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Discovering genetic determinants of vitamin D deficiency in south Asians: A genome-wide association study

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Vitamin D deficiency is implicated in multiple disease conditions and accumulating evidence supports that the variation in serum vitamin D levels, including deficiency, is under strong genetic control. However, the underlying genetic mechanism associated with circulating vitamin D levels is poorly understood. We earlier reported a very high prevalence of vitamin D deficiency associated with an increased risk for type 2 diabetes and obesity in a Punjabi Sikh diabetic cohort as part of the Asian Indian Diabetic Heart Study (AIDHS). Here we have performed the genome-wide association study (GWAS) of circulating serum vitamin D levels on 3,538 individuals. Our discovery GWAS comprised of 1,387 subjects followed by validation of 24 putative SNPs ($P < 10^{-4}$) using an independent replication sample ($n=2,151$) from the same population by direct genotyping. One novel locus at chromosome 20p11.21 with minor allele frequency (MAF) 0.29, [$\beta = -0.13$, $p=4.47 \times 10^{-9}$] between FOXA2 and SSTR4, and another suggestive locus at chromosome 1q21.3 (MAF 0.54) [$\beta = 0.90$; $p=1.36 \times 10^{-6}$] within the regulatory region of the IVL gene were identified to be associated with circulating serum vitamin D levels. Additionally, we replicated 3 of 5 known GWAS genes influencing serum vitamin D levels including GC ($p=0.007$) and CYP2R1 ($p=0.019$) reported in Europeans and the DAB1 ($p=0.003$), reported in Hispanics. Identification of novel association signals in biologically plausible regions with vitamin D metabolism will provide new molecular insights on genetic drivers of vitamin D status and its implications in health disparities.

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Practical tools for the prevention and management of diabetes in South Asians

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South Asians represent almost 25% of the global population. They are at least 3-5 times increased risk of developing diabetes as compared to Caucasians. There is also increased risk of diabetes in South Asians children and adolescents. South Asians have increased prevalence of pre-diabetes states in addition to diabetes. Despite increased prevalence of diabetes among South Asians, majority of the cases remain undiagnosed and poorly controlled. There are several barriers in the prevention and management of diabetes in South Asians which could be at patient, provider or the society level. Primary prevention needs collaboration with health care professionals, community leaders and funding agencies. Our recent Canadian study has shown that that 86% of South Asians diagnosed with diabetes less than 30 years of age were type-2 diabetes. The incidence of type 2 diabetes was highest in South Asians especially in 20-29 year olds with rates 2.2 times that of White and 3.1 times that of Chinese patients. South Asians patients should be screened for diabetes at relatively younger age (preferably starting at age 20) and more frequently than non-South Asians with appropriate prevention efforts in childhood and adolescence. South Asians should be aggressively managed for cardiovascular risk factors due to their high mortality rates from cardiovascular disease. A structured culturally and linguistically relevant program of life style modifications that includes healthy diet, weight control and regular exercise should be implemented to reduce the risk and burden of type 2 diabetes in South Asians.

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