CLINICAL AND LABORATORY PROFILE OF CHRONIC LIVER DISEASE PATIENTS IN A TERTIARY HOSPITAL IN CALABAR, NIGERIA

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ABSTRACT

Background: Chronic Liver Disease (CLD) is a medical condition commonly seen in gastroenterology practice in Nigeria. Thorough evaluation of CLD patients can be expensive; often times being unaffordable for patients and also taking a toll on existing limited health resources. Despite this, the relevant and prompt assessment of CLD patients can significantly reduce the high morbidity and mortality rates associated with this condition.

Objectives: This study aimed to demonstrate the clinical and laboratory patterns of patients with chronic hepatitis (CH), liver cirrhosis (LC) and primary liver cell carcinoma (PLCC).

Methods: This was a cross-sectional descriptive study involving consecutive CLD patients referred to the Gastroenterology unit of the University of Calabar Teaching Hospital. One hundred and six (106) patients were recruited over a 9 month period. These included CLD patients who met the eligibility criteria for CH, LC and PLCC.

Results: Thirty eight (38) patients had findings suggestive of CH, while 36 and 32 had features of PLCC and LC respectively. The predominant symptoms and signs seen among the CLD patients were fatigue (88.9%) and leg swelling (68.8%) in PLCC and LC patients respectively. While hepatomegaly (83.3%) and ascites (71.9%) where reported mostly in PLCC and LC patients respectively. Elevations in gamma-glutamyl transpeptidase (γ-GT) and alkaline phosphatase (ALP) was found to be more deranged in PLCC patients when compared to the other CLD categories and this was statistically significant (<0.005). However, an abnormal international normalized ratio and low platelet count was mostly found in LC patients and this too was statistically significant ($p<0.005$).

Conclusion: This study demonstrated that most of the CLD patients had symptoms and signs suggestive of decompensated liver disease, further manifested by deranged laboratory parameters such as the presence of coagulopathy mostly among LC patients and cholestasis in PLCC patients.

Keywords: Calabar, Chronic hepatitis, Liver cirrhosis, Primary liver cell carcinoma.

INTRODUCTION

The Liver is the largest solid organ of the body weighing an average of 1 to 1.5kg and represents 1.5 to 2.5% of the lean body mass [1]. The cells of the liver perform several important roles in maintaining homeostasis and health. These functions can be broadly grouped as synthetic, excretory and storage [1]. Injury to the liver as a consequence of infections, drugs, toxins etc can result in typical clinical and biochemical manifestations of acute or chronic liver disease.

Loss of hepatocyte mass results in impairment of the biosynthetic functions of the liver [1]. Liver disease (irrespective of its aetiolgy) lasting for at least six months is otherwise referred to as CLD. Patients with CLD may initially be asymptomatic eventually having overt features as a result of pathologic changes (e.g. fibrosis) which reflect the extent of damage to the liver [2]. Loss of hepatocyte function results in jaundice, bleeding diathesis from coagulopathy and fluid retention arising from hypoalbuminemia [2]. Furthermore ascites and bleeding from oesophageal varices (presenting as hematemesis and passage of melaena or bloody stools) arising from portal hypertension are major complications that signify decompensated liver cirrhosis [2].

Certain laboratory tests are quite useful in evaluating the synthetic functions of the liver and assessment of hepatocellular damage [1]. Measurement of the serum albumin concentration and prothrombin time provides a quantitative assessment of functional impairment of the liver [1,3]. The liver transaminases (aspartate amino transferase - AST, alanine amino transferase- ALT) on the other hand are useful screening tools to evaluate underlying hepatocellular damage (especially following acute injury)[3]. There is no singular test that accurately assesses the liver's total functional capacity [1]. Hence a combination of these investigations increases both the sensitivity and the specificity in the detection of liver disease [1]. Serum bilirubin, aminotransferases, alkaline phosphatase, albumin, and prothrombin time tests are routinely carried out when investigating liver disease. A persistent or serial abnormal finding in one or more of these tests raises the probability of liver disease [1]. The role of ultrasonograghy cannot be over- emphasized, as it is non-invasive, cheap, and widely available and provides useful information about the liver parenchyma, biliary tree and vasculature. Certain features like a diffuse increase in liver echogenicity may suggest chronic hepatitis, while masses found in hepatocellular carcinoma may show variable echogenicity (i.e. hyperechoiec or hypoehoiec) with or without features of cirrhosis (increased liver echogenicity and or surface nodularity) [4]. Histological assessment of the liver via liver biopsy is the cornerstone in the assessment and management of patients with liver disease [5]. Information regarding the typical histological findings of necro-inflammation (portal or lobular), hepatocyte necrosis and fibrosis can be obtained. Features that may suggest viral hepatitis may also be seen in autoimmune hepatitis, α_1 anti-trypsin deficiency, drug induced hepatitis and chronic biliary disorders [5]. Comprehensive evaluation of necro-inflammatory activity is based on current semi-quantitative scoring systems e.g. Knodell - Ishak , metavir score etc [3]. The Knodell - Ishak score for instance gives a histological activity index (HAI) that reflects the distribution and severity of inflammation and the presence or absence of fibrosis, it is widely used in evaluating patients with chronic hepatitis B [1,5]. A combination of clinical, biochemical, radiological and histological findings can broadly group CLD patients as either having CH, LC or PLCC (which is a major objective of this study).

MATERIALS AND METHODS

Study design: This was a cross-sectional descriptive study involving patients with chronic liver disease seen at the Gastroenterology Unit of the University of Calabar Teaching Hospital (UCTH).

Eligibility criteria: These patients were aged 18 years and above. The diagnosis of chronic liver disease was made based on typical clinical, biochemical, histological and radiologic features of chronic liver disease.

Sample size estimation: Sample size was calculated using the Leslie and Kish formula as follows:

$$N = z^2pq \div d^2$$

Where: N= the desired sample size (when population is greater than 10,000)

z= the standard deviation usually set at 1.96, corresponds to 95% confidence interval.

p= the proportion in the target population estimated to have a population characteristic i.e. 4.2% by Ansa *et al* [6].

To account for 10% non-response (attrition), the estimated minimal sample size was 106.

Sampling methods: Consecutive CLD patients seen in the gastroenterology unit were recruited into the study.

Data collection: All patients were evaluated using a semi-structured interviewer, administered questionnaire which sought features suggestive of chronic liver disease (jaundice, fatigue and abdominal swelling, finger clubbing, leuconychia, wasting of the thenar/ hypothenar eminences, palmer erythema, superficial distended abdominal veins). Also the presence of hepatomegaly that is firm or hard, nodular, tender or non-tender with a blunt edge or a shrunken liver was sought. Blood samples were taken for transaminase assay, total protein/albumin estimation and quantification of L-γ- glutamyltransferase (γ-GT). Heamatologic work up was done, for full blood count estimation and prothrombin time test (PT) or international normalized ratio (INR). Laboratory investigations suggestive of chronic liver disease include; Prothrombin time > 3seconds or International normalized ratio > 1.2. Normal or elevated aspartate and alanine aminotransaminase (i.e. AST and ALT $\geq$ 40U/L).Elevated alkaline phosphatase > 92 U/L, raised serum bilirubin > 17µmol/l , reduced albumin< 36g/l. Elevated gamma-glutamyl transpeptidase >50 U/L and 32 U/L in men and women respectively. Radiologic features suggestive of chronic hepatitis were the presence of any of these features; diffuse increase in liver echogenicity, coarsening of hepatic echotexture, silhouetting / loss of definition of portal venules (resulting in decreased visualization of the walls of the peripheral portal veins). In Primary Liver Cell Carcinoma (PLCC) the following were suggestive; mass lesions with variable echogenicity- hyperechoic / hypoechoic (due to marked dilatation of sinusoids and solid tumours respectively). PLCC of mixed echogenicity (due to non-liquefactive tumour necrosis) and in rare cases calcifications may be seen. In cirrhosis, suggestive features include; increased liver echogenicity, surface nodularity, heterogenous coarse (usually) / fine echotexture and dilatation of hepatic arteries.

In patients who met the criteria for liver biopsy for histopathologic examination, the histologic features suggestive of chronic hepatitis range from inflammation limited to portal tracts (consisting of lymphocytes, macrophages, occasional plasma cells, and rarely neutrophils or eosinophils). Smoldering hepatocyte apoptosis throughout the lobule may be seen and this may occur in all forms of chronic hepatitis. Other findings include; lymphoid aggregates, bile duct reactive changes in the portal tracts, and focal mild to moderate macrovesicular steatosis. The presence of ground glass cells (usually seen in biopsies that contain little necro-inflammatory activity) are typically seen in chronic HBV infection. In all forms of chronic hepatitis, continued interface hepatitis and bridging necrosis between portal tracts and portal tracts-to-terminal hepatic veins, herald progression of liver damage .The main characteristic of chronic liver damage is the deposition of fibrous tissue (cirrhosis) . At first, only portal tracts show increased fibrosis, but with time periportal septal fibrosis occurs, followed by linking of fibrous septa (bridging fibrosis), especially between portal tracts . The Knodell – Ishak score was used to grade inflammation and hepatocyte destruction and also the severity of fibrosis (stage).

Ethical issues: Ethical clearance for this study was obtained from the Health Research Ethics committee of UCTH, assigned number; UCTH/HREC/33/92.

Statistical analysis: Data collected was sorted out manually and then entered into the Predictive Analytics Software (PASW) version 18 IBM New York USA and subsequently analyzed. Frequency tables and bar charts were used for descriptive statistics. Categorical variables were compared using the Chi-square tests, while ANOVA was used to analyze the differences among group means. A p-value of $\leq$0.05 was considered statistically significant.

RESULTS

Diagnosis of the CLD sub-types: The diagnosis of the sub-types of CLD was made in 91 (85.8%) of the cases based on a combination of clinical, biochemical and liver ultrasound scan findings while in the remaining 15 cases (14.25%), the diagnosis was based on the above parameters and characteristic histological findings (table 1)

There were 38 cases of chronic hepatitis 28 of which were diagnosed based on a combination of clinical, biochemical and radiologic features, while the remaining 10 (26.3%) had additional histological features. The predominant radiologic feature among chronic hepatitis patients was the presence of a uniformly increased echogenic, normal or enlarged

Table 1: Summary of the diagnosis of the CLD sub-types

CLD sub-types	Diagnostic criteria
Chronic hepatitis (38)	
28	Clinical + Biochemical + Radiological
10	Clinical + Biochemical + Radiological + Histological
Liver cirrhosis (32)	
28	Clinical + Biochemical + Radiological
4	Clinical + Biochemical + Radiological + Histological
PLCC (36)	
35	Clinical + Biochemical + Radiological
1	Clinical + Biochemical + Radiological + Histological

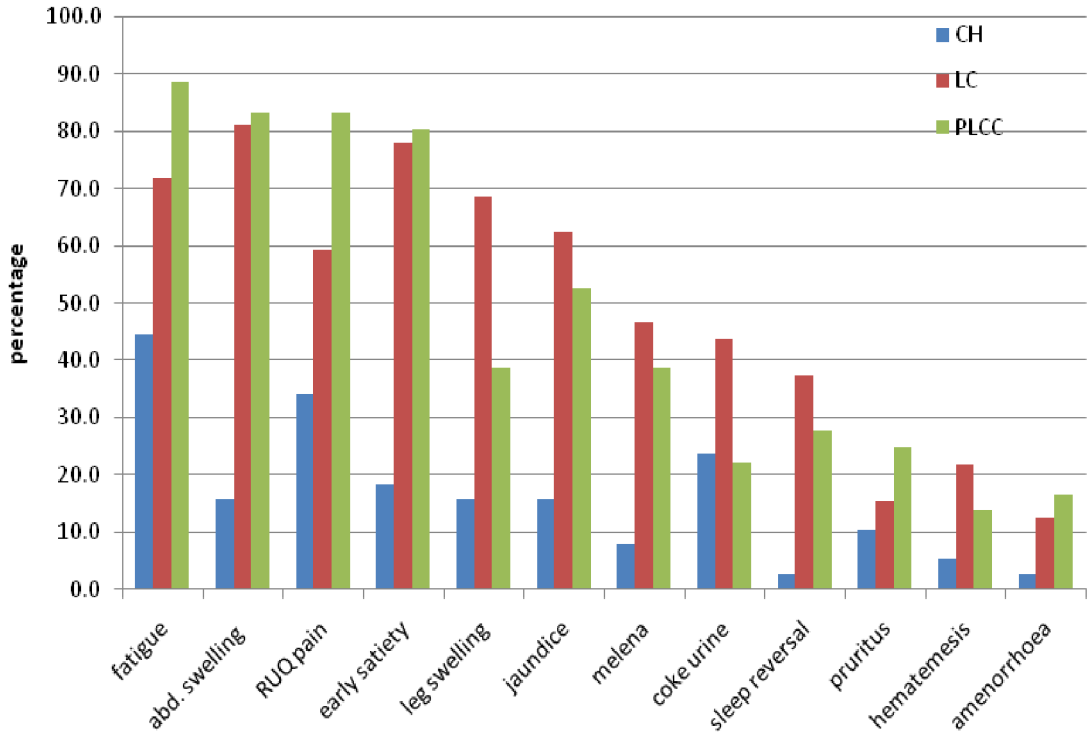

Fig. 1: Clustered bar chart showing the distribution of symptoms among the different sub-types of CLD

liver. Among the 10 chronic hepatitis patients with abnormal histology, the common histological feature was moderate necro- inflammation and fibrosis (stage $^{2}/_{6}$ and grade $^{2}/_{4}$) based on the Knodell-Ishak score. Thirty two of the CLD patients had liver cirrhosis, 28 (87.5%) of which were diagnosed based on a combination of clinical, biochemical and ultrasound features, while the remaining 4 (12.5%) had histological evidence in addition. The typical ultrasound findings were increased liver echogenicity, surface nodularity and a coarse/ fine heterogenous echotexture. Portal hypertension evident by ascites, splenomegaly with or without dilatation of the portal vein was also seen. The typical histological findings in these individuals were the presence of advanced fibrosis and necroinflammation (Knodell- Ishak grade $^{4}/_{6}$ and stage $^{4}/_{4}$).

Thirty six (37.5%) of the CLD patients had PLCC. The presence of hypo/ hyper echoic masses or mixed echogenic masses in the background of an

irregular liver outline (with a few of these masses showing calcifications evident by the presence of an echogenic lesion with a posterior acoustic shadowing). Only one (2.8%) of the PLCC patients had liver biopsy done and the histopathological finding was of a well differentiated variant of PLCC (trabecular pseudoglandular pattern).

Symptoms among the sub-types of CLD: Among the PLCC patients the main symptoms were; fatigue (88.9%), abdominal swelling (83.3%), right upper quadrant pain (83.3%) and early satiety (80.6%). Other symptoms were generalized pruritus (25%) and amenorrhoea (16.7%). Leg swelling (68.8%), jaundice (62.5%), melaena (46.9 %) and haematemesis (21.9%) were the most common complaints among liver cirrhosis patients. Whereas in chronic hepatitis patients; fatigue (44.7%), right upper quadrant pain (34.2%) and passage of coke colored urine (23.7%) were the most predominant complaints (figure1).

Signs among the sub-types of CLD: In patients with PLCC, the most common signs included; hepatomegaly (83.3%) and wasting of the thenar and hypothenar eminences (66.7%). On the other hand ascites (71.9%) and pedal edema (53.1%) were the most common signs elicited among liver cirrhosis patients. The peripheral stigmata of CLD were seen more in PLCC patients and the signs observed were wasting of the thenar and hypothenar eminences (66.7%), distended superficial abdominal veins (52.8%), finger clubbing (27.8%), leukonychia (5.6%), fluffy hair (16.7%) and gynaecomastia / loss of secondary hair (13.9%).

Among patients with chronic hepatitis, hepatomegaly (21.1%), finger clubbing (18.4 %), wasting of the thenar and hypothenar eminences (15.8%) and jaundice (13.2%) were the leading signs.

Biochemical parameters among the Sub-types of CLD: The mean value for AST (92.9, SD ± 34.9 U/L), ALP (173.7, SD ±140.4U/L), GGT (396.9, SD ± 373.9 U/L) and albumin (33.2, SD ± 7.9 g/dl) were significantly associated ($p < 0.05$) with PLCC patients when compared with the mean values from the other sub-types of CLD (table 2).

Among the CLD sub-groups hyperbilirubinaemia was seen mostly in the PLCC cases 23 (63.9%), though it was not statistically significant.

Table 2: Comparison of mean values of the biochemical parameters among the sub- types of CLD

Variable	Chronic hepatitis N = 38	Liver cirrhosis N = 32	PLCC N = 36	F - test	p - value
	Mean ±SD *Range*	Mean ± SD *Range*	Mean ± SD *Range*		
Total bilirubin (µmol / l)	25.5 ± 16.4 *8.6-205.2*	46.2± 52.3 *8.6-246*	47.1± 49.3 *8.6-199.9*	2.609	0.078
AST (U / L)	19.3 ± *28.712-125*	75.3± 36.1*15-125*	92.9± 34.9*28.1-125*	**16.219**	**0.001**
ALT (U / L)	40±29.5*8-125*	56.1± 30.6*4-124*	60.8± 35.6*11.7-125*	3.686	0.028
ALP (U / L)	57.3± 30.8*20-164*	88.1± 6.9*27-232*	173.7± 140.*429-645*	**17.123**	**0.001**
γ-GT **(U / L)**	112.7± 153.*316.5-669.8*	138.3± 106.*218-347*	396.9± 373.9*20.4-1285*	**13.100**	**0.001**
Albumin (g / dl)	38. 9± 6.59*24-56*	33.9± 6.9*18-48*	33.2± 7.9*14-55*	**7.235**	**0.001**

AST / ALT ratio greater than 2 was found in 10 (27.8%) of the PLCC cases, though a majority 15 (41.7%) of them had a ratio greater than 1, this however was not statistically significant ($p = 0.704$) (table 3).

Gamma glutamyl transpeptidase elevation greater than 1 x ($\geq$ 50 U/L) and$\geq$ 2 x ($\geq$ 100 U/L) ULN was found in 3 (12%) and 20 (80%) of PLCC cases respectively, while ALP elevations above $1^1/_2$ and 2 x ULN occurred in 13 (36.1%) and 11 (30.6%) respectively in this category of patients. In both instances these results were found to be statistically significant ($p < 0.05$). Hypoalbuminaemia was found

Table3: Comparison of the biochemical parameters among the CLD sub-types

Variable Total bilirubin (µmol/l)	Chronic hepatitis N = 38 (100%)	Liver Cirrhosis N = 32 (100%)	PLCC N = 36 (100%)	Chi-square tests	p-value
≤ 17	23 (60.5)	12 (37.5)	13 (36.1)	5.568	0.062
≥ 17	15 (39.5)	20 (62.5)	23 (63.9)		
AST (U/L)					
≤ 40	18 (47.4)	5 (15.6)	2 (5.6)	**29.973***	**0.001***
40-60	9 (23.7)	11 (34.4)	9 (25.0)		
$1^1/_2$ x ULN	8 (21.1)	5 (15.6)	5 (13.9)		
2 x ULN	3 (7.9)	11 (34.4)	20 (55.6)		
AST / ALT ratio					
< 1	15 (39.5)	11 (34.4)	11 (30.6)	2.172	0.704
1-2	17 (44.7)	12 (37.5)	15 (41.7)		
> 2	6 (15.8)	9 (28.1)	10 (27.8)		
ALT (U/L)					
≤ 40	22 (57.9)	11 (34.4)	10 (27.8)	8.986*	0.169*
40-60	8 (21.1)	9 (28.1)	12 (33.3)		
$1^1/_2$ x ULN	4 (10.5)	3 (9.4)	5 (13.9)		
2 x ULN	4 (10.5)	9 (28.1)	9 (25.0)		
ALP (U/L)					
22- 92	33 (86.8)	22 (68.8)	12 (33.3)	**27.391***	**0.001***
$1^1/_2$ x ULN	5 (13.2)	8 (25.0)	13 (36.1)		
2 x ULN	0 (0)	2 (6.3)	11 (30.6)		
γ-GT **(U/L)**					
7-50	14 (41.2)	7 (22.6)	2 (8.0)	**15.389***	**0.003***
1 x ULN	10 (29.4)	8 (25.8)	3 (12.0)		
2 x ULN	10 (29.4)	16 (51.6)	20 (80.0)		
Albumin (g/l)					
≤ 36	9 (23.7)	15 (46.9)	21 (58.3)	**9.452**	**0.009**
≥ 36	29 (76.3)	17 (53.1)	15 (41.7)		

**Fisher's exact was used where counts are less than 5 in any cell*

Table 4: Comparison of mean values of the heamatological parameters among the different sub-types of CLD

Variable	Chronic hepatitis N = 38 Mean ± SD *Range*	Liver cirrhosis N=32 Mean ± SD *Range*	PLCC N = 36 Mean ± SD *Range*	F- test	p-value
MCH (pg)	30.4± 8.8*23.7-79.0*	28.6± 3.7*18.7-35.7*	27.2± 4.0*18.4-35.0*	2.587	0.80
MCV (fl)	85.5± 8.982.6-88.4	86.51±10.0782.9-90.1	81.75±12.877.4-86.1	1.911	0.153
MCHC (g/dl)	34.3± 8.7*24.5-84.5*	31.6± 2.9*22.8-36.9*	32.1± 3.0*18-36.2*	2.233	0.112
INR	1.58± 0.50*1.41-1.74*	1.88± 0.33*1.75-1.99*	1.63± 0.49*1.47-1.80*	**11.322**	**0.001**
PCV (%)	38.7± 7.57*10.7-50.2*	31.8± 7.26*14.8-41*	29.2± 7.99*.3-43*	**14.509**	**0.001**
Platelet count x 10^9/L	204.7± 127.9*50-788*	150.5± 95.6*18-380*	267.3± 168.4*78-852*	**6.366**	**0.002**

mostly (21, 58.3%) in the PLCC cases but this finding was not statistically significant, p= 0.009 (table 3).

Haematologic parameters among the Sub- types of CLD: The mean INR among liver cirrhosis patients was 2.15, SD ± 1.19 (0.8 – 1.2), while the mean platelet count among this group was 150.5, SD ± 95.6 x 10^9/ L (18-380). These results were found to be statistically significant, p < 0.05 (table 4).

Anaemia (PCV < 30%) commonly occurred among PLCC patients (15, 41.7%) and this was statistically significant (p= 0.022), while an abnormal INR (i.e. > 1.2) was more frequent among the liver cirrhosis cases (28, 87.5%). Likewise majority of CLD patients with liver cirrhosis had thrombocytopenia (22, 68.8%) and in both instances this was statistically significant, p <0.05(table 5).

DISCUSSION

The diagnosis of CLD was based on a combination of clinical, biochemical, ultrasonographic and histological features. Chronic liver disease was broadly grouped into chronic hepatitis 38 (35.8%), primary liver cell carcinoma 36 (34%) and liver cirrhosis 32 (30.2%). Our findings in this study concurs with that of Lesi and her colleagues in Lagos (Western, Nigeria) who reported a similar frequency among CLD patients presenting with primary liver cell cancer (35%) and liver cirrhosis (29%)[7]. In South eastern Nigeria, Okonkwo *et al* reported an overall higher trend, with PLCC being the commonest (54%) presentation of CLD followed by liver cirrhosis (41%) and chronic hepatitis (5%) [8]. When compared to the above reports (i.e. Lesi and Okonkwo's work), this study found that most CLD patients presented with chronic hepatitis, probably due to the increased

Table 5: Comparison of haematologic tests among the sub-types of CLD

Variable	Chronic hepatitis N = 38 (100%)	Liver Cirrhosis N = 32 (100%)	PLCC N = 36 (100%)	Chi-square test	p-value
International normalized ratio (INR)					
0.8 - 1.2	16 (42.1)	4 (12.5)	13 (36.1)	**7.732**	**0.021**
> 1.2	22 (57.9)	28 (87.5)	23 (63.9)		
Platelet count x 10^9/L					
< 150	12 (31.6)	22 (68.8)	14 (38.9)	**10.586**	**0.001**
> 150	26 (68.4)	10 (31.2)	22 (61.1)		
PCV (%)					
< 30	5 (13.2)	10 (31.2)	15 (41.7)	**7.601**	**0.022**
> 30	33 (86.8)	22 (68.8)	21 (58.3)		
MCV (fl)					
< 96	32 (84.2)	27 (84.4)	32 (88.9)	0.488	0.813*
> 96	6 (15.8)	5 (15.6)	4 (11.1)		
MCH (pg)					
< 31	11 (28.9)	10 (31.2)	17 (47.2)	3.106	0.212
> 31	27 (71.1)	22 (68.8)	19 (52.8)		
MCHC (g/dl)					
< 36	6 (15.8)	9 (28.1)	14 (38.9)	4.977	0.083
> 36	32 (84.2)	23 (71.9)	22 (61.1)		

**Fisher's exact was used where counts are less than 5 in any cell*

awareness of the populace as regards screening for viral hepatitis as part of comprehensive medical examinations for job recruitments, ante-natal screening, and pre-marital / school admission prerequisites etc. Fatigue was a universal complain among the CLD patients, with well over three quarter (89%) of PLCC patients presenting with this symptom. Fatigue is reported to be the most frequent and classical symptom of liver disease[2].

Majority of CLD patients in this study were found to have a more advanced form of the disease; presenting with right upper quadrant pain, ascites, pedal edema, hepatomegaly, jaundice as well as splenomegaly and distended superficial veins. These signs have been found to be associated with the diagnosis of PLCC and liver cirrhosis as shown in other studies [7, 8, 9, 12].

The late presentation of patients with CLD is a common trend among Nigerian CLD patients as reflected in this study and other comparable studies [7, 8, 11]. The explanation could be that CLD being initially asymptomatic runs an indolent course with patients often times being unaware of their underlying disease. However in symptomatic patients, financial constraints and social-cultural or religious beliefs may delay early presentation or hospital referral.

Hyperbilirubinaemia was mainly seen in patients with more severe liver disease i.e. PLCC (23, 63.9%) and LC (20, 62.5%) though this was not statistically significant (p>0.05). A comparable raised serum bilirubin level was also reported in Nnewi among CLD patients with PLCC and LC [13]. The occurrence of even the slightest elevation of serum bilirubin in the presence of elevated liver enzymes should raise the suspicion of hepatocellular injury [12]. Serum bilirubin level is a useful prognostic marker in CLD (it correlates with the extent of damaged hepatocytes or bile ducts). Certain prognostic tools such as; the Child-Pugh score and Model for end-stage liver disease score incorporate the serum bilirubin level into their assessment tools [12, 14]. These scoring systems are frequently applied in clinical practice to evaluate the survival outcome of CLD patients [14]. The higher the serum bilirubin level the poorer the prognosis of the disease[12].

An AST: ALT > 1 and 2 was the most common pattern of transaminase derangement among CLD patients, especially the more advanced forms of CLD (i.e. liver cirrhosis and PLCC) which predominantly had an AST/ALT ratio > 1 though this was not statisticallysignificant (p>0.05). This is in concordance with the finding of Williams & Hoofnagle and Siddiqi *et al* who in respective studies revealed an AST/ALT ratio > 1 suggested a more advanced form of CLD (i.e. cirrhosis) [15, 16]. In the latter study, Siddiqi et al it demonstrated that an AST/ALT > 1 alone had a modest specificity (88%) in predicting cirrhosis [16].

Gamma glutamyl transpeptidase elevation (2 x ULN) was found to be mostly elevated among PLCC patients and this was statistically significant (p= 0.003). Gamma glutamyl transpeptidase elevation has a high sensitivity but low specificity in identifying hepatobilliary disease (usually obstruction) [12]. Traditionally a rise in this enzyme in the setting of alcohol abuse is a sensitive tool in identifying alcoholic liver disease [12]. Nonetheless research has suggested an association between high serum γ-GT levels and the risk of hepatocellular carcinoma [17].

Alkaline phosphatase elevations was predominantly seen among PLCC patients and this finding was statistically significant (p= 0.001). Alkaline phosphatase elevation may be non-specific but in the presence of γ-GT elevation suggests hepatobiliary disease[17]. Researchers have demonstrated that ALP elevations in PLCC can be used as an inflammatory marker especially in the setting of hepatocarcinogenesis induced by HBV [17].Although this was not an expected outcome of this study, primary liver cell carcinoma is associated with ALP rise and has been shown to correlate with poor disease outcome [17].

Hypoalbuminaemia and thrombocytopenia were findings mostly seen in patients with advanced liver disease such as liver cirrhosis and PLCC and this association was statistically significant ($p < 0.05$). Hypoalbuminaemia reflects a marked reduction in hepatic synthetic function and is a key finding in CLD [12]. However thrombocytopenia arises from several factors, including; decreased activity of thrombopoietin, splenic platelet sequestration, bone marrow suppression by chronic hepatitis C infection, and antiviral treatment with interferon-based therapy [18]. Thrombocytopenia is a useful marker of advanced liver disease (fibrosis and portal hypertension), though a correlation between a low platelet count and fibrosis was not sought among the cases in this study [18]. In one study a low platelet count had a correlation with the presence of PLCC[19].

This study showed that the finding of hypoalbuminaemia and thrombocytopenia correlate with advanced liver disease which is in keeping with a similar finding reported by Omoti and her colleagues in Benin [20].

It was also observed that most liver cirrhosis patients in this study had an abnormal INR when compared with PLCC patients and this was statistically significant ($p< 0.05$) in this category. This finding may be due to the fact that coagulopathy is almost universal in patients with cirrhosis [3]. The synthesis of vitamin K–dependent clotting factors is diminished because of a decrease in hepatic mass (from cirrhosis) [3].

In conclusion, this study demonstrated that the diagnosis of CLD requires extensive clinical and laboratory evaluation. Furthermore, it proved that no singular test can conclusively make a diagnosis of CH, LC and PLCC. The various findings of this study revealed that most CLD patients presenting to our facility had evidence of advanced liver disease i.e. PLCC and LC. Considering the dismal outcome of CLD especially in resource poor settings such as ours, the early diagnosis of CLD (via relevant tests) in at risk groups should be encouraged among clinicians practicing in our environment.

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