Prevalence of 1691G>A FV mutation in females from Bosnia and Herzegovina - a preliminary report

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ABSTRACT

Factor V is the liver-synthesized multidomain glycoprotein encoded by a gene localised on chromosome 1q23. The point mutation 1691G>A in this gene results in formation of an altered protein of V Factor resistant to activated protein C (APC) cleavage. This mutation alone is the most frequent cause of inborn thrombophilia and the most widely acknowledged genetic risk factor for venous thrombosis in a Caucasian population. This study was designed to provide the first estimate of the frequency of the allele 1691 A FV in the Bosnian female population. The 1691 G>A FV mutation was examined by polymerase chain reaction-restriction fragment length polymorphism, in a group of 67 women, mean age of 58.6 years with no history of cardiovascular incident. Our findings revealed an absence of the mutated allele 1691 A FV in the studied group.

This is the first report on the 1691 G>A FV mutation in a population from Bosnia and Herzegovina. Further research is needed to establish prevalence of the mutated allele in the population from Bosnia and Herzegovina.

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KEY WORDS: FV, Factor V Leiden, 1691 A FV, thrombophilia, prevalence, recurrent miscarriages

INTRODUCTION

Inherited resistance to activated protein C (APC) is one of the most common genetic defects associated with familial thrombophilia and is now known to be the most common genetic risk factor for venous thrombosis. It is an autosomal dominant disorder caused by a single point mutation in the Factor V gene, which predicts substitution of arginine (R) to a glutamine (Q) at aminoacid position 506. G>C transition occurs at nucleotide position 1691 located in exon 10. This mutation is known as Factor V Leiden (FVL) [1]. Factor V Leiden, in comparison with the active form, is inactivated by protein C at a much slower rate. Since mutated Factor V is resistant to the anticoagulative action of protein C, it cannot be activated by cleavage, causing inactivation of the antithrombotic regulatory pathway [2-3]. Carriers of 1691 G>A FV are more likely to develop abnormal blood clots, which in extreme cases can cause deep vein thrombosis (DVT), pulmonary embolism and superficial thrombophlebitis.

Furthermore, mutation 1691 G>A of the gene coding for Factor V accounts for the most common cause of inherited predisposition to thrombosis. It has been reported that, presumably due to placental thrombosis, Factor V Leiden increases by 2- to 3-fold the risk for recurrent miscarriage and possibly other obstetrical complications such as intrauterine growth restriction and placental abruption [4-8]. The 1691 G>A FV mutation in fertile women might be associated with deep vein thrombosis and pulmonary embolism during pregnancy, increased risk of preeclampsia, recurrent miscarriage and placental development. During postmenopausal period, estrogen replacement therapy is associated with imbalance in coagulation and fibrinolysis especially relevant for 1691 G>A FV mutation carriers. It is known that the frequency of the 1691 G>A FV allele varies worldwide and differences are observed between geographic locations and ethnic populations. Recent studies have concluded that the 1691 G>A mutation is virtually nonexistent in Asia and in some regions of Africa; however, the mutation showed a higher prevalence in the Lebanese population (14.4%) and was extremely high among healthy Palestinians (20.1%) [9-12]. In Europe the 1691 G>A FV provides a mosaic, among South-Eastern European countries the frequency of allele 1691 A FV varied from 3.6% in Bulgaria, 3.5% in Macedonia, 2.2% in Serbia to 1.6% in Croatia, indicating an upward trend in Southeasterly direction.
RESULTS

The results obtained in this study, which included 67 healthy women, reveal that the 1691A allele was absent.
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DECLARATION OF INTEREST

The authors state no conflict of interest.

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(13/185) in the control group [25]. In Iranian women the prevalence of FVL in the healthy women group was 0.0% [26]. These preliminary results of the presence of 1691G–A mutation in the Bosnia and Herzegovina raise the question of future screening for this mutation, including both genders.