Case report

Coronavirus Disease 19 (COVID-19) in a Patient with Chronic HCV while on Direct-Acting Antiviral Therapy with a Worse Prognosis

Running title: COVID-19 disease in Chronic HCV patient while on DAAs.

List of Abbreviations:

COVID-19: Coronavirus Disease.

DAAs: Direct Acting Antiviral Therapy for HCV

WHO: World Health Organization

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2:

RT-PCR: Real-time reverse-transcriptase– polymerase-chain-reaction

ALT: Alanine Aminotransferase

AST: Aspartate Aminotransferase.

ALP: Alkaline Phosphatase

GGT: Gamma-glutamyl transferase

PLT: Platelet count

CPK-MB: creatine phosphokinase-MB

ECG: Electrocardiogram

LFT: Liver function test

INR: International normalized ratio:

Abstract:

Introduction:
The world is suffering a major global health pandemic caused by a new strain of the coronavirus (COVID-19). Herein, we encountered one case with COVID-19 and chronic HCV while on Direct Acting Antiviral Therapy.

Case presentation:
A 58-year male patient had chronic hepatitis C (HCV) without liver cirrhosis. He was on

Direct- Acting Antiviral Therapy for HCV (DAAs) in the form of Sofosbuvir 400 mg daily and Daclatasvir 60 mg daily (on his third month). The patient developed acute respiratory symptoms suggestive of pneumonia. Oropharyngeal swab for COVID-19 was positive as detected by real-time polymerase-chain-reaction (PCR) assay. The treatment for COVID-19 was given according to the Ministry of Health Protocol in addition to oxygen therapy with the continuation of his anti HCV therapy. His symptoms and oxygen saturation progressively deteriorated. The patient died despite supportive measures.

Conclusion:
Clinicians should suspect a worse prognosis of COVID-19 in chronic HCV patient despite supportive therapy for COVID -19. The efficacy of anti HCV therapy as protective or therapy against COVID-19 needs clinical trials.

Keywords: COVID-19; SARS-CoV-2; HCV; Coinfection; DAAs, Case report.

1.INTRODUCTION:

The World Health Organization (WHO) was informed about the emergence of a new virus from CORONA viruses' family on December 31st, 2019 [1]. This virus emerged from Wuhan City of Hubei Province of China and named by WHO as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2, 3, 4]. WHO declared that COVID-19 is considered a pandemic on 11 March 2020 [5]. Globally, 7, 941, 791 cases of COVID-19 have been reported with 434, 796 confirmed deaths as stated in WHO report on 16 June 2020 [6]. Risk factors for poor prognosis are older age, male sex and presence of comorbidities (obesity, diabetes, heart disease, lung disease, kidney disease) [7].

It is unclear to what degree chronic liver diseases could be considered as a risk factors, due to lack of appropriate studies [8]. However, patients with chronic liver disease, especially viral hepatitis B and/or C, may be more vulnerable to liver damage from SARS-CoV-2, but supporting data are limited [9].

To the best of our knowledge, the coinfection of SARS-CoV-2 and chronic HCV cases on treatment may occur in Countries with high prevalence of HCV, but not reported. Here, we present the occurrence of COVID-19 in chronic HCV case while on anti-HCV treatment.

2.PRESENTATION OF CASE:

A 58-year- old male patient had chronic hepatitis C without liver cirrhosis. He was on hepatitis C treatment in the form of Sofosbuvir 400mg daily and Daclatasvir 60 mg daily (on his third month). The patient developed acute respiratory symptoms in the form of high-grade fever and cough four days prior to presentation followed by shortness of breath 1 day prior to his admission to the Emergency Department of Assiut University Hospital on 15th of May 2020.

On physical examination at the time of admission, the patient had fever 38.5^0C, had an arterial blood pressure of 150/80 mmHg, a heart rate of 100 beats/min, respiratory rate of 40 breaths/min and oxygen saturation of 90% on room air. Chest examination revealed bilateral crepitation. On admission, urgent complete blood gas, and routine blood tests, were done. The arterial blood gas on room air showed a PaO_2 of 51 mmHg, $PaCO_2$ of 29 mmHg, HCO3 of 19 mmol, pH of 7.45. Acute respiratory failure type 1 was suggested. Oxygen therapy was given using venturi mask 50%.

Urgent blood tests revealed the following: hemoglobin (Hb) level of 12.9 g/dL, leucocyte count (WBCs) of 13.5 (x 10^3/ul), with 75 % neutrophils, 20.0% lymphocytes (N 20-45), and 2.0% monocytes, platelet count (PLT) of 279 (x10^3/ul), random blood sugar: 150 mg /dL, sodium (Na): 134 mmol/L (136-145), calcium: 8.4 mg/dl (N 8.6-10.2), potassium (K): 3.7 mmol/L (N 3.5-5.1), creatinine: 61 µmol/L (N 66-106), troponin: 0.03 (N up to 0.05), creatine phosphokinase-MB (CPK-MB): 8 U/L (N < 25), and D dimer: (0.8) mg/L (N up to 0.55).

Electrocardiogram (ECG) showed sinus tachycardia. Abdominal Ultrasonography showed mild hepatosplenomegaly and normal both kidneys. High resolution CT chest revealed multiple ground glass alveolar opacities (more evident on bilateral lower lung lobes) goes with diagnosis of COVID-19

(Figure 1). Oropharyngeal throat swab sample for COVID-19 was positive as detected by real-time reverse-transcriptase– polymerase-chain-reaction (RT-PCR) assay.

The patient was admitted to Al-Rajhi Liver Hospital, (COVID-19 quarantine hospital), Assiut, Egypt, on the 16th of May 2020 after confirmed positive PCR for SARS-CoV-2. Treatment was given according to Ministry of Health Protocol in Egypt (Hydroxy chloroquine 400 mg was given twice per day for 1 day then 200 mg every 12 hours, Vitamin C dose was 1 gm per day, Zinc dose was 50 mg per day, and antipyretics was given as needed). In addition, oxygen therapy was given via Venturi mask 50% and the patient was maintained on his anti HCV therapy.

Complete laboratory investigations after admission was as follow, ferritin: 1125 ng/ml (N 22-322), fibrinogen level: 3.34 g/L (N 2-4), high sensitive C-reactive protein (CRP): 202 mg/L (N 0-6). Triglycerides: 74 mg/dl (50-150), Prothrombin time (PT): 13.7 Second, concentration 72%, international normalized ratio: (INR) 1.14, total bilirubin: 8.5 umol/l (N 5-21), total protein: 61 g/L (N 64-83), albumin: 21g/L(N 34-50), aspartate aminotransferase: (AST) 45 U/L(N <34), alanine aminotransferase (ALT): 62 U/L (N 10-49), gamma-glutamyl transferase (GGT): 54 U/L (N <63), and alkaline phosphatase (ALP): 60 U/L (N 46-116).

Two days after hospital admission, follow up Hb 13.4: g/dl, PLT 279($x10^3$/ul), WBCs 18.4 ($x10^3$/ul), lymphocytes 17%, erythrocyte sedimentation rate (ESR) 1st hour 80 mm (N 3-5), 2nd hour 120 mm (N 7-12), creatinine 61 µmol/L, Follow up liver function test (LFT), total bilirubin: 13.6 umol/l, total protein: 59.8 g/L, albumin: 27.7 g/L, AST: 43.6 U/L, ALT: 39.6 U/L, GGT: 40.1 U/L, ALP: 72.4 U/L. ferritin: 2525 ng/ml. D dimer: 1.83 mg/L. Linezolid 600 mg IV every 12 hours and prophylactic dose of low molecular weight heparin were added.

One day later, worsening of oxygen saturation, so the patient was shifted to noninvasive mechanical ventilation. There was no clinical improvement on noninvasive mechanical ventilation and the patient died on the fourth day of hospital admission.

3.DISCUSSION:

We have reported this case with specific interest due to coinfection of SARS-CoV-2 and chronic HCV while on treatment which is not common. The essential factor that discriminates who complains of minor symptoms of COVID 19 and who will be very sick is his baseline state of health. Hepatitis C is a serious, pre-existing health condition. Therefore, a person who is infected with Hepatitis C is more

likely to suffer serious illness and confront a difficult, if not a fatal experience from SARS-CoV-2 infection than a person who does not have Hepatitis C [10].

Several studies stated that Sofosbuvir and other Direct Acting Antivirals (DAAs) could inhibit SARS-CoV-2 replication [10]. Coronaviruses are positive-strand RNA viruses with conserved polymerase, so SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) is suppressed by Sofosbuvir. So, it was hypothesized that SARS-CoV-2 infection could be susceptible to Sofosbuvir [11]. Sofosbuvir, Ribavirin, and Remdisivir can be used to treat COVID -19 disease with promising results [12]. Moreover, Sofosbuvir and Daclatasvir fixed dose combination regimen was used in treating Hepatitis C patients Co-infected with Human Immunodeficiency Virus [13].

A Multicenter trial in Tehran was done and randomized 66 adults hospitalized with severe COVID-19 to either Sofosbuvir and Daclatasvir plus standard of care (hydroxychloroquine with or without lopinavir/ritonavir) (active arm) versus standard of care only (control arm).The clinical recovery rate was 83% in active arm vs 67% in control arm. Time to clinical recovery, was faster in the active arm vs control arm (median: 6 days vs 11 days, p=0.041) [14]. This study was registered with the Iranian Clinical Trials Registry, IRCT202001238046294N2.

However, in our case despite he was on Sofosbuvir and Daclatasvir therapy, he gets infected with SARS-CoV-2 and his prognosis was poor with death at the end despite supportive therapy for COVID -19 and DAAs.

4.CONCLUSION: Clinicians should suspect a worse prognosis of COVID-19 in chronic HCV patients despite supportive therapy for COVID-19. The efficacy of anti HCV therapy as protective or therapy against COVID-19 needs more clinical trials.

5.REFERENCES:

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Figure 1: High resolution CT chest findings suggestive of COVID-19.