IS THE MATERNAL AGE A RISK FACTOR IN CAUSING GENETIC THROMBOPHILIC MUTATION?

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Abstract

Thrombophilia are hereditary or acquired disorders that predispose to clot formation and venous thrombotic events, or thromboembolic disease, based on a variety of structural abnormalities in the fibrinogen molecule. In most studies thrombophilia are associated with an increased risk of fetal loss. This study was conducted in the Department of Obstetrics and Gynecology of the Emergency Clinic Hospital Municipal Deva. Regarding the typology, this study is a prospective cohort study, the patients being monitored for three years. In calculating the risk factors, we consider both risk ratio and odds ratio. For statistical significance test, we applied χ^2 test for equality of proportions. From the database we have made contingency tables, one for each individual gene. The study of the risk ratio concludes that age is a risk/protective factor defining for the appearance of mutation, most likely this mutation might also occurring due to other risk factors than age.

Keywords: genetics, thrombophilia, gene, mutations.

Introduction

Thrombophilia are hereditary or acquired disorders that predispose to clot formation and venous thrombotic events, or thromboembolic disease, based on a variety of structural abnormalities in the fibrinogen molecule. In most studies thrombophilia are associated with an increased risk of fetal loss [1-8].

Pregnant women are investigated mostly for thrombophilia if there are diagnosed delayed growth of the fetus, changes in circulation tubes with increased blood circulation uterine on ultrasound power Doppler examination, increased blood pressure that can lead to extreme manifestations of eclampsia-preeclampsia and pathology of the placenta that is ultrasound detected with "premature aging of placenta" [9-17].

Material and methods

This study was conducted in the Department of Obstetrics and Gynecology of the Emergency Clinic Hospital Municipal Deva. We intended to identify mutations in pregnant women diagnosed with thrombophilia and Factor V Leiden, Factor V R2, Factor II, MTHFR, PAI, Factor XIII, EPCR - correlated with maternal age and the risk factors for the fetus in case of the occurrence of fetal thrombophilia. We considered risk factors analysis to see if the maternal age over 35 years may be regarded as a risk factor in the development of genetic mutations.

Regarding the typology, this study is a prospective cohort study, the patients being monitored for three years. In calculating the risk factors, we consider both risk ratio and odds ratio. For statistical significance test, we applied χ^2 test for equality of proportions. Thus, from the database we have made nine contingency tables, one for each individually gene.

Results and discussion

Descriptive data and results are shown in Tables 1-9 and the conclusions for each case are detailed in the table description. In this follow up study we tasted to see if an age above 35 years can be considered as a main risk factors which can influence the appearance of some gene mutations during pregnancy. So, we gathered information from 40 patients. After running a risk analysis we obtained that the age can't be considered a risk factor. In some cases for some genes the age is a protective factor, but the differences are not significant from the statistical point of view. For the tested mutation we calculated both the risk ratio and the odds ratio.

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For the statistical significance we applied a χ^2 test for proportions. We considered the level of confidence to be $\alpha = 0.05$. The only case where we obtained significant differences is for the MTHMR MTHFR C677T homo-mutation, where the age has a protective factor, the age has a positive influence ($p = 0.03$, $RR = 0.25, RR \in (0.06; 0.99)$, $OR = 0.17, OR \in (0.03; 0.92)$, see Table 5).

Table 1: Analysis of the risk of FV Leiden mutation homo-. In terms of the sample, the age over 35 years can be considered a protective factor risk (RR <1, OR <1) insignificant risk to the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	F V homo+	F V homo -		
>= 35 years	2	18	20	$p = 0.38$ $RR = 0.5$, $RR \in (0.11; 2.43)$ $OR = 0.44$, $OR \in (0.07; 2.76)$
< 35 years	4	16	20	
Total	6	34	40	

Table 2: Analysis of the risk of FV Leiden mutation hetero-. In terms of the sample, the age over 35 years can be considered a risk factor (RR> 1, OR> 1), the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	F V hetero+	F V hetero -		
>= 35 years	6	14	20	$p = 0.73$ $RR = 1.2$, $RR \in (0.44; 3.30)$ $OR = 1.29$, $OR \in (0.32; 5.17)$
< 35 years	5	15	20	
Total	11	29	40	

Table 3: Analysis of the risk of F II mutation homo-. Leiden mutation homo, the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	F II homo+	F II homo -		
>= 35 years	2	18	20	$p = 0.38$ $RR = 0.5$, $RR \in (0.11; 2.43)$ $OR = 0.44$, $OR \in (0.07; 2.76)$
< 35 years	4	16	20	
Total	6	34	40	

In terms of the sample, the age over 35 years can be considered a protective risk factor (RR <1 or <1), analogous to FV

Table 4: Analysis of the risk of F II mutation homo-. In terms of the sample, the age over 35 years can be considered a protective risk factor (RR <1, OR <1), the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	F II hetero+	F II hetero -		
>= 35 years	3	17	20	$p = 0.58$ $RR = 0.75$, $RR \in (0.19; 2.93)$ $OR = 0.71$, $OR \in (0.14; 3.66)$
< 35 years	4	16	20	
Total	7	33	40	

Table 5: Analysis of the risk of MTHMR MTHFR C677T mutation homo-. In terms of the sample, the age over 35 years can be considered a protective risk factor (RR <1, OR <1), the risk is significant for the entire population from which is the study group (p <0.05). In terms of risk analysis conducted on this group, this is the only situation where the registered risk can be generalized to the entire population.

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	MTHMR C677T homo +	MTHMR C677T homo -		
>= 35 years	2	18	20	$p = 0.03$ $RR = 0.25,$ $RR \in (0.06; 0.99)$ $OR = 0.17,$ $OR \in (0.03; 0.92)$
< 35 years	8	12	20	
Total	10	30	40	

Table 6: Analysis of the risk of MTHMR MTHFR C677T mutation hetero-. In terms of the sample, the age over 35 years can be considered a risk factor (RR> 1, OR> 1), the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	MTHMR C677T hetero +	MTHMR C677T hetero -		
>= 35 years	10	10	20	$p = 0.20$ $RR = 1.66,$ $RR \in (0.75; 3.71)$ $OR = 2.33,$ $OR \in (0.67; 8.54)$
< 35 years	6	14	20	
Total	16	24	40	

Table 7: Analysis of the risk of MTHFR A1298C mutation homo-. In terms of the sample, the age over 35 years can be considered a risk factor (RR> 1, OR> 1), the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	MTHFR A1298C homo +	MTHFR A1298C homo-		
>= 35 years	4	16	20	$p = 0.68$ $RR = 1.33,$ $RR \in (0.34; 5.21)$ $OR = 1.42,$ $OR \in (0.27; 7.34)$
< 35 years	3	17	20	
Total	7	33	40	

Table 8: Analysis of the risk of MTHFR A1298C mutation hetero-. In terms of the sample, the age over 35 years can be considered a risk factor (RR> 1, OR> 1), the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	MTHFR A1298C hetero +	MTHFR A1298C hetero -		
>= 35 years	7	13	20	$p = 0.33$ $RR = 0.7,$ $RR \in (0.33; 1.47)$ $OR = 0.54,$ $OR \in (0.15; 1.92)$
< 35 years	10	10	20	
Total	17	23	40	

Table 9: Analysis of risk ratio applicable to other types of mutations than those tested herein. In terms of the sample, the age over 35 years can be considered a risk factor (RR> 1, OR> 1), the risk is insignificant for the entire population from which is the study group (p> 0.05).

Exposure vs Disease	Types of mutation		Total	p - value RR, 95% OR, 95%
	Another types of mutation +	Another types of mutation -		
>= 35 years	14	6	20	$p = 0.51$ $RR = 1.17,$ $RR \in (0.74; 1.85)$ $OR = 1.55,$ $OR \in (0.42; 5.76)$
< 35 years	12	8	20	
Total	26	14	40	

Conclusions

The study of the risk ratio concludes that age is a risk/protective factor defining for the appearance of mutation, most likely this mutation might also occurring due to other risk factors than age.

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