

Ekspresi mRNA Matrik Metalloproteinase-7 (MMP-7) dan Tissue Inhibitor of Metalloproteinase-1 (TIMP-1) pada Endometrium Perempuan Obesitas dengan Infertilitas

ABSTRAK

Latar belakang: Obesitas menyebabkan perubahan pada endometrium yang diyakini menyebabkan perubahan pada protein dan ekspresi gen di endometrium yaitu MMP dan inhibitor alaminya, TIMP. MMP dan TIMP memainkan peran penting dalam remodeling jaringan endometrium. Terdapat 23 jenis MMP, terkhusus MMP-7 yang berperan dalam mendegradasi membran basal dan dalam proses apoptosis sedang TIMP-1 adalah inhibitorynya. Pada perempuan obesitas terjadi proliferasi endometrium berlebih dan apoptosis jaringan yang terhambat sehingga menyebabkan infertilitas oleh karena penurunan reseptivitas endometrium, hal ini terdapat peran MMP-7 dan TIMP-1 didalamnya.

Tujuan: Penelitian ini dilakukan untuk mengetahui ekspresi mRNA MMP-7 dan TIMP-1 di endometrium fase proliferasi perempuan obesitas dengan infertilitas juga hubungannya dengan kadar serum estradiol dan progesteron.

Metode: Penelitian ini dilakukan dengan metode potong lintang dengan kriteria inklusi yaitu perempuan infertil minimal 1 tahun, usia 18-45 tahun, dengan siklus haid teratur 28-35 hari serta tidak mendapatkan terapi kortikosteroid dan hormonal dalam tiga bulan terakhir. Subyek penelitian dibagi dalam dua kelompok berdasarkan IMT yaitu kelompok obesitas ($\geq 25 \text{ kg/m}^2$) dan kelompok IMT normal. Pengambilan jaringan endometrium dilakukan pada hari ke-8 hingga hari ke-13 dalam siklus menstruasinya. Sampel darahpun diambil pada hari yang sama. Jaringan endometrium sebesar $\pm 1 \text{ cm}$ atau $\pm 25-50 \text{ mg}$ diperoleh dengan histeroskopi atau biosi *Pipelle*, kemudian dilakukan pemeriksaan RT-PCR dan diperoleh nilai CT mRNA MMP-7 dan TIMP-1. Darah vena diambil 3 ml, dengan puasa minimal 8 jam, kemudian dilakukan pemeriksaan kadar estradiol, progesteron dan gula darah puasa.

Hasil: Sebanyak 24 sampel jaringan endometrium dari 24 pasien yang terbagi dalam 2 kelompok. Hasil uji *Unpaired Independent T-Test* menunjukkan ekspresi mRNA MMP-7 secara statistik lebih rendah pada perempuan obesitas dengan infertilitas dibandingkan dengan perempuan IMT normal ($p=0,005$, 95% *CI* -3,583; -0,707). Hasil uji regresi linear menunjukkan terdapat hubungan positif kuat antara kadar estradiol dengan ekspresi mRNA TIMP-1 di endometrium fase proliferasi pada perempuan obesitas dengan infertilitas ($p=0,021$, 95% *CI* 0,127; 0,893).

Kesimpulan: Pada endometrium fase proliferasi perempuan obesitas dengan infertilitas, ekspresi mRNA MMP-7 lebih rendah dan ekspresi mRNA TIMP-1 lebih tinggi dibandingkan dengan perempuan IMT normal dengan infertilitas, tidak terdapat hubungan antara kadar estradiol dan kadar progesteron dengan ekspresi mRNA MMP-7, terdapat hubungan positif kuat antara kadar estradiol dengan ekspresi mRNA TIMP-1, tidak terdapat hubungan antara kadar progesteron dengan ekspresi mRNA TIMP-1, juga tidak terdapat hubungan rasio kadar estradiol dan kadar progesteron dengan rasio ekspresi mRNA MMP-7 dan TIMP-1.

Kata kunci: *Matrix Metalloproteinase-7 (MMP-7)*, *Tissue Inhibitor of Metalloproteinase-1 (TIMP-1)*, endometrium fase proliferasi, obesitas

Expression of mRNA Matrix Metalloproteinase-7 (MMP-7) and Tissue Inhibitor of Metalloproteinase-1 (TIMP-1) in the Endometrium of Obese Women with Infertility

ABSTRACT

Background: Obesity causes changes in the endometrium, which is believed to result in alterations in protein and gene expression, specifically MMP and its natural inhibitor, TIMP. MMP and TIMP play a crucial role in endometrial tissue remodelling. There are 23 types of MMPs, specifically MMP-7, which is involved in degrading the basal membrane and apoptosis processes, while TIMP-1 acts as its inhibitor. In obese women, excessive endometrial proliferation and inhibited tissue apoptosis lead to infertility due to decreased endometrial receptivity. MMP-7 and TIMP-1 play a role in this process.

Purposes: This research was conducted to determine the mRNA expression of MMP-7 and TIMP-1 in the proliferative phase endometrium of obese women with infertility and its relationship with serum estradiol and progesterone levels.

Methods: This study was conducted by a cross-sectional method with inclusion criteria, i.e. infertile women of at least 1 year, aged 18-45 years, with a regular menstrual cycle of 28-35 days and not receiving corticosteroid and hormonal therapy in the last three months. The study subjects were divided into two groups based on BMI: the obesity group (≥ 25 kg/m²) and the normal BMI group. Endometrial tissue sampling was performed from day 8 to day 13 of her menstrual cycle. Blood samples were also taken on the same day. Endometrial tissue measuring approximately ± 1 cm or ± 25 -50 mg was obtained using hysteroscopy or Pipelle biopsy. Subsequently, an RT-PCR examination was conducted to obtain CT values of mRNA MMP-7 and TIMP-1. A 3 ml venous blood sample was taken after a minimum 8-hour fasting period, followed by an assessment of estradiol, progesterone, and fasting blood sugar levels.

Results: A total of 24 endometrial tissue samples were obtained from 24 patients divided into 2 groups. The Unpaired Independent T-Test results showed that the mRNA expression of MMP-7 was statistically lower in obese women with infertility compared to women with normal BMI ($p=0005$, 95%CI -3583;-0707). The results of the linear regression test indicate a strong positive relationship between estradiol levels and TIMP-1 mRNA expression in the proliferative phase endometrium of obese women with infertility ($p=0021$, 95%CI 0127; 0893).

Conclusions: In the endometrium of the proliferation phase of obese women with infertility, the expression of mRNA MMP-7 was lower, and the expression of mRNA TIMP-1 was higher compared to normal-weight women with infertility, there was no correlation between estradiol and progesterone levels and expression of mRNA MMP-7. However, there was a strong positive correlation between estradiol levels and expression of mRNA TIMP-1, there was no correlation between progesterone levels and expression of mRNA TIMP-1, and there was no correlation between the estradiol and progesterone ratio and the mRNA expression ratio of MMP-7 and TIMP-1.

Keywords: Matrix Metalloproteinase-7 (MMP-7), Tissue Inhibitor of Metalloproteinase-1 (TIMP-1), proliferative phase endometrium, obesity