

INTISARI

HUBUNGAN VARIASI GENOTIP TNRC9 (TOX3) DENGAN KEJADIAN KANKER PAYUDARA ONSET DINI DI YOGYAKARTA

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Latar Belakang: Kanker payudara merupakan keganasan yang paling sering menyerang wanita di seluruh dunia, termasuk Indonesia. Insidensi kanker payudara onset dini lebih tinggi pada negara-negara berkembang di Asia. Polimorfisme TOX3 rs3803662 teridentifikasi memiliki asosiasi dengan kanker payudara onset dini pada populasi Eropa, Asia, dan Afrika-Amerika, tetapi terdapat hasil yang berbeda dan kontradiktif antar populasi studi.

Tujuan: Mengetahui proporsi variasi genotip TOX3 rs3803662 dan hubungan TOX3 rs3803662 dengan kejadian kanker payudara onset dini di Yogyakarta.

Metode: Penelitian ini merupakan penelitian observasional analitik dengan rancangan kasus kontrol. Subjek penelitian adalah 193 DNA biorepositori penderita kanker payudara RSUP Dr. Sardjito tahun 2006-2013 yang berusia ≤ 40 tahun ($n=93$) dan ≥ 55 tahun ($n=95$) sebagai kelompok kasus dan 60 DNA darah tepi individu normal sebagai kontrol. Varian genetik TOX3 SNP rs3803662 dianalisis dengan TaqMan SNP *Genotyping Assays*. Uji beda proporsi variasi genetik antara kasus dan kontrol dilakukan menggunakan uji *chi-square*. Analisis asosiasi antar model genetik dan risiko terhadap kanker payudara menggunakan perhitungan *odds ratio*.

Hasil: Hasil analisis menunjukkan adanya hubungan antara variasi genotip dan kanker payudara pada kontrol dan seluruh pasien kanker payudara ($p=0,036$). Alel T rs3803662 berhubungan dengan penurunan risiko kanker payudara pada seluruh model genetik, dengan penurunan risiko terbesar terlihat pada genotip TT (OR=0,385 95%CI=[0.160 - 0.924]). Genotip TT merupakan genotip protektif pada kelompok kanker payudara onset dini (OR=0,316 95%CI=[0.115 - 0.864]), sedangkan genotip CT memberikan efek protektif terkuat pada kelompok pasien ≥ 55 tahun (OR=0,388 95%CI=[0.177 - 0.852]). Alel T secara signifikan berhubungan dengan penurunan risiko kanker payudara pada seluruh kelompok kasus (seluruh pasien: OR=0,593 95%CI= [0.389 - 0.905]; ≤ 40 tahun: OR=0,563 95%CI= [0.351 - 0.904]; ≥ 55 tahun: OR=0,624 95%CI=[0.390 - 0.998]).

Kesimpulan: Alel minor T TOX3 rs3803662 memiliki asosiasi yang signifikan terhadap penurunan risiko kanker payudara dan kanker payudara onset dini di Yogyakarta, Indonesia.

Kata Kunci: Kanker Payudara, Onset Dini, SNPs, TOX3 rs3803662

ABSTRACT

ASSOCIATION OF GENETIC VARIANTS AT TNRC9 (TOX3) WITH THE RISK OF EARLY ONSET BREAST CANCER IN YOGYAKARTA

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Background: Breast cancer is the most common cancer in women worldwide, including Indonesia. Early onset breast cancer incidence are higher in developing Asian countries, which carry poorer prognosis. Genetic variants TOX3 rs3803662 was associated with the early onset breast cancer risk in Europe, Asian, and African-American population. However the result were contradictory and differ according to ethnic and race.

Objectives: To determine TOX3 rs3803662 genetic variants and its association on early onset breast cancer initiation in Yogyakarta population.

Methods: This research is an observational analytic studies with case control design. DNA biorepository from 193 breast cancer patients in Dr. Sardjito Hospital from 2006-2013 that aged ≤ 40 years and ≥ 55 years (case group) and DNA from 60 healthy individual (control group) were used on this study. TOX3 SNP rs3803662 were genotyped using TaqMan Genotyping Assay. Chi-square test of independence was used to test for equality of proportion between case and control. Odds ratio (OR) was calculated to measure the strength of association of risk allele and breast cancer under many genetic models.

Results: result suggest that there are correlation between genotype variants and breast cancer risk in breast cancer patients ($p=0,036$). Rs3803662 T Allele was associated with lower risk of breast cancer in all genetic models, with lower OR detected in genotype TT (OR=0,385 95%CI=[0.160 - 0.924]). Genotype TT detected as the protective variant in early onset breast cancer patients (OR=0,316 95%CI=[0.115 - 0.864]). Genotype CT was the protective variant in the older, ≥ 55 years group (OR=0,388 95%CI=[0.177 - 0.852]). There were significant association of allele T rs3803662 with decreased risk breast cancer in all case group (all patients: OR=0,593 95%CI= [0.389 - 0.905]; ≤ 40 years: OR=0,563 95%CI= [0.351 - 0.904]; ≥ 55 years: OR=0,624 95%CI=[0.390 - 0.998]).

Conclusion: rs3803662-T allele were significantly associated with lower risk in breast cancer and early onset breast cancer in Yogyakarta, Indonesia.

Keywords: Breast Cancer, Early Onset, SNPs, TOX3 rs380366