

Indications and Histological Outcomes of Liver Biopsies in Sokoto, Northwestern Nigeria

Abubakar Sadiq Maiyaki^{1*}, Nasiru Altine Dankiri¹

¹Department of Internal Medicine, Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria

DOI: <https://doi.org/10.36348/sjpm.2024.v09i09.005>

| Received: 17.08.2024 | Accepted: 25.09.2024 | Published: 30.09.2024

*Corresponding author: Abubakar Sadiq Maiyaki

Department of Internal Medicine, Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria

Abstract

Background: Various liver disorders require histological assessment for proper diagnosis, staging, treatment, or follow-up. We determine indications and histological outcomes of liver biopsy samples. **Materials and Methods:** Sixty-two patients were consecutively recruited from four health centers within Sokoto metropolis over a five-year period (March 2019 to February 2023). Fifty one subjects that consented had a liver biopsy done for various indications. The tissues obtained were taken for histopathologic evaluations. **Results:** In the majority of the subjects, 39 (76.5%) the clinical indications for liver biopsy was Chronic viral Hepatitis infections (CVHI) while 7(13.7%) and 5(9.8) of the subjects had clinical indications of unexplained liver mass and fatty liver disease respectively. In all, fifty one subjects had liver biopsy. Histological outcomes were: Chronic Hepatitis 37 (72.5%), followed by HCC with 6 (11.8%), steatohepatitis 4(7.8%) then one subjects each for steatosis and secondary metastasis to the liver. Among the subjects with histological findings of Chronic Hepatitis majority of them either having mild necroinflammation 13(35.1%) or moderate necroinflammation 14(40.5%). Significant fibrosis was found in over 40% of the patients, with 2(5.6%) having histological conclusion of liver cirrhosis. The degree of inflammation and fibrosis from chronic hepatitis was not statistically significant between genders. **Conclusions:** Despite advancements made in available facilities in diagnosing liver diseases, tissue still plays a significant role. This is particularly so in regions with hyper- endemicity for CHBVI and low socio-economic standards.

Keywords: Indications, Histological, Liver biopsies, Nigeria, outcomes.

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

The liver is one of the major organs in the body that is prone to various infective, metabolic, and neoplastic insults and conditions. Common diseases affecting the liver include viral hepatitis, non-alcoholic fatty liver disease (NAFLD), liver cirrhosis, hepatocellular carcinoma, and alcoholic liver disease [1]. High prevalence of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma (HCC) have been reported in different studies from Nigeria and other parts of Africa [1]. Hepatitis B virus (HBV) infection is a major health burden of global concern with about two billion people being infected in their lifetime. More than 250 million of those previously infected have current evidence of chronic infection. This burden is more worrisome in developing nations of sub-Saharan Africa, particularly in Nigeria where HBV is hyper endemic with prevalence of more than 8%. HBV is a major cause of morbidity and mortality due to its complications of liver cirrhosis and hepatocellular cancer [2-5]. In such studies, Hepatitis B

(HBV) and Hepatitis C virus (HCV) were the two major hepatotropic viruses implicated in such conditions [6, 7].

Histological assessment of the liver through liver biopsy is a cornerstone in the evaluation and management of patients with different liver diseases and has long been considered to be an integral component for diagnosis, assessing prognosis, and tailoring treatment [8]. Even with the advent of non-invasive techniques, it's still a useful tool in the diagnosis of some cases of liver disease. There are different forms of liver biopsy techniques; percutaneous liver biopsy using a Menghini biopsy needle, the method is simple, rapid, inexpensive, though invasive but quite safe. Laparoscopic and Transjugular liver biopsy techniques yields more information than percutaneous liver biopsy especially in patients with severe coagulopathies [9].

Some of the diagnostic indications of liver biopsy were; Autoimmune hepatitis, primary sclerosing

cholangitis, primary biliary cirrhosis, hemochromatosis, Wilson's disease, overlap syndrome, multiple parenchymal liver diseases, abnormal liver tests of unknown etiology, steatohepatitis, and focal or diffuse abnormalities on imaging studies. It's also a useful tool in the staging and treatment of liver disease. In viral hepatitis liver biopsy is the gold standard to determine the degree of inflammatory activity (grading) and the extent of fibrosis (staging). In hepatitis B infection, the demonstration of a significant degree of fibrosis and/ or inflammation is an integral factor that can determine the indication for treatment [9]. There are other ways to assess the degree of liver fibrosis, such as the use of Fibroscan which is non-invasive; however, however, it is not readily available and is limited is not readily available and limited in most economically underdeveloped areas in sub- Africa [10].

AIM: To determine indications and histological outcomes of liver biopsy samples.

MATERIALS AND METHODS

The ethical approval for this study was obtained from the ethical committees of Usmanu Danfodiyo University Teaching Hospital, Caliphate Multi Specialist Hospital, Saraki Specialist Hospital, and Specialist Hospital Sokoto. The rules guiding human experiments as adopted by the Helsinki declaration was followed throughout the study. The study was a descriptive prospective. Sixty-two patients were consecutively recruited from March 2019 to February 2023. The study population included all adult patients from the four centers with clinical indications for liver biopsy [3]. The subjects that were excluded were; patients that did not consent, or had prothrombin time > 3 seconds, and those with platelet count < 100, 000.

Fifty-one subjects that consented to the procedure and had no other exclusion criteria and contraindications to liver biopsy had percutaneous liver biopsy using a suction menghini biopsy needle after obtaining information such as indication for the procedure and socio-demographic characteristics of each subject. The procedure was done under an aseptic condition with the patient in a supine position after infiltrating the area with plain xylocaine. Menghini needle capped to a 20ml syringe containing 5mls of normal saline was used to obtain the samples. No more than two passes were made to obtain an adequate sample size of at least 1.5cm long. The biopsy tissue was placed in a tissue bottle containing formalin labeled for transport to the histology laboratory. Each patient was observed for six hours with monitoring of vital signs before discharged. No complication was observed in any of the biopsied subjects. The tissues obtained were stained with haematoxylin, eosin and then trichrome stain to demonstrate evidence of liver pathology. Metavir staging system was used for subjects with chronic hepatitis [11].

For this study, the degree of inflammation in Chronic Hepatitis (CH) Subjects were graded as; A0 = No inflammation, A1= Mild necro-inflammation, A2= moderate necro-inflammation, A3= Severe necro-inflammation. While degree of fibrosis was graded as; F0 = No Fibrosis, F1= Portal fibrosis without septa, F2= Portal fibrosis with few septa, F3= Bridging Fibrosis, F4=Cirrhosis. F0 and F1 was termed as non-significant fibrosis while F2 and F3 was termed as significant Fibrosis [12, 13].

Statistical data analysis

Data obtained was imputed into a computer and analyzed using IBM's Statistical Package for Social Sciences software version 25. Categorical data were summarized as frequencies, proportions, and percentages while continuous data were presented as means \pm standard deviation.

Ethical consideration

Approval was obtained from the Research and Ethics Committee from the centers where the study was conducted.

RESULTS

The ages of respondents ranged between 20 and 63 with a mean of 34.12 ± 11.11 years. The dominant age group that had the liver biopsy during the study was 20-29-year which constituted more than forty percent 22 (43.1%) of the respondents. More than two-thirds 38 (54.9%) of the respondents were male and almost all respondents 48 (94%) were seen at Usmanu Danfodiyo University Teaching Hospital as seen in Table 1.

In the majority of the respondents, 39 (76.5%) the clinical indication for liver biopsy was CVHI. However, 7 (13.7%) and 5 (9.8) of the respondents had clinical indications of unexplained liver mass and fatty liver disease respectively. The results are displayed in Figure 1.

The commonest overall histological outcome of the biopsied subjects was CH which was found in more than two-thirds of the subjects 37 (72.5%), followed by HCC with 6 (11.8%), steatohepatitis 4(7.8%) then one subjects each for steatosis and secondary metastasis to the liver. However, the outcome of the remaining two results could not be concluded histologically, Table 2.

Among the subjects with histological findings of CH, majority of them either had mild necroinflammation 13(35.1%) or moderate necroinflammation 14(40.5%) while significant fibrosis (F1 and F2) was found in over 40% of the patients. In addition, 2(5.6%) had histological conclusion of liver cirrhosis (Table 2 and 3). Even though the degree of inflammation from CH was higher among the male subjects, the results were not statistically significant

(p=0.053). Similarly, the degree of fibrosis did not show any statistical difference among male and female gender (p=0.325). (Table 4 and 5).

Table 1: Sociodemographic characteristics of the respondents

Variables	Frequency (n = 51)	Percent (%)
Age group (in years)		
20 – 29	22	43.1
30 – 39	16	31.4
40 – 49	5	9.8
≥ 50	8	15.7
Gender		
Male	38	54.9
Female	23	45.1
Hospital		
UDUTH	48	94.0
SHS	1	2.0
CMSH	1	2.0
SSH	1	2.0
Mean age of the respondents = 34.12 ±11.11		
UDUTH = Usmanu Danfodiyo University Teaching Hospital, SHS = Specialist Hospital Sokoto, CMSH= Caliphate Multi Specialist Hospital, SSS =Saraki Specialist Hospital		

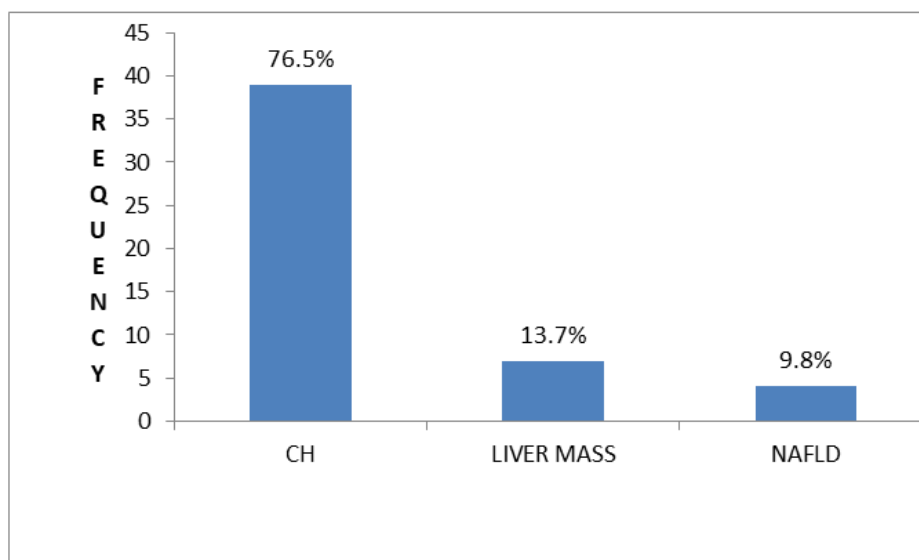


Figure 1: Indications for Liver Biopsy

CH = Chronic Viral Hepatitis NAFLD =Non-Alcoholic Fatty Liver Disease

Table 2: Histological outcome of the Liver biopsy

Findings	Frequency (n = 51)	Percent (%)
Chronic Hepatitis	37	72.5
HCC	6	11.8
Steatohepatitis	4	7.8
Steatosis	1	2.0
MLD	1	2.0
Inconclusive	2	3.9

HCC=Hepatocellular Carcinoma, MLD = Metastatic Liver Disease

Table 3: Degree of Inflammation among Subject with Chronic Hepatitis

Findings	Frequency (n = 37)	Percent (%)
A0	5	13.5
A1	13	35.1
A2	15	40.5
A3	4	10.8

A0 = No inflammation, A1= Mild necroinflammation, A2= moderate necroinflammation, A3= Severe necroinflammation.

Table 4: Degree of Fibrosis among Subject with Chronic Hepatitis

Findings	Frequency (n = 37)	Percent (%)
F0	9	24.3
F1	13	27.0
F2	15	21.6
F3	4	21.6
F4	2	5.4

F0 = No Fibrosis, F1= Portal fibrosis without septa, F2= Portal fibrosis with few septa, F3= Bridging Fibrosis, F4=Cirrhosis

Table 5: CrossTabulation between Gender and Degree of Inflammation in Chronic Hepatitis

Variables	A0 (n=37) n (%)	A1 (n=37) n (%)	A2(n=37) n (%)	A3(n=37) n (%)	P value Test –statistics
Male	0 (0)	7 (35)	10 (50)	3 (15)	P=0.053
Female	5 (29.4)	6 (35.3)	5 (29.4)	1(5.9)	

Table 6: Cross Tabulation between Gender and Degree of Fibrosis in Chronic Hepatitis

Variables	F0(n=37) n(%)	F1(n=37) n(%)	F2(n=37) n(%)	F3(n=37) n(%)	F4(n=37) n(%)	P value Test –statistics
Male	3 (15.0)	5 (25.0)	6 (30.0)	4 (20.0)	2 (10.0)	P= 0.325
Female	6 (35.3)	5 (29.4)	2 (11.8)	4(23.5)	0 (0)	

DISCUSSION

The mean age of the study participants was 34.12±11.11 with male to female ratio of 1.7: These findings were similar to the study on histopathological patterns of liver biopsies by Ugiagbe and colleagues at a tertiary institution in Nigeria where the subjects that had liver biopsy assessment were predominately male [1], however, the 4th decade was her dominant subjects in contrast to our findings where a significant number were in the 3rd decade. Another study in the same country by Ola *et al.*, on the Spectrum of histological diagnoses among clinically suspected HCC also shows a higher male preponderance [14].

Three provisional diagnoses were found in the study as indications for liver biopsy, the commonest being CVH, liver mass, and NAFLD. The mentioned conditions were among the most common diseases that liver biopsy still helps either for diagnosis, prognosis, and staging or in the treatment [9]. The finding of CVH as the main indication is of no surprise as it's the most prevalent cause of liver disease in sub-Saharan Africa [15].

Chronic Hepatitis was the main indication for liver biopsy in over 70% of the subjects primarily due to the high prevalence of the virus in the region and its

potential to cause acute and chronic liver complications. While Hepatocellular carcinoma was the second most common in the study (11.8%) also a chronic sequelae of CHVI. Similarly, studies have shown that the northwestern geopolitical zone of the country where our study area is located has the highest prevalence of CHB infection in the country [16].

A study in a tertiary institution in North-western Nigeria on histopathological findings in liver biopsies and clinical correlation over two years periods also corroborates with our finding even though the study demonstrated a higher prevalence of HCC of 27% compared to our study [17]. This could be due to less number of patients that had liver biopsy during the period as compared to the previous study. It is a recognized fact that there are several non-invasive, cheap and readily available tools with high specificity for the diagnosis of HCC that can serve as alternatives for the diagnosis and surveillance of HCC. HCC as the main finding of the biopsied liver masses in our study was also observed in the study by Adenji and colleagues on the pattern of the malignant tumors of the liver where two-thirds of his patients with liver masses had HCC [18]. HCC is the highest reported liver cancer in Africa with HBV, HCV, aflatoxin-contaminated foods, heavy alcohol consumption, obesity, type 2 diabetes, and smoking as

identifiable risk factor [19]. Non-alcoholic fatty liver disease has been suggested to be associated with metabolic syndrome and has been described as a hepatic component of metabolic syndrome [20]. It is a spectrum of diseases of the liver ranging from steatosis to non-alcoholic steatohepatitis (NASH) and cirrhosis [20]. Majority of individuals with NAFLD are asymptomatic and are typically diagnosed through a combination of medical history, physical examinations, imaging and with liver biopsy being the gold standard, thus a diagnosis of exclusion. The index study revealed the lowest percentage of subjects with hepatic steatosis or steatohepatitis as their histological outcome. This finding could be as a result of a low number of cases with fatty liver disease identified as their clinical indication for liver biopsy coupled with the limited available information which suggests that the prevalence of NAFLD in the general population is lowest in the Africa region hindering identifying subjects with such disease condition [21]. One of the primary reasons for the perceived low prevalence of NAFLD in sub-Saharan Africa faces a high burden of neglected tropical diseases and other infectious diseases, which may overshadow the recognition and diagnosis of NAFLD.

Among the thirty-seven subjects with the histological outcome of chronic hepatitis, the majority of them either had mild or moderate necro-inflammation while over 40% had significant fibrosis, with about 5% of them with histologic findings of liver cirrhosis, however, the results were not statistically significant between males and females. A study by Musa *et al.*, on Hepatic fibrosis among chronic hepatitis B virus-infected patients in North-Western Nigeria experience, where sixty-eight patients had liver biopsies revealed that 61.7% had histologic evidence of necroinflammation, with 22% exhibiting significant inflammation, while 46.5% of them had significant fibrosis [22]. These were in keeping with another study in the same region where out of seventy cases of CHBI that had a liver biopsy over half of the symptomatic individuals among them showed a significant degree of inflammation and fibrosis [23]. These findings highlighted the burden of chronic hepatitis especially B and C and its complications including cirrhosis and HCC in Nigeria and Africa including the index study area [24, 25].

CONCLUSION

Our study indicates CHBV infection as the commonest indication for liver biopsy and HCC among patients with liver masses. It also demonstrates that chronic hepatitis is the most prevalent disease outcome on liver biopsy due to the high burden of HBV and HCV infections in our environment. Significant necro inflammation and fibrosis among chronic hepatitis subjects may prompt early commencement of antiviral initiation and monitoring, evaluation of treatment response and potential adjustment and surveillance

further reducing or retarding progression of the disease to unwanted chronic sequelae like cirrhosis and HCC. Therefore, clinicians are encouraged to consider liver biopsy in any patient with a clear indication without compelling contraindications.

LIMITATION

The two inconclusive liver tissue histology may probably affect the overall result though not significantly as there are a large number of samples that have clear histological outcomes.

REFERENCES

1. Ugiagbe, E. E., & Udoh, M. O. (2013). The histopathological pattern of liver biopsies at the University of Benin Teaching Hospital. *Nigerian journal of clinical practice*, 16(4), 526-529.
2. European Association for the Study of the Liver. (2017). Clinical Practice Guidelines on the management of hepatitis B Virus Infection. *J Hepatol*, 64(2), 370-398.
3. WHO. Global hepatitis report [Internet]. 2017. Available from: www.who.int
4. Makvandi, M. (2016). Update on occult hepatitis B virus infection. *World journal of gastroenterology*, 22(39), 8720-8734.
5. Igetei, R., Awobusuyi, J. O., Wright, O. K., & Olaleye, D. O. (2015). Occult hepatitis B virus infection in Nigerian patients on haemodialysis. *Tropical Journal of Nephrology*, 10(2), 79-86.
6. Takano, S., Yokosuka, O., Imazeki, F., Tagawa, M., & Omata, M. (1995). Incidence of hepatocellular carcinoma in chronic hepatitis B and C: a prospective study of 251 patients. *Hepatology*, 21(3), 650-655.
7. Ojo, O. S., Olude, I. O., & Odesanmi, W. O. (1990). The pathological basis of chronic liver diseases in a tropical population—a biopsy study. *Orient J Med*, 2, 190-193.
8. Rockey, D. C., Caldwell, S. H., Goodman, Z. D., Nelson, R. C., & Smith, A. D. (2009). American association for the study of liver D. *Liver biopsy*. *Hepatology*, 49(3), 1017-44.
9. Tannapfel, A., Dienes, H. P., & Lohse, A. W. (2012). The indications for liver biopsy. *Deutsches Ärzteblatt International*, 109(27-28), 477-483.
10. Liu, C., Wang, L., Xie, H., Zhang, L., Wang, B., Luo, C., ... & Xie, Y. (2018). The relationship between serum hepatitis B virus DNA level and liver histology in patients with chronic HBV infection. *PloS one*, 13(11), e0206060.
11. Mohamadnejad, M., Tavangar, S. M., Sotoudeh, M., Kosari, F., Khosravi, M., Geramizadeh, B., ... & Malekzadeh, R. (2010). Histopathological study of chronic hepatitis B: a comparative study of Ishak and METAVIR scoring systems. *International journal of organ transplantation medicine*, 1(4), 171.

12. Sebastiani, G. (2009). Non-invasive assessment of liver fibrosis in chronic liver diseases: implementation in clinical practice and decisional algorithms. *World journal of gastroenterology: WJG*, 15(18), 2190.
13. Jeanu, C. F., Ungureanu, B. S., Săndulescu, D. L., Gheonea, I. A., Tudorașcu, D. R., Ciurea, M. E., & Purcărea, V. L. (2015). Quantification of liver fibrosis in chronic hepatitis B virus infection. *Journal of medicine and life*, 8(3), 285.
14. Mashor, M. I., Oluwasola, A. O., & Ola, S. O. (2020). Spectrum of histological diagnoses among clinically suspected PLCC patients in a Nigerian teaching hospital. *Nigerian Journal of Gastroenterology and Hepatology*, 12(2), 50-55.
15. Organization WH. Global hepatitis report 2017: World Health Organization; 2017.
16. Ajuwon, B. I., Yujuico, I., Roper, K., Richardson, A., Sheel, M., & Lidbury, B. A. (2021). Hepatitis B virus infection in Nigeria; a systematic review and meta-analysis of data. *BMC Infect Dis*, 21(1), 1120. doi:10.1186/s12879-021-06800-6;PMCID:PM8556927
17. Samaila, A. A., Mohammed, A. Z., Borodo, M. M., & Tijjani, B. M. (2008). Histopathological findings in liver biopsies and clinical correlation at Kano, Nigeria. *Sahel Medical Journal*, 11(1), 20-23.
18. Adeniji, K. A., & Anjorin, A. S. (2004). The pattern of malignant tumours of the liver in a tertiary health institution in Nigeria. *African Journal of Medicine and Medical Sciences*, 33(1), 27-30.
19. El-Kassas, M., & Elbadry, M. (2022). Hepatocellular carcinoma in Africa: challenges and opportunities. *Frontiers in Medicine*, 9, 899420.
20. Zarean, E., Goujani, R., Rahimian, G., & Ahamdi, A. (2019). Prevalence and risk factors of non-alcoholic fatty liver disease in southwest Iran: a population-based case-control study. *Clinical and experimental hepatology*, 5(3), 224-231.
21. Paruk, I. M., Pirie, F. J., & Motala, A. A. (2019). Non-alcoholic fatty liver disease in Africa: a hidden danger. *Global health, epidemiology and genomics*, 4, e3.
22. Musa, Y., Abdulkadir, Y. M., Ibrahim, Y., Maiyaki, A. S., Yakubu, A., Ijeoma, I. M., ... & Muhammad, M. B. (2024). Hepatic fibrosis among chronic hepatitis B virus-infected patients: North-Western Nigeria experience. *Nigerian Journal of Gastroenterology and Hepatology*, 16(1), 8-14.
23. Ndububa, D. A., Ojo, O. S., Adetiloye, V. A., Durosinmi, M. A., Olasode, B. J., Famurewa, O. C., ... & Adekanle, O. A. (2005). Chronic hepatitis in Nigerian patients: a study of 70 biopsy-proven cases. *West African Journal of Medicine*, 24(2), 107-111.
24. Laraba, A., Wadzali, G., Sunday, B., Abdulfatai, O., & Fatai, S. (2010). Hepatitis C virus infection in Nigerians with chronic liver disease. *The Internet Journal of Gastroenterology*, 9(1), 1528-8323.
25. Ali, A., Ikani, O., Onyekwelu, K., Obi, O., & Ogbonna, E. (2020). Epidemiology of chronic liver disease in Nigeria: a review. *Asian Journal of Advances in Medical Science*, 2(1), 63-68.