

**METHYLENTETRAHYDROFOLATE REDUCTASE (*MTHFR*)  
C677T GENE POLYMORPHISM IN INDONESIAN WOMEN  
WITH RECURRENT PREGNANCY LOSS**

***POLIMORFISME GEN METHYLENTETRAHYDROFOLATE  
REDUCTASE (*MTHFR*) C677T PADA WANITA INDONESIA  
DENGAN KEGUGURAN BERULANG***



**THESIS**

**Submitted to fulfill the assignment and fit-out requisite in passing  
Post-graduate Program Majoring Biomedical Science Concentration Genetics  
Counseling Diponegoro University Semarang**

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DIPONEGORO UNIVERSITY  
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I hereby declare that this thesis is my own work and that to the best of my knowledge and belief. It contains no materials previously published or written by another person nor material which to a substantial extent has been accepted for the award of any degree or diploma of the university or other institute of higher learning, except where due acknowledgement is made in the text.

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## LIST OF CONTENTS

Title.....	i
Statement of Originality.....	iv
Curriculum Vitae.....	v
Acknowledgements.....	viii
Contents.....	x
List of Tables and Figures.....	xiii
Abbreviation List.....	xiv
List of Appendix.....	xv
Abstrak .....	xvi
Abstract.....	xvii
CHAPTER I.....	1
INTRODUCTION .....	1
1.1    Background.....	1
1.2    Research Question .....	2
1.2.1    General Research Question .....	2
1.2.2    Research question in detail.....	2
1.3    Research objectives.....	3
1.3.1    General objective .....	3
1.3.2    Specific objectives .....	3

1.4	Research advantages .....	3
1.5	Research originality.....	3
CHAPTER II .....		7
LITERATURE REVIEW .....		7
2.1	Reccurent Pregnancy Loss .....	7
2.2	<i>MTHFR</i> Gene Polymorphism.....	12
2.3	Folate Metabolism .....	13
2.4	Homocysteine and Recurrent Pregnancy Loss.....	14
2.5	Homocysteine and Neural Tube Defect.....	16
CHAPTER III .....		17
THEORETICAL SCHEME .....		17
CHAPTER IV .....		18
CONCEPTUAL SCHEME .....		18
CHAPTER V .....		19
RESEARCH METHOD.....		19
V.1.	Research aspects .....	19
V.1.1	Field.....	19
V.1.2	Location .....	19
V.1.3.	Period.....	19
V.1.4	Design.....	19
V.2	Material .....	20
V.2.1	Population .....	20
V.2.2.	Samples.....	20

V.2.2.1 Inclusion criteria.....	20
V.2.2.2 Exclusion criteria.....	20
V.2.2.3 Subject selection.....	21
V.2.2.4. Clinical examination.....	21
V.2.2.5 Sample collection.....	21
V.2.2.5 Sample estimation.....	21
V.3. Methods.....	22
V.3.1 General.....	22
V.3.2. Laboratory Methods.....	22
V. 4. Variables.....	24
V. 5. Operational definitions.....	25
V. 6. Data Analysis.....	25
V. 7. Research Flow.....	26
CHAPTER VI.....	27
RESULT.....	27
CHAPTER VII.....	31
DISCUSSION.....	31
CHAPTER VIII.....	34
CONCLUSION AND FUTURE DIRECTION.....	34
REFERENCES.....	36
APPENDIX.....	42

## LIST OF TABLE & FIGURES

	<b>Tables</b>	<b>Pages</b>
Table 1.	Research originality.....	4
Table 2.	Distribution of allele C and T in <i>MTHFR</i> C677T gene polymorphism.....	28
Table 3.	Distribution of genotype in <i>MTHFR</i> C677T gene polymorphism.....	28
Table 4.	Distribution of genotype (TT/CC) in <i>MTHFR</i> C677T gene polymorphism.....	28
Table 5.	Distribution of genotype (CT/CC) in <i>MTHFR</i> C677T gene polymorphism.....	28
Table 6.	Distribution of genotype (TT/CC+CT) in <i>MTHFR</i> C677T gene polymorphism..	29
<b>Figures</b>		
Figure 1.	Etiology of recurrent pregnancy loss.....	8
Figure 2.	Scheme of folate metabolism.....	14
Figure 3.	PCR amplification of <i>MTHFR</i> gene from recurrent pregnancy loss patient.....	29
Figure 4.	RFLP result of <i>MTHFR</i> C677T polymorphism from recurrent pregnancy loss patient. ....	30
Figure 5.	RFLP result of <i>MTHFR</i> C677T polymorphism from normal control population .....	30

**ABBREVIATION LIST**

MTHFR	: Methylene TetraHydroFolate Reductase
PCR	: Polymerase Chain Reaction
DNA	: Deoxyribose Nucleated Acid
RPL	: Recurrent Pregnancy Loss
REPL	: Recurrent Early Pregnancy Loss
APS	: Anti Phospholipid Syndrome
PCOS	: Polycystic Ovary Syndrome
NTD	: Neural Tube Defect
IgG	: Immunoglobulin G
IgM	: Immunoglobulin M

## LIST OF APPENDIX

Appendix 1. Statistical Computation.....	42
Appendix 2. Ethical Clearance Certificate.....	8

## ABSTRAK

**Latar Belakang:** : Polimorfisme gen C677T methylenetetrahydrofolate reductase adalah polimorfisme paling sering ditemukan yang dapat menurunkan aktifitas enzim MTHFR menghasilkan hiperhomosisteinemia yang berakibat keguguran berulang.

**Tujuan:** Studi ini bertujuan untuk mengetahui distribusi antara polimorfisme gen methylenetetrahydrofolate reductase (*MTHFR*) C677T dengan kejadian keguguran berulang pada wanita di Indonesia

**Subyek dan Metode:** Partisipan sebanyak 47 pasien yang memiliki riwayat dua atau lebih keguguran berulang secara berurutan dan 46 kontrol dengan riwayat obstetrik baik. Pemeriksaan dari polimorfisme gen *MTHFR* C677T dilakukan dengan PCR dan RFLP menggunakan enzim HinfI.

**Hasil:** Penelitian ini menemukan 26,08% genotip CT dan 4,34% genotip TT pada polimorfisme *MTHFR* C677T dengan pasien keguguran berulang. Dibandingkan dengan kontrol, kasus dengan keguguran berulang menunjukkan frekuensi yang lebih banyak homozigot mutant *MTHFR* C677T meskipun tidak mencapai hasil yang signifikan.

**Kesimpulan:** Polimorfisme gen *MTHFR* C677T pada wanita Indonesia dengan keguguran berulang memiliki frekuensi yang meningkat namun tidak signifikan. Konseling genetika sebaiknya diberikan kepada wanita dengan homozigot TT mengenai kemungkinan risiko homosisteinemia. Interaksi dengan berbagai variasi gen dan metabolisme homosistein perlu dilakukan pada penelitian selanjutnya.

**Kata kunci:** gen *MTHFR*, Keguguran berulang, PCR, RFLP



## ABSTRACT

**Background:** Polymorphism of C677T methylenetetrahydrofolate reductase (*MTHFR*) gene is the most common polymorphism which can reduce *MTHFR* enzyme activity resulting in hyperhomocysteinemia which may lead to recurrent pregnancy loss (RPL).

**Aim:** This study aims to identify the distribution of the *MTHFR* C677T gene polymorphisms among RPL women in Indonesia.

**Subjects and Methods:** A total of 47 participants with history of two or more experiences consecutive pregnancy loss and 46 control women with a good obstetric history. *MTHFR* C677T polymorphism was examined by using polymerase chain reaction (PCR) with restriction fragment length polymorphism (RFLP) using restriction enzymes *Hinf*I.

**Results:** This study found 26,08% CT genotype and 4,34% TT genotype of *MTHFR* C677T gene polymorphism in RPL patients. Compared with controls, cases with RPL showed higher frequency of the homozygous mutant *MTHFR* C677T although statistically not significant.

**Conclusions:** *MTHFR* C677T polymorphism was increased but not statistically significant in Indonesian women with RPL. Genetic counseling should be given to women with homozygote TT for possible risk of homocysteinaemia. Interaction with other genetic variants and homocysteine metabolisms need to be further investigated.

**Keyword.** *MTHFR* gene, Recurrent pregnancy loss, PCR, RFLP