



Original Article

COVID-19's Hidden Impact on Chronic Liver Disease Mortality in Nigeria: Findings from an 18-Year Retrospective Review

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Abstract

Background: The COVID-19 pandemic disrupted healthcare systems globally, disproportionately affecting patients with decompensated chronic liver disease (DCLD) due to interrupted care, resource diversion, and the immunosuppressive state associated with DCLD.

In Nigeria, where viral hepatitis is endemic, evidence on the pandemic's indirect impact on DC LD mortality remains scarce. This study examined 18-year mortality trends among patients who died from DCLD in North-eastern Nigeria and evaluated the influence of the COVID-19 pandemic on DCLD-related mortalities.

Methodology: A retrospective review of 436 adult decedents with confirmed DCLD (2006–2024) was conducted at Modibbo Adama University Teaching Hospital, Adamawa State. Sociodemographic and clinical data were abstracted from records. Mortality trends were analysed using Poisson regression, changepoint detection, and joinpoint analysis to identify inflection years, focusing on 2020–2022 as the pandemic window.

Results: The mean age at death was 50.3 ± 14.4 years; 74.5 % were male, and 76.1 % were from low-income households. Viral Hepatitis B & C infections were linked to 67.8 % of deaths, followed by alcohol use (30.1 %). Common complications included hepatic encephalopathy (83.8 %) and portal hypertension (58.2 %). Mortality rose steadily over 18 years, with an abrupt 8.7 % increase in 2020 ($p < 0.01$). Joinpoint analysis identified 2013 and 2020 as major inflection points.

Conclusion: Mortality from DCLD in North-eastern Nigeria increased sharply during the COVID-19 pandemic. Viral hepatitis remains the dominant cause, compounded by late presentation and poor access to care. Strengthening hepatitis prevention, integrating CLD management into non-communicable disease programs, and maintaining chronic care continuity during health emergencies are crucial to mitigating future excess deaths.

Keywords: chronic liver disease; viral hepatitis; mortality trends; COVID-19 pandemic; Nigeria

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Quick Response Code:



Introduction

The coronavirus disease 2019 (COVID-19) pandemic, which emerged in late 2019, exposed profound deficits in global health preparedness and highlighted the fragility of health-system resilience worldwide [1]. Patients with preexisting comorbidities such as diabetes, cardiovascular disease, and immunosuppressive conditions experienced disproportionately higher rates of severe COVID-19 disease and death [2]. During the pandemic peak, healthcare systems redirected resources to COVID-19, resulting in cancelled elective procedures, suspended outpatient services, and delayed care for chronic diseases [3,4]. As a consequence, mortality from non-COVID-19 conditions increased, yet this collateral impact largely remained unnoticed and underreported [5,6].

Individuals with CLD constituted a particularly vulnerable population at heightened risk of acquiring COVID-19 [7,8]. CLDs are persistent inflammatory or fibrotic liver disorders lasting more than six months and include chronic viral hepatitis (B/C), alcoholic liver disease, autoimmune hepatitis, metabolic liver disorders, cirrhosis, and primary liver cancer (PLCC), etc. [9,10]. The transition from compensated to decompensated disease is often marked by potentially lethal complications such as hepatic encephalopathy, portal hypertension, etc [11]. Globally, DCLDs account for nearly two million deaths annually, approximately 4% of all-cause mortality. Cirrhosis ranks among the ten leading causes of death in the African region [12–14].

Generally, patients with underlying CLD and DCLD are of particular concern during infectious pandemics [15]. The immunosuppression that characterizes an advanced liver disease predisposes them to severe forms of COVID-19, while atypical clinical presentations may delay diagnosis and treatment [3,6]. COVID-19 has been found to trigger acute hepatic decompensation and trigger acute-on-chronic liver failure [16]. Twenty-one percent of people secondarily affected by COVID-19 with a background of CLD showed no respiratory symptoms, thereby evading clinical detection [16]. Emerging global evidence suggests that DCLD-related mortality increased during the COVID-19 pandemic, both due to elevated risk of infection and because of disruptions in the continuity of requisite care [2,7,17]. Marjot et al. [16] reported a multi-centre study that revealed that preexisting CLD increased mortality by 32% among those who developed superimposed COVID-19, compared with 8% among those without background CLD. In addition, this aforementioned study further observed that acute hepatic decompensation occurred in 45% of patients with preexisting stable compensated cirrhosis [16]. COVID-19 increased the risk of death by 3.5-fold in the face of background cirrhosis [18]. However, 12 of the 57 studies analysed by Yan-Fei et al. [19] in a systematic review found no relationship between underlying chronic hepatitis B-related CLD and heightened COVID-19 disease risk.

Post-pandemic assessment of COVID-19's impact on CLD remains unreported, mainly in Nigeria and sub-Saharan Africa. Exploring these insights is essential for strengthening health system preparedness and response and ensuring continuity of chronic disease care during future public health emergencies. In addition, identifying the primary drivers of DCLD could serve as a policy brief for targeted containment measures.

Against this background, we conducted an 18-year retrospective review to quantify mortality trends in DCLD and assess the effect of the COVID-19 pandemic on DCLD-related mortality. To our knowledge, this is the first sub-Saharan analysis examining the COVID-19 impact on DCLD-related deaths.

Materials and method

Study design and population

This retrospective review examined all documented DCLD-related deaths recorded at Modibbo Adama University Teaching Hospital, Adamawa, Nigeria, from 2006 to 2024, using systematically retrieved hard-copy medical records.

The primary outcome of this study was the mortality trend due to DCLD before and during the COVID-19 pandemic. In contrast, the secondary outcome assessed the annual trajectory of DCLD-related mortality over the past two decades. Eligibility for inclusion required that diagnoses of DCLDs be confirmed by clinical presentation supported by radiological and laboratory findings. Folders with incomplete data, missing variables, and insufficient evidence of DCLD diagnoses were all excluded. Decedents younger than 18 years at diagnosis or death were also excluded. Cases in which the aetiology of DCLD could not be clinically established were classified as cryptogenic. Records indicating hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, whether mono- or co-infection, were classified and operationalized as DCLD of viral origin for analytical simplicity, given that viral hepatitis remains the leading cause of CLD and DCLD in Nigeria.

After applying these criteria, 436 case files were retained for analysis from an initial pool of about 500 initially retrieved from the archive.

To ensure data reliability, trained and certified nurses at the facility sieved and retrieved eligible case files in accordance with the above eligibility criteria. They extracted relevant variables, including sociodemographic information, the type and aetiology of the DCLDs, and associated risk factors, such as viral hepatitis. Others were history of alcohol use and cigarette smoking. The data were extracted and uploaded to an electronic mobile data collection tool, KoboToolbox.

Statistical analysis

Data were analysed using Python 3.12.12. Categorical variables (e.g., gender, tribe, marital status, education, occupation) were presented as frequencies and percentages. Continuous variables (e.g., age) were summarized as means.

Change-point analysis identified years when DCLD mortality deviated sharply from prior patterns, while joinpoint regression quantified and confirmed shifts in trends before and after these breaks. Together, these methods more reliably detected pandemic-related disruptions than standard linear or Poisson models, directly supporting our aim to assess whether COVID-19 represented an actual turning point in mortality. COVID-19 was first detected in Adamawa in March 2020 and gradually subsided by late 2021 following non-pharmaceutical interventions and the vaccine rollout. By 2022, COVID-19 was no longer considered a significant public health concern in Adamawa State. This informed the selection of the 2020-2022 pandemic window for analysis.

Standard deviation.

After importing the dataset from Excel, the liver disease types were grouped into 7 major categories. Their proportions were calculated to show the most common causes of DCLD in Adamawa.

To examine changes over time, annual deaths were summarized, and a three-year moving average was used to smooth year-to-year variation. Mortality trends were then assessed using linear and Poisson regression, with the latter applied because the data comprised yearly death counts. Outputs included trend direction, p-values, and model fit statistics.

Trend changes were explored using additional methods. Change-point detection and join-point regression were used to identify years when mortality patterns shifted. A segmented regression model with a fixed break in 2020 was applied to assess the possible impact of COVID-19 on liver-related deaths.

All analyses and graphs were completed using standard Python libraries (pandas, NumPy, SciPy, stats models, and matplotlib).

Results

Sociodemographic Characteristics (Table 1)

Between 2006 and 2024, a total of 436 fatalities associated with DCLD were examined in retrospect. The average age of decedents was 50.3 ± 14.4 years, with a significant male predominance (74.5%) and a male-to-female ratio of approximately 3:1. Mortality was concentrated among married individuals (86%) and those with low income (76.1%). Moreover, one-third (35.8%) were devoid of formal education. Farmers/herders (28.7%), civil servants (22%), and dealers (19.7%) were the most impacted occupational groups. Viral hepatitis (hepatitis B and C) was the predominant aetiology of DCLD, collectively accounting for 68% of cases, while alcohol consumption (30.1%) and tobacco use (9.5%) emerged as significant secondary risk factors.

Variable	n (%)
Total participants	436
Age (years), mean \pm SD	50.3 \pm 14.4
≤ 20	4 (0.9%)
20–29	34 (7.8%)
30–39	60 (13.8%)
40–49	96 (22.0%)
50–59	111 (25.5%)
60–69	84 (19.3%)
70–79	38 (8.7%)
80–89	8 (1.8%)
Male	325 (74.5%)

Female	111 (25.5%)
Divorced	3 (0.7%)
Married	375 (86.0%)
Single	44 (10.1%)
Widowed/Widower	14 (3.2%)
No formal education	156 (35.8%)
Primary	57 (13.1%)
Secondary	110 (25.2%)
Tertiary	113 (25.9%)
Civil servant	96 (22.0%)
Corporate employee	3 (0.7%)
Farmer/Herder	125 (28.7%)
Full-time housewife	0 (0.0%)
Healthcare worker	4 (0.9%)
Military/Paramilitary	15 (3.4%)
Student	10 (2.3%)
Trader/Business	86 (19.7%)
Unemployed	14 (3.2%)
Urban residence	161 (36.9%)
High income	1 (0.2%)
Medium income	103 (23.6%)
Low income	332 (76.1%)
Alcohol use (Yes)	124 (28.4%)
Smoking (Yes)	38 (8.7%)
HCV Positive	59 (13.5%)
HBsAg Positive	174 (39.9%)

Clinical complications of CLD (Table 2) indicated advanced illness at presentation. Hepatic encephalopathy (83.8%) was the predominant terminal DCLD complication, followed by portal hypertension (58.2%), spontaneous bacterial peritonitis (22%), and hepatorenal syndrome (21%).

Complication	n (%)
Hepatic encephalopathy	331 (83.8)
Portal hypertension	230 (58.2)
Spontaneous bacterial peritonitis (SBP)	87 (22.0)
Hepatorenal syndrome	83 (21.0)
Hypoglycaemia	30 (7.6)
Hepatopulmonary syndrome	9 (2.3)
Haemorrhagic shock	1 (0.3)

Annual Temporal Trends in CLD Mortality (Figures 1 and 2) indicated a progressive rise in DCLD mortality from 2006, culminating in a substantial surge in 2020, coincident with the COVID-19 pandemic. In 2020, mortality increased by 8.7% relative to 2019,

Figure 1 illustrates temporal trends in mortality across different etiological categories of chronic liver disease recorded in Adamawa State from 2006 to 2024.

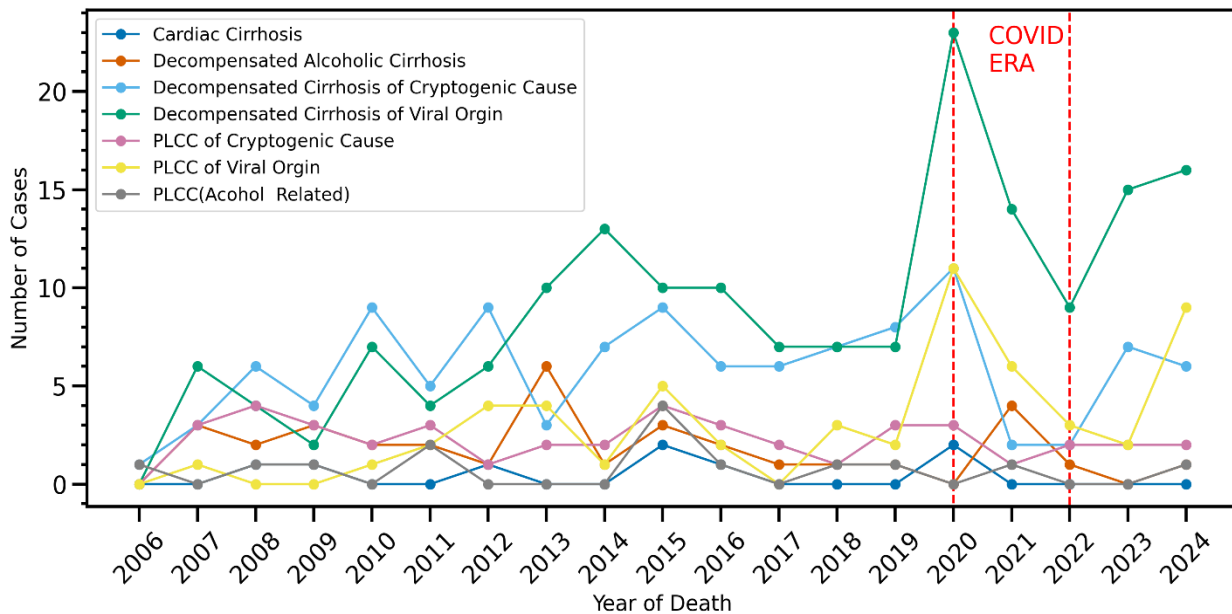


Figure 2 displays the total number of annual deaths and the percentage contribution of deaths attributed to chronic liver disease between 2006 and 2024.

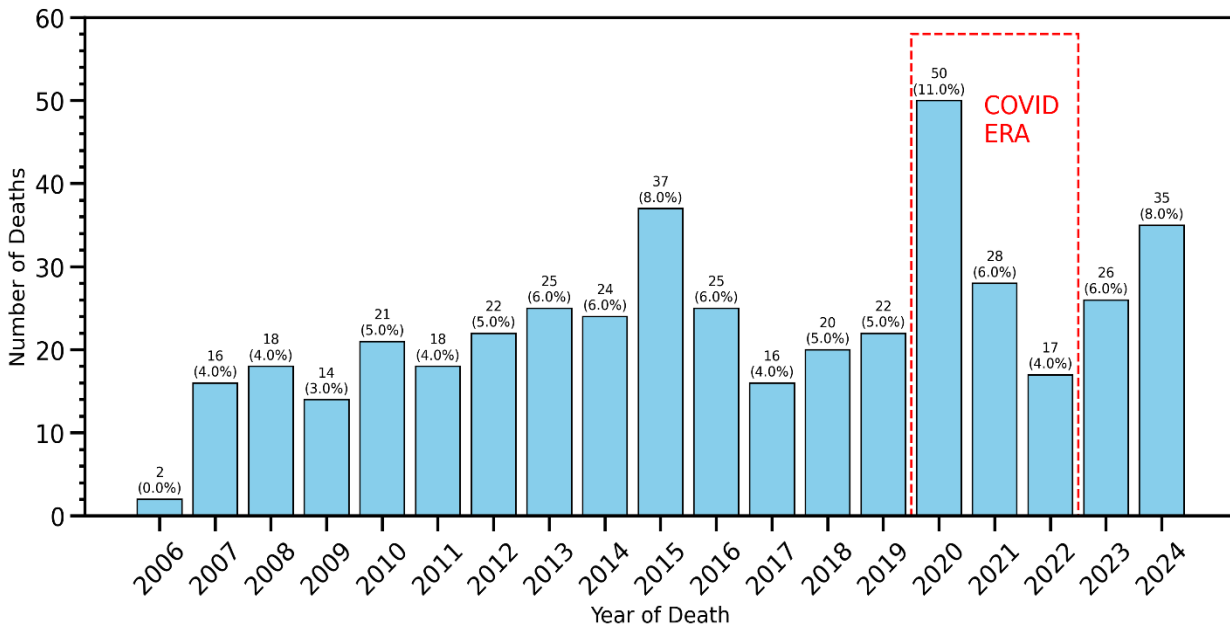


Figure 2 shows a bar chart displaying the total number of deaths from Chronic Liver Disease (CLD) recorded each year in Adamawa from 2006 to 2024. Each bar is annotated with the exact number of deaths and the corresponding percentage of the total deaths over the entire 18 years.

Poisson regression analysis (Figure 3) revealed a statistically significant rising trend ($R^2 = 0.33$, $p < 0.01$), corroborating the higher mortality recorded in 2020. The model's fit closely aligned with the empirical data, validating that the 2020 increase surpassed random annual variations.

Figure 3 Observed and Poisson Fitted Annual Deaths for Overall CLD and Decompensated Cirrhosis of Viral Origin in Adamawa (2006–2024)

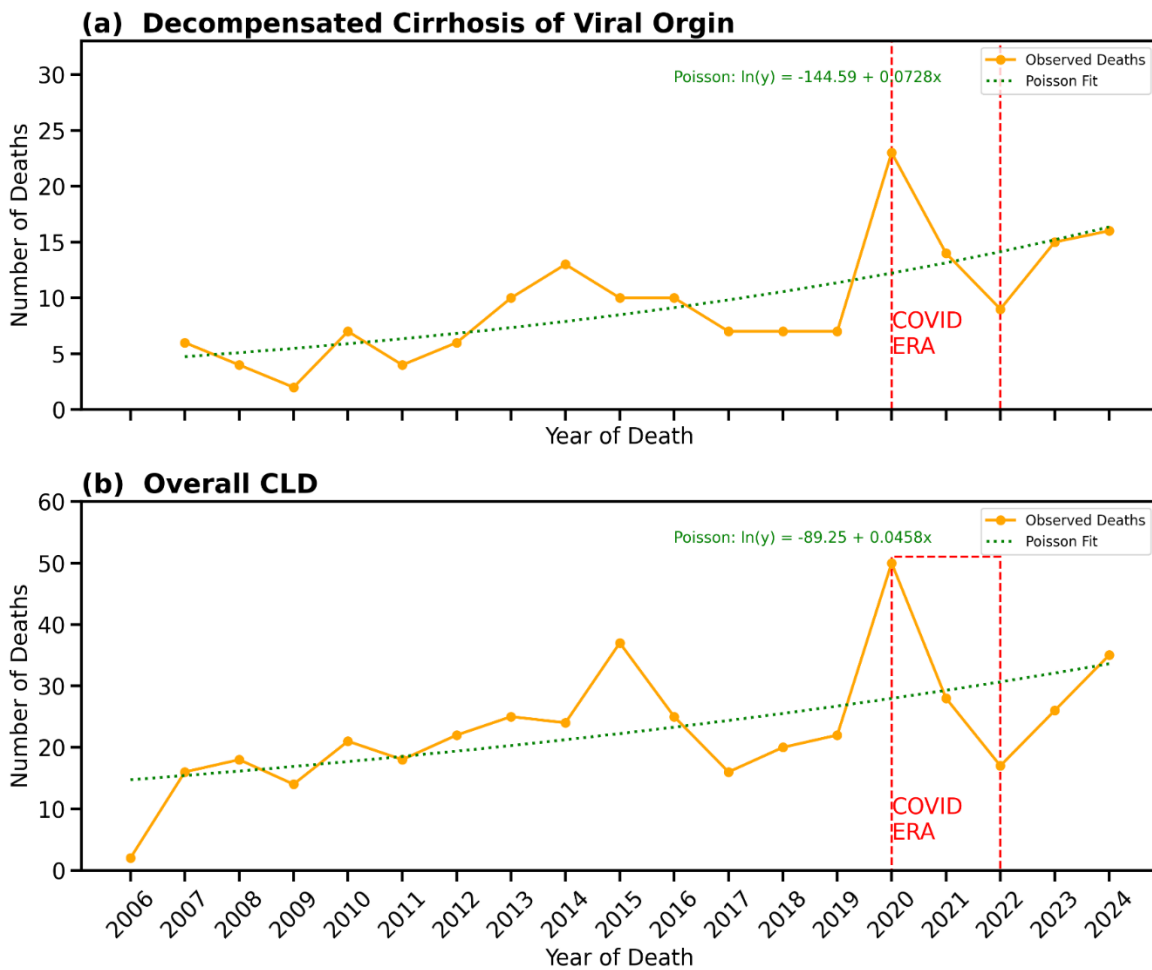


Figure 3 presents two-time series plots. The top plot shows the observed and Poisson-fitted annual deaths for Decompensated Cirrhosis of Viral Origin, while the bottom plot shows the same for all Chronic Liver Diseases (Overall CLD). The dashed lines represent COVID-19-related deaths during the pandemic.

Changepoint analysis (Figure 4). identified 2013 and 2020 as years when mortality patterns shifted sharply. Both detection methods revealed that 2020–2022 represented a distinct high-mortality period relative to prior years.

Figure 4 depicts the changepoint detection outputs identifying years in which chronic liver disease mortality patterns shifted significantly.

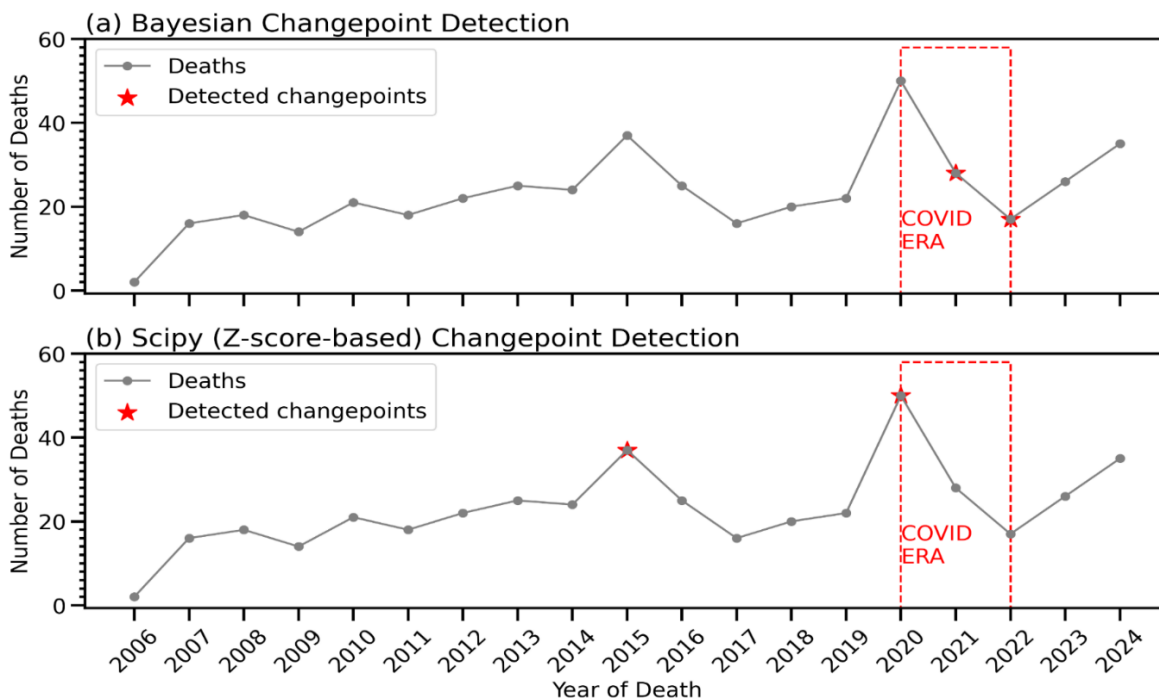


Figure 4 presents the results of two changepoint detection methods applied to the annual Chronic Liver Disease (CLD) death counts in Adamawa. Panel (a) shows the observed deaths and the changepoints detected by the Bayesian method. Panel (b) shows the observed deaths and the changepoints detected using the Scipy (Z-score-based) method. Both plots help identify potential years where the trend in CLD mortality significantly changed. The dashed red rectangle highlights the COVID-19 pandemic period (2020-2022).

Regression models (Figure 5). Comparison of observed deaths with linear and Poisson models demonstrated a gradual upward trend pre-2020, followed by a steeper escalation during 2020–2022. Both models validated that the pandemic period represented a non-linear rise rather than a background annual fluctuation.

Figure 5 shows observed annual death counts plotted against fitted linear and Poisson regression models, demonstrating a progressively rising trend with further elevation during the 2020–2022 pandemic window.

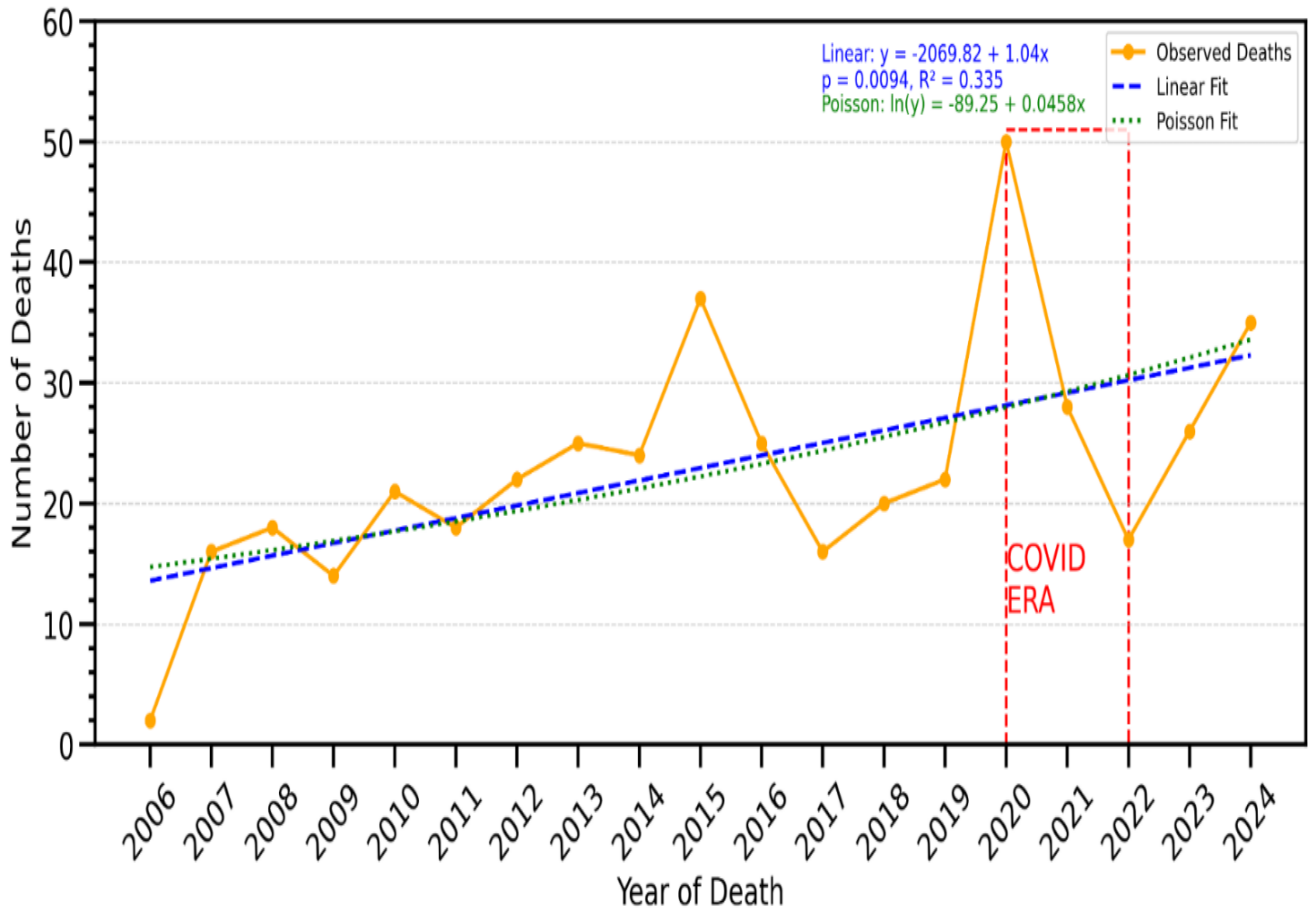


Figure 5 displays the observed annual number of deaths from Chronic Liver Diseases (CLD) in Adamawa alongside fitted lines from linear and Poisson regression. The linear fit provides a simple straight-line trend, while the Poisson fit is suitable.

Joinpoint analysis (Figure 6). Joinpoint analysis detected two significant inflection points (2013 and ~2017), with the steepest slope occurring from 2020–2022.

Figure 6 presents a two-break joinpoint regression curve applied to annual chronic liver disease mortality, highlighting statistically significant inflection years and the sharper upward trajectory during the COVID-19 period (2020–2022)

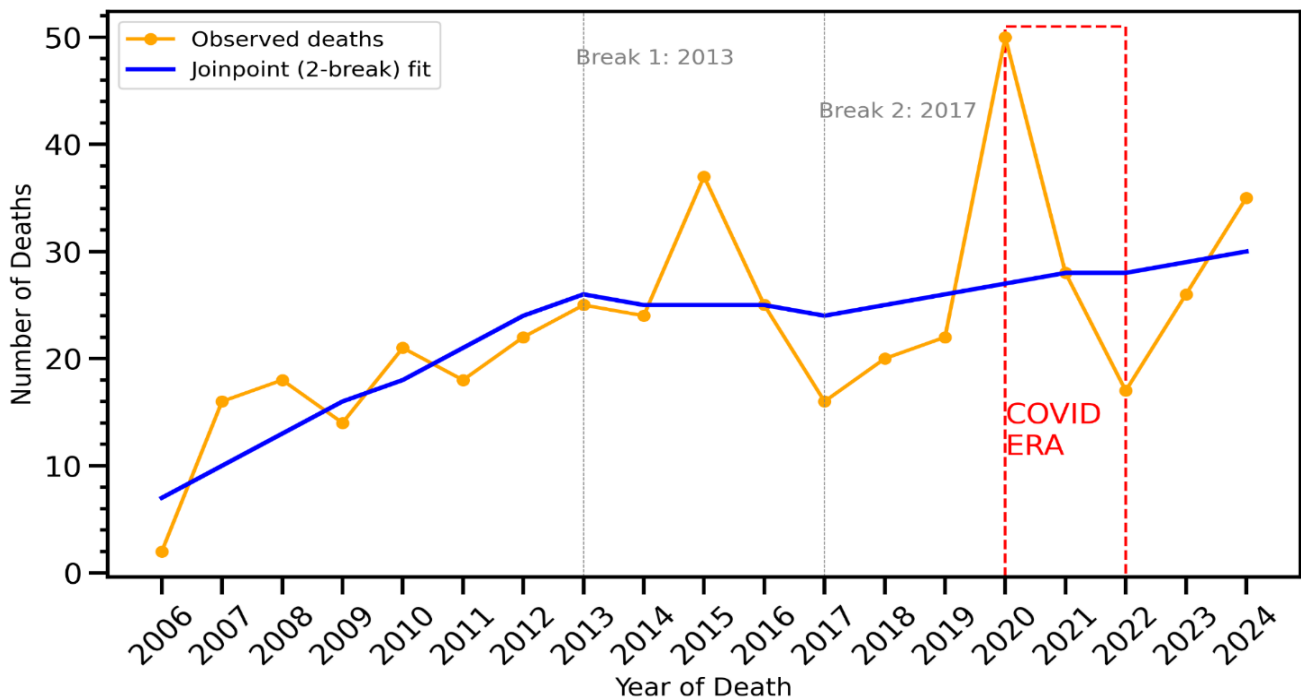


Figure 6 shows the observed annual number of deaths from Chronic Liver Diseases (CLD) in Adamawa from 2006 to 2024, along with a two-break joinpoint regression model fit. The joinpoint analysis identifies statistically significant points in time where the linear trend of the death rate changes. The model estimates the breakpoint years (approximately 2013 and 2017) and the trend slopes in each segment (k_0 , k_1 , k_2). The dashed red rectangle highlights the period between 2020 and 2022, representing the COVID-19 pandemic era.

Ultimately, the Joinpoint analysis identified inflection years at 2013 and approximately 2017, within which mortality rose more steeply, with the sharpest slope occurring during 2020–2022.

In summary, the above results depict that DCLD deaths in North-eastern Nigeria mainly affect disadvantaged, middle-aged men, present late with severe complications, and are primarily driven by viral hepatitis. Mortality rose sharply during the COVID-19 pandemic.

Discussion

The striking finding of this study is the sharp surge in DCLD-related mortality in 2020. Pockets of published reports across the globe are now revealing that the COVID-19 pandemic was accompanied by amplification of DCLD-related mortalities [5]. While our study showed that DCLD-related mortalities increased by 8.7% in 2020 compared with 2019, an Egyptian study found that COVID-19 significantly increased mortality among patients with background DCLD, particularly those with Child–Pugh class C disease ($r = 0.40$, $p = 0.001$) [20].

In the United States, mortality due to DCLD increased by 21% during the pandemic, with hepatitis- and alcohol-related liver diseases contributing the most to the excess deaths [7]. In contradiction, our study depicted spikes in viral-related DCLD. In Brazil, cirrhotic patients secondarily infected with COVID-19 were shown to have experienced a higher case fatality of 51.3% as against 21.7% in non-CLD patients [17].

The relatively younger population structure of sub-Saharan Africa is believed to have conferred some degree of protection, resulting in a lower overall incidence of COVID-19 in the Sub-region during the pandemic [21]. This might plausibly account for the relatively low number of DCLD-related deaths observed in 2020 in this study. The excess mortality in 2020 in this study may plausibly be attributed to the dual vulnerability of DCLD patients to both infection-related mortality and also indirectly due to the interruption of specialized care services.

In this 18-year mortality review, we provided rare insight into the previously underrecognized burden and mortality trends of DCLD in North-eastern Nigeria over the past two decades. These findings imply that both long-standing drivers and the disruptive impact of the COVID-19 pandemic contributed to DCLD mortality. While viral hepatitis infections remain the leading cause of CLD in sub-Saharan Africa and Asia [10], alcoholic liver diseases (ALD) and metabolic-associated fatty liver diseases are the leading causes of DCLDs in the Western world [13, 14]. Our findings are consistent with this global picture [14]. Though DCLD of Cryptogenic cause also accounted for a substantial proportion of DCLD-related deaths in our study, its burden falls within the reported global range of 5-30% [22]. A Brazilian study found that one-third of patients presumed to have cryptogenic CLD were later diagnosed to have metabolic-dysfunction-associated fatty liver disease [22]. The frequent attribution of cases to "cryptogenic DCLD" in our study underscores the substantial diagnostic gaps within the health system. The burden of Metabolically-dysfunction-associated fatty liver disease is on the rise in Africa [23]. In general, the increasing burden of CLD in Sub-Saharan Africa is driven by aflatoxin contamination of food due to poor food storage facilities [24].

Overall, the joint point-confirmed shift in 2020 offers quantitative evidence that the pandemic may have mediated as a catalyst for increased DCLD-related mortality. In addition, the health systems and resources in Nigeria, as in many countries, were redeployed in response to the global pandemic. Most Specialty clinics were suspended; access to antiviral drugs and their logistics were disrupted. These factors likely precipitated the decompensation of previously stable CLD into DCLD, contributing to the excess mortality observed in 2020. The need for a more aggressive viral hepatitis prevention and control program is indicated by the fact that decompensated cirrhosis and PLCC of viral origins accounted for most of the deaths. Due to the low vaccination rates, delayed diagnosis, and limited access to antiviral treatments, virus-related DCLD continue to pose a significant impact in sub-Saharan Africa despite international elimination targets [25].

The advanced stage of the disease in which decedents usually presented in our study is reflected by the high prevalence of complications, notably hepatic encephalopathy (HE) (83.8%), portal hypertension (58.2%), etc. The high cumulative prevalence of hepatic encephalopathy (84%) observed over the 18-year study period slightly exceeds the reported global prevalence range of 20–80% [26].

Generally, outside the COVID-19 pandemic, early diagnosis and timely liver transplantation account for the lower mortality observed in high-income countries [13, 14]. Conversely, mortality from decompensation remains disproportionately high in resource-constrained settings such as Nigeria, driven by late presentation and limited access to specialized hepatology services [27].

Our results highlight the urgent need to strengthen the health system, especially by improving diagnostic capabilities, expanding access to antiviral and antifibrotic treatments, and expanding palliative care services for advanced DCLD.

This study's findings have significant ramifications for public health policy and clinical practice. First, the higher prevalence of viral hepatitis calls for a renewed dedication to eradication goals and programs via enhanced screening, universal immunization, and government-funded antiviral medications. Liver health may be incorporated into non-communicable disease (NCD) programs, given the growing burden of cryptogenic DCLD. To prevent future pandemics from disrupting essential services for immunocompromised populations, DCLD care may be integrated into pandemic preparedness and response frameworks as a core public health policy reform.

Lastly, reducing the death rate from DCLD necessitates both socioeconomic investment policy and antiviral therapies provision. Antivirals are usually unaffordable to the low socioeconomic class [27]. This study's finding that nearly three-quarters of the decedents came from low-income families serves as a reminder that social injustices, poverty, and lack of literacy continue to be significant factors influencing DCLD outcomes [28, 29].

The strength of this study lies in its rare 18-year analysis of DCLD mortality from a major referral centre serving multiple states and nearby countries, providing unusually robust insight into long-term DCLD mortality trends in North-eastern Nigeria. Its large dataset, 18-year longitudinal observation, standardized record review, and application of advanced statistical methods, including Poisson modelling, change-point and join-point analyses, strengthen the reliability of the findings and demonstrate the possibility of a pandemic-related mortality surge.

Limitations included a lack of control, a retrospective design, and reliance on hospital records. All these have their attendant biases. In addition, being a single-centre study, findings may not be generalizable to all regions of Nigeria. Furthermore, excluding case files with substantial missing data and lost records may have led to an underestimation of the actual burden of DCLD mortality in the region. Additionally, the influence of unmeasured confounders cannot be entirely excluded.

Conclusion

In conclusion, viral hepatitis remains the dominant driver of DCLD mortality in North-eastern Nigeria, compounded by a significant burden of cryptogenic DCLD, which may likely reflect an emerging metabolic

liver disease. The COVID-19 pandemic amplified those outcomes, thereby exposing the fragility of healthcare systems in protecting patients with underlying chronic conditions. A multi-Centre study across sub-Saharan Africa is recommended to review the DCLD-related deaths that occurred during the pandemic for more substantial evidence.

Ethical Approval: The study was approved by the Modibbo Adama University Teaching Hospital Health Research Ethics Committee with reference number MAUTH/HREC/23/333 on Jun 24 2024

References

1. Filip R, Gheorghita Puscaselu R, Anchidin-Norocel L, Dimian M, Savage WK. Global challenges to public health care systems during the COVID-19 pandemic: a review of pandemic measures and problems. *Journal of personalized medicine*. 2022 Aug 7;12(8):1295. <https://doi.org/10.3390/jpm12081295>
2. Bigdelou B, Sepand MR, Najafikhoshnoo S, Negrete JA, Sharaf M, Ho JQ, Sullivan I, Chauhan P, Etter M, Shekarian T, Liang O. COVID-19 and preexisting comorbidities: risks, synergies, and clinical outcomes. *Frontiers in immunology*. 2022 May 27;13:890517. <https://doi.org/10.3389/fimmu.2022.890517>
3. Makanjuola S, Shantikumar S. The impact of the COVID-19 pandemic on non-COVID-associated mortality: a descriptive longitudinal study of UK data. *Public Health in Practice*. 2024 Jun 1;7:100489. <https://doi.org/10.1016/j.puhip.2024.100489>
4. Byrnes ME, Brown CS, De Roo AC, Corriere MA, Romano MA, Fukuhara S, Kim KM, Osborne NH. Elective surgical delays due to COVID-19: the patient lived experience. *Medical care*. 2021 Apr 1;59(4):288-94.
5. Gao X, Lv F, He X, Zhao Y, Liu Y, Zu J, Henry L, Wang J, Yeo YH, Ji F, Nguyen MH. Impact of the COVID-19 pandemic on liver disease-related mortality rates in the United States. *Journal of Hepatology*. 2023 Jan 1;78(1):16-27. <https://doi.org/10.1016/j.jhep.2022.07.028>
6. Liao CM, Kao YW, Lin CM, Lai PY. The Impact of the COVID-19 Pandemic on Mortality Rates From Non-Communicable Chronic Diseases in Taiwan: An Interventional Time Series Study. *International Journal of Public Health*. 2025 Mar 28;70:1607723. <https://doi.org/10.3389/ijph.2025.1607723>
7. Paik JM, Shah D, Eberly K, Golabi P, Henry L, Younossi ZM. Changes in mortality due to chronic liver diseases (CLD) during the COVID-19 pandemic: Data from the United States' National Vital Statistics System. *Plos one*. 2024 Sep 3;19(9):e0289202. <https://doi.org/10.1371/journal.pone.0289202>
8. Vujčić I. Outcomes of COVID-19 among patients with liver disease. *World Journal of Gastroenterology*. 2023 Feb 7;29(5):815. <https://doi.org/10.3748/wjg.v29.i5.815>
9. Wen Y, Ma L, Ju C. Recent insights into the pathogenesis and therapeutic targets of chronic liver diseases. *Egastroenterology*. 2023 Oct 19;1(2).
10. Abdelhamed W, El-Kassas M. Hepatitis B virus as a risk factor for hepatocellular carcinoma: there is still much work to do. *Liver Research*. 2024 Jun 1;8(2):83-90. <https://doi.org/10.1016/j.livres.2024.05.004>
11. Fromme M, Strnad P. Pathophysiology of chronic liver disease development. *International Journal of Molecular Sciences*. 2022 Mar 21;23(6):3385. <https://doi.org/10.3390/ijms23063385>
12. Wong VW, Ekstedt M, Wong GL, Hagström H. Changing epidemiology, global trends and implications for outcomes of NAFLD. *Journal of hepatology*. 2023 Sep 1;79(3):842-52. <https://doi.org/10.1016/j.jhep.2023.04.036>

13. Nguyen NT, Hoai LN, Bui LT, Chang YM, Abdi AA, Hsu SC, Lin HJ, Huang CC. Global mortality of chronic liver diseases attributable to Hepatitis B virus and Hepatitis C virus infections from 1990 to 2019 and projections to 2030. *Journal of Infection and Public Health*. 2024;17:102443.
14. Huang DQ, Terrault NA, Tacke F, Gluud LL, Arrese M, Bugianesi E, Loomba R. Global epidemiology of cirrhosis—etiology, trends and predictions. *Nature reviews Gastroenterology & hepatology*. 2023 Jun;20(6):388-98. <https://doi.org/10.1038/s41575-023-00759-2>
15. Marciano S, Diaz JM, Dirchwolf M, Gadano A. Spontaneous bacterial peritonitis in patients with cirrhosis: incidence, outcomes, and treatment strategies. *Hepatic medicine: evidence and research*. 2019 Jan 14;13-22. <https://doi.org/10.2147/HMER.S164250>
16. Marjot T, Moon AM, Cook JA, Abd-Elsalam S, Aloman C, Armstrong MJ, Pose E, Brenner EJ, Cargill T, Catana MA, Dhanasekaran R. Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: an international registry study. *Journal of hepatology*. 2021 Mar 1;74(3):567-77. <https://doi.org/10.1016/j.jhep.2020.09.024>
17. Menezes LS, da Cunha PF, Pires MC, Valle LR, Costa FC, Ferreira MA, Guimarães Júnior MH, Francisco SC, Carneiro M, Silveira DV, Aranha FG. Clinical outcomes of COVID-19 in patients with liver cirrhosis: a propensity-matched analysis from a multicentric Brazilian cohort. *BMC Infectious Diseases*. 2025 Jan 15;25(1):68. <https://doi.org/10.1186/s12879-024-10424-x>
18. Ioannou GN, Liang PS, Locke E, Green P, Berry K, O'Hare AM, Shah JA, Crothers K, Eastment MC, Fan VS, Dominitz JA. Cirrhosis and severe acute respiratory syndrome coronavirus 2 infection in US veterans: risk of infection, hospitalization, ventilation, and mortality. *Hepatology*. 2021 Jul;74(1):322-35.
19. He YF, Jiang ZG, Wu N, Bian N, Ren JL. Correlation between COVID-19 and hepatitis B: A systematic review. *World journal of gastroenterology*. 2022 Dec 14;28(46):6599. <https://doi.org/10.3748/wjg.v28.i46.6599>
20. Samir A, Nabil F, Ashour M, Mahdy A. Impact of chronic liver disease on COVID-19 infection at Zagazig University Hospitals. *African Journal of Gastroenterology and Hepatology*. 2022 Oct 1;5(2):16-31. <https://doi.org/10.21608/ajgh.2022.176239.1020>
21. Taboe HB, Asare-Baah M, Yesmin A, Ngonghala CN. The impact of age structure and vaccine prioritization on COVID-19 in West Africa. *Infectious Disease Modelling*. 2022 Dec 1;7(4):709-27. <https://doi.org/10.1016/j.idm.2022.08.006>
22. Cançado GG, Candolo AC, Nardelli MJ, Zitelli PM, Mazo DF, Oliveira CP, Cunha-Silva M, Greca RD, Araújo RC, Alustau AS, Couto CA. Cryptogenic chronic hepatitis: looking for an ideal diagnostic algorithm. *Frontiers in Gastroenterology*. 2023 Aug 1;2:1209000. <https://doi.org/10.3389/fgstr.2023.1209000>
23. Ahmed MH, Noor SK, Bushara SO, Husain NE, Elmadhoun WM, Ginawi IA, Osman MM, Mahmoud AO, Almobarak AO. Non-alcoholic fatty liver disease in Africa and Middle East: an attempt to predict the present and future implications on the healthcare system. *Gastroenterology research*. 2017 Oct 26;10(5):271. <https://doi.org/10.14740/gr913w>
24. Gemedede HF. Toxicity, Mitigation, and Chemical Analysis of Aflatoxins and Other Toxic Metabolites Produced by *Aspergillus*: A Comprehensive Review. *Toxins*. 2025 Jun 30;17(7):331. <https://doi.org/10.3390/toxins17070331>
25. Spearman CW, Afihene M, Ally R, Apica B, Awuku Y, Cunha L, Dusheiko G, Gogela N, Kassianides C, Kew M, Lam P. Hepatitis B in sub-Saharan Africa: strategies to achieve the 2030 elimination targets. *The lancet gastroenterology & hepatology*. 2017 Dec 1;2(12):900-9.
26. Vilstrup H, Amodio P, Bajaj J, Cordoba J, Ferenci P, Mullen KD, Weissenborn K, Wong P. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the

Study of Liver Diseases and the European Association for the Study of the Liver. *Hepatology*. 2014 Aug;60(2):715-35.

27. Stephen RI, Reyes JA, Dunga JA, Awang SK, Zawaya KP. An unusual survival for 6.5 years with end-stage hepatitis C related advanced liver cirrhosis following sustained virologic response with direct antiviral agents—A case report from A low-resource setting. *Nigerian Medical Journal: Journal of the Nigeria Medical Association*. 2025 Jun 16;66(2):791. <https://doi.org/10.71480/nmj.v66i2.661>
28. Kardashian A, Serper M, Terrault N, Nephew LD. Health disparities in chronic liver disease. *Hepatology*. 2023 Apr 1;77(4):1382-403.
29. Jafree SR, Naveed A, Ahsan H, Burhan SK, Khawar A, Khan MA, Fischer F. Predictors of health-seeking behavior in patients with chronic liver disease and a comparison of health-seeking based on patient-type. *BMC gastroenterology*. 2025 Sep 19;25(1):642. <https://doi.org/10.1186/s12876-025-04235-w>