

Impact of the Covid-19 pandemic on the elimination of hepatitis C virus in Duhok, Kurdistan, Iraq: A retrospective cross-sectional study

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ABSTRACT

Background and Aim: Infection with hepatitis C virus (HCV) is a public health threat worldwide. The World Health Organization aims to eliminate HCV. However, the coronavirus disease (COVID-19) pandemic has led to a severe compromise in health services, and this has halted efforts to eliminate HCV. Herein, we report our experience with the initiative of HCV elimination in Duhok city, Kurdistan Region of Iraq, with a focus on the effect of the COVID-19 pandemic on the HCV elimination plan. **Materials and Methods:** An anti-HCV antibody test was used to screen subjects. All positive results were then confirmed by reverse-transcription polymerase chain reaction (RT-PCR) testing. All patients with current HCV infection were treated with direct-acting antiviral regimens. **Results:** During the study period, 459,015 subjects were tested for anti-HCV antibody positivity, with a monthly average of 9,562 tests for HCV. This number dropped to zero during the lockdown period between 1 March and 31 May 2020. Among the tested samples, 0.29% (1350/459015) tested positive for anti-HCV antibodies. RT-PCR testing of all positive samples revealed that 0.020% (93/459015) were positive. Of the 93 recruited subjects, 3 patients did not complete the treatment course due to the lockdown. All patients who finished the treatment course were cured as determined by sustained virologic response 12 (SVR12) weeks after finishing the treatment course. **Conclusion:** During the COVID-19 pandemic, reductions in health facility utilisation led to a significant decrease in services offered for HCV screening and treatment. Such a decrease in services has had a negative impact on HCV elimination. An urgent plan is needed to resume the services, and strict follow-up is needed for patients whose treatment was interrupted.

Keywords: COVID-19, Duhok, HCV elimination, Iraqi population, Kurdistan

Introduction

HCV infection is a public health issue worldwide^[1] and is predispose to deleterious effects such as hepatic failure and liver cancer. The World Health Organization (WHO) is aiming

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at the elimination HCV as a public health threat by reducing the transmission of HCV and decreasing the morbidity and mortality related to the infection.^[2] The WHO has proposed a 60% reduction in HCV-related mortality and a 90% reduction in HCV transmission globally.^[2] Such reductions can be achieved by improving the following areas: infection control to minimise the risk of transmission within the healthcare system; preventive measures that eliminate the risk of transmission of HCV among vulnerable groups such as patients who need

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multiple blood transfusions; the surveillance system for HCV infection; and the healthcare system so that all patients have access to treatment.^[2] In addition, the approval of direct acting antiviral (DAA) medications for the treatment of the HCV has encouraged healthcare providers working to eliminate HCV. The COVID-19 pandemic has impacted healthcare services, including those offered to HCV patients.^[3,4] The Kurdistan Region of Iraq adopted lockdown and social distancing measures to combat the transmission of the infection.^[5,6] In addition, the government diverted resources to halt the outbreak. In this study, we report our experience about the initiative of HCV elimination in Northern Iraq, with a focus on the effect of the COVID-19 pandemic on the HCV elimination plan.

Methods

Study setting

This retrospective cross-sectional study was conducted in Northern Iraq. The HCV elimination initiative was established on 1 January 2016 and was then adopted by the College of Medicine, University of Zakho. HCV screening checkpoints were set up to test different categories of individuals including blood donors, premarital couples, government job applicants, and preoperative patients. Five cities were included in the study: Duhok, Aqre, Zakho, Amedi, and Sumail. We included all the data obtained between 1 January 2016, and 31 May 2020 in the study.

Confirmation of HCV infection

Enzyme-linked immunosorbent assay

Anti-HCV antibodies (fourth generation) were studied using a commercial ELISA kit (DIA.PRO Diagnostic Bioprobes Srl, Lombardia, Italy) as per manufacturer's instructions.

Quantification of HCV RNA and HCV genotyping

Reverse transcription polymerase chain reaction (RT-PCR) was used for the amplification of HCV RNA using Artus HCV RG RT-PCR kit (Qiagen, Hamburg, Germany) as per manufacturer's instructions. HCV genotyping was performed using the reverse hybridisation technique (NLM, Settala, Italy).

Patients and treatment

This is a retrospective study and all data extracted from medical record. All subjects with HCV were prescribed a direct-acting antiviral (DAA)-based regimen as part of routine clinical practice in infectious disease and gastroenterology units in Duhok City. In the current study, our patients were classified into four groups: subjects without comorbidities, subjects with thalassaemia, subjects with end-stage renal disease (ESRD), and patients with renal transplant who were treated for chronic HCV.

Treatment efficacy was measured as by SVR12 which is defined as an HCV-RNA level below the level of quantification or that is undetected, recorded 12 weeks after treatment was discontinued.

Ethics

The study was approved by the Scientific and Ethics Committee of the College of Medicine, University of Zakho. Oral consent was obtained from all participants before data collection. Written consent was also obtained from all subjects who received treatment.

Results

Prevalence of HCV and its genotypes

In the study period, 459015 subjects were tested for anti-HCV antibody positivity, with a monthly average of 9562 tests for HCV. This number dropped to zero during the lockdown period between 1 March and 31 May 2020. Among the tested samples, 0.29% (1350/459015) tested positive for anti-HCV antibodies. To distinguish between current infections and old resolved infections, all positive samples were sent to testing by RT-PCR. The RT-PCR showed that 0.020% (93/459015) samples were positive. Approximately 60% of the positive samples accounted for samples collected from male subjects. When we performed genotyping of all samples positive on RT-PCR, 46.2% (43/90) of our samples were typed as HCV genotype 4, 46.2% (43/90) as genotype 1, and 7.78% (7/90) as genotype 3 [Table 1].

Patients and treatment

During the study period, 93 subjects had chronic HCV without comorbidities ($n = 82$), thalassaemia ($n = 5$), ESRD ($n = 2$), or kidney transplant ($n = 4$) were treated for HCV. Amongst them, 61.2% (57/93) were males. A total of 83 patients (89.2%) were treatment-naïve without prior exposure to the classical regimen of peg-interferon (PIFN) and ribavirin (RIB) combination. One patient received a PIFN and RIB combination, followed by a combination of sofosbuvir (SOF), RIB, and PIFN, both of which failed to achieve SVR.

Of the 93 recruited subjects, 3 who were receiving SOF/ledipasvir (LED) did not complete the treatment course due to the lockdown. Of the 90 patients who completed the treatment course, 88 received treatment for 12 weeks: 70 were treated with SOF/LED, followed by SOF; 16 patients were treated with PIFG plus RIB; and two patients with ESRD received an SOF 200 mg/daclatasvir-containing regimen. In addition, 2 patients received ribavirin (RBV) plus RIB for 24 weeks [Table 2]. All patients who finished the treatment course were cured, as determined by SVR 12 weeks after finishing the treatment course.

Discussion

During the study period, each month, more than 9000 subjects were tested for HCV. This number dropped to zero during the social distancing and lockdown period. Such a severe compromise in HCV screening highlights the devastating wider impact of the COVID-19 outbreak. To maintain the

Table 1: Characteristics of patients with hepatitis C virus infection who finished the treatment course before the lockdown

Comorbidities	Genotypes			Treatment-naïve	Average age	Male (No.)	Total	Cure rate
	G1	G3	G4					
No comorbidities	37	7	35	77	42±12	46	79	100%
Thalassaemia	1	0	4	1	18.6±4	3	5	100%
ESRD	2	0	0	1	42.5±7.8	2	2	100%
Renal transplant	2	0	2	1	40±8.5	3	4	100%

ESRD: end-stage renal disease

Table 2: Treatment courses used in the treatment of patients with hepatitis C virus infection who finished the treatment course before the lockdown

Comorbidities	Course				Total	RVR	SVR
	SOF/RIB	SOF, RIB and PIFN	SOF/LED	SOF/DAC			
No comorbidities	0	13	68	0	79	58 (73.4%)	81 (100%)
Thalassaemia	0	3	2	0	5	4 (80%)	5 (100%)
ESRD	0	0	0	2	2	2 (100%)	2 (100%)
Renal transplant	2	0	2	0	4	0 (0%)	4 (100%)

DAC=daclatasvir, ESRD=end-stage renal disease, LED=ledipasvir, PIFN=peg-interferon, RIB=ribavirin, SOF=sofosbuvir, SVR=sustained virologic response, RVR=rapid viral response

health system, including the hepatitis elimination initiative in the pandemic and to avoid outbreaks of other diseases, healthy scepticism and the foundation of clinical equipoise should be retained.

There is a great variation in the prevalence of anti-HCV antibody positivity among countries, ranging from 0.4% to 19.2%.^[7-9] Previous studies from Iraq found that 0.5% of recruited samples were positive for HCV.^[10] A previous study from our city, Duhok, showed that 0.2% of the samples were positive for anti-HCV antibodies.^[11] In the same study, RT-PCR was performed to confirm the positivity, and it was shown that 0.013% were currently infected with HCV. In our study, we found that 0.020% of our samples were currently infected with HCV. The difference between our results and the results from previous studies could be explained, in part, by the large sample size recruited in this study. In addition, in this project, different groups of people were recruited rather than a specific group, as was the case in previous reports.

All diagnosed subjects were offered treatment with new powerful medications. Sustained virologic response was achieved in 100% of the patients. Additionally, no medication discontinuation was reported, indicating the noticeable improvement in drugs tolerability compared to the classic interferon-containing regimen. Our data support the success and ease of new HCV DAA-based regimens that we previously showed.^[12,13] Our results extend the experience of DAA treatment to the drugs approved subsequently and in populations with and without comorbidities. The most frequently used regimen in this study was SOF/LED. Impressively, the successful outcomes found in our clinical experience were higher than those observed in clinical trials of carefully selected patients.^[14,15] This might be due to the small sample size recruited in our study or the differences in the population and genetic makeup of patients and viruses in

this region. The significance of our study is that we recruited all patients with and without comorbidities, such as ESRD and renal transplant patients, with a 100% SVR.

It is worth acknowledging the limitations of our data. This report was not randomised clinical study, and our analysis was based on the per-protocol population.

With the high success rates and minor side effects of the new medications, the long-awaited goal of HCV elimination is closer than ever. However, the COVID-19 pandemic has interrupted HCV treatment, which requires high medication adherence to be successful. Such an interruption, which is particularly damaging to our HCV elimination initiative, will have a public health impact.

Before Covid-19 pandemic, the role of primary care physicians was to refer patients with HCV to infectious disease units. With the closure of these units, primary health care physicians can ideally be positioned to offer treatment and long-term care for patients with HCV. Hence, primary care physicians can play a major role in containing the HCV epidemic during covid-19 pandemic.

In summary, our paper showed that the scope and scale of the consequences of covid-19 pandemic on population health is beyond the direct morbidity. The long-term consequences may include weakening of other programs combating infectious diseases such as HCV elimination initiative. After the establishment of the HCV initiative in our city, 459,015 people were tested for HCV. The infection rate was very low, and 93 patients were diagnosed with current HCV infection. All infected subjects were offered treatment that resulted in a 100% success rate. Reductions in health facility utilisation due to the COVID-19 pandemic led to a significant decrease in the services offered for HCV screening and treatment.

Such a decrease in services may negatively impact HCV elimination. Urgent action is required to resume these services, and strict follow-up is needed for patients whose treatment was interrupted.

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Ethical approval

Ethical approval was obtained from the Scientific and Ethics Committee of the College of Medicine, University of Zakho (Ethic reference number: 4/154NW, Approval data of ethic committee was obtained: 02.05.2019).

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Conflicts of interest

There are no conflicts of interest.

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