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Research article

Racial disparity in chronic hepatitis B infection in a predominately African American urban clinic population

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Abstract: African Americans (AA) are 4 times as likely as Caucasians to have chronic Hepatitis B (CHB) and yet are under represented in the literature especially with respect to treatment response. The objective of this study was to compare demographics, treatment decisions and outcomes of AA to Non-AA patients seen in the same GI clinic. Of the 92 patients with CHB, 60% were AA. AA patients had similar ALT and viral load at early visits as compared to Non-AA but significantly less fibrosis as defined by AST Platelet Ratio Index. Treatment rates were lower but not statistically different for AA (38%) vs. Non-AA (46%) and the majority of patients (80%) were HBeAntigen (HBeAg) negative. The patients responded well to treatment, although HBeAg positive AA were less likely to have a decline in HBV DNA than HBeAg negative AA patients. The primary conclusions of this study are that AA as compared to Non-AA patients are less likely to have fibrosis and appear to have a dissimilar response to anti-viral therapy.

Keywords: hepatitis B; racial diversity; African Americans; fibrosis; viral burden

1. Introduction

Although a vaccine has been available for hepatitis B since 1982, this chronic infection is still far from eradicated. In fact, hepatitis B virus (HBV) infects up to 2 million of the US population and African American (AA) patients are 4 times as likely as Caucasians to develop chronic hepatitis B (CHB) [1–8]. Since Asians are the dominant infected population in the US, the most studied population with respect to CHB history and treatment are Asians, the majority of whom have

acquired the infection via vertical transmission.2 This contrasts with most AA and Caucasian patients in the US where the infection is acquired horizontally [3–5]. Thus, understanding HBV status, treatment, response and outcomes especially in AA is needed to serve the predominately AA patients in many urban clinic settings [5]. A small study including subjects from an urban medical center found that only 7% of a predominantly African American and Hispanic population had been initiated on therapy [9]. A more recent example of the disproportion of AA in clinical trials is the two multi-national phase 3 studies comparing tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF), where the black representation was 13/1298 = 1% [10].

The advent of effective antiviral drugs during the past two decades has resulted in considerable advances not only in controlling CHB infection, but also in preventing and reducing the incidence of liver cirrhosis and hepatocellular carcinoma (HCC) [10–16]. Sustained suppression of HBV replication with antiviral therapy (nucleoside/nucleotide analogues) halts the progression of liver disease, may reverse liver fibrosis, and can reduce the development of cirrhosis and HCC [2,12–15].

The decision to treat patients with chronic hepatitis B is to a large extent, individual centric based on age and disease status with respect to stage of fibrosis, levels of HBV DNA in serum, the presence of viral particles as measured by surface Antigen (HBsAg), and liver inflammation as defined by elevated alanine amino transferase (ALT) levels [8–16]. In the minority of patients with detectable serum levels of the soluble secretory HBe Antigen (HBeAg) (i.e. presumably in earlier more active stages of infection), this marker is also useful to define a decline in viral replication. Conversely, HBeAg negative patients may be further along in the course of the disease, are twice as likely to progress to cirrhosis and should perhaps be treated more aggressively. Biopsy to evaluate the presence of significant fibrosis is being used less and fibrosis as defined by fibroscan or serum fibrosure/FIB-4/APRI are now used to identify patients with significant fibrosis who should be treated regardless of viral status. Response to treatment is defined by a decrease in serum HBV DNA level and reduction in ALT. Additional responses with longer term treatment can include: loss of HBeAg with or without seroconversion to anti-HBe antibody, loss of hepatitis B surface antigen (HBsAg) with or without seroconversion to anti-HBs antibody and a decrease in levels of fibrosis.

The primary objective of this outcomes study was to evaluate the use of antiviral drugs and the response to therapy in the predominately African American population of patients with CHB seen in urban clinic settings A secondary objective was to determine whether patient HBeAg status had been determined and if it had an influence on treatment decisions and response to treatment in AA as compared to non-AA patients.

2. Materials and Method

Using the medical records of 250 patients with ICD9/10 codes for hepatitis B who did not have HCC seen between 2013 and 2015, we identified 92 mono-HBV infected patients with CHB who had at least two visit prior to 2016. The remaining patients were not documented with CHB (n = 97) or were co-infected with human immunodeficiency virus (HIV) (n = 61). HIV co-infected patients were being treated “incidentally” with tenofovir in the Infectious Disease Clinics rather than Gastroenterology and were not included in this data analysis. For the 92 mono-infected patients, we reviewed the medical records through the end of 2016 for this study.

Viremia was defined by HBV DNA levels, inflammation by ALT and fibrosis by AST (aspartate aminotransferase) Platelet Index (APRI = ((AST/normal AST)/platelets) × 100). APRI was selected

since biopsy is rarely performed and, in a recent meta-analysis of its use in HBV patients, it was shown to have a sensitivity of 73% for significant fibrosis when using a 0.5 cut-off [17]. Only patients with a known pretreatment positive HBV DNA level (n = 31) were used in the viral load analysis to assure accurate pair-wise evaluation. If patients did not have a pre-treatment HBV DNA, we still included them with respect to ALT and APRI (n = 38). The JMP statistical package from SAS (https://www.jmp.com) was used for data analysis with Pearson chi-square for character variables and Student's t test for numerical data.

3. Results

As shown in Figure 1 and 2, the majority of patients were AA and most were HBeAg negative. At first visit, AA as compared to non-AA were more likely to be female, older (55 years vs. 45 years) and have less fibrosis (APRI 0.44 vs. 0.92; $p < 0.05$). They were similar with respect to inflammation (ALT) and viral load. Patients who were subsequently treated were compared to non-treated patients at first visit (Table 1), Consistent with treatment guidelines, treated patients had higher inflammation (ALT), greater fibrosis (APRI) and were more likely to have elevated HBV DNA.

Table 2 presents the data prior to treatment for treated vs. non-treated by race to assess potential racial diversity. The percent of patients who were treated was greater for Non-AA as compared to AA (46% vs. 38%) but the difference was not statistically different ($p \geq 0.05$). With respect to patients who were not treated, there was minimal racial disparity with AA patients being older (53 years vs. 40 years; $p < 0.005$) and having slightly higher platelets ($p < 0.05$). With respect to patients who were subsequently treated, the only racial disparity was in the lower fibrosis as defined by APRI in AA patients (0.47 vs. 1.40; $p < 0.05$). The HBeAg distribution was also similar with the majority of patients being HBeAg negative (80%) with a positive HBsAg and significant viral load.

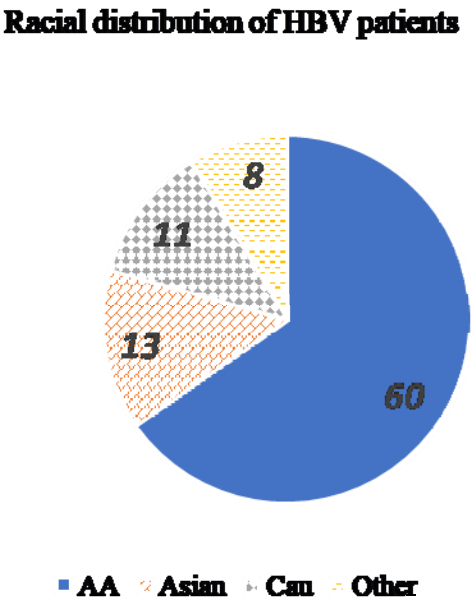

Figure 1. Racial distribution first visit of patients with chronic hepatitis B. The majority of patients were African American (60/92 = 65%)

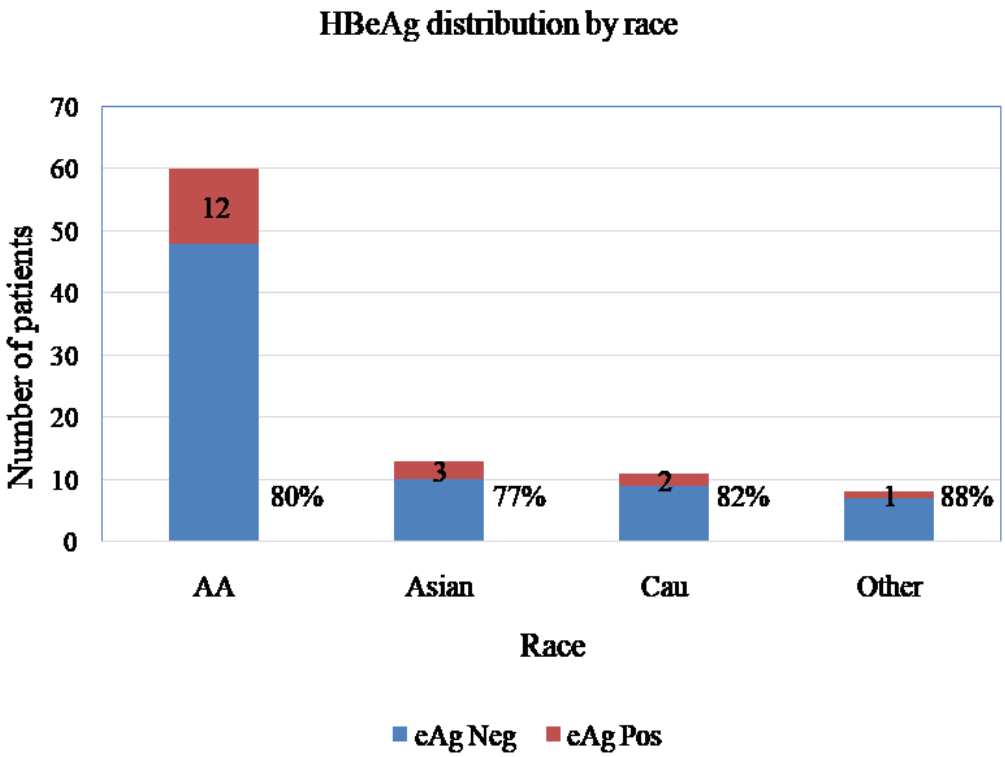

Figure 2. HBeAg status and race at first visit of patients with chronic hepatitis B. The majority of patients were HBeAg- for all races (74/92 = 78%).

Table 1. Patient data at first visit and for treated vs. Non-treated.

Prior to treatment for AA vs. Non-AA				Not treated after earliest visit	Treated after earliest visit	
	AA (n = 60)	Non-AA (n = 32)	p value (NS = p ≥ 00.5)	All Patients	All Patients 38/92 = 41%	p value (NS = p ≥ 0.05)
Male Gender (%)	25 (42%)	20 (63%)	p < 0.05	23 (51%)	22 (49%)	NS
Age (years)	55	45	p < 0.005	49	55	NS
ALT ± SEM (n) (IU/mL)	75 ± 17 (60)	64 ± 25 (29)	NS	40 ± 18 (52)	114 ± 21 (37)	p = 0.0088
AST ± SEM (n) (IU/mL)	46 ± 9 (59)	43 ± 14 (31)	NS	31 ± 10 (52)	63 ± 121 (38)	p = 0.045
Platelets ± SEM (n) ($\times 10^5$)	238 ± 9 (60)	192 ± 13 (28)	p < 0.05	242 ± 10 (51)	197 ± 11 (37)	p = 0.0034
Fibrosis (APRI)	0.44 ± 0.11 (59)	0.92 ± 0.17 (28)	p < 0.05	0.42 ± 0.13 (51)	0.83 ± 0.15	p = 0.38
HBV DNA (n) (%)			NS			p = 0.001
High (>20,000 IU/mL)	20 (34%)	6 (23%)		4 (7%)	22 (71%)	
Low (<20,000 IU/mL)	32 (54%)	16 (62%)		39 (72%)	9 (29%)	
Neg (non-detectable)	7 (11%)	4 (14%)		11 (21%)	0	

Table 2. Racial disparity in patients comparing treated vs. Non-treated.

	Not treated after earliest visit			Treated after earliest visit		
	AA (n = 37)	Non-AA (n = 17)	AA vs. Non-AA p value (NS = p ≥ 0.05)	AA (n = 23)	Non-AA (n = 15)	AA vs. Non-AA p value (NS = p ≥ 0.05)
				23/60 = 38%	15/32 = 47%	p = 0.42
Male gender (%)	14 (38%)	9 (53%)	NS	11 (48%)	11 (73%)	NS
Age (years)	53	40	p = 0.007	57	52	NS
ALT ± SEM (n) (IU/mL)	43 ± 9 (37)	34 ± 15 (15)	NS	126 ± 40	67 ± 51	NS
AST ± SEM (n) (IU/mL)	33 ±7 (36)	26 ± 10 (16)	NS	65 ± 22 (23)	61 ± 27 (15)	NS
Platelets ± SEM (n) ($\times 10^5$)	254 ± 11 (37)	210 ± 18 (14)	p = 0.048	211 ± 13 (23)	174 ± 17 (14)	NS
Fibrosis (APRI)	0.41 ± 0.13 (37)	0.44 ± 0.21 (14)	NS	0.47 ± 0.19 (22)	1.40 ± 0.25 (14)	p = 0.0007
HBV DNA (n) (%)			NS			NS
High (>20,000 IU/mL)	3 (8%)	1 (6%)		17 (77%)	5 (56%)	
Low (<20,000 IU/mL)	27 (72%)	12 (71%)		5 (23%)	4 (44%)	
Neg (non-detectable)	7 (20%)	4 (23%)		0	0	
HBeAg Neg (n) (%)	32 (87%)	15 (88%)	NS	16 (70%)	11 (73%)	NS

Treatment of non-AA patients for an average of 4 years improved disease status as defined by a decrease in ALT, APRI and HBV DNA although HBeAg negative patients were less likely to have an improvement in fibrosis as compared to positive patients (Figure 3). For AA patients, treatment for an average of 3.4 years improved ALT, APRI and HBV DNA (Figure 3). Unlike Non-AA, the improvement in APRI was minimal since pretreatment levels of fibrosis were low. HBV DNA decline was least likely in the AA HBeAg positive patients as compared to non-AA and AA HBeAg negative patients.

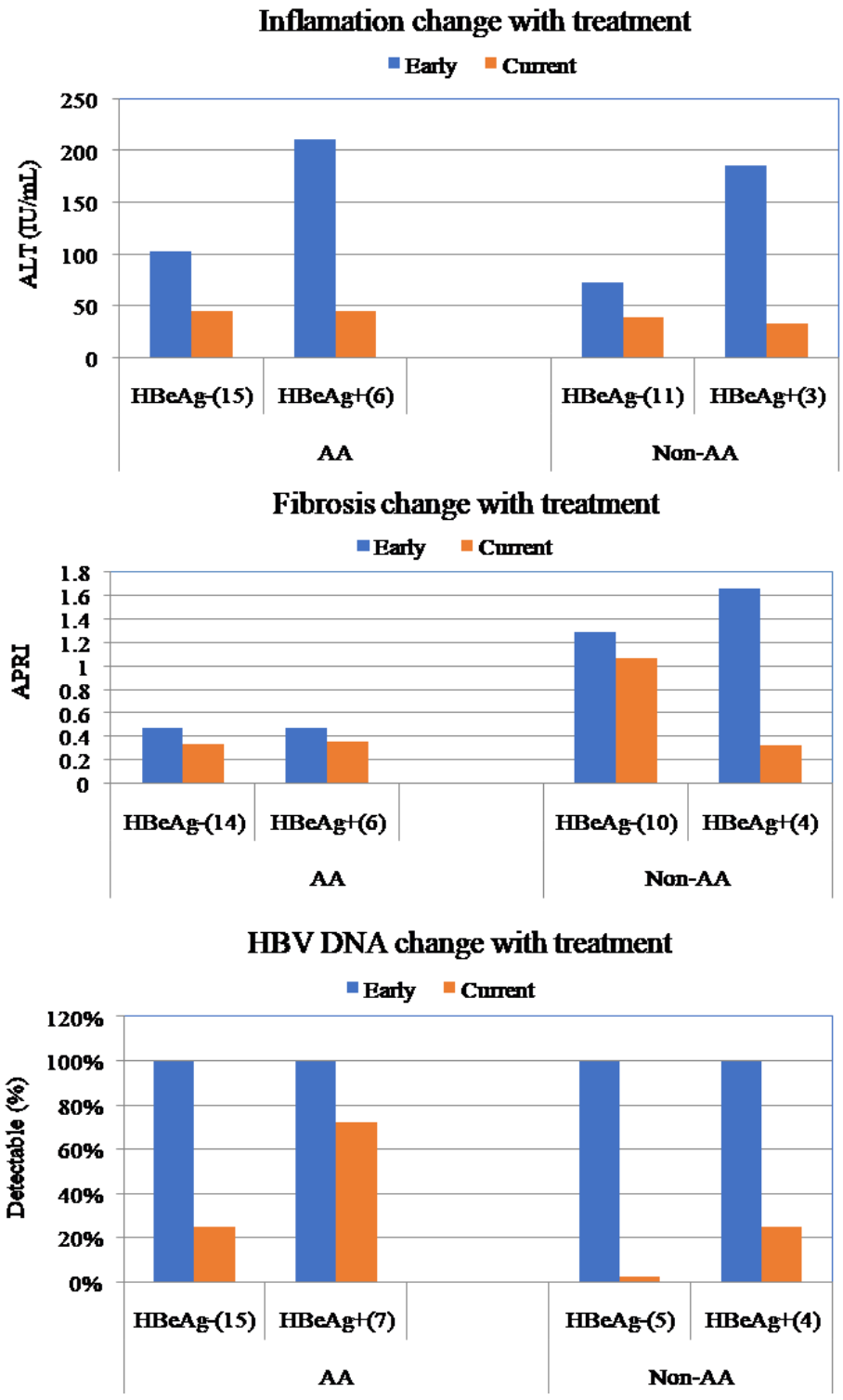

Figure 3. Change with treatment for chronic HBV patients. Treatment decreases viral load, fibrosis and inflammation in the majority of patients. HBeAg+ positive AA patients were least likely to have a decrease in viral load compared to Non-AA but had similar declines in inflammation as non-AA. Fibrosis by APRI was low in AA at entry with minimal decrease after treatment. Due to the variability and small numbers in the subgroups, using pair wise analysis for Inflammation and APRI were not statistically significant

4. Conclusion

African Americans are 4 times as likely as Caucasians to have CHB yet even in the most recent clinical trial comparing tenofovir alafenamide to tenofovir disoproxil fumarate, blacks represented only 1% (n = 13) of the 1298 patients in the clinical trial [10]. Thus, the data presented here with 60 AA (n = 60), whom were treated with direct acting antivirals (n = 23) provides important information regarding AA patients as compared to Non-AA.

Racial diversity in HBV infected patients was found between AA and Non-AA with respect to gender (female), age (older), and fibrosis (lower). Treatment for mono-infected patients was predominately in patients with high viral load, elevated ALT and significant fibrosis as defined by APRI. Treatment was successful in the majority of patients with respect to reducing viral load, inflammation (ALT) and fibrosis (APRI). HBeAg positive AA patients were less likely to have a decline in HBV DNA following treatment as compared to other three patients groups. APRI was not as useful a parameter of fibrosis response in AA patients as compared to Non-AA patients since the values were significantly lower than for non-AA. While all patients were treated for at least 1 year, compliance to medication could not be assessed in this retrospective study. Future studies with this group of patients should be directed toward the use of Fibroscan to follow improvement in fibrosis, changes in response when switching AA patients to newer antivirals, additional measures of treatment endpoint responses, and the role of patient compliance in the response to treatment.

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Conflict of interest

The authors have no financial, commercial, or other relationships that might be perceived by the academic community as representing a potential conflict of interest.

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