Lipid profile in Jordanian patients with first ever ischemic stroke

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ABSTRACT

الأهداف: دراسة العلاقة بين مستوى الدهنيات في الدم: الكولسترول الكلي (TC)، الكولسترول قليل الكثافة (LDL)، الكولسترول عالي الكثافة (HDL)، والدهنيات الثلاثية (TG)، في المرضى الأردنيين الذين أدخلوا للمستشفى اثر تعرضهم لسكتة دماغية احتباسية (IS) خلال 3 سنوات، ومقارنتهم مع مجموعة ضابطة.

الطريقة: أُجريت دراسة استعادية مضبوطة لجميع المرضى الذين تم تشخيصهم بسكتة دماغية احتباسية (IS)، واللذين تم إدخالهم إلى مستشفى الجامعة الأردنية – الأردن، خلال الفترة ما بين يناير 2004م وحتى 31 ديسمبر 2006م، والذين تم قياس مستوى الدهنيات بالدم خلال 48 ساعة من إدخالهم.

النتائج: شملت الدراسة 98 مريضاً مصاباً بالسكتة الدماغية الاحتباسية (IS)، وتمت مقارنتهم بـ 98 مريضاً من المجموعة الضابطة. كانت المجموعتان متشابهتين من حيث العمر، الجنس، معدل انتشار ارتفاع الضبط الشرياني(HTN)، السكري (DM)، أمراض القلب الوعائية الإحتباسية (IHD)، والتدخين. أظهرت الدراسة انخفاضاً ملموساً ومهماً في نسبة الكولسترول عالي الكثافة (HDL) في مرضى السكتة دماغية الاحتباسية (IS) بالمقارنة مع مجموعة التحكم. لم يكن هناك اختلاف بين المجموعتين في أنواع الدهنيات الأخرى (TC, LDL, TG). كان استخدام الأدوية الخافضة للكلسترول (ستاتينس) أكثر في المجموعة الضابطة (28%) مقارنة بالمرضى (10%) (p=0.002). ظهرت عوامل الخطر الأساسية في كلا المجموعتين.

خاتمة: رغم أن هذه الدراسة محدودة بكونها استعادية، إلا أنها أظهرت انخفاضاً ملحوظاً في الكولسترول عالي الكثافة (HDL)، لدى مرضى السكتات الدماغية الاحتباسية (IS).

Objective: To study the relationship between lipid profile, total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), and triglycerides (TG) in Jordanian patients admitted with first ever ischemic stroke (IS) to a teaching hospital over a 3-year-period, and compared them to a control group.

Methods: A retrospective case control study of all patients with diagnosis of IS who were admitted to the Jordan University Hospital, Amman, Jordan from January 2004 to December 2006 and had a documented fasting lipid profile within 48 hours of their admission. They were compared to controls without IS.

Results: Ninety-eight patients with IS were studied and compared to 98 control subjects. Both patients and control groups were similar regarding age, gender distribution, prevalence of hypertension, diabetes mellitus, ischemic heart disease (IHD), and smoking. The lipid profile showed a significantly lower HDL level in IS patients compared to the control group. There were no significant differences between the patients and control regarding TC, LDL, or TG levels. Control group used statins more frequently than patients (28% versus 10%, p=0.002). Both groups had high prevalence of risk factors.

Conclusions: Though this study is limited by its retrospective design, it suggests that IS patients have significantly lower levels of HDL.

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Cerebrovascular diseases (CVD), both ischemic stroke (IS) and intracerebral hemorrhage (ICH) are the leading causes of disability and the second leading causes of mortality in the developed countries.[1] There is striking lack of information regarding the epidemiology of stroke in the Arabic population. According to the World Health Organization report from United Arab Emirates, CVD ranked second as a cause of mortality (16.2%) after ischemic heart disease (IHD) (28%) and preceded road traffic accidents (15%).[2] Well known

modifiable risk factors for IS include hypertension, cigarette smoking, IHD, and diabetes mellitus (DM). Though the relationship between IHD and dyslipidemia are well established both by observational and interventional studies, the relationship between CVD and dyslipidemia is still controversial.[3,4] While observational studies did not find a direct relationship between serum cholesterol levels and IS, interventional studies aiming at reducing low-density lipoprotein (LDL) levels by statins in patients with IHD showed significant reduction in the incidence of non fatal IS.[5] Previous studies suggested an inverse relationship between mortality rate from ICH and cholesterol level. This lead to the finding of a J shape relationship between cholesterol level and CVD increasing at both ends of the range (higher mortality incidence of ICH with low cholesterol levels, and higher IS incidence with higher cholesterol levels).[6,7] Studies regarding relationship of lipid profile and CVD in Jordanian patients are lacking. The aim of this paper is to study the relationship between lipid profile on admission in patients with IS, and compared it to the control group without IS who were tested in the same period (2004-2006).

Methods. Files of all adult patients (age ≥18 years) with the following inclusion criteria were included in the study: 1) confirmed diagnosis (by neuroimaging) of first ever IS and who had 2) fasting (of least 12 hours) lipid profile carried out within 48 hours of admission in the period from January 2004 to December 2006 were reviewed. The study took place in Jordan University Hospital, Amman, Jordan. The Ethics Committee of Jordan University approved this study. Exclusion criteria included patients with clinical, although not confirmed, history of IS or no documented lipid profile or patients with transient ischemic attacks defined as patients with short lasting neurological deficit of less than 24 hours. Data including age, gender, final diagnosis IS with no attempt to classify the etiology or type of IS, risk factor status at the time of diagnosis including hypertension (HTN) defined as being known hypertensive (documented readings of >140/90 mm Hg) from the history record or the list of medications used, DM defined by use of insulin or other antidiabetic agents or fasting blood sugar of more than 126 mg/dl. Ischemic heart disease with confirmed history of angina, myocardial infarction, coronary intervention such as bypass surgery, angioplasty, or stenting or documented atherosclerosis of coronaries by angiography. History of smoking and use of lipid lowering agents (statins) was also recorded for each patient or control. The control group included randomly selected patients either admitted to the hospital or seen in the outpatient departments for reasons other than CVD during the same study period and who had lipid profile tested in the same period. Fasting lipid profiles were recorded in patients and controls. They were measured in mg% instead of millimoles/liters. We used the reported values (from our laboratory) without changing them to the international standard values.

We used SPSS statistical package version 11.5. Mean, ranges, standard deviations, 95% confidence intervals for age, total cholesterol (TC), LDL, high density lipoprotein (HDL), and triglycerides (TG) for patients with IS, and controls were calculated and tabulated. For continuous variables, 2 independent sample T tests were used to look for any significant difference. We used 2 -tail tests with an alpha of 0.05. Categorical variables were compared by cross tabulation using chi square testing to assess any significant differences. Correlations between different variables were calculated using Spearman correlation coefficient.

Results. The prevalence of classical risk factors was quite high, and similar in both groups (**Table 1**). The lipid profile findings showed significant difference in the level of HDL, which was lower in patients with IS compared to control. There were no differences between groups in TC or LDL or TG levels (**Table 1**). If we excluded the remaining patients and control subjects with IHD (56 patients and 51 control), there will be a comparison with regards to their age (61.8±10.5 versus 58.7±13.0, p=0.17) and the lipid profile showed only significant

Table 1 - Demographic data, lipid profile and risk factors in ischemic stroke (IS) and control groups.

Parameters	IS group (N=98)	Control (N=98)	*P*-value
Age (years) (mean±SD)	62.8±10.6	60.3±11.5	0.18
Range (years)	40-89	32-89	
Gender (%) Male/Female	53/47	49/51	0.67
TC (mg%) (mean±SD)	195.0±47.8	186.1±39.6	0.16
LDL (mg%) (mean±SD)	123.1±42.3	126.0±46.1	0.65
HDL (mg%) (mean±SD)	39.3±10.6	44.2±11.8	0.003
TG (mg%) (mean±SD)	174.5±93.4	182.7±96.9	0.55
HTN (%)	71.4	73.5	0.87
DM (%)	44.9	38.8	0.22
IHD (%)	42.9	48.0	0.31
Smoking (%)	44.9	40.8	0.67
Statins use (%)	10.2	28.6	0.001

TC - total cholesterol, LDL - low density lipoprotein, HDL - high density lipoprotein, TG - triglycerides, HTN - hypertension, DM - diabetes mellitus, IHD - ischemic heart disease

difference regarding HDL (p=0.002) level and was not significant for the levels of TC (p=0.54), LDL (p=0.83) or TG (p=0.63). The finding of significantly low HDL level in IS was still correct (p=0.04), even if we considered patients and control subjects who did not use statins (88 patients and 70 control) with comparable age (62.4±10.7 versus 59.7±10.8 p=0.12), and no difference regarding TC (p=0.74), LDL (p=0.97), and TG (p=0.60).

Discussion. The lack of association between TC levels and IS is similar to the previous reports.[8-11] One Italian study showed a linear relationship between TC level and risk of stroke.[12] The positive association of lower levels of HDL and IS is quite interesting, and worth further confirmation. A study from Britain reported an inverse relationship between HDL level and the incidence of stroke in British men.[10] This was reported in other studies as well,[13,14] while another American study showed only a tendency for women with higher HDL level to get less IS.[13] An old study of clofibrate, which is quite potent in elevating HDL level and lowering TG levels than other lipid lowering agents seemed to increase, rather than decrease the incidence of IS despite the 8% reduction of TC.[15] The role played by HDL is now getting more insight, as this seems to be quite important for the whole process for atherosclerosis. Investigators of the Jordan Hyperlipidemia and Related Targets Study (JoHARTS) study[16] showed significantly lower levels of HDL in Jordanian patients with IHD regardless of their gender compared to those without IHD. In this study, the HDL level was still significantly lower in the patient group compared to the control group in the subgroup of patients and control without IHD (40.4±11.5 versus 47.8±12.2, p=0.002). This confirms the fact that low HDL is a risk factor for both IHD and IS, and even in the absence of IHD, a low HDL level would remain a significant risk factor for IS. We do believe that the lower levels of HDL are a real risk factor for IS in this population. Anyhow, the reason behind this lower level of HDL cannot be ascertained from this study. Factors known to be associated with low levels of HDL (such as the metabolic syndrome) or high levels were not examined in this retrospective study. Smoking is such a risk factor, and it was similar in the 2 groups as a whole (**Table 1**). The British study quoted above[10] showed the difference in HDL was still significant regardless of smoking status. Another reason for the difference in HDL level is the higher percentage of control group using statins compared to IS patients. This would have been more reasonable if the effect on LDL was also significant as these drugs (statins) would have affected LDL levels more than HDL levels as reported in different interventional trials.[17] We also showed that even if we exclude patients and controls who were using statins still patients with IS had significantly lower levels of HDL compared to controls.

The presence of the classical risk factors across both groups in high proportion is quite alarming. Compared to other series and meta-analyses these figures are quite high.[17] It is very clear that the control population in this study does not represent the healthy Jordanian population as this group represented a hospital rather than general community population. There were some limitations, however, some of them are unavoidable. The retrospective design, single center, the timing of lipid profile testing (within 48 hours of event), the lack of classification of IS types and etiologies, and the presence of some confounding factors that we did not consider (such as body mass index) are some of them. For the stroke subtypes, a previous report from Jordan[18] showed that the majority of IS are lacunar, and the incidence of atrial fibrillation and extracranial carotid disease was quite small.

Conclusions that can be drawn and definitely need further confirmation include low HDL levels in IS patients and the relatively high rate of classical risk factors in the studied population. A recent publication of the REACH registry confirms the high prevalence of these risk factors in patients with cerebrovascular events.[19] A major effort needs to be carried out at the public level to decrease the incidence of these risk factors and to consider low HDL levels as an important risk factor for IS.

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Related topics

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