

Total and LDL cholesterol as risk factors of ischemic stroke in Emirati patients

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Citation

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Abstract

The role of total and LDL-cholesterol as independent risk factors of ischemic stroke remains uncertain. The aim of this hospital based prospective observational study is to investigate the association between total and LDL cholesterol levels and ischaemic stroke in Emirates patients admitted to hospital between June 2007 and June 2009 with atherothrombotic stroke. One hundred and seventy one Emirati patients, 89 males and 82 females with acute ischemic stroke were diagnosed and investigated for risk factors, including hypertension, diabetes mellitus, cardiac diseases, cigarettes smoking and past history of transient ischemic attack (TIA) and past history of stroke. Exclusion criteria were patients with acute or chronic atrial fibrillation and patients receiving "statins". Brain CT scan, echocardiogram and carotid ultrasound were done on hospital admission. One hundred and twelve patients (65.5%) had hypercholesterolemia (total cholesterol level ≥ 5.2 mmole/L, LDL cholesterol ≥ 4.2 mmole/L). One hundred and thirty patients (76.0%) were hypertensive. Ninety patients (52.8%) were diabetic. Twenty two (12.9%) were heavy smokers. Fifty patients (29.2%) had past history of cardiac disease. Twenty eight patients (16.4%) had previous stroke Twelve patients (12%) had TIA. Out of the one hundred and twelve patients with hypercholesterolemia nine patients (5%) only had isolated hypercholesterolemia. The commonest risk factor associated with hypercholesterolemia is hypertension (78.8%). In conclusion, the results of this study do not support the association between isolated hypercholesterolemia and atherothrombotic stroke. Hypercholesterolemia is not an independent risk factor for ischaemic stroke but it can interact with other risk factors mainly hypertension to promote atherosclerosis.

INTRODUCTION

Stroke is the third most common cause of death and leading cause of severe disability in both developed and developing world¹. Treatment of stroke is still unsatisfactory and the best management for stroke is primary prevention. Management of the common reversible atherosclerotic risk factors such as hypertension, diabetes mellitus, carotid stenosis, atrial fibrillation, heavy smoking and excessive alcohol intake is crucial for primary prevention of ischaemic stroke². Controversy remains on the relation between serum cholesterol levels and ischaemic stroke. A meta-analysis of the literature that was limited to ischaemic stroke, showed no association between total cholesterol levels and ischemic stroke incidence^{3,4}. In contrast, authors of meta-analysis of seven other cohort studies reported a positive association between cholesterol and ischemic stroke⁵. Meta-analysis of early trials of lipid – lowering therapy using dietary or drug intervention rather than statins, provides evidence that reducing cholesterol levels per se does not reduce the risk of ischaemic stroke⁶. In contrast, use of 3-hydroxy – 3-methyl glutaryl coenzyme A (HMG – COA) reductase inhibitors

(statins) among such patients has been reported to produce about 24% relative risk reduction of all strokes and a 30% relative risk reduction of ischemic stroke^{7,8}. At present, the prevailing evidence is not supportive of the hypothesis that cholesterol is an important risk factor for ischaemic stroke, although this issue has been clouded by the observation of a reduced risk of ischaemic stroke with the use of statins.

The objective of this study is to investigate the role of total and LDL cholesterol as an independent risk factor for ischemic stroke in Emirati patients.

SUBJECTS AND METHODS

The prospective observational study was done at Al-Qassimi hospital – Sharjah, UAE between June 2007 and June 2009. One hundred and seventy one Emirati patients diagnosed with acute ischaemic stroke including both large artery disease and small artery disease (lacunar infarcts). Inclusion criteria were clinical diagnosis of acute stroke with a brain CT scan confirming cerebral or brain stem infarcts. Exclusion criteria were patients with intracerebral hemorrhage or brain tumor on brain CT scan, atrial

fibrillation on ECG or patients on statins therapy before the onset of stroke. Baseline data and measurements collected including demographics, history of atherosclerotic risk factors as hypertension (BP> 140/90), diabetes mellitus (fasting blood sugar > 8 mmol/L), cardiac diseases confirmed by echocardiogram, carotid stenosis ($\geq 70\%$) shown by carotid ultrasound, past history of transient ischaemic attack (TIA), heavy cigarette smoking (≥ 20 cigarettes /day for 5 years or more) and hypercholesterolemia (fasting serum total cholesterol level ≥ 5.2 mmol/L and LDL – cholesterol level > 4.2 mmol/L). Categorical variables are expressed as frequencies and percentages. There were 89 males and 82 females ranging between the ages of 30 and 90 years. All investigations were done according to standard procedures.

RESULTS

Eighty nine males and eighty two females with acute ischemic stroke were included. The mean age of the males was 70 years with the range between 30-90 years and the mean age of the females was 72.3 years with the range between 60-85 years. The age group between 50-69 years

old shows the highest risk of ischemic stroke (Tab.1). Tab II shows that 59.6% of the patients with hypercholesterolemia had ischemic stroke between the ages 50-69 years old. Out of the 112 patients with hypercholesterolemia, nine patients (5%) only had isolated hypercholesterolemia (Tab III). Tab VI shows the frequencies of cerebral infarction according to the risk factors of ischemic stroke in 171 patients; one hundred and thirty patients (76.0%) were hypertensive one hundred and twelve patients (65.5%) had hypercholesterolemia, ninety patients (52.8%) were diabetic, fifty patients (29.2%) had cardiac disease (28 patients had ischemic heart disease, 14 patients had aortic stenosis and 8 patients had cardiomyopathy), twenty eight patients (16.4%) had past history of stroke, twenty two patients (12.9%) were heavy smokers, sixteen patients (9.4 %) had significant carotid stenosis and twelve patients (7.0%) had past history of TIA.

There were no cases of ischemic stroke due to independent risk factors of TIA, diabetes or carotid artery stenosis. Two patients (1.1%) had cardiac disease or were smokers and seven patients (3.9%) had hypertension as independent factors for ischemic stroke.

Figure 1

Table I

Frequency of cerebral infarct amongst the age groups

Frequency of cerebral infarct in males and females

Gender	Frequency	Percent
Males	89	52.0%
Females	82	48.0%

Table VI

Frequencies of cerebral infarct according to risk factors

Risk Factor	Frequency	Percent
H.T.	130	76.0%
Hypercholesterolemia	112	65.5%
D.M.	90	52.8%
History of cardiac disease	50	29.2%
Previous stroke	28	16.4%
Smoking	22	12.9%
Carotid artery stenosis	16	9.4%
TIA	12	7.0%

Table II

Hypercholesterolemia distribution by Age in patients with cerebral infarct

Age Groups (years)	Frequency	Percent
30-39	2	1.7%
40-49	6	5.0%
50-59	34	28.1%
60-69	38	31.4%
70-79	23	19.0%
80-89	9	7.4%
Total	121	100

Table III

Patients with two risk factors (Age & hypercholesterolemia) and cerebral infarct

Age Groups (years)	Frequency	Percentage
30-39	6	3.5%
40-49	27	15.8%
50-59	52	30.4%
60-69	50	29.2%
70-79	27	15.8%
80-89	9	5.3%
Total	112 (out of 171)	

Patients with cerebral infarct due to two risk factors (Hypercholesterolemia plus a second risk factor)

Risk Factor	Hypercholesterolemia	Percent	Total	% compared to the total patients with hypercholesterolemia (112)
Gender:				
Males	54	48.2%	112	48.2%
Females	58	51.8%		51.8%
H.T.	86	50.0%	130	76.8%
Diabetes	60	66.7%	90	53.6%
Cardiac disease	33	66.0%	50	29.5%
Previous stroke	18	64.3%	28	16.1%
Smoking	16	72.7%	22	14.3%
Carotid stenosis	10	62.5%	16	8.9%
TIA	7	58.3%	12	6.3%

Frequencies of outcomes of stroke patients

Outcomes	Frequency	Percent
Died	25	14.6%
Wheel chair bound	57	33.3%
Reasonably mobile	89	52.0%
Total	171	100%

Independent Risk Factors and ischemic stroke

Risk Factor	Frequency	Percent
H.T.	9	5.0%
Hypercholesterolemia	7	3.9%
D.M.	0	0%
History of cardiac disease	2	1.1%
Previous stroke	0	0%
Smoking	2	1.1%
Carotid artery stenosis	0	0%
TIA	0	0%

DISCUSSION

Most clinical trials which investigated the association between hypercholesterolemia and stroke were mostly done in Western Europe, North America and Australia, few were conducted in Japan, China, Malaysia and India. In this study the association between hypercholesterolemia and ischemic stroke was investigated in a Middle East population which has different genetic patterns, culture and dietary habits from Western and Asian populations. Hypercholesterolemia appears to be a problem in most Middle East populations specially the Gulf countries. One community-based study conducted in the United Arab Emirates showed the prevalence of hypercholesterolemia varied from 47.2% – 53.0% in Arab nationals and from 22.7% – 44.5% in non-Arabs, and it afflicts nearly 50% of the population⁹. Another epidemiologic study from Saudi Arabia showed that the maximum prevalence of hypercholesterolemia (6.2 mmole/L) achieved at an age of 56-64 years in urban Saudi subjects¹⁰; similar to age groups found in this study. A hospital-based prospective observational study done in Qatar showed that the prevalence of hypercholesterolemia (27.5%) was one of the most common risk factors of young ischemic stroke in Qatar¹¹.

The relatively small number of patients with ischemic heart disease can be explained by the exclusion of patients in statin. The patients with ischemic heart disease included in the study were diagnosed on hospital admission with ECG changes and echocardiogram. We found that there was no difference in the concentration of total and LDL cholesterol levels between patients with lacunar infarct strokes and atherothrombotic large artery strokes. This is in agreement with other studies which reported no difference in total and LDL cholesterol level between different subtypes of ischemic stroke and the controls¹². We found a strong positive association between serum total and LDL cholesterol is in middle aged men and women. A result of the clinical trial of the elderly in Europe showed that the use of statins in the elderly population did not result in a decrease in the incidence of stroke, while there was a substantial decrease in coronary events¹³. Our study showed that hypertension is the most common risk factor associated with hypercholesterolemia for ischemic stroke. Therefore hypercholesterolemia in hypertensive patients can increase the risk of atherosclerotic stroke. Another prospective observational studies reported negative association of cholesterol level and high blood pressure and stroke patients¹⁴. We found only 5% of the patients had isolated

hypercholesterolemia as an independent factor for ischemic stroke. This result does not match the results from randomized trials that reducing hypercholesterolemia with statins reduces stroke rate. It remains arguable however whether the reduced risk of ischemic stroke associated with the use of statins is attributed to other properties of statin^{15,16,17}. Statins are known to ameliorate endothelial dysfunction, stabilize atherosclerotic plaques and modify inflammatory responses and thrombus formation⁸. We used total and LDL cholesterol levels as indicators of hypercholesterolemia as LDL cholesterol fraction is believed to induce atherosclerosis. However HDL-cholesterol has been emphasized as a predictor of coronary heart disease in Western countries¹⁸ and recently in Japan¹⁹ it was found that low HDL cholesterol alone to be associated with increased risk of cerebral infarction^{3,20}. Other studies did not disclose an association between HDL cholesterol and ischemic stroke²¹.

CONCLUSION

Hypercholesterolemia is not found to be an independent risk factor for atherothrombotic stroke in Emirati patients but it could interact with other atherosclerotic risk factors, especially hypertension to increase the risk of ischaemic stroke. There is now more evidence that the ratio of total cholesterol to HDL-cholesterol is more informative to determine the risk to ischemic stroke than total and LDL-cholesterol levels.

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