

Pengaruh Aktivitas *Matrix Metalloproteinase-9* (MMP-9) dan Ekspresi *Tissue Inhibitor of Metalloproteinase-1* (TIMP-1) pada Skor Invasi Jaringan Endometrioma yang Ditransplantasikan pada *Chorioallantoic Membrane* (CAM)

ABSTRAK

Latar belakang: Invasi jaringan endometriosis pada lapisan peritoneum merupakan proses awal yang penting terbentuknya endometriosis. Proses ini tergantung pada kemampuan proteolisis jaringan endometriosis yang diperankan oleh enzim *matrix metalloproteinases* (MMPs) dimana aktivitasnya diatur oleh inhibitor alaminya yaitu *Tissue Inhibitor of Metalloproteinases* (TIMPs). Penelitian terdahulu mengungkapkan adanya peningkatan ekspresi MMP-9 dan penurunan TIMP-1 pada endometrium endometriosis dan endometrioma, tetapi hubungan antara MMP-9 dan TIMP-1 terhadap proses invasi melalui proses remodeling matriks ekstraseluler belum bisa dijelaskan.

Tujuan: Penelitian ini dilakukan untuk mengukur aktivitas MMP-9 dan ekspresi TIMP-1 endometrioma ovarium dan melihat hubungannya terhadap skor invasi endometrioma dengan menggunakan CAM ayam sebagai model.

Metode: Populasi pada penelitian ini adalah semua wanita usia 18-49 tahun dengan gejala klinis berupa endometrioma yang belum mendapatkan terapi hormonal dalam 3 bulan terakhir. Jaringan endometrioma dipotong 2 - 3 mm dan ditransplantasikan ke dalam CAM kemudian diinkubasi selama 5 hari. Skor invasi dinilai berdasarkan tingkat regularitas epitel korion CAM yang ditemplei endometrioma dengan menggunakan metode pengecatan *hematoxilin-eosin* (HE). Aktivitas MMP-9 dianalisis menggunakan metode gelatin zimografi. Ekspresi TIMP-1 dianalisis menggunakan metode *western blot*. Hubungan antara aktivitas MMP-9 dan ekspresi TIMP-1 terhadap skor invasi pada CAM dianalisis menggunakan *Spearman correlation test*.

Hasil: Total sebanyak 30 sampel jaringan endometrioma didapatkan dari 24 pasien yang menjalani prosedur laparoskopi atau laparotomi di RSUP Dr. Sardjito, Yogyakarta. Hasil *Spearman correlation test* menunjukkan terdapat hubungan positif yang kuat antara peningkatan aktivitas MMP-9 dan peningkatan skor invasi jaringan endometrioma pada CAM, serta hubungan negatif antara penurunan ekspresi TIMP-1 dan peningkatan skor invasi jaringan endometrioma pada CAM meskipun lemah.

Kesimpulan: Aktivitas MMP-9 dan ekspresi TIMP-1 berhubungan dengan skor invasi jaringan endometrioma pada CAM. Peningkatan aktivitas MMP-9 memiliki hubungan yang kuat dengan peningkatan skor invasi jaringan endometrioma pada CAM. Sementara itu, penurunan ekspresi TIMP-1 memiliki hubungan yang lemah dengan peningkatan skor invasi jaringan endometrioma pada CAM.

Kata kunci: *Endometrioma, Chorioallantoic membrane (CAM), Matrix metalloproteinase-9 (MMP-9), Tissue Inhibitor of Metalloproteinase-1 (TIMP-1)*

Correlation Between *Matrix Metalloproteinase-9* (MMP-9) Activity and *Tissue Inhibitor of Metalloproteinase-1* (TIMP-1) Expression on The Invasion Score of Endometrioma Tissue Transplanted on *Chorioallantoic Membrane* (CAM)

ABSTRACT

Background: The invasion of endometrial tissue in the peritoneal layer is an important precursor to the formation of endometriosis. The mechanisms rely on the proteolytic ability of endometrial tissue that is regulated precisely by matrix metalloproteinases (MMPs) enzyme and their natural inhibitor, which are called by Tissue Inhibitor of Metalloproteinases (TIMPs). A previous study revealed that high expression levels of MMP-9 and low expression levels of TIMP-1 are related to the presence of endometrial endometriosis and endometriomas. However, the correlation between MMP-9 and TIMP-1 on the invasion level of endometriomas tissue through extracellular matrix (ECM) remodelling has not been elucidated.

Objective: To investigate the MMP-9 activity and TIMP-1 expression of ovarian endometriomas, as well as to observe their correlation to the invasion level of endometriomas using CAM as a model.

Methods: The study population was women aged 18-49 years with endometriomas who had not received hormonal therapy in the last 3 months. Endometrioma tissue was cut off 2 - 3 mm, transplanted into CAM, then incubated for 5 days. The invasion level was assessed based on the level of regularity of the CAM chorionic epithelium attached to endometrioma tissue using the haematoxylin-eosin (HE) staining. The MMP-9 activity and TIMP-1 expression were analysed using gelatine zymography and western blot. Moreover, the correlation between MMP-9 activity and TIMP-1 expression on the invasion level of endometrioma tissue was analysed using the Spearman correlation test.

Results: A total of 30 endometrioma tissues were obtained from 24 patients who underwent laparoscopic or laparotomy procedures. The Spearman correlation test showed that there was strong positive correlation between MMP-9 activity and invasion level of endometriomas tissue, while TIMP-1 expression was inverse with weak negative correlation.

Conclusion: MMP-9 activity and TIMP-1 expression were correlated with the invasion level of endometrioma tissue.

Keyword: Endometrioma, Chorioallantoic membrane (CAM), Matrix metalloproteinase-9 (MMP-9), Tissue Inhibitor of Metalloproteinase-1 (TIMP-1)