

ASSESSMENT OF SOME ATHEROSCLEROSIS RISK FACTORS IN CHILDREN OF PATIENTS WITH YOUNG STROKE

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Abstract

INTRODUCTION: Cerebral strokes below the age of 45 account for up to 3% of all strokes. Given that atherosclerotic thrombotic factors are the most frequent etiology of cerebrovascular accidents (CVA) second to cardioembolic causes, and that children of families with sequels of premature atherosclerosis are considered to be at risk, we assessed atherosclerosis risk factors and antiphospholipid antibody (APL-Ab) levels in children of patients with young stroke (YS) and without cardioembolic causes in comparison to controls.

METHODS: This cross-sectional study was conducted on 27 children of patients with YS due to non-cardiac causes (case group) and 2 control groups, one with 52 children of patients with stroke after the age of 50, and the other with 55 children without the history of stroke in their parents. Findings were analyzed with SPSS using ANOVA test.

RESULTS: The mean values of systolic and diastolic blood pressure, LDL-C and ApoB₁₀₀ in the case group were significantly higher and mean HDL-C and ApoA₁ were significantly lower in the case group. The number of APL-Ab-positive cases was larger in the case group. The other assessed variables were not different between the two control groups.

CONCLUSIONS: Atherosclerotic thrombotic risk factors were more prevalent in children of patients with atherosclerotic thrombotic cerebral YS than in controls. Primordial and primary prevention of these risk factors should be considered in children of these families.

Key Words: Young stroke, risk factors, children, prevention.

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Introduction

Atherosclerotic thrombosis is well documented as the second most frequent cause of young stroke (YS) (i.e. stroke under the age of 40) and is most important in the 4th and 5th decades of life.^{1,2}

The atherosclerosis phenomenon starts early in life and becomes symptomatic in late adulthood. Many risk factor e.g. hypertension (HTN), dyslipidemia, high plasma levels of fibrinogen, antiphospholipid antibodies (APL-Ab) and diabetes mellitus accelerate the atherosclerotic process.^{3,4}

HTN increases the risk of ischemic stroke up to 3-4-fold and decreasing the systolic blood pressure below 11-12 mmHg decreases the rate of ischemic stroke by up to 38%. HTN induces lipohyalinosis in blood vessels and subsequent endothelial damage.⁵⁻⁷

Dyslipidemia, especially high levels of LDL-C, induces cholesterol deposits in damaged endothelium and accelerates atherosclerosis.

Other studies revealed that the risk of ischemic stroke decreased by up to 28% with the treatment of hypercholesterolemia.^{8,9}

There are numerous studies on the role of fibrinogen (Fb) in pathogenesis of thrombotic events. Some have revealed that high levels of Fb are a risk factor for ischemic stroke.¹⁰⁻¹³

In addition, APL-Ab is known as a risk factor of premature atherosclerosis.

The pathophysiology of stroke in APL-Ab syndrome is not well understood, but non-inflammatory thrombosis of medium-sized brain vessels is suggested as the main cause.¹⁴

Given that the children of patients with early atherosclerosis are considered to be at risk, the aim of this study was to assess thrombotic risk factors in the offspring of patients with YS compared to controls.

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TABLE 1. Comparison of mean variables in the case and control groups

	Case (n=27)	Control 1 (n= 55)	Control 2 (n= 52)
	Mean \pm SD	Mean \pm SD	Mean \pm SD
Age (year)	12.7 \pm 2.7	12.7 \pm 2.2	12.9 \pm 3.1
BMI (kg/m ²)	22.1 \pm 2.1	22.4 \pm 3.1	21.2 \pm 2.7
SBP (mmHg)	112 \pm 11.2*	107 \pm 1.4*	104.1 \pm 10.8*
DBP (mmHg)	76.2 \pm 3.1*	67.1 \pm 2.1*	69.2 \pm 2.7*
Total cholesterol (mg/dl)	177.1 \pm 28.2	169.2 \pm 33.2	174.2 \pm 31.1
LDL-C (mg/dl)	104.1 \pm 21.2*	95.4 \pm 17.2*	98.7 \pm 18.1*
HDL-C (mg/dl)	34.1 \pm 5.2*	40.1 \pm 5.3	38.2 \pm 4.7
TG (mg/dl)	148.2 \pm 27.1	142.7 \pm 15.1	146.1 \pm 21.2
Fibrinogen (mg/dl)	227.2 \pm 22.1*	214.7 \pm 5.5*	212.1 \pm 21.4*
ApoA ₁ (mg/dl)	117.1 \pm 14.1*	122.1 \pm 12.4*	125.2 \pm 15.7*
ApoB ₁₀₀ (mg/dl)	90.7 \pm 11.2*	82.7 \pm 10.1*	84.2 \pm 10.7*
Fasting blood sugar (mg/dl)	87.1 \pm 7.2	84.7 \pm 7.2	85.2 \pm 6.1

*P<0.05 (difference between the case and two control groups)

SBP: Systolic blood pressure; DPB: diastolic blood pressure; HDL-C: High-density lipoprotein cholesterol
LDL-C: Low-density lipoprotein cholesterol; TG: Triglycerides; Apo: Apolipoprotein

TABLE 2. The frequency of positive antiphospholipid antibodies (APL-Ab) in the case and control groups

Group	Positive APL-Ab	OR (95%CI)	P
Case	38%	2.7 (1.4-3.9)	0.02
Control 1	21%		
Case	38%	2.9 (1.7-4.1)	0.03
Control 2	19%		

Materials and methods

The subjects were recruited from amongst offspring of patients with YS referred to Alzahra Hospital, Isfahan, Iran. The case group consisted of 27 children of patients with thrombotic stroke under the age of 45 and two control groups, one consisting of 52 children of patients with stroke after 45 years of age and the other with 55 children of parents with no parental history of cerebrovascular accidents (CVA) or cardiac disease.

All subjects were aged 12-18 years and had no history of smoking, alcohol consumption and/or systemic diseases. The cases were selected from among children of patients with YS. All of the subjects underwent transesophageal echocardiography (TEE) to exclude cardiac diseases.

The biochemical parameters were assessed using venous blood samples taken in fasting state. APL-Ab measurement was conducted using ELISA (Cardivlisa kit, France) and values \geq 15 SI were considered as positive. Data were analyzed with SPSS using ANOVA. P values below 0.05 were considered as significant.

Results

The mean levels of systolic blood pressure (SBP), diastolic blood pressure (DBP), low-density lipoprotein cholesterol (LDL-C), APOB₁₀₀, and Fb in the case group were significantly higher than in the two control groups. HDL-C and APOA₁ levels were significantly lower in the case group.

There was no significant difference between BMI, total cholesterol, TG and FBS in the case and control groups (Table 1). As shown in Table 2, the frequency of positive APL-Ab in the case group was higher than in controls.

Discussion

Levels of SBP, DBP, Fb, LDL-C, and HDL-C were significantly different between the case and control groups. Given that essential HTN is the most common cause of HTN and its familial nature is well documented,¹⁴ higher blood pressure in the case group would be a reasonable expectation. Obesity is an atherosclerosis risk factor,¹⁵ however, in our study, there was no significant difference between BMI of the three groups studied.

Different studies have shown contradictory results about the role of Fb in ischemic stroke. In our study, the mean Fb level was significantly higher in the case group. In light of the ethnic and genetic differences in our society, we suggest that high Fb levels should be considered as an important thrombosis risk factor. Our study is in line with some other works in showing higher levels of LDL-C and lower levels of HDL-C in the case group.⁸ ApoB₁₀₀ is the main lipoprotein of VLDL and contains a domain recognized by the LDL receptor. ApoA₁ is the main apolipoprotein of HDL-C and its levels correlate with those of HDL-C in blood. ApoB₁₀₀ levels provide information on the number of potentially atherogenic particles.¹⁶ In this study, levels of ApoA₁ and ApoB₁₀₀ were significantly different between the case and control groups. Given the higher frequency of positive APL-Ab in the case group, assessment of this parameter as a risk factor of thrombosis might be important. The findings of this study show the necessity of screening for atherosclerosis risk factor in the offspring of patients with YS. Prevention of modifiable atherosclerosis risk factors and lifestyle improvement are essential to primary prevention of atherosclerotic diseases.

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