IBOM MEDICAL JOURNAL
Vol.19 No.3 | July - September 2026 | Pages 660-668
www.ibommedicaljournal.org

Treatment Outcomes of Patients with Chronic Hepatitis B at a tertiary hospital in Nigeria: A 5 Year Retrospective study

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Abstract

Context: Hepatitis B virus infection (HBV) is a global public health problem and a major cause of morbidity and mortality in Nigeria. This study determined the different treatment outcomes of patients with chronic hepatitis B virus infection and their associated factors in Nigeria.
Materials and Methods: This was a retrospective descriptive cross sectional study carried out at a tertiary hospital in Nigeria from January, 2018 to December 2022. The records of the adults diagnosed and managed for chronic HBV infection were retrieved. Data extracted included demographics, biochemical and hematological parameters, HBV panels and viral loads. These were analyzed using descriptive and inferential statistics.
Results: A total of 362 patients aged between 17 and 80 years, with a mean age (SD) of 42.4 (11.7) years were studied and 285(79.0%) were alive and in care. Majority of our patients achieved adequate virologic response 257(90.2%) and biochemical normalization 262 (92%). Virologic breakthrough was observed in 18(6.3%). Ten (3.5%) patients achieved HBsAg loss, which was more prevalent in patients treated with pegylated interferon plus nucleoside analogue (NA) therapy 5(50%) than those treated with nucleotide analogue only 3(30%). Poor drug adherence (86.7%), APRI Score ≥ 0.6 (66.7%), co-infections hepatitis C virus 9 (60%) and presence of diabetes mellitus (DM) (73.3%) were associated with poor treatment outcomes (P<0.005).
Conclusion: Adequate virologic response and biochemical normalization were the common treatment outcomes achieved in this cohort. HBsAg loss was achieved in few patients (higher with pegylated interferon plus NA therapy). Individuals with poor drug adherence, APRI Score≥ 0.6, Co-infection with HCV and DM need to be closely monitored to prevent virologic failure.

Keywords: Treatment outcomes, chronic hepatitis B, Nigeria.

Introduction

Hepatitis B virus(HBV) infection is a global health problem, about 2 billion people [One-third of the world's population] have been affected with HBV,[1] majority in sub-Saharan Africa where Nigeria falls in, South East Asia and Far East.[2]
Approximately 250 million people have lifelong chronic infection world wide and 0.5% spontaneously seroconvert annually.[1] More than one million people with chronic Hepatitis B die annually. About 20-30% of patients with chronic HBV infection would develop Cirrhosis and Hepatocellular Carcinoma.[3] HBV is the 2nd most important carcinogen worldwide after tobacco.[4] In Nigeria, about 7.3-24% of the population have serological evidence of HBV infection (average 13.7%) with

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DOI: 10.61386/imj.v19i3.1197

20 million Nigerians currently infected,[5] and approximately 5 million will die of HBV-related complications.[5] Other areas of high incidence include: South East Asia, (10-20%), Alaskan Eskimos (45%), pacific Islands (50%) and Australian Aborigines (85%). Modes of transmission include parental exposure to blood and blood products, percutaneous and mucous membrane(heterosexual, homosexual and needle pricks), maternofetal (vertical) and child to child (horizontal).[1] Treatment outcomes of chronic HBV infection had been studied in Europe, The USA and Asia[6,7,8]. An ideal therapy must ensure a degree of virological suppression that will then lead to biochemical remission, histological improvement and prevention of complications. Responses can be divided into biochemical, serological, virological and histological.[6-8]

HBsAg loss, with or even without seroconversion to anti-HBs (Functional cure). The ideal end point for HBeAg-positive and HBeAg-negative patients which however is infrequently achievable with the currently available anti-HBV agents. This is associated with a complete and definitive remission of the activity of CHB and an improved long-term outcome (A1).[6]

Virological responses vary according to the timing (on or after therapy) and type of therapy. Two different types of drugs can be used in the treatment of CHB: Conventional or pegylated interferon alpha (IFN or PEG-IFN) and nucleoside/nucleotide analogues referred to collectively as NAs in this document

Conventional or Pegylated interferon alpha, virological response is defined as an HBV DNA concentration of less than 2000 IU/ml. It is usually evaluated at 6 months and at the end of therapy as well as at 6 and 12 months after the end of therapy. Sustained virological response is defined as HBV DNA levels below 2000 IU/ml for at least 12 months after the end of therapy.[6,7]

Using Nucleoside/Nucleotide Analogues (NA therapy), adequate virological response is defined as undetectable HBV DNA by a sensitive PCR assay. It is usually evaluated every 3–6 months during therapy depending on the severity of liver disease and the type of NA(s).

Sustained off-treatment virological response may be defined similarly to the definition used for IFN therapy. Discontinuation is a not common practice to date. However, NA(s) may be discontinued in some patients

Primary non-response is defined as less than 1 log10 IU/ml decrease in HBV DNA level from baseline at 3 months of therapy. This may be caused by drug resistance. Partial virological response is defined as a decrease in HBV DNA of more than 1 log10 IU/ml but detectable HBV DNA after at least 6 months of therapy in compliant patients.

Virological breakthrough (Treatment failure) is defined as a confirmed increase in HBV DNA level of > 1 log10 IU/ml compared to the nadir (lowest value) on therapy; it may precede a biochemical breakthrough. The main causes of virological breakthrough on NA therapy are poor adherence to therapy and/or selection of drug-resistant HBV variants (resistance).[6,7] Histological response is the decrease in necroinflammatory activity (by P2 points in HAI or Ishak's system) without worsening in fibrosis compared to pre-treatment histological findings.[7] In addition, biochemical response is defined as normalization of ALT levels. It can be evaluated at several time points on-therapy, at the end and after the end of therapy. Since ALT activity often fluctuates over time, a minimum follow-up of at least 1 year post-treatment, in some cases 2 years with ALT determinations at least every 3 months is required to confirm sustained off-treatment biochemical response.[6,7]

The studies found that the majority of their patients achieved good treatment outcomes. Also, determinants of poor outcomes in these studies were: poor drug adherence, late commencement of treatment co-infections with HIV and HCV infections. However, in Africa, and particularly in Nigeria there is paucity of data on outcomes of HBV treatment and its determinants. There is therefore a need for data on the possible treatment outcomes of HBV Infection in our resource-limited settings like Nigeria. This information is needed public health planning on the management of chronic HBV infection and the possible ways of improving favorable treatment outcomes. Moreover, this data will be useful in informing future review of the National guidelines in treatment of HBV infection. This study determined different treatment outcomes of patients with chronic HBV infection and factors responsible for them.

Materials and Methods

Study Location: This study was conducted at the Alex Ekwueme Federal University Teaching Hospital Abakaliki (AEFUTHA), Ebonyi State of Nigeria from 1st January 2018 to 31 December 2022.

Study Design: This retrospective hospital-based descriptive cross-sectional design of patients who were diagnosed for and received treatment for chronic HBV infection over a five-year period, allowing for a comprehensive review of the treatment outcome

Study Population: included all eligible adults (17 years or more) with chronic Hepatitis B who met criteria for treatment using the EASL (European Association for the Study of the Liver) guidelines and receiving antiviral treatment under the period of study at AEFUTHA, Ebonyi State of Nigeria. Patients who had liver cirrhosis and or Primary liver cell cancer prior to commencement of treatment were excluded. Patients with incomplete follow-up records were also excluded All patients who met the inclusion criteria were studied.

The operational definition of HBV infection was established using EASL criteria the presence of HBsAg establishes the diagnosis of hepatitis B. Chronic infection is defined by the presence of HBsAg for at least 6 months or presence of total Anti-HBcAb in the absence of IgM-anti-HBcAb or Presence of IgG-Anti-HBcAb in the absence of IgM-Anti-HBcAb.

Data collection: The case notes of these patients were systematically retrieved, and data extracted by trained researchers using a standardized data abstraction form. Data extracted includes demographics, comorbidities, biochemical and hematological parameters, HBV Panels and Viral loads. To minimize selection bias inherent in retrospective studies, all eligible patients with chronic HBV infection receiving Antiviral treatment under the period of study were studied.

Indications for treatment was made using the EASL Guidelines and includes:[7]

1. Patients with HBeAg-positive or -negative chronic hepatitis B, defined by HBV DNA [2,000 IU/ml, ALT [ULN and/or at least moderate liver necroinflammation or fibrosis.
2. Patients with HBV DNA [20,000 IU/ml and ALT [2xULN regardless of the degree of fibrosis.
3. Patients with HBeAg-positive chronic HBV infection >30 years, defined by persistently normal ALT and high HBV DNA levels, regardless of the severity of liver histological lesions.
4. Patients with HBeAg-positive or HBeAg-negative chronic HBV infection and family history of HCC or cirrhosis and extrahepatic manifestations.
5. Additional indications include the prevention of mother to child transmission in pregnant women with high viremia and prevention of HBV reactivation in patients requiring immunosuppression or chemotherapy.
6. Patients with compensated or decompensated cirrhosis need treatment, with any detectable HBV DNA and regardless of ALT levels were not studied as one of our primary objectives was to determined patients with chronic HBV infections on treatment who developed complications such as liver cirrhosis and Hepatocellular carcinoma.

The treatment outcomes of the patients with chronic HBV infection studied included HBsAg loss (functional cure), Biochemical Normalization, HbeAg Seroconversion, On treatment Sustained Virologic response (SVR), Anti-HBs detection and Virologic Failure (breakthrough).

Statistical Analysis

The data were entered in numerical codes and analyzed using Statistical package for social sciences (SPSS) 20 Software. Categorical data were summarized as frequencies and percentages while continuous data were summarized as mean + standard deviation. Chi-Square was used to compare the relationship between two qualitative variables. Student t- test and Analysis of Variance (ANOVA) was used to assess for significant associations between group means in quantitative (continuous) normally distributed variables and Man Whitney U Test for variables not normally distributed. A P value of <0.05 at confidence interval of 95% was considered as being statistically significant.

Ethical Concerns

Ethics Declarations: This study was conducted according to the principle expressed in the declaration of Helsinki and approved by the Alex-

Ekwueme Federal University Teaching Hospital Ethics and Research Committee (approval numbers NHREC/16/05/22/503). Due to the retrospective study design, the requirement for written consent was waived (Alex-Ekwueme Federal University Teaching Hospital Ethics and Research Committee).

Benefits: Determination of the treatment outcomes of patients with chronic hepatitis B and factors responsible for them will improve future treatment outcomes as factors responsible for poor outcome may be addressed.

Confidentiality: Patients initials and codes were used in identifying all the data. Data was stored in pass-worded computer. No part of the information shall be divulged to anybody.

Results

Table 1: Socio-demographic characteristics of participants

Variables	Frequency N=362	Percent (%)
Age groups(years)		
18 -30	102	(28.2)
31 – 50	144	(39.8)
51 – 70	98	(27.1)
>70	18	(4.9)
Age(years), Mean ± SD	42.4 ± 11.7	
Gender		
Male	185	(51.0)
Female	177	(49.0)
Level of Education		
Primary	78	(21.5)
Secondary	96	(26.5)
Tertiay	190	(52.5)
Ethnicity		
Igbo	262	(72.4)
Coss-River/Effik	62	(17.1)
Yoruba	18	(4.9)
Idoma	12	(3.3)
Hausa/Fulani	8	(2.2)
Marital Status		
Single	148	(40.9)
Married	184	(50.8)
Widowed	30	(8.3)
Religion		
Christianity	352	(97.2)
Islam.	10	(2.8)
Occupation:		
Civil servants	188	(51.9)
Artisans	64	(17.7)
Traders	52	(14.1)
Farmers	40	(11.1)
Unemployed	28	(4.9)

About 1670 of patient with chronic HBV infection presented to our health facility within a 5-year study period, and 362 of them met criteria for treatment. Table 1 shows the socio-demographic characteristics of the subjects. The age range of the patients was between 17 and 80 years, with a mean age (SD) of 42.4 (11.7) years.

Majority 144 (39.8%) of the patients were 39-50 years old, while 18 (4.9%) were greater than 70 years old. A greater proportion of the patients were males (185, 51%), with a female to male ratio of 1:1.1. Most of the subjects belonged to the Igbo ethnic group (262, 72.4%), were married (184, 50.8%), and were Christians (352, 97.2%). There were 188 civil servants (51.9%), 28 unemployed/retired (4.9%), 64 traders (17.7%), 64 artisans (17.7%).and 40 farmers (11.1%)

A high proportion of subjects had tertiary education (190, 52.6%). This was followed by secondary education (96, 26.5%) and primary education (78, 21.5%).

Table 2: Clinical outcomes of chronic HBV infected patients on treatment

Outcome	Total n= 362 (%)	Male n= 185 (%)	Female n= 177 (%)
Alive and in care	285(79.0%)	161(87.0%)	124(70.0%)
Lost to follow-up	56(15.5%)	20(10.8%)	36(20.3%)
Transferred out	10(2.8%)	2(1.1%)	8(4.5%)
Developed complication (6 LC,2 HCC)	8(2.2 %)	2(1.1%)	6 (3.4%)
Dead	3 (0.8%)	0(0%)	3(1.7%)

LC=Liver Cirrhosis, **HCC**=Hepatocellular Carcinoma

LC=Liver Cirrhosis, HCC=Hepatocellular Carcinoma

Table 2 showed the clinical outcomes of the chronic HBV infected patients on treatment

Among the 362 patients, 3 (0.8%) died, 56 (15.5%) were lost to follow-up, 10 (2.8%) transferred to another health facility, 8(2.2 %) developed liver cancer and Cirrhosis and 285 (79.0%) were still on treatment (Table 2).

HBsAg=Hepatitis B Surface Antigen, Anti-HBS=Anti-Hepatitis B Surface Antibody

Table 3 showed the various treatment outcomes of the patients who are alive and in care. A high proportion of patients achieved adequate virologic response (AVR) (257, 90.2%) which was higher in females (91.9%) than males (88.8%) (p =0.879). A 262 of the subjects (92%) achieved biochemical Normalization which was slightly higher in females

Table 3: Treatment Outcomes of the Patients with Chronic HBV Infection who are Alive and in Care

Outcomes		Total n= 285	Male n=161	Female n=124	p-value
HBsAg loss (functional cure)	Yes	10(3.5%)	4(2.5%)	6(4.8%)	
	No	275(96.5%)	157(97.5%)	118(95.2%)	0.360
Biochemical Normalization(<40iu/L)	Yes	262(92%)	147(91.3%)	115(92.7%)	
	No	23(8.1%)	14(8.7%)	9(7.3%)	0.786
HbeAg Seroconversion	Yes	20(91%)	8(89%)	12(92.3%)	
	No	2(9%)	1(11%)	1(7.7%)	0.79
Adequate Virologic response	Yes	257(90.2%)	143(88.8%)	114(91.9%)	
	No	28 (9.8%)	18(11.2%)	10(8.1%)	0.879
Anti-HBs detected	Yes	3(1.1%)	1(0.6%)	2(1.6%)	
	No	282(99%)	160(99.4%)	122(98.4%)	0.416
Virologic Failure (breakthrough)	Yes	18(6.3%)	12(7.5%)	6(4.8%)	0.047
	No	267(93.7%)	149(92.5%)	118(95.2%)	

HbeAg (Hepatitis B Seroconversion (HbeAg loss + Anti HB Seroconversion)

than in males (92.7% vs. 91.3%)). Virologic Failure (breakthrough) was observed in 18(6.3%) of the patients and was higher in males than in females 6(4.8%) Few 10(3.5%) patients achieved HBsAg loss (functional cure) and only 3(1.1%) developed Anti-HBs.

Table 4: Factors associated with the various treatment outcomes in the chronic HBV subjects

Variables		Good treatment outcome N (%)N=267	Treatment failure N (%)N=18	Statistics	p-value
Age:	<40years	157(58.8%)	6(33.3%)	X^2 = 0.432	**0.511**
	>40years	110 (41.2%)	12(66.7%)	df= 1	
Sex:	Male	149(55.8)	12(66.7%)	X^2 0.809	**0.368**
	Female	118(44.2%)	6(33.3%)	df= 1	
Drug:	NA use	250 (93.6 %)	14(77.8%)	X^2 = 5.011	**0.025**
	Interferon based	17(6.4%)	4(22.2%)	df= 2	
Drug Adherence:	>95%	248(92.9%)	2(11.1%)	X^2 = 120.606	**0.001**
	<95%	19(7.1%)	16(88.9%)	df= 1	
PT-VL:	2000-19.999iu/ml	180(67.4%)	11(61.1%)	X^2 = 1.341	**0.247**
	>20.000iu/ml	87(32.6%)	7(38.9%)	df= 1	
HbeAg Status:	Positive	18(6.7%)	2(11.1%)	X^2 = 9.259	**0.002**
	Negative	249(93.3%)	16(88.9%)	df 1	
APRI Score:	<0.6	190(71.2%)	6(33.3%)	X^2 = 9.259	**0.002**
	>0.6	77(28.8%)	12(66.7%)	df 1	
Co-infections HCV:	Yes	20(7.5%)	10(55.6%)	X^2 = 18.208	**0.001**
	No	247(92.5%)	8(44.4%)	df 1	
Co-infections HIV:	Yes	18(6.7%)	3(16.6%)	X^2 = 120.909	**0.001**
	No	249(93.3%)	15(83.3%)	df= 1	
Co-morbidity: DM:	Yes	25(10.4%)	12(66.7%)	X^2 = 52.864	**0.001**
	No	242 (90.6%)	6(33.3%)	df= 1	

PT-VL –Pre-treatment viral load
APRI- Aspartate Platelet ratio Index
Good Treatment outcome (HBsAg loss + adequate virologic response +AntiHBsAb)

Table 4 showed factors associated with the treatment outcomes in the chronic HBV patients.
High proportion of patients were aged > 40years (66.7%) and male sex (66.7%). Poor drug adherence (88.9%) and HbeAg negative status (88.1%) had significantly poor treatment outcomes. (P<0.005). APRI Score more than 0.6 (66.7%), co-infections HCV 9(60%) and presence of DM (73.3%) were also significantly associated with poor treatment. (P<0.005).

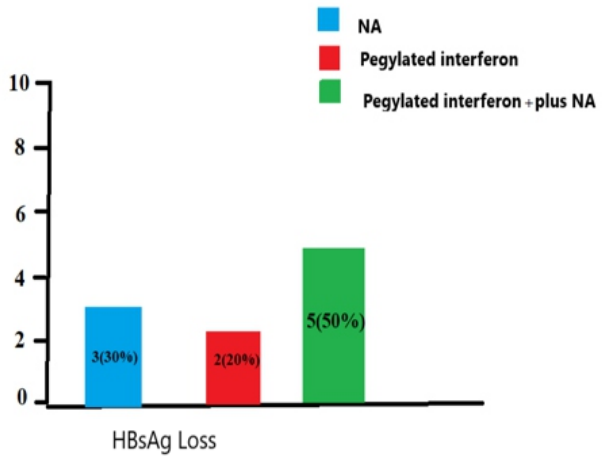

Figure 1: Frequencies of HBsAg loss with type of medication used by the patients

Figure 1 showed the frequencies of HBsAg loss with type of medication used by the patients. A high proportion (50%) of patients who used pegylated interferon plus nucleoside analogue (NA) achieved HBsAg loss, followed by those that used Pegylated interferon only (30%). And least proportion (20%) of HBsAg loss was observed in those who used NA only.

Discussion

Studying treatment outcomes in patients with Hepatitis B virus infection may help review the effectiveness of the current treatment options and guidelines and may help draw up recommendations that will improve future treatment outcomes.
Majority of our patients achieved biochemical normalization and virologic response, this may be related to the high rate use of highly active nucleoside analogue and adherence by majority of the patients. There is paucity of data on the outcome of treatment of chronic Hepatitis B in the South-Eastern and other regions of Nigeria. A study conducted in by Raheem et al.[9] on the treatment of chronic hepatitis B infection in Nigeria suggested a need for a paradigm shift and recommended test and treatment of all patient seropositive for HBsAg. Their study did not discuss the different treatment outcomes.
Desalegn et al.[10] in Ethiopia, Northern Africa, in their five-year results of a treatment program for 1303 chronic hepatitis B patients, of whom 291 (22.3%) started antiviral therapy. Their results

showed estimated 5-year hepatocellular carcinoma-free survival of 99.0% in non-cirrhotic patients which was similar to our findings. They also reported 5-year hepatocellular carcinoma-free survival 88.8% in compensated cirrhotic patients and 54.2% in decompensated cirrhotic patients. Their study was slightly different from ours as patients with HCC and liver cirrhosis were excluded in our study.

Our findings on virologic response and biochemical normalization were similar with reports in Europe[11], USA[13] and Asia[14]. In Europe, Liaw et al.[11] and Chang et al[12] reported virological remission rates of >90% with ongoing entecavir or tenofovir adherent to treatment after 3 years.

In the USA, Younossi et al.[13] compared outcomes between patients taking oral nucleoside analogues (tenofovir, entecavir, adefovir, lamivudine, or telbivudine) and those on vesatolimod (an oral agonist of Toll-like receptor 7) or placebo. They observed that majority of the patients achieved virologic response which also correlated with biochemical normalization. There was no significant differences in outcomes in the groups.

A study in India by Isaakidis et al.[14] on the treatment outcomes in a cohort of patients with chronic hepatitis B and human immunodeficiency virus co-infection in Mumbai. The majority of their patients achieved adequate biochemical normalization and good virologic response while very few four (7%) achieved serum HBsAg seroclearance and developed anti-HBs-antibodies (functional cure).

Hepatitis B Surface antigen seroclearance (functional cure): Only very few of our patients achieved hepatitis B Surface antigen seroclearance and majority of them were young (<40 years), received tenofovir plus pegylated interferon (those on PEG who switched to NA either due to failed or incomplete treatment) and had no evidence of fibrosis on APRI score. This agrees with the finding of Zhang et al.[15] who also reported higher incidence of functional cure in younger patients. Clinical trials using combination therapy with direct acting antivirals and immune modulatory agents especially Pegylated interferon had shown increased frequency of functional cure[16]. Although, achieving functional cure is rare, the long-term outcome of HBsAg clearance is excellent if there is no pre-existing advanced fibrosis, cirrhosis, super infection and remains the optimal goal of therapy for chronic HBV infection[17]. The European Association for the of study of liver diseases [EASL] recommends additional antiviral therapy for 12 months then withdrawal for patients who achieved HBsAg clearance during treatment for HBV infection.[18] Hepatitis B Surface antigen (HBsAg) seroclearance in patient with chronic HBV Infection occurs at annual rate of 1-2%. Based on some studies, the rate of disappearance of Hepatitis B Surface antigen actually based on the type of treatment given. After 48 weeks of Antiviral therapy, HBsAg clearance was slightly higher for Pegylated interferon (3-5%) than the Oral nucleosides (1-2%).[16-18] Pegylated interferon has both Antiviral and immune regulatory functions, prevents infection of new liver cells, and also clears infected liver cells. Chronic hepatitis B is very difficult to cure due to formation of covalently closed circular DNA, cccDNA, a highly stable reservoir of the virus , that serve as a template for viral RNA ensuring continued viral replication.

The current antiviral target the viral replication process but don't directly affect the cccDNA.[19] Secondary, HBV DNA can integrate into the host DNA becoming a permanent part of the host's genetic materials. Thirdly, Chronic HBV infection can lead to T-cell exhaustion, fatigued and less effective at targeting the virus. Others are viral reservoirs and clinical heterogeneity.[20]

Marcellin et al.[21-22] in their study in Europe observed HBsAg loss following 12 months of treatment of 3–7% with PEG-IFN, 1% with lamivudine, 0% with adefovir, 2% with entecavir, 0.5% with telbivudine, and 3% with tenofovir. HBsAg loss rates increase after the end of (PEG-) IFN therapy in patients with sustained off-treatment virological response. These reports were similar to our findings. In patients adherent to treatment, virological remission rates of >95% can be maintained with entecavir or tenofovir at P3–5 years.[23]

Lok et al.[16] in Beijing, China reported HBsAg loss rates increase to 9% at 3 years and 12% at 5 years following PEG-IFN-2a therapy. In contrast, Liaw et al.[24] HBsAg loss was exceptionally low during the first 4–5 years of NA(s) therapy in HBeAg-negative CHB patients. The rates of HBsAg loss was higher in their study than ours, this may be related to genetic factors and environmental such as difficulty in maintenance of cold chain due to inadequate

power supply in our environment.

Virologic failure (virologic breakthrough) was observed commonly males patients older than forty years. Those with poor drug adherence, high APRI score, HCV co-infections and diabetes mellitus also had high treatment failures.

Several factors from literatures have been found to be associated with poor treatment outcomes in chronic HBV infection, these may include; viral factors such as high HBV DNA Levels, genotypes C n D, mutation etc[25]. Host/patient factors including genetic and environmental such as immune status-insufficient B cell responses and compromised T cell function pose barriers to HBV clearance, fibrosis, cirrhosis, older age, and male gender, use of alcohol, tobacco smoking and underlying health conditions like metabolic syndrome etc.[26]

A study of 478 chronic HBV patients in China by Jia et al.[27] showed that older age, male sex, HBeAg positive status, higher HBV DNA levels were associated with poor treatment outcomes disease progression.

Alemnew Aval et al.[28] in Ethiopia in their study of 213 patients with chronic hepatitis B also found poor drug adherence, late stage of the disease and treatment duration among the factors associated with poor treatment outcomes.

Marcellin P et al.[29] in their study that also compared treatment response of PEG-INT with NA, reported off-treatment SVR of 20% at 6 months following 12 months of PEG-IFN therapy and <5% following discontinuation of 12 months of NA(s) therapy in HBeAg negative patients. Liac et al also got similar resilts[30]. In our, study off-treatment SVR was only applied for patients that received interferon and their population was too small to draw any significant conclusion.

Treatment related factors such as type, duration, adherence and timing also affects treatment outcomes. For example, NAs can directly inhibit HBV DNA but unable to act on covalently closed circular DNA (cccDNA), hence clearing HBsAg or inhibiting its production is extremely challenging.[31] Whereas HBsAg clearance is higher with Peg interferon though 10% may relapse within 48 weeks after functional cure. Pegylation of interferon with polyethylene glycol extends its half, allowing for less frequent dosing and potentially fewer side effects.[32]

Pegylated interferon Alfa 2a (Pegasys) binds to cell surface receptors primarily type 1 interferon receptors in cascade of protein interactions through JAK/STAT pathway resulting in gene transcription. These stimulated genes inhibit viral replication and assembly in infected cells, cell proliferation and immunomodulation, shift the immune response from Th2-dominant profile to Th1-dominant which is more effective against antiviral. It also enhances the activities of cytolytic T-cell and natural killer cells.[33]

The study has some limitations. This is a retrospective descriptive cross sectional study, some of the data were missing due to loss to follow up.

Conclusion: Virologic response and biochemical normalization were the common treatment outcomes achieved in our patients. HBsAg loss was achieved in few patients and was achieved in majority of patients who used pegylated interferon plus NA therapy. This findings was very significant as it may be necessary to conduct similar study in study larger population of patients with chronic Hepatitis B who used combined therapy of Interferon and NA. Also, CHB patients who are older age > 40years, male sex, poor drug adherence, APRI Score≥ 0.6, co-infections HCV and presence of DM need to be closely monitored to prevent virologic failure.

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Consent for publication: Not applicable due to the retrospective study design

Author's contributions: Dr. Obasi Emmanuel conceptualize the study, collected the data, interpreted the data and drafted the manuscript, Dr. Ajayi and other authors helped to draft the manuscript, participated in the interpretation and critical appraisal.

Competing interests: Authors declare no competing interests

Funding: This study was funded by the researchers.

Some general things to know about the study:

This study is sets to look out for treatment outcomes of patients with chronic hepatitis B at AEFUTHA over a 5 year period and determine the factors responsible for favourable and poor outcomes