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# EFFICACY OF SOFOSBUVIR, DACLAVIR AND RIBAVIRIN IN TREATMENT OF HCV INFECTION WITH DIFFERENT STAGES OF LIVER DISEASE

By
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## ABSTRACT

**Background:** Hepatitis c virus (HCV) is a serious worldwide problem which has a great impact on health status in the field of liver diseases with an estimation of 170 million people infected worldwide. HCV infection is gaining increasing attention as a global health problem, with approximately 3% of the world's population infected. Egypt reports the highest prevalence of HCV worldwide, ranging from 6% to more than 40% with an average of 13.8%. Today, many direct-acting antivirals (DAAs) are available with encouraging results in terms of both virologic response and safety.

**Objectives:** The aim of this study was to evaluate the prevalence of SVR (12-24 weeks) in Egyptian patients with different Child-Pough classification, the complications and its frequency during, and after treatment with combination of antiviral agents.

**Patients and Methods:** This study was performed at Internal Medicine Department, Ahmed Maher Teaching Hospital, Cairo, Egypt,. The study included 650 patients with chronic hepatitis C that were categorized into 3 groups according to Child-Pugh classification as follows: Group A: included 300 patients with Child-Pugh score of 5-6 points, Group B: included 300 patients with child-Pugh score of 7-9 points, and Group C: included 50 patients with Child-Pugh score of 10-15 points Patients enrolled in the study were prospectively evaluated as outpatients by the study staff after 4, 8, 12 weeks and at 12 and 24 weeks post- treatment.

**Results:** There was a statistically highly significant difference in PCR before treatment (100% +ve) and after treatment (100% -ve)at 1st mo,3rd mo, 6th mo in group A. There was a statistically highly significant difference in PCR before treatment (100% +ve) and after treatment -ve at 1st mo,3rd mo 6th mo (100%, 100%, 91.6% respectively) in group B; and there was a statistically highly significant difference in PCR before treatment (100% +ve) and after treatment –ve at 1st mo,3rd mo, 6th mo (100%, 82%, 54% respectively) in gourp C. Throughout the study, most of the patients were responders (95.1% achieved SVR12).

**Conclusion:** Use of SOF-DCV in patients with chronic HCV-G4 proved to be safe and associated with a high SVR12 rate, in patients with different stages of fibrosis.

**Key words:** HCV, complications, incidence, Sofosbuvir, Daclavir, Ribavirin, compensated cirrhosis.

## INTRODUCTION

Hepatitis C virus (HCV) infection is the most common blood-borne infection. The worldwide prevalence of (HCV) infection is estimated to be 2.0% overall, corresponding to approximately 120 million persons *(Messina et al., 2015)*.

There is a substantial variation by region, with the highest prevalence in North Africa and the Middle East, particularly Egypt (>3.0%), followed by rest of African countries, China and other Asian countries. In more developed countries, transmission seems to be primarily a result of illicit drug use; whereas, in less developed countries the modes of transmission are unsafe therapeutic injection practices, inadequate disinfection practices in medical and dental settings *(Perz et al., 2004)*.

HCV- related squeal such as cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC) are expected to increase over the course of the next decade *(Razavi et al., 2015)*. Importantly, chronic HCV infection not only increases liver -related mortality, but also mortality from extrahepatic disease *(Lee, 2012)*.

The goal of antiviral therapy is to cure hepatitis C via a sustained elimination of the virus. A sustained elimination of HCV is achieved if the HCV RNA remains negative six monthes after the end of treatment (sustained virological response, SVR) *(Bertino et al., 2016)*.

The standard therapy was based on interferon therapy either as a monotherapy with SVR rate from 5-20%, or with a combination of INF and ribavirin (RBV) with a SVR rate from 40-50% *(Rosen, 2011)*.

Different HCV genotypes shows different SVR rates, patients with the most frequent HCV genotype 1 require longer treatment duration with IFN/RBV and still get a lower SVR compared to HCV genotype 2 and 3. The development of pegylated interferon α(PEG-INF) improved the pharmacokinetics of INF, allowing more convenient dosing intervals and resulting in higher SVR especially for HCV genotype 1 *(McHutchison et al., 2009)*.

The development of direct –acting antiviral agents (DAAs) against HCV has revolutionized the treatment of chronic hepatitis C. The main targets for DAAs are the NS3/4A protease, NS5B polymerase and the NS5A replication complex. Combinations of different classes allow very potent treatment *(Zeuzem et al., 2011)*.

The aim of this study was to evaluate the prevalence of SVR at 12 weeks and at 24 week after treatment in Egyptian patients with different Child-Pough classification and the complications and its frequency during and after treatment with combination of antiviral agents.

## SUBJECTS AND METHODS

This study was performed at Internal Medicine Department, Ahmed Maher Teaching Hospital, Cairo, Egypt, from February 2017 to February 2018.

All procedures were followed according to Al- Azhar University Ethical Committee regulations.

A written consent was taken from every patient before collecting any information or starting any procedure.

The study included 650 patients with chronic hepatitis C that were categorized into 3 groups according to Child-Pugh classification as follows:

- **Group A:** included 300 patients with Child-Pugh score of 5-6 points.

- **Group B:** included 300 patients with child-Pugh score of 7-9 points.

- **Group C:** included 50 patients with Child-Pugh score of 10-15 points.

All patients were subjected to the following at the beginning of research, after 3 months and after 6 months:

1. Full history including:
   a- The presenting symptoms with a special emphasis on:
   - Symptoms – free, accidentally discovered.
   - Fatigue.
   - Loss of weight.
   - Right hypochondrial pain.
   - Dysphagia.
   - Bleeding tendency.
   - Anorexia.
   - Jaundice.
   - Arthralgia.

   b- Special emphasis on risk factors associated with transmission of infection:
   - Blood transfusion.
   - Dental invasive maneuvers.
   - Intravenous drug use.
   - Surgery.
   - Wound suturing.
   - Tattoos.
2. Complet general and abdominal examination.
3. Virological assessment: Anti HCV antibody detected by enzyme immunoassay (EIA), HCV RNA by a sensitive molecular method.
4. Laboratory investigation: CBC, blood urea and creatinine, LFT (ALT, AST, BIL (total &direct), serum albumin, prothrombin, INR and ALP.
5. Abdominal ultrasound and upper GI endoscope for patients with Child B.C group to evaluate the pressure of portal hypertension – esophageal and gastric varices.
6. Assessment of fibrosis by measurement of liver stiffness by fibroscan: It was not included in the Egyptian protocol of HCV treatment but used as an evaluation technique to differentiate between closed group as A, B or C as a non-invasive method for determination of fibrosis degree.

**Inclusion criterion:**

All patients with chronic hepatitis C virus: naive and treatment experienced patients who were willing to be treated:

- Patient age was above 18 years.
- Positive anti- HCV and HCV RNA in sera.
- Compensated liver.
- White blood cells > 4000/cc.
- Plateles > 75000/cc.
- Fasting blood sugar < 115mg/dl.
- If the patient was diabetic, glycosylated hemoglobin was < 8.5%.
- Serum creatinine within normal.
- ANA <1:160.
- Prothrombin time ≤ 2 seconds above the upper limit of normal.

All inclusion criteria were based upon Egyptian protocol of HCV treatment (2018).

**Exclusion criteria:**

- Any cause of liver disease other than chronic HCV based on the patient history and laboratory findings are excluded as:
  i. Autoimmune hepatitis.
  ii. Hemochromatosis.
  iii. Wilson's disease.
  iv. Alcoholic liver disease.
  Laboratory markers that exclude treatment included:
  • ANA.
  • Serum ferritin.
  • Urinary copper.
  • ALT/AST ratio.
  • HBsAg.
  • Hepatic tumors excluded by both AFP level (less than 500ng/ml) and abdominal ultrasonography.
  • Hbs Ag +ve patients.
  • Pregnancy or breast feeding.
  • Serious systemic disease (e.g. ischemic heart disease).
  • Severe pre-existing psychiatric condition.
  • Poorly controlled diabetes (Hb A1C >8.5%).
- All patients were subjected to treatment with oral direct antiviral therapy that included Sofosbuvir (400 mg tab)+daclatasvir (60 mg tab) ± ribavirin (1000-1200 mg) according to body weight.
- The duration of therapy was 12 weeks.
- The goal of therapy was to cure HCV infection to prevent hepatic cirrhosis, decompensation of cirrhosis, HCC, severe extrahepatic manifestation and death.
- The endpoint of therapy was undetectable HCV RNA in blood by a sensitive assay (lower limit of detection is ≤ 15 IU /ml) at 12 weeks (SVR12), at 24 weeks (SVR24) and after the end of treatment.
- Evaluation of complications of treatment was monitored frequently. A reasonable schedule of monthly visits was done during the course of treatment. At each visit, the patient was questioned regarding the presence of complications. Laboratory monitoring included measurement of the complete blood count, ALT and AST levels, serum creatinine and serum bilirubin.

**Statistical analysis:**

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

**The following tests were done:**

- A one-way analysis of variance (ANOVA) when comparing between more than two means.
- Post Hoc test: Least Significant Difference (LSD) was used for multiple comparisons between different variables.
- Paired sample t-test of significance was used when comparing between related sample.
- Chi-square (x2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the P-value was considered significant when it was ≤ 0.05.

## RESULTS

Mean age was 39.78±8.41 years in group A, 54.59±4.8 years in group B and 57.6±5.42 years in group C. There were 152 males (50.7%) and 148 females (49.3%) in group A, 134 males (44.7%) and 166 females (55.3%) in group B, 21 males (42%) and 29 females (58%) in group C (Table 1).

**Table (1): Comparison between groups according to demographic data**

| Groups / Demographic Data | Group A (n=300) | Group B (n=300) | Group C (n=50) |
|---|---|---|---|
| **Age (years)** | | | |
| Mean ± SD | 39.78 ± 8.41 | 54.59 ± 4.8 | 57.6 ± 5.42 |
| Range | 22 - a59 | 39 - a67 | 48 - a68 |
| **Sex** | | | |
| Male | 152 (50.7%) | 134 (44.7%) | 21 (42%) |
| Female | 148 (49.3%) | 166 (55.3%) | 29 (58%) |

There were highly statistically significant differences between groups according to laboratory data in general (AST, ALB, INR, BIL, PLAT, HB, TLC and fibroscan) (Table 2).

**Table (2): Comparison between groups according to laboratory data in before treatment**

| Groups / Laboratory Data | Group A (n=300) | Group B (n=300) | Group C (n=50) | ANOVA | p-value |
|---|---|---|---|---|---|
| **AST** | | | | | |
| Mean ± SD | 47.89±16.92 | 42.35±6.6† | 42.6±5.16†‡ | 5.283 | <0.001 |
| Range | 18-a142 | 24-a58 | 32-a53 | | |
| **ALT** | | | | | |
| Mean ± SD | 56.06±16.64 | 54.57±6.9 | 56.2±6.5 | 1.433 | 0.153 |
| Range | 28-a152 | 38-a57 | 44-a70 | | |
| **ALB** | | | | | |
| Mean ± SD | 3.95±0.17 | 3.07±0.22† | 2.78±0.16†‡ | 86.806 | <0.001 |
| Range | 3-a4.9 | 2.8-a5.2 | 2.5-a3.1 | | |
| **INR** | | | | | |
| Mean ± SD | 1.001±0.011 | 1.21±0.15† | 2.04±0.16†‡ | 112.210 | <0.001 |
| Range | 1-a1.1 | 1-a1.9 | 1.7-a2.3 | | |
| **BIL** | | | | | |
| Mean ± SD | 1.01±0.03 | 1.28±0.18† | 2.89±0.29†‡ | 111.689 | <0.001 |
| Range | 0.9-a1.2 | 1-a2 | 2.2-a3.5 | | |
| **CBC** | | | | | |
| **PLAT** | | | | | |
| Mean ± SD | 239.91±42.47 | 156.5±25.1† | 107.34±8.47 †‡ | 53.022 | <0.001 |
| Range | 159-a360 | 89-a210 | 90-a124 | | |
| **HB** | | | | | |
| Mean ± SD | 13.2±1.28 | 10.5±0.59† | 10.6±0.6† | 31.856 | <0.001 |
| Range | 10-a16 | 9.2-a12.3 | 9.7-a12.3 | | |
| **TLC** | | | | | |
| Mean ± SD | 4.45±0.82 | 5.13±1.11† | 6.26±0.86†‡ | 26.382 | <0.001 |
| Range | 2.8-a7.3 | 2.8-a7.5 | 4.8-a7.8 | | |
| **Fibroscan** | | | | | |
| Mean ± SD | 6.49±3.43 | 11.3±3.17 | -- | t=17.838 | <0.001 |
| Range | 3.9-a15 | 7.1-a14 | -- | | |

†Significant difference between group A
‡Significant difference between group B
ANOVA: A one-way analysis of variance

There were highly significant differences between the four groups as regards U/S finding (P<0.001). There were normal 99 (33%), Bright liver 179 (59.7%) and Chronic parenchymal liver disease 22 (7.3%) in group A, Bright liver 25 (8.3%), Chronic parenchymal liver disease 271 (90.3%) and Liver cirrhosis 4 (1.3%) in group B, Bright liver 1 (2%), Chronic parenchymal liver disease 0 (0%) and Liver cirrhosis 49 (98%) in group C (Table 3).

**Table (3): Comparison between groups according to U/S finding**

| Groups / U/S finding | Group A *(n=300)* | Group B *(n=300)* | Group C *(n=50)* | x2 | p-value |
|---|---|---|---|---|---|
| Normal | 99 (33%) | 0 (0%)† | 0 (0%)‡ | 21.410 | <0.001 |
| Bright liver | 179 (59.7%) | 25 (8.3%)† | 1 (2%)†‡ | 54.835 | <0.001 |
| Chronic parenchymal liver disease | 22 (7.3%) | 271 (90.3%)† | 0 (0%)‡ | 194.650 | <0.001 |
| Liver cirrhosis | 0 (0%) | 4 (1.3%) | 49 (98%)†‡ | 333.769 | <0.001 |

†Significant difference between group A
‡Significant difference between group B
x2: Chi-square test

There were highly statistically significant differences between groups according to ALT from 1st month of treatment to 3rd month of treatment (Table 4).

**Table (4): Comparison between groups according to ALT**

| Groups / ALT | Group A (n=300) | Group B (n=300) | Group C (n=50) | ANOVA | p-value |
|---|---|---|---|---|---|
| Before treatment | 56.06±16.64 | 54.57±6.9 | 56.2±6.5 | 1.433 | 0.153 |
| 1st month of treatment | 32.91±8.01 | 32.81±6.31 | 41.0±5.6†‡ | 14.012 | <0.001 |
| 2nd month of treatment | 27.09±8.02 | 28.26±4.8 | 37.02±5.5†‡ | 17.321 | <0.001 |
| 3rd month of treatment | 32.71±7.66 | 24.81±4.3† | 30.6±4.4‡ | 12.137 | <0.001 |

†Significant difference between group A
‡Significant difference between group B
ANOVA: A one-way analysis of variance

**Table (5): Comparison between groups according to abnormal CBC**

| Abnormal CBC | Group A (n=300) | Group B (n=300) | Group C (n=50) | x2 | p-value |
|---|---|---|---|---|---|
| Before treatment | 300 (100%) | 300 (100%) | 50 (100%) | 0.000 | 1.000 |
| 1st month of treatment | 0 (0%) | 0 (0%) | 14 (28%)†‡ | 80.360 | <0.001 |
| 2nd month of treatment | 0 (0%) | 0 (0%) | 17 (34%)†‡ | 99.976 | <0.001 |
| 3rd month of treatment | 0 (0%) | 0 (0%) | 22 (44%)†‡ | 133.483 | <0.001 |

†Significant difference between group A
‡Significant difference between group B
x2: Chi-square test

There were statistically significant differences between groups according to positive PCR at 3rd months of treatment and 6th months of treatment (Table 6).

**Table (6): Comparison between groups according to positive PCR**

| Positive PCR | Group A (n=300) | Group B (n=300) | Group C (n=50) | x2 | p-value |
|---|---|---|---|---|---|
| Before treatment | 300 (100%) | 300 (100%) | 50 (100%) | 0.000 | 1.000 |
| 1st mo of treatment | 0 (0%) | 0 (0%) | 0 (0%) | 0.000 | 1.000 |
| 3rd mo of treatment | 0 (0%) | 0 (0%) | 9 (18%)†‡ | 48.473 | <0.001 |
| 6th mo of treatment | 0 (0%) | 25 (8.3%)† | 23 (46%)†‡ | 140.309 | <0.001 |

†Significant difference between group A
‡Significant difference between group B
x2: Chi-square test

There were statistically significant differences over the periods through abnormal CBC in each group (Table 7).

**Table (7): The extent of the difference over the periods through abnormal CBC in the each group**

| Abnormal CBC | Group A (n=300) | | | Group B (n=300) | | | Group C (n=50) | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. (%) | $x^2$ | p-value | No. (%) | $x^2$ | p-value | No. (%) | $x^2$ | p-value |
| Before treatment | 300 (100%) | | | 300 (100%) | | | 50 (100%) | | |
| 1st month of treatment | 0 (0%) | 596 | <0.001 | 0 (0%) | 596 | <0.001 | 14 (28%) | 25.168 | <0.001 |
| 2nd month of treatment | 0 (0%) | 596 | <0.001 | 0 (0%) | 596 | <0.001 | 17 (34%) | 23.314 | <0.001 |
| 3rd month of treatment | 0 (0%) | 596 | <0.001 | 0 (0%) | 596 | <0.001 | 22 (44%) | 18.161 | <0.001 |

x2: Chi-square test

There were statistically significant differences over the periods through positive PCR in each group (Table 8).

**Table (8): The extent of the difference over the periods through positive PCR in the each group**

| Positive PCR | Group A (n=300) | | | Group B (n=300) | | | Group C (n=50) | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. (%) | $x^2$ | p-value | No. (%) | $x^2$ | p-value | No. (%) | $x^2$ | p-value |
| Before treatment | 300 (100%) | | | 300 (100%) | | | 50 (100%) | | |
| 1st mo of treatment | 0 (0%) | 596 | <0.001 | 0 (0%) | 596 | <0.001 | 0 (0%) | 96 | <0.001 |
| 3rd mo of treatment | 0 (0%) | 596 | <0.001 | 0 (0%) | 596 | <0.001 | 9 (18%) | 66 | 0.004 |
| 6th mo of treatment | 0 (0%) | 596 | <0.001 | 25 (8.3%) | 504 | <0.001 | 23 (46%) | 34 | 0.022 |

x2: Chi-square test

There were statistically significant decrease 1st, 2nd and 3rd months from before treatment over the periods through ALT in each group (Table 9).

**Table (9): The extent of the difference over the periods through ALT in the each group**

| ALT | Group A (n=300) | | | Group B (n=300) | | | Group C (n=50) | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | t | p-value | Mean ± SD | t | p-value | Mean ± SD | t | p-value |
| Before treatment | 56.06±16.64 | | | 54.57±6.9 | | | 56.2±6.5 | | |
| 1st month of treatment | 32.91±8.01 | 21.712 | <0.001 | 32.81±6.31 | 40.309 | <0.001 | 41.0±5.6 | 12.527 | 0.021 |
| 2nd month of treatment | 27.09±8.02 | 27.164 | <0.001 | 28.26±4.8 | 54.216 | <0.001 | 37.02±5.5 | 15.945 | 0.0017 |
| 3rd month of treatment | 32.71±7.66 | 22.078 | <0.001 | 24.81±4.3 | 63.401 | <0.001 | 30.6±4.4 | 23.062 | <0.001 |

t: Paired Sample t-test

## DISCUSSION

Chronic hepatitis C virus (HCV) infection is estimated to globally affect 70-100 million people *(The Polaris Observatory, 2017)* Genotype 4 infects 10-15 million persons; a large percentage of whom are living in Egypt, where HCVG4 represents more than 90% of the infected population *(Messina et al., 2015)*.

During the last few years, management of HCV became more effective with the appearance of different classes of direct antiviral agents (DAA). They raised the sustained virological responses (SVR) rates from around 40% with pegylated interferon (PEG) and ribavirin (RBV) *(Asselah et al., 2011)* to more than 90% *(Asselah, 2014)*. Different combinations afforded the possibility of interferon-free regimens with unprecedented success rates *(Wantuck et al., 2014)*.

Daclatasvir (DCV) is a potent HCV NS5A replication complex inhibitor which is active against HCV-G4 *(Bunchorntavakul and Reddy, 2015)*. Sofosbuvir (SOF) is a pan-genotypic NS5B polymerase inhibitor that showed a good safety profile as well as a high barrier to resistance *(Stedman, 2014)*.

The combination of both drugs led to appreciable success rates *(Sulkowski et al., 2014)* including patients in different special populations as HIV-coinfected patients, advanced liver diseases, pre- and post-transplant settings, and hemodialysis patients *(Poordad et al., 2016)*.

In Egypt, the National Committee for the Control of Viral Hepatitis (NCCVH) started a mass treatment program that was initially based on SOF in combination with RBV for a treatment duration of 24 weeks or in combination with PEG and RBV for 12 weeks, during the period from October 2014 till May 2015, with SVR12 rates of 78.4% and 94% respectively. This was followed by an era of combined SOF and simeprevir (SMV) therapy that provided an overall 94% SVR12 *(Elsharkawy et al., 2017)*. Starting November 2015, generic SOF+DCV (with or without RBV) became the main line of therapy in the national program, due to efficacy and safety on a large scale of patients *(Omar et al., 2017)*.

This study used DCV and SOF with or without RBV for treating patients with HCV-G4. Although genotyping was not performed at baseline, more than 90% of

patients in Egypt are infected with HCV-G4, and this report can thus be taken to represent results of HCV-G4 treatment *(Waked et al., 2014).*

Optimising treatment outcomes in patients with cirrhosis includes either the addition of RBV or prolonging treatment duration *(Majumdar et al., 2016).*

**All patients in the present work of group a received Sofosbuvir 400 mg /day and daclatasvir 60 mg /day for 12 weeks:**

SVR at end of treatment EOT reached 100%, with SVR12 that also reached100%. This was similar with results obtained from a study done by *(Omar et al., 2017)*. Similar high response rates have been reported with the use of SOF plus DCV with or without RBV from real-life cohorts, even in elderly patients with several concomitant medications *(Hezode et al., 2015).* The ANRS-CUPILT report of treating post-liver transplant patients with SOF-DCV in France included 11 HCV-G4 patients, and the SVR12 rate was 91% *(Coilly et al., 2016).*

The High SVR was also reported in a study done in EGYPT by the tropical department Mansoura University and Zoology department Damietta University and published in Egypt-J-Zool 2017 that concluded in HCV genotype 4 infection once daily oral dose of Sofosbuvir plus daclatasvir with or without ribavirin for 12 weeks appear to be a very good treatment option with the lowest adverse effect and the highest SVR rate.

The Ally study -3 also reported "A 12-week regimen of daclatasvir plus sofosbuvir achieved SVR12 in 96% of patients with genotype 3 infection without cirrhosis and was well tolerated".

**All patients of group B received Sofosbuvir 400 mg /day and daclatasvir 60 mg /day for 12 weeks:**

SVR 12 of 91.6% with 25 patients (8.3%) that relapsed after treatment. This was with a real-world report from Europe on compassionate use of SOF-DCV in patients with HCV and advanced liver disease included 19 HCV-G4 patients, and the SVR12 rate was 100% *(Welzel et al., 2016)*.

This was concomitant with results obtained from a study done by *(Welzel et al., 2016* and *Omar et al., 2017)*.

**All patients of group C received Sofosbuvir 400 mg /day and daclatasvir 60 mg /day with ribavirin 1200mg in patients above 75 kg, 1000mg in patients below 75 kg for 12 weeks:**

*(Poordad et al., 2016)* found lower albumin levels associated with non-response in Child C patients as a reflection of impaired hepatic function *(Poordad et al., 2016)*. We found several factors that could impact SVR12 rates. These include gender, bilirubin, albumin, INR and platelets.

Treatment was well tolerated. Only 0.3% of our patients reported adverse events. This also with a study done by *(Omar et al., 2017)* that revealed, among patients who failed treatment, more patients treated with SOF-DCV-RBV discontinued therapy than those treated with SOF- DCV, while primary non response occurred slightly more among those treated without RBV. Relapse rates were similar in both cohorts. *(Young et al., 2017)* reported that the estimated rate of

SVR12 was 87% in patient with advanced liver disease, and concluded that patients with decompensated cirrhosis have always been difficult to treat with direct acting antivirals, efficacy is reduced in such patients and it is not yet clear which treatments are best.

All previous studies concluded that SOF-DCV combination is safe with limited adverse events. High incidence of serious complications was reported by *(Coilly et al., 2016)* as they managed HCV recurrence in transplanted patients. Such patients are a peculiar situation due to multiple factors that coexist as multi drug intake, immunosuppression and possible drug-drug interactions. Although DAAs provide high cure rates, their high prices could be a barrier to rapid universal treatment uptake *(Hill et al., 2016).*

As the Egyptian programme for the control and eradication of HCV infection escalated, the need arose for much larger drug production at much lower costs *(Vermehren et al., 2016)*. The MoH strongly supported local producers of generic DAAs by providing "fast track registration" of generic DAAs including SOF and DCV provided they reduced their prices. Several publications compared the efficacy of brand and generic drugs produced in Egypt or used generic SOF with DAA molecules, that proved safe and effective *(Fouad et al., 2016).*

This regimen was associated with good safety results with high response rate in patients with different stages of liver disease.

## CONCLUSION

DAAs are effective in treatment of HCV infection in Egyptian patients and percentage of SVR correlated with the degree of liver state according to Child-Pugh classification; and the incidence of complications of therapy is minimal and it is recommended to make more prolonged follow up and apply the therapy on other groups of patients like those with chronic liver disease with renal or cardiac failure, thyroid diseases or DM.

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# فعالية ونسبة حدوث المضاعفات بعد علاج مرضى الالتهاب الكبدي الوبائي س بعقار السوفوسبيوفير والداكلافير والريبافيرين في حالات تليف الكبد المتكافئ

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**خلفية البحث :** يعتبر الالتهاب الكبدي الفيروسي المزمن (سى) أحد المشكلات الصحية الخطيرة على مستوى العالم، حيث أن له تأثيراً كبيراً على الحالة الصحية في مجال أمراض الكبد، حيث يقدر عدد المصابين به في جميع أنحاء العالم بحوالي ١٧٠ مليون شخصاً. وتكتسب الإصابة بفيروس الالتهاب الكبدى اهتماماً متزايداً كمشكلة صحية عالمية، بما يقرب من ٣٪ من سكان العالم. وقد سجلت مصر أعلى معدل انتشار لمرض الالتهاب الكبدي الفيروسي المزمن (سى) على مستوى العالم، حيث تراوحت الإصابة بين ٦٪ وأكثر من ٤٠٪ بمتوسط ١٣، ٨٪. واليوم، تتوافر العديد من الأدوية المضادة للفيروسات ذات المفعول المباشر بنتائج مشجعة من حيث الاستجابة الفيروسية والسلامة.

**الهدف من البحث:** تهدف هذه الدراسة بهدف تقييم مدى انتشار الاستجابة الفيروسية المستدامة (١٢-٢٤ أسبوعاً) لدى المرضى المصريين الذين يعانون من تصنيفات مختلفة على مقياس بيشوب وتقييم المضاعفات معدل الإصابة أثناء وبعد العلاج بمجموعة من العوامل المضادة للفيروسات.

**المرضي وطرق البحث:** أجريت هذه الدراسة بقسم الأمراض الباطنة بمستشفى أحمد ماهر التعليمي بالقاهرة. وقد اشتملت الدراسة على ٦٥٠ مريضًا يعانون من فيروس الالتهاب الكبدى المزمن (سى) وقد تم تصنيفهم إلى ٣ مجموعات وفقًا لتصنيف تشايلد-باف على النحو التالي:

المجموعة (أ): شملت ٣٠٠ مريضاً بمقياس ٥-٦ نقاط على تصنيف تشايلد-باف.

المجموعة (ب): شملت ٣٠٠ مريض بمقياس ٧-٩ نقاط على تصنيف تشايلد-باف.

فى حين شملت المجموعة (ج): ٥٠ مريضًا بمقياس ١٠-١٥ نقاط على تصنيف تشايلد-باف.

وقد تم تقييم المرضى المسجلين في الدراسة المستقبلية كمرضى العيادات الخارجية من قبل فريق الدراسة خلال ٤ و ٨ و ١٢ أسبوعًا وبعد ١٢ أسبوعًا و ٢٤ أسبوعًا من العلاج.

**النتائج:** أظهرت الدراسة وجود فروق ذات دلالة إحصائية كبيرة في مستوى البروتين التفاعلي سى قبل العلاج (١٠٠٪ إيجابى) وبعد العلاج (١٠٠٪ سلبى) فى الشهر الأول والشهر الثالث والشهر السادس فى المجموعة (أ)، وكانت هناك اختلافات ذات دلالة إحصائية عالية في مستوى البروتين التفاعلي سى قبل العلاج (١٠٠٪ إيجابى) وبعد العلاج (١٠٠٪ سلبى) فى الشهر الأول والشهر الثالث والشهر السادس فى المجموعة (ب) (١٠٠٪، ١٠٠٪، ٩١، ٦٪ على الترتيب)؛ كما أظهرت الدراسة اختلافات ذات دلالة إحصائية في مستوى البروتين التفاعلي سى قبل العلاج (١٠٠٪ إيجابى) وبعد العلاج (١٠٠٪ سلبى) فى الشهر الأول والشهر الثالث والشهر السادس فى المجموعة (ج) (١٠٠٪، ٨٢٪، ٥٤٪)؛ وقد أظهر جميع المرضى إستجابة للعلاج؛ وحقق٩٥، ١٪ منهم إستجابة مستدامة لمدة ١٢ شهراً).

الاستنتاج: أثبت العلاج بالسوفوسبيوفيروالداكلافير في المرضى المصابين بفيروس (سى) من النوع الجيني الرابع المزمنة أنه آمن ويرتبط بمعدل استجابة مستدامة ومرتفعة للعلاج في المرضى الذين يعانون من مراحل مختلفة من التليف.