DIAGNOSTIC VALUE OF LIPID PROFILE IN HEMORRHAGIC STROKE PATIENTS

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ABSTRACT

The relation between lipid profile and hemorrhagic stroke is controversial till now. Many epidemiological studies show inverse association of total cholesterol and triglycerides with hemorrhagic stroke. We analyze diagnostic role of lipid profile parameter in hemorrhagic stroke via case control study. The aim was to investigate lipid profile in hemorrhagic stroke patients and healthy control persons. Total 100 subject's case and control were included in this study and divided in two groups. 50 are hemorrhagic stroke patients and 50 are healthy control. Patients age <18, renal and hepatic impairment and familial hypercholesterolemia and hyperthyroidism were excluded. The inclusion of age group was between (64.8±11.9) and (48.9 ±9.9). Statistical analysis was done by using SPSS version 21.0. p value was calculated by ANOVA unpaired t- test. The p<0.05 was considered a statistically significant. The mean value of Total cholesterol (p=0.0001*) and Triglycerides (p=0.0254) were significantly low in hemorrhagic stroke patients compared with healthy control respectively. The mean LDL-C and VLDL-C were also significantly low in hemorrhagic stroke compared to healthy individuals (p=0.016 and p=0.025) respectively. Similarly, the mean HDL-C was also low in hemorrhagic stroke patients compare to healthy individuals. The hemorrhagic stroke patient's serum total cholesterol and triglycerides (r=-0.0854,p=0.0001 and r=-0.200 and p=0.046) were show significantly negative correlation with healthycontrol. The LDL –C and VLDL-C (r=-0.121 p=0.230 and r=-0.200, p=0.460) were show non-significant negative association in hemorrhagic stroke compare to healthy control respectively. HDL-C of hemorrhagic stroke patient's shows positively non-significantly associated with healthy control (r=0.0891, p=0.3785). This present study concluded that lipid profile levels play significant diagnostic role in hemorrhagic stroke patients. The lower concentration of total cholesterol and triglycerides may predispose individual towards the higher risk of hemorrhagic stroke.

KEYWORD: Hemorrhagic stroke, Lipid Profile, Diagnostic role, Diabetic, Hypertension.

INTRODUCTION

Stroke, is the condition of neurological defects attributed acute focal vascular injury by obstruction of blood vessel in central nervous system include cerebral infraction and cerebral hemorrhage (1). Hemorrhagic stroke is rupture of blood vessel in focal region of the brain and spills of blood in surrounding area of brain parenchyma (2). Collected hematoma increase intracranial pressure then cause neuronal injury (3). It is second most common subtype of stroke it accounts approximately 10-20 % of all stroke events. However, compared to ischemic stroke, it causes more severe disability with higher mortality. Stroke is second leading cause of death and disability worldwide. 15.2 million People have to face stroke throughout the world till 2015, in which 5 million die and left over are disabled. The low- and middle-income countries suffers 80% mortality rate of hemorrhagic stroke (4-5).

The occurrence of ischemic stroke is highest in number but high mortality and disability-adjusted life-years (DALY] is allocated to hemorrhagic stroke. In middle- and low-income country the disability adjusted life years (DALY] rate of hemorrhagic stroke 137/100000 per year till 2013 (6). The incidence rate of hemorrhagic stroke is differing in different countries across the world. Low- and middle-income countries having double incidence rate of hemorrhagic stroke as compare to high income countries (7). In general, the mammalian cells, Cholesterol act as precursor molecule for Vitamin D synthesis, steroid hormone, sex hormone and it is also a constituent of bile salt (8-9) LDL, VLDL and HDL are major lipoprotein which transports cholesterol and triglycerides throughout body. In human body LDL is used for deliver cholesterol to different cells for different purposes while HDL is used to transport excess cholesterol from cell to liver (10) Sometimes LDL particles penetrate the endothelium of arterial

walls and oxidized as results promote inflammation, injury and long-term fate is arthrosclerosis that's why LDL is "Bad Cholesterol" (11). Excess cholesterol is removed by HDL so it called "Good Cholesterol".

The relationship between serum lipid and hemorrhagic Stroke is not well established. Studies of lipids in hemorrhagic stroke have verity of findings. A population based cohort study in San Francisco also observed association between low serum cholesterol level and hemorrhagic stroke was confirmed in elderly men (12). An epidemiological study of Japan reveals that the hemorrhagic stroke was independently predicted by lower total cholesterol concentration in men(13). A collaborative study between total HDL and stroke in Europe and conclude that stroke could be related to HDL cholesterol level differently in men than women (14). A pooled cohort shows that low LDL and low level of cholesterol increase the risk of hemorrhagic stroke (15). A similar study found in Honolulu Heart program the scientist observes significant and inverse non-linear association between serum cholesterol and intracerebral hemorrhage but not of subarachnoid hemorrhage (16).

MATERIALS AND METHODS

The present case control study was conducted from October 2017 to October 2018.

Blood sample of Hemorrhagic stroke patients were collected form Neurology clinic of KPS institute of Medicine and OPD of Medicine wards of LLR and associated Hospitals, G.S.V.M. Medical College, Kanpur as cases where as age and sex matched normal healthy individuals residing around Kanpur as control and blood sample collected from dept. of biochemistry G.S.V.M. Medical college Kanpur.

Patients admitted with in 24 hrs. of first ever hemorrhagic stroke and age >30 years were included in this study. Patients with familial hypercholesterolemia with associated significant co morbidities like hypothyroidism and age <18 years were excluded from this study.

DATA COLLECTION

In this study total 100 individuals wereselected; 50 cases of hemorrhagic stroke patients and 50 healthy control subjects include in this study. Hemorrhagic stroke patients were enrolled on the basis of their Computed tomography/ Magnetic Resonance Imaging scan report. A questionnaire was prepared for collect information of disease profile, demographic variables, risk factors, and medications used.

SAMPLE COLLECTION

Blood sample of hemorrhagic stroke cases were taken within 48 hrs. after having stroke. For lipid profile blood sample of hemorrhagic stroke cases and control

persons were taken after overnight fasting. The lipid profile of both groups has done by photometry based Selectra pro M machine.

STATISTICAL ANALYSIS

Data were analyzed using SPSS 21.0 version (Chicago, Inc., USA) software. Quantitative data and expressed as mean and standard deviation. Qualitative data were expressed as percentage. Unpaired t- test was used as a test of significance; with p value < 0.05 was taken to be significant. Pearson co-relation coefficient test was used to check correlation between parameters of both groups.

RESULTS

In case group 50 consecutive patients of hemorrhagic stroke (28 male and 22 Female with age mean ± SD 64.8 ±11.9) were included. In 50 healthy persons (40 male and 10 females with 48.9 ± 9.9 mean ±SD) were included in control group. Table 1 shows baseline characteristics of case and control group. 30 (60%) persons of case group and 24 (48%) persons of control group were addicted with smoke, Alcohol and tobacco. Rest people were non- addicted.

Base line characteristics		Case (n=50)	Control (n=50)	p-Value*
Age (Mean ± SD) year		64.8 ±11.9	48.9 ±9.9	0.0001
Sex	Male	28 (56%)	40 (80%)	0.0100
	Female	22 (44%)	10 (20%)	0.0100
Addicted (Smoke, Alcohol and Tobacco)		26 (52%)	29 (58%)	0.5464 **
Diabetic		24 (48%)	13 (26%)	0.0227
Hypertensive		36 (72%)	14 (28%)	0.0001

Table 1: Comparison Between Case and Control in Base Line Characteristics

* p value <0.05 significant

** p value > 0.05 is non-significant

Table 1 shows significant level of hypertensive and diabetic patients in case group Hypertension (72%) and diabetic (48%) as compared to control group hypertensive (26%) and diabetic (28 %). Hypertension and diabetes are common risk factor for hemorrhagic stroke.

Parameter's	Case (n=50) (Mean ± SD)	Control (n=50) (Mean ± SD)	p-Value*
Total cholesterol	157.04 ± 36.03	172.18 ± 38.35	0.00001
Triglycerides	103.68 ± 30.49	115.99 ± 31.45	0.0254
LDL cholesterol	112.91 ± 37.82	121.11± 22.07	0.0165
HDL cholesterol	26.97 ± 8.78	51.062 ± 16.27	0.0001
VLDL	20.74 ± 6.10	23.20 ± 6.23	0.025

Table 1: Serum Cholesterol and Risk of Hemorrhagic Stroke

* p value >0.05 significant

Table 2: shows that mean value of Total cholesterol in hemorrhagic stroke patients were significantly lower compared to control group (157.04 ± 36.03 vs.172.18 ± 38.35, p=0.0001). Mean triglycerides and LDL-c were significantly lower in hemorrhagic stroke patients as compared of control group (103.68 ± 30.49 vs 115.99 ± 31.45, p= 0.0254); (112.91 ± 37.82 vs 121.11± 22.07, p=0.0165) respectively. The mean HDL is significantly higher in control group compare with case group (28.26± 7.68 vs 51.06± 16.27, p=0.0001) and case group have low mean VLDL as compare to control group (20.74±6.10 vs 23.20 ±6.23, p=0.025).
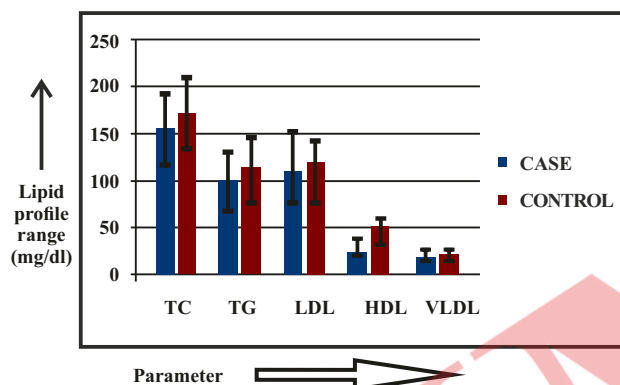

Fig 1: Graphical Representation Of Comparison Between Lipid Profile of Case and Control

Parameter	Case (n=50) (Mean ± SD)	Control (n=50) (Mean ± SD)	p-Value*
Total cholesterol (men)	159.96 ±38.72	169.24 ± 42.05	0.0004
Total cholesterol (women)	153.09 ± 32.85	170.10 ± 41.59	0.004

Table 3: Subgroup Analysis Of Total Cholesterol

* p value >0.05 significant

Table 3: shows subgroup analysis of cholesterol in men and women of case and control group. There was significantly lower total cholesterol in men and women of case group as compared to control.
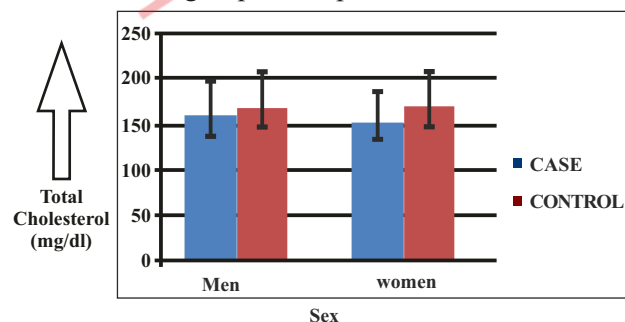

Fig 2: Comparison Of Total Cholesterol Level Between Sexes Of Case And Control Group

Pearson correlation of Lipid profile in case and control group			
Parameter's	r-Value*	r²-Value	P Value**
Total Cholesterol	-0.0854	0.007	.00001
Triglycerides	-0.200	0.0402	0.046
LDL-C	-0.1214	0.0147	0.230 (NS)
HDL-C	0.0891	0.0079	0.3785 (NS)
VLDL-C	-0.200	0.0402	0.460 (NS)

Table 3: Shows Subgroup Analysis of Cholesterol In Men And Women of Case and Control Group. There Was Significantly Lower Total Cholesterol In Men And Women Of Case Group As Compared To Control

* r = 1 means a perfect positive correlation and the value r = -1 means a perfect negative correlation

** p value >0.05 significant

Table-3 represents Pearson correlation between case and control group of lipid profile. Total cholesterol and triglycerides of case and control have significant negative correlation (TC r=-0.0854 and p=0.0001, TG r=-0.200 and p=0.046) respectively. LDL-C and VLDL-C were non-significantly and negatively correlated (LDL-C r=-0.121, p=0.230 and VLDL-C r=-0.200, p=0.460) respectively. HDL-C has non-significant positive correlation (r=0.0891, p=0.378).

DISCUSSION

Hemorrhagic stroke is heterogeneous patho-physiological entity in which vastly different pathways might lead to indistinguishable clinical presentations. Major cause of hemorrhagic stroke is hypertension it covers up to two third of hemorrhagic stroke. Hemorrhagic stroke is also links to brain tumors, amyloid angiopathy and various malformation and the location of hemorrhagic stroke is also important.. The hypertension cause small vessel damage by microaneurysms at bifurcation of arteriols and chronic elevation of intraluminal arterial pressure (3). In a model of hemorrhagic stroke (hypertensive rat) suggesting that there is a gradual weakening of vascular integrity that eventually lead to rupture (17).

Cholesterol is a major component of plasma membrane in all mammalian cells where phospholipid and cholesterol ratio are 1:1 (18). Changes in membrane cholesterol level cause major effect on physical properties of plasma membrane like membrane fluidity, phospholipids arrangement and it also cause membrane deformability (19-20).The brain contain 20 % of body cholesterol and use for formation synapse and dendrites (21-22).

The arterial stiffening a possible pathogenic factor caused by depletion of cholesterol, which change properties of arterial wall and promote to vascular rupture in response to acute elevation in intravascular

pressure. Many clinicians try to reduce arterial stiffness to reduce incidence of hemorrhagic stroke (23-24).

Our findings show strong inverse association of serum lipid concentration between hemorrhagic stroke patients and healthy control persons. It means Very low serum concentration of total cholesterol, triglycerides, LDL, VLDL and HDL increase risk of hemorrhagic stroke. There is no significant difference between total cholesterol of men and women of case and control group.

There are so many previous studies which show similar results. An observational study of Japan elucidates that low serum cholesterol [<160mg/dl] is strongest risk factor for hemorrhagic stroke (25). In a study of multi risk factor intervention Trail, people which have total cholesterol <4.13 mmol/L the risk of hemorrhagic stroke is three times higher than that of normal (26).A prospective study of Finland was observed the total cholesterol positively associated with ischemic stroke and negatively associated with hemorrhagic stroke (27). A study showed risk of death from subarachnoid hemorrhage among men was significantly associated with serum cholesterol level and this association was U shaped (28). From the results of our study we found significant negative association between total cholesterol and hemorrhagic stroke. In another observational study showed low triglycerides and LDL-C levels were associated with increase risk factor of hemorrhagic stroke in women and also state that person's which have LDL-C levels <70 mg/dL increase in 2.17 times the risk of hemorrhagic stroke (29). A Meta-analysis observed that 15 % hemorrhagic stroke risk was decrease with increment of 1mmol/L of total cholesterol concentration. Lower LDL- C concentration was significantly associated with increased risk of hemorrhagic stroke (30). An observational study reveals that the association between hemorrhagic stroke and LDL-C are independently associated (31). In our study we found that the triglyceride level is negatively significant and LDL-C has non-significant negative association with hemorrhagic stroke.

Wang et al 2011also found that hemorrhagic stroke is inversely associated with plasma serum high density lipoprotein cholesterol (HDL-C) (32). A study of Zeng et al 2019 observed that serum HDL and ratio of LDL and HDL was not associated with hemorrhagic stroke (33). Similarly in our study we found non- significant negative correlation between serum HDL-C and hemorrhagic stroke.

A Meta-Analysis of Ziff et al 2019observed use of statin non-signignificantly increase intracranial hemorrhage (34).Vergouwen et al 2008 observed that beneficiary effect of statins is lost in hemorrhagic stroke patients (35). In another study of Goldstein 2008observed that the use of atorvastatin reducerisk of stroke by aggressive reduction in cholesterol level. Statins or HMG Co-A reductase are enzymes that inhibits cholesterol biosynthesis, used as lipid lowering medication that increase risk of hemorrhagic stroke (36).

CONCLUSION

This present study concluded that lipid profile levels play significant diagnostic role in hemorrhagic stroke patients. The lower concentration of total cholesterol and triglycerides may predispose individual towards the higher risk hemorrhagic stroke.

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