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Short Communication

Prevalence of hereditary risk factors for thrombophilia in Belém, Brazilian Amazon

France Keiko Nascimento Yoshioka[1], Amélia Góes Araújo[2], Marli Haydee Tavella[2], Igor Guerreiro Hamoy[1] and João Farias Guerreiro[1]

[1]*Universidade Federal do Pará, Centro de Ciências Biológicas, Departamento de Patologia, Laboratório de Genética Humana e Médica, Belém, PA, Brazil.*
[2] *Universidade de São Paulo, Faculdade de Medicina de Ribeirão Ribeirão Preto, Departamento de Medicina Clínica, Laboratório de Hematologia,Ribeirão Preto, SP, Brazil.*

Abstract

Different risk factors for venous thromboembolism (VTE) have been identified, including hereditary abnormalities in the mechanisms of coagulation and fibrinolysis. We investigated five genetic polymorphisms (*FVL G1691A*, *FII G20210A*, *MTHFR C677T, TAFI A152G* and *TAFI T1053C*) associated with VTE in individuals from the city of Belém in the Brazilian Amazon who had no history of VTE. No significant difference was found between the observed and expected genotype frequencies for the loci analyzed. We found high frequencies of *MTHFR C677T* (33.9%) and *TAFI T1053C* (74%) and low frequencies of *FVL* (1.6%), *FII G20210A* (0.8%) and *TAFI A152G* (0.8%). The *FVL G1691A*, *FII G20210A* and *MTHFR C677T* frequencies were similar to those for European populations and populations of European descent living in the city of Ribeirão Preto in the Brazilian state of São Paulo. The frequency of the two TAFI mutations in the Belém individuals was not significantly different from that described for individuals from Ribeirão Preto. We suggest that the risks for VTE in the population of Belém are of the same magnitude as that observed in European populations and in populations with an expressive European contribution.

Key words: factor V Leiden, prothrombin, MTHFR, TAFI, thrombophilia.

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Thrombophilia can be defined as an increased tendency towards thrombosis (venous and arterial) through enhanced coagulation. Over the past few decades genetic defects in proteins regulating blood coagulation have been established as risk factors predisposing to venous thromboembolism (VTE). Such genetic defects are relatively frequent, the most important of which are antithrombin, protein C or protein S deficiency or resistance to activated protein C due to the factor V Leiden (*FVL G1691A*) or factor II prothrombin (*FII G20210A*) gene mutations (Lane and Grant, 2000). Other potential genetic polymorphisms have also been studied, including the thermolabile variant of the methylenetetrahydrofolate reductase (MTHFR) gene (Arruda *et al*., 1997) and polymorphisms in the 5'-untranslated region (5'-UTR) of the thrombin-activatable fibrinolysis inhibitor (TAFI) gene (*TAFI A152G* and *TAFI T1053C*), which plays an important role in hemostasis by functioning as a potent fibrinolysis inhibitor (Franco *et al*., 2001

The available studies show a high prevalence of *FVL G1691A, FII G20210A* and *MTHFR C677T* polymorphisms in Europeans (Adamczuk *et al*., 2000; Angelopoulou *et al*., 2000; Araújo *et al*., 2000) but the frequency of the *TAFI A152G* and *TAFI T1053C* polymorphisms are less well-known.

We present the results of a study designed to evaluate the prevalence of five polymorphisms (*FVL G1691A*, *FII G20210A*, *MTHFR C677T*, *TAFI A152G* and *TAFI T1053C*) in a population sample from the city of Belém, the capital of the state of Pará in the Brazilian Amazon.

The general Belém population has resulted from an intense process of admixture between Caucasians (principally of Portuguese descent), Blacks (descendants of African slaves) and Amerindians. This study was approved by the ethics committee of our institution.

Blood was collected after informed consent from 73 females and 54 males, (n = 127, median age 23 years, range 18-44) with no history of VTE and the DNA extracted by the standard phenol-chloroform method. Genotyping for

Send correspondence to João Farias Guerreiro. Universidade Federal do Pará, Centro de Ciências Biológicas, Departamento de Patologia, Laboratório de Genética Humana e Médica, 66075-970 Belém, PA, Brazil. E-mail: joaofg@ufpa.br.

Table 1 - Allele and genotype frequencies of the factor V Leiden (*FVL G1691A*), factor II prothrombin (*FII G20210A*), methylenetetrahydrofolate reductase (*MTHFR C677T*) and thrombin-activatable fibrinolysis inhibitor (*TAFI A152G* and *TAFI T1053C*) polymorphisms in a population sample (N = 127) from the Brazilian city of Belém.

	Genotype frequency						Allele frequency	
Locus	Genotype	Frequency (%)	Genotype	Frequency (%)	Genotype	Frequency (%)	Allele	Frequency (%)
FVL G1691A	GG	123 (97)	GA	4 (3)	AA	0	A	1.6
FII G20210A	GG	125 (98)	GA	2 (2)	AA	0	A	0.8
MTHFR C677T	CC	56 (44)	CT	56 (44)	TT	15 (12)	T	33.9
TAFI A152G	AA	125 (98)	AG	2 (2)	GG	0	G	0.8
TAFI T1053C	TT	8 (6.3)	TC	50 (39.4)	CC	69 (54.3)	C	74

the five polymorphisms were performed by PCR amplification followed by *Mnl*I, *Hind*III, *Hinf*I, *Ssp*I and *Msp*I restriction digestion, respectively, using primers described previously (Bertina *et al*., 1994; Poort *et al*., 1996; Frosst *et al*., 1995; Franco *et al*., 2001).

The genotype and allele frequency distributions recorded for the five loci are presented in Table 1. We found high frequencies of *MTHFR C677T* (33.9%) and *TAFI T1053C* (74.0%) but the other variants were less frequent, *i.e. FVL G1691A* (1.6%), *FII G20210A* (0.8%) and *TAFI A152G* (0.8%). For all loci the genotype distributions were consistent with the expected Hardy-Weinberg values.

The factor V Leiden allele is present in about 4-5% of the normal white population, but is rare or absent among Asia, Africa, America and Australia indigenous populations (Zivelin *et al.*, 1997). In our study the observed *FVL G1691A* frequency (1.6%) did not differ significantly from the frequencies observed in most of Caucasian populations (Adamczuk *et al*., 2000) or from that reported by Franco *et al*. (1999) in Brazilians of European origin (1.3%) and Brazilian Amerindians (0.3%), but was significantly lower than the 6.9% found in Greeks (Angelopoulou *et al*., 2000).

The *FII G20210A* frequency is 1-8% in the general European population (Zivelin *et al*., 1998; Angelopoulou *et al*., 2000) but this gene is rare or absent in black Africans, Amerindians and Asians (Cumming *et al*., 1997; Rosendaal *et al*. 1998; Angchaisuksiri *et al*., 2000). In our study the observed *FII G20210A* frequency (0.8%) was similar to that reported for most Caucasian populations, including Brazilians of European origin in a population sampled by Franco *et al*. (1998) in the Brazilian state of São Paulo where the frequency of this gene was also 0.8%.

The frequency (34%) of the *MTHFR C677T* gene in our sample was high and similar to that found in Europeans, Asians and Brazilian Amerindians (Franco *et al*. 1998; Botto and Yang *et al*., 2000), this frequency being significantly higher than those described in African populations and populations of North American and Brazilian blacks (Franco *et al*. 1998; Angelopoulou *et al*., 2000; Araújo *et al*., 2000; Wilcken *et al*., 2003).

Little is known globally about the frequency of polymorphisms in the 5'-UTR region of the TAFI gene, the only available data having been published by Franco *et al*. (2001) who reported a frequency of 2% for *TAFI A152G* and 75.6% for *TAFI T1053C* in a population sample from city of Ribeirão Preto in the Brazilian state of São Paulo. Our results for the TAFI polymorphisms (*TAFI A152G* = 0.8% and *TAFI -1053C* = 74.0%) did not differ significantly from those reported by Franco *et al*. (2001).

Our results show that in the population studied by us the frequency of polymorphisms related to the risk of VTE were in accordance not only with the expected values based on the available date on the distribution of these polymorphisms in human populations but also with the estimates by Santos and Guerreiro (1995) of the relative contributions of European (47%), African (12%) and Amerindian (41%) genes to the population of Belém.

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