likely in agreement with the finding of *Stefanova-Petrova et al.* [38] who reported that fatigue was the most frequent non-specific clinical symptoms in chronic HCV infection in female patients. The elevated fatigue score is probably related to an increase in serum leptin levels which may interact with serotonin neurotransmission, Fatigue can be considered a part of the clinical picture of HCV-associated cryoglobulinemia developed during treatment with DDA.

The present work also demonstrated decrease at calcium and phosphorus levels during treatment period, while the most decrease was at female groups. The contrast of findings between male and female subjects may be because of sex-based differences in the practice of circumcision: boys are sometimes circumcised in groups at communal ceremonies, whereas girls are generally circumcised individually [39].

Another hypothesis, that severe vitamin D deficiency was an independent risk factor for the presence of mixed cryoglobulins in a cohort of patients with chronic HCV infection in various stages of the disease. However, it is noteworthy that a high prevalence of vitamin D deficiency was found increased during the treatment period, it is well known that vitamin D apart from its classical role as a key regulator of calcium homeostasis as reported by *Gentile et al.* [40]

The main finding of our study is that was hyperlipidemia and hypercholesterolemia which was clear at all treated groups which in agreement with *Morales et al.* [41] who estimate lipid profile in HCV treated with Sovaldi patients 6 months before and after treatment and found that there was significant hyperlipidemia and also increase in total cholesterol level and LDL-C.

Also, *Meissner et al.*, [42] demonstrated rapid changes in serum lipoprotein particle concentration during treatment infected patients with SOF with observed rapid increase at LDL-C and decrease in VLDL, these changes reflected a shift in lipid metabolism in the setting of inhibition of HCV replication and implicate a direct viral effect on serum lipoprotein concentrations.

The increase in LDL-C we observed after the suppression of HCV was suggesting a direct effect of viral suppression. Whereas larger LDL-C particle size is associated with decreased cardiovascular risk, the changes observed in particle size here using the NMR Lipid Profile were

transient and returned to pretreatment values after the end of treatment. As such, the observed changes likely reflect a physiological response to viral clearance, and any impact of viral clearance on atherosclerotic potential requires assessment in larger cohorts followed longitudinally.

In the current study, the effect of DAAS (sofosbuvir) treatment regime of HCV infection was evaluated and their effect on potential cardiac toxicity focusing on cardiac muscles affection was assessed. However, the use of DAAs has raised some concerns about the possibilities of cardiac toxicity during the treatment which resolves after stopping the treatment without leaving any permanent cardiac damage, recent studies reported death for cardiac causes after administration of a sofosbuvir metabolite at blood concentrations much higher than the therapeutic index used in humans [43]. Currently, there is a lack of data on the effects of sofosbuvir on heart function. Such data are important to confirm the safety of sofosbuvir because we are currently treating aging populations with a significant prevalence of heart diseases. Our study showed significant increase at cardiac enzymes especially at group III (male 41-60 y) this in agreement with *Biomy et al.*, [44] who reported an increase in CK level with no cardiac complication or symptoms of any cardiac dysfunctions.

These findings were also in agreement with a previous report confirming that the patient developed myocarditis after starting the treatment with DAAs associated with a reduction in the LV EF and in RV systolic function [45].

Our study also revealed nonsignificant increase at Lactate dehydrogenase (LDH) as cardiac enzyme except at young female group (IV), these findings in agreement with *Tadokoro et al.* [45] who reported non-significant changes during treatment period at old male patients. while *Linetal* [46], was reported significantly elevated lactate dehydrogenase at lymphoma patients. Also, *Ewers et al* [47], recorded an elevated level of LDH associated with the treatment of HCV infection at large B-cell lymphoma patients treated with sofosbuvir.

Several potential explanations may account for this observation, the aggressive may be pure coincidence with HCV treatment in regard to timing, development was accelerated by HCV infection and/or treatment. This is supported by the proposed molecular model of multistep. Alternatively, sofosbuvir, a new class of specific nucleotide analog inhibitor of HCV NS5B polymerase, may have had an unwanted effect on multistep lymphomagenesis, even though it is active in treating HCV.

The cardiotoxicity caused by SOF may be attributed to another HCV DAATs, A previous study showed the manifestation of cardio-toxic disorder correlated to the use of DAAs as a medication of chronic HCV [48]. Cardio-toxicity was confirmed in HCV nucleotide-polymerase-inhibitor and HCV NS3 inhibitors [47], rapidly progressive heart failure and cardio-toxicity were later identified [48].

The current results considered of maximum clinical potency that DAAs are becoming significant for hepatitis C medication and the patients exposed to sofosbuvir is supposed to elevate in a proportion that exceeds the number of patients included in the clinical experiment. Interestingly, the possibility of a small absolute risk increase is not excluded by the current evaluation.

Thus, the main goal of this study was to assess and determine the changes associated with treatment with Sovaldi during all treatment period (12 weeks) and the

comparison between male and female at different ages. This aim was achieved by monitoring the data of a specific number of patients from each category.

Conclusion

The clinical observations and experiences from this study demonstrate that full-dose SOF-based regimens can be tolerated and effective with minimal side effects observed in patients with significant renal and cardiac history; We show that in HCV-infected patients treated with SOF-containing regimens, SVR rates are not significantly influenced by baseline renal dysfunction, but more renal and cardiac safety events needed. Also to determine whether this is a direct SOF effect or not. In addition, the mild side effects experienced did not lead to treatment discontinuation in any of patients. Additional longitudinal studies, are needed to confirm our findings, would help to clarify the riskgroups and the need for close monitoring for renal and cardiac safety events during treatment.

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