

# Analisis metilasi DNA dan korelasinya dengan ekspresi mRNA Epidermal Growth Factor Receptor dan Matrix Metalloproteinase 2 Pengkode Protein Pengatur Sitoskeleton pada Jaringan Endometriosis Peritoneum = Analysis of DNA Methylation and its Correlation with mRNA Expression of Epidermal Growth Factor Receptor and Matrix Metalloproteinase 2 Encoding for Cytoskeleton Regulating Protein in Peritoneal Endometriosis Tissue

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## Abstrak

Latar Belakang: Endometriosis merupakan penyakit multifaktorial yang mempengaruhi 10% wanita usia subur. Diketahui bahwa gen EGFR dan MMP-2 mengalami peningkatan ekspresi pada endometriosis sehingga memiliki peran dalam perkembangan endometriosis, dan gen yang dapat meregulasi sitoskeleton. Tujuan dari penelitian ini adalah untuk mengevaluasi hubungan antara tingkat metilasi gen EGFR dan MMP-2 dengan ekspresi mRNA-nya pada jaringan endometriosis peritoneum.

Metode Penelitian: Penelitian ini menggunakan desain cross sectional. Sampel yang digunakan sebanyak 20 wanita endometriosis dan 20 wanita bukan endometriosis yang usianya sekitar 20-45 tahun. Pada wanita endometriosis diambil jaringan endometriosis peritoneum dengan tindakan laparoskopik, sedangkan 20 wanita bukan endometriosis diambil jaringan endometrium normal dengan tindakan mikrokuretase. Tingkat metilasi DNA gen EGFR dan MMP-2 dianalisis dengan metode Methylation Specific PCR (MSP) dan Ekspresi mRNA gen EGFR dan MMP-2 dianalisis dengan metode qRT-PCR.

Hasil: Tingkat metilasi DNA pada gen EGFR dan MMP-2 mengalami hipermetilasi. Pada gen EGFR, tingkat metilasi DNA antara jaringan endometriosis peritoneum dibandingkan dengan jaringan endometrium normal terdapat perbedaan yang bermakna ( $p=0,001$ ), sedangkan pada gen MMP-2 tingkat metilasi DNA-nya tidak terdapat perbedaan yang bermakna ( $p=0,596$ ) antara jaringan endometriosis peritoneum dibandingkan dengan jaringan endometrium normal. Nilai ekspresi relatif mRNA EGFR dan MMP-2 mengalami peningkatan ekspresi pada jaringan endometriosis peritoneum. Penelitian ini tidak menunjukkan korelasi yang bermakna antara tingkat metilasi dengan tingginya ekspresi mRNA baik gen EGFR maupun MMP-2. (gen EGFR ( $p=0,947$  dan  $r=-0,016$ ) dan gen MMP-2 ( $p=0.769$  dan  $r=0.070$ ))

Kesimpulan: Tingginya ekspresi mRNA EGFR dan gen MMP-2, kemungkinan bukan hanya disebabkan karena faktor metilasi DNA, melainkan faktor lainnya.

**Background:** Endometriosis is a multifactorial disease that affects 10% of women of childbearing age. It is known that the EGFR and MMP-2 genes have increased expression in endometriosis and thus have a role in the development of endometriosis, and genes that can regulate the cytoskeleton. The purpose of this study was to evaluate the relationship between the level of methylation of the EGFR and MMP-2 genes with their mRNA expression in peritoneal endometriosis tissue.

**Method:** The study used a cross sectional design. The sample used was 20 women with endometriosis and 20 women without endometriosis who were around 20-45 years old. In endometriosis women are taken to peritoneal endometriosis tissue by laparoscopic, while 20 women without endometriosis are taken to normal endometrial tissue by microcurettage. The levels of EGFR and MMP-2 gene methylation were analyzed by

the Methylation Specific PCR (MSP) method and the mRNA expression of the EGFR and MMP-2 genes were analyzed by the qRT-PCR method.

Results: The level of DNA methylation in the EGFR and MMP-2 genes was hypermethylated. In the EGFR gene between peritoneal endometriosis tissue compared to normal endometrial tissue there were significant differences ( $p=0,001$ ), whereas in the MMP-2 gene there was no significant difference ( $p=0.596$ ) between peritoneal endometriosis tissue compared to normal endometrial tissue. The relative expression value of EGFR and MMP-2 mRNA has increased expression in peritoneal endometriosis tissue. This study did not show a significant correlation between the level of methylation and the high mRNA expression in both the EGFR and MMP-2 genes. (EGFR gene ( $p=0.947$  and  $r=-0.016$ ) and MMP-2 gene ( $p=0.769$  and  $r=0.070$ ))

Conclusion: The high expression of EGFR mRNA and MMP-2 gene, the possibility is not only due to hypermethylation factors, but other factors.