

Impaired Psychomotor Speed Functions in Patients Who Recovered from Acute Lassa Fever Infection: A 30-Days Follow-Up Study

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Abstract

Background: Some Patients with lassa fever patients do present with delirium and encephalitis symptoms during the vital period that there is paucity of information on the cognitive and mental status of patients who have recovered from acute lassa fever infection.

Aim and Objectives: To determine the cognitive functions of patients who recovered from Lassa fever during a 30-day follow up study.

Methods: Fifty patients with Acute Lassa fever infection were studied along with fifty healthy normal controls who are seronegative to Lassa antibody test. Sociodemographic profile and clinical of the patients were collected along that of the normal, sex and educationally matched controls. Some Blood Investigation were collected from the patients for haematological test, renal and liver functions tests. Patients and Normal controls had neuropsychological test battery and the result were documented. The statistical data were analyzed by SPSS version 22.

Result: The mean age of Lassa fever patients was 41.94 ± 14.54 years while that of the controls was 37.34 ± 12.89 . There was no significant difference in the sociodemographic profiles of the Lassa fever patients and the controls subject ($p > 0.05$). The Lassa patient has significantly prolonged auditory and binary choice reaction times when compared with normal controls ($p < 0.05$). while there was no difference in the visual reaction times between the Lassa fever patients and controls ($p < 0.05$). There was severe impairment in auditory reaction times in 14% of Lassa fever patients in the Auditory reaction times subtest.

Conclusion: Patients who recovered from Lassa fever presented with features of psychomotor speed impairment during a 30-day follow up period and this was severe in auditory support is advocated for these patients to improve their cognitive and self-management practices.

Keywords: Lassa Fever; Viral Haemorrhagic Fever; Cognitive Functions; Nigeria

Abbreviations

ART: Auditory Reaction Time; BCRT: Binary Choice Reaction Time; BCRA: Binary Choice Accuracy; β : Beta; CDC: Centre for Disease Control; CVST: Computerized Visual Searching Task; δ : Delta;

Fepsey: Iron Psychology; LF: Lassa Fever; n: Number; p: Level of Significance; RMT: Recognition Memory Test; t: Student t-test; χ^2 : Chisquare Test

Introduction

Lassa fever infection is one of the haemorrhagic fever diseases in West Africa including Nigeria [1]. The Primary host for the Virus is a Multimammate rat (*Mastomys Nataliensis*). About 100,000 to 300,000 Lassa fever infections occur annually leading to approximately 5,000 death annually [1,2].

The Initial presentation Lassa fever ranges from asymptomatic infection to multisystemic disease with a case fatality rate of about 24% [3].

The Africa Centre for Disease Control (CDC) reported in 2018 that 114 out of 413 patients died from Lassa virus infection in Nigeria [4]. Central nervous centre presentation of Lassa fever (LF) infection include aseptic meningitis, encephalitis, seizures and global encephalopathy [5,6], ataxia, bilateral hearing loss among others . In the recently published report from Federal Medical Centre, Owo [7], where 510 patients were studied prospectively and the clinical spectrum of specific CNS presentation in LF infection are as follows; seizure (5%), Delirium (4%), Confusion (4%) Headache (37%),focal neurologic defect (1%) and impaired hearing/Vision (1%). There is paucity of information on the cognitive function on cognition on the patients who received from LF infection in Nigeria.

Cognitive impairment in post – discharge period could affect patient quality of life, medication adherence and follow -up clinical attendance.

Objectives of the Study

- To determine the prevalence of cognitive impairment in the first 30days period in patients who have recovered from LF infection.
- To determine the pattern of cognitive impairments in patients with LF infection within 30 days post recovery period.

Methodology

Study Site: the study was conducted in the medical outpatient clinic of Federal Medical Centre ,Owo, Ondo State, Nigeria over a twelve month period.

Study design and population

The study was a prospective study aimed to determine the prevalence and patterns of cognitive function in Lassa fever Virus patients within 30days post recovery period. Fifty consecutive patients that were discharged from the Infectious Disease Centre

(IDC) Unit, FMC Owo and have tested negative to repeat ELISA blood test would he studied along with 50 - age, Sex and educationally matched normal seronegative control subjects.

Inclusion criteria

All Confirmed Cases of LF patients that were discharged from the IDC ward and have tested negative to repeat polymerase chain reaction (PCR) for LF virus infection would be recruited within the first 30 days in the post recovery period.

The patients and controls must be ≥ 16 years old.

Exclusion criteria

- Age of Patients ≤ 16 years old presence of co-morbid illnesses that could affect cognitive function in the study participants such as head Injury, other central nervous system infection other than Lassa virus infection, presence of premorbid dementing illnesses such as Parkinsons disease, stroke, use of psychoactive drugs or presence of co-morbid major psychiatric illnesses.
- Lassa Fever Patients with Positive PCR test result in the post recovery period. Similar inclusion and exclusion criteria were used for recruitment of the matched controls.
- Ethical Consideration and Informed consent. Ethical Clearance would be obtained from Research and Ethics Committee of the Federal Medical Centre, Owo before commencing the Study. In addition, verbal and duly signed Informed consent would be obtained from the patients and control Subjects Participating in the study.

Procedure

Fifty patients who tested negative to Lassa virus Infection after being discharged from the infections Disease control centre of the hospital were recruited during follow up clinic attendance period and studied along with 50 age, sex and educationally matched normal control subjects. A structured questionnaire which contains information on the sociodemographic and clinical information about the patients were completed. Thereafter an automated neuropsychological Test Battery “Fepsy” (Iron Psychology) was administered to each patient and control subject. “Fepsy” have been used extensively in Nigeria to assess cognitive functions of the Patients previously [7-9]. The Memory function,(verbal and non-verbal) would be assessed by the Recognition Memory Task aspect of the “Fepsy” while the psychomotor speed of patients were assessed

with the visual reaction times and auditory reaction times aspect of Fepsy. The patients attention and concentration function were assessed with the aid of Binary choice reaction times and continuous performance aspects of the “Fepsy” Instrument. The “Fepsy” Instruments was used to administer the neuropsychological test via a computer to both the patients and controls subjects and the results were usually displayed on the screen and stored in the computer thereafter.

Data analysis

The Statistical package software for social Sciences (SPSS) version 21.0 was used to analyze the data collected from the study. Frequencies and proportions were generated and presented in Tables and Figures where necessary. Comparison of proportions and percentages were done using the Chi square test or Fischer’s exact test. The Independent student t-test was used for comparison of means for continuous variable as necessary. Analysis of Variance (ANOVA) was used to compared differences in variables that are more than two while Pearson’s moment of correlation would be used in the analyses were necessary. The level of significance was set at 0.05 and $p < 0.05$ was taken as being significant.

Results

Sociodemographic profile

The mean age of the Lassa fever patients was 41.94(14.54) while that of the normal controls was 37.34 +12.89 There were 29 males and 23 females in the Lassa fever patients group. The other aspect of sociodemographic features of the Lassa fever patients are as highlighted in table 1.

Variable	Cases n %	Controls n %	Statistic	p
Age (years)				
16-29	11(49)	14(56.0)	1.281	0.527
29-45	19(51.4)	18(48.6)		
>45	20(58.8)	14(41.2)		
Level of Education (years)				
6-12	25(52.1)	23(47.9)	1.293	
12-16	20(46.5)	23(53.5)		0.524
>16	1(10.0)	0(0.0)		
Sex				
Male	29(47.4)	30(52.6)	-1.250	
Female	23(59.0)	16(41.0)		0.264

Table 1: Demography of the cases and Coatreole.

Frequency distribution of sociodemographic profile of patient with lassa fever

The frequency distribution of the sociodemographic and clinical characteristics of the Lassa fever patients are as shown in table 2. The Lassa fever patients had prolonged auditory reaction times when compared with the normal controls ($P < 0.05$).

Variables	n	%
Time Spent on admission		
1-10	28	56.9
11-30	21	42.0
>30	1	2.0
HIV		
+ve	0	0
-ve	18	100.0
HBsAg		
+ve	0	0.0
-ve	18	100.0
Anti HCV		
+ve	0	0.02
-ve	18	100.0
PCV (%)		
<25	3	8.1
25-45	12	32.4
>45	22	159.5
Serum Creatinine (mmol/L)		
<50	20	12.8
50-132	27	69.2
>132	7	17.9
Serum Urea(mmol/L)		
<2.5	20	40.0
2.5-5.8	17	34.0
>5.8	13	26.0
Serum Potassium (mmol/L)		
<3.0	3	7.7
3.0-5.0	31	79.5
>5.0	5	12.8

Table 2: Clinical and laboratory Characteristics of patients with lassa fever.
n- Number of variables
%- Percentage.

Cognitive functions in patients with Lassa fever Vs Normal controls

The binary choice reaction times were also prolonged among the Lassa fever patients when compared to the normal controls (P > 0.05). There was no significant difference in visual reaction times between the Lassa fever patients and normal controls. (p > 0.05). This is as highlighted in table 3.

Cognitive Sub-tests	Lassa fever Patient (n=50) Mean	Controls (n=50) Mean	Statistics	p
Mean age	41.94 ± 14.54	37.34 ± 12.89	3.453	0.097
ART (ms)				
ART Dom	621.68300.9	435.30217.3	2.575	0.001
ART (Non Dom)	571.02 3 63.63	378.20 274.76	1.814	0.012
VRT(ms)				
VRT(Dom)	538.56 363.63	434.93 139.29	0.774	0.073
VRT(Non Dom)	502.92 395.00	413.43 132.43	0.156	0.147
BCR (Ms)				
BCR (Mean Time)	614.04177.68	529.52145.44	2.510	0.007
BCR Accuracy	0.95 0.12	0.95 0.75	0.156	0.876

Table 3: Cognitive performance of Lassa Fever patients within 30 days of discharge Vs normal controls.

Analysis done by student T-test.

p = Level of significant .

p < 0.05 = Significant.

Prevalence of severe cognitive impairment with Lassa fever

Table 4 showed the burden of severe cognitive impairment in various cognitive functions subtests in patients with Lassa fever.

Impact of sociodemographic and clinical factors on cognitive functions in patient with Lassa fever

Table 5 highlighted in details the impact of sociodemographic and clinical factors on the cognitive functions of the Lassa fever patients. Patients who were older and have 12 – 16 years of education have prolonged auditory and visual reaction times when compared to other Lassa fever patients groups in the 30 day follow up period.

Cognitive Subjects	Lassa fever + Severe Cognitive Impairment n	Lassa fever patients with normal cognitive score n	Percentage of Lassa Fever patient with severe cognitive impairment	Statistics	p
ART (Dom)	7	43	14.0	4.498	0.034
ART (Non -Dom)	3	47	61.0	2.627	0.162
VRT (Dom)	9	41	18.0	0.276	0.600
VRT (Non-Dom)	5	45	10.0	0.168	0.602
BCRT (mean)	4	45	8.0	0.167	0.075
BCR Accuracy	0	48	0.0	-	-

Table 4: Proportions of lassa fever patients with severe cognitive Impairment.

% - Percentages

N= numbers

P== level of significance

P<0.05 = significant

Analysis done by Chisquare test.

Discussion

In this study the Lassa fever patients were majorly females and this due to the hospital attendance pattern that are typical of Africans where male tend attend hospitals more than their female counter parts due to some social and economic reasons [10,11]. The majority of the patient were in the middle age group and this may not be surprising because this age groups are more exposed to the risk factors and contact with infected individuals.

In this study the patients with Lassa fever had prolonged psychomotor speed when compared to control subjects and this may be an important issues to focus on as information processing speed is essential determinant of learning of self management skills such medication adherence, understanding doctors prescription and adherence to other preventive strategies recommended by the health practitioners of the patients [12-14]. Complex information processes/attention functions that were impaired in these patients could also worsened their medication adherence.

Variables	n	ART Dom (ms)	ART Non- Dom (ms)	VRT Dom (ms)	VRT Non- Dom (ms)	BCR mean (ms)	BCRA
Sex							
Male	29	495.68 ± 287.22	450.07 ± 389.29	485.54 ± 306.39	452.35 ± 328.17	550.89 ± 148.39	0.96 ± 0.06
Female	23	586.00 ± 260.80	520.36 ± 359.65	493.82 ± 248.74	471.28 ± 260.92	592.24 ± 193.12	0.94 ± 0.13
t		-1.570	-0.896	-0.140	-0.301	-1.167	0.825
p		0.120	0.373	0.889	0.764	0.246	0.411
Level of Education							
6-12 years	25	580.58 ± 301.86	523.29 ± 415.66	547.00 ± 339.40	502.15 ± 355.79	614.87 ± 187.53	0.94 ± 0.13
12-16 years	20	477.40 ± 255.90	440.09 ± 347.45	438.05 ± 207.16	419.77 ± 238.34	516.17 ± 131.60	0.96 ± 0.05
>16 years	1	715.00 ± 0.00	568.00 ± 0.00	518.00 ± 0.00	674.00 ± 0.00	711.00 ± 0.00	0.97 ± 0.00
F		(2,89) = 1.738	(2,89) = 0.553	(2,89) = 1.663	(2,89) = 1.056	(2,86) = 4.392	(2,86) = 0.534
P		0.182	0.577	0.195	0.352	0.015	0.588
Age group							
16-29	11	440.72 ± 225.29	361.52 ± 181.25	438.56 ± 181.99	415.60 ± 175.04	541.96 ± 162.54	0.93 ± 0.16
30-44	19	502.82 ± 267.97	429.43 ± 281.24	424.70 ± 130.92	390.46 ± 99.47	548.27 ± 160.65	0.96 ± 0.05
≥45	20	631.94 ± 302.04	618.26 ± 515.96	595.44 ± 411.70	568.44 ± 457.49	611.90 ± 178.25	0.96 ± 0.07
F		(2,93) = 3.954	(2,93) = 4.101	(2,93) = 4.012	(2,93) = 3.651	(2,90) = 1.629	(2,90) = 0.827
P		0.022	0.020	0.021	0.030	0.202	0.441
Time spent at admission							
1-10	28	606.89 ± 276.99	582.04 ± 499.48	535.71 ± 443.05	540.79 ± 507.50	591.92 ± 144.71	0.97 ± 0.02
10-30	21	634.00 ± 341.42	554.29 ± 352.22	547.95 ± 241.18	450.67 ± 172.08	635.05 ± 215.59	0.93 ± 0.18
>30	1	777.00 ± 0.00	614.00 ± 0.00	421.00 ± 0.00	540.00 ± 0.00	769.00 ± 0.00	0.97 ± 0.00
F		(2,47) = 0.178	(2,47) = 0.028	(2,47) = 0.058	(2,47) = 0.308	(2,44) = 0.713	(2,44) = 0.906
P		0.837	0.972	0.944	0.736	0.496	0.412

Table 5: Impact of Demography and clinical factors on community functions in Lassa fever patients.

Older patients exhibited poorer psychomotor speed when compared with controls and this is similar to what was observed in other medical conditions in which cognition such as epilepsy, Africa, Diabetes [13-17]. The reason for these may be due to cognitive decline that accompany aging process [18,19].

Previous reports on the central nervous system presentation of Lassa fever infections in Nigeria were few case series reports lassa fever presentation with features of sensorineural deafness (2D), Lassa fever encephalitis and Lassa fever delirium [21] and there is paucity of literature on the cognitive functions of Lassa fever in Nigeria.

Conclusion

The patients with Lassa fever presented with measures of prolonged psychomotor speed and impaired attention during the 30 days follow up period. It is recommended that these patients should be given psychosocial support to improve their medication adherence and vocational support. The result findings from his study need to be confirmed in further large studies Lassa fever endemic areas.

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