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Factors influencing treatment outcome in hepatitis C virus minority patients at an inner-city hospital

A STROBE-complaint article

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Abstract

Chronic hepatitis C virus (HCV) infection disproportionately affects African-Americans (AAs) and is a major contributor to liver failure and mortality. Genetic factors may not be the only cause in outcome disparity. We retrospectively investigated whether genetic host factors, viral genotypes, and treatment compliance in AA patients impacted the efficacy and the sustained virological response (SVR) rate of the interferon (IFN)-based treatment regimen. The medical chart review included 76 African-American patients (age ranging from 26 to 76) with varying levels of hepatitis condition. Fifty-seven (75%) of them had a clinically verifiable HCV infection and were followed by a hepatologist for 2 years at Howard University Hospital in Washington, DC. Both comprehensive metabolic profile and complete blood count analyses were performed. Among the 57 patients whose viral and IL28B genotypes were determined, sixty-eight percent (68%) were infected with viral genotype 1 and 71% harbored the CT allele of the *IL28B* gene. Among the 12 patients who completed treatment with IFN-based dual or triple therapy, 58% had achieved SVR 12 weeks following completion of treatment; 33% had a partial response with under 6000 viral count after 16 weeks of treatment; and there was one patient with viral genotype 1a and CT allele who did not respond to the medications. The results of this study prove that the PEG IFN-based regimen was effective in treating HCV-infected AA patients despite the current availability of new direct-acting antivirals. The major obstacles contributing to a low reduction in HCV infection and outcome in the AA community were avoidance or lack of treatment or compliance; contraindications, medication side effects, non-adherence, and payer eligibility restrictions.

Abbreviations: AA = African-American, DAA = direct-acting antivirals, HCV = hepatitis C virus, HUH = Howard University Hospital, IL28B = interleukin 28B, SVR = sustained virological response.

Keywords: African-American, HCV, interleukin 28B, PEG-interferon, Ribavirin, SVR, Telaprevir

1. Introduction

Hepatitis C virus is the most common but rarely recognized form of blood-borne diseases in the United States; and chronic hepatitis C virus (HCV) infection is a leading cause of virus-associated morbidity and mortality affecting about 2.7 to 3.9 million people in the United States and resulting in about 16,500 deaths annually.[1] This prevalence is, however, an underestimation of the real rate since the homeless people, incarcerated individuals, active military, veterans, and healthcare workers were not included in the National Health and Nutrition Examination Survey (NHANES).[2]

Among the HCV-infected population in the United States, only 7% to 11% had been medically treated over the years[3] and it is expected that the percentage will be much higher now with the advent of the direct-acting anti-viral drugs (DAA) that have a cure rate of over 90%. Most people are still unaware of their infection. Baby boomers are especially vulnerable and account for more than 75% of individuals chronically infected with HCV and are specifically singled out for screening.[1] African-American (AA) male patients have a high rate of exposure (8.3%) in this birth cohort.[2] Overall, AAs with chronic HCV infection experience higher rates of mortality due to cirrhosis and liver cancer and are disproportionately underrepresented in clinical trials.[4,5] One of the findings for a poor prognosis in this ethnic group is a non-CC

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IL28B (*IFNL3*) genotype (i.e., CT or TT) that exhibits a weaker immune response and efficacy to the pegylated IFN-alpha (PEG-IFN α)-based treatments.[6,7] The SNP, rs8099917 in gene *IL28B*, is reported to be associated with risk of chronic infection by HCV but is not associated with response to treatment.[8] In contrast, the reported toxicity and side-effect of IFN, which sometimes can culminate in neutropenia and thrombocytopenia, are especially concerning for AAs who have lower counts of leukocytes and neutrophils than do Caucasians.[9] Therefore, avoidance of treatment, which is common in this group may not be due to low socio-economic status.[10] Furthermore, AA patients do not exhibit some of the risk factors associated with a faster liver fibrosis progression such as stage, HCV-onset after 40 years of age, and persistently elevated alanine transaminase (ALT), all of which are the hallmarks of progressive disease state in non-AAs.[3] Therefore, along with the host factors studied in our research work including gender, age, body mass index (BMI), obesity, diabetes, HIV co-infection, compromised immunity, steatosis (fatty liver), iron overload, and genetics, we also hypothesize that substance abuse, life-style behaviors and low expectations play significant roles and may impact the development and progression of liver disease.

A significant segment of HCV patients who undergo anti-viral therapy have recurrent viremia and succumb to fibrosis and cirrhosis due to lack of sustained virological response (SVR). SVR is an indicator of an effective and long-lasting response to treatment signaling the elimination of HCV in years of follow-up after the end of treatment. HCV genotype 1 is the most common viral strain in infected Americans and the most prevalent in AAs with subtype 1a as the most refractory and thus the need for prolonged therapeutic prescription.[11–13] The SVR rates have been highest for genotype 2 (>80%) and lower for genotypes 3 to 6 (50–70%) based on the stage of the disease. The homozygous CC host genotype is associated with a greater rate of SVR in chronically infected HCV genotype 1 individuals treated with pegylated-interferon-ribavirin (PEG-INF/RBV) dual therapy.[14] This has been the standard of care for many years despite the known side effects of IFN and the precipitation of anemia by RBV. Also, the dual therapy, to which HCV genotype 1 is more refractory, has remained a mainstay regimen for genotypes 2 through 6 until the arrival of Telaprevir.[15–17] In this study, we investigated various host factors that might have impacted the SVR rate and treatment efficacy in a predominantly AA cohort at an inner-city hospital located in Washington, DC.

2. Patients and methods

2.1. Patient selection

This retrospective chart study of HCV-infected patients between 2011 and 2014 was conducted at Howard University Hospital (HUH) in Washington, DC. HUH is a teaching hospital located on the campus of a historically Black university; and serves predominantly underrepresented minority populations in the Washington Metropolitan area. There was a total of 76 primarily African-American patients (ranging in age from 26 to 76) whose medical records were reviewed and evaluated for HCV infection. The patients' medical chart review included positive HCV antibody reaction (n=57); dual (PEG-IFN-α-RBV) or triple therapy ((PEG-IFN-α-RBV and Telaprevir); *IL28B* (i.e., *IFNL3*) polymorphism, viral genotype variant, HCV viral load, iron load, ferritin content, platelet count, neutrophil count, liver enzymes, and BMI associated with age and gender. Furthermore, the clinical data of the patients were compared with the grading and staging of liver biopsies using the Batts-Ludwig scoring methods.[18] These host and viral factors were crucial for the determination of treatment outcome. Patients were included in the study if they completed a full course of anti-HCV therapy, achieved an end-of-treatment response and complied with the 12 and 24 weeks post-treatment follow-up for serum HCV-RNA determination. There were only 12 patients who adhered to the treatment guidelines and qualified for this study, which was approved by the ethics committee of the Howard University Institutional Review Board (IRB-12-CMED-76). This study protocol also conforms to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) as reflected in a prior approval by the institution's human research committee. Although the patients have provided informed consent for publication of their cases, they are anonymized in this study.

2.2. Liver histology

Analysis of Howard University Hospital's histopathology database by an experienced histopathologist indicated that 32 of the 57 patients (56.1%) underwent liver biopsies with all original biopsy slides retrospectively identified, graded and staged using the Batts-Ludwig scoring method for chronic hepatitis C. *HCV RNA Measurement* patient blood samples were analyzed at LabCorp Center for Molecular Biology and Pathology (Research Triangle Park, NC). Hepatitis C quantitation or viral titer was accomplished by HCV Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) Amplification method using COBAS Taqman HCV test., V2.0. (Roche Molecular Diagnostics, Pleasanton, CA). The quantitative range of the assay was 15 IU/mL to 100 million IU/mL.

2.3. Host IL28B and viral genotyping

HCV genotyping was performed using a system of detection for the six major types and their most common subtypes, by LabCorp Center for Molecular Biology and Pathology (Research Triangle Park, NC).

IL28B genotyping was performed by Real-time PCR with allele-specific TaqMan probes to detect a Single Nucleotide Polymorphism (SNP) (rs12979890 C/T on chromosome 19q13.

Host Factors Besides the *IL28B and HCV* genotypes, the patients' clinical measurements of iron load, ferritin content, liver enzymes, α-feto protein (AFP), neutrophils and platelet counts were determined pre- and post-treatment by complete blood count and comprehensive metabolic analyses using standard clinical laboratory test procedures.

2.4. Treatment regimen

The standard dual regimen consisted of 180 mcg PEG-IFN injected subcutaneously weekly and 600 mg of RBV oral tablet taken twice daily. A protease inhibitor, Telaprevir, 375 mg oral tablet, taken twice daily, was added to the triple therapy. In 2011, patients with genotypes 2 and 3 were treated only with IFN and RBV for 24 weeks. However, for genotype 1, the treatment schedule included PEG-IFN plus RBV and Telaprevir, initially for 12 weeks and then following a response-guided therapy with PEG IFN and RBV, for either 12 more weeks (total of 24 weeks) or 36 more weeks (total of 48 weeks).[19–21] Response-guided therapy

Table 1

Characteristics of HCV patients (n = 76).

Characteristic	Frequency	Percentage
Gender		
Male	44	57.89
Female	32	42.11
Race*		
African American	73	96.1
European American	1	1.33
Hispanic American	1	1.33
Biopsy†	32	42.1
Fibrosis	18	56.3 (18/32)
Cirrhosis	14	43.8 (14/32)
Steatosis	5	6.6
Alcohol	24	31.6
Hepatocellular carcinoma	7	9.2
Human immunodeficiency virus	5	6.6
Anti-HCV antibody‡	57	75
-HCV RNA count	41	71.9 (41/57)
Number of patients treated	12	15.8

* One patient's race was undetermined.
† Physician's chart indicates that 37 biopsies were ordered but only 32 were completed.
‡ Only 57 were tested for HCV antibody test.

refers to a patient who has achieved eRVR (extended r\Rapid Virological Response), with a negative HCV RNA at 4 and 12 weeks after commencing treatment. This would allow the patient to continue PEG IFN and RBV for 24 weeks. However, under conditions where the patient did not achieve eRVR, but was still within the stopping rule, the patient was allowed to continue treatment with PEG IFN and RBV for up to 24 weeks and if HCV RNA remained negative then treatment was continued for up to 48 weeks.

In this study, SVR would be achieved when the HCV RNA remained negative for 24 weeks after successful completion of treatment. In contrast, virologic failure was defined as an HCV RNA level greater than 1000 IU/mL after 4 weeks of treatment, a decline from baseline by <2 log10 units in the level of detectable HCV RNA at week 12, or a detectable HCV RNA level at any time between weeks 24 and 36. According to the standard therapy protocol, cessation of treatment with Telaprevir included the detection of any HCV RNA >1000 IU/mL at week 4 and 12.[22]

2.5. Statistical analysis

Continuous variables were presented with median (interquartile range) and categorical with frequency. We tested the effect of treatment on viral load and measures of liver function using the Wilcoxon singed-rank test. *P* values for tables were calculated using unpaired student's *t* test.

3. Results

3.1. Cohort characteristics

A total of 76 patients with likelihood of HCV infection (73 AA; 1 Hispanic-American (HA), one European-American (EA), and one male patient whose race was not identified) were evaluated. Fifty-seven of the patients representing AA, EA and HA had a positive HCV-antibody identification (75%) and 41 of 57 (71.9%) had detectable HCV RNA counts. The rest were undetermined. The mean age and BMI were 59.2 years and 28.2 kg/m^2, respectively. The general characteristics of the patients are shown in Table 1 with male patients featuring predominantly in the study. There were 32 patients (out of the 76) that were biopsied including 6 out of the 12 who had completed the full regimen (see Table 2 and Fig. 1). In these 32 biopsied patients, liver fibrosis was more common than cirrhosis. Seven out of the 76 (9.2%) patients had advanced stage liver disease with hepatocellular carcinoma (HCC).

Most (85%) of the patients were treatment-naïve at the beginning of their diagnosis. However, the full course of treatment was not administered to five patients that were HCV/HIV co-infected; four patients who were decompensated; 23 patients with contraindications (drug–drug interactions); and five patients who had renal disease. Eight of the remaining patients either did not qualify for insurance reimbursement or had difficulty complying with the administration of the medications and therefore were not included in this study. As such, there were only 12 patients who completed the IFN-based 24-weeks treatment regimen for HCV infection resulting in 58% of them acquiring SVR. Table 3 shows the prevalence of HCV genotypes in the 41 of 57 (71.9%) patients who had detectable HCV RNA counts. Viral genotypes 1a and 1b were more prevalent (close to 88%) than genotypes 2 (2.4%), 3 (4.9%), or 4 (4.9%) in this study group; and subtype 1a was the most resistant to IFN-based therapy. Figure 2 represents the distribution of the

Table 2

Host factors and liver stages.

Chart data	Low liver stage (1/2) N = 18	High liver stage (3/4) N = 14	*P*
Age, median (IQR)	60 (58–65)	60 (57–62)	.9
Male, n (%)	8 (44%)	10 (71%)	.1
BMI, median (IQR)	26.7 (22.9–31.6)	30.1 (24.9–35.0)	.5
Viral load (×1000), median (IQR)	320 (135–775)	450 (553–1891)	.9
Platelet count (×1000), median (IQR)	224 (181–258)	123 (100–175)	.001*
Neutrophil count (×100), median (IQR)	24 (16–29)	26 (16–31)	.9
Serum iron, median (IQR)	101 (82–102)	106 (80–117)	.9
Serum ferritin, median (IQR)	170 (126–520)	212 (95–653)	.6
ALT, median (IQR)	49 (27–56)	65 (40–115)	.1
AST, median (IQR)	49 (27–59)	71 (53–127)	.027*
AFP, median (IQR)	3.6 (2.8–5.8)	8.4 (6.5–20.1)	.025*

Liver stages 1 and 2 indicate fibrosis; whereas 3 and 4 represent cirrhosis.
*Significant numbers = $P<.05$
IQR = Interquartile range

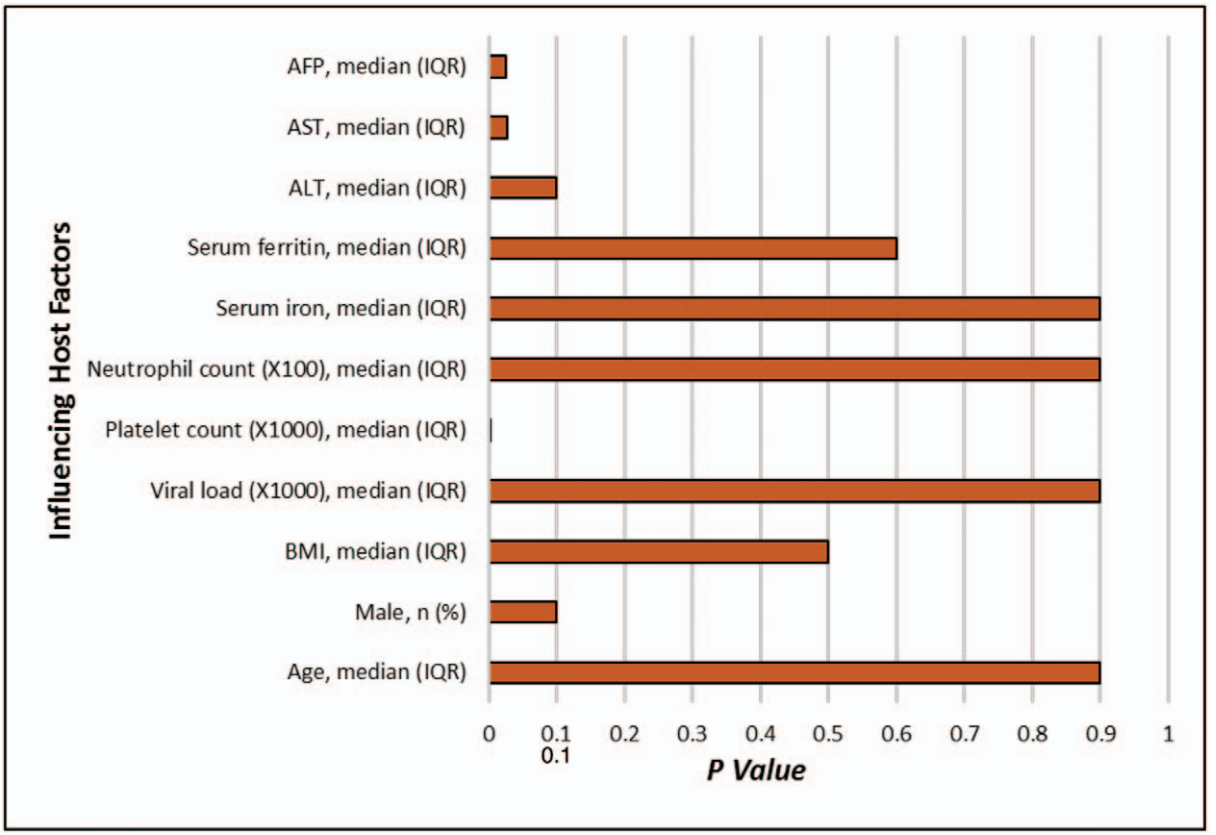

Figure 1. Influencing host factors on viral load in low (fibrosis, n = 18) and high (cirrhosis, n = 14) liver staging. IQR (interquartile range) measures the statistical dispersion of the dataset.

IL28B genotypes for the 51 of the 57 HCV antibody-positive patients (89.5%) in the study. The heterozygous CT was the most frequently represented *IL28B* genotype (70.6%) in this cohort that also includes the sole European American patient.

3.2. Pre- and post-treatment of the 12 HCV-positive cohort

Eleven of the 12 patients had a negative HCV RNA at 12 weeks after triple treatment with PEG IFN, RBV and Telaprevir. There was a patient who did not achieve eRVR but was within stopping rule of the HCVRNA at <1000 IU/mL at 4- and 12-weeks following treatment. Among the final 12 HCV patients who completed the full treatment regimen, the effect of treatment on the status of several host factors including viral load and liver enzyme markers are shown in Table 4. Prior to treatment, viral RNA copy number ranged from 9.02×10^4 (or 16,107 IU/mL) to 6.84×10^7 copies/mL (or 12,214,285 IU/mL). However, following treatment, the median viral load (HCV RT-RNA) declined significantly from >2,280,000 (or 407,142 IU/mL) to 0 with a *P* value of .003. Conversely, ferritin and iron overload, although relatively high in the HCV-infected patients, did not significantly decline in response to therapy; whereas the ALT level did decline precipitously following treatment ($P = .04$). Also, there was no significant difference in the serum neutrophil count ($P = .9$) between pre-treatment and post-treatment regimens.

Table 3

The prevalence of HCV genotypes.

Genotype	Sub-genotype	Respective # of patients (%) (n = 41)*	Subtotal
1	1a, 1b	28 (68.3), 8 (19.5)	36 (87.8)
2	–	1 (2.4)	1 (2.4)
3	–	2 (4.9)	2 (4.9)
4	–	2 (4.9)	2 (4.9)
Total	2	41 (100)	41 (100)

* HCV patients whose genotypes have been determined.

Figure 3 shows the sustained virological response (SVR) rates by *IL28B* genotype and HCV genotype prior to treatment and after treatment. Twelve (12) HCV patients were treated with the standard triple therapy (except patients 1 and 5 who were treated with PEG-INT and RBV only). The *IL28B* genotype of 10.5% of patients including the only Hispanic patient was not determined. There was no significant difference in viral load or virological response rates among the different host genotypes of *IL28B* although one patient with a CC genotype (patient #1) and the four patients with CT genotype (patients #s 2, 3, 5, and 6), as well as both patients with TT strains (patient #s 11 and 12) all had viral clearance after treatment. The documented SVR for patients harboring genotype 1 (for both 1a and 1b subtypes) was (50%) compared to patients infected with genotype 3 (100%) (Fig. 3). There was a sustained virological response (SVR: 58%) 24 weeks post-treatment and a partial response rate (TR: 33%) for some of the patients treated with the standard triple regimen from 12 weeks to up to 2 years. There was only one patient (shown as

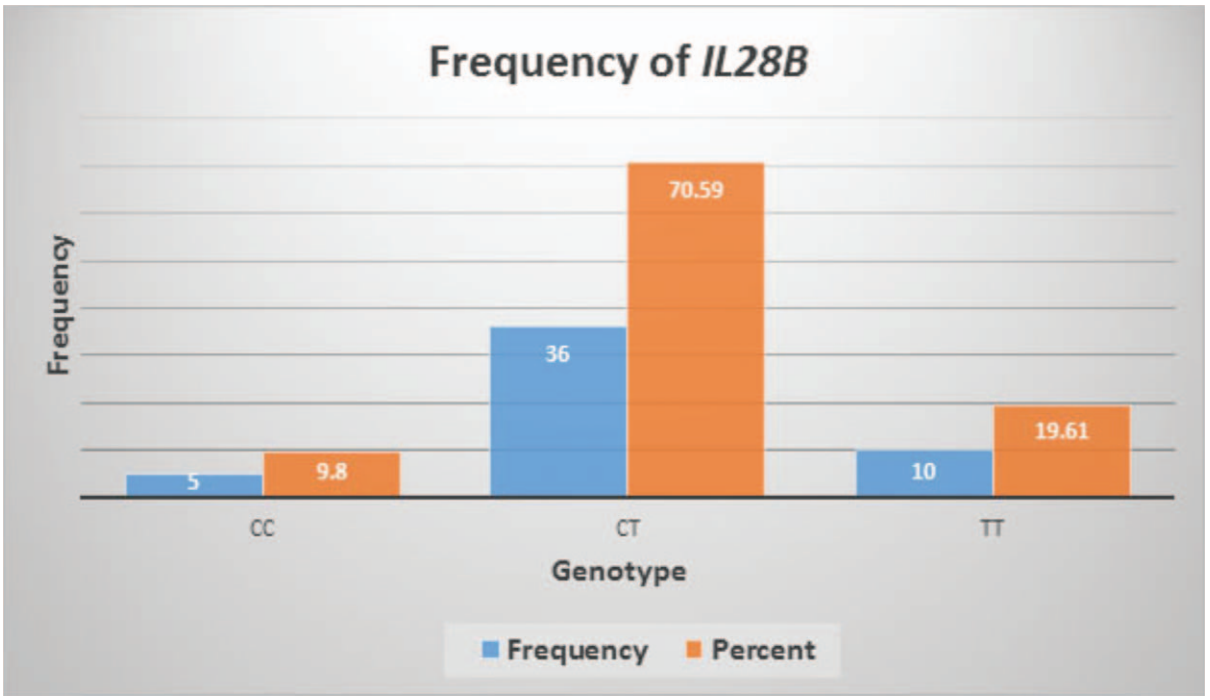

Figure 2. The distribution of the *IL28B* genotype among the HCV patients under study. There were 51 patients whose genotypes were determined.

#9 in Fig. 3) who did not respond at all to the therapy. He was infected with genotype 1a and had the CT variant of *IL28B*. The HCV genotypes for patients 10 and 11 were not determined.

3.3. Pre- and post-treatment variables

Although the viral load was drastically reduced following therapy, only ALT ($P < .04$) showed significant reduction; whereas AST ($P < .1$) was not significantly affected (see Table 4). In contrast, the AST level ($P < .027$) correlated significantly with higher degree of liver injury (cirrhosis, F score = 3 or 4) than a lower state of injury (F score 2 or less) (Table 2). Moreover, the alpha-feto protein (AFP) level, a marker for hepatocellular regeneration and HCC, was not significantly affected by treatment ($P < .9$, Table 4) but was significantly higher ($P < .025$) as expected in cirrhotic patients than fibrotic patients. Two of these cirrhotic patients developed HCC.

Finally, analyses of complete blood count indicated that blood platelet count was significantly lower ($P = .001$) at the cirrhosis stage than the fibrosis stage (Table 4). There was no significant difference in the baseline viral load and liver staging ($P = .9$) and the liver stage had no effect on the neutrophil count. Furthermore, there was no significant difference in the viral load between the fibrosis and cirrhosis stages of the liver ($P = .9$). There was also no correlation between the degree of liver injury (grade or stage) and serum viral load before or after treatment ($P = .9$) (Fig. 4).

4. Discussion

Chronic hepatitis C infection presents a significant public health concern in the United States. It is the leading cause of liver transplantation and liver disease-associated mortality where AAs are disproportionately represented. For over a decade, IFN-based treatments have yielded modest cure rates (38–55%) but with much lower efficacy for AAs (8–28%).[23] Interestingly, none of the host factors that are known to affect treatment outcome such as age, gender and BMI were significant in our study cohort.

Table 4

***P* values in viral load and host factors pre- and post-treatment.**

Clinical data	Normal reference value	Pre-treatment N = 12	Post-treatment N = 12	*P*
Viral load (×1000), median (IQR)	<0.015 IU/mL	308 (550–552)	0 (0–0.3)	.003*
Platelet count (×1000), median (IQR)	140–415/μL	187 (128–211)	179 (147–211)	.8
Neutrophil count (×1000), median (IQR)	1.8–7.8/μL	16 (16–24)	17 (15–26)	.9
Serum iron, median (IQR)	40–155 μg/dL	116 (95–193)	116 (90–176)	.3
Serum ferritin, median (IQR)	22–322 ng/mL	491 (126–1404)	454 (128–853)	.08
ALT, median (IQR)	0–55 IU/L	67 (24–123)	22 (15–71)	.04*
AST, median (IQR)	0–40 IU/L	59 (25–142)	40 (26–69)	.1
AFP, median (IQR)	0–6 ng/mL	8.8 (3.6–17.4)	8.5 (3.6–38.5)	.9

* Statistically significant difference.

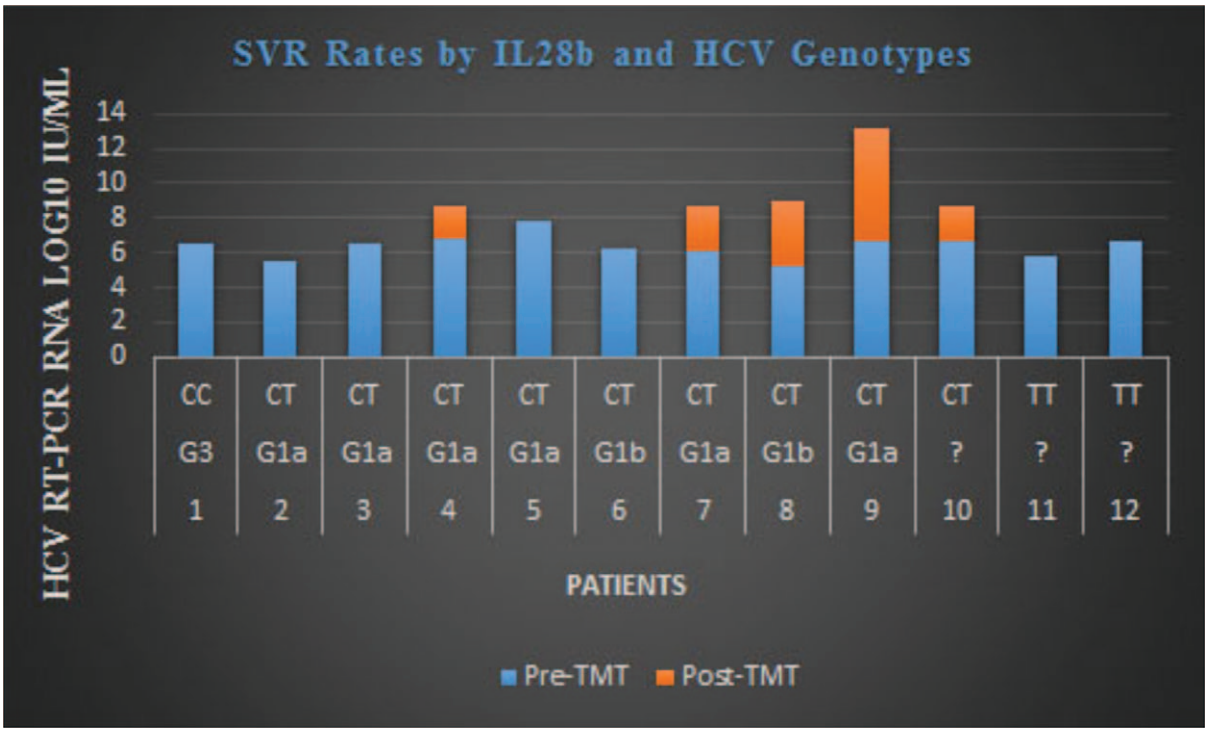

Figure 3. The sustained virological response (SVR) rates by *IL28B* genotype and HCV genotype prior to treatment and after treatment. Twelve (12) HCV patients were treated with the standard triple therapy (except patients 1 and 5 who were treated with PEG-INT and RBV only). "G" before numbers on the X-axis denotes the genotype designation for HCV. The viral load is represented by $\log_{10}$ of International Unit (IU) of RT-PCR RNA copies per milliliter of blood.

While the normal course of treatment should run up to 24 weeks, many patients dropped out of treatment for different reasons such as lack of insurance coverage or approval. This reduced our sample size in the study to 12 patients who completed treatment.

The study reveals that potent IFN-based combination therapy (dual or triple) worked relatively well for AA HCV patients treated at HUH at a >58% SVR rate. We can confidently state that if the HCV-infected HUH patients were able to tolerate the

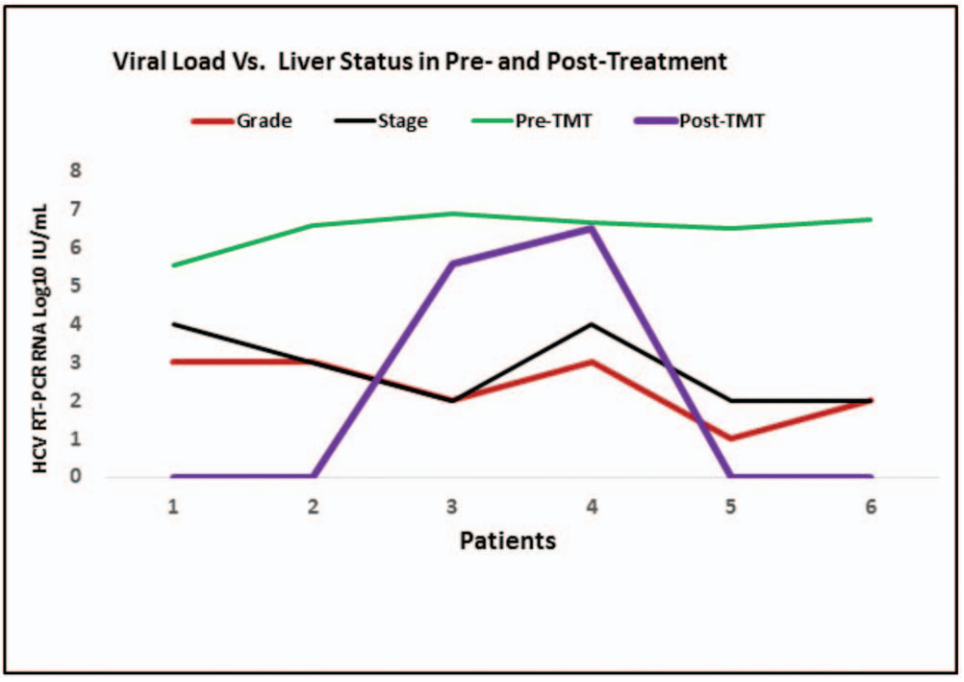

Figure 4. The HCV RT-RNA level in different grading and staging forms of the liver before and after treatment with IFN-based combination therapy.

harsh side effects of the PEG IFN treatment and complied with the strict administration of the medications, and continued until the end of the regimen, most of the 57 patients would have had a better treatment outcome despite having unfavorable *IL28B* genotypes. The low efficacy of IFN-based therapy for AAs has been reported to be mainly—but not completely—due to a variation in an inherited genetic factor involved in IFN-alpha pathway and the interleukin-28B (*IL28B*) polymorphism.[24] Despite the identification of a SNP upstream of the *IL28B* gene by Genome-Wide Association Studies, the mechanism by which the *IL28B* genotype mediates PEG-IFN/RBV treatment response in HCV genotype 1 is not yet understood. In our sample-size study, the majority of the patients harboring viral genotype 1 and possessing the CT *IL28B* subtype still managed to attain SVR although the CC genotype has been associated with a 3-fold increase in the rate of spontaneous clearance of HCV.[25] The CT variant is known to confer resistance to IFN-based treatment as shown in Figure 2. This highlights the presence of other relevant clinical and host factors that can modulate response rates to pegylated-IFN/RBV therapy.

Our results validate that receiving the double or triple therapy (PEG-IFN/RBV/ and/or Telaprevir) from 24 weeks up to 2 years of follow-up treatment at HUH had a drastic reduction in viral load despite harboring a predominant non-CC genotype (92%) and being infected by the most therapeutic-resistant viral genotype 1 (68%). This means that IFN-based therapy treatment for these patients was relatively effective especially for those who tolerated its severe side effects. The viral genotype will also determine the duration of therapy and the likelihood of response to a combination of therapies even though in this study, genotype 1 perhaps is not a predominant factor affecting SVR. Furthermore, the viral load reduction was not linked to a specific host *IL28B* genotype or viral genotype or stage of liver disease. It should be emphasized, however, that the patients treated with triple therapy after 2011 (with the emergence of direct-acting antivirals) had a significant increase in SVR compared with the dual-therapy given to a cohort before 2011 despite receiving multiple treatment modalities to tolerate side effects. Even so, the initial reduction (in the first 4 weeks of treatment) in viral load is extremely important because it is a good indicator of efficacy and patient response to medication.[26] The 2-log viral reduction is critical 12 weeks following treatment, otherwise the medication was stopped altogether. A *significantly* reduced viral load of a 100-fold meant that treatment was working and eventually the virus would become undetectable. Although it was expected that the neutrophil count would also be reduced because of neutropenia caused by IFN treatment, we have found no significant difference in the serum neutrophil count ($P=.9$) between pre- and post-treatment regimens. Reduction of viral load does not guarantee clinical benefit as there will be relapse and it is not proven to have a net histological improvement.

Another significant factor in our study was the decrease in platelet count with the higher degree of liver cirrhosis. It is interesting that treatment did not have a significant effect in reversing the decline in platelet count. The expectation now is that for AA patients, the new era of oral direct-acting antiviral medications that are protease or polymerase or NS5A inhibitors will have shorter durations and better cure rates without the genetic complications or the intolerable side-effects of IFN or RBV. However, if resistance to these new medications develop, IFN and RBV may still be used in combination with one of the new DAAs.

This study does not show data with respect to compliance with appointments and adherence to medications, which are vital and critical for the successful treatment of HCV in minority communities. From the electronic database of the 76 patients analyzed, about 12% were non-compliant for various reasons one of which was negative expectation. Patient motivation is the most important factor in medical adherence. But there may also be other barriers to treatment in AA communities that have not been previously addressed.[27–29] The physician's chart review reveals that most of the 76 patients in our study did not receive treatment for one or combination of reasons based on either provider determination or patient motivation; IFN-intolerance or ineligibility (over 41%), the presence of contraindications and significant comorbid illnesses such as advanced fibrosis, high depressive symptoms, anemia, cardiovascular disease, autoimmune disorder, renal dysfunction, HIV, and regular drug abuse—which ties into eligibility restrictions set by the payer. All these conditions precluded most of the patients in our study from receiving the IFN-based treatment. The decline in treatment may also be based on race in addition to the side effects of the medications.[30] In our study, we did not find access to a care center as a significant factor delaying or impeding treatment. We did, however, find from the chart review that some of the insurance companies declined payment for medications to specific patients, particularly to persons with intravenous drug abuse.

As our study shows, the old standard treatment regimen in an ***era of protease inhibitor-based therapy*** that included PEG-INF and RBV should be used for SVR for a ***significant number*** of AA patients regardless of their *IL28B* genotypes. Therefore, again getting the treatment is paramount in the fight against hepatitis C infection and progression in underrepresented communities. If access is not an obstacle to treatment, then awareness and positive reinforcement to visit the hospital, to comply with and adhere to the treatment regimen as well as follow-up on scheduled visits are the pivotal factors in the fight against the spread of HCV in AA communities. In contrast, care providers and payers should also consider early treatment for AAs with lower fibrosis scores and should not delay therapy until it progresses to cirrhosis as HCC and mortality rates are higher in AAs than any other ethnic group even at similar fibrosis stages. SVR for AAs has also dramatically lagged Caucasians owing to differential contributions by both viral and host factors. To narrow this health disparity with respect to HCV infection, specialists such as gastroenterologists and hepatologists as well as primary care physicians must address the risk factors and treatment outcomes in a more aggressive manner including attracting AA enrollment in clinical trials.

Future prospective, randomized controlled trials will be urgently needed to understand the natural history of HCV infection in AAs.

5. Conclusions

Most of the subset of HCV patients receiving the standard IFN-based triple therapy between 12 and 24 weeks had a drastic reduction in viral load; and most of those treated attained end of treatment response (ETR) despite harboring a predominant *IL28B* heterozygous CT or homozygous TT genotypes (92%) and being infected by the most therapeutic-resistant viral genotype 1 (68%). This retrospective study clearly demonstrates that screenings, awareness, early detection as well as the

immediate initiation of treatment, however suboptimal, for hepatitis C are pivotal for the eventual eradication of the disease in the AA community. The IFN-based combination therapy may not be a first line of choice for patients but nevertheless, compliance and adherence may play an important role in the treatment regimen. The efficacy of combination treatments (old or new) for naïve or experienced AA patients clearly mandates awareness and full participation in the treatment program.

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