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Plasma Level of Homocysteine and Lipid Profile in Patients with Cerebrovascular Accident in Tertiary Health Centre in Ogbomoso Oyo State South-West Nigeria

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Abstract

Apart from the traditional risk factors, there are newer risk factors such as high plasma level of Homocysteine, Folate deficiency and Vitamin B12 deficiency, associated with cardiovascular disease. Plasma Homocysteine level has been link to the level of LDL-C and functionality of HDL-C. This study is therefore designed to correlate plasma level of Homocysteine with Lipid profile in patient newly diagnosed of cerebrovascular accident. Seventy-Two newly diagnosed stroke patients were consecutively recruited into the study. Seventy-Two apparently healthy, age and sex matched volunteers were recruited from the community as controls. The data obtained were analyzed using SPSS version 20. Level of significance for the study was set at $p<0.05$. High plasma level of Homocysteine (12.72 ± 5.10 µmol/L), Total-Cholesterol (4.58 ± 1.40 mmol/L) and LDL (3.34 ± 1.41 mmol/L) were obtained from the study population when compared with Homocysteine (7.60 ± 1.80 µmol/L), Total-Cholesterol (3.93 ± 0.91) and LDL (2.23 ± 0.80 mmol/L) obtained from the controls and the difference was highly significant ($p<0.01$). The difference in the mean plasma level of HDL was statistically significant among study population (0.74 ± 0.32 mmol/L) when compared with Control (1.26 ± 0.38 mmol/L) $p<0.001$. Homocysteine had weak positive correlations with T-Cholesterol (r=0.172), LDL (r=0.213), Body Fat (r=178) and negative correlation with HDL (r=-0.178) but statistically significant $p<0.05$. We concluded that elevated plasma level of Homocysteine has significant correlation with abnormal lipid profile which is one of the major risk factors for cerebrovascular accident.

Keywords: ***Cerebrovascular accident; Homocysteine; Lipid profile; HDL-C; LDL-C***

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Introduction

The theme for World Stroke Day in 2008 was “Little stroke, big trouble” focusing on the importance of stroke as a critical warning sign of more debilitating vascular events or death. Presently, stroke constitutes a leading cause of mortality and long term physical and mental disability throughout the world [1,2].

The management is largely conservative, therefore primary prevention is the key to reducing the increasing burden of stroke worldwide especially in developing world like Nigeria [3,4]. A key component of the secondary prevention strategies for stroke advocated by the World Health Organization (WHO) is intensified reduction in exposure to major cardiovascular risk factors [5-7]. There are traditional risk factors associated with cardiovascular events, newer independent risk factors such as high plasma level of homocysteine, folate deficiency and vitamin B12 deficiency have come to limelight and have been focus of research lately. High plasma homocysteine level has been linked to the level of Low-Density Lipoprotein-Cholesterol (LDL-C) and functionality of High-Density Lipoprotein-Cholesterol (HDL-C) [4,8].

High plasma homocysteine concentrations have been associated with increased risk of Cardiovascular Diseases (CVD) [9,10]. However, several large randomized clinical trials have not been able to show a direct link between lowering homocysteine plasma levels with vitamin B therapy and reduction in the risk of CVD or mortality among subjects with known CVD [11]. Endothelial dysfunction, increased oxidative stress, alterations of lipid metabolism, and induction of thrombosis have been suggested to be pathogenesis of CVD in Hyperhomocysteinemia [12,13]. However, the mechanism by which homocysteine could promote atherogenesis and thromboembolic disorders is far from clear and the role of Homocysteine in human CVD is largely unclear and subject of debate [11].

This study was, therefore, designed to see the relationship between plasma Homocysteine level and well established risk factor for CVD-abnormal lipid profile.

Materials and Methods

Bowen University Teaching Hospital (BUTH) and Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital (LTH) both located in Ogbomoso, Oyo State, Nigeria, were used as the sites of the study. The subjects were new clinically diagnosed with Cerebrovascular Accident (CVA) with CT scan confirmation. Patients with complications such as renal, liver pathology or other medical illnesses were excluded. Patients on lipid regulating drugs were also excluded from the study. History and physical examination were taken from the subjects and blood samples were collected for analysis

It was a cross-sectional study with semi-structured questioner administered as a survey instrument. Seventy-Two newly diagnosed CVA patients presenting at Accident and Emergency units of both institutions were consecutively recruited into the study after obtaining their informed consent. Another seven-two apparently healthy normotensive, age, and sex-matched volunteers were recruited from Ogbomoso Community as controls after obtaining their informed consent.

Ethical clearances for the study were obtained from the Ethical Review Committee of Ladoke Akintola University of Technology Teaching Hospital and Bowen Teaching Hospital.

Blood sample collection, storage and laboratory analysis

A fasting venous blood was collected into 0.1% Na EDTA bottle from each subject and control using the standard technique of phlebotomy. Each sample was centrifuged at 3,000 xg for 5 minutes. The plasma obtained was stored frozen at -200°C

before analysis. Plasma from both subjects and controls were analyzed in batches using standards and controls for all the biochemical parameters. The enzymatic endpoint was used for lipid profile parameters except LDL-Cholesterol, using kits from Randox Laboratories Limited, (Batch Number; CH 200 Lot 363904/97QX, TR 210 325799 87 D8, CH203 2344CH) Crumlin, UK. Low-density lipoprotein cholesterol was calculated using freidwald's formula [14]. Homocysteine was measured by Enzyme-Linked Immune-Sorbent Assay (ELISA) using commercial kits (Human) purchased from Span Biotech Limited (Batch Number; E201509198050), Hong Kong.

The data obtained were analyzed using Statistical Package for Social Sciences (SPSS) version 20. Frequency distribution tables were generated from variables like age, sex, religion, marital status, and ethnicity, while cross-tabulation and test statistics were done. The Chi-square test was used to compare proportion, while Student 't' test was used to compare means of continuous variables. The Analysis of Variance (ANOVA) test was used to compare the means of more than two variables. Pearson's correlation analysis was used to test the strength and direction of relationship between continuous variables. The level of significance was set with p-value less than or equal to 0.05.

Results

TABLE 1. **Demographic profile of the respondents.**

Variables	**Categories (%)**			**X2**	**df**	**p-value**
	Study population (n=72)	**Control (n=72)**	**Total (N=144)**			
Age group (in years)				**6.455**	**4**	**0.168**
30-39	3 (4.2)	4 (5.6)	7 (4.9)			
40-49	8 (11.1)	14 (19.4)	22 (15.3)			
50-59	14 (19.4)	22 (30.6)	36 (25.0)			
60-69	15 (20.8)	11 (15.3)	26 (18.0)			
≥70	32 (44.4)	21 (29.2)	53 (36.8)			
Gender				**2.418**	**1**	**0.12**
Male	31 (43.1)	22 (30.6)	53 (36.8)			
Female	41 (56.9)	50 (69.4)	91 (63.2)			
Education				**1.972**	**3**	**0.578**
No formal education	30 (41.7)	35 (48.6)	65 (45.1)			
Primary	16 (22.2)	18 (25.0)	34 (23.6)			
Secondary	14 (19.4)	12 (16.7)	26 (18.1)			
Tertiary	12 (16.7))	7 (9.7)	19 (13.2)			
Religion				**0**	**1**	**1**
Christianity	57 (79.2)	57 (79.4)	114 (79.2)			
Islam	15 (20.8)	15 (20.8)	30 (22.8)			
Employed				**4.079**	**1**	**0.043***
Yes	35 (48.6)	47 (65.3)	82 (56.9)			

No	37 (51.4)	25 (34.7)	62 (43.1)			
Occupation status				**5.482**	**2**	**0.065**
Unskilled	15 (42.9)	28 (59.6)	43 (52.4)			
Semiskilled	12 (34.3)	6 (12.8)	18 (22.0)			
Skilled	8 (22.9)	13 (27.2)	21 (25.6)			
Marital status				**8.125**	**4**	**0.087**
Never married	0 (0.0)	2 (2.8)	2 (1.4)			
Currently married	44 (61.1)	41 (56.9)	85 (59.0)			
Separated	3 (4.2)	0 (0.0)	3 (2.1)			
Divorced	0 (0.0)	3 (4.2)	3 (2.1)			
Widowed	25 (34.7)	26 (36.1)	51 (35.4)			
*Statistically significant						

TABLE 1 shows the socio-demographic characteristics of the study population and controls. The study population included 72 patients with stroke and 72 apparently healthy people as controls. The age range for controls and subjects were between 30-95years. There was no significant difference in the mean age when compared to subjects with controls. The employment status in subjects compared with controls was significantly different ($p<0.05$) as shown above. All other socio-demographic characteristics were not statistically significant.

TABLE 2. **Assessment of risk factors for stroke.**

Variables	**Categories (%)**			**X2**	**df**	**p-value**
	Study population (n=72)	**Control (n=7)**	**Total (n=144)**			
Alcohol intake				**6.477**	**3**	**0.091**
Yes frequently	8 (11.1)	2 (2.8)	10 (6.9)			
Yes occasionally	6 (8.3)	2 (2.8)	8 (5.6)			
No but in the past	6 (8.3)	6 (8.3)	12 (8.3)			
No never before	52 (72.2)	62 (86.1)	114 (79.2)			
Tobacco				**4.114**	**2**	**0.128**
Yes frequently	0 (0.0)	2 (2.8)	2 (1.4)			
No but in the past	0 (0.0)	2 (2..8)	2 (1.4)			
No never before	72 (100.0)	68 (94.4)	140 (97.2)			
Hypertension (HNT)				**86.4**	**1**	**<0.001****
Yes	54 (75.0)	0 (0.0)	54 (37.5)			
No	18 (25.0)	72 (100.0)	90 (62.5)			
Diabetic Mellitus (DM)				**8.471**	**1**	**0.004****
Yes	8 (11.1)	0 (0.0)	8 (5.6)			
No	64 (88.9)	72 (100.0)	136 (94.4)			

Exercise				**24.167**	**1**	**<0.001****
Yes	6 (8.3)	32 (47.2)	38 (26.4)			
No	66 (91.7)	38 (52.8)	104 (72.2)			
Family history HNT				**14.3954**	**2**	**0.001****
Yes	28 (38.9)	11 (15.3)	39 (27.1)			
No	32 (44.4)	54 (75.0)	86 (59.7)			
Don't know	12 (16.7)	6 (8.3)	18 (12.5)			
Family history DM				**8.508**	**2**	**0.014***
Yes	14 (19.4)	3 (4.2)	17 (11.8)			
No	38 (52.8)	49 (68.1.2)	87 (60.4)			
Don't know	20 (27.8)	20 (27.8)	40 (27.8)			
Family history of stroke				**2.165**	**2**	**0.339**
Yes	6 (8.3)	6 (8.3)	12 (8.3)			
No	55 (76.4)	48 (66.7)	103 (71.5)			
Don't know	11 (15.3)	18 (25.0)	29 (20.1)			
Waist hip ratio				**3.575**	**1**	**0.059**
Normal	24 (33.3)	14 (19.4)	38 (26.4)			
Elevated	48 (66.7)	57 (79.2)	105 (72.9)			
Body mass index				**16.784**	**3**	**0.001****
Underweight	0 (0.0)	6 (8.3)	6 (4.2)			
Normal	27 (37.5)	43 (59.7)	70 (48.6)			
Overweight	26 (36.1)	13 (18.4)	39 (27.1)			
Obesity	19 (26.4)	10 (13.9)	29 (20.1)			

*Statistically significant $p<0.05$; **Highly significant $p<0.01$

TABLE 2 shows above statistically significant differences were observed in those who had hypertension, Family history of hypertension, involved in exercise, had DM and had a family history of DM ($p<0.005$) in study population compared to controls. More people had abnormal BMI in study population compared with controls and were statistically significant. Although, more people had abnormal waist/hip ratio among study population the differences were not statistically significant.

TABLE 3. **Comparison of anthropometric measurements and biochemical parameters.**

Variables	Study population	Controls	t-test	p-value
HCY(μmol/L)	12.72 ± 5.10	7.60 ± 1.80	8.073	**<0.001
Total- Chol (mmol/L)	4.58 ± 1.40	3.93 ± 0.91	3.136	**0.002
HDL-C (mmol/L)	0.74 ± 0.32	1.26 ± 0.38	8.89	**<0.001
LDL-C (mmol/L)	3.34 ± 1.41	2.23 ± 0.80	5.521	**<0.001
TRIG (mmol/L)	1.12 ± 0.68	0.98 ± 0.45	1.431	0.155

SBP (mmHg)	152.69 ± 29.80	117.23 ± 16.93	8.927	**<0.001
DBP (mmHg)	89.38 ± 17.47	71.13 ± 11.59	7.514	**<0.001
BODYFAT (%)	33.3 3± 6.49	29.79 ± 7.97	2.33	*0.021
*Statistically significant p<0.05; **Highly significant p<0.01; SBP-Systolic Blood Pressure (mm Hg); DBP: Diastolic Blood Pressure (mmHg)				

TABLE 3 shows high level of plasma Homocysteine (12.72 ± 5.10 μmol/L), Total Cholesterol (4.58 ± 1.40 mmol/L) and LDL-C (3.34 ± 1.41 mmol/L) in the study population when compared with Homocysteine (7.60 ± 1.80 μmol/L), Total Cholesterol (3.93 ± 0.91) and LDL-C (2.23 ± 0.80 mmol/L) than that of control and the difference was highly significant (p<0.01). The difference in the mean plasma level of HDL-C was statistically significant among study population (0.74 ± 0.32 mmol/L) when compared with Control (1.26 ± 0.38 mmol/L) p<0.001 The mean value of SBP (152.69 ± 29.80 mmHg) and DBP (89.38 ± 17.47 mmHg) for study population and SBP (117.23 ± 16.93 mmHg) and DBP (71.13 ± 11.59 mmHg) for controls and they were significantly elevated in study population (p<0.001). The Mean Body Fat (33.33 ± 6.49) in subjects compared with mean body fat (29.79 ± 7.97) in controls were significantly different (p<0.005).

TABLE 4. **Correlation of plasma level of homocysteine, T-Chol, HDL-C, LDL-C, TRIG, BMI, WHR and % body fat in patients with stroke.**

		HCY	T-Chol	HDL-C	LDL-C	TRIG	BMI	Waist/hip	Body fat
HCY (μmol/L)	r	1	0.172	-0.178	0.213	0.058	0.91	-0.011	0.178
	p		*0.040	*0.033	*0.010	0.487	0.278	0.994	*0.033
T-Chol (mmol/L)	r	0.172	1	-0.101	0.932	0.309	-0.006	-0.095	0.025
	p	*0.040		0.226	**<0.001	**<0.001	0.943	0.256	0.768
HDL-C (mmol/L)	r	-0.178	-0.101	1	-0.239	-0.17	-0.048	-0.182	-0.106
	p	*0.033	0.226		*0.043	*0.042	0.564	*0.029	0.206
LDL-C (mmol/L)	r	0.213	0.932	-0.398	1	0.145	-0.001	0..003	0.041
	p	*0.010	**<0.001	**<0.001		0.084	0.99	0.967	0.625
TRIG (mmol/L)	r	0.058	0.309	-0.17	0.145	1	0.055	-0.163	0.088
	p	0.487	**<0.001	*0.042	0.084		0.512	0.051	0.295
BMI	r	0.91	-0.006	-0.048	-0.001	0.055	1	0.126	0.676
	p	0.278	0.943	0.564	0.99	0.512		0.133	**<0.001

Waist/hip	r	-0.011	-0.095	-0.182	0.003	-0.163	0.126	1	0.215
	p	0.994	0.256	*0.029	0.967	0.051	0.133		*0.010
Body fat (%)	r	0.178	0.025	-0.106	0.041	0.088	0.676	0.215	1
	p	*0.033	0.768	0.206	0.625	0.295	**<0.001	*0.010	
*Statistically significant p<0.05; **Highly significant p<0.01									

TABLE 4 shows that HCY had weak positive correlations with T-Chol (r=0.172), LDL-C (r=0.213), Body Fat (r=178) and negative correlation with HDL (r=-0.178) but statistically significant p<0.05. T-Chol had a positive correlation with LDL-C (r=0.932 strong) and TRIG (r=0.309) both were highly significant, p<0.01. HDL-C showed a weak negative correlation with LDL-C (r=-0.231), TRIG (r=-0.170) and Waist/Hip ratio. The correlations were significant p<0.05. There was strong and highly significant correlation between percentage Body Fat and BMI (r=0.678), p<0.01. Also, a significant but weak positive correlation exists but percentage Body Fat and Waist/Hip ratio (r=0.215), p<0.5.

Discussion

The aim of this study is to access the correlation between major risk factors of cerebrovascular accident for the purpose of primary prevention. The major risk factor for cerebrovascular accident in this study was hypertension. Seventy-five percent of the study population was hypertensive and was highly significant when compared with controls (p<0.001), this has been documented in studies [15,16]. Family history of hypertension, DM, and lack of regular exercise had been shown to play a significant role in development of the cardiovascular event, as well as abnormal anthropometric measurements such as BMI and Waist/Hip Ratio, are established risk factors for cardiovascular event and those were significantly high in the study population. Weight reduction and prescribed regular exercise have been found to be integral part of primary preventive measures [17,18].

Abnormal lipid profile was found to be high among the study population when compared with that of controls, that is, elevated plasma level of total cholesterol and LDL-Cholesterol while plasma level of HDL-Cholesterol was low. This abnormal pattern has been established and documented in many journals as primary risk factors for cardiovascular events. Primary and secondary preventive measures have been centered on the treatment of abnormal lipid profile [19,20].

A high significant plasma level of Homocysteine was observed in the study population when compared with that of controls. This is similar to a study done by Suleiman et al. in Northwest Nigeria [21]. Elevated plasma level of Homocysteine has been implicated in pathogenesis of vascular events and now regards as isolated newer risk factor for stroke [13,22].

Pearsons correlation was done to see if there was any correlation between plasma level of Homocysteine and lipid parameters and various degrees of correlations were observed. We found that Total Cholesterol, LDL-Cholesterol, and Triglyceride have positive though weak correlation with plasma level of Homocysteine. This is similar to a report obtained from Brain Hospital, Affiliated Hospital of Xuzhou Medical University [23]. Elevated plasma homocysteine levels have been linked with abnormal lipid profile. Homocysteine level was found to interfere with metabolism of lipids, especially Apo A1 in HDL-Cholesterol. Statistically significant, negative correlation between plasma level of Homocysteine and HDL-Cholesterol was observed in this study. This explained one of the pathophysiologies of elevated plasma Homocysteine levels as independent risk factor for

cardiovascular disease [24,25]. Although, abnormal anthropometric measures have been linked with risk of cardiovascular event no significant correlation was found with plasma level of Homocysteine.

Conclusion

We concluded that elevated plasma level of Homocysteine has a significant correlation with abnormal lipid profile which is one of the major risk factors for cerebrovascular accident.

Conflicts of Interest

The authors declare that they have no conflicts of interest with the contents of this article.

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