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Prevalence and pattern of cognitive impairment among Nigerians with heart failure

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ABSTRACT

Introduction

Cognitive impairment following heart failure is a major determinant of clinical outcomes and the patient's ability to adhere to the treatment regimen. It significantly affects their quality of life. Among patients with heart failure, rates of anxiety and depression are reported to be between 13– 39% and have further negative impacts on their cognitive function.

Methods

Our study enrolled 78 heart failure patients, diagnosed using Framingham's criteria. The aim of our study was to determine the prevalence of cognitive and mood impairment among these patients with heart failure. We also evaluated them for the pattern of cognitive dysfunction. Community Screening Instrument for Dementia (CSID) and Trail Making Test A (TMTA) were used to assess the subjects for cognitive impairment across several domains. The Hospital Anxiety and Depression Scale (HADS), a self-assessment instrument, was used for assessing mood disorders. Significance level was set at a p-value <0.05.

Results

The mean age of subjects was 51.5±14 years. Cognitive impairment was present in 42% using the CSID and 26% on the TMTA. We noted anxiety and depression in 5% of the subjects. A significant correlation was observed between the performance of cognitive tasks by the patients and their age (p-value = 0.037) and estimated glomerular filtration rate (p-value = 0.002). Logistic regression of the variables with performances assessed using CSID performance was significant for age (p-value = 0.032), total cholesterol (p-value = 0.052), low density lipoprotein (LDL) (p-value = 0.017) and eGFR (p-value = 0.046).

Conclusion

We observed a high prevalence of cognitive and mood impairment among the heart failure patients enrolled in this study. The CSID is a better predictor of cognitive impairment for the different cohorts enrolled in our study.

Keywords: Heart failure, Cognitive impairment, Depression and Anxiety

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INTRODUCTION

Cardiac failure is a rapidly increasing health problem worldwide with global prevalence reported to be more than 37 million cases annually.[1] The prevalence of cognitive impairment in cardiac failure varies depending on the population studied, the diagnostic criteria for heart failure used, the study design and the neuropsychiatric test administered[1] but is documented in 25–75% of patients with cardiac failure and is an important determinant of their quality of life and mortality.[2,3] Anxiety and depression also occur frequently among heart failure patients and are important determinants of the occurrence of cognitive impairment.[4, 5] Ansa et al [4], in a prospective cross-sectional screening of 100 consecutive heart failure patients presenting at two cardiac clinics in Southern Nigeria, observed a prevalence of anxiety, depression and combination of both anxiety and depression of 16%, 13% and 39% respectively. They also observed that younger age was the main predictor of psychological distress among their cohort of heart failure patients.

Despite the high prevalence of cognitive dysfunction in heart failure, it is still under-reported because of its subtle occurrence, poor assessment skills by clinicians and lack of a consensus guideline of assessment tools.[3,6] The presence of cognitive impairment in patients with heart failure results in increased risk of worsening symptoms and hospital readmission possibly due to impairment of executive function, self-care and decision making.[1,7,8] This will impair the patient's ability to adhere to treatment regimens and instructions regarding behavioural adjustments needed for their optimal care.[1, 7]

The exact pathogenesis and course of cognitive impairment in cardiac failure is not fully understood,[7] but both structural and functional changes have been documented in brain imaging of patients with cardiac failure.[1] Some of the changes observed at a higher rate in cardiac failure patients include cerebral infarct, atrophy in the cortex, reduced size of the mammillary bodies with hypoxic-ischemic changes, reduced putamen volume, decreased parietal creatinine levels and sodium concentration.[8-11] Čelutkienė et al listed atrial fibrillation, atherosclerosis, diabetes, anaemia, physical inactivity, depression and malnutrition as contributing factors to cognitive impairment in heart failure.[3]

The cognitive impairment in heart failure commonly involves memory, attention, language, visuospatial function, executive function and psychomotor speed.[2,6] Other studies have observed that delayed and immediate memory are more likely to be impaired in heart failure patients than semantic memory.[7, 12]

Despite several reports on cognitive assessment in patients with heart failure, no consensus instrument has been agreed for its evaluation,[13] though Montreal Cognitive Assessment (MoCA) is a very useful tool for screening heart failure patients for cognitive dysfunction in the domains commonly affected.[6] Other neuropsychological tests, all of which have limited domain assessment, have been used including the Mini Mental State Examination (MMSE), Six-Item Screener (SIS), Hodkinson Abbreviated Mental Test (AMT), Short Portable Mental Status Questionnaire, Blessed Orientation-Memory and the Clock drawing test (CDT), which can detect deficit in executive function but is not suitable in evaluating short-term memory and verbal learning.[6]

METHODS AND MATERIALS

Our cross-sectional single-centre descriptive study enrolled 78 patients (37 male and 41 female) aged 14 years and above with various types of heart failure diagnosed on Framingham's criteria,[14] who presented consecutively at the cardiac clinic and medical wards of the University of Calabar Teaching Hospital between January 2018 to December 2020. We excluded patients with a previous history of stroke, traumatic brain injury and psychiatric illness. Patients with delirium and renal failure were also excluded. Patient demographics and clinical data were obtained using a semi-structured questionnaire after informed written or verbal consent was obtained. The objective of this study was to determine the prevalence and pattern of cognitive impairment among patients of all New York Heart Association (NYHA) classes of heart failure.[15] We also aim to determine the correlates of cognitive impairment. We further determined the relationship between mood disorders and the severity

of cognitive impairment in our cohort. These issues have not been widely studied and reported in the sub-Sharan Africa region.

Participants were screened for cognitive and mood impairment using CSID, TMTA and HADS. The CSID assesses several cognitive domains including memory, language, attention, calculation and praxis. It has been validated for reliability and suitability in assessing cognitive function among several patient groups in Nigeria.[16-18] In order to apply the CSID to the evaluation of our subjects, we pre-tested it in the study environment among healthy subjects and obtained an average total CSID score of 61.2. Performance below two standard deviations from this population score, which gave a score of 45, was set as the cut-off point below which interviewees were seen as having cognitive impairment.

TMTA is a neuropsychological pen-and-paper instrument that tests for ability to shift between tasks (cognitive flexibility), psychomotor speed, sequencing and visual attention; these are key components of executive function. Participants were expected to draw a line linking numbers 1 to 25 scattered in space. Performance was judged based on time taken to complete the task. Subjects who spent more than 78 seconds to complete the task are judged to have cognitive impairment,[19, 20] this timeframe has been validated in previous studies in our environment. [16, 17] The Hospital Anxiety and Depression scale (HADS) categorizes mood assessment into normal, borderline or abnormal depression and anxiety respectively based on their scores.[21]

Standard M-Mode and 2D transthoracic echocardiography was obtained for all subjects using a CHISON IVi-60 Echocardiography machine with a 3.5 MHz phased array transducer. Measurements of left ventricular internal diameter, interventricular septum and posterior wall thickness was performed according to the guidelines of the American Society of Echocardiography.[22] Left ventricular (LV) systolic function was determined using the Ejection fraction. LV diastolic function was assessed using trans-mitral flow velocity. Peak velocities of the E wave and A waves were measured using Pulsed Wave Doppler. The ratio of the E wave to A wave was used in determining the presence and grade of diastolic dysfunction. The fasting lipid and electrolyte assay results for each participant was obtained from their hospital records.

Data from this study was analyzed using Statistical Package for Social Science (SPSS) software version 21. Categorical variables were compared using the Chi-squared test. Multivariate analysis was carried out using logistic regression models to identify correlates. The level of statistical significance was fixed at $p \leq 0.05$.

This study conformed to the ethical guidelines on Human Research of the 1973 declaration of Helsinki as modified in 2004.[23] Informed written or verbal consent was obtained from all subjects after the study was carefully explained to them. Information regarding each subject was treated with strict confidentiality. Participation in the study had no financial benefits and involvement or otherwise had no bearing on the standard or quality of care offered to the participants.

RESULTS

The mean age of the subjects was 51.5±14 years; 51% were aged 46-65 years. Among the study population, 55 (70.5%) had hypertension, 16 (20.5%) had type 1 or 2 diabetes mellitus (DM), while 16 (12.5%) had both hypertension and DM. The functional class of our subjects based on NYHA functional classification stage 1 to 4 was 15.4%, 44%, 35% and 6% respectively. Hypertensive heart disease was responsible for the aetiology of heart failure in 63% of the subjects. Most of our subjects had very low atherogenic risk, with 94% having <0.11 atherogenic index of plasma. The detailed summary of the demographic, laboratory and clinical characteristics of study participants are as shown in Table 1, 2 and 3.

Table 1 Demographic distribution of the study group

Variable	Frequency (n= 78)	Percentage (%)
Gender		
Male	41	53
Female	37	47
Age category (years)		
<30	3	4
30-45	24	31
46-65	40	51
>65	11	14
Educational status		
No formal education	12	15
Primary (0-6 years of education)	20	26
Secondary (7–12 years of education)	21	27
Tertiary (> 13 years of education)	25	32
Marital status		
Single	2	3
Married	63	81
Divorced	1	1
Widowed/widower	12	15
Occupation		
Unemployed	6	8
Self-employed	25	32
Trader	15	19
Civil servant	27	34
Military/paramilitary	2	3
Others	3	4
Alcohol use		
Yes	21	27
No	57	73
Tobacco use		
Yes	5	6
No	73	94

Table 2 Mean Demographic, Clinical and Laboratory Characteristics of Patients

Variable (N= 113)	Mean (SD)
Systolic Blood Pressure	125 (±22.5) mmHg
Diastolic Blood Pressure	80.8 (±11.8) mmHg
BMI of Patients	27.0 (±6.1) Kg/m^2
Total Cholesterol	4.2 (±1.1) mmol/l
HDL	1.7 (±2.2) mmol/l
LDL	2.4 (±0.8) mmo/l
VLDL	0.7 (±0.5) mmol/l
TG	1.2 (±0.5) mg/dl
Atherogenic Index of Plasma	-0.1(±0.3)
Left Ventricular Ejection Fraction	47.2 (±14.9)
E/A Ratio	1.6 (±0.8) mL/min/1.73 m^2

Estimated GFR	73.0 (±2.6)
Urea	5.9 (±3.1) mmol/l
Sodium	137 (±5.2) mmol/l
Potassium	4.0 (±13.4) mmol/l
Chloride	101.8 (±13.4) mmol/l
Bicarbonate	22.5 (±8.5) mmol/l
Creatinine	101 (±13.4) umol/l

Table 3 Clinical characterization of heart failure patients

Variable	Frequency (n= 78)	Percentage (%)
BMI category (Kg/M²)		
< 18 (Underweight)	6	8
18.5-24.9 ((Normal)	27	35
25.0-29.9 (Overweight)	20	26
30-34.9 (Class I obesity)	19	24
35-40 (Class II obesity)	4	5
> 40 (Class III obesity)	2	3
Presence of co-morbidities		
Co-existence of Hypertension		
Yes	55	70.5
No	23	29.5
Co-existence of DM		
Yes	16	20.5
No	62	79.5
Co-existence of SCD		
Yes	1	1.3
No	78	98.9
Atherogenic risk		
Low risk (AIP < 0.11)	73	93.6
Intermediate risk (AIP 0.11-0.21)	3	3.8
High Risk (AIP >0.21)	2	2.6
Aetiology of HF among our subjects		
Hypertensive heart disease	49	62.9
Cardiomyopathy	24	30.7
Valvular heart disease	4	5.1
NYHA functional classification		
Stage 1	12	15.4
Stage 2	34	43.6
Stage 3	27	34.6
Stage 4	5	6.4
Estimated GFR		
Stage 1 (>90)	21	26.9
Stage 2 (60-89)	30	38.5
Stage 3 (30-59)	24	30.8
Stage 4 (15-29)	2	2.6
Stage 5 (<15)	1	1.3

BMI - Body Mass Index, DM- Diabetes mellitus, SCD- Sickle cell disease, GFR- Glomerular filtration rate, DM – Diabetes mellitus, SCD – Sickle cell disease, HF – Heart failure AIP - Atherogenic Index of Plasma, NYHA – New York Heart Association, GFR – Glomerular filtration rate

Table 4 Relationship between JADS (anxiety and depression) and risk of cognitive impairment

	HADS Category	No cognitive impairment	Cognitive impairment	Chi square	p-value
Based on CSID Scores	No anxiety	37 (61%)	24 (39%)		
	Abnormal (borderline + anxiety)	8 (47%)	9 (53%)	0.316	0.407
	No depression	38 (62%)	23 (38%)		
	anxiety (borderline + depression)	7 (41%)	10 (59%)	0.119	0.166
Based on TMTA Scores	No anxiety	47 (77%)	14 (23%)		
	Abnormal (borderline + anxiety)	11 (65%)	6 (35%)	0.303	0.351
	No depression	47 (77%)	14 (23%)		
	Depression (borderline + depression)	11 (65%)	6 (35%)	0.303	0.351

Table 5 Correlation between variables and their scores (TMTA and CSID)

Variable	TMTA Score		CSID Score	
	Pearson Correlation	P-Value	Pearson Correlation	p-value
Age	-0.237	0.037	-0.229	0.044
Systolic Blood Pressure	-0.088	0.444	0.148	0.194
Diastolic Blood Pressure	-0.064	0.575	0.086	0.455
Body Mass Index	-0.110	0.337	0.096	0.404
Total Cholesterol	0.018	0.874	-0.010	0.931
High Density Lipoprotein	-0.103	0.371	0.064	0.579
Low Density Lipoprotein	0.069	0.547	0.023	0.842
Very Low Density Lipoprotein	0.010	0.934	0.143	0.211
Triglyceride	-0.016	0.887	-0.077	0.504
Atherogenic Index of Plasma	0.003	0.981	0.003	0.981
Left Ventricular Ejection Fraction	-0.142	0.216	0.074	0.521
E/A Ratio	0.147	0.199	0.098	0.392
Estimated GFR	-0.339	0.002	0.273	0.015
HADS Anxiety Score	-0.008	0.942	0.074	0.518
HADS Depression	0.012	0.915	-0.140	0.223
Serum Urea	0.112	0.330	-0.068	0.553
Serum Sodium	0.125	0.274	-0.094	0.414
Serum Potassium	-0.005	0.966	0.101	0.381
Serum Chloride	0.066	0.566	0.057	0.622
Serum Bicarbonate	-0.125	0.276	0.100	0.386
Serum Creatinine	0.042	0.66	0.045	0.441
New York Ass. Functional Class.	0.634	0.889	1.364	0.714

Table 6 Logistic regression of variables with cognitive impairment assessed with CSID and TMTA

Variable	CSID			TMTA		
	Expo B	CI	P-Value	Expo B	CI	P-Value
Age	1.041	1.003 – 1.080	0.032	1.007	0.968 – 1.046	0.742
Systolic Blood Pressure	0.974	0.941 – 1.008	0.133	0.962	0.922 – 1.003	0.070
Diastolic Blood Pressure	1.008	0.948 – 1.072	0.801	1.050	0.978 – 1.128	0.181
Body Mass Index	0.974	0.895 – 1.061	0.550	1.030	0.940 – 1.129	0.521
Total Cholesterol	2.717	0.993 – 7.435	0.052	1.008	0.375 – 2.710	0.987
High Density Lipoprotein	0.906	0.592- 1.386	0.649	0.594	0.169 – 2.086	0.417
Low Density Lipoprotein	0.245	0.077 – 0.779	0.017	1.096	0.341 – 3.518	0.878
Very Low Density Lipoprotein	0.445	0.139 – 1.431	0.174	1.771	0.539 – 5.823	0.347
Triglyceride	0.575	0.139 – 1.431	0.465	1.952	0.584 – 6.517	0.277
Atherogenic Index of Plasma	2.363	0.173 – 32.295	0.519	0.415	0.045 – 3.817	0.437
Left Ventric. Ejection Fraction	0.995	0.963 – 1.030	0.791	0.988	0.952 -- 1.024	0.499
E/A Ratio	0.737	0.390 – 1.394	0.348	1.031	0.510 – 2.085	0.932
Serum Urea	1.010	0.843 – 1.211	0.913	1.100	0.916 – 1.320	0.307
Serum Sodium	1.173	1.001 – 1.375	0.049	1.061	0.940 – 1.197	0.337
Serum Potassium	1.775	0.727 – 4.332	0.207	0.976	0.392 – 2.429	0.958
Serum Chloride	0.883	0.764 – 1.021	0.092	0.990	0.941 – 1.042	0.696
Serum Bicarbonate	0.881	0.696 – 1.114	0.289	1.009	0.802 – 1.271	0.936
Estimated Glomerular Filtration Rate	0.980	0.960 – 1.000	0.046	0.991	0.970 – 1.013	0.414

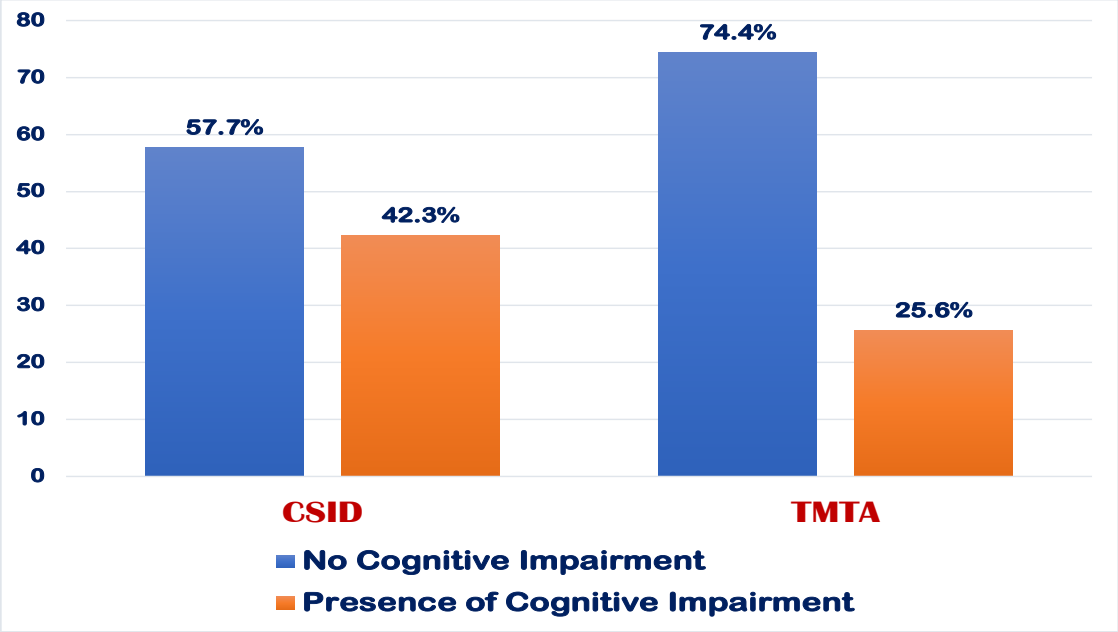

Fig 1: Prevalence of cognitive impairment based on CSID and TMTA

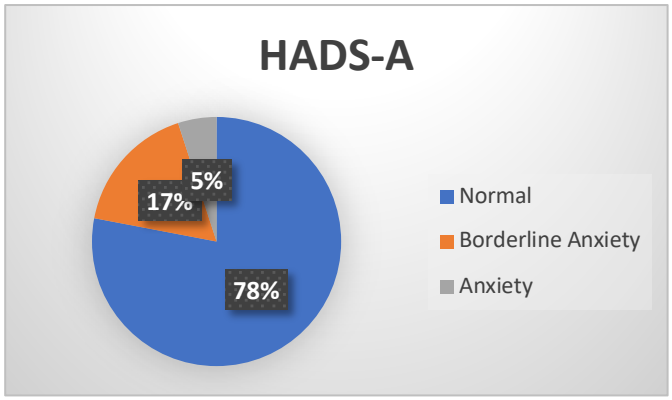

Fig 2 Patients with anxiety based on HADS

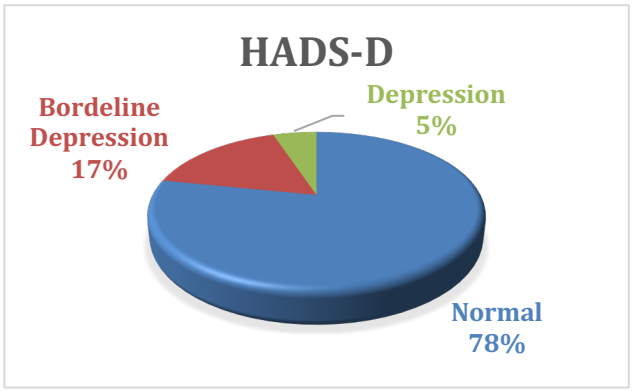

Fig 3 Patients with depression based on HADS

The proportion of patients with cognitive impairment was 42% using the CSID and 26% on the TMTA. 5%of the patients had anxiety and depression respectively. These are demonstrated in Figure 1, 2 and 3 respectively. We also observed that cognitive dysfunction is higher among subjects with depression and anxiety when cognitive function is assessed using both CSID and TMTA, though this was not statistically significant (see Table 4).

A significant correlation was observed between TMTA scores of the participants and their age and estimated glomerular filtration rate (eGFR), with p-values of 0.037 and 0.002 respectively. There was also significant correlation between the CSID score, age of participants and their eGFR, with p-values of 0.044 and 0.015 respectively (see Table 5).

Logistic regression of the variables with CSID performance was weakly significant for age (p-value =0.032), total cholesterol (p-value=0.052), Low Density Lipoprotein (p-value=0.017), Serum Sodium (p-value=0.049) and eGFR (p-value=0.046). A weak positive relationship was observed for Serum Chloride (p-value=0.092). Logistic regression of the variables with TMTA performance observed only a weak correlation for Systolic Blood pressure (p-value=0.070). These are shown in Table 6.

DISCUSSION

This cross-sectional single-centre descriptive study reported clinical and demographic characteristic of 78 patients with heart failure, a cohort that was relatively younger than Caucasian in the United State of America with heart patients, who are usually in their sixth and seventh decade .[24] The age of our patients suggest they have a lower risk of age-related cognitive impairment as most of them (51%) were within the middle age range. The majority of our heart failure patients were within NYHA functional stage II and III, as compared to the earlier report by Ansa *et al* which had 98% of patients in functional stages III and IV.[4]

We observed a prevalence of cognitive impairment of 42% using the CSID and 25% when using the TMTA. This prevalence rate is within the previous range of 25–75% reported among heart failure patients.[2,3] The CSID had a greater sensitivity in detecting cognitive impairment in our population. This had also been observed in an earlier report among patients with stages 3– 5 chronic kidney disease.[16] This might be due to the fact that broader cognitive domain is tested on the CSID compared to TMTA, which evaluates mainly the ability to shift between tasks (a measure of cognitive flexibility), psychomotor speed, sequencing and visual attention, all of which are key components of executive function.

Predictors of cognitive function reported in earlier studies include: presence of symptoms of advanced heart failure and a history of recent admissions,[6] NYHA class and American College of Cardiology/American Heart Association (ACC/ AHA) stage of heart failure, reduced cardiac output, reduced systolic component of blood pressure, presence of obesity and depression, left ventricular ejection

fraction, elevated ß-type natriuretic peptide (BNP), hyponatraemia, low serum albumin, increased serum homocysteine, impaired diastolic filing, low testosterone in male and the presence of cerebral atrophy.[3,7,8,10,12] Brain imaging to evaluate for any brain abnormalities was not carried out in our study population due to lack of funds. We observed that there was a positive correlation between age of our patients and the occurrence of cognitive impairment when assessed using TMTA but not with CSID. This is in keeping with reports that suggested that older patients in the general population have a greater propensity for cortical atrophy, which is a marker for age-related cognitive impairment.[23, 24.]

On logistic regression of the variables with the CSID score, a significant positive relationship was seen for total cholesterol, LDL, Serum Sodium and eGFR. When the CSID score is replaced with TMTA performance, a weak relationship was only observed for systolic blood pressure. The relationship between cognitive impairment and biochemical parameters such as serum creatinine is in keeping with an earlier report.[25] This relationship might be due to the co-existence of some form of chronic kidney disease in this cohort of heart failure patients, as most of them had DM or hypertension. CKD as demonstrated by reduce eGFR had been reported as a predictor of neurocognitive dysfunction in our population.[16] Contrary to a study by Celutkiene et al,[3] which noted that depression was a predictor of cognitive impairment among their heart failure patients, we were unable to establish any significant relationship between these parameters. Nor were we able to establish any significant correlation between the presence of cognitive impairment assessed by either CSID or TMTA and basic echocardiography cardiac parameters such as ejection fraction, left ventricular ejection fraction or E/A ratio. There was also no correlation between cognitive impairment and the propensity for vascular disease as measured by their atherogenic index of plasma.

Our study observed a combined prevalence of anxiety and /or depression of around 10%, which was lower than the 13–39% reported in by Ansa et al.[4] The findings in their study was closer to that observed in black Hispanic minorities, African-Americans and Caucasians in the United States which was between 13–42%.[27] This may be attributable to improvement in the care given to heart failure patients with an attendant improvement in their quality of life. Cognitive dysfunction was higher among the subjects in our study, who had anxiety and depression when assessed using both CSID and TMTA compared to earlier reports.[2, 3]

Limitations of this study include the lack of a control arm and the relatively small sample size. These may have reduced the strength of the study. Absence of the control group means the pattern of cognitive impairment could not be established. Inability to carry out cranial imaging studies for these patient means we could not rule out the presence of infarcts or cortical atrophy, which could have accounted for the high prevalence of cognitive impairment observed.

CONCLUSION

A significant proportion of patients with heart failure in Nigeria have cognitive and mood impairment. The CSID was a better predictor of cognitive impairment among different cohorts in our population. For patients with heart failure eGFR, total cholesterol and LDL are possible predictors of cognitive impairment. Given that occurrence of cognitive impairment is a major determinant of the patient's quality of life, further studies to fully understand this topic, develop the best instruments for assessing it and modalities of managing it will greatly improve the care available for patients with heart failure.

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