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Genetic Factors Related to the Incidence of Type II Diabetes in Adults

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ABSTRACT

As the seventh leading cause of death in the United States, diabetes affects 29.1 million people. In May 2017, the U.S. CDC reported, the estimated total financial burden for diabetes in the United States at greater than $245 billion ($95 billion attributed to disability, lost days at work and premature death). The purpose of this study was to investigate genetic variants in parallel with type II diabetes. Through a five-year prior search of Cochran, Medline and PubMed, this review of the literature examined studies regarding type II diabetes related genetic variants specific to non-ethnic and ethnic populations of otherwise healthy adults aged 18-69 year olds. Methods encompassed extracting DNA from nuclear pellets. Further genotyping was conducted using SNPs or Taqman allelic discrimination less than 5% and considered statistically significant. Literature reviews utilized centre-stratified analysis, combining evidence from each center using fixed-effect meta-analyses. The authors then assessed research subjects against controls utilizing measured genotype and additive genetic models adjusted for age and gender. Significance thresholds were then adjusted where a p-value of < 0.05 was considered statistically significant. Francescochini et al. (2013), Wu et al. (2014), Hanson et al. (2013), Kato (2013), Hanson et al. (2013), Wu et al. (2014) and Pal and McCarthy (2013) all suggest evidence of genetic loci have been identified in candidate genes and genome-wide association studies. Of the genetic variants discovered, Wu et al. (2014) and Yagootak and Frayling (2013) determined variants at TCF7L2 resemble the most robust association with type II diabetes. Wu et al. (2014) found a 50% concordance rate among monozygotic twins with type II diabetes, as well as a 40% incidence rate of developing type II diabetes among those who have first-degree relatives with the disease. However, Kato (2013) suggests previous studies only account for 5% of heritability associated with type I diabetes. Sun and Hu (2014) reported the concept of pharmacogenomics, drug molecular mechanisms related to gene variants and drug efficacy may eventually drive clinical decision making regarding type II diabetes drug selection, dose titration and adverse side effect avoidance. Based on the results of the studies in this review, accurate genetic data reveals potential to evolve clinically into a valuable instrument, thereby facilitating optimized therapeutics and deferring or ameliorating the onset of type II diabetes.

LITERATURE REVIEW

According to Francescochini et al. (2013) and Wu et al. (2014) evidence to date suggests there exists a utility regarding genetic evaluation of glycemic deterioration from hyperglycemia to type II diabetes. Francescochini et al. (2013), Wu et al. (2014) Han. et al. (2013), Kato (2013), Yagootak and Frayling (2013), Sun, Yu and Hu (2014) and Pal and McCarthy (2013) all concur that over 60 genetic loci have been identified in candidate gene and genome-wide association studies regarding type II diabetes. Francescochini et al. (2013) suggest several of the loci identified are located in or near genes affecting pancreatic beta cell development and function, related to insulin secretion.

Kato (2013) suggests KLQ4 is more commonly found in Europeans with type II diabetes, however not in East and South Asians. (See Figure 1.) Kato (2013) suggests some gene variant loci are not in fact neighboring observable candidate genes, however are often located in areas known as intergenic regions. (See Figure 2.) Wu et al. (2014) propose a 50% concordance rate among monozygotic twins with type II diabetes, as well as a 40% incidence rate of developing type II diabetes among those who have first-degree relatives with the disease.

Hanson et al. (2013) suggest there exists a strong parent of origin effect within recently identified gene single nucleotide polymorphisms which confirm susceptibility to type II diabetes among Native American peoples. Kato (2013) suggests previous studies only account for 5% of heritability associated with type I diabetes. Sun and Hu (2014) reported the concept of pharmacogenomics, drug molecular mechanisms related to gene variants and drug efficacy may eventually drive clinical decision making regarding type II diabetes drug selection, dose titration and adverse side effect avoidance. Based on the results of the studies in this review, accurate genetic data reveals potential to evolve clinically into a valuable instrument, thereby facilitating optimized therapeutics and deferring or ameliorating the onset of type II diabetes.

INTRODUCTION

The global epidemic of type II diabetes has proven to exist as one of the greatest chronic diseases of the twenty-first century. Current diagnostic tests suggest type II diabetes is a multicausal disease with robust genetically related components. According to Sanghera and Blackett (2012), genome-wide association studies have successfully identified common risk alleles correlated with associated loci that have been reported in meta-analyses of genome-wide association studies regarding type II diabetes. Of the genetic variants discovered, Wu et al. (2014) and Yagootak and Frayling (2013) determined variants at TCF7L2 resemble the most robust association with type II diabetes.

Kato (2013) suggests previous studies only account for 5% of heritability associated with type I diabetes. Sun and Hu (2014) reported the concept of pharmacogenomics, drug molecular mechanisms related to gene variants and drug efficacy may eventually drive clinical decision making regarding type II diabetes drug selection, dose titration and adverse side effect avoidance. Based on the results of the studies in this review, accurate genetic data reveals potential to evolve clinically into a valuable instrument, thereby facilitating optimized therapeutics and deferring or ameliorating the onset of type II diabetes.

LITERATURE REVIEW

What genetic factors are responsible for the increasing incidence of type II diabetes among adults?

DISCUSSION

• Wu et al. (2013) conducted research that resulted in genetic loci related to hyperglycemia progression to type II diabetes.

• Francescochini et al. (2013) conducted research that resulted in genetic loci in proximity to genes which affect pancreatic beta cell development.

• Kato (2013) conducted research resulting in the discovery of type II diabetes genes located in intergenic regions.

• Wu et al. (2014) conducted research resulting in type II diabetes concordance rates between twins.

• Hanson et al. (2013) conducted a study resulting in inherited type II diabetes genes in Native American people.

• Su, Yu and Hu (2014) conducted research resulting in the utility of a concept known as pharmacogenomics.

• Pal and McCarthy (2013) conducted research resulting in clinical application of type II diabetes genetic data.

APPLICABILITY TO CLINICAL PRACTICE

• With more than 70 genetic loci identified that correlate to type II diabetes susceptibility, further investigation and narrowing of these novel findings is advised by those within the research community.

• Although several genetic variants have been identified and further studied for prediction value of type II diabetes, these genetic variants only marginally improved prediction beyond nominative characteristics in previous studies. Specific genetic loci such as KCNQ1 and PPARG serve as therapeutic targets for specific antihyperglycemic agents such as sulfonylureas and thiazolidinediones.

• Research suggests variations of multiple gene loci are correlated with clinical outcomes of hyperglycemia, tolerance, effect avoidance. Based on the results of the studies in this review, accurate genetic data reveals potential to evolve clinically into a valuable instrument, thereby facilitating optimized therapeutics and deferring or ameliorating the onset of type II diabetes.

According to the Centers for Disease Control, diabetes is the 7th leading cause of death in the United States. Enhanced predictive, preventative and therapeutic methodologies are warranted to delay morbidity and mortality from this debilitating and deadly disease.

STATEMENT OF THE PROBLEM

According to the Centers for Disease Control, diabetes is the 7th leading cause of death in the United States. Enhanced predictive, preventative and therapeutic methodologies are warranted to delay morbidity and mortality from this debilitating and deadly disease.

REFERENCES


Frayling, T. M. (2007). Recent progress in the role of genetics to understand links between type 2 diabetes and related metabolic traits. Genome Biology, 8(2).


