Author(S): Gulzar Bhat[1],Ashaqullah Bhat[1], Aadil Wani[1], Nida Sadiq[1],Samoon Jeelani[2],Rajinder Kaur[3],Akbar Masood[1],Bashir Ganai[1]*

Title: Polymorphic Variation in Glutathione-S-transferase Genes and Risk of Chronic Myeloid Leukaemia in the Kashmiri Population

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Institute: [1]Department of Biochemistry, University of Kashmir,
[2]Department of Clinical Hematology, SKIMS, Srinagar,
[3]Department of Human Biology, Punjabi University, Patiala, India

Abstract

Cancer is a complex disease and the genetic susceptibility to it could be an outcome of the inherited difference in the capacity of xenobiotic metabolizing enzymes. Glutathione-S-transferases (GSTs) are phase II metabolizing enzymes whose various genotypes have been associated with increased risk of different types of cancer. Null mutations caused by the deletion of the entire gene result in the absence of the enzymatic activity and increase in the risk of developing cancer including chronic myeloid leukaemia (CML). In the present case-control study we evaluated the effect of null mutations in GSTM1 and GSTT1 genes on the risk of developing CML. The study included 75 CML patients (43 males and 32 females; age (mean ${\pm}$ S.D) $42.3{\pm}13.4$ years) and unrelated non-malignant controls (76 male and 48 females; age (mean ${\pm}$ S.D) $41.5{\pm}12.9$). The distribution of GSTM1 and GSTT1 genotypes in CML patients and controls was assessed by multiplex-PCR method. Logistic regression was used to assess the relationship between GSTM1 and GSTT1 genotypes and risk of CML. Chi-square test was used to evaluate the trend in modulating the risk to CML by one or more potential high risk genotype. Although GSTM1 null genotype frequency was higher in CML patients (41%) than in the controls (35%), it did not reached a statistical significance (OD = 1.32, 95% CI: 0.73-2.40; P value = 0.4295). The frequency of GSTT1 null genotypes was higher in the CML patients (36%) than in the controls (21%) and the difference was found to be statistically significant (OD = 2.12, 95% CI: 1.12-4.02; P value = 0.0308). This suggests that the presence of GSTT1genotype may have protective role against the CML. We found a statistically significant (OD = 3.09, 95% CI: 1.122-8.528; P value = 0.0472) interaction between the GSTM1 and GSTT1 null genotypes and thus individuals carrying null genotypes of both GSTM1 and GSTT1 genes are at elevated risk of CML.

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