

Distribution and Determinants of Etiologies and Complications of Chronic Liver Diseases Among Patients at a Tertiary Hospital in a Lower Economic Region of Ghana

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Abstract: There is dearth of data on the epidemiology of chronic liver diseases (CLDs) in northern Ghana. To this extent, we intended to investigate the distribution and determinants of the etiologies and complications of CLDs at the Tamale Teaching Hospital, a referral hospital of northern Ghana. The medical records of patients with CLDs admitted at the medical ward of Tamale Teaching Hospital from June to December 2019 were reviewed in a retrospective cross-sectional study. Out of 180 patients reviewed, 130 (72.2%) were males; the age range was 18–86 years, with a mean age of 44.3 years. Etiologies of CLDs comprised hepatitis B viral infection (53.3%), hepatitis C viral infection (21.7%), unknown (9.4%), hepatocellular carcinoma (8.9%), and alcoholic liver disease (6.7%). Among the complications of CLDs; cirrhosis (71.1%), hypoalbuminemia (59.4%), ascites (58.3%) and jaundice (52.2%) occurred in more than half of the patients. Age ($p < 0.001$), education ($p = 0.005$) and intake of herbal medicine ($p = 0.001$) were associated with the etiologies of CLDs. There was a significant association between the etiologies of CLDs and complications; cirrhosis ($p < 0.001$), hypoalbuminemia ($p = 0.003$), ascites ($p < 0.001$), and jaundice ($p = 0.009$). Hepatitis B and hepatitis C viral infections were the main etiologies of CLDs. Young/middle age, non-education and intake of herbal medicine were risk factors for the main etiologies of CLDs. Cirrhosis, hypoalbuminemia, ascites, and jaundice were the major complications of CLDs. Chronic hepatitis B and C viral infections were risk factors for developing the major complications of CLDs. Implementation of integrated public health strategies targeted at risk groups (young/middle age adults, illiterates, consumers of herbal medicine, patients with hepatitis B and C viral infections) may help curtail the burden of CLDs in northern Ghana.

Keywords: Chronic, Complications, Determinants, Diseases, Distribution, Etiologies, Liver

1. Introduction

Chronic liver diseases (CLDs) are persistent inflammatory conditions of the liver in which the biochemical and histopathological abnormalities of the liver are present over a long period [1]. It consists of a wide range of liver pathologies of different etiologies existing on a continuum between chronic hepatitis, cirrhosis and hepatocellular carcinoma.

CLDs exemplify a critical global public health problem,

because it causes substantial morbidity and mortality worldwide. It has been estimated that about 844 million people globally have CLDs, with 2 million deaths per year, which is comparable to the morbidity and mortality of other major public health diseases like diabetes mellitus (422 million cases, and 1.6 million deaths), respiratory diseases (650 million cases, and 6.17 million deaths) and cardiovascular diseases (540 million cases, 17.7 million deaths) [2].

Globally, the distribution of CLDs comprises non-alcoholic fatty liver diseases [NALD] (60%), hepatitis B viral infection [HBV] (29%), hepatitis C viral infection [HCV] (9%), and alcoholic liver diseases [ALD] (2%) [3]. However, depending on the geographical prevalence of etiologies (hepatitis viruses, alcohol consumption, and metabolic syndrome), a large degree of geographical variation exist in the pattern of CLDs [4]. For instance, viral hepatitis is prevalent in Africa, Asia and Latin America, whereas ALD and NALD is predominant in Western countries [2]. The morbidity and mortality of CLDs are mainly due to its complications (ascites, hepatic encephalopathy, hepatorenal syndrome, variceal hemorrhage and hepatocellular carcinoma). Yet again, the distribution of complications of CLDs will differ due to the common etiologies of CLDs in a setting. For example, chronic HBV infection accounts for more than 70% of hepatocellular carcinoma cases in Africa and Asia, but about 50% of cases globally [5]. It is therefore important to identify the geographical epidemiology of CLDs to help implement specific strategies to curtail the burden of CLDs in that setting.

From search of the literature there was dearth of data on the epidemiology of CLDs in northern Ghana. This research, was thus aimed to study the distribution and determinants of the etiologies and complications of CLDs among patients presenting at a tertiary hospital in northern Ghana.

2. Methods

2.1. Study Design and Site

A retrospective cross-sectional study was carried out on patients with CLDs at the medical ward of the Tamale Teaching Hospital. The Tamale Teaching Hospital is a tertiary and referral hospital for the northern sector of Ghana, as well as an institution for training of health professionals.

2.2. Patients and Inclusion Criteria

Patients on admission at the medical ward of Tamale Teaching Hospital from June–December 2019 were included in the study. Only patients diagnosed of CLD and ≥ 18 years of age were eligible for the research. Diagnosis of CLD was made among patients with evidence of liver disease (elevated liver enzymes, high bilirubin, and/or low albumin levels) by liver function test (S1 Table) The diagnosis was done according to the following criteria: (i) abdominal imaging (ultrasound) showing hepatic parenchyma heterogeneity and/or surface irregularity suggestive of chronic hepatitis, cirrhosis, or hepatocellular carcinoma [6] or (ii) presence of clinical features of decompensated liver diseases such as ascites, bleeding, jaundice, and hepatic encephalopathy [7].

2.3. Data Collection

Data from the medical records of all eligible patients were collected into an excel spread sheet. Data collected included socio-demographic characteristics (sex, age, and educational background); history of alternative medical treatment (intake of herbal medicine); and clinical characteristics (etiologies and complications of CLDs). Etiologies and complications of

CLD were defined according to the criteria in (S2 Table) and (S3 Table) respectively.

2.4. Data Analysis

Descriptive information on the patients' demographic and clinical characteristics were performed and illustrated in proportions with the aid of tables and figures. Analysis of the determinants of the etiologies and complications of CLDs was performed using Statistical Package for the Social Sciences (SPSS) Version 25. Fisher exact test was used to investigate for a significant association between (demographics and etiologies of CLD) and (etiologies and complications of CLD) at p-value of less than 0.05. Multinomial logistic regression with 95% confidence interval was utilized to determine the predictive effects of associated variables.

2.5. Ethical Consideration

Permission was sought from the management of the Tamale Teaching Hospital to conduct the study through an application containing a summary of the study proposal to the research and ethics committee of TTH. Authorization was granted before the study commenced.

3. Results

3.1. Demographic Characteristics of Patients

A total of 180 patients with CLDs were included in the study. Gender composition of the patients indicated that males were majority; 72.2% (Table 1). The age range of the patients was 18 to 86 years, with a mean age of 43 years. A greater proportion of the patients were in the age group of 18–39 years (43.9%) and 40–59 years (40.6%). More than half of the patients had no formal education 136 (75.6%). Drug history of intake of herbal medicine showed that majority of the patients (59.4%) had consume herbal medicine (Table 1).

Table 1. Demographic characteristics of the patients.

Characteristic	Frequency	Percentage
Gender		
Male	130	72.2
Female	50	27.8
Age range		
18–39	79	43.9
40–59	73	40.6
≥ 60	28	15.6
Education		
Educated	44	24.4
Non-educated	136	75.6
Intake of herbal		
Yes	107	59.4
No	73	40.6

3.2. Distribution of Etiologies of Chronic Liver Diseases

The etiologies among the patients showed that hepatitis B viral infection was the major cause of CLDs 96 (53.3%), followed by hepatitis C viral infection 39 (21.7%), unknown

17 (9.4%), hepatocellular carcinoma 16 (8.9%), and alcoholic liver disease 12 (6.7%) (Figure 1).

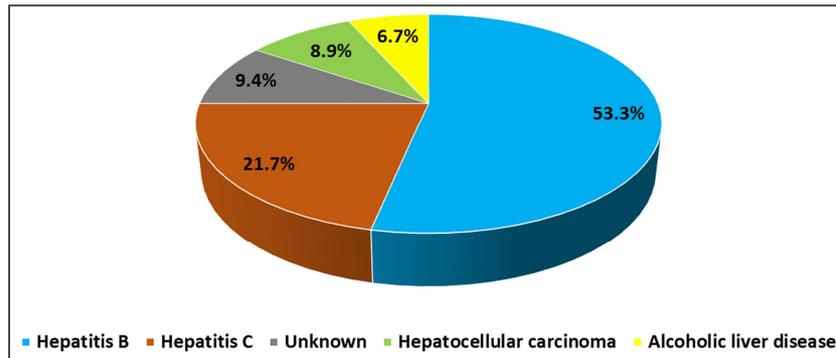


Figure 1. Distribution of etiologies of chronic liver diseases.

3.3. Distribution of Complications of Chronic Liver Diseases

The following were major complications among the CLD patients; cirrhosis 129 (71.7%), hypoalbuminemia 107 (59.4%), ascites 105 (58.3%) and jaundice 94 (52.2%)

(Figure 2). These complications: infections, upper gastrointestinal bleeding, hyponatremia, hepatorenal syndrome, hepatic encephalopathy, and varices occurred in less than 50% of the patients.

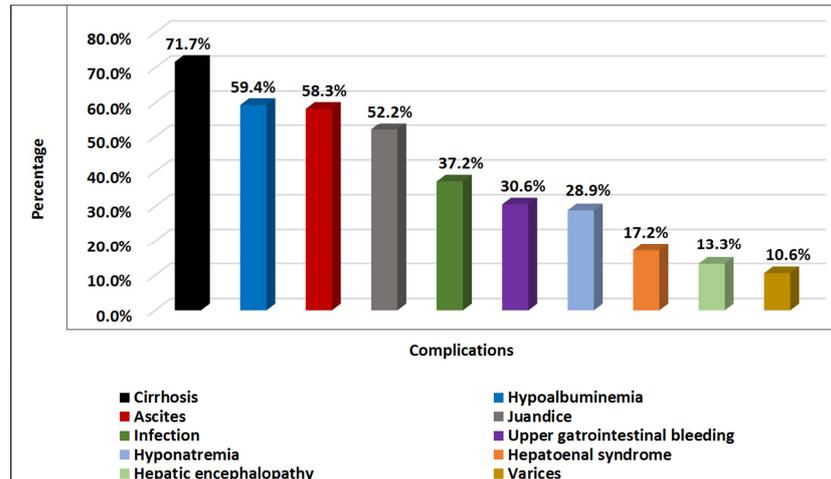


Figure 2. Distribution of complications of chronic liver disease

3.4. Determinants of Etiologies of Chronic Liver Diseases

Analysis of etiologies among the CLD patients revealed that age, education background, and history of intake of

herbal medicine were significantly associated with the etiologies of CLD; (p=<0.001), (0.005) and (0.001) respectively (Table 2).

Table 2. Association between demographic characteristics and etiologies of CLD.

Demographic characteristics	Etiologies of CLD					Fisher exact P-value
	ALD (n=12)	HBV (n=96)	HCV (n=39)	HCC (n=16)	Unknown (n=17)	
Gender						0.199
Male	9 (75.0)	75 (78.1)	23 (59.0)	10 (62.5)	13 (76.5)	
Female	3 (25.0)	21 (21.9)	16 (41.0)	6 (37.5)	4 (23.5)	
Age (years)						<0.001
18-39	3 (25.0)	60 (62.5)	4 (10.3)	5 (31.3)	7 (41.2)	
40-59	7 (58.3)	31 (32.3)	21 (53.8)	9 (56.3)	5 (29.4)	
≥ 60	2 (16.7)	5 (5.2)	14 (35.9)	2 (12.5)	5 (29.4)	
Education						0.005
Non-educated	7 (58.3)	76 (79.2)	35 (89.7)	9 (56.3)	9 (52.9)	
Educated	5 (41.7)	20 (20.8)	4 (10.3)	7 (43.8)	8 (47.1)	
Intake of herbal						0.001
Yes	5 (41.7)	66 (68.8)	26 (66.7)	4 (25.0)	6 (35.3)	
No	7 (58.3)	30 (41.1)	13 (33.3)	12 (75.0)	11 (64.7)	

Patients between age 18–39 years and 40–59 years were 8.6 times and 6.2 times more likely to have chronic HBV infection. Non-educated patients were more at risk of developing chronic HBV (AOR=3.4, 95% CI: 1.2–9.8, $p=0.026$), and chronic

HCV infections (AOR=7.8, 95% CI: 1.9–31.7, $p=0.004$). There was 4 times and 3.7 times higher likelihood to develop CLD from HBV and HCV infections among patients with history of intake of herbal medicine (Table 3).

Table 3. Multinomial logistic regression analysis of demographic characteristics and etiologies CLD.

Etiologies of CLD	Demographic characteristics							
	Age (years) ¹				Education ²		Intake of herbal ³	
	18–39		40–59		Non-educated		Yes	
	P-value	AOR (CI: 95%)	P-value	AOR (CI: 95%)	P-value	AOR (CI: 95%)	P-value	AOR (CI: 95%)
ALD	0.949	1.1 (0.1–8.9)	0.220	3.5 (0.4–25.9)	0.774	1.2 (0.3–5.5)	0.728	1.3 (0.3–6.0)
HBV	0.004	8.6 (2.0–37.1)	0.022	6.2 (1.3–29.5)	0.026	3.4 (1.2–9.8)	0.012	4.0 (1.4–11.9)
HCV	0.051	0.2 (0.1–1.0)	0.574	1.5 (0.4–6.2)	0.004	7.8 (1.9–31.7)	0.033	3.7 (1.1–12.1)
HCC	0.570	1.8 (0.2–13.2)	0.135	4.5 (0.6–32.3)	0.849	1.1 (0.3–4.5)	0.522	0.6 (0.1–2.8)
Unknown		1.0 (ref)		1.00 (ref)		1.00 (ref)		1.00 (ref)

¹Age ≥ 60 is the reference category.

²Educated is the reference category.

³No intake of herbal medicine is the reference category.

3.5. Determinants of Complications of Chronic Liver Diseases

The risk of developing cirrhosis ($p<0.001$), hypoalbuminemia ($p=0.003$), ascites ($p<0.001$) and jaundice ($p=0.009$) were significantly associated with the etiologies of CLD (Table 4).

Table 4. Association between etiologies and complications of CLD.

Complications of CLD	Etiologies of CLD						Fisher exact P-value
	ALD (n=12)	HBV (n=96)	HCV (n=39)	HCC (n=16)	Unknown (n=17)		
Cirrhosis	4 (33.3)	81 (84.4)	32 (81.1)	4 (25.0)	8 (47.1)	<0.001	
Hypoalbuminemia	4 (33.3)	62 (64.6)	29 (74.4)	6 (37.5)	6 (35.3)	0.003	
Ascites	3 (25.0)	68 (70.8)	26 (66.7)	2 (12.5)	6 (35.3)	<0.001	
Jaundice	7 (58.3)	60 (62.5)	18 (46.2)	4 (25.0)	5 (29.4)	0.009	
Infection	5 (41.7)	36 (37.5)	15 (38.5)	5 (31.3)	6 (35.3)	0.987	
UGIB	4 (33.3)	33 (34.4)	13 (33.3)	2 (12.5)	3 (17.6)	0.333	
Hyponatremia	6 (50.0)	27 (28.1)	13 (33.3)	3 (18.8)	3 (17.6)	0.306	
HRS	1 (8.3)	15 (15.6)	10 (25.6)	1 (6.3)	4 (23.5)	0.333	
HE	2 (16.7)	15 (15.6)	4 (10.3)	1 (6.3)	2 (11.8)	0.826	
Varices	2 (16.7)	11 (11.5)	4 (10.3)	1 (6.3)	1 (5.9)	0.880	

Multinomial regression indicated that patients who had HBV (AOR=6.1, 95% CI: 2.0–18.3, $p=0.001$) and HCV infections (AOR=5.1, 95% CI: 1.5–18.0, $p=0.011$) were more at risk to develop cirrhosis (Table 5). The risk of developing hypoalbuminemia was 3.3 and 5.3 times more likely among CLD patients with HBV and HCV etiologies respectively.

Additionally, patients with viral hepatitis B and C as the cause of their CLD had 45% and 37% respectively, higher likelihood to develop ascites. A complication of jaundice was more likely to occur in patients who were infected with chronic HBV (AOR=4.0, 95% CI: 1.3–12.3, $p=0.015$) (Table 5).

Table 5. Multinomial logistic regression analysis of etiologies and complications of CLD.

Etiologies of CLD	Complications of CLD							
	Cirrhosis ¹		Hypoalbuminemia ²		Ascites ³		Jaundice ⁴	
	P-value	AOR (CI: 95%)	P-value	AOR (CI: 95%)	P-value	AOR (CI: 95%)	P-value	AOR (CI: 95%)
ALD	0.462	0.6 (0.1–2.6)	0.913	0.9 (0.2–4.4)	0.557	0.6 (0.1–3.2)	0.126	3.4 (0.7–15.8)
HBV	0.001	6.1 (2.0–18.3)	0.028	3.3 (1.1–9.8)	0.007	4.5 (1.5–13.2)	0.015	4.0 (1.3–12.3)
HCV	0.011	5.1 (1.5–18.0)	0.008	5.3 (1.6–18.1)	0.033	3.7 (1.1–12.1)	0.246	2.1 (0.6–7.0)
HCC	0.194	0.4 (0.1–1.6)	0.895	1.1 (0.3–4.5)	0.141	0.3 (0.1–1.6)	0.776	0.8 (0.2–3.7)
Unknown		1.0 (ref)		1.00 (ref)		1.00 (ref)		1.00 (ref)

¹Presence of cirrhosis.

²Presence of hypoalbuminemia.

³Presence of ascites.

⁴Presence of jaundice.

4. Discussion

4.1. Demographic Characteristics of Patients

The study found out a male gender preponderance among the CLD patients and this was comparable to observations from studies elsewhere in Africa [8] Asia [9] Europe [10] and America [11]. This may imply that male gender is a high-risk group for CLDs. The mean age of the CLD patients (43 years) was similar to the findings in another study in Nigeria (44 years) [12]; and Nepal (42 years) [13]. Additionally, CLD was higher among patients with younger age (18–39 years) and middle age (40–59 years) [14]. The young and/or middle age are mostly at high risk of environmental (heavy alcohol use, smoking) and human exposure (unprotected sex, blood and body fluids) which may point to the high incidence of CLD in this age group. It was also noted that majority of the patients did not have formal education (illiterates). The Northern region is the region with the highest adult illiteracy rate in Ghana [15], which may explain the higher non-educated adult study participants. Drug history of the study population showed that majority (59.4%) were exposed to herbal medicine consumption, which was comparatively higher than the (45.5%) in Enugu state [8], but lower compared with the (68.5%) in Calabar [16]. It is estimated that more than 75% of the populace in sub-Saharan Africa depend on traditional herbal medicine for primary health care [17]. Thus, the observation in this study reflects the use of herbal medicine in a sub-Saharan African setting for health care including liver diseases.

4.2. Distribution and Determinants of Etiologies of Chronic Liver Diseases

A review of the etiologies indicated that HBV was the major etiology of CLD (53.3%). Other studies in African countries have identified a comparable major pattern of HBV infection among CLD patients: (57.7%) in Ethiopia [18] and (58.0%) in Nigeria [12]. A greater proportion of the patients (21.7%) had HCV as the cause of their CLD which was similar to the (22.5%) obtained in Ethiopia [19], however very low compared to the (43.1%) in Italy [4]. The geographical variations may have contributed to this findings, which implies that the prevalence of HCV infection among individuals with CLD is higher in Europe compared to Africa.

There was high risk of HBV infection among young and middle age adults. Other studies in Ghana have identified high prevalence of HBV among young and middle age adults [20, 21]. Young and/or middle age adults are more likely to engage in high-risk sexual activities; one of the most frequent routes of transmission for HBV among adults [22]. Again, young/middle age adults are likely to have more social contacts, and frequently visit settings (e.g. barber, and beauty care centers) which have been associated with transmission of HBV infection [23].

Patients with no formal education (illiterates) were associated with higher likelihood of being infected with HBV

and HCV. It has been noted that both HBV and HCV infections are rapidly increasing in developing countries due to lack of health education, poverty and illiteracy [24]. Illiteracy has direct impact on human health, as it prevents people from access to the vast global store of written information [25]. This implies that written information on modes of transmission and preventive measures of infectious diseases including HBV and HCV infections are likely to be oblivious to individuals without formal education. Limited health literacy has been associated with reduced adoption of protective behaviours such as immunization, less participation in health-promotion and disease-detection activities. [26, 27].

Patients with history of intake of herbal medicines were more likely to develop CLD from HBV and HCV infections. Herbal medicines have been associated with liver fibrosis and increased risk of developing CLDs [28, 29]. Therefore, liver injury due to consumption of herbal medicines either prior or post HBV and HCV infection are highly likely to progress to chronic HBV and HCV infections. Patients may use herbal medicines because they believe these are products of natural origin and thus safe for consumption. However the literature has proven this ideology to be untrue with reports of hepatotoxicity from the use of herbal medicines [17]. Hepatotoxicity from herbal medicines can result from; use of herbs with unknown toxicity; incorrect identification of herbs leading to substitution of non-poisonous herb with a toxic herb; potentiation of the toxic effect of a conventional drug; and the presence of chemicals and heavy metals [30, 31].

4.3. Distribution and Determinants of Complications of Chronic Liver Diseases

It was found out that cirrhosis, hypoalbuminemia, ascites, and jaundice were the major complications among the CLD patients. This indicates that majority of the patients were in decompensated cirrhotic phase of CLD at the time they were presenting to the hospital. The prognosis among these patients are likely to be poor because the estimated one-year mortality among decompensated patients is high; 20–57% [32]. This obviously indicates the need for early testing and treatment among high risk populations as this is necessary to reduce the burden of liver diseases.

It was observed that there was a high risk of developing liver cirrhosis among CLD patients who were infected with HBV and HCV. Infection with HBV and HCV particularly lead to CLD and, together have been the major causes of liver cirrhosis worldwide [33, 34]. It is known that about 8–20% of patients who get infected with HBV will progress to chronicity and develop cirrhosis within 5 years of infection [35], whereas 15–30% of persons who contract HCV will get chronic and then advance to cirrhosis within 20 years [36]. The progression of chronic HBV or HCV to cirrhosis depends on a number of factors (host and virus). In the case of HBV infection, these factors include; alcohol consumption, smoking, male gender, co-infection with hepatitis C or D virus and HBV genotype (C > B; D > A) [37]. Others are

elevated serum levels of total bilirubin, AST/ALT ratio, HBV DNA, and positivity of HBeAg [38, 37]. Important factors for the progression of chronic HCV infection to cirrhosis include non-modifiable (male sex, age at which infection was acquired, and race), modifiable (alcohol abuse, smoking, insulin resistance, and co-infection with hepatitis B, HIV or schistosomiasis) [39] and HCV genotypes (HCV 2 <HCV 4 <HCV 1 <HCV 3) [40].

In this study, the risk of developing hypoalbuminemia was more likely to occur among patients with chronic viral hepatitis. Since majority of the patients with chronic HBV and HCV infections in this study had clinical decompensated complications (advanced cirrhosis) it could explain the association between hypoalbuminemia and viral infections. Patients with advanced cirrhosis almost always have hypoalbuminemia caused by both decreased synthetic function of the liver cells and water and sodium retention that dilutes the content of the albumin in the extracellular compartment [41]. A significant association have been found between the severity of hepatic cirrhosis and decreased albumin levels in patients with chronic HBV [42]. Similarly, the risk of hypoalbuminemia increased significantly in chronic HCV patients with advanced fibrosis [43].

We found out that, HBV and HCV infections were significant risk factors for a patient to develop ascites. Liver cirrhosis is the most common cause of ascites [44]. In patients with liver cirrhosis ascites develops mainly due to portal hypertension [45]. Additionally, hypoalbuminemia favors the extravasation of fluid from plasma to the peritoneal cavity and therefore, ascites is rare in patients with liver cirrhosis unless there is existence of both portal hypertension and hypoalbuminemia [46]. Since patients with chronic HBV and HCV infections were more likely to have cirrhosis, and hypoalbuminemia, it may offer a basis for the relationship between HBV and HCV infections and the development ascites.

Patients with HBV infection had significant risk of developing jaundice as a complication, a finding that has been demonstrated by other studies in Ghana [47] and Kenya [48]. Jaundice is an indication of hepatic decompensation and occurs as a result of impaired conjugation of bilirubin and biliary excretion of conjugated bilirubin.

5. Conclusion

HBV and HCV infections were the main etiologies of CLDs. Young/middle adult age, non-education and intake of herbal medicine were risk factors associated with chronic HBV and HCV infections. Cirrhosis, hypoalbuminemia, ascites, and jaundice were the major complications of CLDs. HBV and HCV infections were risk factors for developing the major complications of CLDs. Implementation of integrated public health strategies such as education, screening, vaccination among high risk groups (young/middle age adult, illiterates, herbal medicine consumers), and early treatment of patients with HBV and HCV infections may help curtail the burden of CLDs in

northern Ghana as well the entire country.

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