Safety and Efficacy of Direct Acting Antivirals in Chronic Hepatitis C Cirrhotic Patients with Ascitis or Esophageal Varices

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Abstract: Chronic liver injury of any etiology most commonly results in liver fibrosis and eventually cirrhosis and portal hypertension with the attendant risks of decompensated liver failure, hepato-cellular carcinoma (HCC) and death. Therefore, The introduction of direct-acting antiviral agents, has revolutionized the treatment for chronic HCV. Higher cure rates and shorter duration of treatment have been achieved. In our study, we studied safety and efficacy of Daclatasvir and Sofosbuvir combination (±Ribavirin) in chronic hepatitis C cirrhotic patients with ascitis or esophageal varices **Methods:** one hundred Egyptian patients of HCV with cirrhotic liver disease and ascitis or esophageal varices & fifty age matched cirrhotic patients of HCV without ascites or esophageal varices as a control group were subjected to Careful history talking and full physical examination, Routine laboratory investigations for all liver functions, Hepatitis C RNA quantitation using polymerase chain reaction (PCR) before the start of treatment, at end of treatment and twelve weeks after treatment to asses for sustained virologic response and Radiological assessment by; **(**Abdominal ultrasonography) **Results:** There were statistically high significant PCR changes between the two studied groups regarding SVR and positivity ($p < 0.001$), a significant difference before treatment ($p < 0.05$) and a non-significant difference after treatment ($p > 0.05$). All Patients developed response at the end of treatment (end of treatment response 100 %), after three month of the end of treatment, seventy six (76%) of responding patients In Group I develop sustained virological response (SVR) and the other twenty four (24%) of patients were relapsers, and fifty (100%) of responding patients In Group II develop sustained virological response (SVR) with zero % of patients were relapsers. There were statistically significant changes between the results of CTP score in cirrhotic patients with ascites and/or esophageal varices. In group I, before treatment, CTP was 14.7 ± 0.50; after treatment, it was 9.90 ± 1.37 and twelve weeks after treatment, it was 8.81 ± 1.54. There were statistically significant changes between the results of MELD score in cirrhotic patients with ascites and/or esophageal varices. In group I, before treatment, MELD was 23.5 ± 1.3; after treatment, it was 17.4 ± 2.3 and 12 weeks after treatment, it was 13.6 ± 2.7. **Conclusion** 12 weeks of oral treatment with the combination of daclatasvir with sofosbuvir and ribavirin achieved high SVR rates in cirrhotic patients with ascites and/or esophageal varices (Child-Pugh class C disease). Importantly, SVR rates are in general lower in individuals with decompensated cirrhosis compared to those seen in individuals with compensated cirrhosis (CTP class A). Treatment was well tolerated without treatment-limiting pharmacokinetic interactions or toxicities and was associated with improvements in liver function.
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Key words: direct acting antivirals, chronic hepatitis C, cirrhotic patients.

1. Introduction

Hepatitis C virus (HCV) infection, 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 2015 concluded that 6.3% of the population have been infected, making this the highest prevalence in any population in the world.1 In the Nile Delta and Upper Egypt, infection rates can be much higher at around twenty six % and twenty eight %, respectively. With incidence rates between two and six per thousand every year, this leads to an estimated 170,000 new cases every year to add to the 11.5 million patients suffering from the disease.

Patients with chronic hepatitis C virus (HCV) infection with advanced fibrosis or cirrhosis are at increased risk of hepatocellular carcinoma, liver failure, liver transplantation, and both liver-related and all-cause mortality.2.

HCV infection occurs through blood contact (3). Apart from the usual modes of transmission, such as intravenous drug use, the main risk factors for transmission in Egypt historically have included the now archaic parenteral antischistosomal therapy, shared or reused needles, poorly sterilized surgical or dental equipment, and blood transfusions (4). In the

past, it was primarily the use of widespread tartar emetic injections, which were used to treat schistosomiasis in Egypt in the 1950s to the early 1980s, which laid the foundation for the HCV epidemic currently seen. Since it can take up to 20–30 years for HCV infection to become clinically evident, there has been a lag phase of several decades before the problem became apparent. While currently, Egypt is still seeing a few new cases of hepatitis C-related liver disease presenting from the initial antischistosomal campaign, with some patients displaying a lag phase of 40 years before clinical presentation, in practice, poor infection control and equipment sterilization procedures used in medical and dental settings also led and continue to lead to iatrogenic HCV infections to the present day, which further stimulate the spread of the disease and continue to fuel the current epidemic. (3)

Virology of hepatitis C virus:

HCV is a member of the family Flaviviridae and the genus Hepacivirus. The HCV genome is a positive-stranded RNA, which encodes a core protein (C), two envelope glycoproteins (E1 and E2), and several non-structural proteins (NS1, NS2, NS3, NS4A, NS4B, NS5A and NS5B). (5)

Direct acting antivirals in decompensated liver disease:-

DAAs targeting various viral proteins such as the NS5B (sofosbuvir) and NS5A (ledipasvir, daclatasvir, velpatasvir) are in general well-tolerated by individuals with decompensated cirrhosis. In contrast, NS3/4A protease inhibitors such as simeprevir, grazoprevir, and paritaprevir are contraindicated in individuals with decompensated cirrhosis due to increased drug levels as well as post-marketing reports of worsening hepatic decompensation and liver failure in few individuals treated with agents in this class (6). If no contraindications exist (i.e., anemia), concomitant administration of ribavirin is recommended in all individuals with decompensated cirrhosis receiving antiviral therapy with regimens containing DAAs (regardless of the genotype) as it improves SVR (7). The recommended initial dose for ribavirin in individuals with severe hepatic decompensation (CTP class C) is 600mg orally once daily, which can be subsequently increased as tolerated. If ribavirin is contraindicated, extending the duration of therapy from 12 to 24weeks is an alternative for all regimens containing DAAs (8).

We conducted this study to determine the efficacy and safety of Daclatasvir and Sofosbuvir combination (±Ribavirin) in chronic hepatitis C cirrhotic patients with ascitis or esophageal varices.

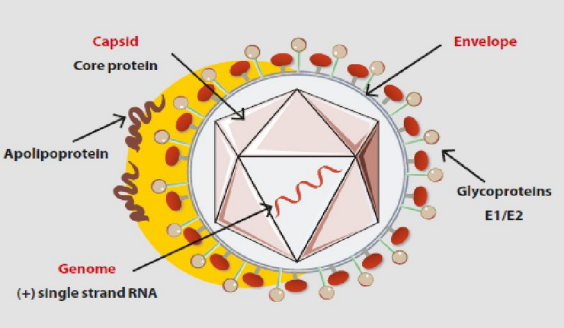

Figure (1): The structure of the hepatitis C virus lipo-viro-particle. E, envelope protein; RNA, ribonucleic acid

2. Patients and methods

Subjects:

This was a cross-sectional The study will be conducted on 100 Egyptian patients of HCV with cirrhotic liver disease and ascitis or esophageal varices selected from GIT outpatient clinics and inpatient wards of Kobry El Qubba Armed Forces Medical Compound and 50 age matched cirrhotic patients of HCV without ascites or esophageal varices as a control group. Patients presented with chronic hepatitis C either accidentally discovered or presented by any symptoms related to liver disease or portal hypertention will be enrolled. This study was approved by the ethical committee of the faculty of medicine, Al-Azhar University at June 2018. Objectives of the study were briefly and clearly described to participants. The written consent to participate or their relatives in the study was done.

The Patients were divided into following groups:

100 Egyptian patients of HCV with cirrhotic liver disease and ascitis or esophageal varices **(group I)** and 50 age-matched cirrhotic patients of HCV without ascites or esophageal varices as a control group **(group II)**.

Inclusion Criteria:

Patients presented with chronic hepatitis C either accidentally discovered or presented by any symptoms related to liver disease or portal hypertention were enrolled.

Exclusion criteria;

Co infection with heptatitis B, Co infection with HIV, Patients with hepatocellular carcinoma and extra-hepatic malignancies.

Control group:

Age matched cirrhotic patients of HCV without ascites or esophageal varices.

Methods:

All patients were subjected to the following;

Careful history talking

Clinical history based on interview with patients and their relatives with special emphasis on:-1-

History of shistosomiasis or exposure to canal water.2- History of frank viral hepatitis or exposure to high risk factors (blood transfusion, operations, health care workers and people dealing with infected blood like laboratory staff). 3- History suggestive of liver cell failure. The history taking sheet was based on the aphasia clinic sheet of Internal medicine Department, Al- Azhar university.

Clinical examination;

Clinical examination to review other systems and discover any associated conditions. the clinical examination sheet of Internal medicine Department, Al- Azhar University.

Routine laboratory investigations

Complete blood picture using Sysmex SF-3000 (Hb WBCs and platelet count), Liver and kidney function tests (albumin, ALT, AST, INR and creatinine) using Dimension RXL (Dade Bhring), Enzyme Linked Immuno-Sorbent Assay of HbsAg. Hepatitis C RNA quantitation using polymerase chain reaction (PCR): Before the start of treatment, at end of treatment and 12 weeks after treatment to asses for sustained virologic response.

Radiological assessment by Abdominal ultrasonography:

All patients underwent US of the abdomen by using sonoscape S11. A specific protocol was performed to evaluate the characteristics consistent with liver cirrhosis (liver and spleen size, liver texture, diameter of the portal, splenic, and mesenteric veins). This study was made in the **Ultrasonography** unit of radio diagnosis department of Kobry Al Kobba Military Medical Complex.

3. Results

Demographic and clinical characteristics;

Age was 51.2 ± 6.2 years with minimum 42 and maximum 62 years in group I and 52.8 ± 7.3 years with minimum 43 and maximum 62 years in group II. Males represent 80% in group I and 84% in group II and females represent 20% in group I and 16% in group II. Statistically, there were no significant differences between the two groups regarding age, sex, smoking, hypertension and diabetes mellitus ($p > 0.05$), but there was statistically significant difference regarding encephalopathy ($p < 0.001$).

There were statistically high significant differences between the two studied groups regarding spleen, ascites and oesophageal varices ($p < 0.001$) and a significant difference regarding polymerase chain reaction ($p < 0.05$).

Table (1): Demonstrating demographic and clinical characteristics:-

	Group I (n = 100)	Group II (n = 50)	t	P
Age (years) Mean ± SD Range	 51.2 ± 6.2 42-62	 52.8 ± 7.3 43-62	 1.4	 0.15 (NS)
Sex Male Female	 80 (80%) 20 (20%)	 42 (84%) 8 (16%)	 X^2 = 0.35	 0.55 (NS)
Smoking -ve +ve	 35 (35%) 65 (65%)	 22 (44%) 28 (56%)	 X^2 = 1.15	 0.2 (NS)
Hypertension -ve +ve	 60 (60%) 40 (40%)	 323 (64%) 18 (36%)	 X^2 = 0.22	 0.63 (NS)
DM -ve +ve	 60 (60%) 40 (40%)	 36 (72%) 14 (28%)	 X^2 = 2.08	 0.14 (NS)
Encephalopathy -ve +ve	 0 (0%) 100 (100%)	 50 (100%) 0 (0%)	 X^2 = 150	 < 0.001 (HS)

Table (2): Clinical findings

	Group I (n = 100)		Group II (n = 50)		X^2	P
	No	%	No	%		
Spleen -ve +ve	 28 72	 28 72	 30 20	 60 40	 14.3	 < 0.001 (HS)
Ascites -ve +ve	 0 100	 0 100	 50 0	 100 0	 150	 < 0.001 (HS)
Child Pugh	15 ± 0					
OV -ve +ve	 28 72	 28 72	 50 0	 100 0	 69.2	 < 0.001 (HS)
PCR Mean ± SD Range	 60869 ± 16085 67000-671000		 996000 ± 1811000 75000-7000000		 2.1	 0.03 (S)

Table (3): Hb changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**p**
Hb_0	13.1 ± 2.1	14.1 ± 1.5	3	0.003 (S)
HB_1	10.2 ± 1.3	12.1 ± 1.3	8.3	< 0.001 (HS)
HB_2	10.4 ± 1.1	12.9 ± 1	13.1	< 0.001 (HS)

In group I, before treatment, Hb baseline was 13.1 ± 2.1; after treatment, Hb was 10.2 ± 1.3 and 12 weeks after treatment, Hb was 10.4 ± 1.1. In group II, before treatment, Hb baseline was 14.1 ± 1.5; after treatment, Hb was 12.1 ± 1.3 and 12 weeks after treatment, Hb was 12.9 ± 1. Statistically, there were significant changes between the two studied groups regarding hemoglobin.

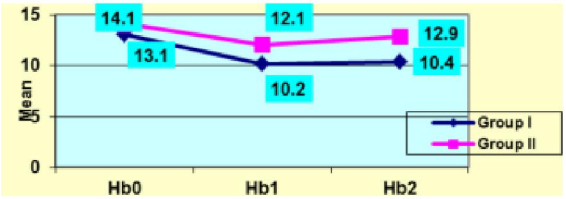

Figure (1): Hb changes among the studied groups

Table (4): WBC changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**P**
WBC_0	5.9 ± 1.6	7.3 ± 2.1	4.7	< 0.001 (HS)
WBC_1	6.1 ± 1.4	6.7 ± 1	2.6	0.01 (S)
WBC_2	5.79 ± 1.5	6.3 ± 1.3	1.97	0.05 (S)

In group I, before treatment, WBC baseline was 5.9 ± 1.6; after treatment, WBC was 6.1 ± 1.4 and 12 weeks after treatment, WBC was 5.79 ± 1.5. In group II, before treatment, WBC baseline was 7.3 ± 2.1; after treatment, WBC was 6.7 ± 1 and 12 weeks after treatment, WBC was 6.3 ± 1.3. Statistically, there were significant changes between the two studied groups regarding white blood cell.

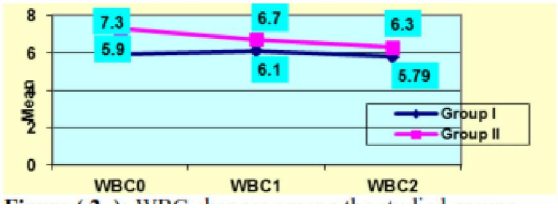

Figure (2): WBC changes among the studied groups

Table (5): PLT changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**P**
PLT_0	91.2 ± 27.7	168.2 ±48.3	12.3	< 0.001 (HS)
PLT_1	116.8 ±27.3	205.9 ±52.3	13.7	< 0.001 (HS)
PLT_2	119.6 ±24.3	211.7 ±62.3	12.9	< 0.001 (HS)

In group I, before treatment, PLT baseline was 91.2 ± 27.7; after treatment, PLT was 116.8 ±27.3 and 12 weeks after treatment, PLT was 119.6 ±24.3. In group II, before treatment, PLT baseline was 168.2 ±48.3; after treatment, PLT was 205.9 ±52.3 and 12 weeks after treatment, PLT was 211.7 ±62.3.

Statistically, there were high significant changes between the two studied groups regarding platelet count.

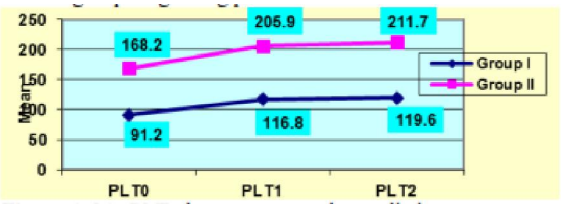

Figure (3): PLT changes among the studied groups

In group I, before treatment, creatinine baseline was 0.9 ± 0.08; after treatment, creatinine was 0.88 ± 0.09 and 12 weeks after treatment, creatinine was 0.88 ± 0.09. In group II, before treatment, creatinine baseline was 0.8 ± 0.1; after treatment, creatinine was 0.75 ± 0.08 and 12 weeks after treatment, creatinine was 0.76 ± 0.08. Statistically, there were high significant changes between the two studied groups regarding creatinine.

Table (6): Creatinine changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**T**	**P**
Cr_0	0.9 ± 0.08	0.8 ± 0.1	7.3	< 0.001 (HS)
Cr_1	0.88 ± 0.09	0.75 ± 0.08	8.4	< 0.001 (HS)
Cr_2	0.88 ± 0.09	0.76 ± 0.08	8.3	< 0.001 (HS)

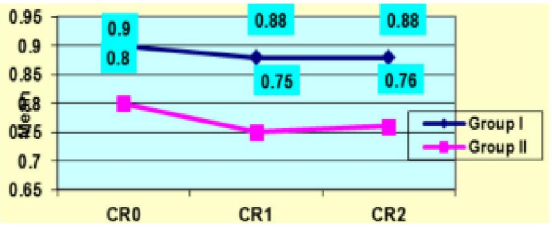

Figure (4): Creatinine changes among the studied groups

In group I, before treatment, ALT baseline was 74.3 ± 41.7; after treatment, ALT was 51.7 ± 23.2 and 12 weeks after treatment, ALT was 46.1 ± 15.3. In group II, before treatment, ALT baseline was 65.6 ± 21.5; after treatment, ALT was 34.9 ± 9.8 and 12 weeks after treatment, ALT was 28.2 ± 5.4. Statistically, there were high significant changes between the two studied groups regarding ALT after treatment and 12 weeks after treatment and no significant ALT changes before treatment.

Table (7): ALT changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**P**
ALT_0	74.3 ± 41.7	65.6 ± 21.5	1.39	0.16 (NS)
ALT_1	51.7 ± 23.2	34.9 ± 9.8	4.8	< 0.001 (HS)
ALT_2	46.1 ± 15.3	28.2 ± 5.4	8.03	< 0.001 (HS)

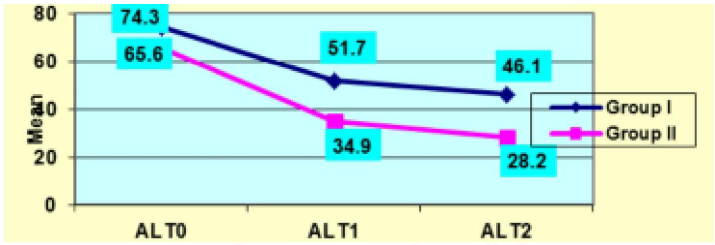

Figure (5): ALT changes among the studied groups

Table (8): AST changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**p**
AST_0	67.5 ± 27.9	65.5 ± 19	0.45	0.64 (NS)
AST_1	50.5 ± 19.8	33.3 ± 12	5.6	< 0.001 (HS)
AST_2	40.4 ± 11.3	34 ± 8.1	3.5	< 0.001 (HS)

In group I, before treatment, AST baseline was 67.5 ± 27.9; after treatment, AST was 50.5 ± 19.8 and 12 weeks after treatment, AST was 40.4 ± 11.3. In group II, before treatment, AST baseline was 65.5 ± 19; after treatment, AST was 33.3 ± 12 and 12 weeks after treatment, AST was 34 ± 8.1. Statistically, there were high significant changes between the two studied groups regarding AST after treatment and 12 weeks after treatment and no significant AST changes before treatment.

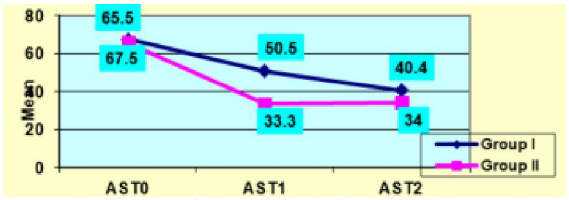

Figure (6): AST changes among the studied groups

Table (9): Bilirubin changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**P**
Bil_0	2.9 ± 0.13	0.97 ± 0.5	34.3	< 0.001 (HS)
Bil_1	1.9 ± 0.3	0.8 ± 0.15	26.7	< 0.001 (HS)
Bil_2	0.9 ± 0.1	0.7 ± 0.1	10.4	< 0.001 (HS)

In group I, before treatment, bilirubin baseline was 2.9 ± 0.13; after treatment, bilirubin was 1.9 ± 0.3 and 12 weeks after treatment, bilirubin was 0.9 ± 0.1. In group II, before treatment, bilirubin baseline was 0.97 ± 0.5; after treatment, bilirubin was 0.8 ± 0.15 and 12 weeks after treatment, bilirubin was 0.7 ± 0.1. Statistically, there were high significant changes between the two studied groups regarding bilirubin.

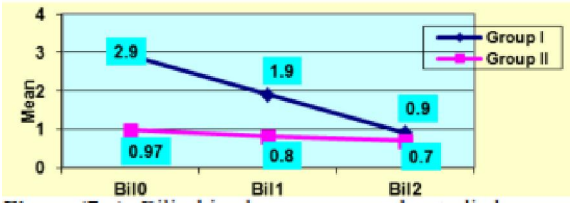

Figure (7): Bilirubin changes among the studied groups

Table (10): Albumin changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**p**
Albumin 0	2.3 ± 0.2	4 ±0.3	40.2	< 0.001 (HS)
Albumin 1	2.5 ± 0.2	4 ± 0.3	35.6	< 0.001 (HS)
Albumin 2	2.54 ± 0.2	4 ± 0.3	34	< 0.001 (HS)

In group I, before treatment, albumin baseline was 2.3 ± 0.2; after treatment, albumin was 2.5 ± 0.2 and 12 weeks after treatment, albumin was 2.54 ± 0.2. In group II, before treatment, albumin baseline was 4 ±0.3; after treatment, bilirubin was 4 ± 0.3 and 12 weeks after treatment, bilirubin was 4 ± 0.3. Statistically, there were high significant changes between the two studied groups regarding albumin.

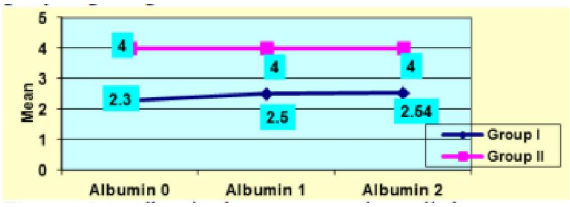

Figure (8): Albumin changes among the studied groups

Table (11): INR changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**t**	**p**
INR_0	2.7 ± 0.1	1.1 ± 0.1	71	< 0.001 (HS)
INR_1	1.9 ± 0.18	1.06 ± 0.07	30.2	< 0.001 (HS)
INR_2	1.8 ± 0.3	1.1 ± 0.07	17.9	< 0.001 (HS)

In group I, before treatment, INR baseline was 2.7 ± 0.1; after treatment, INR was 1.9 ± 0.18 and 12 weeks after treatment, INR was 1.8 ± 0.3. In group II, before treatment, INR baseline was 1.1 ± 0.1; after treatment, INR was 1.06 ± 0.07 and 12 weeks after treatment, INR was 1.1 ± 0.07. Statistically, there were high significant changes between the two studied groups regarding INR.

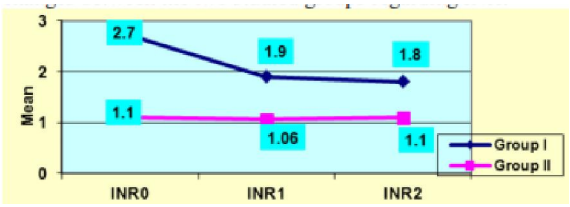

Figure (9): INR changes among the studied groups

Table (12): PCR changes among the studied groups

	Group I (n = 100) Mean ± SD	**Group II (n = 50) Mean ± SD**	**T**	**p**
PCR_0	608629±161005	996000±1811000	2.1	0.03 (S)
PCR_1	0	0	0	1 (NS)
SVR	23220 ± 40054	0	3.9	< 0.001 (HS)
+ve	24 (24%)	0 (0%)		< 0.001 (HS)

There were statistically high significant PCR changes between the two studied groups regarding SVR and positivity ($p < 0.001$), a significant difference before treatment ($p < 0.05$) and a non-significant difference after treatment ($p > 0.05$).

CTP Score

Table (13): changes in group I patients

	Mean ± SD	**T**	**P value**
CTP0	**14.7±0.50**	**34.4**	**0.001**
CTP1	**9.90± 1.37**		
CTP1	**9.90± 1.37**	**9.4**	**0.001**
CTP2	**8.81±1.54**		
CTP2	**8.81±1.54**	**36.3**	**0.001**
CTP0	**14.7±0.50**		

In group I, before treatment, CTP was 14.7 ± 0.50; after treatment, it was 9.90 ± 1.37 and 12 weeks after treatment, it was 8.81 ± 1.54. There were statistically significant changes between the results of CTP score in cirrhotic patients with ascites and/or esophageal varices.

Table (14): Wilcoxon signed ranks test for ascites at initiation, after completion, and 12 weeks after DAAs therapy

	No. of cases		Z	P value
Ascites0	N	0	5.05	0.001
	P	100		
Ascites 1	N	60		
	P	40		
Ascites 1	N	60	0	1.0
	P	40		
Ascites 2	N	60		
	P	40		
Ascites 0	N	0	5.047	0.001
	P	100		
Ascites 2	N	60		
	P	40		

There was a statistically significant improvement in clinically detectable ascites between ascites 0 and ascites 1, between ascites 0 and ascites 2, but no significant improvement in clinically detectable ascites between ascites 1 and ascites 2.

Table (15): Wilcoxon signed ranks test for esophageal varices at initiation, after completion, and 12 weeks after DAAs therapy

	No. of cases		Z	P value
OV0	N	28	2.0	0.046
	P	72		
OV 1	N	24		
	P	76		
OV 1	N	24	2.0	0.046
	P	76		
OV 2	N	28		
	P	72		
OV 0	N	28	0	1.0
	P	72		
OV2	N	28		
	P	72		

There was a significant increase in the number of OV cases between OV 0 and OV 1, between OV 1 and OV 2, but no change in the number of OV between OV 0 and OV 2.

Table (16): Wilcoxon signed ranks test for Hepatic encephalopathy at initiation, after completion, and 12 weeks after DAAs therapy in

	No. of cases		Z	P value
Encephalopathy 0	N	0	8.0	0.000
	P	100		
Encephalopathy 1	N	64		
	P	36		
Encephalopathy 1	N	64	3.5	0.001
	P	36		
Encephalopathy 2	N	76		
	P	24		
Encephalopathy 0	N	0	8.7	0.000
	P	100		
Encephalopathy 2	N	76		
	P	24		

There was a statistically significant improvement in the number of encephalopathy cases between encephalopathy 0 and encephalopathy 1, between encephalopathy 1 and encephalopathy 2, and between encephalopathy 0 and encephalopathy 2.

4. Discussion

Hepatitis C virus (HCV) infection, and its long-term resultant consequences, is a major endemic medical health problem in Egypt (9). HCV infection transmitted through blood contact (10). A part from the usual modes of transmission, such as intravenous drug use, the main risk factors for transmission in Egypt historically have included the now archaic parenteral antischistosomal therapy, shared or reused needles, poorly sterilized surgical or dental equipment, and blood transfusions (11). Once cirrhosis is established complications such as ascites, gastroesophageal variceal hemorrhage, hepatic encephalopathy, hepatocellular carcinoma, and/or acute or chronic liver failure may develop and result in diminished quality of life and survival without liver transplantation. Effective antiviral therapy that results in sustained virological response (SVR) is the only strategy that positively alters the natural history of liver disease associated with HCV infection by reducing the frequency of hepatic decompensation, liver-related mortality, all-cause mortality, need for liver transplantation, and hepatocellular carcinoma (12) Furthermore, SVR is also associated with improved quality of life and increased work productivity (13). Licensure of new generation direct-acting antiviral agents (DAAs) revolutionized treatment of HCV infection, as these agents have very high virological efficacy, low frequency of severe adverse events (AEs), and overall high barrier to resistance. Treating patients with advanced liver disease has been historically associated with limited success (14). In addition to the intrinsic fragility of these patients, decompensated liver disease may result in impaired hepatic metabolism, affecting the plasma concentrations of HCV direct-acting antiviral agents (DAAs) (15). Therefore, treatment options must be carefully considered. Furthermore, it has been reported that some DAAs may cause liver injury in patients with underlying cirrhosis (16). The efficacy of all-oral antiviral regimens in the management of patients with compensated liver disease due to chronic HCV infection is now established (17) and data on patients with decompensated cirrhosis are emerging (18). This study was conducted on 150 patients infected with HCV; 100 patients of HCV with cirrhotic liver disease and ascitis or esophageal varices and 50 age-matched cirrhotic patients of HCV without ascites or esophageal varices as a control group to study the safety and efficacy of DAAs in the form of Daclatasvir and Sofosbuvir combination (±Ribavirin). Their mean age (± SD) was 51.2 ± 6.2 years, 80% were male, all were had cirrhosis with ascites or esophageal varices, all were treatment-naive, and the baseline mean HCV RNA concentration was 60869 ± 16085 (Range, 67000-671000) IU/mL. Overall, 100 % completed the full course of therapy and the SVR12 rate was 75 %. In our study, the strongest predictors of response included no prior treatment, and baseline platelets ≥ 90 $^{x}10^{3}$/mL. Improving response in patients with the most advanced disease requires further study; potentially, extending treatment beyond 12 weeks may be beneficial and worthy of evaluation in a larger cohort of patients with Child-Pugh class C disease.

Conclusion

We concluded that:

12 weeks of oral treatment with the combination of daclatasvir with sofosbuvir and ribavirin achieved high SVR rates in cirrhotic patients with ascites and/or esophageal varices (Child-Pugh class C disease). Importantly, SVR rates are in general lower in individuals with decompensated cirrhosis compared to those seen in individuals with compensated cirrhosis (CTP class A). This combination, achieved high SVR12 rates in patients with potentially life-threatening liver disease (with ascites and/or esophageal varices). Treatment was well tolerated without treatment-limiting pharmacokinetic interactions or toxicities and was associated with improvements in liver function.

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