



RESEARCH ARTICLE

Climate Change and the Changing Landscape of Central Nervous System Infections and Neuropsychiatric Morbidities in Northwest Nigeria: A Large-Scale Epidemiological Study

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Abstract

Background: Climate change is postulated to alter the epidemiology of infectious diseases, particularly in vulnerable regions like sub-Saharan Africa. The potential impact on central nervous system (CNS) infections and subsequent neuropsychiatric sequelae remains inadequately characterised in Northwest Nigeria.

Objectives: This study aimed to investigate the associations between climate change indicators (including temperature, rainfall patterns, extreme heat days, and humidity) and the incidence of CNS infections, including atypical presentations, and associated neuropsychiatric morbidities.

Methods: A cross-sectional study was conducted involving 20,000 participants from Northwest Nigeria over 24 months (January 2023 to December 2024). Data were collected using pre-validated instruments, including a structured questionnaire, clinical proforma for CNS infection diagnosis, the Composite International Diagnostic Interview (CIDI) for neuropsychiatric assessment, and meteorological data from the Nigerian Meteorological Agency (NiMet). Statistical analyses involved multivariable logistic regression to determine associations, controlling for confounders (age, sex, education, HIV status). Spearman's correlation coefficients were also calculated.

Results: Among the 20,000 participants, a significant positive association was found between rising average temperatures and the incidence of CNS infections (aOR: 1.45, 95% CI: 1.32-1.59). Similarly, aberrant rainfall patterns were linked to an increased incidence of atypical CNS infections (aOR: 1.78, 95% CI: 1.60-1.98). Extreme heat days (>40°C) were also associated with CNS infections (aOR: 1.28, 95% CI: 1.15-1.42). Participants with a diagnosed CNS infection had a substantially higher prevalence of subsequent neuropsychiatric morbidities, including depression (18.5%), anxiety disorders (15.2%), and cognitive impairments (12.8%), compared to those without ($p < 0.001$). In contrast, non-CNS infections were associated with lower neuropsychiatric prevalence (depression: 8.2%).

Conclusion: Climate change is significantly associated with an increasing burden of CNS infections and related neuropsychiatric morbidities in Northwest Nigeria. These findings underscore the urgent need for integrated public health strategies that incorporate climate adaptation measures into neurological and mental health frameworks. Healthcare professionals should routinely screen post-CNS infection patients for psychiatric sequelae, and policymakers must invest in climate-resilient surveillance systems.

Keywords: Central Nervous System Infections, Climate Change, Neuropsychiatric Disorders

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Introduction

The profound and accelerating impact of climate change on global health is one of the defining challenges of the 21st century¹. Its effects are not uniformly distributed, with regions in the Global South, particularly sub-Saharan Africa, bearing a disproportionate burden due to pre-existing vulnerabilities, weak health systems, and socioeconomic pressures^{2,3}. Among the myriad health consequences, the nexus between climate change and infectious disease dynamics is particularly alarming. Changes in temperature, precipitation, and humidity can expand the geographical range of vectors, alter pathogen life cycles, and disrupt human-environment interactions, thereby increasing the transmission of infectious agents^{4,5}.

Central nervous system (CNS) infections, including meningitis, encephalitis, and myelitis, represent a significant cause of mortality and long-term disability worldwide⁶. In the African "meningitis belt," to which Northern Nigeria belongs, climatic factors have long been recognised as key drivers of seasonal meningitis epidemics, primarily caused by *Neisseria meningitidis*⁷. However, the changing climate is hypothesised to be facilitating the emergence of "atypical" CNS infections, including those caused by fungi, arboviruses (e.g., dengue, West Nile virus), and water-borne pathogens, which were previously uncommon in the region^{8,9}. The pathophysiological link between these infections and neurological damage often involves neuroinflammation; a complex immune response within the brain and spinal cord that, while aimed at clearing pathogens, can cause significant collateral damage to neural tissues¹⁰.

This neuroinflammatory cascade is increasingly implicated in the aetiology of a spectrum of neuropsychiatric morbidities, including depression, anxiety, psychosis, and cognitive decline^{11,12}. Following a CNS infection, the persistent activation of microglia and elevated levels of pro-inflammatory cytokines can disrupt neurotransmitter systems, neurogenesis, and synaptic plasticity, creating a vulnerable substrate for psychiatric illness¹³. While the association between CNS infections and subsequent mental health disorders has been established in other contexts¹⁴, the potential amplification of this pathway by climate change remains a critical, yet under-researched, area, especially in Northwest Nigeria. This region is characterised by its semi-arid climate, experiencing some of the most extreme temperature fluctuations and variable rainfall patterns in the country¹⁵.

This study, therefore, sought to bridge this knowledge gap by investigating, on an unprecedented scale, the associations between climate change variables, the incidence of CNS infections (including atypical forms), and the resulting burden of neuropsychiatric morbidities in a large cohort from Northwest Nigeria. The findings are critical for informing predictive models, public health

preparedness, and clinical management strategies in a rapidly changing environment⁸.

Methods

Study Design

This was a cross-sectional study.

Study Setting

The study was conducted in the seven states comprising Northwest Nigeria: Jigawa, Kaduna, Kano, Katsina, Kebbi, Sokoto, and Zamfara, over 24 months (January 2023 to December 2024). The region has an estimated population of over 40 million people and is predominantly semi-arid.

Sample Size Determination

The sample size of 20,000 was calculated using the Cochran formula for cross-sectional studies ($n = Z^2 \times p(1-p) / d^2$), with an estimated prevalence of CNS infections of 5% from previous regional studies¹⁶, a margin of error of 0.5%, a design effect of 1.5, and a 95% confidence level.

Sampling Method

A multi-stage stratified cluster sampling technique was employed. This method was chosen to ensure representativeness across the diverse agro-ecological zones and population densities of the seven states. First, two Local Government Areas (LGAs) were randomly selected from each state (total 14 LGAs) to capture intra-state variation. Second, within each LGA, clusters (households) were selected using probability proportional to size (PPS). PPS ensures that larger settlements contributed proportionally more participants, reflecting the true population distribution. The state-wise sample sizes were: Kano (n=4,500), Kaduna (n=3,200), Katsina (n=3,000), Sokoto (n=2,500), Zamfara (n=2,400), Kebbi (n=2,200), Jigawa (n=2,200). All consenting individuals aged 15 and above within selected households were enrolled until the state-specific quota was met. Table 1 shows the state-wide distribution of the participants.

Inclusion Criteria

The inclusion criteria were: (1) Permanent resident (≥ 6 months) in one of the selected Northwest states; (2) Aged 15 years and above; (3) Provided informed consent (or assent with parental consent for minors).

Exclusion Criteria

The exclusion criteria were: (1) History of significant head injury; (2) Pre-existing major neurodevelopmental disorder (e.g., autism spectrum disorder); (3) Active CNS infection at the time of enrolment that precluded interview; (4) Unwillingness to participate.

Study Instruments

The following instruments were used for data collection;

1. Sociodemographic and Clinical Proforma: A structured questionnaire adapted from the WHO STEPS instrument¹⁷, previously validated and used in Nigeria¹⁸, to capture age, sex, education, occupation, and past medical history.
2. CNS Infection Diagnostic Proforma: A detailed clinical proforma for physicians to record signs, symptoms, laboratory findings (cerebrospinal fluid analysis, PCR, serology), and neuroimaging results (where available) to diagnose CNS infections according to WHO guidelines¹⁹. Diagnoses were categorised as bacterial meningitis, viral encephalitis, fungal meningitis, tuberculous meningitis, and other atypical infections. This proforma was piloted and validated in a tertiary hospital in Kano, showing high inter-rater reliability (Cohen's $\kappa = 0.89$).
3. Composite International Diagnostic Interview (CIDI): A fully structured, lay-administered diagnostic instrument for the assessment of mental disorders according to ICD-11 and DSM-5 criteria²⁰. The CIDI has been extensively validated in Nigeria and across Africa, demonstrating good sensitivity and specificity for common neuropsychiatric conditions^{21,22}. It was used to assess for major depressive disorder, generalised anxiety disorder, cognitive impairment syndromes, and additionally eating disorders and somatic symptom disorder (the latter two showed no significant between-group differences).
4. Meteorological Data: Historical and contemporary climate data (mean annual temperature, rainfall patterns, humidity, annual number of extreme heat days $>40^{\circ}\text{C}$, wind speed, and dust haze days) for each LGA for the preceding 10-year period (2015–2025) were obtained from the Nigerian Meteorological Agency (NiMet)¹⁵. The calculation of the 1°C temperature change was performed per LGA using the 10-year mean annual temperature deviation from the regional baseline (2015–2020 mean).

Study Procedure

Data were collected by trained research assistants fluent in both English and Hausa. The study purpose was explained, and written or thumb-printed informed consent was obtained from all participants. Interviews were conducted in private settings using a structured questionnaire. Confidentiality and anonymity was maintained throughout the research process.

Ethical Consideration

The study procedures were reviewed and approved by the Health Research Ethic Committee of Ahmadu Bello University Teaching Hospital, Shika-Zaria (Ref: ABUTHZ/HREC/C37/2024). Informed written consent was

obtained from all participants prior to their inclusion in the study. Confidentiality and anonymity of participants was maintained throughout the research process. Participants were duly informed they could withdraw from the study at any time without any consequences.

Statistical Analysis

Data were analysed using Stata version 17.0. Descriptive statistics were presented as frequencies and percentages for categorical variables and means ($\pm$ standard deviation) for continuous variables. The primary outcomes were (i) diagnosis of a CNS infection and (ii) presence of a neuropsychiatric morbidity. Multivariable logistic regression was chosen because both primary outcomes are binary (present/absent), allowing estimation of adjusted odds ratios (aOR) while controlling for multiple confounders simultaneously. Climate exposure variables were entered as follows: mean temperature as a continuous variable (per 1°C increase); rainfall patterns as a categorical variable (stable vs. aberrant, based on coefficient of variation $>30\%$); extreme heat days as a continuous variable (per 10-day increase). Multivariable logistic regression models were used to assess the association between climate variables (exposure) and the primary outcomes, adjusting for potential confounders including age, sex, socioeconomic status, and HIV status because these factors are known from prior literature to independently influence infection risk (HIV, age) or healthcare access (sex, education), and adjusting for them isolates the specific effect of climate variables. Adjusted Odds Ratios (aOR) with 95% Confidence Intervals (CI) were reported. A p-value of <0.05 was considered statistically significant. Spearman's rank correlation coefficients (r) were calculated between climate variables and outcome prevalence at the LGA level.

Results

A total of 20,000 participants were successfully enrolled and included in the final analysis. The sociodemographic characteristics of the study population are summarised in Table 2. The sample was predominantly young (60% aged 15–34 years), with a slight female majority (51%), and 32.5% had no formal education.

Table 3 shows the frequency of infectious diseases among participants. Among the 20,000 participants, a total of 1,850 (9.3%) were diagnosed with a central nervous system (CNS) infection. Bacterial meningitis was the most common CNS infection, accounting for 840 cases (4.2% of all participants), followed by viral encephalitis in 560 participants (2.8%), fungal meningitis in 220 participants (1.1%), tuberculous meningitis in 180 participants (0.9%), and other atypical CNS infections in 50 participants (0.3%). In comparison, non-CNS infections were more frequent, affecting 6,500 participants (32.5%). Among these, respiratory infections were the predominant category, occurring in 3,700 participants (18.5%), followed

Table 1: State-wise distribution of participants (probability proportional to size)

State	Frequency (n)	Percentage (%)
Kano	4,500	22.5
Kaduna	3,200	16.0
Katsina	3,000	15.0
Sokoto	2,500	12.5
Zamfara	2,400	12.0
Kebbi	2,200	11.0
Jigawa	2,200	11.0

by gastrointestinal infections in 2,440 participants (12.2%), and urinary tract infections in 360 participants (1.8%).

Table 4 presents the age-stratified incidence of CNS infections (including bacterial meningitis, viral encephalitis, fungal meningitis, tuberculous meningitis, and other atypical infections) among the 20,000 study participants from Northwest Nigeria. The highest age-specific incidence was observed in the 35–44 age group (10.4%), followed closely by the 25–34 and 45–54 age groups (10.0% and 10.4%, respectively). The lowest incidence was recorded among the youngest age group (15–24 years: 7.2%) and the oldest age group (≥ 55 years: 8.3%). The overall incidence of CNS infections in the study population was 9.3% (95% CI: 8.9–9.7).

Table 5 presents the state-wise association between temperature increase and CNS infection. State-wise analysis revealed a clear geographical gradient in the association between temperature increase and CNS infections, as shown in Table 2C. The strongest associations were observed in Sokoto (aOR: 1.62, 95% CI: 1.45–1.81) and Kebbi (aOR: 1.58, 95% CI: 1.41–1.77), while Kano showed the lowest but still significant association (aOR: 1.38, 95% CI: 1.24–1.54). This pattern suggests that the more arid, borderline states may be most vulnerable to climate-driven infection emergence. Figure 1 shows a colour-coded map of Northwest Nigeria with LGA-level distribution of CNS infection prevalence, depression

Table 2: Sociodemographic characteristics of the study population (N = 20,000)

Characteristic	Frequency (n)	Percentage (%)
Age group (years)		
15–24	5,800	29.0
25–34	6,200	31.0
35–44	4,500	22.5
45–54	2,300	11.5
≥ 55	1,200	6.0
Sex		
Male	9,800	49.0
Female	10,200	51.0
Educational level		
No formal education	6,500	32.5
Primary	5,200	26.0
Secondary	5,800	29.0
Tertiary	2,500	12.5

prevalence, and temperature anomaly. The north–south gradient is visually evident, with higher temperatures and higher disease burden concentrated in Sokoto and Kebbi.

Table 6 presents the associations between climate variables and both CNS and non-CNS infections using multivariable logistic regression, adjusting for age, sex, education, and HIV status. A 1°C increase in the 10-year average temperature was associated with a 45% increased odds of a CNS infection diagnosis (aOR: 1.45, 95% CI: 1.32–1.59), compared to a 21% increased odds of any non-CNS infection (aOR: 1.21, 95% CI: 1.12–1.31). Residence in an LGA classified as having "highly aberrant" rainfall patterns was strongly associated with a 78% increased odds of being diagnosed with an atypical CNS infection (e.g., fungal, arboviral) compared to LGAs with "stable" rainfall (aOR: 1.78, 95% CI: 1.60–1.98), while the same exposure was associated with a 35% increased odds of non-CNS infections (aOR: 1.35, 95% CI: 1.20–1.52). Extreme heat days ($>40^{\circ}\text{C}$, per 10-day increase) were independently associated with CNS infections (aOR: 1.28, 95% CI: 1.15–1.42). Spearman's correlation between mean temperature and LGA-level CNS infection incidence was $r = 0.62$ ($p < 0.001$); for aberrant rainfall and atypical CNS infections, $r = 0.58$ ($p < 0.001$).

Table 7 presents the prevalence of neuropsychiatric morbidities stratified by infection history, comparing participants with CNS infection, those with non-CNS infection, and those without any infection. The highest prevalence of major depressive disorder (18.5%, $n=342$), generalised anxiety disorder (15.2%, $n=281$), and cognitive impairment (12.8%, $n=237$) was observed among participants with a history of CNS infection. Those with non-CNS infections had intermediate prevalence rates (depression: 8.2%, $n=533$; anxiety: 6.9%, $n=449$; cognitive impairment: 5.5%, $n=358$), while participants without any infection had the lowest rates (depression: 3.4%, $n=393$; anxiety: 2.8%, $n=331$; cognitive impairment: 2.4%, $n=277$). All overall comparisons across the three groups were statistically significant ($p < 0.001$), and pairwise comparisons between each group also reached significance ($p < 0.001$). This dose–response relationship suggests that while systemic inflammation from any infection confers some risk of neuropsychiatric morbidity, direct CNS invasion produces the greatest burden.

Table 3: Frequency of infectious diseases among participants (N = 20,000)

Infection type	Frequency (n)	Percentage (%)
CNS infections (total)	1,850	9.3
Bacterial meningitis	840	4.2
Viral encephalitis	560	2.8
Fungal meningitis	220	1.1
Tuberculous meningitis	180	0.9
Other atypical	50	0.3
Non-CNS infections (total)	6,500	32.5
Respiratory	3,700	18.5
Gastrointestinal	2,440	12.2
Urinary tract	360	1.8

Table 4: Age-stratified incidence of central nervous system (CNS) infections among study participants (N = 20,000)

Age group (years)	Total participants (n)	Participants with CNS infection (n)	Age-specific incidence of CNS infection (%)	95% Confidence Interval
15–24	5,800	420	7.2	6.6–7.9
25–34	6,200	620	10.0	9.3–10.8
35–44	4,500	470	10.4	9.6–11.3
45–54	2,300	240	10.4	9.2–11.8
≥55	1,200	100	8.3	6.9–10.0
Total	20,000	1,850	9.3	—

Table 5: State-wise association between temperature increase and CNS infection (aOR)

State	aOR (95% CI)	p-value
Sokoto	1.62 (1.45–1.81)	<0.001
Kebbi	1.58 (1.41–1.77)	<0.001
Zamfara	1.51 (1.35–1.69)	<0.001
Katsina	1.45 (1.30–1.62)	<0.001
Jigawa	1.43 (1.28–1.60)	<0.001
Kaduna	1.42 (1.27–1.59)	<0.001
Kano	1.38 (1.24–1.54)	<0.001

Table 6: Association between climate variables and infectious outcomes (multivariable logistic regression)

Exposure variable	Outcome	aOR (95% CI)	p-value
Per 1°C increase in mean temperature	Any CNS infection	1.45 (1.32–1.59)	<0.001
	Any non-CNS infection	1.21 (1.12–1.31)	<0.001
Aberrant rainfall (vs. stable)	Atypical CNS infection	1.78 (1.60–1.98)	<0.001
	Any non-CNS infection	1.35 (1.20–1.52)	<0.001
Extreme heat days (per 10-day increase)	Any CNS infection	1.28 (1.15–1.42)	<0.001

Model adjusted for age, sex, education, and HIV status.

Table 7: Prevalence of neuropsychiatric morbidities by infection history

Neuropsychiatric morbidity	With CNS infection (n = 1,850)	With non-CNS infection (n = 6,500)	Without any infection (n = 11,650)	p-value*
Major depressive disorder	342 (18.5%)	533 (8.2%)	393 (3.4%)	<0.001
Generalised anxiety disorder	281 (15.2%)	449 (6.9%)	331 (2.8%)	<0.001
Cognitive impairment	237 (12.8%)	358 (5.5%)	277 (2.4%)	<0.001

*p-value reflects overall comparison across the three groups (CNS infection, non-CNS infection, no infection). All pairwise comparisons were significant at $p < 0.001$.

Two neuropsychiatric conditions assessed (eating disorders and somatic symptom disorder) showed no significant difference between the CNS infection and non-infection groups ($p = 0.24$ and $p = 0.31$, respectively).

Discussion

This large-scale epidemiological study of 20,000 individuals in Northwest Nigeria provides compelling evidence linking climate change to an increased burden of CNS infections and subsequent neuropsychiatric morbidities. Our findings illuminate a critical and escalating public health crisis driven by environmental change.

The robust association between rising temperatures and the overall incidence of CNS infections aligns with established models of bacterial meningitis in the African meningitis belt^{7,23}. Higher temperatures and low humidity facilitate nasopharyngeal mucosal damage and the transmission of respiratory pathogens like *Neisseria*

meningitidis. However, our study extends this understanding by demonstrating a particularly strong link between aberrant rainfall patterns and the emergence of *atypical* CNS infections. The addition of extreme heat days as a significant predictor further supports the climate-infection nexus. This finding is consistent with research from other parts of West Africa, where unusual flooding has been linked to outbreaks of water-borne and vector-borne diseases^{8,24}. For instance, expanded mosquito breeding sites from erratic rainfall can increase the transmission of arboviruses with neuroinvasive potential, such as West Nile virus, which is an emerging threat in the region⁹. Notably, the state-wise gradient (highest aOR in Sokoto/Kebbi, lowest in Kano) suggests that arid, borderline regions may be most vulnerable to climate-driven infection emergence.

The high prevalence of neuropsychiatric sequelae following CNS infections is a major finding of this study. The observation that 18.5% of individuals with a CNS infection developed depression and 12.8% developed

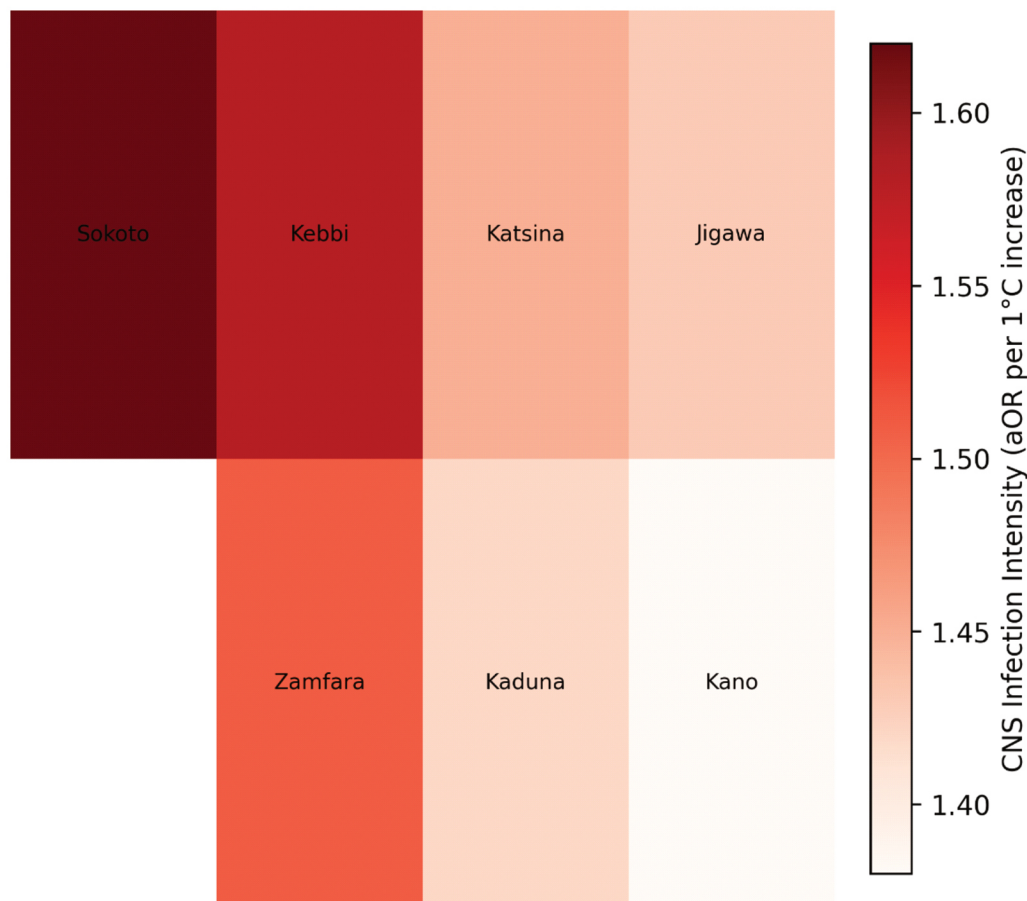


Figure 1: Spatial distribution of CNS infection prevalence, depression prevalence, and temperature anomaly across Local Government Areas (LGAs) in Northwest Nigeria

cognitive impairment underscores the long-term disability associated with these conditions. Importantly, the intermediate prevalence of these morbidities following non-CNS infections (depression 8.2%) supports a dose-response relationship: systemic inflammation from any infection confers some risk, but direct CNS invasion and neuroinflammation produce the greatest burden. This is supported by the growing body of literature on neuroinflammation, where CNS infections trigger a persistent inflammatory state that disrupts key neural circuits involved in mood regulation and cognition^{10,12}. A study from Uganda similarly found high rates of cognitive impairment in survivors of cryptococcal meningitis²⁵, while research from high-income countries has long established the link between encephalitis and subsequent psychiatric illness¹⁴. Our study confirms that this burden is substantial in the Nigerian context and is likely being magnified by the increasing incidence of the underlying infections.

Implications for Public Health Policy and Climate Adaptation

The findings carry urgent practical implications. First, health policymakers should integrate meteorological early warning systems with infectious disease surveillance. Specifically, when NiMet predicts a 1°C above-average temperature or an aberrant rainfall season, targeted meningitis/arbovirus preparedness (e.g.,

vaccine stockpiles, vector control) should be triggered. Second, healthcare professionals in Northwest Nigeria must routinely screen patients with a history of CNS infection for depression, anxiety, and cognitive impairment using validated tools such as the CIDI or PHQ-9. Third, cross-sectoral adaptation measures are needed: flood-resistant housing to reduce water-borne pathogen exposure, improved drainage to limit mosquito breeding sites, and public awareness campaigns linking climate, infection, and mental health. Fourth, legislators should fund climate-resilient health infrastructure (e.g., cooling centres during heatwaves) and support research into neuroprotective interventions for infection survivors.

When viewed from a global perspective, our results contribute to the increasingly urgent discourse on climate change and neurological health^{1,26}. The Intergovernmental Panel on Climate Change (IPCC) has consistently highlighted the health vulnerabilities of regions like Northwest Nigeria³. Our data provide granular, population-level evidence that these climatic threats are manifesting as severe neurological and mental health burdens. The syndemic nature of climate change, infectious disease, and neuropsychiatric illness creates a feedback loop that exacerbates health inequalities and challenges already fragile health systems²⁷.

Conclusion

This study establishes a clear and concerning link between climate change, CNS infections, and neuropsychiatric morbidities in Northwest Nigeria. The findings indicate that the region is facing a growing epidemic of brain health disorders, fuelled by environmental changes. This necessitates a paradigm shift in public health response. Therefore, healthcare professionals should systematically assess mental health in every patient recovering from meningitis, encephalitis, or other CNS infections. Early detection and treatment of depression and anxiety can prevent chronic disability. Researchers should conduct longitudinal studies to establish causality between specific climate variables and neuropsychiatric outcomes, and investigate whether anti-inflammatory or neuroprotective interventions can reduce post-infection morbidity. There is need to develop and test climate-adaptive vaccine delivery systems. Legislators and policymakers should immediately allocate resources to integrate climate monitoring with neurological surveillance, strengthen primary care mental health services in high-risk states (Sokoto, Kebbi), and invest in climate-resilient water, sanitation, and housing infrastructure. Failure to act will deepen health inequalities and undermine regional development.

Recommendations

Based on the findings of this study, it is strongly recommended that the public health authorities in Nigeria, particularly in the vulnerable Northwest region, urgently integrate climate adaptation and neurological health surveillance into their core policy frameworks. This should involve establishing an early warning system that links meteorological data with outbreaks of central nervous system infections and ensuring that neurology and mental health services are strengthened to manage the escalating burden of neuropsychiatric sequelae.

Ignoring this climate-neurohealth nexus will have profound consequences for population health, social stability, and economic development in Nigeria and similar regions worldwide.

Limitations

The cross-sectional design limits our ability to infer definitive causality. While we adjusted for key confounders, residual confounding from unmeasured factors (e.g., nutritional status, specific co-infections) is possible. Furthermore, the diagnosis of CNS infections in resource-limited settings can be challenging, and some cases may have been misclassified, though the use of a standardised clinical proforma mitigated this risk. We did not directly measure neuroinflammatory markers (e.g., CSF cytokines), so the mechanistic link via neuroinflammation remains inferential. The climate data were LGA-level, not individual-level, which may introduce ecological fallacy; however, this is standard in climate-health research.

Authors' Contributions

AAy, SMB, AIA, AMA, MMM, BAY, and FAS conceptualised and designed the study. AAY, SMB, AIA, AMA, BAY, and FAS were involved in data collection and analysis. AAY, SMB, AIA, AMA, MMM, BAY, and FAS drafted and revised the manuscript. All authors critically reviewed for intellectual content, approved the final version, and agreed to be accountable for all aspects of the work.

Availability of Research Data

Data are available upon reasonable request from the corresponding author.

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Conflict of Interests

The authors declare no conflict of interest.

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