Brief Communication

Maternal methyltetrahydrofolate reductase gene mutation in patients with missed abortions

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Abstract

**Background:** Missed abortions are a common problem, often caused by thrombophilia in both recurring and non-recurring cases.

**Aim:** To determine whether the presence of a mutation in the methyltetrahydrofolate reductase (Mthfr) gene correlates with missed abortions.

**Patients and methods:** We selected two hundred patients for this study in two groups: the study group, which consisted of one hundred patients with a history of missed abortion; and the control group, which consisted of one hundred patients with no history of missed abortion.

**Results:** Of the 200 patients, mutations in Mthfr were only found in forty-four patients—thirty-four from the study group and ten from the control group.

**Conclusions:** Mthfr gene mutation is a common cause of both recurring and non-recurring missed abortions.

**Keywords:** Habitual abortion; Missed abortion; Mthfr; Recurrent miscarriage; Thrombophilia

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Introduction

Missed miscarriage is a common multifactorial disease that may be recurrent; recurrent pregnancy loss refers to cases where the patient experiences two or more consecutive missed miscarriages. Missed miscarriages affect approximately 1% of fertile couples.  

The World Health Organization defines miscarriage as the loss of a foetus or embryo weighing less than 500 g, which corresponds to approximately 20–22 weeks of gestation.

Recurrent missed abortions can often cause psychological and emotional distress for affected couples.

Abortions for either clinically recognized or unrecognized pregnancies affect 10–12% of couples. The risk of recurrent missed abortions increases based on previous abortions: there is a 24% chance of recurrence in patients who have had one abortion, a 26% chance in patients who have had two abortions, and a 32% chance in patients who have had three abortions.

Many factors are associated with recurrent miscarriages in terms of maternal, foetal, or paternal gene polymorphisms. Maternal polymorphisms may be caused by many factors, such as genetic causes, haematological causes, anatomy, and endocrine problems. Up to 50% of cases of recurrent missed abortions remain unexplained.

Normal placental circulation and foetal vasculature are important for maintaining a normal healthy pregnancy; any abnormalities in placental circulation can lead to severe complications, including termination of the pregnancy.

Thrombophilia may be an inherited or acquired condition that increases the risk of thromboembolism. Inherited thrombophilia is a well-known cause of spontaneous pregnancy loss.

Folate is important for normal RNA and DNA synthesis and is required for homocysteine metabolism. It is also important for normal foetal growth and development; during pregnancy, folate requirements are increased. The level of
homocysteine in the body is mainly affected by dietary intake of folate and vitamin B12, as well as polymorphisms in genes that encode enzymes or transport proteins involved in folate- and vitamin B12-dependent homocysteine metabolism.

Decreased folate intake will affect homocysteine metabolism and lead to an increase in homocysteine levels in the blood.

Methylenetetrahydrofolate reductase (MTHFR) is an important regulatory enzyme in the metabolism of homocysteine, which catalyses the reduction of 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate. Mutations in the Mthfr gene can cause decreased enzyme activity and hyperhomocysteinaemia, which induces platelet aggregation by enhancing endothelial oxidative damage. Many mutations within the Mthfr gene have been identified; the two most common and important mutations are C677T and A1298C. The former mutation has been shown to cause early pregnancy loss.

Aim
The aim of this study is to determine whether mutations in the Mthfr gene are a cause of missed abortions.

Materials and Methods
Two hundred pregnant women were recruited for this study from the outpatient clinic of the El Shatby Maternity University Hospital. They were divided into two groups:

The first group included one hundred women with a history of one or more missed first trimester abortions, where the cause was unknown.

The second group included one hundred women with no history of abortion; all participants in this group were previously pregnant without complications, and have living children.

All women agreed to participate in this research and signed a written consent form.

All the women in this study were aged 20–30 years old.

Pregnancy was diagnosed by ultrasound, B-HCG, and physical examination. All diagnoses of missed abortions in the first trimester were made after excluding other possible causes of spontaneous pregnancy loss, such as anatomical or endocrine-related causes.

Blood serum was taken from the patients, and presence of the maternal Mthfr C677T mutation was determined by PCR.

Patients were categorised into groups based on the presence or absence of this mutation, as well as the number of abortions received.

Results were compared between different groups.

Statistical analysis
Data were collected and analysed bioinformatically. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version 20.0) software.

The following statistical tests were performed:

The Chi square test (X²) was used for categorised parameters. The arithmetic mean and standard deviation were also calculated. The Student’s paired t-test was used for parametric data. A value of P < 0.05 was considered statistically significant.

Results
The mean age of patients was 25.6 years old in the first group and 24.9 years old in the second group (Table 1).

In the studied group, 31% of patients had two abortions, and 23% had five abortions (Table 2).

In the control group, all women delivered a living child at least once (Table 3).

Presence of the Mthfr gene mutation was significantly higher in patients with missed abortions than in the control group (Table 4).

Presence of the Mthfr gene mutation significantly differed depending on the number of abortions (Table 5 and Figure 1).

Discussion
Many factors may contribute to sporadic and recurrent missed abortions. The presence of Mthfr gene mutations was studied as a potential cause for this phenomenon.

In this study, the age of patients ranged from 20 to 30 years in both groups; the mean age was 25.6 years in the study group, and 24.9 years in the control group.

In a study performed by L. Zhu, patients were aged between 22 and 44 years, with a mean age of 29.8 ± 4.3 years. Their control group consisted of 174 participants aged between 21 and 24 years, with a mean age of 28.5 ± 4.0 years. The age difference between the two groups was not statistically significant (P > 0.05).

In a study by Wendell Vilas Boas et al., the median age of the women in the study group was 29.4 ± 5.4 years, while the average age in the control group was 23 ± 5.5 years. The median abortion number in the study group was 3.2 ± 1.9, ranging from two to thirteen abortions in which forty-one (47%) women had two spontaneous abortions, twenty-five

| Table 1: Comparison of ages of patients in the two studied groups. |
|---------------------------------------------------------------|
|                  | First group | Second group |
| Range            | 21−30       | 20−29        |
| Mean ± S.D.      | 25.65 ± 2.65| 24.92 ± 2.46 |
| T                | 0.106       |              |
| P                | 0.69        |              |

| Table 2: Distribution of the number of abortions in the studied group. |
|---------------------------------------------------------------|
| No. of abortions | No. | %  |
|------------------|-----|----|
| 1                | 7   | 7.0|
| 2                | 31  | 31.0|
| 3                | 17  | 17.0|
| 4                | 19  | 19.0|
| 5                | 23  | 23.0|
| 6                | 1   | 1.0|
| 7+               | 2   | 2.0|
women had three spontaneous abortions, and twenty-one (24%) women had more than three abortions. In our study, 31% of patients had two abortions, and 23% of patients had five abortions. Our study showed a strong association between \textit{Mthfr} gene mutation and missed abortions. This is in line with the results of previous studies such as Cao Y et al., Govindaiah V et al., Puri M et al., and Nair RR. However, some studies failed to find a correlation, such as Wendell Vilas Boas et al., Sinem Yalcintepe et al., and Puri M et al.

Conclusions

Mutations in the \textit{Mthfr} gene are a common cause of recurring or non-recurring missed miscarriages.

Conflicts of interest

The author has no conflict of interest to declare.

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