INTISARI

Latar Belakang: Kanker ovarium merupakan salah satu kanker yang mempunyai prevalensi yang tinggi pada wanita. Indonesia termasuk dalam 5 besar negara penderita kanker ovarium terbanyak di Asia. Penderita kanker ovarium hanya 20% yang terdiagnosis pada stadium awal. Sebagian besar (90%) kanker ovarium adalah *epithelial ovarian cancer (EOC).* Banyak penelitian sebelumnya menemukan bahwa *microenvironment* pada tumor mempunyai pengaruh besar terhadap invasi dan metastasis kanker. Salah satu sel imun yang terbanyak terdapat pada *microenvironment* adalah *tumor associated macrophage (TAM)*. Penelitian sebelumnya mendapatkan rasio Makrofag 1/Makrofag 2 berbanding terbalik dengan ekspresi MUC2 dan mempengaruhi *survival rate* pasien EOC. Berdasarkan studi *insilico*, ekspresi MUC2 diregulasi oleh miR-34c. MikroRNA mempunyai peranan penting dalam regulasi ekspresi gen dan dapat menjadi salah satu kandidat biomarker.

Tujuan Penelitian: Tujuan utama penelitian ini adalah untuk melihat hubungan ekspresi miR-34c dan mRNA MUC2 pada plasma pasien EOC dibanding kontrol sehat dan pengaruhnya terhadap ekspresi mRNA TNF-α dan MMP7 sebagai penanda *tumor associated macrophage (TAM).*

Metode: Sampel menggunakan plasma dari pasien di RSUP Dr. Sardjito dengan 29 pasien EOC dan 25 kontrol sehat yang sudah ada di *Biobank* FKKMK UGM. Total RNA diisolasi dari plasma pasien EOC dan kontrol sehat. Selanjutnya dilakukan sintesis cDNA. Ekspresi miR-34c, mRNA MUC2, mRNA TNF-α dan MMP7 diperiksa menggunakan qRT-PCR. Hasil qRT-PCR dinormalisasi dengan *Biorad CFX Manager Software* dan dilanjutkan analisis dengan metode Livak and Schmittgen dan analisis statistik menggunakan SPSS 19 dan *GraphPad 7.0*.

Hasil: Hasil analisis mendapatkan bahwa ekspresi miR-34c menurun 6,40 kali (p-value = 0,455*) pada pasien EOC dibanding kontrol sehat, tidak signifikan secara statistik (p value≥ 0,05). Ekspresi mRNA MUC2 menurun 1,40 kali (p-value = 0.350*) pada plasma pasien EOC dibanding kontrol sehat. Ada korelasi negatif lemah antara miR-34c and mRNA MUC2 (r= -0.145, p>0.05). Terdapat korelasi positif lemah antara ekspresi miR-34c dan mRNA MUC2 terhadap perbandingan ekspresi mRNA TNF-α/MMP7 pada pasien EOC (p=0.173, r= 0.254 and p=0.581, r=0.106).

Kesimpulan: Penelitian membuktikan bahwa ekspresi miR-34c mengalami *downregulation* pada pasien EOC dibanding kontrol sehat dan adanya korelasi negatif yang lemah antara ekspresi miR-34c dengan ekspresi mRNA MUC2 pada pasien EOC. Ekspresi miR-34c dan mRNA MUC2 mempunyai korelasi positif lemah dengan polarisasi makrofag .

Kata kunci: *kanker ovarium, plasma, miR-34c, MUC2, tumor associated macrophage*

ABSTRACT

Background: Ovarian Cancer (OC) is one of the high prevalence cancer in woman in the world. Indonesia include in five country that have highest rate incidence OC in Asia. Only 20 % of OC patient are diagnosed in early stage. Most of ovarian cancer (90%) is epithelial ovarian cancer (EOC). Many study has found that microenvironments of cancer cells lead progression and metastasis. One of the most among immune system in microenvironments of cancer cells is tumor associated macrophage (TAMs). Ratio M1/M2 is inversely associate to MUC2 expression and it influence survival rate of EOC patient. Based on insilico study, production of MUC2 is direct regulated by miR-34c. MicroRNAs have important role in gen regulation and also one of biomarker candidate.
Objective: The aim of this study is to determine whether there are associated between the expression of miR-34c and mRNA MUC2 in plasma EOC patients and it influence to expression of mRNA TNF-α and MMP7 as mark tumor associated macrophage.
Methods: The samples is plasma from patients of RSUP Dr. Sardjito with 29 EOC patients and 25 healthy control. Total RNA was isolated from blood plasma samples of EOC patients. cDNA synthesis from total RNA was performed to obtain cDNA. The expression of miR-34c, mRNA MUC2, mRNA TNF-α and MMP7 were calculated using qRT-PCR. qRT-PCR results were analyzed using CFX Manager Software. All data was analized with Livak and Schmittgen methods, SPSS 19 software and GraphPad 7.0.
Result: The analysis showed that the expression of miR-34c were 6,40 times lower (p-value = 0,455*) in the plasma of EOC patienst compared the healthy control, the differences were not statistically significant (p value≥ 0,05). Whereas the mRNA expression MUC2 were 1,40 times lower (p-value = 0.350*) in the plasma of EOC compared with healthy control. There is low negative correlation beween expression miR-34c and mRNA MUC2 (r= -0.145, p>0.05). There is low positive correlation among expression miR-34c and mRNA MUC2 to ratio expression of mRNA TNF-α/MMP7 in EOC (p=0.173, r= 0.254 and p=0.581, r=0.106).
Conclusion: This study has proved that miR-34c expression is downregulated in EOC compared healthy control and there is low negative correlated among miR-34c expression to expression of mRNA MUC2 in EOC. Expression miR-34c and mRNA MUC2 is low posssitive correlated with polarization of macrophage.

key word :ovarian cancer, plasma, miR-34c, MUC2, tumor associated macrophage