ABSTRAK

Latar belakang. Kanker paru adalah tumor ganas yang berasal dari epitel bronkus sebagai penyebab kematian kanker terbanyak laki-laki di dunia. Kanker paru karsinoma bukan sel kecil (KPKBSK) merupakan 85% dari seluruh kanker paru. Mortalitas tinggi disebabkan sebagian besar penderita datang *stage* lanjut dan resisten terapi. Hanya 16,6% pasien kanker paru yang hidup 5 tahun setelah didiagnosis. Perlunya petanda molekular untuk membantu tatalaksana terapi, salah satunya miRNA. Penelitian ini menggunakan miR-34 dan miR-222. Saat ini belum ada studi mengenai data genetik tersebut pada populasi Indonesia.

Tujuan. Membuktikan serum miR-34 dan miR-222 dapat menjadi petanda biologi prognosis KPKBSK. Penelitian ini akan membuktikan hubungan kesintasan miR-34 tinggi memiliki prognosis baik dan miR-222 tinggi prognosis buruk.

Bahan dan cara kerja. Metode penelitian kohort retrospektif, subjek pasien KPKBSK *stage* lanjut di RS Kanker "Dharmais" dari Januari 2017 - Desember 2017. Subjek yang memenuhi kriteria inklusi dan eksklusi diambil spesimen serum darah untuk pemeriksaan miRNA. Hasil patologi anatomi dilanjutkan pemeriksaan mutasi gen EGFR. Pengamatan selama 1 tahun dan evaluasi RECIST tiap 3 bulan. Teknik RT *q*-PCR mendeteksi ekspresi miR-34 dan miR-222 sediaan darah dengan kit komersial.

Hasil. Didapatkan 52 pasien status terbanyak T4-N2-M1b *stage* IVb metastasis multiorgan, adeokarsinoma 82,7%, mutasi gen EGFR 19,2%. Ekspresi serum miR-34 rendah (53,85%) dan miR-222 tinggi (32,69%). Hubungan miR-222 tinggi terhadap *performance status* p = 0,018. Korelasi miR-222 terhadap kreatinin p = 0,027; r = -0,308, CEA p = 0,002; r = 0,542, Cyfra 21-1 p = 0,001; r = 0,519 dan korelasi miR-34 terhadap kalium p = 0,008; r = 0,366. MiR-34 tinggi sebagai diagnostik prediktif terhadap metastasis M1b multipel p = 0,020, jenis sel kanker adenokarsinoma p = 0,009 dan adenokarsinoma mutasi gen EGFR negatif p = 0,031. Analisis kesintasan KPKBSK *stage* lanjut terhadap ekspresi serum miRNA didapatkan miR-34 tinggi median kesintasan (MK) 244 hari dibandingkan miR-34 rendah MK 70 hari p = 0,968, miR-222 tinggi MK 81 hari dibandingkan miR-222 rendah MK 92 hari p = 0,283. Prognosis buruk KPKBSK *stage* lanjut metastasis M1b, didapatkan miR-222 tinggi MK 27 hari, miR-222 rendah MK 67 hari *log rank test* p = 0,049. Prognosis buruk KPKBSK *stage* lanjut mutasi gen EGFR positif didapatkan miR-222 tinggi MK 74 hari, miR-222 rendah MK 293 hari *log rank test* p = 0,049.

Kesimpulan. KPKBSK *stage* lanjut memiliki ekspresi serum miR-34 dan miR-222. Ekspresi miR-34 rendah dan miR-222 tinggi merupakan prognosis buruk, terutama miR-222 tinggi terhadap kasus metastasis M1b dan mutasi gen EGFR positif.

Kata Kunci: KPKBSK, miR-34, miR-222, Kesintasan Hidup.

ABSTRACT

Background. Lung cancer is a malignant tumor originating from the bronchial epithelium as the leading cause of cancer death for most men in the world. Non-small cell lung carcinoma (NSCLC) lung cancer is 85% of all lung cancer. High mortality is caused by most patients who come in advanced stages and are resistant to therapy. Only 16.6% of lung cancer patients lived 5 years after being diagnosed. There is need for molecular markers to help in managing therapy, one of which is miRNA. This study uses miR-34 and miR-222 for this purpose. At the present, there are no studies on this genetic data in the Indonesian population.

Objective. The purpose of this study is to prove that miR-34 and miR-222 can be used as biology markers of prognostic. This study will prove that high miR-34 has a good prognosis and high miR-222 has a poor prognosis. This study will also prove the relationship between high miR-34 and low miR-222 with survival in NSCLC.

Materials and methods. Retrospective cohort research method, subjects are advanced stage NSCLC patients at the "Dharmais" Cancer Hospital from January 2017 - December 2017. Subjects who met the inclusion and exclusion criteria underwent blood serum specimens for miRNA examination. The results of anatomy pathology were followed by examination of EGFR gene mutations. Observation for 1 year and evaluation of RECIST every 3 months. The RT q-PCR technique detects the expression of miR-34 and miR-222 from serum with a commercial kit.

Results. Subject with 52 pts had the expression of low miR-34 (53.85%) and high miR-222 (32.69%). There was significant correlation between high miR-222 to performance status p = 0.018, creatinine p = 0.027; r = -0.308, CEA p = 0.002; r = 0.542, Cyfra 21-1 p = 0,001; r = 0,519 and correlation high miR-34 to potassium p = 0,008; r = 0,366. High miR-34 as diagnostic predictive to M1b multiple metastasis p = 0.020, adenocarcinoma cancer cells type p = 0.009 and adenocarcinoma EGFR gene mutation negative p = 0.031. Survival analysis relationship between advanced stage NSCLC with miRNA were found that prognosis of high miR-34 median survival (MS) 244 days compared to low miR-34 MS 70 days p = 0.968, prognosis of high miR-222 MS 81 days, compared with low miR-222 MS 92 days p = 0.283. There was significant correlation of high miR-222 as a poor prognosis in cases of M1b metastasis and positive EGFR gene mutation. Advanced stage NSCLC with metastasis M1b obtained a poor prognosis with high miR-222 MS 27 days while low miR-222 MS 67 days, log rank test p = 0.049. Advanced stage NSCLC with positive EGFR gene mutations obtained a poor prognosis with high miR-222 MS 74 days while low miR-222 MS 293 days, log rank test p = 0.049.

Conclusion. Advanced stage of NSCLC has expression of miR-34 and miR-222 serum. Low miR-34 and high miR-222 expressions are a poor prognosis, especially high miR-222 against cases of M1b metastasis and positive EGFR gene mutations.

Keywords: Advanced Stage NSCLC, miR-34, miR-222, Survival.