



Visuo-Spatial Impairment in Patients Who Recovered from Lassa Fever Infection: A 30 Day Follow Up Observatory Study

Sunmonu Taofiki Ajao^{1*}, Owhin Sampson Omagbemi¹, Abejegah Chukwuyem², Kareem Adesola Olawumi², Etafo Ijeoma² and Ogunmodede Adebimpe Funmilola³

¹Department of Medicine, Federal Medical Centre Owo, Ondo State, Nigeria

²Department of Community Health, Federal Medical Centre, Owo, Ondo State, Nigeria

³Department of Medicine, Federal Medical Centre, Owo, Ondo state, Nigeria

*Corresponding Author: Sunmonu Taofiki Ajao, Department of Medicine, Federal Medical Centre, Owo, Ondo State, Nigeria.

Received: August 21, 2023

Published: September 22, 2023

© All rights are reserved by Sunmonu Taofiki Ajao., et al.

Abstract

Introduction: Lassa Fever infection is one of the viral haemorrhagic fevers that occur in epidemics in west African countries. It could affect the central nervous system and present with cognitive function impairment.

Aims and Objective: This study aimed to examine the visuo-spatial function in patients who recovered from Lassa fever infection especially within the 30 day follow up period.

Methods and Materials: Fifty patients who presented with serologically positive Lassa fever infection were studied along with fifty age, sex and educationally matched controls. The sociodemographic and clinical variables of the participants were obtained with structured questionnaire. Thereafter the patients were examined neurologically. and automated neuropsychological test were administered to all study participants. Blood samples were also collected from the patients for HIV and Hepatitis virus screening. Blood samples for Serum electrolytes, Urea and creatinine and full blood count were also collected. The results obtained were documented and analyzed with SPSS version 21.0 (Chicago Illinois).

Results: The mean age of the Lassa Fever patients was 41.94 ± 14.5 years while that of the normal controls was 37.34 ± 12.89 ($p > 0.05$). There were 27 males and 23 females in the Lassa fever group while there were 30 males and 16 females in the control group. The mean CVST time in the Lassa group was 22.59 ± 10.89 seconds while that of the control group was 17.89 ± 6.55 seconds ($p < 0.05$). Only prolonged hospital stay was associated with significantly prolonged mean CVST time ($p < 0.05$). The serum electrolytes level, degree of anaemia serum urea and creatinine had no impact on the patients mean CVST mean time. The prevalence of severely prolonged mean CVST time in the patients with Lassa fever was 18.8% while that of controls was 8%.

Conclusion: Prolonged mean CVST time was observed in patients from acute Lassa fever infection with recovery. Prolonged hospital stay was identified as a significant risk factor for this

Keywords: Cognition; Viral Haemorrhagic Fever; Lassa Fever

Introduction

Lassa fever is one of the viral haemorrhagic fevers which occurs in epidemics in West African Countries [1]. The disease was first identified in Borno State, Nigeria in 1969 and is endemic in Nigeria. Transmission occurs throughout the year however large sea-

sonal outbreaks occurs during the diseases on typically from December to April [2,3]. The vector for this virus is a multimammate rat (*Mastomys Nataliensis*) and more than 100,000 to 200,000 individuals are infected annually with Lassa fever virus leading to approximately 3,000 deaths annually [1,4]. The clinical presenta-

tion of Lassa fever ranges from asymptomatic disease to fulminant multi-systemic disease and case fatality could be up to 24% [4]. The central nervous system could be affected and patients may present with clinical features in keeping with meningitis, encephalitis, stroke, seizure disorders and sensorineural deafness [5].

There is paucity of literature on the cognitive functions in patients with acute Lassa fever infection in Nigeria and hence the need for this study.

Methodology

This was a prospective case-control study conducted at the infectious diseases ward and clinics of the hospital. About fifty serologically confirmed Lassa fever patients were studied along with fifty healthy age, sex and educationally matched seronegative controls over a period of eleven months.

Inclusion criteria for the patients included age greater or equal to 16 years, education of at least 6 years (many of the tests required reading and writing). Patients with blood seropositivity to Lassa virus antibodies (PCR) discharged within 30 days from the Infectious disease centre having tested negative to antibodies to Lassa virus (PCR).

Exclusion criteria

Patients lesser than 16 years of age, cognitive impairment such as Parkinsons disease, Alzheimers disease, traumatic brain, injury, use of anticholinergic drugs, stroke, epilepsy and patients who have major psychiatric disorders. Similar inclusion and exclusion criteria was applied to the normal controls that were recruited into the body.

Laboratory tests

Blood samples were collected from the patients for evaluation of serum electrolytes, urea and creatinine, liver enzymes (Liver function test) complete full blood count and erythrocytes sedimentation rate. Serological testing for hepatitis B surface antigen, anti HCV antibodies and retroviral screening was also done.

Ethical consideration and informed consent

Ethical clearance was obtained from the Research and ethics department of the Hospitals before the commencement of the study. In addition, written and informed consent was obtained from each study participant. The study was performed in conformation with

the World Medical Association declaration of Helsinki published in Journal of American Medical Association.

The study had three phases namely: the interview phase, physical/examination phase and cognitive assessment phase. During the interview phase, a structured questionnaire capturing the socio-demographics and clinical history of the participants was obtained followed by detailed general physical and neurological examination. The third phase of the study entailed the administration of the CVST subtest of the Iron Psychology "Fepsy" automated neuropsychological test battery to each study participant. Details on the use of the FePsy has been described elsewhere [6].

Assessment of brain damage

This was done with the aid of computerized visual searching Task (CVST) subtest of FePsy. The CVST has been accurate in correct discrimination of brain damage from psychiatric illness by previous studies [7-9]. A Nigerian study also reported sensitivity of CVST in identifying cognitive impairment in patients with epilepsy to be about 81.77% and 81.77% respectively [9]. The qualities of CVST tool that make it to be more sensitive than some other cognitive tools in detecting cognitive impairment include the fact that it is a mentally demanding test that uses visual information processes to interpret complex stimulus pattern and it also has a long testing duration; these were the reasons while a study on cognitive impact of epileptic form discharges showed that it was only CVST test that was sensitive to detection of epileptic form discharges on EEG in children with epilepsy [10]. Some search (CVST) could neutrally reflect actual visual search in real word naturalistic environment [11].

CVST assessment procedure

This task (CVST) has been adapted for microcomputer by Moorland, *et al.* as part of the Fepsy "Iron Psychology" in 1986. The task consists of finding a grid pattern out of 24 which matches the one in the centre of the screen (Figure 1). Grid patterns are displayed in a checkerboard fashion and are numbered 1 to 24. The target pattern is at the centre of the screen (with arrow pointing at it). The tester is expected to select a pattern identical to the target pattern in the centre of the screen by tapping the keyboard. Twenty four patterns are presented. After the 12 presentation the surrounding grid change. Each subject had a total of 24 trails and the participants is instructed to react as fast as possible. Result shows accuracy and speed of responses within the context of complex

visual information processing and perception mental changes. An abnormal prolonged CVST mean time duration indicate cognitive impairment (brain damage). The test was administered to the participants by an expert who gave technical advice and support.

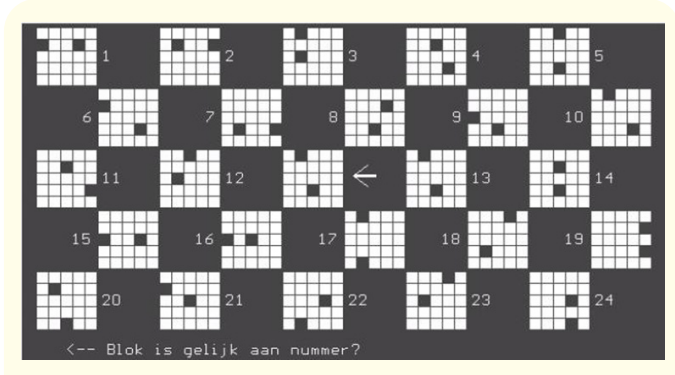


Figure 1: The Computerized Visual Scanning Test (CVST).

Statistical analysis

The data collected were analyzed with statistical package for social sciences (Version 21.0, Chicago Illinois). Frequencies and proportions were generated and they were compared by Chi-square test or Fischer’s Exact test. The Student-test and analysis of variance (ANOVA) were used to compare the variables as the case applied. Pearson’s moment of correlation was used as applicable and the level of significance was set at 0.05; p value < 0.05 was taken as being significant.

Results

Sociodemographic details

The mean age (SD) of the Lassa fever patients was 41.94(14.54) years while the mean age (SD) of the normal controls was 37.34 (12.69) years. There were 27 males and 21 females in the Lassa Fever group while there were 30 males and 16 females in the control group (p > 0.50). There were no significant differences in the sociodemographic details between the Lassa fever patients and controls (P > 0.05). This is illustrated in Table 1.

Variable	Cases		Controls		Statistic	P
	n	%	n	%		
Gender						
Male	27	(47.4)	30	(52.6)	1.281	0.20
Female	23	(59.0)	16	(41.0)	1.0250	
Level of Education						
6-12 years	25	(52.1)	23	(47.9)	1.293	0.52
13-16 years	20	(46.5)	23	(53.5)		
> 16 years	1	(1)	0	(0.0)		
Age groups						
16-24	11	(44.0)	14	(56.0)	1.281	0.53
30-44	19	(51.4)	18	(48.6)		
≥45	20	(58.8)	14	(41.2)		

Table 1: Sociodemographic Clinical Characteristics of patients with Lassa Fever infection and normal controls.

The cognitive function (CVST) performances of Lassa Fever patients and controls

The CVST (mean time) of the Lassa fever patients was significantly lower than the controls 22.5910.89 Vs 17.89 6.55 seconds (p < 0.05).

Impact of sociodemographic variables on CVST performances in patients with lassa fever

There was no statistically significant difference in CVST performances among age groups and educational status categories of the Lassa Fever patients (p > 0.05). Also, the gender of the patients had no influence on the CVST performances (p > 0.05) but the dura-

tion of admission significantly affected the cognitive function of the patients as patients who had prolonged hospital stay during admission performed poorly on CVST test ($p < 0.05$). This was i as shown in Table 2.

Impact of laboratory variables on cognitive functions in lassa fever patients

There was no significant impact of serum electrolytes and urea, platelets count, and anaemia on CVST performance of the Lassa fever patients ($P > 0.05$). This is as illustrated in Table 3.

Variables	n	CVST mean (seconds)	Statistics	P
Gender				
Male	27	19.650.74	-0.749	0.456
Female	22	21.1318.52		
Level of Education (Years)				
6-12	22	21.73 9.19	0.995	0.74
13-16	19	19.119.59		
> 16	1	15.28 0.00		
Age group (Years)				
16-29	11	19.87 9.82	1.688	0.191
30-44	13	5.82 0.96		
≥45	18	11.70 2.14		
Time spent at Admission (days)				
1-10	28	20.64 8.51	4.646	0.015
10-30	21	23.60 11.82		
> 30	1	51.47 0.00		

Table 2: Impact of sociodemographic variables on cognitive functions in Lassa Fever patients.

Variables	n	CVST Mean (second)	Statistic	P
Serum Chloride (mmol/L)				
<95	12	23.75	1.894	0.163
95-110	30	20.26		
>110	8	28.45		
Serum potassium (mmol/L)				
<3	3	18.06	7.078	0.352
3-5	31	21.57		
>5	5	28.17		
Serum Sodium (mmol/L)				
<120	12	22.38	0.316	0.731
120-140	32	22.05		
>140	6	26.29		
Serum Creatinine(umol/L)				
<50	5	23.45	0.033	0.965
50-132	27	22.14		

>132	7	22.39		
Serum Urea(mmol/L)				
<2.5	20	21.97	0.084	0.919
2.5-5.8	17	22.59		
>5.8	13	23.64		
Serum Calcium (mmol/L)				
<2.25		20.80	0.504	0.609
2.25 -		23.68		
>2.75		15.13		
PCV(%)				
<25	3	23.06	0.393	0.678
25-35	12	25.05		
>35	22	21.72		
Platelet Point (000,000/mm ³)				
<150	28	21.29	0.665	0.519
150-400	18	23.01		
>400	7	26.98		

Table 3: Laboratory variables on cognitive functions in Lassa fever patients.

Prevalence of severe Impairment in computerized visual searching task among the study participants

Out of 48 Patients with Lassa fever about 9 of the patients had severely prolonged CVST mean time (18.8%) while 4 Out of 50 normal controls studied had severely prolonged CVST mean time (8.0%).

The severely prolonged CVST mean time = CVST mean time + 2 standard Deviation = 17.89s + 2(6.55)s = 30.99s.

Therefore mean CVST time greater or equal to 30.99s was taken as severely prolonged CVST mean time.

Discussion

The Study evaluated the cognitive functions of Lassa fever patients and controls using the CVST subtest of Fepsy. The patients cohort consisted majorly of male patients which reflected the typical pattern of hospital attendance in Nigeria hospitals [13,14]. Only a few number of patients had tertiary education and there may be reason to suspect that Lassa Fever infections are commoner among individuals with lower educational level and low socio-economic status which was corroborated by a previous study in Ibadan, Oyo state Nigeria that found a low level of Knowledge of preventive

measures against Lassa fever infection among individuals in rural communities with Low level of education [15].

The length of hospital stay was prolonged (greater than 10days) in significant proportion of the patients and this was due to presence of complication from the illness especially those with clinically severe infection.

In this study patients with Lassa fever performed poorly on CVST task relative to normal controls and this may suggest that Lassa fever patients had poor relative to normal controls and this may suggest the presence of brain damage in these patients [7,8]. On careful analysis, it was found that the Lassa fever with prolonged hospital stay had worse performance on CVST assessment which may suggest that patients with severe Lassa infections with complications had susceptibility to development of residual brain damage after recovery from the illness. This findings aligned with the previous studies that found positive association between severity of illness and prolonged hospital stay [16-18].

The other sociodemographic variable such as age and gender had no influence on the patients performances on CVST test in this study which was in contrast to the previous studies which showed

that sociodemographic characteristics such as age, and level of education of the individuals have impacts on cognitive performances of the individuals [19-21]. Another plausible reason for this finding could be due to small sample size of the study in which majority of the patients had secondary level of education (6-12 years) and majority of the patients that were predominantly in the middle age group (30 - > 65 years).

Previous studies showed that derangement of serum electrolytes could influence the cognitive performances in patients with medical illness [22,23] But this study showed no association of serum electrolyte levels with performance on CVST task in patients with Lassa fever infection and this is in contrast to the findings in previous studies which serum electrolyte imbalances such as hyponatraemia, hypocalcaemia and hypochloraemia resulted in cognitive dysfunction [24-26]. The plausible reason for these findings could be because majority of the patients had normal serum electrolyte levels.

Elevated serum creatinine and urea were shown to be associated with worse cognitive functions in previous studies in Nigeria [27,28] but in this present study there was no demonstrable influence of elevated creatinine and urea on CVST task performance probably also because a large number of the patients had normal serum creatinine and Urea levels.

Previous studies [29,30] confirmed that anaemia could influence cognitive functions of some patients but this study was not in keeping with this findings probably because patients with severe anaemia were not included in this present study.

A recent study which evaluated cognitive functions among patients with chronic immune thrombocytopenia showed that cognitive impairment are common in the patients due to possible brain micro bleeds from auto-antibody mediated platelet destruction resulting is impaired memory and attention [31]. This was not corroborated in this study and the reason for the lack of association between cognitive performances and platelets count found in this study would need to be explored in further large scale studies in Lassa fever patients in the future.

In this study, the prevalence of severe impairment of performance task was 18.8% which was significantly higher than that of the controls (8%), prolonged hospital stayed due to complications

were present in these patients and further studies are needed to confirm the disease burden of the Lassa fever in the future.

Authorship Contributions

All the authors contributed to data collection, data analysis and writing of the manuscript.

Conflicts of Interest

All the authors have no conflict of interest with the study.

Acknowledgements

The authors thanked the Management of Federal Medical Centre, Owo, Nigeria for providing a conducive working environment for the study. The authors also thanked the staff of the Infectious diseases centre of Federal Medical centre, Owo for the recruitment of the Lassa fever patients for this study.

Data Sharing and Data Accessibility

The authors declared that the data supporting the findings in this study are available in the supplementary files section of this article.

Bibliography

1. Centre for Disease control (DSC). Lassa fever (2023).
2. World Health organization (WHO). Seasonal Variations in Lassa fever epidemics (2023).
3. Bakare EA, *et al.* "Mathematical modelling and analysis of transmission dynamics of lassa fever". *Journal of Applied Mathematics* (2020): 6131708.
4. Okokhere F, *et al.* "Clinical and Laboratory predictors of Lassa Fever outcome in a dedicated facility in Nigeria; an observational cohort study". *Lancet Infectious Disease* 18 (2018): 687-695.
5. Okokhere PO and Akpede GO. "Central nervous system manifestation of Lassa fever in Nigeria and the effect on mortality". *Journal of the Neurological Sciences* 1 (2013): ebo4.
6. Fepsy. 'The Iron Psyche'. A system for automated neuropsychological testing (2023).
7. Goldstein G and Kgc F. "Performance of Brain damaged schizophrenia and normal subjects on a visual searching task". *Perceptual and Motor Skills* 45 (1978): 731-734.

8. Da Mita MA, et al. "The validity of a computerized searching task as an indicator of brain damage". *Behavior Research methods and Instrumentation* 13 (1981): 592-594.
9. Ogunrin O, et al. "Predictive Validity and usefulness of visual scanning task in HIV/AIDS A case-control analysis". *African Journal of Neurological Sciences* 26.1 (2007): 1-7.
10. Aldenkamp AP, et al. "The cognitive impact of epileptiform EEG discharges: Relationship with type of cognitive task". *Child Neuropsychology* 19.4 (2004): 297-305.
11. Botch TL, et al. "Active Visual search in naturalistic environments reflects individual difference in classic visual search performance". *Scientific Report* 13 (2023): 631.
12. Moreland MC, et al. "A neuropsychological test battery for the Apple Ile". *International Journal of Man-Machine Studies* 25 (1986): 453-467.
13. Ulasi I. "Gender bias in access to health care in Nigeria. A study of end-stage renal disease". *Tropical Doctor* 38.1 (2008): 50-52.
14. Odelola TD. "Healthcare utilization among rural women of child-bearing age; a Nigerian experience". *Pan African Medical Journal* (2015): 171.
15. Awosanya EJ. "Post -epidemic awareness and knowledge of Lassafever among residents of affected community in Ibadan, Oyo state". *Veterinary World* 11.8 (2018): 1059-1063.
16. Horn Sd, et al. "The relationship between severity of illness and hospital length of stay and mortality medical Care". 29.4 (1991): 305.
17. Setareh M, et al. "Severity of illness affecting the length of stay and outcomes in patients admitted to intensive care units, Iran 2019". *Journal of Education and Health Promotion* 10 (2021): 142.
18. Plante J, et al. "Cognitive impairment and length of stay in acute care hospitals: A scoping review of the literature". *Canadian Journal of Aging/La Revue Canadienne av vitalissement* 40.3 (2019): 405-423.
19. Ogunniyi A, et al. "Influence of education on aspects of cognitive functions in non - demented elderly Nigerians". *Neuroepidemiology* 10.5-6 (1991): 246-250.
20. Rijnen SJM, et al. "Evaluation of normative data of a widely used copmputerized neuropsychological test battery Applicability and effect of sociodemographic variables in a Dutch Sample". *Assessment* 27.2 (2020): 373-383.
21. Corlier FW. "Principal component analysis suggests multiple dimensions of memory inhabitation are differently affected by age". *Frontiers in Psychology* (2023): 13.
22. Rondanelh M, et al. "Electrolytes and cognitive function in the elderly; relationship between serum sodium and chloride concentration and psychometric scores". *Panminerva Medica* 40.3 (1998): 191-195.
23. Bialecka Debek A and Pietruszka B. "The association between hydration status and cognitive function among free-living elderly, volunteers". *Aging, Clinical and Experimental Research* 31 (2019): 695-703.
24. Brin Kkoeter RT, et al. "Impact of resolution of hyponatraemia on neurocognitive and motor performance in geriatric patients". *Scientific Reports* 29.1 (2019): 12526.
25. Lee S, et al. "Serum sodium in relation to various domains of cognitive function in the elderly US population". *BMC Geriatrics* 21 (2021): 328.
26. Saponaro F, et al. "Serum calcium levels are associated with cognitive functions in hypoparathyroidism; an neuro - psychological study in an Italian cohorts of patients with chronic post surgical hypoparathyroidism". *Journal of Endocrinological Investigation* 45.10 (2021): 1909-1918.
27. Owolabi LF, et al. "Cognitive functions assessment in patients with end stage renal disease in Nigeria: A single centre experience". *Annals of African Medicine* 15.13 (2016): 138-144.
28. Egbi OG, et al. "Prevalence and determination of cognitive impairment in patients with chronic Kidney disease; a cross-sectional study in Benin - City, Nigeria". *Annals of African Medicine* 14.2 (2015): 75-81.
29. Sunmonu TA, et al. "Cognitive functions in patients with newly diagnosed HIV infection in a tertiary health facility in south - west Nigeria. Assessment using computer assisted neuropsychological test battery". *eNuerological Science* 3 (2016): 54-59.

30. Qin T, *et al.* "Association between anaemia and cognitive decline among middle- aged elderly; evidence from Chinese health and retirement Longitudinal study". *BMC Geriatrics* 19 (2019): 305.
31. Kuter DJ, *et al.* "Cognitive impairment among patients with chronic immune". *Thrombocytopenia Blood* 140 (2022): 8422-8424.