During the Era of Pandemic Corona Virus Disease 19, is Telemedicine Effective in the follow-up of Hepatitis C Virus Patients Receiving Direct anti-Viral Therapy?

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Background and study aims: A novel severe acute respiratory syndrome corona virus (SARS COV2) outbreak resulting in corona virus disease (COVID- 19) which is known as a pandemic infectious disease. Chronic hepatitis C virus (HCV) is a well-known major cause of chronic liver disease and its subsequent major complications. Telemedicine refers to the remote practice of medical care for patients when the provider and patient are not physically present with each other. We aim to assess use of telemedicine in the follow up of chronic HCV patients during treatment by direct antiviral therapy in this era of COVID- 19.

Patients and Methods: this study included cross matched 300 patients consulted for HCV treatment. 150 patients were treated in 2019 and followed by routine classic visits (routine classical group). Another 150 patients were treated in 2020 and followed up via virtual visits by telemedicine (telemedicine group).

Results: There is no significant statistical difference between the two groups regarding the sustained virological response (SVR) and the recorded side effects during treatment (P= 0.275, P= 0.523) respectively.

Conclusion: Use of telemedicine in the follow up of chronic HCV patients during treatment is as effective as the classic way and safer especially in the era of pandemic COVID19.

INTRODUCTION

A new severe acute respiratory syndrome corona virus outbreak has led to corona virus disease 2019 which has begun in Wuhan city in December 2019, then has rapidly spread throughout China and became worldwide **[1]**. The World Health Organization (WHO) has declared that COVID-19 is a pandemic infectious disease that was on 11 March 2020, and the number of confirmed COVID-19 cases has increased to more than 372000 globally by 24 March 2020 **[2]**.

About 1099 patients were diagnosed as COVID-19 from Wuhan city were studied and showed that typical clinical spectrum of symptoms of COVID- 2019 included fever, sore throat, fatigue, cough, and shortness of breath. Over 40% of patients had had a history of contact with confirmed COVID-19 cases and 56.2% didn't have history of fever **[3]**. Gastrointestinal symptoms of COVID-19 were less common when compared with SARS or MERS **[4, 5]**. The overall mortality was about 1.4%, and the mortality increases with the severity of cases up to 22.4% in more complicated cases **[6, 7]**.

There are over 185 million worldwide are infected with chronic hepatitis c virus (HCV), which is considered a known cause of chronic liver disease and its life threatening medical burdens such as liver cell failure, portal hypertension and hepatocellular carcinoma within 10 to 30 years **[8]**.

Telemedicine refers to the remote practice of medical care for patients when the health care provider and patient are not physically present with each other. It is recognized as the remote delivery of health care services, as distance is a limiting factor, by all health care professionals using informational technologies and modern communication methods for the exchange of valid and clear information for diagnosis, prevention of disease and injuries and treatment, also telemedicine can be used for research and evaluation **[9]**.

Technology has become as a great enabler of patient continuity through remote medical consultation, ongoing monitoring, and patient education using telephone and videoconferencing in the COVID-19 era **[10]**.

In this study, we want to assess retrospectively patients who received anti- HCV treatment and were followed via telemedicine and different communications methods during this current era of COVID- 19 in 2020.

PATIENTS AND METHODS

This current retrospective study has included 300 naive chronic HCV patients who asked for medical advice at viral hepatitis clinic, Minia university hospital, Egypt, were treated with sofosbouvir 400 mg, daclatasvir 60 mg for 12 weeks. 150 chronic HCV naive patients were treated during the period of 2019 and were followed by regular routine visits during the treatment (routine classical group). Another 150 cross matched chronic HCV naïve patients during 2020 after beginning of the era of COVID 19 (telemedicine group). Patients were included in the study according to the following criteria (positive HCV RNA, age is ranging from 18 to 65 years, and treatment naïve patients). Exclusion criteria from the study if patients had any of the following : treatment experienced patients, patients with current or previously treated hepatocellular carcinoma, extra-hepatic malignancy, liver transplanted patients, patients with severe extra-hepatic manifestations, pregnancy, or inability to use effective contraception, poorly controlled diabetes mellitus, patients suffering from advanced kidney disease, and patients with child B or C liver cirrhosis. Patients were subjected before treatment to detailed medical history including treatment of accompanying chronic medical comorbid diseases, meticulous clinical examination, assessment of body mass index and laboratory measures including HCV antibodies using the ELISA technique, HCV RNA quantitative PCR before treatment, follow-up at the end of treatment and at 12 weeks after the end of treatment, liver function tests including aspartate aminotransferase, alanine aminotransferase, international normalized ratio, serum albumin, total and direct serum bilirubin, plus HBs Ag, HIV antibody by ELISA, complete blood count, fasting blood glucose, and HbA1c (in diabetic patients), serum creatinine, calculation of estimated glomerular filtration rate **[11]**, alpha fetoprotein, pregnancy test for females in the child-bearing period, and pelvic-abdominal ultrasonography. Child Pough assessment of cirrhotic patients was done **[12]**. Patients had been treated with Sofosbouvir 400 mg, Daclatasvir 60 mg for 12 weeks. During the treatment period, 2019 group (routine classical group) of patients were followed up by regular routine classic visits every 2-4 weeks while 2020 group (telemedicine group) of patients were followed up by telemedicine and different communication methods as the patients received three doses of sofosbouvir 400 mg and daclatasvir 60 mg once and were instructed to send their follow up laboratory results and follow up symptoms checklist sheet via whatsApp application to well defined certain mobile numbers and this is the preferred method or via certain e mail at the end of every dose. There is also a well-known hot line for emergent clinical problems and video communications if needed at specific preset dates, complete blood count, creatinine, bilirubin, AST, ALT were monitored, Quantitative PCR for HCV RNA at 12 weeks after the end of treatment was done.

The gathered data were inserted, and statistically analyzed using statistical package for social sciences program (SPSS) software version number 24. Qualitative data were expressed as proportions while quantitative data were expressed as mean $\pm$ standard deviation (SD) and median plus inter quartile range (IQR). Statistical significance was defined when p values are less than 0.05.

RESULTS:

The present retrospective study included cross matched 300 patients were suffering of chronic HCV and were treated by direct acting antiviral regimen for 12 weeks, were divided into two

equal groups; routine classical group of patients were followed up by regular routine classic visits every 2-4 weeks till the end of treatment and telemedicine group of patients were followed up by telemedicine and different modern communication methods. Table 1 shows the baseline characters of both groups; as regard age, sex, residence and the presence of comorbid diseases; baseline characteristics were generally balanced between the studied groups. Table 2 shows that there are no significant statistical changes between routine classical group of patients and telemedicine group of patients regarding the different laboratory measures. Table 3 shows that the treatment response in telemedicine group of patients is about (98.6%), two patients (1.4%) didn't achieve SVR, the response to treatment in routine classical group of patients is about (99.3%) only one patient didn't achieve SVR, no significant difference between both groups regarding response to treatment (P value > 0.05), all patients in the studied groups completed the course of treatment. Table 4 shows that total number of patients experienced adverse effects in telemedicine group of patients is 17(11.3%) versus 13(8.6%) in routine classical group of patients as follow; headache occurred in 2 patients (1.3%) in telemedicine group of patients also in 2 patients (1.3%) in routine classical group of patients. fatigue occurred in 3 patients (2%) in telemedicine patients versus 2 patients (1.3%) in routine classical patients. lower GIT symptoms occurred in 2 patients in 2020 group (1.3%) versus one patient (0.7%) in routine classical group. Upper GIT symptoms occurred in 2 patients (1.3%) in telemedicine group of patients versus 3 patients (1.3%) in routine classical group of patients. Itching occurred in 2 patients (1.3%) in telemedicine patients versus one patient (0.7%) in routine classical patients, chest symptoms occurred in one patient in telemedicine patients (0.7%) and also in one patient (0.7%) in routine classical patients, hemoglobin drop below 10g occurred in one patient (0.7%) in telemedicine group of patients also in one patient (0.7%) in routine classical group of patients, no record for affection of white blood cells, no record for fever or severe complications such as development of ascites, hepatic encephalopathy or upper and lower GIT hemorrhage in studied groups, no significant difference between telemedicine patients or routine classical patients regarding adverse effects (P value > 0.05). Table 5 shows that in telemedicine HCV group of patients 135 patients (90%) are satisfied by the telemedicine way as a method of communication between the doctor and the patient while 15 ones aren't satisfied (10%). In routine classical HCV group of patients 125 patients (83.3%) are satisfied by the classic way for follow up between patient and doctor in the form of regular routine visits while 25 ones (16.7%) aren't satisfied no significant difference between both groups regarding patient satisfaction (P value >0.05).

Table (1): Demographic data of studied groups.

		Telemedicine Group of patients	**Routine classical group of patients**	**P value**
		N=150	**N=150**	
Age	Range Mean ± SD	(31-66) 43.1±8.3	(22-69) 48.±7.8	>0.05
Sex	Male Female	69(46%) 81(54%)	73(48.6%) 77(51.4%)	>0.05
Residence	Rural Urban	89(59.3%) 61(40.7%)	81(54%) 69(46%)	>0.05
Comorbid diseases	No Yes	122(81.3%) 28(18.7%)	116(77.4%) 34(22.6%)	>0.05
Comorbid diseases	hypertension Diabetes hypertension and diabetes	11(7.3%) 13(8.7%) 4(2.7%)	13(8.7%) 19(12.7%) 2(1.3%)	>0.05

SD (standard deviation)

Table (2): Laboratory data before treatment.

		Telemedicine Group of patients N=150	Routine classical group of patients N=150	P value
ALT	Median IQR	46 (40-65)	49 (41-74)	0.170
AST	Median IQR	52 (43-75)	60 (51-86)	0.053
Creatinine	Mean ± SD Median IQR	0.98±0.21 1 (0.8-1.1)	0.95±0.19 0.9 (0.8-1)	0.320
Platelets	Median IQR	190 (150-215)	187 (139.5-208)	0.063
Bilirubin	Median IQR	1.1 (0.9-1.3)	1.2 (0.9-1.4)	0.982
Albumin	Median IQR	4.1 (3.8-4.7)	4.2 (3.7-4.9)	0.566
INR	Range Mean ± SD	(1-1.7) 1.3±0.2	(1-1.6) 1.2±0.2	0.532

- ***Independnet samples T test for parametric quantitative data between the two groups***
- ***Mann Whitney test for non- parametric quantitative data between the two groups***

****: Significant level at P value < 0.05, ALT (alanine transferase), AST(aspartate transferase), INR(international normalized ratio) , IQR(interquartile range), SD(standard deviation)***

Table (3): Response and compliance on treatment.

		Telemedicine group of patients N=150	Routine classical group of patients N=150	P value
Response	SVR Relapse	148(98.6%) 2(1.4%)	149(99.3%) 1(0.7%)	0.275
Continuation of treatment		150(100%)	150(100%)	
Patient satisfaction	Yes No	135(90%) 15(10%)	125(83.3%) 25(16.4%)	0.175

****: Significant level at P value < 0.05*** SVR (sustained virological response)

Table (4): Adverse effects and morbidity.

	Telemedicine group of patients	Routine classical group of patients	P value
	N=150	N=150	
Headache	2(1.3%)	2(1.3%)	1
Fatigue	3(2%)	2(1.3%)	0.413
Lower GIT symptoms	2(1.3%)	1(0.7%)	0.096
Upper GIT symptoms	2(1.3%)	3(2%)	0.417
Itching	2(1.3%)	1(0.7%)	0.096
Fever	0	0	
Chest symptoms	1(0.7%)	1(0.7%)	1
Abdominal pain	4(2.6%)	2(1.3%)	0.123
Ascites	0	0	
Hepatic encephalopathy	0	0	
GIT haemorrhage	0	0	
Haemoglobin drop below 10g/dl	1(0.7%)	1(0.7%)	1
Drop of white blood cells below 3,000	0	0	
total	17(11.3%)	13(8.6%)	0.523

- ***Independnet samples T test for parametric quantitative data between the two groups***
- ***Chi square test (if less than 20% of cells have expected count <5) or Fisher exact test (if more than 20% of cells have expected count <5) for qualitative data between the two groups***

****: Significant level at P value < 0.05***

DISCUSSION

The present study designed to assess the use of telemedicine and modern communication methods in the follow-up of chronic HCV patients receiving direct antiviral therapy instead of classic routine visits during the treatment period in the era of COVID-19. The process of clinical care has been shifted to telemedicine communications after the era of pandemic COVID- 19 **[13]**. In the pre COVID time, routine home based patient doctor telemedicine care was little due to lack of reimbursement. The pandemic COVID-19 has made a lot of changes in medical practice. Now patients and physicians were struggling to reduce classic visits for public health reasons **[14]**. Telemedicine can be determined as an integration of several components such as information and communication technologies, hardware and software technologies and medical services reacting together so as to provide required features or services to users **[15]**.

In our study we have found that the SVR in chronic HCV patients who were treated by Sofosbuvir 400 mg and Daclatsvir 60 mg direct antiviral therapy for 12 weeks during the era of COVID- 19 and were monitored by virtual visits via telemedicine and different communication procedures was nearly similar to those HCV patients who received also same treatment and were followed by routine classic visits without significant statistical difference. Recording of side effects to treatment by the virtual visits via telemedicine was possible like the classic routine visits and it could be done during any part of the day which may be an advantage for the patients. Most of patients who were followed by telemedicine program were satisfied by this easier and safer way for communication with their doctors and to receive public health services with little costs. We conclude that use of telemedicine in the follow- up of chronic HCV patients during treatment is as effective as the classic way and safer especially in the era of pandemic COVID-19.

Ethical Approval: Informed and written consent was obtained from all individual participants included in the study, and also, for publication of the work. Local research Ethics Committee for human subject research reviewed and approved the research protocol and consent forms. All procedures performed in the study were in accordance with the ethical standards of the national research committee.

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HIGHLIGHTS

- Chronic hepatitis C virus (HCV) is considered a major cause of chronic liver disease and its major complications
- Telemedicine refers to the practice of medical caring for patients remotely when the provider and patient are not physically present with each other.
- Use of telemedicine in the follow up of chronic HCV patients during treatment by direct antiviral therapy is as effective and safer as the classic way.

REFERENCES

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* 2020; 382(13):1199–207.
2. WHO. Corona virus disease (COVID-2019) situation reports. Situation report – 64, 2020. Available: https://www.who.int/docs/default source/corona-viruse/situationreports/ 20200324-sitrep-64-covid-19.pdf? sfvrsn=703b2c40_2.
3. Guan WJ, ZY N, Hu Y, Liang W, Shan H, Liu L et al. China medical treatment expert group for COVID-19. clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020 ; 382:1708-1720.
4. Wong S, Lui R, Sung J. COVID-19 and the digestive system. *J. Gastroenterol. Hepatol*. 2020. 35 (5), 744-748.
5. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; 323(11):1061-1069.
6. Coronavirus COVID-19 global cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. https://doi.org/10.1101/2020.03.26.20044743
7. Chen N, Zhou M, Dong X, Lee MH, Archelueta S, Bagdasarian N et al. Epidemiological and clinical characteristics of 9 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395.10223: 507-513
8. Jazwinski A B, Muir AJ. Direct-Acting Antiviral Medications for Chronic Hepatitis C Virus Infection. *Gastroenterol Hepatol (N Y).* 2011; 7(3):154–162.
9. Ittipong K, Watsawee S, Manachai T. Telemedicine – Meaning, Challenges and Opportunities, *Siriraj medical journal*, 2019, 71.3: 246-252
10. Sonu B, Sian B, Vijy K, Anil A, Alma N, Saltanat K et al. Telemedicine As The New Outpatient Clinic Gone Digital: Position Paper From The Pandemic Health System REsilience PROGRAM**.** Public Health |accepted 10 july 2020 *Frontiers in public health*, 2020, 8: 410 doi: 10.3389/fpubh.2020.00410.
11. Levey AS, Greene T, Kusek I, Beck G. A simplified equation to predict glomerular filtration from serum creatinine (Abstract). *J Am Soc Nephrol* 2000; 11:155A.
12. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973 Aug;60(8):646-9.
13. U.S. Centers for Medicare & Medicaid Services. Telehealth services. 2020, mbMar Accessed 2020 Apr 14. https://www.cms.gov/Outreach-and-Education/MedicareLearning- Network-MLN/MLNProducts/ Downloads/TelehealthSrvcsfctsht.pdf.
14. Duffy S, Lee TH. In-person health care as Option B. *N Engl J Med* 2018:378:2: 104-106.
15. Hollander JE, Carr BG. Virtually perfect? Telemedicine for Covid-19. N Engl J Med 2020;382: 1679-1681.