Abstract ID:- 208

Abstract Topic:- Complex traits and polygenic disorders

Abstract Title:- Association of PI3K (rs3730089), IRS-1 (rs1801278) and KCNJ11 (rs5219) with type 2 diabetes in three endogamous groups of North-West India (Punjab)

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Aims:-The chronic and progressive epidemic of T2D has a major societal and economic impact worldwide. India is amongst the countries with the largest number of adults with T2D reporting a prevalence of 74.2 million in 2021(IDF, 2021). The identification of T2D susceptibility loci have extensively contributed in understanding the genetic architecture of the disease. However, there are several inconsistencies in the association of susceptibility loci in the background of ethnic heterogeneity. Although presumed to be homogeneous, Indian population is ethnically diverse with different subgroups exhibiting varied cultural and lifestyle practices. In line to this fact there is extensive stratification within the North-West Indian (Punjab) population also. Considering the high ethnic/genetic heterogeneity, there is scarcity of data on ethnic disparities in association of genetic variants with T2D from North-West, India (Punjab). The present case-control association study investigated the role of three candidate gene polymorphisms in the insulin signaling pathway i.e. PI3K (rs3730089), IRS-1 (rs1801278), and KCNJ11 (rs5219) towards T2D susceptibility among three endogamous groups i.e. Jat Sikhs, Banias and Brahmins of North-West India (Punjab).

Methods:- The study enrolled 573 T2D cases (200 Jat Sikhs, 208 Banias and 165 Brahmins)and 590 controls (204 Jat Sikhs, 216 Banias and 170 Brahmins). The genotyping of all the SNPs was done using PCR-RFLP method. Statistical analysis was done using SPSS V.16 software. Gene-gene interactions were studied through MDR. v. 3.0.2 software.

Results:- The variant allele of rs3730089 and rs1801278 showed association with T2D in the Bania population only [p=5.1x10-4, OR=1.72(1.26-2.38)], [p=7 x10-4* OR=2.38 (1.43-4.0)], respectively. However, rs5219 is significantly associated with T2D in all three studied population groups. Model analysis revealed a 2-4 fold increased risk of diabetes under different genetic models. Gene-gene interactions depicted redundant interactions between rs1801278 and rs5219 in all three endogamous groups.

Conclusions:- In conclusion, the present study implicates the variants of PI3K (rs3730089), IRS-1 (rs1801278), and KCNJ11 (rs5219) polymorphism with T2D susceptibility. The study also reveals the role of ethnicity in differential genetic susceptibility to T2D.

Keywords:- T2D, PI3K,IRS-1, KCNJ11, Ethnicity