

SCREENING WOMEN WITH MISCARRIAGES FOR MTHFR POLYMORPHISMS. IS THERE ANY CLINICAL UTILITY?

T Kanellopoulou*¹, M Bellia¹, V Daskalaki¹, A Apostolopoulou¹, G Apergis^{1,2}, V Tsevrenis¹, E Nomikou¹

¹Blood Bank & Haemophilia Unit, Hippokratio Hospital Of Athens, Greece, ²Molecular Biologist

Problem Statement

- Abnormalities within the methionine pathway such as polymorphisms in MTHFR gene may lead to elevated homocysteine levels, which is a risk factor for venous thromboembolism (VTE).
- The most common polymorphic variant of MTHFR is C677T and less frequent is A1298C.
- These disorders have not only been implicated in VTE but also in placental diseases and miscarriages.
- However, there is still a debate whether MTHFR screening should be performed in the evaluation for thrombophilia in pregnancy or other adverse events and miscarriages.

Method

- We performed a retrospective analysis of women with miscarriages, pregnancy complications or infertility, who were tested for plasma homocysteine levels and MTHFR polymorphisms as a part of thrombophilia screening

Results

WOMEN CHARACTERISTICS	
Median age	35 years
VTE HISTORY	
Before conception	4.5%
Antepartum	2.1%
Postpartum	1.2%
Family History	40.0%
Other risk factors (obesity, smoking, dyslipidemia, CVD)	30.3%
Obstetric Complications	11.8%
ABORTIONS	
Number	
No history	16.1%
1 abortion	30.3%
2 abortions	34.2%
≥3 abortions	19.4%
Trimester	1 st 69.1%

- High levels of plasma homocysteine and/or MTHFR polymorphisms were detected in 66% of the women.

MTHFR POLYMORPHISMS			
MTHFR C677T	39.1%	MTHFR A1298C	24.5%
<i>Heterozygosity</i>	17.9%	<i>Heterozygosity</i>	8.2%
<i>Homozygosity</i>	10 %	<i>Homozygosity</i>	4 %
Double Heterozygosity 11.55%			

- There was a statistically significant association with high levels of homocysteine and/or the presence of MTHFR variant with first trimester miscarriages (p=0.013).
- However, separate analysis of variants showed that only A1298C variant, even in a heterozygous state, was associated with the miscarriages (p=0.036).
- The statistically significant finding remains even in women with no other thrombophilia factors, such as the presence of antiphospholipid antibodies and/or the mutations in FV-Leiden or FII-R20210A

Conclusion

- MTHFR screening for women with miscarriages is still controversial and Current American and European guidelines do not include this yet.
- In our study the rare A1298C variant was found to be associated with first trimester miscarriages and that could represent a genetic risk factor for pregnancy loss.

* Acknowledgement: T. Kanellopoulou has fellowship of Hellenic Society of Haematology