

# Ekspresi Phosphatase Regenerating Liver-3 dan E- Cadherin pada Kanker Serviks Stadium Awal dan Lanjut Lokoregional

*by Sharvianty Arifuddin*

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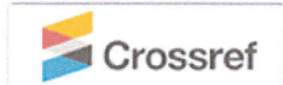
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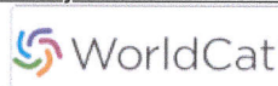
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## Eksresi Phosphatase Regenerating Liver-3 dan E-Cadherin pada Kanker Serviks Stadium Awal dan Lanjut Lokoregional

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### ABSTRACT

*Purpose: To investigate the relationship between the expression of PRL-3 and E-cadherin to the stages, histopathological types and tumor grades of cervical cancer. Material and Methods: Analytic study with cross-sectional approach in several hospitals at the Department of Obstetrics and Gynecology, Makassar from January to June 2011. Expression of PRL-3 and E-cadherin was detected by immunohistochemistry in 16 early-stage and 15 locally advanced stage of cervical cancer cases. The relationship between the expression of PRL-3 and E-cadherin to several clinicopathologic factors were analyzed. Result: PRL-3 expression was not significantly different between early stage and locally advanced stage, histopathological types and tumor grades ( $p>0.05$ ). E-Cadherin expression also showed no significant difference between stages, types and grades ( $p>0.05$ ). There were no significant correlations between the expression of PRL-3 and E-Cadherin. Conclusion: There was no relation between PRL-3 and E-cadherin expression to the stages, histopathological types and tumor grades of cervical cancer.*

**Keywords:** Early-stage cervical cancer, locally advanced stage cervical cancer, adenocarcinoma, squamous cell carcinoma, tumor grade, PRL-3, E-cadherin.

### ABSTRAK

Tujuan: untuk menyelidiki hubungan antara ekspresi PRL-3 dan E-Cadherin dengan stadium, jenis histopatologi, dan derajat diferensiasi kanker serviks. Metode: penelitian ini merupakan studi analitik dengan pendekatan potong lintang di beberapa rumah sakit pendidikan Bagian Obstetri dan Ginekologi, Makassar, mulai Januari hingga Juni 2011. Ekspresi PRL-3 dan E-Cadherin diperiksa dengan pengecatan imunohistokimia pada 16 kanker serviks stadium awal dan 15 stadium lanjut lokoregional. Hasil: ekspresi PRL-3 tidak berbeda bermakna antara kanker serviks stadium awal dengan stadium lanjut lokoregional, antara berbagai jenis histopatologi dan derajat diferensiasi ( $p>0,05$ ). Ekspresi E-Cadherin juga menunjukkan tidak ada perbedaan bermakna antara berbagai stadium, jenis histopatologi, dan derajat diferensiasi ( $p>0,05$ ). Tidak didapatkan korelasi bermakna antara ekspresi PRL-3 dengan E-Cadherin pada penelitian ini. Kesimpulan: tidak ada hubungan antara ekspresi PRL-3 dan E-Cadherin dengan stadium, jenis histopatologi, dan derajat diferensiasi kanker serviks.

**Kata Kunci:** Kanker serviks stadium awal, kanker serviks stadium lanjutlokoregional, adenokarsinoma, karsinoma sel skuamosa, derajat diferensiasi, PRL-3, E-Cadherin.

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### PENDAHULUAN

Kanker serviks merupakan kanker pada traktus genitalia perempuan yang tersering dan merupakan penyebab kematian akibat kanker tertinggi pada populasi

sediaan diinkubasi *overnight* pada suhu  $-4^{\circ}\text{C}$  dengan primer PRL-3 antibodi (AttoGen) yang diencerkan 1:100. Sediaan dicuci lagi sebanyak 3 kali dengan  $\text{dH}_2\text{O}$  sebelum diinkubasi dengan *secondary antibody* dan streptavidin selama masing-masing 30 menit. Untuk pewarnaan digunakan 3,3 diamino benzidine tetrahydrochloride kurang lebih 10 menit sampai didapatkan reaksi pewarnaan yang dapat dideteksi dengan pemeriksaan mikroskopis. Setelah itu, diwarnai lagi dengan hematoksin untuk memperjelas inti sel selama 30 detik dan dicuci dengan air mengalir selama 5 menit. Sediaan didehidrasi dengan menggunakan alkohol yang konsentrasinya dinaikkan secara bertahap dari 70%, 80%, 90%, sampai 100% selama masing-masing 2 menit. Setelah itu, sediaan dicelupkan ke dalam xylene selama 5 menit. Terakhir, sediaan diberi malinol sebelum ditutup dengan kaca penutup.

Sebelum dilakukan pembuatan imunohistokimia, terlebih dahulu dilakukan deparafinisasi jaringan dengan melakukan inkubasi ke dalam larutan berturut-turut: xylene 3 x 15 menit, etanol 100% 3 x 5 menit, etanol 90% 5 menit, etanol 80% 5 menit, akuades 5 menit, Antigen Retrieval masking (Novocastral®)  $100^{\circ}\text{C}$  15 menit, 1 x PBS (Sigma®) 2 x 5 menit, H2O2 3% dalam methanol 10 menit, dan 1 x PBS (Sigma®) 2 x 5 menit. Jaringan kemudian diinkubasi dalam blocking solution serum (Novocastral® Prediluted normal horse serum) selama 10 menit, lalu diinkubasi dengan antibodi primer (Novocastral® Mouse monoclonal antibody antibody) selama 30 menit pada suhu kamar, kemudian dicuci dengan 1 x PBS (Sigma®) 2 x 5 menit. Kemudian, jaringan diinkubasi dengan link antibody (antibodi sekunder yang dilabel dengan biotin) (Novocastral® Biotinylated Universal secondary antibody p53) selama 10 menit pada suhu kamar, kemudian dicuci lagi dengan 1 x PBS (Sigma®).

Jaringan kemudian diinkubasi dengan Streptavidin (Novocastral®) selama 10 menit pada suhu kamar kemudian dicuci dengan 1 x PBS (Sigma®). Untuk pewarnaan, jaringan diinkubasi dengan DAB/AEC kromogen (Novocastral®) yang dilarutkan dalam H2O2 3% selama 25 menit. Setelah preparat dicuci dengan akuades mengalir selama 2-3 menit, dilakukan *counter staining* (mewarnai sel negatif). Jaringan diinkubasi dengan larutan Meyer Hematoxylin selama 2-5 menit pada suhu kamar. Setelah dibilas dengan akuades mengalir, dilakukan dehidrasi dengan memakai alkohol bertingkat (70%,80%,90%), masing-masing 1 menit dan dijernihkan dengan xylene 2

menit. Jaringan kemudian ditetesi malinol lalu ditutup dengan kaca penutup.

Derajat ekspresi pewarnaan PRL-3 dan E-Cadherin dilihat dari persentase kelompok sel yang terwarnai dan intensitas pewarnaan. Persentase didapatkan dari hasil penjumlahan sel yang positif pada seluruh lapangan pandang sediaan tumor yang diperiksa dengan memakai mikroskop cahaya. Saat ini tidak terdapat sistem *scoring* yang baku, namun berdasarkan berbagai referensi, sistem *scoring* yang lazim digunakan adalah sebagai berikut: - (skor 0) bila sel positif <5%; positif 1 (skor 1) bila sel positif berjumlah 5-25%; positif 2 (skor 2) bila sel positif 26-75%; dan positif 3 (skor 3) bila sel positif >75%.<sup>1</sup>

Uji statistik yang dilakukan untuk menganalisis hubungan antara ekspresi PRL-3 dan E-Cadherin dengan stadium kanker serviks serta beberapa faktor klinikopatologik adalah uji Kruskal Wallis atau Wilcoxon - Mann Whitney. Uji statistik untuk menganalisis korelasi antara ekspresi PRL-3 dengan E-Cadherin pada kanker serviks adalah uji korelasi Spearman.

#### HASIL

Penelitian ini dilakukan secara *cross-sectional* analitik terhadap 31 sampel, yaitu 16 sampel kanker serviks stadium awal dan 15 sampel kanker serviks *locally advanced*. Subyek penelitian ini diambil dari Januari hingga Juni 2011, dengan mengambil jaringan biopsi serviks uteri. Pemeriksaan dilakukan di bagian Patologi Anatomi untuk menilai jenis histopatologi, derajat diferensiasi, serta level ekspresi PRL-3 dan E-Cadherin dengan menggunakan metode imunohistokimia.

Tabel 1 menyajikan profil klinikopatologik penderita. Karakteristik yang dievaluasi adalah umur, stadium, jenis histopatologi, dan derajat diferensiasi kanker serviks. Sampel penelitian sebanyak 31 orang dengan data rerata umur penderita 48,23 tahun ( $\text{SD} \pm 9,99$ ). Umur termuda 25 tahun dan tertua 68 tahun, paling banyak ditemukan pada umur lebih dari 51 tahun, yaitu 11/31 (35,45%). Pada penelitian ini didapatkan penderita kanker serviks stadium awal sebanyak 16/31 (51,61%) dan stadium lanjut lokoregional sebanyak 15/31 (48,39%). Berdasarkan jenis histopatologi, terbanyak adalah jenis karsinoma sel skuamosa, yaitu 24/31 (77,42%). Derajat diferensiasi sedang dan buruk dijumpai pada penderita dengan jumlah yang sama, masing-masing 14/31 (45,16%).



berhubungan dengan derajat diferensiasi.<sup>22</sup> Penelitian ini juga menunjukkan bahwa tidak terdapat korelasi yang bermakna antara ekspresi PRL-3 dengan E-Cadherin. Hal ini dapat dijelaskan karena ekspresi PRL-3 tidak mengalami peningkatan secara bermakna pada berbagai stadium sehingga tidak berhubungan dengan ekspresi E-Cadherin pada kanker serviks. Pada penelitian ini, ekspresi E-Cadherin cenderung menurun pada stadium lanjut, akan tetapi tidak bermakna secara statistik yang mungkin disebabkan oleh jumlah sampel yang kecil. Ekspresi E-Cadherin sendiri, selain dipengaruhi oleh PRL-3, juga diatur oleh berbagai jalur sinyal yang tidak diteliti pada penelitian ini. Oleh karena itu, masih perlu dilakukan penelitian lebih lanjut untuk mengetahui mekanisme biomolekuler dalam mempelajari perilaku kanker serviks, khususnya untuk mempelajari mekanisme regulasi gen PRL-3 dan E-Cadherin pada kanker serviks.

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