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Predictive Value of CTLA-4/PD1 Genes Polymorphisms and Susceptibility of Pediatric Acute Lymphoblastic Leukemia

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INTRODUCTION

Immune checkpoint mechanisms depend heavily on programmed death-1 (PD-1) and cytotoxic T lymphocyte-associated antigen-4 (CTLA-4). There have been reports linking the single nucleotide polymorphisms (SNPs) of PD-1 and CTLA-4 to an increased risk of developing various autoimmune disorders and malignancies. It is currently unknown if SNPs in these immune checkpoint genes may be linked to an increased risk of acute lymphoblastic leukaemia (ALL).

AIM

This study aimed to clarify the effect of PD-1 and CTLA-4 SNPs on the risk of developing ALL and the prognosis of the disease.

METHOD

This study was carried out on 100 B-ALL pediatric patients (56 males and 44 females) attending to Pediatric Outpatient Clinic of Mansoura University Oncology Center with median age of 7.8 years. A total number of 100 healthy controls of matched age and gender were included in the study. The PD-1, CTLA-4 and SNPs were examined by RFLP technique.

RESULTS

The study revealed that CTLA-4 (rs 11571316) was associated with high risk of B-ALL developments [OR 1.492 (CI: 1,157-1,924) (p= 0.002)]. PD-1 (rs 36084323) GA genotype was significantly associated with protective effect against non-remission (p= 0.007). PD-1 (rs 36084323) and A allele were associated with protective effect against relapse (p= 0.008). CTLA-4 and PD-1 genotypes did not have significant impact on B-ALL patients' outcome.

	Cases (n=100)
Age (year)	7.8 (0.5-18)
Males	56 (56.0%)
females	44 (44.0%)
WBCs (X10^9/L)	28 (1-160)
Hb (g/dL)	8.9 (5.9-14.8)
RBCs (X10^9/L)	3.3 (2.0-5.6)
platelet (X10^9/L)	40 (8.0-374)
BM blast %	80 (33-95)
LDH (U/L)	682 (105-10575)
Lymphadenopathy	22 (22.0%)
Organomegaly	17 (17.0%)
NCI Risk stratification	
Standard Risk	
Age (1- 10 years) WBCs (<50.0 x 10^9 cells/L)	55 (55%)
High risk	
Age : (<1 years , ≥ 10 years) WBCs (≥50.0 x 10^9 cells/L)	45 (45%)
Philadelphia chromosome positive	6 (6.0%)
Cytogenetic Findings by FISH	
Standard risk	45 (45.0%)
High Risk	55 (55%)
Induction remission response	79 (79.0%)
Percentage of relapse	20/79 (25.3%)

Table 1. Features of studied B-ALL cases

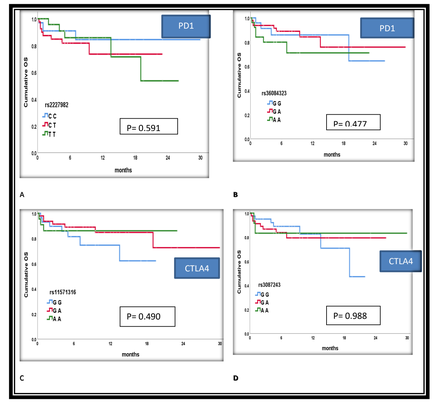


Figure 1. Kaplan-Meier curve assessed that OS according to different genotypes in studied SNPs. The figures showed that neither PD1 nor CTLA4 polymorphisms have significant effect on B-ALL OS.

CONCLUSIONS

The current study displayed for the first time that genetic variations of the CTLA-4 were associated with susceptibility to B-ALL and that PD-1 (rs 36084323) GA genotype was significantly associated with protective effect against non-remission, while PD-1 (rs 36084323) and A allele were associated with protective effect against relapse.

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No conflict of interest

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