

## INTISARI

### Ekspressi miR-141 dan mRNA PTEN (*Phosphatase and Tensin Homolog*) pada Plasma Darah Penderita Tumor Ovarium dan Kanker Ovarium

**Latar Belakang:** Kanker ovarium merupakan keganasan ginekologis yang paling mematikan pada wanita. Sebagian besar kanker ovarium terdiagnosis pada stadium lanjut akibat gejala yang tidak khas dan belum adanya metode deteksi dini yang efektif. Diperlukan adanya biomarker deteksi dini yang minimal invasive untuk meningkatkan keberhasilan pengobatan. microRNA merupakan regulator ekspresi gen pada tingkatan postranskripsi dan memainkan peranan penting dalam karsinogenesis kanker ovarium. microRNA juga dapat dideteksi di sirkulasi darah sehingga berpotensi sebagai biomarker minimal invasive untuk kanker ovarium. Penelitian sebelumnya menemukan bahwa miR-141 menghibridisasi secara langsung sekuens 3'UTR mRNA PTEN, dan upregulasi miR-141 menyebabkan downregulasi ekspresi PTEN in vivo. PTEN merupakan tumor suppressor gen yang mengalami inaktivasi pada berbagai kanker, termasuk kanker ovarium. Penelitian pada jaringan kanker ovarium menemukan downregulasi ekspresi mRNA dan protein PTEN, namun masih sedikit data yang menunjukkan ekspresi mRNA PTEN pada sirkulasi darah kanker ovarium epitel.

**Tujuan:** Penelitian ini bertujuan untuk mengukur dan membandingkan ekspresi miR-141 dan mRNA PTEN pada plasma penderita tumor ovarium dan kanker ovarium epitel.

**Desain :** Penelitian ini merupakan penelitian analitik observasional dengan desain *cross sectional*. Penelitian ini menggunakan 25 plasma pasien kanker ovarium epitel dan 25 plasma pasien tumor ovarium jinak. Ekspresi relatif miR-141 dan mRNA PTEN dikuantifikasi menggunakan *reverse transcription Real Time Quantitative PCR* (qRT PCR). Metode  $2^{-\Delta\Delta Cq}$  digunakan untuk menghitung kuantifikasi relatif miR-141 dan mRNA PTEN.

**Hasil:** Ekspresi miR-141 pada plasma darah pasien kanker ovarium epitel mengalami peningkatan sebesar 7,59 kali lipat dibanding plasma darah pasien tumor ovarium ( $p=0,001$ ). Ekspresi mRNA PTEN plasma darah pasien kanker ovarium epitel mengalami penurunan sebesar 11,63 kali dibanding plasma darah pasien tumor ovarium ( $p=0,001$ ). Terdapat korelasi negatif antara ekspresi miR-141 dengan ekspresi mRNA PTEN pada plasma darah pasien kanker ovarium epitel dengan kekuatan korelasi sedang ( $p=0,033$ ;  $r = -0,428$ ).

**Kesimpulan:** Ekspresi miR-141 dan mRNA PTEN berbeda antara plasma darah pasien kanker ovarium epitel dan tumor ovarium jinak. Terdapat korelasi negatif antara ekspresi miR-141 dan mRNA PTEN plasma pasien kanker ovarium epitel.

**Kata Kunci:** Kanker Ovarium Epitel, microRNA sirkulasi, miR-141, mRNA PTEN

## ABSTRACT

### Expression of Circulating miR-141 and mRNA PTEN (Phosphatase and Tensin Homolog) in Blood Plasma of Ovarian Tumor and Ovarian Cancer Patient

**Background:** Epithelial Ovarian Cancer (EOC) is the most lethal gynecological malignancies among woman. The majority of this disease is diagnosed at the advanced stage due to lack of specific symptoms and effective screening methods. Therefore, an adequate biomarker for early detection is needed and may improve patient survival. microRNA is a small non-coding RNA that regulates gene expression in post-transcriptional level. Several studies have shown the ability to detect microRNA in blood circulation so microRNA may be used as a minimally invasive biomarker for EOC. microRNA-141 (miR-141) plays a major role in EOC by regulating expression of several tumor suppressor gene. Previous study have confirmed that miR-141 regulated PTEN gene directly by interacting with 3'UTR sequence of PTEN mRNA. PTEN is important tumor suppressor gene that its inactivation found in various human cancer. When various studies found that PTEN mRNA and protein expression is significantly downregulated in EOC tissue, little is known about the expression of PTEN mRNA in blood circulation of EOC patient, especially in Yogyakarta population.

**Objective:** The aims of this study is to measure and compare expression of miR-141 and mRNA PTEN in blood plasma of ovarian tumor patient and epithelial ovarian cancer patient.

**Methods:** This study used cross-sectional design. 25 blood plasma of ovarian tumor and 25 blood plasma of EOC were collected. Total RNA was isolated and reverse transcribed to obtain cDNA. The expression of miR-141 and mRNA PTEN were measured by quantitative real-time polymerase chain reaction assay (qPCR). The  $2^{-\Delta\Delta Cq}$  method was used to calculate relative quantification of miR-141 and mRNA PTEN using miR-16 as reference gene for microRNA and beta-actin mRNA as reference genes for PTEN mRNA.

**Result:** Expression of miR-141 is significantly elevated in blood plasma of epithelial ovarian cancer patient compared to the ovarian tumor ( $p=0,001$ , fold change=7,59). Expression of PTEN mRNA significantly downregulated in blood plasma of epithelial ovarian cancer patient compared to the ovarian tumor ( $p=0,001$ , fold change=11,63). There was a significant negative correlation between miR-141 expression and mRNA PTEN expression in blood plasma of epithelial ovarian cancer patient ( $p=0,033$ ;  $r=-0,428$ ).

**Conclusion:** miR-141 and mRNA PTEN differentially expressed in blood plasma of ovarian tumor and epithelial ovarian cancer patient. There was a negative correlation between miR-141 and mRNA PTEN expression in blood plasma of epithelial ovarian cancer patient.

**Keywords:** Epithelial ovarian cancer, Circulating microRNA, miR-141, mRNA PTEN