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Adipocytokine and inflammatory gene polymorphisms and risk of metabolic syndrome and coronary artery disease in north Indian population

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Obesity is a central marker of the metabolic syndrome and strongly associated with insulin resistance and T2DM. Obese patients are at a higher risk for developing CVD and several studies have suggested obesity to be an independent marker. T2DM with IR has been found to increase cardiovascular risk in metabolic syndrome subjects. Metabolic syndrome known to be polygenic in nature and several pathways are implicated in the pathogenesis of this syndrome. Adipose tissue has a major role in secretion of significantly important proteins, collectively known as adipocytokines, which function as cytokines and have important role in the development or progression of CAD and metabolic syndrome.

Aims and Objectives: To check the association of the various Adipocytokines like TNF-alpha-308G>A, LEPRser492thrG>C, APM+45T>G and APM+276G>T. To check the risk for inflammatory gene IL-18-137G>C and *VEGF-1154G>A* gene polymorphism with MetS and CAD.

Material and Methods: The NCEP-ATPIII Panel was used to enroll the MetS subjects with age of 20-80 years. PCR-RFLP was done for *LEPR* ser492thrG>C with *PstI* enzyme, Nested PCR was done for APM+45T>G with SmaI enzyme and APM+276G>T polymorphism with BgII enzyme, while PCR-ARMS and PCR-SSP was used for *TNF-alpha 308G>A, VEGFA-1154G>A* and *IL-18-137G>C* polymorphism. The 2 by 2 Contingency tables were used for assessing the OR and 95%C.I. and Multiple regression analysis was done for calculating the risk after correcting for confounding variables, assuming $P<0.05$ to be significant using SPSS 11.5 software.

Results: The GG, AG, AA and combined AA + AG genotypes of TNF-308 polymorphism were significantly associated with CAD as well as MetS. Similarly GG, GC and CC+GC genotypes of LEPR were significantly associated both with MetS and CAD. Different genotypes of *VEGFA-1154* gene showed significantly strong association with MetS (GG, AA, GG+AG) and CAD (GG, AG, AA and AA+AG). The GG/GC genotypes of IL-18 polymorphism showed as association with MetS while GC and CC did so with CAD. In case of APM +45T>G polymorphism different genotype like TG, GG and TG+GG showed association with MetS, while in CAD, TG along with TG+GG had a significant impact on CAD. The polymorphisms GG/TT and TT+GT of APM+276 G>T had significant impact on risk of MetS. Similarly, GG/GT, TT and TT+GT genotype were strongly associated with CAD subjects. There were certain protective genotypes of these genes for MetS and CAD.

Discussion and Conclusions: The present study is a preliminary evidence of association of adipocytokines as well as *VEGF -1154G>A* polymorphisms with CAD and MetS. It has been demonstrated that -308 A polymorphic variant and -308G/A heterozygous polymorphic variant of TNF-alpha seems to be a major risk factor in MetS, but may confer protection in CAD. This novel finding denotes that heterozygosity in this population may be playing a major role in the development of MetS and CAD. In *LEPR ser492thr* polymorphism, the GG genotype showed a 3.5 and 7.5 fold risk of MetS and CAD respectively. The GC and C alleles of *VEGF-1154G>A* were protective both for MetS and CAD. There was 4.9 and 10 folds risk for CAD with heterozygous GA genotype and A allele but in case of MetS the risk was 3 and 1.9 folds respectively. The *IL-18-137 G>C* polymorphism may have a significant effect on development of CAD as well as MetS. In MetS, GC genotype may be a risk factor, while in CAD, GG genotype showed a major 6.7 fold risk. In CAD, C while in MetS the G alleles may have a protective role. APM+45 T/G polymorphism may be a major predictor of CAD while the mutant T allele of APM+276G/T polymorphism showed a high risk in both MetS and CAD. While the GT genotype indicated a 2.4 fold risk in CAD, G allele indicated a protective role.

This preliminary study provides evidence that polymorphic forms of adipocytokine genes may prove to be biomarkers for the risk for MetS and CAD and hence more comprehensive studies on a larger population group are required.

Biography

R. C. Sobti is association with academia-as a teaching assistant in 1974 to the Vice Chancellorship of one of the top ten universities in India-spans close to four decades. His contribution as a ground-breaking biotechnologist, skilled orator, efficient administrator and futuristic Vice-Chancellor has won him accolades at both the national and the international levels a fact recognized by the Government of India while honoring him with the Padma Shree in 2009

Professor Sobti began his teaching career in the Department of Zoology, Panjab University in 1976 and went on to become the founder-Chairperson of the Biotechnology Department as a Professor of Cell Biology. Currently he has over 246 publications and 22 books to his credit. His research work, particularly in the areas of Cancer and Environmental Biology, has more than 1100 citations with an 18 H factor (Citation gadget) and has seen him head or be a part of the editorial boards of respected national and international journals such as Molecular Cell Biochemistry, Cytology and Genetics, Indian Journal of Human Genetics etc. He has also been awarded over 23 joint and independent projects by the UGC, CSIR, ICMR, DOE, DBT for policy-driven research in genetic markers and cancer-environment linkages.

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