

Serum Lipids, Lipid Ratio Pattern among Stroke Patients in a Nigerian Tertiary Care Hospital

Olufisayo Gabriel Ayoade^{1,*}, Timothy Ekwere², Franklin O. Dike³

¹Department of Chemical Pathology, University of Uyo/ University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria

²Department of Haematology, University of Uyo/ University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria

³Department Internal Medicine, Neurology Unit, University of Uyo/ University of Uyo Teaching Hospital, Uyo, Akwa Ibom State, Nigeria

Abstract Background: The impact of cerebrovascular accident (CVA) has been on the rise especially in developing countries. Abnormalities in lipids and lipoprotein ratios are an important factor in development of stroke despite the varied reports on evaluation of relationship between dyslipidemia and the risk of stroke. The aim of the study is to evaluate the pattern of dyslipidemia vis-à-vis serum lipoproteins and lipoprotein ratios among Stroke patients and to determine some of its correlates in patients attending tertiary hospital in South-South Nigeria. **Methods:** This is a prospective case-control study. A total of 61 participants consisting of 41 stroke patients (cases) and 20 healthy persons (controls) were consecutively recruited into the study in Neurology unit of University of Uyo Teaching Hospital (UUTH) over a period of 6 months. Fasting lipids, total cholesterol (TC), triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) were estimated. **Results:** The TC, LDL-C, HDL-C and Non-HDL-C levels were significantly higher in stroke cases than in controls. Among stroke cases, elevated LDL-C was the most frequent abnormality in absolute lipid values, found in 78.0% of stroke cases. This was significantly higher ($p=0.001$) than the percentage amongst the controls (30.0%). Among stroke cases and controls, abnormalities in lipid ratios were significantly higher among stroke cases than in controls ($p<0.001$). **Conclusion:** The most common dyslipidemia among stroke patients is elevated LDL-C which is an atherogenic lipoprotein implicated in atherosclerosis. The pattern of dyslipidemia among the stroke patient also includes raised TC and low HDL levels with elevated LDL-C/HDL-C ratio.

Keywords Stroke, Lipoprotein ratios, Lipids, Cardiovascular disease

1. Introduction

Stroke (Cerebrovascular accident) is defined as a rapidly developed global or focal neurological deficit lasting more than 24 hours or leading to death with no apparent cause other than vascular origin [1]. It is recognized to be one of the major causes of mortality and long-term severe disability with significant socio-economic burden especially in post-stroke care worldwide [2]. There has been an increase in the global burden of Cerebrovascular accident (CVA), as the impact is worse in many developing countries. World Health Organization (WHO) has projected that 80% of stroke cases will occur in these countries by year 2030 [3]. Sub-Saharan Africa seems to bear the largest burden of stroke as the prevalence and case fatality is higher due to marked cases of hypertension and other risk factors like dyslipidemia among the general population [4-5].

In Nigeria, even though there has been lack of community-based data on the prevalence, hospital-based

studies show that stroke accounts for 0.9 to 4.0% of patient's hospitalization, up to 45% of neurological admissions. It also accounts for 3.7% of emergency medical admission and it is the eighth leading cause of death [6-7]. CVA can be classified as ischemic or hemorrhagic with the former being predominant (88%) and the latter accounts for 12% which can either be subarachnoid (9%) or intracerebral (3%) [8]. The modifiable risk factors which commonly predispose to stroke include Dyslipidemia, Hypertension, Cardiac diseases especially atrial fibrillation and diabetes mellitus (DM) amongst others. Effective primary prevention of stroke by early identification of risk factors is key as over 80% of the global stroke burden is attributed to few factors that improve significantly with interventions [9].

Dyslipidemia is an important factor in the development of stroke playing an essential role in the initiation and progression of atherosclerosis. [10]. Studies evaluating the relationship between lipid biomarkers and the risk of stroke have reported varied associations. [11-12] The discrepancies reported is very much base on the studied population differences and in varying methods utilized in the process [12].

* Corresponding author:

ayofissy07@gmail.com (Olufisayo Gabriel Ayoade)

Received: Dec. 6, 2021; Accepted: Jan. 7, 2022; Published: Jan. 13, 2022

Published online at <http://journal.sapub.org/ajmms>

Plasma lipids and lipoproteins levels have consistently been associated with cardiovascular diseases including myocardial infarction and stroke. Despite ample evidence suggesting that increased levels of total cholesterol (TC) and low levels of high-density lipoprotein cholesterol (HDLc) are strong and important risk factors for coronary heart disease, many observational studies have yielded inconsistent results for lipid profile and stroke. [12-13] The predictive role of serum lipid level in the occurrence of stroke still remains unclear despite several empirical evidences that support the use of lipid lowering agent such as statins as a means of reducing cardiovascular disease risk [14].

Traditional lipid parameters, represented by increased concentrations of total cholesterol (TC), triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), and decreased high-density lipoprotein cholesterol (HDL-C), have been identified as risk factors and predictors of cardiovascular disease, including stroke [15]. The assessment of lipid ratios such as TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C is recognized as a better predictor of vascular risk compared to traditional lipid parameters [15,16].

This study sought to examine the plasma lipoproteins and lipoprotein ratios in patient with stroke and its association with other risk factors. Stroke, not only has it been on increase in many developing nations but it is the leading cause of morbidity and mortality in the world. There has been mixed and inconsistent reports on the plasma lipid levels in stroke patients as it affects other risk factors especially in Nigeria. The obvious inadequate knowledge necessitates more research in this area. This study has the potential to provide valuable information on the predictive role of lipids in occurrence of stroke.

2. Materials and Methods

Study Design: This was a prospective case-control study designed to achieve the set objectives of the study.

Study Population: Adult Patients diagnosed with stroke in line with the WHO clinical definition of stroke and confirmed by computer tomography scan (CT-scan) of the brain were recruited consecutively into the study over a 6 months period (March-August 2019). Age and sex matched healthy individuals were used as controls for the study. A total of 61 participants consisting of 41 stroke patients (cases) and 20 healthy persons (controls) were consecutively recruited into the study.

Sample Collection/ Analytical Procedure: After informed consent were taken, 5 mls of blood was drawn from each participant after an overnight fast of 8-10 hours. It was collected in plain tube, allowed to clot and separated through centrifugation (1500× g for 30 minutes). It was then stored at -20°C until assay was run. The assays were run in 3 batches, the duration storage of each batch of samples is between 6-8 weeks.

Biochemical Analysis

The lipid profile (Total Cholesterol, Triglycerides, High density Lipoprotein-Cholesterol) was assayed using the enzymatic method, cholesterol oxidase phenol 4-aminoantipyrine peroxidase (CHOD-PAP) on Automated Chemistry Analyzer (Selectra ProM, ELITech Group, Holland). LDL was calculated using the Friedewald formula.

Inclusion Criteria: Newly diagnosed adult patients with stroke in line with WHO definition and confirmed by CT-scan of the brain and who gave oral and signed informed consent were recruited into the study during the study period (March–August 2019).

Exclusion Criteria: Patients less than 18 years of age, patients whose diagnosis were not confirmed by CT- scan and those who did not give informed consent were excluded from the study.

Data Collection: Data was collected in a profoma designed for the study. This include; age, sex, blood pressure, plasma fibrinogen level, co-morbid risk factors including hypertension, diabetes mellitus, obesity and chronic cigarette smoking.

Data Analysis: Data was analysed using SPSS for windows version 20. The results were presented in simple tables. Descriptive and inferential statistics such as t-test were used as appropriate. The level of significance was set at $p < 0.05$.

Ethical Consideration: Ethical approval was obtained from the Health Research Ethics Committee of the Hospital before the commencement of this study. Also, all participants in this study signed a written informed consent before being recruited in the study.

3. Results

A total of Forty-one (41) stroke patients and twenty (20) age and sex matched controls were recruited for this study within the study duration. The male to female ratio in both arm of the study was 1:1. The mean age range of both the subjects and controls were 60.6 years and 59.8 years respectively with no statistical difference between the 2 groups. (Table 1) The mean systolic and diastolic blood pressure between the subjects and controls were $168.2 \pm 32.9 / 119.2 \pm 12.8$ and $106.9 \pm 29.8 / 94.7 \pm 94.7$ respectively. ($p = 0.0001$ both cases).

The absolute lipid values for the stroke cases and the control group are also shown in Table 1. The TC, LDL-C, HDL-C and Non-HDL-C levels were significantly higher in stroke cases than in controls with mean \pm SD of 5.34 ± 0.68 v. 4.70 ± 0.51 ; 3.80 ± 0.58 v. 3.11 ± 0.36 ; 1.07 ± 0.13 v. 1.14 ± 0.14 and 4.27 ± 0.66 v. 3.56 ± 0.40 respectively. No significant difference was observed between the TG values in both groups i.e., 1.04 ± 0.36 v. 0.97 ± 0.17 ($p = 0.30$).

Among stroke cases, elevated LDL-C was the most frequent abnormality in absolute lipid values, found in 78.0% of stroke cases. This was significantly higher

($p=0.001$) than the percentage amongst the controls (30.0%). Among the controls, low HDL-C was the most frequent dyslipidemia found in 40.0% of the controls (see Table 3).

Lipid ratios for the stroke cases and the control group are shown in Table. The TC/HDL-C, LDL-C/HDL-C and TG/HDL-C levels were significantly higher in stroke cases than in controls with mean \pm SD of 4.9 ± 1.6 v. 4.21 ± 1.3 ($p<0.0001$); 3.43 ± 1.5 v. 2.8 ± 1.2 ($p<0.001$); and 2.9 ± 1.8 v. 2.2 ± 1.34 ($p<0.001$) respectively.

Among stroke cases and controls, abnormalities in lipid ratios were significantly higher among stroke cases than in controls ($p<0.001$). Elevated LDL-C/HDL-C was the most frequent abnormality found in 83% of stroke cases and 25% of controls ($p<0.001$), while elevated TG/HDL-C was the least commonly found in 14.6% of stroke cases and none of the controls (see Table 3).

4. Discussion

Several observational studies have shown conflicting findings regarding the association of dyslipidemia with cerebrovascular accident and there is lack of sufficient data on the prevalence and pattern of dyslipidemias among stroke patients in Nigeria. [17-18] This study was designed to determine the pattern of dyslipidemia among stroke patients and its association with risk factors of stroke. Our results showed a high prevalence of dyslipidemia with higher TC, LDL-C and non-HDL-C values, i.e., more than the respective cut-off values, with about 78% of the patients fulfilling at least 1 criterion for dyslipidemia according to the NCEP ATP III guideline for the detection, evaluation, and management of dyslipidemia [19]. This is consistent with reported rates of dyslipidemia among stroke patients in Spain, which has ranged between 60-80% [20].

Table 1. Baseline characteristics of study participants

Parameters	Stroke patients Mean (SD) n=41	Healthy Control Mean (SD) n=20	P-value
Characteristics			
Age (years)	60.6 (10)	59.8 (8.7)	0.744
Systolic BP (mmHg)	168.2 (32.9)	119.3 (12.8)	0.000*
Diastolic BP (mmHg)	106.9 (29.8)	69.9 (9.9)	0.000*
Traditional lipid parameters			
TC	5.34 (0.68)	4.70 (0.51)	0.000*
TG	1.04 (0.36)	0.97 (0.17)	0.449
HDL-C	1.07 (0.13)	1.14 (0.14)	0.045
LDL-C	3.80 (0.58)	3.11 (0.36)	0.000*
Non-HDL-C	4.27 (0.66)	3.56 (0.40)	0.000*
Lipoprotein ratios/ Atherogenic indices			
TC/HDL-C	5.02 (0.66)	4.11 (0.28)	0.000*
LDL-C/HDL-C	3.57 (0.60)	2.72 (0.28)	0.000*
TG/HDL-C	2.24 (0.80)	1.95 (0.29)	0.124
AIP	0.32 (0.16)	0.28 (0.06)	0.295
AC	4.02 (0.67)	3.11 (0.28)	0.000*

LDL-C=Low density lipoprotein cholesterol; HDL-C=High density lipoprotein cholesterol; TG=Triglycerides; TC=Total cholesterol. The lipoprotein cut-off values are all in mmol/L units

Table 2. Age and Sex distribution of the respondents across the study group

Variables	Study groups n (%)		Total (n=61)	Statistical indices
	Stroke (n=41)	Control (n=20)		
Sex				Df=1
Male	22 (53.7)	10 (50.0)	32 (52.5)	X ² =0.0721
Female	19 (46.3)	10 (50.0)	29 (47.5)	P value=0.788
Age (years)				
40-49	6 (14.6)	4 (20.0)	10 (16.4)	
50-59	12 (29.3)	4 (20.0)	16 (26.2)	
60-69	15 (36.6)	11 (55.0)	26 (42.6)	Df=3
70 and above	8 (19.5)	1 (5.0)	9 (14.8)	P value=0.310+
Median (range)	60 (85-40)	62 (78-45)	61 (85-40)	

+fischer.exact test

Table 3. Prevalence of dyslipidemia in stroke patients and healthy controls

Variables	Stroke cases n=41	Healthy Control n=20	Total n=61	Statistical indices
SPB (mmHg)				
Less than 140	6 (14.6)	19 (95.0)	25 (41.0)	Df=1
140 and above	35 (85.4)	1.0 (5.0)	36 (59.0)	P value <0.0001*
DBP (mmHg)				
Less than 90	12 (29.3)	18 (90.0)	30 (49.2)	Df=1
90 and above	29 (70.7)	2.0 (10.0)	31 (50.8)	P value <0.0001
Total Cholesterol (mmol/l)				
Less than 5.2	19 (46.3)	17 (85.0)	36 (59.0)	Df=1
5.2 and above	22 (53.7)	3 (15.0)	25 (41.0)	P value=0.004+*
TG (mmol/L)				
Less than 1.7	38 (92.7)	20 (100.0)	58 (95.1)	Df=1
1.7 and above	3 (7.3)	0 (0.0)	3 (4.9)	P value=0.544
HDL				
Abnormal	25 (61.0)	8 (40.0)	33 (54.1)	Df=1
Normal	16 (39.0)	12 (60.0)	28 (45.9)	P value=0.123
LDL-C				
Less than 3.37	9 (22.0)	14 (70.0)	23 (37.7)	Df=1
3.37 and above	32 (78.0)	6 (30.0)	38 (62.3)	P value <0.0001
Non-HDL-C				
Less than 4.14	18 (44)	20 (100)	38 (62.3)	Df=1
4.14 and above	23 (54)	0 (0.0)	23 (37.7)	P value <0.0001
TC/HDL-C				
Less than 5.0	21 (51.2)	20 (100)	41 (67.2)	Df=1
5.0 and above	20 (48.8)	0 (0.0)	20 (32.8)	P value <0.0001
LDL-C/HDL-C				
Less than 3.0	7 (17)	15 (75)	22 (36.1)	Df=1
3.0 and above	34 (83)	5 (25)	39 (63.9)	P value <0.0001
TG/HDL-C				
Less than 3.0	35 (85.4)	20 (100)	55 (90.2)	Df=1
3.0 and above	6 (14.6)	0 (0.0)	6 (9.8)	P value <0.124
AC				
Less than 3.0	1 (97.6)	8 (40)	9 (4.8)	Df=1
3.0 and above	40 (3.4)	12 (60)	52 (85.2)	P value <0.0001
Number of risk factors				
No risk factors	0 (0.0)	14 (70.0)	14 (23.0)	Df=1
At least one risk factor	41 (100.0)	6 (30.0)	47 (77.0)	P value<0.0001*

LDL-C=Low density lipoprotein cholesterol; HDL-C=High density lipoprotein cholesterol; TG=Triglycerides; TC=Total cholesterol. The lipoprotein cut-off values are all in mmol/L units

The male to female ratio was almost similar to other studies in South-western Nigeria [17,21]. higher incidence of stroke among male may be attributed to high prevalence of smoking among men and the consumption of more fatty food. In addition, the hormonal effects of estrogen also have a protective effect against stroke in females. Although a study from Oxford shire, showed that males are more affected than females by genetic factors, the family history are more likely to be found in females than in males [22].

Regarding the age distribution of stroke patients in the study, the mean age was 60.6 years (± 10.7) which is similar to a result of a study by Olamoyegun et al, that showed a mean age of 69 years [20]. The majority, 23 (56.5%) patients, were above the age of 60 years. Again, this result is almost

similar to the previous study conducted in Ibadan, south west Nigeria that found 58% of patients were above the age of 60 years [23]. These results indicate that the incidence of stroke is higher for those who are above 60 years old.

The most common dyslipidemia pattern in our study is hypercholesterolemia and reduced HDL-C. The lipid profile of stroke patients was studied and it was found that there were 22 (53.7%) patients with total cholesterol level ≥ 5.2 mmol/L and the mean total cholesterol was 5.34 mmol/L (± 0.68), while elevated LDL-C occurs in 78% of stroke patients compared to 30% in healthy controls. This finding is in agreement with similar studies around the world that has demonstrated hypercholesterolemia among stroke patients and as there has been significant correlation between

cholesterol level and the risk of stroke [24,25].

This study also recorded low HDL-C among stroke patients statistically significant compared to the healthy controls. This is similar to findings from Olamoyegun *et al* [17]. Several studies showed similar findings and suggested that lower levels of HDL are associated with increased risk of stroke, while high levels of HDL are considered as a slight protective indicator against stroke [25,26]. On the other hand, a study conducted in Hawaii, showed no clear relationship between low levels of HDL and the risk of having stroke [27].

We found out that there is no statistical difference in TG in stroke patients and healthy controls. TG level was normal in 92.7% of stroke patient with mean of 1.04 ± 0.36 . These results are similar to several studies that showed the TG level ranging from 1.12 to 1.54 mmol/l among stroke patients [28-29]. This indicate that the relationship between elevated TG levels and the risk of stroke is still lacking, and this is in agreement with previous studies showed that no clear relationship between elevated TG levels and risk of stroke [29-31].

Lipid ratios have been demonstrated by several published studies to be better predictors of vascular risk than traditional lipid parameters. More than 80% of the stroke cases in our study has abnormal LDL-C/HDL-C ratio with mean of 3.57 ± 0.60 , statistically higher than in healthy controls with mean of 2.72 ± 0.28 . In their study of some stroke patients in northern Nigeria, Glew and his colleagues observed that despite normal lipid values both control and stroke patients, the LDL/HDL ratio distinguished the stroke patients from the control, and has shown to have more predictive power in assessing dyslipidemia in stroke patients [32].

The main limitation of our study was the fact that it was hospital-based study, making it difficult to generalize our findings to reflect the whole country. Also, it was a cross-sectional study, and thus cannot be used to predict some of the causal relationships indicated. More prospective studies with larger sample sizes are therefore suggested.

5. Conclusions

The prevalence of dyslipidemia in our study population is high and increases with age. The most common dyslipidemia among stroke patients is elevated LDL-C which is an atherogenic lipoprotein implicated in atherosclerosis. The pattern of dyslipidemia among the stroke patient also includes raised TC and low HDL levels with elevated LDL-C/HDL-C ratio. Determination of lipoprotein ratios should complement the other investigations in evaluation of patient with Stroke.

ACKNOWLEDGEMENTS

We are thankful to the resident doctors of department of Chemical Pathology, Haematology and Neurology unit,

Internal Medicine for their assistance.

Statement of Ethics

The authors had the approval from the University of Uyo Teaching Hospital Institution Health Research Ethical Committee.

Disclosure Statement

The authors have no conflicts of interest to disclose.

Funding Sources

The authors did not receive funding from any source.

REFERENCES

- [1] Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: Result of WHO collaborative study. *Bull World Health Organ.* 1980; 58(1): 113-30.
- [2] Caprio FZ, Sorond FA. Cerebrovascular disease: primary and secondary stroke prevention. *Med Clin North Am.* (2019) 103: 295–308. doi: 10.1016/j.mcna.2018.10.001.
- [3] Feigin, VL, Forouzanfar, MH, Krishnamurthi, R, et al. Global and regional burden of stroke during 1990–2010 findings from the Global Burden of Disease Study 2010. *Lancet* 2014; 383: 245–254.
- [4] Owolabi, M, Olowoyo, P, Popoola, F, et al. The epidemiology of stroke in Africa: a systematic review of existing methods and new approaches. *J Clin Hypertens* 2018; 20: 47–55.
- [5] Adoukonou T, Kossi O, Fotso Mefo P, et al. Stroke case fatality in sub-Saharan Africa: Systematic review and meta-analysis. *International Journal of Stroke.* February 2021. doi:10.1177/1747493021990945.
- [6] Ojini FI, Danesi MA. Pattern of neurological admissions at the Lagos University Teaching Hospital. *Nig J Clin Pract.* 2003; 5(1): 38-41. PubMed | Google Scholar.
- [7] World Health Organisation (WHO) Country mortality Fact Sheet 2006 Nigeria. Death and DALY estimates by cause, 2002. Available at <http://www.who.int/entity/healthinfo/statistics/bodgbddeathdalyestimates.xis>.
- [8] American Heart Association. Heart disease and stroke statistics-2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Committee. *Circulation.* 2006; 113(6): e85-e151.
- [9] Akinyemi, R.O., Ovbiagele, B., Adeniji, O.A. et al. Stroke in Africa: profile, progress, prospects and priorities. *Nat Rev Neurol* 17, 634–656 (2021). <https://doi.org/10.1038/s41582-021-00542-4>.
- [10] Roberts WC. Factors linking cholesterol to atherosclerotic

- plaques. *Am J Cardiol.* 1988; 62:495–499.
- [11] Pikula A, Beiser AS, Wang J, Himali JJ, Kelly-Hayes M, Kase CS, Yang Q, Seshadri S, Wolf PA. Lipid and lipoprotein measurements and the risk of ischemic vascular events: Framingham Study. *Neurology.* 2015 Feb 3; 84(5): 472-9.
 - [12] Berger JS, McGinn AP, Howard BV, Kuller L, Manson JE, Otvos J, Curb JD, Eaton CB, Kaplan RC, Lynch JK, Rosenbaum DM, Wassertheil-Smoller S. Lipid and lipoprotein biomarkers and the risk of ischemic stroke in postmenopausal women. *Stroke.* 2012 Apr; 43(4): 958-66. doi: 10.1161/STROKEAHA.111.641324. Epub 2012 Feb 2. PMID: 22308251; PMCID: PMC3547588.
 - [13] Kloska A, Malinowska M, Gabig-Cimińska M, Jakóbkiewicz-Banecka J. Lipids and Lipid Mediators Associated with the Risk and Pathology of Ischemic Stroke. *Int J Mol Sci.* 2020 May 20; 21(10): 3618. doi: 10.3390/ijms21103618. PMID: 32443889; PMCID: PMC7279232.
 - [14] Mihaylova B, Emberson J, Blackwell L, et al.. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: Meta-analysis of individual data from 27 randomised trials. *Lancet.* 2012. doi:10.1016/S0140.
 - [15] Millan J, Pinto X, Munoz A, et al. Lipoprotein ratios: physiological significance and clinical usefulness in cardiovascular prevention. *Vasc Health Risk Manag.* 2009; 5: 757-765.
 - [16] Liu L, Yin P, Lu C, Li J, Zang Z, Liu Y, Liu S, Wei Y. Association of LDL-C/HDL-C Ratio With Stroke Outcomes Within 1 Year After Onset: A Hospital-Based Follow-Up Study. *Front Neurol.* 2020 May 15; 11: 408. doi: 10.3389/fneur.2020.00408. PMID: 32499753; PMCID: PMC7242747.
 - [17] Olamoyegun MA, Akinlade AT, Fawale MB, Ogbera AO. Dyslipidaemia as a risk factor in the occurrence of stroke in Nigeria: prevalence and patterns. *Pan Afr Med J.* 2016 Oct 4; 25: 72. doi: 10.11604/pamj.2016.25.72.6496. PMID: 28292035; PMCID: PMC5324148.
 - [18] Gezmu T, Schneider D, Demissie K, Lin Y, Giordano C, Gizzi M. Lipid profiles and ischemic stroke risk: variations by sex within racial/ethnic groups. *Int J Womens Health.* 2014; 6:585-595.
 - [19] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) *JAMA.* 2001; 285: 2486–97.
 - [20] de la Sierra, A., Pintó, X., Guíjarro, C. et al. Prevalence, Treatment, and Control of Hypercholesterolemia in High Cardiovascular Risk Patients: Evidences from a Systematic Literature Review in Spain. *Adv Ther* 32, 944–961 (2015). <https://doi.org/10.1007/s12325-015-0252>.
 - [21] Desalu OO, Wahab KW, Fawale B, Olarenwaju TO, Busari OA, Adekoya AO, Afolayan JO. A review of stroke admissions at a tertiary hospital in rural Southwestern Nigeria. *Ann Afr Med.* 2011 Apr-Jun; 10(2): 80-5. doi: 10.4103/1596-3519.82061. PMID: 21691011.
 - [22] Touzé E, Rothwell PM. Sex differences in heritability of ischemic stroke: a systematic review and meta-analysis. *Stroke.* 2008 Jan; 39(1): 16-23. doi: 10.1161/STROKEAHA.107.484618. Epub 2007 Nov 21. PMID: 18032738.
 - [23] Owolabi MO, Ugoya S, Platz T. Racial disparity in stroke risk factors: the Berlin-Ibadan experience; a retrospective study. *Acta Neurol Scand.* 2009; 119(2): 81–87.
 - [24] Woodward M, Barzi F, Feigin V et al. For the Asia Pacific Cohort Studies Collaboration, Associations between high-density lipoprotein cholesterol and both stroke and coronary heart disease in the Asia Pacific region. *Eur Heart J.* 2007; 28(21): 2653-60. PubMed | Google Scholar.
 - [25] Zhang Y, Tuomilehto J, Jousilahti P et al. Total and high-density lipoprotein cholesterol and stroke risk. *Stroke.* 2012; 43(7): 1768-74.
 - [26] Reina SA, Llabre MM, Allison MA, Wilkins JT, Mendez AJ, Arnan MK, Schneiderman N, Sacco RL, Carnethon M, Delaney JA. HDL cholesterol and stroke risk: The Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis.* 2015 Nov; 243(1): 314-9. doi: 10.1016/j.atherosclerosis.2015.09.031. Epub 2015 Sep 28. PMID: 26425994; PMCID: PMC4609625.
 - [27] Curb JD, Abbott RD, Rodriguez BL, Masaki KH, Chen R, Popper JS, et al. High-Density Lipoprotein Cholesterol and the Risk of Stroke in Elderly Men: The Honolulu Heart Program. *American Journal of Epidemiology*; 160(2), 15 July 2004, Pages 150–157.
 - [28] Jain M, Jain A, Yerragonda N, Brown RD, Rabinstein A, Jahromi BS, et al. The Triglyceride Paradox in Stroke Survivors: A Prospective Study. *Neurosci J.* 2013; 2013:870608. doi: 10.1155/2013/870608. Epub 2013 Feb 25. PMID: 26317103; PMCID: PMC4437270.
 - [29] Bowman TS, Sesso HD, Ma J, Kurth T, Kase CS, Stampfer MJ, Gaziano JM: Cholesterol and the risk of ischemic stroke. *Stroke* 2003; 34: 2930–2934.
 - [30] Sridharan R. Risk factors for ischemic stroke: a case control analysis. *Neuroepidemiology* 1992; 11: 24–30.
 - [31] Rossner S, Kjellin KG, Mettinger KL, Siden A, Soderstrom CE. Normal serum-cholesterol but low HDL-cholesterol concentration in young patients with ischemic cerebrovascular disease. *Lancet.* 1978; i: 577–579.
 - [32] Glew RH, Okolie H, Crossey M, Suberu O, Trujillo M, Pereyra M, et al. Serum lipid profiles and homocysteine levels in adults with stroke or myocardial infarction in the town of Gombe in northern Nigeria. *J Health Popul Nutr.* 2004 Dec; 22(4): 341-7. PMID: 15663167.