The Potential Effect of Lipid Profile on Deep Seated Versus Lobar Intracerebral Hemorrhage

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ABSTRACT:

BACKGROUND:

Brain hemorrhage is defined as the extravasation of blood from the vascular bed into the intracranial space, resulting in clinical dysfunction of nervous system. Intracerebral hemorrhage is a heterogeneous disease with deep and lobar subtypes. The amount of serum lipid may also affect the integrity of blood vessel wall and abnormal lipid profile may consider as a risk factor for intracerebral hemorrhage.

OBJECTIVE:

The present study was designed to evaluate the relationship between serum lipids and the site of intracerebral hemorrhage.

METHOD:

A cross-sectional study for 100 patients (50 with deep seated, 50 with lobar intracerebral hemorrhage) from Al-Kadhymia teaching hospital and Bagdad Teaching Hospital between August 2012 and June 2014. Case subjects included those patients from 20 to 89 years of age experiencing ICH within first 48 hours of presentation. Total cholesterol (TC), High-density lipoprotein (HDL) cholesterol, Low-density lipoprotein (LDL) cholesterol and Triglycerides **(**TG) serum level, was compared in deep seated and lobar intracerebral hemorrhage.

RESULTS:

There was significant relationship between high HDL level in deep seated compared to lobar hemorrhage, while there was no statistical significant relationship between the site of hemorrhage by TC, LDL and TG level

CONCLUSION:

High HDL level is a risk factor for deep seated rather for lobar intracerebral hemorrhage.TC, TG, LDL have no effect on the site of hemorrhage.

KEY WORLDS: lipid, intracerebral hemorrhage.

INTRODUCTION:

Brain hemorrhage is defined as the extravasation of blood from the vascular bed into the intracranial space, resulting in clinical dysfunction of nervous system [(1)].

Intracerebral hemorrhage (ICH) is a heterogeneous disease with deep and lobar subtypes distinguishable on an epidemiologic basis. The different patterns of these two subtypes should no longer be treated as a single entity [(2)].

Deep intracerebral hemorrhage is a type of stroke due to bleeding within the deep structures of the brain. These structures include the thalamus, basal ganglia, pons, and cerebellum [(3)].

Lobar intracerebral hemorrhage is an intracranial hemorrhage of the frontal, parietal, temporal, or occipital cortex which represents one third of cases of primary, non-traumatic ICH [(3)].

Previous studies identified bleeding location as a potent influencing factor of ICH volume. Lobar hemorrhages were consistently found to be larger than those located in deep structures of the brain [(4)].

The biological pathways that lead to ICH differ depending on the location of the hemorrhage [(5)].

In addition to the well-known etiological factors for primary ICH, such as hypertension and cerebral

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amyloid angiopathy, dyslipidemia has a significant role as well [6,7]. Hypocholesterolemia may be defined by a serum total cholesterol level lower than the 5th percentile for age and gender, or by the cut-of value that predicts an adverse prognosis by epidemiological studies [8]. Its prevalence varies according to populations and reaches 2% to 3% in the general population and 6.2% in patients hospitalized in the department of internal medicine [9].

Disorders of certain lipoprotein fractions, mainly hypocholesterolemia, hypertriglyceridemia, hypo-low density-lipoprotein cholesterolemia (hypo-LDL) and hypo-high density- lipoprotein cholesterolemia (hypo-HDL), are considered risk factors for ICH [10, 11].

The pathophysiological mechanism that links dyslipidemia and ICH is still unclear; however, it is possible that total cholesterol has effect on the preservation of the integrity of the blood vessel wall, and consequently its low levels may contribute to necrosis of smooth muscle cells. On the other hand, cholesterol levels modify platelet aggregability, affecting platelet activating factor, and hypo-Cholesterol may lead to decreased platelet aggregation which may contribute to an increase in the size of ICH [12].

Some experts have suggested that a plasma low density lipoprotein cholesterol level of 25 mg/dL is sufficient to supply peripheral cholesterol needs [13]. Both low and high serum total cholesterol levels have been reported to be associated with increased mortality, thus demonstrating a U- or J-shaped relationship [14,15]. Among various clinical factors, high blood pressure and alcohol consumption increased the risk for hemorrhagic stroke in subjects with low total cholesterol (TC) [15,16]. An intensive therapeutic strategy has led to very low LDL-C (≤ 40 mg/dL) in statin-treated subjects in many clinical trials of intensive statin treatment; however, an increased incidence of ICH has not been confirmed [17]. Aggressive reduction in cholesterol levels increased incidence of ICH in subjects treated with 80 mg of atorvastatin after a recent (within 1 to 6 months) stroke or transient ischemic attack [18]. Nevertheless, no association was found between the risk for ICH and the baseline or recent LDL-C level in statin-treated patients [19]. LDL level can be considered as a risk factor for both ischemic and hemorrhagic cerebral events [20].

The present study was designed to evaluate the relationship between serum lipids and the site of intracerebral hemorrhage.

PATIENTS AND METHODS:

Study Design

This was a hospital-based cross-sectional study which conducted to determine the effect of TC, LDL, and HDL level in patients with lobar vs. deep seated intracerebral hemorrhage.

Setting

Hundred patients with ICH who have been received at Al-Kadhimiya teaching hospital and Baghdad teaching hospital between August 2012 and June 2014 was seen at neurology wards and general medical wards. A structured questionnaire filled by the researcher by taking history from the patients and sends them lipid profile as part of routine work-up in the ward.

Study Sample

The following clinical and demographic data was collected: age, sex, risk factors.

The Inclusion and exclusion criteria for the cross-sectional study groups were as follows:

a) Inclusion criterion:

Case subjects included those patients from 20 to 89 years of age both male and female experiencing ICH within first 48 hours of presentation diagnosed by head CT-scan.

b) Exclusion criterion:

1. Children less than 18 year because of the likely different etiologies.
2. Diabetic patients because diabetes mellitus may affect the lipid profile.
3. Those with history of familial hyperlipidemia.
4. Patients with history of coagulopathies.
5. Secondary ICH due to tumor, aneurysm, vascular malformations.
6. Patients had taken lipid lowering drugs.
7. Obese patients (BMI above 25).

Data collection and analysis

Complete cholesterol test (also called a lipid profile) measures the amount of “good” and “bad” cholesterol and the level of triglycerides in the blood. Cholesterol is a soft, waxy fat that the body needs to function properly.

Complete cholesterol test measures four types of lipids (fats) in the blood:

- Total cholesterol
- Low-density lipoprotein (LDL) cholesterol: this is referred to as “bad” cholesterol.

- High-density lipoprotein (HDL) cholesterol: this is referred to as "good" cholesterol.
- Triglycerides

The test is usually done in the morning, as you'll probably have fasted since the night before. A blood test is an outpatient procedure, usually performed at a diagnostic lab. The procedure takes only a few minutes and is relatively painless. Cholesterol levels are measured in milligrams (mg) of cholesterol per deciliter (dL) of blood. Ideal results for most adults are:

LDL: 70-130 mg/dL. HDL: more than 40 mg/dL. Total cholesterol: less than 200 mg/dL. Triglycerides: less than 150 mg/dL.

Serum was separated and all samples were analyzed within 6 hours of collection .Serum cholesterol and triglyceride was estimated by enzymatic methods using diagnostic kits (Accurex Biomedical). HDL-C was measured in the serum after a precipitation with phosphotungstic acid in presence of magnesium chloride. LDL-C were estimated using the formula of Friedewald with modification of Bachorik. Quality control was maintained using quality control sera of Technicon (Bayer Corporation, USA). The laboratory values of serum lipids were compiled and analyzed using appropriate statistical methods. The intraassay and interassay coefficient of variations for these investigations were found to be between 4% to 6% which is well within the recommended range.

Hypertension and diabetes were considered present when patients reported being diagnosed by their physician.

Statistical Analysis

Statistical analysis was carried out using SPSS version 20. Categorical variables were presented as frequencies and percentages. Independent sample t-test was used to compare between two groups. Pearson's chi square (X^2) test and fisher exact test were used to find the association between the categorical variables. A p-value of ≤ 0.05 was considered as significant.

RESULT:

Hundred patients were involved in this study; they were divided according to site of intracerebral hemorrhage into two groups; 50 patients with deep seated ICH and other 50 patients with lobar ICH. LDL, TG, HDL, total cholesterol were measured and compared in both groups.

In this study 74 patients were male (39 deep seated , 35 lobar) and 26 were female (11 deep seated and 15 lobar),53 patients were 60 year and above (22 deep seated , 31 lobar) and 47 patients were below 60 years of age (28 deep seated ,19 lobar). Most of hemorrhages were in the right hemisphere (54% for deep seated and 60% for lobar).

The mean differences of patients' lipid profile by site of intracranial hemorrhage. There was significant mean difference of deep seated intracranial hemorrhage and lobar site by patients HDL. However, there were no significant mean differences of deep seated intracranial hemorrhage and lobar site by LDL, triglyceride as well as total cholesterol. HDL mean was measured in both deep seated and lobar ICH and the result was high HDL level in deep seated compared to lobar hemorrhage and by using t-test result was highly significant as shown in table 1.

There were no significant association between site of hemorrhage by age and sex as shown in table 2.

History of hypertension was found in deep seated ICH (74%) compared with lobar ICH (64%) as shown in figure 1. By using Chi squared test the result was statically significant as shown in table 3.

To exclude confounding factors, we do logistic reassign model for LDL, HDL, TG and total cholesterol. Only HDL variable showed significant contribution to this model as shown in table 4 and 5.

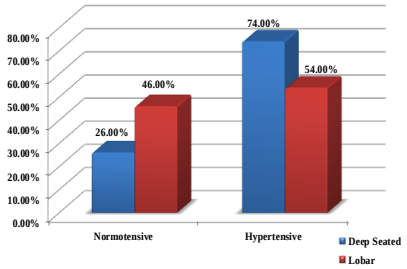

Figure 1: Distribution of patients with intracranial hemorrhage by Blood pressure.

Table 1: Mean differences of patients' lipid profile by site of intracranial hemorrhage

Variable	Groups	N	Mean	t-test	P value
LDL	Deep Seated	50	96.06	0.915	0.363
	Lobar	50	89.10		
HDL	Deep Seated	50	42.10	3.171	0.002*
	Lobar	50	39.22		
Triglyceride	Deep Seated	50	92.82	0.092	0927
	Lobar	50	92.28		
Total Cholesterol	Deep Seated	50	163.02	1.482	0.141
	Lobar	50	150.48		

*p value ≤ 0.05 is significant

Table 2: Association of site of intracranial hemorrhage by age and sex.

Variable	Site of Intracranial Haemorrhage		χ^2	*P* values
	Deep Seated (%)	Lobar (%)		
Age Groups < 60 years ≥ 60 years	28 (56.0) 22 (44.0)	19 (38.0) 31 (62.0)	3.252	0.071
Sex Male Female	39 (78.0) 11 (22.0)	35 (70.0) 15 (30.0)	0.832	0.362

*p value ≤ 0.05 is significant

Table 3: Association of site of intracranial hemorrhage by blood pressure

Variable	Site of Intracranial Haemorrhage		χ^2	*P* values
	Deep Seated (%)	Lobar (%)		
Blood pressure Normotensive Hypertensive	13 (26.0) 37 (74.0)	23 (46.0) 27 (64.0)	4.3402	0.037*

*p value ≤ 0.05 is significant

Table 4: Logistic regression for LDL, HDL, TG and total cholesterol.

Variable	Wald	df	P value	Odds Ratio	95% C.I. for Odds Ratio	
					Lower	Upper
LDL	0.904	1	0.342	0.974	0.922	1.029
HDL	8.898	1	0.003*	1.252	1.080	1.451
TG	1.438	1	0.230	0.986	0.963	1.009
Total Cholesterol	3.295	1	0.069	1.049	0.996	1.104
Constant	12.171	1	0.000	0.000		

*p value ≤ 0.05 is significant

Table 5: Logistic regression for blood pressure, LDL, HDL, TG and total cholesterol.

Variable	Wald	df	P value	Odds Ratio	95% C.I.for Odds Ratio	
					Lower	Upper
Blood pressure Normal** Hypertensive	1.048	1	0.038	2.851	1.058	7.684
LDL	-0.028	1	0.323	0.973	0.921	1.027
HDL	0.236	1	0.003*	1.266	1.086	1.476
TG	-0.011	1	0.387	0.989	0.965	1.014
Total Cholesterol	0.045	1	0.083	1.047	0.994	1.102
Constant	-13.718	1	0.000	0.000		

**reference group
*p value ≤ 0.05 is significant

DISCUSSION:

The study shows that the site of ICH whether deep seated or lobar was affected by HDL level and blood pressure while LDL, TC, TG levels have no statistically significant effect on the site of hemorrhage.

ICH recurs more frequently in lobar hemorrhage than in deep hemorrhage; indeed, recurrent hemorrhage is part of definition of cerebral amyloid angiopathy [21].The only predictor of recurrent ICH includes age, sex, history of hypertension, and lobar location [22]. In our study the mean HDL level in deep seated ICH was 42.10 which mean that high HDL level may be a risk factor for deep seated hemorrhage which is near the result achieved by Xiang Wang [23]. This can explain by high HDL level lead to thinning of arterial wall predisposing to microaneurysms formation.

In the current study there was significant mean difference between the site of hemorrhage and HDL level (P value 0.002). The mean HDL level in lobar hemorrhage was 39.22 this mean that low level of HDL may be a risk factor for lobar hemorrhage, this may explained by HDL level may decreased with age and the patients with lobar hemorrhage were older age group.

The mean total cholesterol level in deep seated ICH was 163.02, while the mean level of total cholesterol in lobar hemorrhage was 150.48. This result mean that there were no significant difference between the site of hemorrhage and total cholesterol level, and the level of total cholesterol is inversely related to the primary intracerebral hemorrhage. This can explained by increased erythrocyte fragility in vitro and in vivo with reduced levels of cholesterol, it has been proposed that lower cholesterol results in a weakened endothelium that more readily leads to arterial fragility, hemorrhage, or slower repair after small hemorrhages [24].

Lipid profile changes are thought to be a risk factor in the occurrence of stroke. On the other hand, stroke itself is also associated with changes in the lipid levels probably because of the accompanying stress and catecholamine overproduction that occurs during an acute stroke [20].

The present study showed that LDL level in deep seated ICH was 96.06 which mean that there is inverse relationship between LDL and deep hemorrhage; so that low level of LDL may be a risk factor for deep seated ICH and this result is near to result achieved by Sturgeon JD [25].This can explain by adequate cholesterol maintain the integrity of vessel wall and their resistant to rupture. Low cholesterol may play a role in promoting arterial medial layer smooth muscle cell necrosis.

In the current study the mean LDL level in lobar hemorrhage was 89.10 which mean that low LDL level is also a risk factor for lobar hemorrhage [23].

When you eat, your body converts the calories it doesn't need into triglycerides, which are stored in fat cells. People who are overweight or diabetic or who eat too many sweets or drink too much alcohol can have high triglyceride levels. Different opinions about triglyceride levels as risk factors for ICH exist: some authors consider low triglyceride values associated with an increased risk of ICH and

the others found that higher levels of triglycerides correlate with higher risk for ICH(10,11), in this study the mean level of TG in patients with deep seated ICH was 92.82, the mean level of TG in lobar ICH was 92.28 and this mean that low level of TG is a risk factor for primary ICH independent on the site of hemorrhage which is near the result achieved by Bonaventure A(10).

There is no significant mean differences in TC, LDL and TG level and site of hemorrhage and there was no previous studies to do comparison of the results.

The risk of primary ICH increase with increasing age in both lobar and deep seated hemorrhage, although patients with lobar hemorrhage are older age than those with deep seated ICH the results were non statically significant.

The overall prevalence of hypertension in patient with ICH was 64%. There was significant association between the site and hemorrhage and blood pressure (P value 0.037) where the hypertension is a risk factor for deep seated hemorrhage this can be explained by hypertension-induced lipohyalinotic changes in penetrating blood vessels and associated amyloid angiopathy. This finding differs from Farah I. Al-Saffar study may be due to younger age group in this study [(26)].

The hypertension may be a confounding factor affecting the site of hemorrhage in addition to lipid profile and to exclude this effect we do logistic regression model for blood pressure, HDL, LDL, TC, TG; only HDL variable show significant contribution to this model p value (0.003) odd ratio (1.266) this mean that HDL level affecting the site of ICH independent on blood pressure level which is near the results achieved by Xiang Wang[(23)].

CONCLUSION AND RECOMMENDATIONS:

Increase HDL level is a risk factor for deep seated ICH. Low LDL level is a risk factor for both.

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