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Original Article

Effect of direct acting antiviral therapy of Chronic Hepatitis C virus on insulin resistance and Type2 DM in Egyptian patients (prospective study)

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ABSTRACT

Background and objectives: sustained virologic response (SVR) can be achieved in high percentage of HCV patients with the availability of direct acting antiviral agents DAAs. However, the effect of DAAs on insulin resistance and T2DM has yet to be clearly documented in spite of higher prevalence of T2DM in chronic HCV patients. This study tested the hypothesis that eradication of HCV is associated with either complete recovery or improvement of the symptoms of IR and T2DM.

Patients and methods: In our study 240 Chronic HCV patients candidate to centers of NCCVH with Coordination to departments of internal medicine and clinical pathology, Zagzig University for treatment with DAAs. Measurement of HbA1c, FPG and fasting insulin hormone and calculation of HOMA-IR before and 3 months after DDAs therapy is done. Statistical analysis was done for these data.

Results: After SVR; HbA1c decreased from 7.6 ± 0.69 to 6.7 ± 0.78 in diabetic group and from 5.8 ± 0.5 to 5.1 ± 0.3 in non-diabetic group, with decreased in the percentage of uncontrolled T2DM patients from 22.4% to 5.2% after treatment. HOMA-IR decreased in diabetic group from 4.9 ± 0.7 to 3.7 ± 0.75 and in non-diabetic group from 3.1 ± 0.56 to 2.3 ± 0.4 with complete improvement of IR to ≤ 2.5 in 20.7% of diabetic patients. 20% of diabetic patient needed to decrease oral hypoglycemic dose and 13.3% of them needed to decrease insulin dose.

Conclusions: This study shows that eradication of HCV by DAAs will result in a parallel decrease in IR and improve clinical outcomes in patients with established T2DM.

1. Introduction

Chronic Hepatitis C virus (HCV) has worldwide distribution. On average, 2–3% of the world's population is infected with HCV. The highest prevalence was reported in Egypt (10%) according to the Egyptian health issues survey (EHIS) in 2015 [1]. Some studies revealed that T2DM is four times more common in patients with HCV than in control patients without liver disease or in patients with other liver [2]. An estimated 47 million individuals worldwide have type 2 diabetes mellitus (T2DM) secondary to chronic HCV infection [3]. Insulin resistance (IR) is a pathophysiological state and is more common in patients with chronic HCV infection and has been associated with increased disease severity, extra hepatic manifestations and decreased response to antiviral therapy. Understanding the basis of such associations is of paramount importance to predict and follow up T2DM and IR [4]. IR occurs in approximately 30%–70% of persons with chronic HCV but in only 10%–25% of the general population [3] . This association has been described in cirrhotic as well as in non-cirrhotic patients with HCV infection [5].

The clinical impact of successful direct-acting antiviral agents (DAAs) on the long-term outcome of T2DM in diabetics with chronic HCV remains largely unknown. This is mainly due to the lack of prospective studies that specifically address this important issue [6,7].

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Aim of the work: This study aims to predict the impact of eradication of HCV by DDAs on IR and T2DM.

1.1. Patients and methods

Study design: This Prospective case control study was carried out in the centers of National Committee for Control of Viral Hepatitis (NCCVH) in Sharkia governorate **(Egypt)** with Coordination to departments of internal medicine and clinical pathology, Zagazig University during period from January 2017 to January 2018.

Patients: 240 Chronic HCV patients' candidate for treatment with DAAs after fulfillment the inclusion and exclusion criteria according to NCCVH Treatment Protocol Update, November 2015. Patients are divided into two groups: ***Non-diabetic Group (A):*** as a ***Control***, it includes 120 non-diabetic chronic HCV patients. ***Diabetic Group (B):*** This group consists of 120 diabetic chronic HCV patients. All patients treated with Sofosbuvir + daclatasvir with or without ribavirin for 12 weeks then followed up for another 12 weeks ***(NCCVH treatment protocol 2015)***.

Inclusion criteria; Informed Medical consent; HCV-RNA positivity; Age: ≥ 18 and Patients' ≥ 65 years old should underwent cardiological assessment prior to therapy by ECG, echocardiography and cardiological consultation and **non-cirrhotic patients or cirrhotic patients up to child score 8**.

Exclusion criteria;Child score< 8 cirrhotic patients; platelets count >50000/mm3**;** HCC or Extra-hepatic malignancy and inadequately controlled DM (HbA1c > 9).

Methods: All patients included in this study were subjected to: **thorough history** taking, complete **physical and clinical** examination, calculation of body mass index, Pelvi-abdominal ultrasound and ECG for patient ≥65 years as a cardiological assessment.

Samples collection: Blood was collected by venipuncture, and drown into; EDTA tube; Citrate tube for CBC and PT respectively; and into plain tube for other investigations; where serum was separated and can be frozen at −20 °C for 3 months prior to assay.

1.1.1. Laboratory investigations including

CBC *(by Sysmex KX-21 N)*, ALT, AST, serum albumin, total bilirubin, S. creatinine and Fasting blood glucose before and 3 months after HCV treatment *(By auto analyzer dimension RLX, Siemens, USA)*. Prothrombin time, concentration and INR *(by Coadata, Germany)*. HCV antibody, HBs antigen by Elisa technique and Quantitative PCR for HCV RNA before treatment and 3 months later for SVR by Real-time PCR *(Rouche diagnostics, Switzerland)*. **HbA1c** is done, before and 3 months after the treatment, by using the Tina-Quant turbidimetric inhibition immunoassay *(on a Hitachi 911 autoanalyzer, Roche Diagnostics, Indianapolis, IN)*. Fasting **insulin** hormone before and 3 months after the treatment: By using DRG Insulin ELISA kits EIA-2935 Ver. 9.0 (2016). *(DRG International, Inc., USA, 841 Mountain Ave., Springfield)*. **Insulin resistance** was calculated for all patients before and 3 months after the treatment by using homeostatic model assessment of insulin resistance (HOMA-IR):

[Fasting insulin level (μUnits/ml) × fasting glucose level (mmol/l)]/22.5 or.

[Fasting insulin level (mIU/L) × fasting glucose level (mg/dl)]/405 [8].

IR was considered normal when HOMA-IR was ≤2.5 [9].

-Liver cirrhosis was assessed by Child-Pugh score for Severity of Cirrhosis.

1.1.2. Statistical analysis

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA)).

2. Results

FPG, HbA1c, insulin level and HOMA-IR were significantly lower in non-diabetic patients (p = 0.0001) (Table 1). SVR was achieved by 98.3% in non-diabetic patients and by 96.7% in diabetic patients. As regarding regimen of treatment, SVR was achieved by 98.8% in patients treated with SOF/DAC and by 93.3% in patients treated with SOF/DAC/RBV. While as regard Child-Pugh score; SVR was achieved by 99.1% In patients with Child-Pugh score A and by 80% in patients with Child-Pugh score B (Figs. 1 and 2). There were no significant differences of laboratory paramaters of Diabetic and Non-diabetic patients whom achieved SVR (Tables 2 and 3).

When we compare sugar profile of non-diabetic patients whom achieved SVR and non-responder; there were no significant differences with P-valu > 0.05. In contrast there were significant differences of sugar profile of diabetic patients whom achieved SVR and non-responders to treatment, Non responders have higher values than patients Whom Achieved SVR for FPG (125±7 mg/dl; p = 0.01), HbA1c (8.3 ± 0.35; p = 0.008), insulin level (16.5 ± 2; p = 0.03) and HOMA-IR (5.1 ± 0.94; p = 0.008) (Table 4). There were highly statstical significant differences as regard Child-Pugh score(p = 0.02) and Serum albumin (P = 0.0001),on comparing the responders and non responders (Table 5). When we compare the HbA1c, HOMA-IR before and after HCV treatment in non-diabetic group there were highly statstical significant differences (p = 0.0001) (Table 6).

In diabetic group, there were highly statstical significant differences of HbA1c before and after DAAs therapy (mean decrease

Table 1
Child-Pugh score for severity of liver disease [10].

Parameter	Points		
	1	2	3
Encephalopathy	none	Grade 1-2	Grade 3-4
Ascites	None	Mild to moderate2	Sever
Total bilirubin (mg/dl)	>2	2–3	<3
Serum albumin (g/dl)	˃ 3.5	2.8–3.5	˂ 2.8
Prothrombin time(Sec. over control) or INR	>4 ˂ 1.7	4-6 1.7–2.3	<6 ˃ 2.3

	A- Easy to treat group	B-Difficult to treat group
Criteria	Treatment naïve T. bilirubin ≥1.2 mg/dl. S. albumin ≥3.5 g/dl INR ≥1.2 Plat. count ≥150 × 10^3/mm3	Peg-IFN treatment experienced. Total bilirubin ≥1.2 mg/dl. Serum albumin ≥3.5 g/dl INR ≥1.2 Platelet count >150 × 10^3/mm3
Regimens treat.	Sofosbuvir + daclatasvir	Sofosbuvir + daclatasvir + ribavirin
Timeof ttt	12 weeks	12 weeks

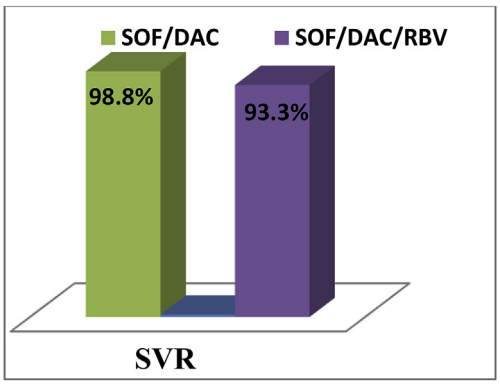

Fig. 1. SVR as regard treatment protocol.

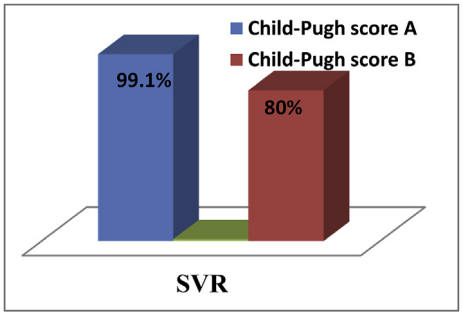

Fig. 2. SVR as regard Child-Pugh score.

from 7.64 ± 0.69 to 6.78 ± 0.81; and p = 0.0001). Fortunately there were decreased percentage of uncontrolled T2DM patients from 22.4% before DAAs therapy to 5.2% after treatment and also, there were significant differences of HOMA-IR before and after DAAs therapy (mean decrease from 4.9 ± 0.7 to 3.7 ± 0.75 and p = 0.0001) with complete improvement of IR to ≤ 2.5 in 20.7% (Table 7). After three months of DAAs therapy, 20% of diabetic patients needed to decrease oral hypoglycemic dose and 13.3% of them needed to decrease insulin dose. Unfortunately 6.7% of them needed to increase oral hypoglycemic dose.

As regarde child Pugh score of diabetic patients, there were significant decrease in the FPG, insulin level, HOMA-IR and HbA1c before and after DAAs therapy in patients with child-Pugh score A ($p < 0.05$), but in patients with Child-Pugh scor B the changes were statsticaly insignificant (Table 7).

As regard treatment protocol,there were significant differences in sugar profile before and after therapy with SOF/DAC and SOF/DAC/RBV with p value < 0.05 (Table 8).

3. Discussion

Chronic HCV infection affects 2–3% of the world population and is a primary cause of liver morbidity and mortality including liver cirrhosis and HCC [3].

It is now widely recognized that chronic HCV is a metabolic disease that is strongly associated with T2DM and IR [11].

Several epidemiological studies on the seroprevalence of HCV have shown higher prevalence in diabetic patients than in controlled [12]. This association has been described in cirrhotic as well as in non-cirrhotic patients with HCV infection [13].

IR can occur early in the course of HCV infection, independent of BMI, viral load and the severity of liver disease [14].

The high therapeutic efficacy of novel antivirals ensured that large number of diabetic cirrhotic patients achieved eradication, this enabled us to understand the relative contribution of the virus on T2DM outcome [6].

HOMA-IR is a valid and reliable surrogate measure of insulin resistance and can give a more physiological estimate of glucose homeostasis [15].

HbA1c is a standard biomarker of long term glycemic control and plays a critical role in the management of diabetic patients and correlates well with both micro- and macro-vascular complications [16]. In this study we thought that as HCV is directly involved in the development of IR and T2DM and its eradication by DAAs will result in a parallel improvment in IR and decreases the risk of onset of T2DM in predisposed individuals.

In our Prospective case control study, as regard treatment protocol; SVR was achieved by 98.8% in patients treated with SOF/DAC and by 93.3% in patients treated with SOF/DAC/RBV.

With the agreement of us, ***Welzel et al. (2016)*** [17] stated that SVR rate after 12 weaks was achieved by 97% of patients treated with SOF/DAC and achieved by 96% of patients treated with SOF/DAC/RBV.

In the present study, as regard cirrhotic state, SVR was achieved by 99.1% In patients with Child-Pugh score A and by 80% in patients with Child-Pugh score B.

Table 2
Baseline characteristics of the patients.

	Diabetic (No = 120)	Non-diabetic (No = 120)	*t*	*p*
	X±SD	X±SD		
Age (year)	52.1 ± 8.4	50.4 ± 9.4	1.1	0.28 (NS)
BMI	28 ± 3	27.3 ± 2.5	1.4	0.17
Hemoglobin (g/dl)	11.6 ± 1.2	11.9 ± 1.3	01.5	0.12
Platelets ($x10^3/mm^3$)	164 ± 53	167 ± 42	0.38	0.7
WBC (103/mm3)	5.6 ± 1.2	5.4 ± 0.9	1.4	0.18
AST (U/L)	16 ± 3.3	15.4 ± 3.6	1.2	0.25
ALT (U/L)	16.5 ± 3.4	15.4 ± 3.5	1.8	0.07
Albumin	3.7 ± 0.47	3.8 ± 0.4	0.65	0.51
Total bilirubin	0.87 ± 0.2	0.88 ± 0.2	0.18	0.86
INR	1.24 ± 0.19	1.19 ± 0.19	1.6	0.1
Creatinine (mg/dl)	0.73 ± 0.14	0.7 ± 0.14	1	0.32
PCR per thousand	3345 ± 2822	3149 ± 2488	**	0.97
FPG(mg/dl	121 ± 7	98 ± 7	18.7	0.0001(s)
Insulin level	16.1 ± 1.7	13 ± 1.7	9.9	0.0001(s)
HOMA-IR	4.9 ± 0.7	3.1 ± 0.56	14.6	0.0001(s)
HbA1c	7.64 ± 0.69	5.8 ± 0.46	17.4	0.0001(s)

t = *t*-test of significant **Mann-Whitney test NS= Non-significant.

Table 3
Comparison of laboratory finding of responders, Diabetic and non-diabetic, patients.

	Diabetic Responders (No = 116)	Non-diabetic responders (No = 118)	*t*	*p*
	X±SD	X±SD		
Hemoglobin (g/dl)	11.6 ± 1.2	11.9 ± 1.3	1.5	0.14
WBC (10^3/mm^3)	5.5 ± 0.9	5.4 ± 0.9	1.1	0.27
Platelets (x10^3/mm^3)	166 ± 52	167 ± 42	0.19	0.85
AST (U/L)	16 ± 3.38	15.±3.6	1.08	0.28
AlT (U/L)	16.6 ± 3.4	15 ± 3.5	1.8	0.07
Albumin	3.76 ± 0.054	3.77 ± 0.05	0.2	0.83
Total bilirubin	0.88 ± 0.2	0.87 ± 0.23	0.01	0.98
INR	1.2 ± 0.2	1.19 ± 0.19	1.5	0.13
Serum creatinine (mg %)	0.74 ± 0.14	0.71 ± 0.14	1.15	0.25
PCR per thousand	3123 ± 2794	3158 ± 2493	[a]	0.88

[a] Mann-Whitnney *U* test.

Table 4
Comparison of sugar profile of non-diabetic &diabetic patients; responders and non-responder.

Sugar profile	N-DM No, = 118 R X±SD	N-DM No, = 2 NR X±SD	t X±SD	p	DM No, = 116 R X±SD	DM No, = 4 NR X±SD	t X±SD	p
FPG(mg/dl) before	98 ± 7	92	0.82	0.41	121 ± 6.7	129 ± 7	1.6	0.1
FPG(mg/dl) after	91 ± 5.5	91	0.03	0.97	112.6 ± 6.6	125 ± 7	2.7	0.01(s)
Insulin level before	13 ± 1.7	12	0.58	0.56	16 ± 1.8	17 ± 1.4	0.68	0.52
Insulin level after	10.23 ± 1.3	10	0.19	0.85	12.6 ± 2.4	16.5 ± 2	2.2	0.03(s)
HOMA-IR before	3.14 ± 0.6	2.72	0.75	0.45	4.8 ± 0.68	5.4 ± 0.74	1.18	0.24
HOMA-IR after	2.3 ± 0.38	2.25	1.9	0.85	3.5 ± 0.8	5.1 ± 0.94	2. 7	0.008(s)
HbA1c before	5.78 ± 0.47	5.6	0.38	0.7	7.6 ± 0.69	8.2 ± 0.5	1.07	0.29
HbA1c after	5.1 ± 0.3	5.1	0.1	0.9	6.7 ± 0.8	8.3 ± 0.35	2.7	0.008(s)

N-DM: non diabetic R: responders NR: non responder DM:diabetic.

Table 5
Comparison of demographic, clinical laboratory parameters of non-responder and responder patients to DAAs.

Laboratory finding	Non-responder (n = 6)	Responder (n = 234)	***t***	***p***
	X±SD	X±SD		
Age	53.3 ± 11.8	51.2 ± 8.9	0.4	0.8
BMI	26 ± 0.4	27.8 ± 2.8	1	0.3
Sex no (%)				
Male	1(33)	65(55.6)	f	0.58
Female	2(67)	52(44.4)		
Child-Pugh score, no (%):				
A	1(33%)	109(93.2%)	f	0.02(s)
B	2(67%)	8(6.8%)		
Hemoglobin (g/dl)	11 ± 0.47	11.8 ± 1.2	0.6	0.5
WBC (10^3/mm^3)	7.8 ± 2.7	5.1 ± 0.7	1.1	0.25
Platelets (x10^3/mm^3)	113 ± 24	167 ± 48	1.9	0.054
AST (U/L)	15.6 ± 1.5	15.8 ± 3.5	0.05	0.96
ALT (U/L)	16 ± 0	15.9 ± 3.5	0.1	0.9
Serum Albumin	2.8 ± 0.6	3.8 ± 0.4	4	0.0001(s)
Total bilirubin	0.63 ± 0.06	0.72 ± 0.14	0.7	0.48
INR	1.32 ± 0.09	1.2 ± 0.14	0.92	0.36
Creatinine (mg/dl)	0.6 ± 0.06	0.72 ± 0.14	1.1	0.26
PCR per thousand	5948 ± 3017	3185 ± 2612	[a]	0. 1
Insulin	15 ± 3	14.6 ± 2.3	0.58	0.56
HOMA −IR	4.5 ± 1.6	4 ± 1	0.8	0.4
HbA1c	7.30 ± 1.5	6.7 ± 1.1	0.9	0.3

[a] Mann-Whitnney *U* test.

Whatever the diference in numbers, both of ***Doss et al., (2015)*** [18] and ***Lionetti et al., (2018)*** [19] agreed us in that patients with cirrhosis at baseline had lower rates of SVR (63% 12 weeks, 78% 24 weeks and 91.5%) than those without cirrhosis (80% 12 weeks, 93% 24 weeks and 83.3), respectively [20,21]**.** In our study, by comparing basic demographical and laboratory parameters of non-responders and responders patients there was difference as regard serum albumin, Child-Pugh score, platelets, HOMA−IR, HbA1c but by Logestic regression analysis to predict non-responders patients only serum lbumin is statsticaly significant with (P = 0.04). Also in our study most of non-responders were have child scor B.

Our results was agreed with that of ***Welzel et al.*****, (2016)** [17] which stated that the SVR was lower in patients with Child−Pugh C and correspondingly, indicators of advanced liver disease such as low platelet count or low albumin level were associated with increased risk of failure**.** Also, ***Hum et al, (2017)*** [22] showed that

Table 6
Comparison of sugar profile before and after DAAs treatment.

	Diabetic group		t	p	Non-Diabetic Group		t	P
	Before	After			**Before**	**After**		
HbA1c%	7.6 ± 0.69	6.7 ± 0.78	18	0.0001 (s)	5.8 ± 0.5 (5–6.5)	5.1 ± 0.3 (4.5–5.7)	17	0.0001 (s)
X*±*SD	6–9.5	5.2–8.6						
Range	45 (77.6%)	55(94.8%)						
Controlled ≤8	13 (22.4%)	3(5.2%)						
Uncontrolled >8								
HOMA-IR	4.8 ± 0.7	3.5 ± 0.8	17	0.0001 (s)	3.1 ± 0.56	2.3 ± 0.4	16	0.0001 (s)
X* ±*SD	3.32–6.9	2.49–6			2.2–4.35	1.78–3.27		
Range	-	12(20.7%) 46(89.3%)						
Normal value ≤ 2.5 insulin resistant>2.5	58(100%)							

Table 7
Comparison between sugar profile before and after DAAs therapy of diabetic patients regard Child-Pugh classification.

Diabetic patients		Child-Pugh-A (No = 106)		t	p	Child-Pugh-B (No = 14)		t	p
before	after	before	after			before	after		
FPG	121 ± 6.6	111 ± 5.7	14.7	0.0001	127 ± 5	124 ± 6	1.6	0.15	
Insulin level	16 ± 1.6	12.3 ± 2.2	17	0.0001	18 ± 2	16.7 ± 1.7	2.4	0.052	
HOMA-IR	4.7 ± 0.6	3.4 ± 0.7	20.7	0.0001	5.8 ± 0.8	5 ± 0.7	2.4	0.056	
HbAC1	7.6 ± 0.7	6.7 ± 0.8	18.4	0.0001	8.1 ± 0.5	7.6 ± 0.8	1.7	0.13	

Table 8
Comparison of glycemic data before and after therapy of diabetic patients regard treatment protocol.

Diabetic patients	SOF/DAC (No = 80)		t	p	SOF/DAC/RBV (No = 40)		t	p
	before	after			before	after		
FPG	121 ± 6.6	112 ± 5.7	12	0.0001	121 ± 7.4	115 ± 9.3	6	0.0001
Insulin level	16 ± 1.6	12.3 ± 2.2	15.4	0.0001	16.8 ± 2	14.3 ± 2.8	6.7	0.0001
HOMA-IR	4.7 ± 0.6	3.4 ± 0.7	17.8	0.0001	5 ± 0.9	4 ± 1	7.5	0.0001
HbAC1	7.7 ± 0.7	6.7 ± 0.7	17	0.0001	7.6 ± 0.7	6.9 ± 1	5.9	0.0001

patients achieved SVR were less likely to have cirrhosis.

With the main interest of our study, the patients who achieved SVR in both groups (diabettic and non-diabetic) showed significant difference in the sugar profile ($p < 0.05$) before and after DAAs therapy, with decrease in the percentage of uncontrolled T2DM patients. While there were non significant difference in the sugar profile of non-responders patients. A study by ***Ciancio et al, (2018)*** [21] agreed us by stating that diabetic responders patients showed a statistically significant decrease of FPG and HbA1c ($P < 0.001$). With no significant variation in FPG ($P = 0.707$) and HbA1c ($P = 0.780$) In non responders patients. [22–24]**.** In contrary, some studies as Stine **et al, (2017)** [25]**, Chaudhury et al, (2017)** [26] ***and*** **Giordanino et al. (2008)** [27] stated that there were no significant differences when comparing pre-treatment HbA1c to post-treatment HbA1c in responders patients with ($p = 0.268$). These studis may be affected by the lower efficacy of antiviral used (IFN ± RBV), older ages and more advanced liver disease, higher mean BMI, and steatosis as in ***Giordanino et al., (2008)*** study. Or may be attributed to a small number of diabetic participants; besides the insulin determinations and HOMA-IR were not included in a study of ***Chaudhury et al., (2017)*** [26]**.** In our study, the patients who achieved SVR in both groups had significant differences of HOMA-IR ($p = 0.0001$) with 20.7% of diabetic patients achieved HOMA-IR score ≤ 2.5**.** This is going on the results obtained by ***Adinolfi et al, (2018)*** [28].

Controversally, a study showed that HOMA-IR in patients who achieved SVR was not significantly different from baseline ($P = 0.75$). These results done on prediabetic and subclinical diabetic patients; these special populations are in the early phase of glucose abnormalities and all of them had genotype-1**.** However, they observed a significant improvement of beta-cell function at the end of treatment, especially among those who had baseline high IR [29].

In our study, as regarding, RBV intake, there were significant differences in sugar profile in patients receiving RBV and in patients not given RBV.

Ciancio et al.,(2018) [21]**,** go on line with us when analyzed treated patients who achieved SVR according to the type of the medication: a significant decrease of HbA1c levels was observed both in patients receiving RBV ($P = 0.024$) and in patients not given RBV ($P = 0.007$).

In our study there were significant difference of sugar profile before and after DAAs therapy ($p < 0.005$) in patients with child-Pugh score A. But in patients with Child-Pugh scor B the changes were statsticaly insignificant.

Our results was agreed also with study of ***Pavone et al.*** which showed that patients who did not experience improvement of glycaemic control had advanced liver disease with Child-Pugh score B [24] **.**As regarding dose of hypoglycemic agents, In our study; some of diabetic patient who achieve SVR needed to decrease oral hypoglycemic dose and others needed to decrease insulin dose. This was agreed with study of ***Dawood et al.*** **(2017)** [30]**,** which stated that (26.7%) of patients achieving SVR needed to decrease the dose of antidiabetic treatment **.**

Our study had some limitations, as the results issued from the study included a relatively small and selected population and need to be confirmed by larger studies. Also the patients with advanced cirrhosis as patient with Child-Pugh score c not included in our study as those patients excluded from ttt According to the national HCV treatment program.

In conclusion, glycemic control improved in patients with diabetes achieving SVR after DAAs and the patients not only have an improvement in HbA1c level but also less likely to require insulin. Improvement of glycemic control was greater in patients with mild liver disease (Child-Pugh score A) and not related to age, sex, and BMI. These endocrine benefits of SVR provide additional justification for considering antiviral treatment in all patients with diabetes. Future studies are needed to confirm our findings, to determine how durable the SVR-induced improvement in glycemic control is over time, and to assess the long-term effect on complications of diabetes such as nephropathy, neuropathy, and cardiovascular disease.

Conflicts of interest

No conflict of interest exists for any of the authors. There was no funding obtained in the development and writing of this article. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Informed consent was obtained from all patients for being included in the study.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.dsx.2019.07.032.

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