Joint Associations of Genetic Risk and Diet Quality with Incident Type 2 Diabetes

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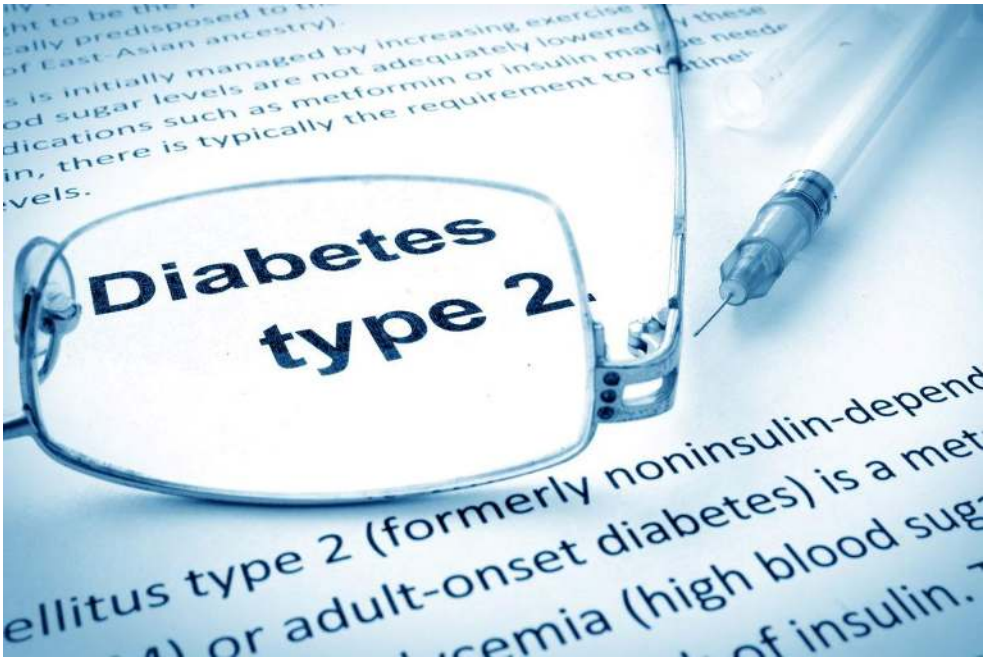
In a recent study published in *PLOS Medicine*, researchers assessed the impact of polygenic scores and diet quality on type 2 diabetes.



Study: Polygenic scores, diet quality, and type 2 diabetes risk: An observational study among 35,759 adults from 3 US cohorts. Image Credit: Vitalii Vodolazskyi/Shutterstock

Studies have observed unequal distribution in the manifestation of type 2 diabetes in adults. These differences are believed to be based on environmental factors within human populations. Extensive research is needed to ascertain the impact of diet, lifestyle, and genetic susceptibility on the risk of type 2 diabetes.

About the study

In the present study, researchers analyzed longitudinal cohorts to investigate the influence of genetic risk and diet quality on the risk of type 2 diabetes.

The team collected data from three prospective group studies conducted in the US, including the health professional's follow-up study (HPFS), the nurses' health study (NHS), and the NHS II. The baseline of the study was set to 1,986 for the NHS with 121,700 female registered nurses and HPFS with 51,529 male health professionals, and 1991 for the NHS II with 116,340 women. At the baseline, the participants answered questionnaires regarding their medical history, diet, and lifestyle.

Genetic determinations were conducted using participants who depicted a representative sample from the original participants. Demographic characteristics, participant health status, and genetic information were obtained for the participants. The team also collected information regarding genotype, imputation, and quality control of genetic data of the genomes.

The authors identified cases of type 2 diabetes via biennially mailed questionnaires, which were confirmed by a supplementary questionnaire regarding related symptoms, laboratory test results, and hypoglycemic therapy. In the case of patients diagnosed before 1998, type 2 diabetes was reported if the participants satisfied at least one of the following criteria recommended by the National Diabetes Data Group: (1) raised glycemia and at least one symptom reported that was related to diabetes including hunger, excessive thirst, polyuria, or weight loss; (2) asymptomatic manifestation with elevated glucose concentrations found on two occasions; and (3) undergoing therapy with either insulin or other hypoglycemic medications.

For cases diagnosed post-1998, the cut-off point for the levels of elevated fasting plasma glucose was lowered to 7.0 mmol/l according to the criteria by the American Diabetes Association. The team also considered hemoglobin A1C (HbA1c).

A global polygenic score was developed for type 2 diabetes to assess the overall genetic burden by conducting a genome-wide association analysis using linear mixed models. The team subsequently estimated the effect sizes by reweighing them. The performance of the polygenic score on a global scale was predicted and applied to the study population. Furthermore, polygenic scores specific to the pathways were also estimated because they captured biological processes relevant to diabetic pathophysiology. These processes included impaired insulin secretion with one polygenic score each for beta-cell dysfunction and proinsulin synthesis. Increased resistance to insulin with a polygenic score correlated to obesity-related resistance, hepatic metabolism, and body fat distribution.

The team quantified overall diet quality by calculating the alternate healthy eating index (AHEI) score estimated as per 11 foods and nutrients that emphasized a higher intake of fruits, vegetables, whole grains, legumes and nuts, polyunsaturated fatty acids, and long-chain fatty acids. Each component was scored from zero (unhealthiest) to 10 (healthiest) points.

Results

The study results showed that a total of 9,417 participants from the HPFS, 14,454 participants from the NHS, and 11,888 participants from the NHS II were a part of this analysis. The mean baseline age of the HPFS participants was 54 years, that of the NHS participants was 53 years, and that of the NHS II participants was 37 years. The mean baseline AHEI score was between 48.9 in the NHS II cohort to 52.6 in the HPFS cohort.

The hazard ratio (HR) adjusted for age in type 2 diabetes was 1.42 in the global polygenic score, while the global polygenic score had an HR of 1.29, indicating a high risk of type 2 diabetes. In the HPFS, NHS, and NHS II cohorts, the multivariable-adjusted HR were 1.23, 1.26, and 1.46 for the risk of type 2 diabetes, respectively. Consistent correlations were also observed between pathway-specific polygenic scores and increased type 2 diabetes risk and genetic risk. Furthermore, the multivariable-adjusted HR for pathway-specific polygenic scores were 1.26 for beta-cell dysfunction and 1.09 for obesity-mediated insulin resistance.

There was also a risk gradient with growing genetic risk and deteriorating diet quality. The multivariable-adjusted HR for type 2 diabetes risk for the low quality of diet was 1.31 among those reporting a lower genetic risk, 1.53 among participants with an intermediate genetic risk, and 2.12 among persons with high genetic risk. Also, the contribution to type 2 diabetes was 53.5% to genetic risk, 38.6% to quality of diet, and 7.8% to the interaction of these factors.

Conclusion

Overall, the study findings showed that diet quality and genetic risk are independently correlated to the risk of type 2 diabetes, without any additive or multiplicative effect on the risk of the disease.

Journal reference:
Merino, J. et al. (2022) "Polygenic scores, diet quality, and type 2 diabetes risk: An observational study among 35,759 adults from 3 US cohorts", PLOS Medicine, 19(4), p.
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