Sequencing studies for rare variants in pedigrees can be used to screen for genetic variants that cause disease. One strategy is to compare the cases from pedigrees with unrelated controls, making efficient use of prior existing resources. This approach, however, requires accounting for correlations among pedigree members. A part of the presentation will present new statistical methods that account for related subjects in case-control data. A second strategy is to evaluate whether affected pedigree members carry the same variant – an evaluation of co-segregation of variant with disease. This approach, however, requires conditional probabilities, because pedigrees without any carriers are not informative. That is, statistical assessment of co-segregation requires comparing the observed number of affected carriers with random expectation, where expectation is based on Mendelian segregation of variants, conditional on at least one affected pedigree member carrying a variant. We developed new statistical methods to test for co-segregation of genetic variants with disease, for studies that genotype only affected pedigree members. Our methods, a simple comparison of observed and expected carrier counts, as well as methods based on quasi-likelihood score (QLS) statistics, provide ways to perform gene-level tests, important for situations where different pedigrees have different segregating variants, yet all within the same gene. Our gene-level test allows use of weights for different variants, such as weights based on allele frequencies or based on likely function. Furthermore, our QLS method accounts for correlations in the data, such as correlations from related subjects, or correlation among multiple variants (e.g., linkage disequilibrium). We will present simulations to illustrate the power of our approach.