

“A combined Test for Genetic Association that Incorporates Information about Hardy Weinberg Disequilibrium in Cases”

Sanjay Shete, PhD.

**Associate Professor of Epidemiology
The University of Texas
M.D. Anderson Cancer Center**

Abstract

To assess genetic association between single nucleotide polymorphisms (SNPs) and diseases status, typically either logistic regression model or general linear model is employed for testing associations. However, deviation from Hardy-Weinberg equilibrium could be another approach for genetic association study. The Hardy-Weinberg equilibrium (HWE) is one of important principles in population genetics. Deviation from Hardy-Weinberg equilibrium, among case (patients) group, may provide additional evidence for association between SNPs and diseases. Our purpose here is to combine evidence from Hardy-Weinberg departures in case subjects and standard regression approaches that use case and control subjects, so that a more powerful statistical test would be developed for genetic association study. In this paper, we propose two new approaches to combine such information. One approach is using the mean based tail strength measure and another is the median! Based tail strength measure to integrate logistic regression and Hardy-Weinberg equilibrium test, to study the association between a binary disease outcome and a SNP on the basis of case-control data. For both mean based and median based tail strength measures, we derived exact formulas to compute p-values. We also developed an approach to obtain empirical p-values values using a re-sampling procedure. Results from simulation studies and real diseases studies demonstrate that the new approach is more powerful than the traditional logistic regression model. And the type I error probabilities of our approach were also well controlled.