Correlation between MTHFR and Clinical Risk Factors in Ischemic Stroke

BALAR Khalid¹, NADIFI Sellama¹ and GRAVCM Study Group²

¹Laboratory of Human Genetics and Molecular Pathology
University Hassan II/ Faculty of Medicine
Casablanca, Morocco

²Academy Hassan II of Science and Technology
Department of Neurology at University Hospital Center
Casablanca and Rabat, Morocco

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Abstract

MTHFR (Methylenetetrahydrofolate reductase) is a genetic factor that has multiple alleles, the presence of certain types of CT and TT alleles as increase cardiovascular risk.

The objective of our study is to evaluate the prevalence and vascular risk factors associated with *MTHFR* CT and TT genotypes in patients with the acute phase of cerebral ischemia and address the issue of the presence of correlation between *MTHFR* and other clinical factors in ischemic stroke.

It was a prospective study during 3 years, on 165 patients, victims of ischemic strokes, in the Laboratory of Human Genetics and Molecular Pathology, University Hassan II- Faculty of Medicine in Casablanca and the department of neurology at the campus teaching hospital of Casablanca and Rabat.

According to the sex, we had 93 men and 72 women with a sex-ratio of 1.3. *MTHFR* CC was normal in 37.6% of patients. *MTHFR* TT was founded in 13.4% of patients and *MTHFR* CT in 49%. There was no correlation between *MTHFR* and other risk factors of stroke (age, sex, hypertension, diabetes, smoking, alcoholism and cholesterol). The high frequency of *MTHFR* CT/TT (62%) among patients with acute ischemic strokes dictates the management of this risk factor.

Keywords: Correlation, Logistic regression, Ischemic stroke, Genetic risk factors *MTHFR*, Clinical risk factors

Introduction

The enzyme methylenetetrahydrofolate reductase is 5,10-called MTHFR. It is a homodimeric protein in the cytoplasm. MTHFR is located in the spleen, lymph nodes and bone marrow as it's a genetic risk factor that has multiple alleles, the presence of certain types of alleles as CT / TT increase cardiovascular risk [11]. Many publications show an association between MTHFR CT / TT genotype and increased risk of coronary and vascular disease, cerebrovascular diseases [2], [3], [6], [9]. Still others emphasize the importance of this genotype on the incidence of thromboembolic events, both arterial and venous, and the risk of venous thrombosis or recurrent juvenile [1], [5], [7], [8]. Variable MTHFR CT / TT is considered a risk factor for cardiovascular and cerebral-vascular independent [3].

A study was set up in 1948 by Framingham [10] to monitor the heart health of the population of a small American town and correlate different parameters with the risk of disease occurrence of stroke. The first two risk factors, hypertension and hypercholesterolemia, were able to be identified in the early 1960s. These data were confirmed by those of other countries, particularly in Helsinki [13].

Rare and recent publications suggest the existence of a probable correlation between the genetic factor with MTHFR alleles (CT / TT) and clinical risk factors associated with ischemic stroke [11].

The epidemiology of this association remains poorly understood in the Moroccan population. The purpose of this study was to evaluate the prevalence and vascular risk factors associated with MTHFR CT / TT patients at the acute phase of cerebral ischemia in the laboratory of Genetics and Molecular Pathology, Faculty of Medicine, Casablanca (LGPM) in collaboration with the departments of neurology of the University Hospital of Casablanca and Rabat to find a correlation between MTHFR genetic factor and other clinical factors such as (age, sex, hypertension, diabetes).

1 Methodology

1.1 Material

This is a prospective study for 3 years. It focused on 165 consecutive patients admitted for ischemic stroke victims and in the laboratory of Genetics and Molecular Pathology, Faculty of Medicine, Casablanca LGPM in collaboration with the departments of neurology of the University Hospital of Rabat and Casablanca, the diagnosis of ischemic stroke was made on clinical criteria.

Each patient had received a clinical examination with 5 main research cardiovascular risk factors: hypertension, diabetes, smoking, alcoholism and cholesterol. A patient is hypertensive when blood pressure above 140/90 mmHg, a diabetic if fasting glucose greater than 1.20g / l.

LGM and neurology CHU Casablanca and Rabat told us the results of the genetic and clinical analysis of 165 samples, this analysis consisted of 9 genes (MTHFR, FII, ACE, FV, APOE, IPA, ENOS, APOA5, ALOX5AP) and several clinical factors (Hypertension, diabetes, smoking, alcoholism and cholesterol)

1.2 Method

Results are presented as mean. Data are analyzed using the "SPSS" software. Averages MTHFR factor were compared in different categories from test "ANOVA" Logistic regression and correlation coefficient were used to analyze the relationship between MTHFR, age, sex, hypertension, diabetes, smoking, alcoholism and cholesterol.

It was then necessary to study and analyze the links between each of the explanatory variables and the dependent variable (MTHFR) was performed bivariate correlation analysis with the method of Karl Pearson in 1986 which offers a mathematical formula for the notion correlation and an estimator of this quantity [4],[12]; odds ratios calculated are gross.

The principle of correlation: There is a correlation between two variables if there is a link between them.

It showed an explanatory variable (Hypertension, Diabetes ...) on which you can easily find information and a dependent variable related (eg MTHFR). We will then investigate whether these two variables move together.

The correlation coefficient: it can check whether two variables move together.

It is calculated as follows:

$$r = \frac{\sum X_i Y_i}{\sqrt{\sum X_i^2} \times \sqrt{\sum Y_i^2}} \text{ with } -1 < r < +1 \text{ or :}$$

- $X_i = x_i - \bar{x}$ x_i representing the values taken by the explanatory variable.

- $Y_i = y_i - \bar{y}$ y_i representing the values taken by the dependent variable.

More r is close to 1 or -1, the correlation is stronger and both variables are related. We consider that the link correlation is significant when $r > 0.85$ or $r < -0.85$.

If r is positive, the two variables move in the same direction.

If r is negative, the two variables move in opposite directions.

2. Results

Our analysis included 165 consecutive patients who have experienced stroke and met our inclusion criteria. The average age was 57 years with extremes of 34 and 76 years. We identified 93 men (56.4%) and 72 women (43.6%) or a men /

women ratio of 1.3.

Table 1 show the distribution by age and sex of patients. On 83 clinical or 50.5% of patients had arterial hypertension deficit; 35 is 21.3%, a deficit of diabetes; 18 or 11% had cholesterol. [cf. Table 1]

62 (37.6%) patients had MTHFR CC; 81 patients (49%) had MTHFR CT and 22 (13.4%) had MTHFR TT. Table 1 shows the MTHFR in the study population and the distribution of subjects with CC and those with MTHFR CT / TT by age group and sex.

In total 83 (50.5%) patients had hypertension, 82 (49.5%) were not. In hypertensive subjects, and non-hypertensive patients ($P = 0.485$). In contrast 35 (21.3%) patients were diabetic, 130 (78.7%) patients were not. There was no significant difference between MTHFR in diabetic and non-diabetic; ($P = 0.218$). The same for other clinical factors, the p-value ($p > 0.05$), the difference was not statistically significant (MTHFR and smoking ($P = 0.509$), MTHFR and alcoholism ($P = 0.115$), MTHFR and cholesterol ($P = 0.366$)).

Table 1. MTHFR in 165 patients victims of ischemic stroke

Age group	Population <i>Studied</i>		Population with <i>MTHFR CC</i>		Population with <i>MTHFR CT/TT</i>	
	N =	%	N =	%	N =	%
<40	7	4,2	3	4,8	4	3,9
40-50	34	20,6	16	25,8	18	17,5
51-60	62	37,6	21	33,9	41	39,8
>60	62	37,6	22	35,5	40	38,8
Total	165	100	62	100	103	100

Table 2 MTHFR crosses the dependent variable and the other explanatory variables (vascular risk factors) such as diabetes and hypertension, smoking, alcoholism, cholesterol. [cf. Table 2].

Table 2. *MTHFR and other vascular risk factors (hypertension, diabetes, smoking, alcoholism, cholesterol).*

		Population Studied	Population with <i>MTHFR</i> CC	Population with <i>MTHFR</i> CT/TT
		N= 165 patients	N= 62 Patients	N= 103 patients
HTA	Yes	83	29	54
	No	82	33	49
Diabetes	Yes	35	10	25
	No	130	52	78
Smoking	Yes	56	23	33
	No	109	39	70
Alcoholism	Yes	14	8	6
	No	151	54	97
Cholesterol	Yes	18	5	13
	No	147	57	90

3. Conclusion

The overall average age of our patients was 57 years. This confirms the occurrence of stroke in high proportion in general and stroke in particular after 50 years. Patients under the age of 40 accounted for 4.2% effect of the total number of our study. We did not notice any significant difference between *MTHFR* factor ($p = 0.58$) depending on the age.

In our study, 21.2% of our patients were diabetic. It was not established significant correlation between the *MTHFR* and diabetes. However, it is noted that a diabetic may *MTHFR* CT / TT as abnormally high levels of insulin to prevent the body and maintain a reducing *MTHFR* CC.

Indeed, it has been demonstrated that this genotype had a significantly stronger effect on diabetes, compared to non-diabetics: *MTHFR* CT/ TT genotype associated with diabetes is a risk of death of 5 years of 90% higher than non-diabetic with a high rate of normal homocysteine (9.14).

Overall, the multivariate analysis (logistic regression) between the *MTHFR* variable (patients with *MTHFR* CT / TT patients without CT / TT) and other factors (sex, age, hypertension, diabetes, smoking, alcoholism, cholesterol) did not reveal no significant correlation.

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