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The Pattern of Common Cholesterol Fractions in Stroke Patients

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims/Purpose: The aim of this study was therefore to document the frequency and pattern of serum cholesterol in stroke patients admitted in a tertiary hospital in Enugu.
Methods: This was a descriptive cross-sectional study carried out at Enugu State University Teaching Hospital Enugu. Serum cholesterol levels were classified based on the current international cut off points for people with cardiovascular disease. Statistical analysis of data was carried out using SPSS version 22.
Results: Data from a total of 180 subjects were collected and analyzed. The mean (sd) of serum cholesterol fractions and their distributions are: Low density lipoprotein 2.4± 1.18 mmol/l, High density lipoprotein, 1.17± 0.62 mmol/l, Total Cholesterol, 4.43± 1.34 mmol/l, and triglycerides 1.21±0.77 mmol/L. HDL-cholesterol was significantly lower in patients 50 years and older. P=0.02. A total of 12 (6.7%) of the patients had high levels of LDL, 92(51.1%) had poor levels of HDL. Between stroke types, 10(7.2%) of patients with ischemic stroke had high serum LDL compared to 2(4.8%) with hemorrhagic stroke p= 0.32. Among those with hemorrhagic stroke, 22(52.4%) had

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poor levels of HDL compared to 70(50.7%) of those with ischemic stroke p= 0.17. Total cholesterol and triglycerides were also found in a higher proportion of those with ischemic stroke than hemorrhagic although these differences were not statistically significant.
Conclusions: There mean level of serum LDL, HDL and TC are higher in stroke patients than recommended values. Current recommended universal use of statins after stroke should be encouraged in both ischemic and hemorrhagic stroke.

Keywords: Ischemic stroke; hemorrhagic stroke; cholesterol; Nigeria.

1. INTRODUCTION

Stroke is generally defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction or hemorrhage [1]. Clinically stroke may be defined as symptoms and/or signs of focal and global loss of cerebral function lasting for at least 24 hours with no apparent cause other than of vascular origin [1]. The incidence and prevalence of stroke in sub-Saharan Africa has increased over the recent decades due to increased rates stroke risk factors [2-8].

Some of the commonest population attributable risk factors for stroke in sub-Saharan Africa (SSA) predispose to stroke via atherosclerosis. The effects of these risk factors are additive when they co-exist together. In case of ischemic stroke, the mechanism by which atherosclerosis cause stroke is primarily through plaque rupture and thrombus formation which may lead to embolus or in-situ vessel occlusion. Atherosclerotic plaques may also break off and cause occlusion at distant sites. In intracerebral hemorrhage, atherosclerosis and arteriosclerosis form the pathological basis of fibrinoid necrosis and hyalination of intracerebral arteries and arterioles. These vessels may rupture under rupture under appropriate conditions leading to intracerebral hemorrhage. Lacunar strokes result from similar changes in small arteries and arterioles [9].

The mechanism of atherosclerosis involves the uptake of cholesterols moieties by the endothelial cells of the blood vessels thus forming foam cells. Over time if increased serum concentrations serum cholesterol persists these pathological changes will lead to formation of plaques especially in the presence of low-density lipoprotein (LDL) [10-11]. Although hypercholesterolemia may cause atherosclerosis in people with hereditary dyslipidemias, this process is accelerated in the presence of risk factors such as hypertension, diabetes, smoking and obesity [10-11] thus, atherosclerosis may develop at a varying concentration of different cholesterol fractions less that the recommended cut-off levels. Abnormal ratio of different lipid fractions may also increase the risk of atherosclerosis [12].

Data on the pattern cholesterol fraction among stroke patients vary widely in different studies. A study from Iran found reported a significantly higher levels of triglycerides (TG) in patients with ischemic compared to hemorrhagic stoke [13]. In another study conducted in Palestinian Arabs [14], about 28.6% of patients had high LDL. High Total Cholesterol (TC) was reported in 17.1% and 15.7% had high TG. Low levels of High Density Cholesterol (HDL) was reported in 61.3% of the stroke patients. In Abuja, Nigeria hypercholesterolemia was reported in 18.4% of stroke patients [15]. In another study from the same city dyslipidemia was reported in 35.8% of stroke patients. Further review of the pattern of lipid profile in the same study 31% had elevated TC, 13% had elevated LDL while low HDL was found in 33%. In Maiduguri, Bornu state in northeast Nigeria, Watila et al. [16] reported a 15.1% rate of hypercholesteremia. The same study showed that hypercholesterolemia to be the second commonest risk factor for stroke among hospital admitted patients. To the best of our knowledge no study in southeast Nigeria has documented the pattern of dyslipidemia among stroke patients. With a stroke prevalence of about 12/1000, in an urban slum in Enugu metropolis [17], documenting the pattern of dyslipidemia among stroke patients will be useful for both clinicians and public health officials.

The aim of this study was therefore to document the frequency and pattern of serum cholesterol in stroke patients admitted in a tertiary hospital in Enugu.

2. METHODS

2.1 Study Location and Data Collection

This was a descriptive cross-sectional study carried out among stroke patients admitted in the

medical wards of the Enugu State University Teaching Hospital Enugu. At the time of data collection stroke patients were admitted into the 4 medical wards of the hospital. For discharged patients, folders were retrieved from the medical records department. All cases of stroke were included in the study. Where diagnosis was not clear or where the patients were not fully investigated, they were excluded. The diagnosis of stroke was made using CT scan. Lipid profile data were collected from case notes. Cholesterol measurements in all cases was carried out according to the ATP III classification for identification of dyslipidemia [18]. All samples were taken after an overnight fasting (at least 12 hours). Serum cholesterol levels were classified based on the current international cut off points for people with cardiovascular disease [18].

Statistical analysis of data was carried out using SPSS version 22 (IBM Chicago Illinois).Data were expressed in tables, the median, mean, standard deviation and chi-square test for various lipid fragment were calculated. Mean ages of the patients were calculated using the students T test. Leve of significance is fixed at 5%. P-value>0.05

3. RESULTS

Data from a total of 180 subjects were collected and analyzed. Males were slightly more in number than females (males 103(56,6%), females 79(43.4%), p=0.08). The mean age of the patients was 63.7±12.6 years, similar in both sexes. Table 1. The age distribution, and mean admission blood pressures and blood glucose are also shown in Table 1. Admission systolic blood pressure was higher in males. P=0.02. The frequency distribution of signs and symptoms of stroke is shown in Fig. 1. Most patients presented with limb weakness (72.2%), headache (27.8%) and facial weakness (24.4%).

The mean (sd) and median of serum cholesterol fractions and their distributions are shown in Table 2. There were no statistically significant differences gender and age distribution of lipid fractions. HDL-cholesterol was significantly lower in patients older than 50 years. P=0.02. The mean LDL, HDL, TG and TC were similar in males and females as well as in those with ischemic and hemorrhagic strokes.

The percentage distributions of serum cholesterol levels based on international recommendations are shown in Tables 3 and 4. A total of 12 (6.7%) of the patients had high levels of LDL, equal in males and females but slightly more between the ages of 50-69 years. A much higher proportion 92(51.1%) had poor levels of HDL while 26.1% (47) of the patients had high HDL levels. This is equally distributed among males and females and different age groups. Sixteen (8.9%) had high levels of TC and 43 (23.9%) high levels of TG.

Between stroke types, 10(7.2%) of patients with ischemic stroke had high serum LDL compared to 2(4.8%) with hemorrhagic stroke although this was not statistically significant. Among those with hemorrhagic stroke, 22(52.4%) had poor levels of HDL compared to 70(50.7%) of those with ischemic stroke. Total cholesterol and triglycerides were also found in a higher proportion of those with ischemic stroke than hemorrhagic although these differences were not statistically significant.

Table 1. Basic clinical characteristics of the patients

	Males	Females	Total	P-value
Mean age	63.95±12	63.4±13.4	63.7±12.6	0.77
Age group				
<50	10(9.7)	12(15.6)	22(12.2)	
50-59	30(29.1)	18(23.4)	48(26.7)	
60-69	26(25.2)	20(26)	46(25.6)	
≥70	37(35.9)	27(35.1)	64(35.6)	0.61
Side affected				
Right	49(50)	39(52.7)	88(51.2)	0.73
Left	49(50)	35(47.3)	84(48.8)	
Blood pressure measurements				
Mean systolic blood pressure (mmHg)	158.1±25.4	148.6±28.9	154±27.2	0.02*
Mean Diastolic blood pressure (mmHg)	89.2±10	87.7±14.5	88.3±12	0.24
Mean admission random blood glucose (mg/dl)	160.2±52.6	171.3±57.1	164.8±54.6	0.2
Total	103(56.6)	79(43.4)	180(100)	0.08

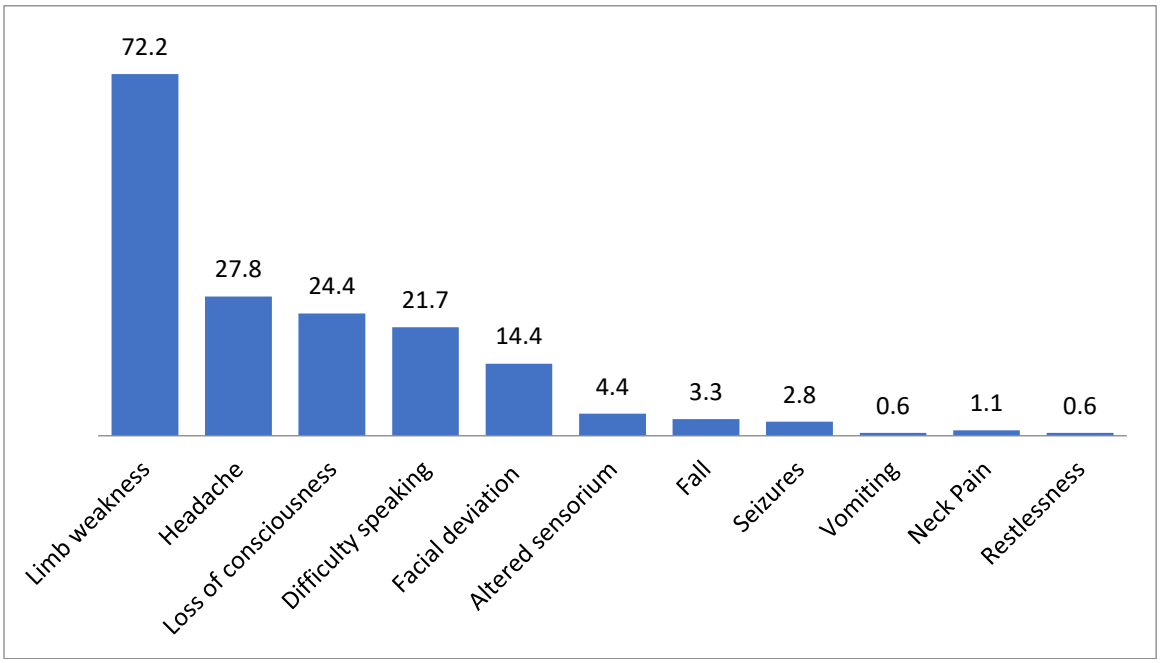

Fig. 1. Frequency of signs and symptoms of stroke observed in percentages

Table 2. Distribution of mean(sd), median and ranges of serum cholesterol levels and other variables

	LDL cholesterol (mmol/L)	HDL Cholesterol (mmol/L)	Total Cholesterol (mmol/L)	Triglycerides (mmol/L)
Gender				
Males				
Mean	2.38±1.24	1.16±0.63	4.4±1.36	1.79±0.82
Median (range)	2(0.3-5.5)	1(0.3-3.7)	4.5(1.2-6.8)	1.8(0.3-3.8)
Females				
Mean	2.44±1.1	1.19±0.6	4.48±1.33	1.62±0.68
Median (range)	2.2(0.1-5)	1.3(0.1-3.5)	4.2(1.5-7)	1.6(0.4-3.2)
P-value for mean	0.77	0.68	0.71	0.11
Stroke type				
Ischemic stroke				
Mean	2.46±1.2	1.19±0.48	4.52±1.33	1.73±0.77
Median (range)	1.2(0.3-5.5)	0.66(0.1-3.7)	4.45(1.33)	1.8(0.3-3.6)
Hemorrhagic stroke				
Mean	2.22±1.1	1.13±0.48	4.14±1.3	1.67±0.74
Median (range)	2(0.1-5.5)	1(0.2-2.2)	4.2(1.3-7)	1.6(0.4-3.8)
P-value for mean	0.47	0.6	0.26	0.58
Age group				
<50 years	2.41±1.17	1.53±0.79	5.04±1.37	1.84±0.76
50-59 years	2.49±1.13	1.15±0.73	4.51±1.21	1.75±0.68
60-69 years	2.531±1.3	1.16±0.56	4.34±1.37	1.73±0.75
≥70 years	2.25±1.17	1.08±0.46	4.25±1.38	1.63±0.84
p-value	0.59	**0.02***	0.14	0.78
Total				
Mean	2.4±1.18	1.17±0.62	4.43±1.34	1.21±0.77
Median (range)	2.05(0.1-5.5)	1.1(0.1-3.7)	4.36(1.3-7)	1.7(0.3-3.8)

**statistically significant*

Table 3. age and sex distribution of normal and abnormal levels of serum cholesterol levels

Cholesterol (mmol/L)	Males	Female	<50 years	50-59 years	60-69 years	≥70 years	Total
LDL							
Best /optimal	73(70.9)	57(74.2)	14(63.6)	37(77.1)	30(65.2)	49(76.6)	130(72.2)
Borderline	22(21.4)	16(20.8)	7(31.8)	6(12.5)	12(26.1)	13(20.3	38(21.1)
High/very high	8(7.8)	4(5.2)	1(4.5)	5(10.4)	4(8.7)	2(3.1)	12(6.7)
*p-value		0.84				0.05	
HDL							
Poor	47(45.6)	45(58.4)	8(36.4)	25(52.1)	22(47.8)	37(57.8)	92(51.1)
Better	29(28.2)	12(15.6)	3(13.6)	9(18.8)	13(28.3)	16(25)	41(22.8)
Best	27(26.2)	20(26)	11(50)	14(29.2)	11(23.9)	11(17.2)	47(26.1)
p-value		0.11				0.11	
Total cholesterol							
Desirable	68(66)	51(66.2)	9(40.9)	32(66.7)	32(69.6)	46(71.9)	119(66.1)
Borderline	28(27.2)	17(22.1)	8(36.4)	13(27.1)	10(21.7)	14(21.9)	45(25)
High	7(6.8)	9(11.7)	5(22.7)	3(6.3)	4(8.7)	4(6.3)	16(8.9)
p-value		0.44				0.13	
Triglycerides							
Desirable	47(54.7)	38(49.4)	7(31.8)	21(43.8)	22(47.8)	35(54.7)	85(47.2)
Borderline	28(27.2)	24(31.2)	6(27.3)	19(39.6)	10(21.7)	17(26.6)	52(28.9)
High	28(27.2)	15(19.5)	9(40.9)	8(16.7)	14(30.4)	12(18.8)	43(23.9)
p-value		0.48				0.18	
Total	103(57.2)	77(42.8)	22(12.2)	48(26.7)	47(25.8)	64(35.4)	180(100)

**p-value for differences between sexes and age groups*

Table 4. Distribution of cholesterol levels by stroke type

Cholesterol	Hemorrhagic stroke	Ischemic stroke	Total
LDL			
Best /optimal	35(83.3)	95(68.8)	130(72.2)
Borderline	5(11.9)	33(23.9)	38(21.1)
High/very high	2(4.8)	10(7.2)	12(6.7)
p-value		0.32	
HDL			
Poor	22(52.4)	70(50.7)	92(50.5)
Better	13(31)	28(20.3)	41(22.8)
Best	7(16.7)	40(29)	47(26.1)
p-value		0.17	
Total cholesterol			
Desirable	32(76.2)	87(63)	119(66.1)
Borderline	7(16.7)	38(27.5)	45(25)
High	3(7.1)	13(9.4)	16(8.9)
p-value		0.28	
Triglycerides			
Desirable	21(50)	64(46.4)	85(47.2)
Borderline	13(31)	39(28.3)	52(28.9)
High	8(19)	35(25.4)	43(23.9)
p-value		0.7	
Total	42(23.3)	138(76.7)	180(100)

Competing Interests

4. DISCUSSION

Stroke is the most common cause of neurologic admissions in Nigeria adults [19-22]. Common modifiable risk factors for stroke such as diabetes, hypertension, cigarette smoking, and obesity/sedentary lifestyle share a common pathway in the etiopathogenesis of stroke via the

formation of atherosclerosis. All these risk factors accelerate the rate and frequency of atherosclerosis in the general population. Atherosclerosis may also occur at younger ages [23,24] hence impaired lipid profile under appropriate conditions may increases the risk of stroke at any age. All common cholesterol fractions have been associated with risk of stroke [25-26].

In this study we have reported the data of 180 subjects equally distributed by gender and age with a mean age of 63.7±12.6 years. There were no statistically significant differences in gender and age distribution of lipid fractions, however the values of cholesterol fractions were higher than recommended cut off values. HDL-cholesterol was significantly higher in younger patients (<50 years). P=0.02. The mean LDL, HDL, TG and TC were similar in males and females as well as in those with ischemic and hemorrhagic strokes. A total of 12 (6.7%) of the patients had high levels of LDL, equal in males and females. A much higher proportion 92(51.1%) had poor levels of HDL. Sixteen (8.9%) had high levels of TC and 43 (23.9%) high levels of TG. Between stroke types, 10(7.2%) of patients with ischemic stroke had high serum LDL compare to 2(4.8%) with hemorrhagic stroke although this was not statistically significant. Among those with hemorrhagic stroke, 22(52.4%) had poor levels of HDL compared to 70(50.7%) of those with ischemic stroke. Total cholesterol and triglycerides were also found in a higher proportion of those with ischemic stroke than hemorrhagic although these differences were not statistically significant. Mean LDL in males and females was higher than 1.8mmol/L recommended for patients for coronary artery disease. HDL serums level was 1.16mmol/L in males and 1.19 mmol/L in females, values also less than the recommended 1.5 mmol/L. The pattern is similar with TG where the mean level reported in our patients were higher than recommended level.

Studies have disclosed varying relationship between cholesterol units and stroke [27-32]. The Copenhagen City Heart Study [27] reported a 47% reduction in the risk of non-hemorrhagic stroke for every 1-mmol/L increase in HDL and the Northern Manhattan Stroke Study [28], there was an inverse relationship between ischemic stroke and HDL level ≤35 mg/dL. Similarly, in the Cardiovascular Health Study [29], high HDL cholesterol level was associated with a decreased risk of ischemic stroke but this association was different in males and females. This association was positive in males but not in females. The Atherosclerosis Risk in Communities study there was no relationship between HDL and ischemic stroke [31]. Thus, the clinical significance of cholesterol fractions in the genesis of stroke may be heterogenous [26,31-33].

The index study is similar to some studies and different from others. Gurmeet Singh et al. [34] reported that serum HDL was raised in 44% of patients with stroke compared to 26.1% in the index study. Similar to the index study they also reported that hemorrhagic stroke patients had lower levels of normal HDL compared to ischemic stroke patients however there was no statistical difference. In other studies Vakilian et al. [13] reported a significant association between the type of stroke and serum HDL cholesterol while Zheng et al. [33] did not find any association between HDL and stroke.

In the index study 12 (6.7%) of the patients had high levels of LDL, and between stroke types, 10(7.2%) of patients with ischemic stroke had high serum LDL compared to 2(4.8%) with hemorrhagic stroke. This is lower than what was reported by Singh et al. [34]. A positive relationship between TG and ischemic stroke was documented by other studies [35,36] while others have reported the opposite [14] Overall, data on the relationship between cholesterol fractions and hemorrhagic stroke has not been consistent. An inverse relationship between TC level and the risk of hemorrhagic stroke while a positive relationship between HDL level and the risk of intracerebral hemorrhage [37] have all been documented. In other studies, for example opposite findings have been reported. In one paper an increment of 1 mmol/L in TC concentration was associated with a 15% decreased risk of hemorrhagic stroke and low LDL-C concentration was also associated with a higher risk of hemorrhagic stroke [38].

Studies have also shown that the relationship between cholesterol fragments may affect carotid intima thickness and may present a greater risk factor than any one of the components [34,39]. TC/HDL cholesterol ratio is a powerful predictor cardiovascular diseases [39-42]. Zheng et al. [35] reported that LDL/HDL was associated with a higher risk of ischemic stroke than other lipids and should be considered for clinical diagnosis and future

disease prevention. The role of serum cholesterol as a risk factor for stroke may be affected by several other common risk factors for stroke. With increasing rates of the major risk factors for stroke in our community, early detection of lipid derangements is important in stroke prevention and the universal use of statins in stroke patients should be implemented.

5. CONCLUSIONS

There mean level of serum LDL, HDL and TC are higher in stroke patients than recommended values. HDL-cholesterol was significantly higher in younger patients (<50 years). About 6.7% of the patients had high levels of LDL, 51.1% had poor levels of HDL, 8.9% had high levels of TC and 23.9%. current recommended universal use of statins after stroke should be encouraged in both ischemic and hemorrhagic stroke.

LIMITATIONS

The current study has some limitations. Firstly, we did not document past medical history of use of lipid lowering agents. It is possible therefore that some patients might have been on lipid lowering agents before the onset of stroke. Furthermore, because of possible temporal changes in lipid profile after acute stroke, it would be appropriated to have a follow up lipid profile report. Secondly, Carotid ultrasound was not done to check for the presence of atherosclerotic plaques. This would offer a better way of stratifying the subjects because stroke may occur irrespective of the size of a carotid plaque. Lastly, various risk factors for stroke that were not included in the study might act as confounders. Notwithstanding. the current study will act as a basis for comparison for further studies in this field in Nigeria.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

CONSENT

Patients' data were retrieved from the case noted after an informed consent.

The authors have nothing to declare. Data was collected from our patients after obtaining the necessary clearance. The work was sponsored by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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