

ABSTRAK

**MEKANISME STRES RETIKULUM ENDOPLASMIK DAN EKSPRESI
CYCLIN D2 TERHADAP PERUBAHAN SIKLUS SEL GRANULOSA OVARIUM
WANITA ENDOMETRIOSIS DENGAN INFERTILITAS**

Pendahuluan: Endometriosis merupakan penyakit inflamasi kronis yang ditandai peningkatan sitokin proinflamasi di zalir peritoneum. Retikulum endoplasmik merupakan organel penting di sel granulosa untuk sekresi hormon. Penelitian bertujuan menganalisa pengaruh TNF α terhadap karakteristik sel granulosa di zalir folikel ovarium wanita endometriosis khususnya fungsi endoplasmik retikulum dan siklus sel.

Metode: Studi ini bersifat potong lintang observasional, dilaksanakan bulan Januari 2016 hingga mei 2018. Pengambilan sampel penelitian wanita endometriosis ini dilakukan dengan prosedur laparoskopi saat dideteksi folikel berukuran 17mm guna diaspirasi zalir folikel dominan dan zalir peritoneum. Kemudian kadar TNF α dizalir peritoneum dengan ELISA, Sel granulosa diisolasi dari zalir folikel dan dievaluasi mRNA GRP78, eIF2 α , CHOP dengan qPCR, siklus sel diperiksa dengan Flowcytometry. Protein Cyclin D2 dievaluasi dengan western blotting.

Hasil : Didapatkan 13 wanita endometriosis dan 4 wanita non endometriosis. Kadar TNF α di zalir peritoneum lebih tinggi pada kelompok endometriosis (48,66 \pm 3,9 ng/mL) dibanding non endometriosis (37,6 \pm 3,8 ng/mL), $p < 0,001$. Pada Sel granulosa zalir folikel dominan kelompok endometriosis didapatkan mRNA GRP78 3,32 kali , eIF2 α 8,54 kali, dan CHOP 1,78 kali lebih tinggi dari non endometriosis. Ekspresi protein Cyclin D2 kelompok endometriosis adalah 97,056% dibanding non endometriosis 86,217% ($p > 0,05$). Sel granulosa pada endometriosis menunjukkan fase G0/G1 lebih tinggi, fase S dan M lebih rendah dibanding non endometriosis ($p < 0,001$). Analisis jalur menunjukkan TNF α zalir peritoneum berpengaruh terhadap GRP78 di sel granulosa.

Kesimpulan: Wanita endometriosis memperlihatkan stres RE di sel granulosa serta perubahan distribusi siklus sel yang disebabkan kadar TNF α zalir peritonuem yang lebih tinggi dbandingkan non endometriosis.

Keyword: Endometriosis, Retikulum endoplasmik, Cyclin D2, siklus sel, infertilitas

ABSTRACT

**THE MECHANISM OF ENDOPLASMIC RETICULUM STRESS AND
THE CYCLIN D2 EXPRESSION ON OVARIAN GRANULOSA CELL CYCLE IN
INFERTILE ENDOMETRIOSIS WOMEN**

Background: Endometriosis, benign gynecological disease is defined by chronic inflammatory disease with dominated inflammatory cytokine. The such endometriosis related secretory cell namely granulosa cell provide its important organell of endoplasmic reticulum. This study aimed to analyze the influence of TNF α against the characteristic of granulosa cell specially the function in its organell of endoplasmic reticulum and the cell cycle.

Methods: This observed cross sectional study was done from January 2016 through May 2018 in DR. Soetomo Hospital Surabaya. Samples was found by laparoscopy at the time of 17 mm sized follicle was detected. Assesment of peritoneal fluid's TNF α level by ELISA, the marker of mRNA-GRP78, eIF2 α and CHOP taken from isolated granulosa cell assessed by qPCR, flowcytometry use to observe cell cycle, Westernblotting spent to evaluate Cyclin D2.

Results: We observed 13 women with endometriosis and 4 women non endometriosis. The study showed that peritoneal fluid TNF α higher in endometriosis group compared to non endometriosis (48,66 \pm 3,9 vs 37,6 \pm 3,8 ng/mL, p<0,05). The study apparently indicated sharply increased that all markers mRNA GRP78, eIF α and CHOP with respectively 3.32, 8.54 and 1.78- fold, but Cyclin D2 was also increased (97,056% vs 86,217%; p>0,05) in endometriosis women group. the granulosa cell's cycle showed the higher result on G0/G1 phase but lowering S/M phase on endometriosis group compared to control. It seemed peritoneal fluid TNF α influence occured against GRP78.

Conclusion: Endometriosis women having higher TNF α level suggested to lead ER stress were playing the importan role in the granulosa cell cycle

Keywords: Endometriosis, endoplasmic reticulum, Cyclin D2 and cell cycle., Infertility