

Study enrollment and methodology

The study was performed on those who implemented the criteria of inclusion of the National Committee for Control of Viral Hepatitis, Ministry of Health and Population (MOHP), Egypt, and included male and female patients aged 18 to 75 years old, easy to treat group [treatment-naïve patients with PCR positive serum HCV RNA, total serum [bilirubin ≤ 1.2 mg/dL, albumin ≥ 3.5 g/dL, INR ≤ 1.2 , and platelet count $\geq 150,000/\text{mm}^3$]. And difficult-to-treat group [interferon treatment-experienced, total serum bilirubin > 1.2 mg/dL, serum albumin < 3.5 g/dL, INR > 1.2 , and/or platelet count $< 150,000/\text{mm}^3$]. For an ethical reason, there was no control group for this study because it was immoral to allocate an infected group without care. Also excluded were individuals with inadequately managed diabetes mellitus (HbA1c $> 9\%$), total serum bilirubin, serum albumin, INR, platelet count > 3 mg/dL, > 2.8 g/dL, ≥ 1.7 , and $< 50,000/\text{mm}^3$ respectively. co-infection with HIV, HBV, any chronic liver disease other than hepatitis C, poorly controlled hypothyroidism, hepatocellular carcinoma with exception of 4 weeks after treatment with no proof of dynamic imaging activity (CT or MRI), extra-hepatic malignancy except after two years of disease-free interval, patients with Child's Paugh C.

Patients' demographics, laboratory test results, and abdominal ultrasounds reports were collected. Verbally communicated information, *via* phone or directly from the patients, about the drug side effects were included. Medical records were screened for evidence of medication error and interaction occurrence taking into consideration that all the medication orders were handwritten. 150 patients were allocated into two groups according to their physical examination and lab parameters: difficult-to-treat group taking sofosbuvir/daclatasvir/ribavirin(S/D/R) and easy-to-treat group taking sofosbuvir/daclatasvir (S/D). Figure 1 shows the methodology and primary results in a graphical image.

Lab parameters of the study participants were tested three times. At baseline, all participants were subjected to medical assessment, lab tests as well as quantitative HCV-RNA, fasting blood sugar levels or HbA1C if diabetes present as comorbidity, serum creatinine, CBC, AST, ALT, concentration of prothrombin or INR, total bilirubin, serum albumin, a test of pregnancy (childbearing aged females), alfa fetoprotein (AFP) as an HCC biomarker. Any participants who were (men > 40 years old, women > 50 years old). underwent abdominal ultrasonography and electrocardiogram before start of the treatment.

Virological response to treatment was evaluated using quantitative HCV RNA assessment, by PCR. Laboratory tests for the participants including, serum creatinine, ALT, AST, CBC, HbA1C if diabetic, INR, serum total bilirubin, albumin, AFP. Abdominal ultrasonography was repeated and any suspected focal lesion of the liver was examined with a triphasic CT scan or MRI to investigate the occurrence or the recurrence of HCC at the antiviral treatment end (12 weeks from the start) and SVR 12 (24 weeks from the start).