

## ABSTRACT

### **Genetic polymorphisms of MDR1 (*Multidrug Resistance 1*) C3435T, NQO1 (NAD(P)H *quinone oxidoreductase 1*) C609T dan GSTP1 (*Glutathione S-transferase 1*) A313G as risk factors of subclinical acute anthracycline-induced cardiotoxicity in childhood Acute Lymphoblastic Leukemia**

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**Background:** Acute Lymphoblastic Leukemia (ALL) is the most common childhood malignancy. Improvement in the treatment of ALL has caused a serious adverse effect such as cardiotoxicity induced anthracycline. Anthracycline has a complex metabolic pathway involving various metabolic enzymes and transporters. Genetic polymorphism of MDR1 C3435T causes decrease of DNR transporter protein, resulting in increased cardiotoxicity. Polimorphisms gene of NQO1 C609T and GSTP1 A313G can cause decrease of detoxification process that lead to cardiotoxicity.

**Objective:** To prove genetic polymorphisms of MDR1 C3435T, NQO1 C609T and GSTP1 A313G as risk factors of subclinical acute anthracycline-induced cardiotoxicity in childhood ALL

**Methods:** Gene polymorphism of MDR1 C3435T, NQO1 C609T and GSTP1 A313G was examined with PCR-RFLP technique. Subclinical acute cardiotoxicity was considered as a decrease in EF or FS examined using echocardiography, or elevated cTnT levels examined using ECLIA techniques in asymptomatic patients.

**Result:** Forty eight ALL patients enrolled the study. Genetic polymorphism of MDR1 C3435T was found in 38 (79.2%) patients. Twenty eight (58.3%) patients had NQO1 C609T gene polymorphism and 24 (50%) patients had GSTP1 A313G gene polymorphism. Subclinical acute cardiotoxicity was found in 33 (68.8%) patients. Logistic regression analysis showed that MDR1 C3435T and GSTP1 A313G gene polymorphism were not risk factors for subclinical acute cardiotoxicity and ( $p=0.568$  and  $p=0,982$ ). NQO1 C609T gene polymorphism was a risk factor for subclinical acute cardiotoxicity ( $p = 0.022$ ) with RR 1.64 (95% CI 1.026 - 2.631).

**Conclusion:** NQO1 C609T gene polymorphism was a risk factor for subclinical acute cardiotoxicity.

**Keywords:** childhood ALL, genetic polymorphims, anthracycline-induced cardiotoxicity