Treatment of Hepatitis C Genotypes 1 to 5 in Sub-Saharan Africa Using Direct-Acting Antivirals

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Abstract. There is limited knowledge of the use of direct acting antivirals (DAAs) for the treatment of hepatitis C virus (HCV) in sub-Saharan Africa. We prospectively evaluated individuals infected with HCV genotypes 1 to 5 in Addis Ababa, Ethiopia. Liver fibrosis was assessed by AST–platelet ratio index score and cirrhosis by imaging and laboratory values. All 164 individuals completed treatment. The majority of patients had genotype 4 (76%), and 19% of participants showed evidence of cirrhosis. Sustained virologic response (SVR) across all genotypes was 98.8%. In those with cirrhosis, SVR was 93.5% and in non-cirrhotics 100%. Our study demonstrates broad genotype successful treatment of HCV with DAAs in sub-Saharan Africa, demonstrating the feasibility of HCV elimination in resource-limited settings.

In the last 5 years, treatment of hepatitis C virus (HCV) with direct-acting antivirals (DAAs) has shown an extraordinary cure rate and completely changed gastroenterologists' approach to HCV.¹ There is now ongoing discussion regarding the eradication of HCV worldwide. Envisioning this aim requires implementation of treatment across the globe, including low-income countries.² Indeed, the short duration of treatment and low–side effect profile suggest that DAAs would prove most beneficial in resource-limited settings. Nonetheless, there is limited knowledge of the use of DAAs in sub-Saharan Africa.³ In this study, we evaluated the use of DAAs in a cohort of patients in Ethiopia. We prospectively evaluated all individuals diagnosed with hepatitis C who were eligible and agreeable for treatment in Adera Medical Center (Addis Ababa, Ethiopia), from February 2016 to June 2017. Patients were not enrolled in a trial style but rather followed in an observational study approach. Diagnosis of HCV infection was performed with antibody detection (Assure Tech, Hangzhou, China) and confirmed with HCV quantitative RNA level (COBAS TaqMan PCR, Roche, Basel, Switzerland). All patients underwent examination of liver enzymes, HCV genotyping, abdominal ultrasonography (US), and general laboratory analyses. The AST–platelet ratio index (APRI) score and US were used to evaluate liver fibrosis. Imaging and laboratory values were used to evaluate the presence of cirrhosis. Hepatitis C virus RNA was measured before treatment and 12 weeks after completion of therapy. Non-cirrhotic patients with genotypes 1, 4, and 5 were treated with ledipasvir/sofosbuvir (LDP/SOF) for 12 weeks, and those with cirrhosis had addition of ribavirin (RBV) or extension of therapy to 24 weeks. Individuals with genotype 2 and 3 infections were treated with SOF/ribavirin (RBV). All statistical analyses were performed using the SPSS version 22.0 statistical package (Armonk, NY). Ethical approval was obtained from Adera Medical Center.

A total of 164 HCV-infected patients were treated with DAAs over a period of 18 months, and all patients completed treatment. The mean age of patients was 52 years (interquartile range [IQR] 42–60), and females accounted for 55% (*N*: 90) of the cohort (Table 1). Seventy-six percent of patients (*N*: 110)

had HCV genotype 4, 14% genotype 2, 6% genotype 1, 2.5% genotype 5, and 1.5% genotype 3 (Table 1). The median HCV RNA level before treatment was 1,300,555 IU/L (IQR 649,825–3,182,800), and the median APRI score was 1.49 (IQR 1.13–2.24), with 19% (*N*: 31) of participants showing evidence of cirrhosis. The median platelet count in patients with cirrhosis was 95,300 (IQR 68,300–150,000). All, but three patients, were HCV treatment naive. Sixty-seven percent (*N*: 110) of patients were treated using LDP/SOF, 18.5% with LDP/SOF/RBV, and 14.6% with SOF/RBV. The treatment period was 12 weeks in 96% (*N*: 157) of the participants and 24 weeks in the remaining 4% (the latter group length of therapy was because of the presence of cirrhosis and previous treatment experience). The rate of sustained virologic response (SVR) across all genotypes was 98.8% (*N*: 162). In those individuals with cirrhosis, SVR was 93.5% (*N*: 29 of 31) and in non-cirrhotics 100%, regardless of the APRI-based fibrosis level. Only two patients, both with HCV genotype 4 infection, failed to achieve SVR. Both showed evidence of decompensated cirrhosis, and one had failed previous therapy with interferon, both of which have previously shown to impact SVR in other studies.⁴ Among reported side effects, fatigue was most commonly reported in 11% (*N*: 18) of participants, followed by nausea in 1.2% (*N*: 2). All side effects subsided after the end of treatment.

Our study shows the successful real-life treatment of HCV, in all genotypes, but 6, in a cohort of patients in sub-Saharan Africa. Importantly, all participants finished the prescribed treatment, indicating that adherence is unlikely to be a barrier in resource-limited settings. Our findings are comparable with findings from Egypt, the United States, and Europe in terms of SVR rates across all subjects.^{4,5} In the case of non-cirrhotics, the success rates in our study were higher than those in most real-life reports.⁶

In our cohort, HCV genotype 4 was the most frequent genotype identified, and the high SVR rate in this group indicates that if treatment is escalated globally, a favorable response can be expected. This is of importance as recent reports have highlighted the need for treatment assessment in this population.⁷ One of the limitations of studies from predominantly Western and Asian population has been the small number of patients with genotype 4. In this regard, our study adds to the growing evidence in the treatment of this group of patients.⁷ As prioritization of treatment of HCV expands in Africa, there is a need to understand the effectiveness of antiviral treatment in

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TABLE 1
Variables of direct-acting antiviral-treated patients

Variable	Frequency (total %)
Male	74 (45)
Female	90 (55)
Hepatitis C virus genotype	
1	10 (6.1)
2	23 (14)
3	2 (1.2)
4	125 (76.2)
5	4 (2.4)
Treatment experience	
Naive	161 (98.2)
Interferon failure	3 (1.8)
AST-platelet ratio index score	
< 1.5	81 (49.4)
1.5–2.0	35 (21.3)
> 2.0	48 (29.3)
Treatment regimen	
LDV/SOF	110 (67.1)
LDV/SOF + RBV	30 (18.3)
SOF + RBV	24 (14.6)
Treatment outcome	
Sustained virologic response-12	162 (98.8)

LDV = ledipasvir; RBV = ribavirin; SOF = sofosbuvir.

the region. Moreover, as recent studies suggest a lower response in black race, studies as ours become critical in understanding the real response of DAAs in the continent.⁸

A potential limitation of the present study is that the patients were not evaluated using transient elastography which was not available at the center. However, the diagnostic modality is also currently not available in most parts of Africa, and evaluation of liver disease using simple algorithms will be necessary to contemplate eradication. In addition, our study did not address hepatitis B virus (HBV) infection or exposure before HCV treatment. Hepatitis B virus is highly prevalent in the area, and likely, a significant proportion of the HCV-infected population expresses HBV core antibody.⁹ Concern has been raised recently about potential reactivation of HBV in those previously exposed.¹⁰ It should be noted, however, that none of the participants in our study experienced flare of liver enzymes during or after treatment. Further studies and treatment strategies in the region will require assessment of HBV infection and exposure before treatment initiation. Subsequent evaluation of the DAAs in other African countries is needed. Nonetheless, our study indicates that successful treatment of HCV in sub-Saharan Africa is achievable, contributing to the vision of HCV elimination worldwide.

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