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## Abstract

Thymidylate synthase (TS) is a crucial enzyme in folate metabolism and plays a vital role in DNA synthesis and repair. The most common polymorphism in TS is a unique double (2R) or triple (3R) 28-bp tandem repeat sequence in the enhancer region of the TS gene (TSER). This genetic variation in TSER has been widely investigated and has been implicated as a risk factor for the development of various cancers, including acute lymphoblastic leukemia. It has also been found to influence sensitivity to anti-cancer drugs, such as methotrexate. We evaluated this polymorphism in acute lymphoblastic leukemia patients in the Kashmir population. In order to determine whether a double (2R2R) versus a triple (3R3R) 28-bp tandem repeat in the TSER modulates risk for acute lymphoblastic leukemia, 72 acute lymphoblastic leukemia cases and 144 age and gender matched, unrelated healthy individuals from the Kashmir region of India were evaluated for this polymorphism by PCR and direct sequencing. We found the frequency of the TS 2R allele to be 32.6 and 26.0%, in cases and controls, respectively. The TS 2R/2R genotype was found to be present in 15.27% of the cases and 9.72% of the controls, the 2R/3R variant in 34.72% of the cases and 32.63% of the controls, and the 3R/3R genotype in 50.0% of the cases and 57.63% of the controls. There was a significant association between the TS 2R/2R genotype and gender of acute lymphoblastic leukemia patients with males harboring the 2R/2R genotype exhibiting a higher risk of developing acute lymphoblastic leukemia than females (P = 0.009) We concluded that the TSER polymorphism appears not to be a risk factor for susceptibility to acute lymphoblastic leukemia in the Kashmir population.

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