

## **Histopathological Findings and Relationship with Liver Function Tests on Patients with Chronic Hepatitis B Infection Attending Federal University Teaching Hospital, Lafia, North Central Nigeria**

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### **Abstract**

*Objective: The study aims to determine the histopathological findings in patients with chronic Hepatitis B infection and their relationship to liver function tests. Materials and methods: A total of 200 HBV-positive patients aged 16 years or older who attended the gastroenterology unit of the Federal University Teaching Hospital, Lafia, were recruited using convenience sampling. The socio-demographic characteristics were recorded; venous blood was sampled for HBV serological marker testing using Enzyme-linked immunosorbent assay kits; a Tru-Cut biopsy needle was used for liver biopsy; and liver pathology was assessed using a magnetic resonance imaging machine. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 23.0. The results were presented in the table, with a significance level of  $p < 0.05$ . Results: The mean age of patients was  $34.87 \pm 10.78$  years. There were (70.5%) males, and (29.5%) females. Histology results revealed ballooning degeneration (9.5%), Fibrosis (5.5%), inflammation (6.0%), Steatosis and ground-glass (1.5%), fatty liver and necrosis (1.0%). The liver function test revealed that (15.0%), (52.5%), (32.5%), and (6.5%) had elevated platelet prothrombin ratio, international normalization ratio, protein, and albumin, with (35.5%), (44.0%), and (29.0%) had elevated alkaline phosphatase, alanine transaminase (ALT), and aspartate transaminase (AST). The patient with normal AST had the greatest ballooning compared with those with elevated AST (13.6% vs 4.5%), a difference that was statistically significant. Patients with normal ALT had higher inflammation than those with high ALT (9.2% vs 1.4%), with a statistically significant difference ( $p=0.033$ ). Conclusion: Liver biopsy will be recommended for patients with chronic hepatitis B showing normal AST and ALT levels.*

**Keywords:** Ballooning Generation, Fatty Liver, Fibrosis, Hepatitis, Histopathology, Liver Biopsy.

### **Introduction**

#### **Background Study**

The liver is the largest digestive organ in the human body and plays a role in metabolizing

most substances [1]. Therefore, liver damage, which can occur for various reasons, significantly impacts a large proportion of the body's metabolism, including the metabolism of blood lipids, blood sugar, uric acid, and

proteins [2]. However, histopathological evaluation of liver biopsy specimens remains the gold standard for diagnosing liver injuries, including steatosis, lobular inflammation, hepatocellular ballooning, and fatty liver [3]. Hepatitis B virus (HBV) is a Hepadnavirus belonging to the family of Hepadnaviridae with small enveloped spherical virions that contain a circular-double-stranded Deoxyribonucleic acid (DNA) molecule that infects liver cells, and subsequently develops hepatocellular carcinomas (HCC). However, more than 2 billion people worldwide are estimated to have had hepatitis B virus (HBV) infection, with 350–400 million being chronic carriers of the virus [4]. Also, HBV accounts annually for an estimated one million deaths worldwide [5]. An estimated 3.6% of the global population was affected by chronic Hepatitis B virus infection [6]. An estimation of 5–15% of adults in sub-Saharan Africa are chronically infected with HBV [7]. There was a 15–25% risk of dying prematurely in adulthood from HBV-related cirrhosis and hepatocellular carcinoma. At the same time, a small proportion of those with acute infections may succumb to fulminant liver failure [6]. In Africa, approximately 60 million people live with chronic HBV infection with an estimated prevalence of 6.2% [8]. In Africa, Nigeria was ranked among the countries with hyperendemic HBV infection (>8%) [9]. Approximately nine in ten Nigerians who live with chronic HBV are unaware of their infection status and are missing from the global public health statistics due to a lack of resources, awareness, and political will for addressing Nigeria's HBV plight [10]. Consequently, Nigeria has one of the highest rates of HBV-attributable cancer in West Africa, with an age-standardized incidence estimate of 2.6 to <5.1 cases per 100,000 person-years [11]. HCC is a highly aggressive cancer with limited treatment options, often lacking in resource-constrained settings [12]. The lack of affordable diagnostics, especially specialized immunoassays and nucleic acid tests, as well as

the out-of-pocket cost for vulnerable populations, constitute potential barriers in eliminating viral hepatitis B in Nigeria, thus making HBV a significant threat to public health. North Central Nigeria was a highly endemic region that experienced higher morbidity and mortality from this disease, which is why this study was conducted [13, 14]. Liver biopsy was considered the most accurate method for assessing neuroinflammatory activity (grading) [15]. The degree of aminotransferase elevation does not adequately reflect disease severity and correlates poorly with histologic grading. Therefore, a histological study was the easiest way to determine the disease stage by assessing the type and extent of fibrosis, along with the recognition of architectural disturbances (staging) [16]. According to the European Association for the Study of the Liver (EASL) and the Society for Gastroenterology and Hepatology in Nigeria (SOGHIN) Guidelines [17], treatment for CHB were indicated in patients with an HBV DNA level above 2000 IU/ml and serum alanine aminotransferase (ALT) levels more than twice the upper limit of normal in Hepatitis B envelope antigen (HBe-Ag) negative CHB. However, liver biopsy was indicated if there was a discordance between the ALT and HBV-DNA levels. Also, the clinical guidelines published by the American Association for the Study of Liver Diseases (AASLD) recommend liver biopsy only for specific groups of patients, stating that it is usually unnecessary in young patients who are HBe-Ag negative and have persistently normal ALT levels [18]. The Nigerian guidelines for HCC surveillance recommend surveillance for all hepatitis B surface antigen (HBsAg) positive individuals over 20 years of age, including CHB patients in the inactive phase and those with cirrhosis [19]. This excludes individuals younger than 20 years, and many of these patients may be lost to follow-up, later presenting with complications of CHB. The present study, aimed at assessing

histopathological findings and correlating them with liver function tests in patients with chronic hepatitis B viral infection attending a specialist hospital in north central Nigeria, was designed to determine the histopathological impairments, the liver function tests, and their relationship. The outcomes of this research could be very useful to the Federal Ministry of Health, the Pharmacists' Council of Nigeria, the State Ministry of Health, and, especially, to gastroenterologists in making informed decisions when managing patients with chronic hepatitis B.

## Materials and Methods

### Study Area

The research was conducted at Federal Teaching Hospital, Lafia, North Central Nigeria. Nasarawa State was one of the 36 states in Nigeria, with its Capital in Lafia. The State Capital was one of the 13 local government areas of the state, located at 8.480° North latitude and 8.520° East longitude, with an elevation of 290 meters above sea level and a land area of 27,117 km. Nasarawa State and its surroundings were in Nigeria's middle belt (north-central region), characterized by an average temperature of 31 °C and an average humidity of 64% [20]. Nasarawa State was bounded in the North by Plateau State, South by Benue State, East by Cross-River State, and West by the Federal Capital Territory (FCT) Abuja.

### Study Site

The study was carried out at the Department of Internal Medicine [Gastroenterology unit], Federal University Teaching Hospital, Lafia, North Central Nigeria. This clinic serves over 10,000 hepatitis B-positive patients, including adolescents on antiviral therapy. The clinic operates every Tuesday, with all positive patients in attendance.

## Study Design

This research work was a hospital-based cross-sectional study.

## Study Population

The study population comprises all patients with chronic hepatitis B aged 16 years or older who attend the Federal University Teaching Hospital in North Central Nigeria.

## Inclusion Criteria

1. All patients diagnosed with Hepatitis B were recruited for this study.
2. All the patients who signed the consent were recruited for this Study.
3. All the patients who are 16years and above were recruited for this study.

## Exclusion Criteria

1. Patients co-infected with hepatitis C, the Delta virus, or human immunodeficiency virus.

## Sample Size Determination

The sample size was determined using the Leslie Kish formula for calculating proportions in a large population [21].

$$\text{Sample Size } (n) = \frac{Z^2 pq}{\delta^2}$$

n = the desired minimal sample size when the population is more than 10,000.

z = is the standard normal deviation corresponding to the level of significance and is constant at 95% confidence interval (1.96). therefore  $Z^2 = 1.96^2 = 3.842$ .

p = Prevalence of the outcome of interest, which is histopathological findings and relationship with liver function test on patients with hepatitis B, and was found to be 35.7% [22] = 0.36.

q = 1-p, the power of the study is 1 – 0.36 = 0.64.

δ = the expected precision is 5% = (p value of 0.05), therefore  $\delta^2 = 0.05^2 = 0.0025$ .

$$n = \frac{3.84(0.36 \times 0.64)}{0.0025}$$

$$n = 347.$$

The population N was 38 (the number of chronic hepatitis B patients who attended the clinic per week)  $\times$  4 weeks  $\times$  3 months (the study duration) = 456. Therefore, N = 456.

nf = the desired sample size when the population is less than 10,000. For this study, the population was 200.

$$nf = \frac{n}{1} + \frac{(n-1)}{(N)}$$
$$nf = \frac{347}{1} + \frac{(347-1)}{(200)}$$
$$nf = 203.7 \text{ (approx. 200).}$$

### Sample Techniques

Convenience sampling was used to recruit participants. This sampling method involved recruiting individuals primarily because they are available, willing, or easy to contact. A total of 200 participants were recruited for the study, and the target population size was 456; any additional participants who could be reached will be recruited. An average of 38 participants attends the clinic every week. This means that, to recruit 200 participants, the duration will be 200 divided by 38, which is 10.97 (approx. 11) weeks. This will be approximately 2.75 months (approx. 3 months).

### Data Collection Method

The data collection was in four phases.

1. **First phase:** The first phase involved the social demographic characteristics, such as age and sex, by the staffing nurse during the clinic.
2. **Second phase:** The second phase involved the venous blood sampling for testing of Hepatitis B Virus profile, such as (HBsAg, HBsAb, HBcAb, and HBeAB, respectively). It was assayed using an enzyme-linked immunosorbent assay (ELISA) kit from Diagnostic Bioprobes Srl, Milan, Italy, with sensitivity and specificity of 100% and 98.8%, respectively. In contrast, the HBV surface antigen (HBsAg) was assayed using the ELISA kit by Bio-Rad

Laboratories, Berkeley, CA, with a sensitivity of 100% and specificity of 99.4%. Other parameters assayed include packed cell volume, white blood cell, platelets, and serum biochemical parameters such as alkaline phosphatase, aspartate aminotransferase, gamma-glutamyl transferase, creatinine, albumin, total bilirubin, conjugated bilirubin, platelets thrombin ratio (PTR), partial thromboplastin time (PTT), international normalization ratio (INR), etc. The laboratory test results for individuals were anonymously linked to individual and household questionnaire information through their unique identifiers.

3. **Third phase:** it involved the liver biopsy, which was performed using a liver biopsy needle (Trucut biopsy needle). The biopsy samples were fixed in buffered formaldehyde for 24 hours and then processed by routine procedures. It was evaluated by a pathologist who was blinded to clinical and virological findings, using hematoxylin- and eosin-stained sections and periodic acid-Schiff stain. Masson's trichrome and Sweet's reticulin stains were reviewed for fibrosis and structural change. Other pathological lesions studied included ballooning degeneration, steatosis without fibrosis, chronic inflammatory cells, mild to moderate microvascular steatosis, plasma cell infiltration, Periportal inflammation, etc.
4. **Fourth phase:** it involved the use of a scanning machine to obtain pathological features such as fatty livers, hepatomegaly, shrunken liver, masses, ascites, etc.

### Data Management

#### Measurement of Variables

The variables were the dependent and independent variables. The dependent variable, also known as the outcome variable, was Histopathological findings and hepatitis B. In contrast, the independent variables were the factors that determined the spread of Hepatitis B infections, liver function test results, and sociodemographic characteristics.

### Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) version 23.0 was used to process data, and statistical analyses were performed and summarized using appropriate measures of central tendency and dispersion.

Significance tests were conducted using the chi-square test; p-values < 0.05 were considered statistically significant at the 95% confidence level. Results were displayed in tables.

### Limitations

1. This study was a single facility-based study that included only clients who were in care at the time, which limits its generalizability.
2. There was limited research concerning hepatitis in Nigeria, which made it difficult to access information.

### Results

**Table 1.** Shows the Socio-Demographic Characteristics of Study Participants (n=200)

Variables	Frequency	Percent
<b>Age (in years)</b>		
15-25	46	23.0
26-35	74	37.0
36-45	45	22.5
46-55	26	13.0
56-65	9	4.5
<b>Mean=34.87±10.78</b>		
<b>Sex</b>		
Male	141	70.5
Female	59	29.5
<b>Occupation</b>		
Farmers	5	2.5
Civil Servant	118	59.0
Students	36	18.0
Housewife	19	9.5
Traders	22	11.0

A total of 200 patients were recruited for the study; their ages ranged from 15 to 65 years, with a mean age of 34.87±10.78 years. There were (70.5%) males, and (29.5%) females. The

majority (59%) of the patients were civil servants, and the fewest (5; 2.5%) were farmers (Table 1).

**Table 2.** Histological Findings of Study Participants (N=200)

Variables	Yes (%)	No (%)
Ballooning	19(9.5)	181(90.5)
Fibrosis	11(5.5)	189(94.5)
Inflammatory cells	12(6.0)	188(94.0)
Steatosis	3(1.5)	197(98.5)

Ground glass	3(1.5)	197(98.5)
Fatty liver	2(1.0)	198(99.0)
Necrosis	2(1.0)	198(99.0)

Histology results of participants showed ballooning generation (9.5%). Fibrosis (5.5%), inflammation (6.0%). Steatosis and ground

glass (1.5%), fatty liver and necrosis (1.0%), respectively (Table 2).

**Table 3.** Liver Function Tests of Study Participants (n=200)

Variables	Frequency	Percent
<b>Platelet Prothrombin ratio</b>		
Normal	125	62.5
High	30	15.0
Not documented	45	22.5
<b>International normalization ratio</b>		
Normal	50	25.0
High	105	52.5
Not documented	45	22.5
<b>Protein</b>		
Normal	125	62.5
High	65	32.5
Not documented	10	5.0
<b>Albumin</b>		
Low	54	27.0
Normal	123	61.5
High	13	6.5
Not documented	10	5.0
<b>Bilirubin Total</b>		
Low	1	0.5
Normal	160	80.0
High	30	15.0
Not documented	9	4.5
<b>Bilirubin Conjugated</b>		
Normal	141	70.5
High	50	25.0
Not documented	9	4.5
<b>Alkaline Phosphatase</b>		
Normal	134	67.0
High	58	29.0
Not documented	8	4.0
<b>Alanine Transaminase (ALT)</b>		
Normal	120	60.0
High	71	35.5
Not documented	9	4.5
<b>Aspartate Aminotransferase (AST)</b>		

Normal	103	51.5
High	88	44.0
Not documented	9	4.5

The liver function test of the participants showed that (15.0%), (52.5%), (32.5%), and (6.5%) had elevated platelet prothrombin ratio, international normalization ratio, protein, and albumin, respectively. The result also showed that (15.0%), (25.0%), and (29.0%) had elevated total bilirubin, conjugated bilirubin,

and alkaline phosphatase, respectively. The liver function test also revealed that (29.0%), (35.5%), and (44.0%) had elevated alkaline phosphatase, alanine transaminase (ALT), and aspartate transaminase (AST), respectively (Table 3).

**Table 4.** Association Between Fibrosis, Ballooning Histology, and Liver Function Tests

Variables	Fibrosis		Test statistics	p-value	Ballooning		Test statistics	p-value
	Yes n(%)	No n(%)			Yes n(%)	No n(%)		
Platelet Prothrombin ratio			0.47	0.490			2.07	0.150
Normal	8(6.4)	117(93.6)			13(10.4)	112(89.6)		
High	3(10.0)	27(90.0)			6(20.0)	24(80.0)		
International normalization ratio			2.90	0.088			0.20	0.648
Normal	1(2.0)	49(98.0)			7(14.0)	43(86.0)		
High	10(9.5)	95(90.5)			12(11.4)	93(88.6)		
Protein			0.25	0.617			0.19	0.662
Normal	8(6.4)	117(93.6)			12(9.6)	113(90.4)		
High	3(4.6)	62(95.4)			5(7.7)	60(92.3)		
Albumin			2.62	0.269			0.28	0.869
Low	2(3.7)	52(96.3)			4(7.4)	50(92.6)		
Normal	7(5.7)	116(94.3)			12(9.8)	111(90.2)		
High	2(15.4)	11(84.6)			1(7.7)	12(92.3)		
Bilirubin Total			3.79	0.150			0.72	0.695
Low	0(0.0)	1(100.0)			0(0.0)	1(100.0)		
Normal	7(4.4)	153(95.6)			14(8.8)	146(91.3)		
High	4(13.3)	26(86.7)			4(13.3)	26(86.7)		
Bilirubin Conjugated			0.62	0.429			0.52	0.468
Normal	7(5.0)	134(95.0)			12(8.5)	129(91.5)		
High	4(8.0)	46(92.0)			6(12.0)	44(88.0)		
Alkaline Phosphatase			0.21	0.647			0.05	0.813
Normal	7(5.2)	127(94.8)			13(9.7)	121(90.3)		
High	4(6.9)	54(93.1)			5(8.6)	53(91.4)		
Alanine Transaminase (ALT)			0.34	0.558			0.75	0.386
Normal	6(5.0)	114(95.0)			13(10.8)	107(89.2)		
High	5(7.0)	66(93.0)			5(7.0)	66(93.0)		
Aspartato transaminasi (AST)			0.06	0.798			4.55	0.033*
Normal	5(4.9)	98(95.1)			14(13.6)	89(86.4)		
High	5(5.7)	83(94.3)			4(4.5)	84(95.5)		

Table 4: Association between fibrosis, ballooning, and liver function test. The results show no statistically significant association between fibrosis and any of the liver function tests. ( $P > 0.05$ ). On the other hand, only patients

with normal AST had the highest prevalence of ballooning compared with those with elevated AST (13.6% vs 4.5%), a statistically significant difference.

**Table 5.** Association Between Fatty Liver, Ground Glass, and Liver Function Tests

Variables	Fatty Liver		Test statistics	p-value	Ground Glass		Test statistics	p-value
	Yes n(%)	No n(%)			Yes n(%)	No n(%)		
Platelet Prothrombin ratio			0.48	0.486			0.38	0.536
Normal	2(1.6)	123(98.4)			2(1.6)	123(98.4)		
High	0(0.0)	30(100.0)			1(3.3)	29(96.7)		
International normalization ratio			0.29	0.589			1.45	0.22
Normal	1(2.0)	49(98.0)			0(0.0)	50(100.0)		
High	1(1.0)	104(99.0)			3(2.9)	102(97.1)		
Protein			0.22	0.636			0.00	0.974
Normal	1(0.8)	124(99.2)			2(1.6)	123(98.4)		
High	1(1.5)	64(98.5)			1(1.5)	64(98.5)		
Albumin			6.14	0.046*			1.66	0.436
Low	0(0.0)	54(100.0)			0(0.0)	54(100.0)		
Normal	1(0.8)	122(99.2)			3(2.4)	120(97.6)		
High	1(7.7)	12(92.3)						
Bilirubin Total			1.79	0.407			0.59	0.744
Low	0(0.0)	1(100.0)			0(0.0)	1(100.0)		
Normal	1(0.6)	159(99.4)			3(1.9)	157(98.1)		
High	1(3.3)	29(96.7)			0(0.0)	0(0.0)		
Bilirubin Conjugated			0.59	0.441			0.08	0.776
Normal	1(0.7)	140(99.3)			2(1.4)	139(98.6)		
High	1(2.0)	49(98.0)			1(2.0)	49(98.0)		
Alkaline Phosphatase			0.87	0.350			0.01	0.905
Normal	2(1.5)	132(98.5)			2(1.5)	132(98.5)		
High	0(0.0)	58(100.0)			1(1.7)	57(98.3)		
Alanine Transaminase (ALT)			1.19	0.274			0.01	0.890
Normal	2(1.7)	118(98.3)			2(1.7)	118(98.3)		
High	0(0.0)	71(100.0)			1(1.4)	70(98.6)		
Aspartato transaminasi (AST)			0.01	0.911			2.60	0.107
Normal	1(1.0)	102(99.0)			3(2.9)	100(97.1)		
High	1(1.1)	87(98.9)			0(0.0)	88(100.0)		

Table 5: Association between fatty liver, ground glass, and liver function test. The result

shows that patients with high albumin had the highest prevalence (7.7%) of fatty liver

compared with those with normal (0.8%) and low (0.0%) albumin. This was statistically significant ( $p < 0.05$ ). On the other hand, there is

no statistically significant association between ground glass and any liver function test. ( $P > 0.05$ ).

**Table 6.** Association Between Steatosis, Inflammation, and Liver Function Tests

Variables	Steatosis		Test statistics	p-value	Inflammation		Test statistics	p-value
	Yes n(%)	No n(%)			Yes n(%)	No n(%)		
Platelet Prothrombin ratio			0.73	0.392			0.06	0.806
Normal	3(2.4)	122(97.6)			10(8.0)	115(92.0)		
High	0(0.0)	30(100.0)			2(6.7)	28(93.3)		
International normalization ratio			0.00	0.968			0.00	0.934
Normal	1(2.0)	49(98.0)			4(8.0)	46(92.0)		
High	2(1.9)	103(98.1)			8(7.6)	97(92.4)		
Protein			0.22	0.636			1.75	0.186
Normal	1(0.8)	124(99.2)			10(8.0)	115(92.0)		
High	1(1.5)	64(98.5)			2(3.1)	63(96.9)		
Albumin			1.10	0.577			6.87	0.032*
Low	0(0.0)	54(100.0)			2(3.7)	52(96.3)		
Normal	2(1.6)	121(98.4)			7(5.7)	116(94.3)		
High	0(0.0)	13(100.0)			3(23.1)	10(76.9)		
Bilirubin Total			0.59	0.744			17.02	0.000*
Low	0(0.0)	1(100.0)			1(100.0)	0(0.0)		
Normal	3(1.9)	157(98.1)			11(6.9)	149(93.1)		
High	0(0.0)	30(100.0)			0(0.0)	30(100.0)		
Bilirubin Conjugated			8.59	0.003*			0.599	0.439
Normal	0(0.0)	141(100.0)			10(7.1)	131(92.9)		
High	3(6.0)	47(94.0)			2(4.0)	48(98.0)		
Alkaline Phosphatase			0.01	0.905			1.11	0.291
Normal	2(1.5)	132(98.5)			10(7.5)	124(92.5)		
High	1(1.7)	57(98.3)			2(3.4)	56(96.6)		
Alanine Transaminase (ALT)			1.13	0.287			4.56	0.033*
Normal	1(0.8)	119(99.2)			11(9.2)	109(90.8)		
High	2(2.8)	69(97.2)			1(1.4)	70(98.6)		
Aspartato transaminasi (AST)			0.19	0.655			0.10	0.752
Normal	2(1.9)	101(98.1)			7(6.8)	96(93.2)		
High	1(1.1)	87(98.9)			5(5.7)	83(94.3)		

\*= Statistically significant

Table 6: Association between steatosis, inflammation, and liver function tests. The result shows that only patients with high conjugated bilirubin had the highest prevalence of steatosis compared with those with normal conjugated bilirubin. (6.0% vs 0.0%) This was statistically significant ( $p < 0.05$ ). On the other

hand, patients with a high albumin level (23.1%) had the highest prevalence of inflammation, whereas those with a low albumin level (3.7%) had the lowest. This was statistically significant ( $p = 0.032$ ). Patients with low total bilirubin (100%) had a higher prevalence of inflammation than those with

normal (6.9%) or high (0.0%) bilirubin. This was statistically significant ( $p < 0.01$ ). Patients with normal ALT had the highest prevalence of inflammation compared with those with high ALT (9.2% vs 1.4%). This was statistically significant ( $p = 0.033$ ).

## Discussion

This study recruited 200 patients with CHBV aged 15-65 years, with a mean age of  $34.87 \pm 10.78$  years. In this study, more patients contracted this virus between the ages of 15 and 35. This was similar to the findings of Mei-hwei (2008), who reported that HBV acquisition occurs in early childhood in areas of high endemicity, such as Nigeria, and is mostly asymptomatic [23]. According to Andersson et al. (2015), early HBV acquisition was either vertical or horizontal, both of which are common in sub-Saharan Africa [24]. Age was an important factor in the prevalence and incidence of HBV infection, particularly in the age at acquisition [25]. The early acquisition of HBV was similar to that reported by Moses *et al.* (2010) [26]. In this Study, the majority of the patients were Males because males indulge in activities that predispose them to the acquisition of HBV, such as sexual harassment, alcoholism, non-adherence to HBV medications, etc. This finding was similar to that of Oje et al. (2024), in which males were more than females [27]. In this study, the histology reports include ballooning degeneration, Fibrosis, inflammation, steatosis, ground-glass appearance, fatty liver, and necrosis. However, hepatocyte ballooning was characterized by enlarged hepatocytes with pale, rarefied cytoplasm, usually with a large, hyperchromatic nucleus and a prominent nucleolus, indicating hepatocellular injury [28]. Again, hepatic fibrosis recorded in this study was caused by the excessive production, deposition, and net accumulation of extracellular matrix by activated hepatic stellate cells and other myofibroblasts [29]. According to Leow et al., steatosis, or fatty change, was the

accumulation of fat droplets in the hepatocyte cytoplasm and could be classified as macrovesicular or microvesicular based on the size of the lipid droplets [30, 31]. Fatty liver was caused by excessive accumulation of fat in hepatocytes [32]. The findings in this study were similar to those of Cataldo et al. [33].

The results of this study also showed that both ALT and AST levels were significantly higher in patients with liver disease than in normal subjects ( $p = 0.000$ ). ALT and AST are both useful in assessing liver function alterations, although ALT is more specific [34, 35].

The results showed that alkaline phosphatase levels were significantly elevated in patients with liver disease compared with those in normal individuals. Alkaline phosphatase is useful in assessing liver injury but may not specifically indicate liver disease [36]. The findings above were similar to those of Asirri et al. [37]. The results showed that patients with liver disease had significantly elevated bilirubin levels compared with normal persons ( $p = 0.000$ ). This is consistent with other studies in which elevated bilirubin levels reflect damage and inflammatory conditions [38]. According to Musarrat (2009), patients with chronic hepatitis B have prothrombin time prolonged along with significantly raised bilirubin, albumin, and transaminase, which is similar to the findings in this study [39]. According to li *et al.* [2023], revealed that liver enzymes (AST and ALT) are indicators of hepatocyte injury, which do not correlate well with the severity of underlying histological changes like inflammation, fibrosis, or ballooning since the patients can have normal liver function tests with significant non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH) and active liver damages [40]. This is because in many liver diseases, like cirrhosis, the number of functional hepatocytes decreases, which can lead to near-normal levels of AST and ALT, even in advanced stages of hepatocyte

ballooning, which was a critical feature in the diagnosis of steatohepatitis (both alcoholic and non-alcoholic) and was strongly associated with the progression to more severe fibrosis and adverse liver-related outcomes [40]. The study underscores the importance of assessing histological features directly (via biopsy or advanced imaging techniques like FibroScan) rather than relying solely on standard blood tests for accurate disease staging and prognosis. The lack of a significant association between fibrosis and all liver function tests ( $P > 0.05$ ) further supports the idea that traditional LFTs are poor standalone markers for assessing the presence or severity of liver scarring (fibrosis) [41]. There was a statistically significant association between fatty liver and high albumin levels, with patients having high albumin showing the highest prevalence of fatty liver (7.7%) compared to those with normal (0.8%) or low (0.0%) albumin. The liver synthesizes albumin, the most abundant protein in plasma, and low albumin indicates liver dysfunction. According to Takahashi *et al.* (2023), cases of significant liver damage, such as advanced fatty liver disease (cirrhosis), show that the liver's ability to produce albumin decreases, leading to low blood albumin levels. Low albumin was a key indicator of severe or long-term liver issues and is associated with a poorer prognosis and increased mortality risk [42].

## Conclusions

This study concluded that standard liver function tests do not capture the full extent of liver pathology, including significant microscopic damage, such as hepatocyte ballooning, which is seen in some patients with normal or near-normal AST levels. However,

this study suggested that a comprehensive diagnostic approach, potentially involving liver biopsy or non-invasive imaging, is necessary for accurate assessment of liver health in patients with chronic hepatitis B.

## Ethical Consideration

Ethical approval for this Research was sought and obtained from the Research and Ethics Committee of the Federal University Teaching Hospital, Lafia, North Central, Nigeria, with reference number FUTHREC/578. Informed and written consent were obtained from all participants.

## Conflict of Interest Statement

The authors declare no conflict of interest.

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## Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon request.

## Authors' Contributions

BRN and NAN were involved in the experiment and data processing, as well as in revising the original draft. AE and NJ contributed to data curation, experiment, methodology, and project administration. AE, DN, and MRK were involved in writing, review, editing, and data curation.

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## References

- [1]. Mitra, V., and Metcalf, J., 2009, Functional Anatomy and blood supply of the liver. *Anesthesia and Intensive Care Medicine*, 10(7), 332-333.
- [2]. Hiroi, K., Matsuzaki, T., Kaku, R., Umeda, Y., Yagi, T., Morimatsu, H., 2019, Postoperative course of serum albumin levels and organ dysfunction after liver transplantation. *Transplant Proc*, 51:2750–2754. Doi:10.1016/j.transproceed.01.199.0041-1345/19.
- [3]. Yakalashi, Y., and Fukusato, T., 2014, Histopathology of Nonalcoholic fatty liver disease/Nonalcoholic steatohepatitis. *World Journal of Gastroenterology*. 2014, 20(42), 15539-15543: <https://dx.doi.org/10.3748/wjg.v20.i42.15539>
- [4]. Takahashi Y, Fukusato T., Histopathology of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. *World J Gastroenterol*, 2014; 20(42): 15539-15548 [PMID: 25400438 DOI: 10.3748/wjg.v20.i42.15539].
- [5]. Lok, A. S., & McMahon, B. J., 2007, Chronic hepatitis B., *Hepatology*, 45(2), 507-539, Doi: 10.1002/hep.21513.
- [6]. WHO, 2014, Hepatitis B. Available at: <http://www.who.int/inf-s/en/fact204.html> Accessed July 28, 2013. <https://www.who.int/inf-s/en/fact204.html>
- [7]. Global Burden of Disease Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2013;385(9963):117–71. December 18, 2014, [http://dx.doi.org/10.1016/S0140-6736\(14\)61682-2](http://dx.doi.org/10.1016/S0140-6736(14)61682-2)
- [8]. World Health Organization. Global health sector strategy on viral hepatitis, 2016.
- [9]. World Health Organization, 2021, Hepatitis B fact sheet. 2019. <https://www.who.int/newsroom/factsheets/detail/hepatitis-b>
- [10]. Kramvis, A., Kew M. C., 2007, Epidemiology of hepatitis B virus in Africa, its genotypes, and clinical associations of genotypes. *Hepatology Res*, 2007;37(s1): S9–19. Doi: 10.1111/j.1872-034X.2007.00098.x.
- [11]. World Hepatitis Alliance, 2018, Find the missing millions: Global report on barriers to diagnosis. 2018.
- [12]. de Martel, C., Georges, D., Bray, F., Ferlay, J., Cliford, G. M., 2020, Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*, 8(2): e180–90. Doi: 10.1016/S2214-109X (19)30488-7.
- [13]. Howell, J., Lemoine, M., Thursz, M., 2014, Prevention of materno-fetal transmission of hepatitis B in sub-Saharan Africa: the evidence, current practice and future challenges. *J Viral Hepatitis*, 21(6):381–96. Doi: 10.1111/jvh.12263.
- [14]. Dwiartama, A., Nirbayati, W. F., Giri-Rachman, E. A., Niloperbowo, W., Tan, M. I., & Anin, A., 2022, Knowledge, attitude, and practice towards hepatitis B infection prevention and screening among Indonesians. *International Journal of Environmental Research and Public Health*. 19(8), 464. Doi: 10.3390/ijerph19084644.
- [15]. Ndubuisi, J. C., Aisha, M., Ugboaja, I., & Ubani, C. D., 2022, Prevalence of hepatitis B virus among students of Faculty of Natural and Applied Sciences, Nasarawa State University, Keffi, Nasarawa State, Nigeria. *South Asian Journal of Parasitology*. 5(3), 86–90. <https://journalsajp.com/index.php/SAJP/article/view/125>
- [16]. Rockey, D. C., Caldwell, S. H., Goodman, Z. D., et al., 2009, Liver biopsy. *Hepatology*, 49:1017–1044. [PubMed: 19243014]. Doi: 10.1002/hep.22742.
- [17]. Anka, Y., Rampal, L., Ibrahim, N., Sidik, S., & Iliyasu, Z., 2016. The effectiveness of an education intervention program for improving knowledge, attitude, and practice related to hepatitis B infection among non-medical and non-veterinary undergraduate university students in Northern Nigeria: A randomized controlled trial. *Pan African Clinical Trials Registry*. 15(11), 114–12. Doi: 10.21010/Ajidv19i1.6.
- [18]. Asaye, Z., Aferu, T., Asefa, A., Feyissa, D., Regasa, T., Kebede, O., Feyisa, D., & Feyisa, M., 2021, Prevalence of hepatitis B virus among

- pregnant women on antenatal care follow-up at Mizan-Tepi University Teaching Hospital and Mizan Health Center, Southwest Ethiopia. *International Journal of General Medicine*, 14, 195–200. Doi: 10.2147/IJGM.S292070.
- [19]. Balegha, A., Yidana, A., & Abihiro, G., 2021, Knowledge, attitude, and practice of hepatitis B infection prevention among nursing students in the Upper West Region of Ghana: A cross-sectional study. *PLoS ONE*, 16(10), 1-18. <https://doi.org/10.1371/journal.pone.0258757>
- [20]. Bigna, J. J., Kenne, A. M., Hamroun, A., Ndongang, M. S., Foka, A. J., Tounouga, D. N., Lenain, R., Amougou, M. A., & Nansseu, J. R., 2019, Gender development and hepatitis B and C infections among pregnant women. Doi: 10.1186/s40249-019-0526-8.
- [21]. Ngbalaga, G. A., Fuh, N. J., Upla, P. U., Akeh, M. A., Ombugadu, A., Ablaku, A. A., & Goche, N. I., 2023, Microbiological evaluation of street-vended *Saccharum officinarum* (sugarcane) sold within Lafia Metropolis, Nasarawa State, Nigeria. *Transactions on Science and Technology*, 10(1), 21–27. <https://doi.org/10.21010/Ajid.v19i.1.6>
- [22]. Shabi, O. M., Omolayo, T., 2018, Sample size determination. *NFMJ*. 1(1): 32-3828. <https://www.journalcra.com>
- [23]. Zhan, Z., Hao, H., Bi, X., Lin, Y., Yang, L., Wang, S., Shen, G., Chang, M., Jiang, T., et al., 2022, Study on Liver histopathology of chronic Hepatitis B virus-infected patients with different normal ALT values. *Frontiers in Immunology*. 13:1069792. <https://doi.org/10.3389/fimmu.2022.1069752>
- [24]. Mei-hwei, C., 2008, Natural history and clinical management of chronic hepatitis B virus infection in children. *Hepato Int*. 2:28–36. Doi: 10.1007/s12072-008-9050-9
- [25]. Andersson, M. I., Rajbhandari, R., Kew, M. C., Sandro, V., Wolfgang, P., Andy, I. M. H., 2015. Mother-to-child transmission of hepatitis B virus in sub-Saharan Africa: time to act. *Lancet*, 3(7):358–9. e358-9. Doi: 10.1016/S2214-109X(15)00056-X
- [26]. Agbede, O. O., Iseniyi, J. O., Kolawole, M. O., Ojuawo, A., 2007, Risk factors and seroprevalence of hepatitis B surface antigenemia in mothers and their preschool-age children in Ilorin. *Nigeria Therapy*, 4(1):67–72. 14750708.4.1.67.
- [27]. Moses, A. P., Gyar, S. D., Pechulano, S., Obadiah, D. B., Samuel, E. E., Timothy, Z., et al., 2010, Hepatitis B virus infections in apparently healthy urban Nigerians: data from pre-vaccination tests. *J Infect Dev Ctries*, 4(6):397–400. Doi: <https://doi.org/10.3855/jidc.591>
- [28]. Modupeola, O. M., Kolawale, O. J., Ijarotimi, O., Adekunle, O., Jegede, O. S., Ndububa, D. A., 2024, Liver histology patterns of young patients with inactive chronic hepatitis B virus infection from a Hospital in Southwest Nigeria. *BMC Gastroenterology*. 24:438. Doi: <https://doi.org/10.1186/s12876-024-03501-7>
- [29]. Takahashi, Y., Fukusato, T., 2014, Histopathology of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. *World J Gastroenterol*, 20:15539-15548.
- [30]. Schwabe, R. F., Tabas, I., Pajvani, U. B., 2020, Mechanisms of fibrosis development in non-alcoholic steatohepatitis. *Gastroenterology*. 158:1913-1928. Doi: 10.1053/j.gastro.2019.11.311
- [31]. Leow, W. Q., Chain, A. W., Mendoza, P. Q., LO, R., Yap, K., Kim, H. Y., 2023, Non alcoholic fatty liver disease: The Pathologist's Perspective. *Clinical and Molecular Hepatology*. 29(Suppl)S302-S318. Doi: 10.3350/cmh.2022.0329.
- [32]. He, T., Li, J., Ouyang, Y., Lv, G., Ceng, X., Zhang, Z., & Ding, J., 2020, FibroScan detection of fatty liver/liver fibrosis in 2266 cases of chronic hepatitis B. *Journal of Clinical and Translational Hepatology*, 8. 109-112. Doi: 10.14218/JCTH.2019.00053
- [33]. Whitehead, M. W., Hawkes, N. D., Hainsworth, I., et al., 1999, A prospective study of the causes of notably raised aspartate aminotransferase of liver origin. *Gut*, 45: 129. Doi:10.1136/gut.45.1.129.
- [34]. Cataldo, I., Sarcognato, S., et al., 2021, Pathology of nonalcoholic fatty liver disease. *Pathologica*, 113: 194-202. Doi: 10.32074/1591-951X-242.
- [35]. Daniel, S., Ben-Menachem, T., Vasudevan, G., et al., 1999, Prospective evaluation of unexplained

chronic liver transaminase abnormalities in asymptomatic and symptomatic patients. *Am J Gastroenterol.* 94:3010– 4. Doi:10.1111/j.1572-0241.1999.01451.

[36]. Newsome, P. N., Cramb, R., Davison, S. M., et al., 2018, Guidelines on the management of abnormal liver blood tests. *Gut.* 67:6-19. Doi: 10.1136/gutjnl-2017-314924

[37]. Asirri, A. M., Joumah, B. A., Alharthi, Y. S., et al., 2022, The assessment of liver Disease utilising a panel of liver function tests. *International Journal of Pharmaceutical and Bio-Medical Science.* 2(8):327-332. Available on: <https://ijpbms.com/>

[38]. Li, H., Wang, Y J., Tan, K, Zeng, L., Liu, L., Liu, F J., et al., 2009, Prevalence and risk factors of fatty liver disease in Chengdu, Southwest China. *Hepatobiliary Pancreat Dis Int,* 8(4):377–82. <https://pubmed.ncbi.nlm.nih.gov/19666406/>

[39]. Musarrat, N., 2009, Prothrombin time is an indicator of the severity of liver disease. *JPMI,* 23(1):102-108.

[40]. Fallatah, H. I., Akbar, H. O., Fallatah, A. M., 2016, FibroScan compared to FIB-4/APRI and AST/ALT Ratio for assessment of liver fibrosis in Saudi patients with Nonalcoholic Fatty Liver Disease. *Hepatology,* 16(7). Doi: 10.5812/hepatmon. 38346

[41]. LI, Y. Y., Zheng, T. L., Xiao, S. Y., Wang, P. Y., Yang, W. J., et al., 2023, Hepatocytic Ballooning in Non-Alcoholic Steatohepatitis: Delimmas and Future Direction, *Willy: Liver International,* 43.1170-1182e38346. 10.5812/hepatmon. 38346

[42]. Gallaher, H., Mehkri, S., 2023, Advanced Stage Hepatic Fibrosis with Normal Liver Chemistries: A Case Report. *Cureus,* 15(6): e40732. Doi: 10.7759/cureus. 40732

[43]. Takahashi, H., Kawanaka, M., Fujii, H., Iwaki, M., Hayashi, H., Toyoda, H., et al., 2023, Association of serum albumin level and long-term prognosis in patients with biopsy-confirmed Non alcoholic Fatty Liver Disease. MDPI. *Nutrients.*15,2014. <https://doi.org/10.3390/nu15092014>