Obesity linked to a nearly 6-fold increased risk of developing type 2 diabetes

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Obesity is linked to a nearly 6-fold increased risk of developing type 2 diabetes (T2D), with high genetic risk and unfavorable lifestyle also increasing risk but to a much lesser extent. These are the conclusions of new research presented at this year's Annual Meeting of the European Association for the Study of Diabetes in Barcelona, Spain (16-20 Sept), by Hermina Jakupovic, University of Copenhagen, Novo Nordisk Foundation Center for Basic Metabolic Research, Copenhagen, Denmark, and colleagues.

Genetic predisposition, obesity, and unfavorable lifestyle have an important role in the development of type 2 diabetes, an increasingly common disorder that contributes majorly to the global burden of disease. According to the International Diabetes Federation, approximately 425 million adults (20-79 years) were living with diabetes in 2017; by 2045 this is expected rise above 600 million.

The current strategy to prevent T2D is underlined by the maintenance of normal body weight and the promotion of a healthy lifestyle. Lifestyle interventions designed for weight loss have been shown to delay the onset of T2D among high-risk subjects. However, the effects of lifestyle factors and obesity on T2D risk may vary between individuals depending on genetic variation. Thus, it is important to understand the interplay between genetic predisposition, obesity, and unfavorable lifestyle in the development of T2D. In this new research, the authors aimed to study whether the genetic risk for T2D is accentuated by obesity and unfavorable lifestyle.

They applied statistical modelling to a case-cohort sample of 9,556 men and women from the Danish prospective Diet, Cancer and Health cohort (49.6% women, 50.4% men, mean age 56.1 (range 50-65)). Almost half (49.5%) of the participants developed T2D during an average 14.7 years of follow-up. A favourable lifestyle was defined as having at least three of the following healthy lifestyle factors: no current smoking, moderate alcohol consumption, regular physical activity, and a healthy diet. An unfavorable lifestyle was defined as zero or only one healthy lifestyle factor while the remaining participants were defined as having an intermediate lifestyle. Genetic risk was assessed by a genetic risk score (GRS) comprising 193 genetic variants known to be strongly associated with T2D. The GRS was stratified into low (lowest 20%), intermediate (middle 60%) and high risk (top 20%) groups.

The researchers found that having an unfavorable lifestyle and obesity are associated with a greater risk of developing T2D regardless of their genetic risk. Obesity (defined as a body mass index of 30 kg/m2 or higher) increased T2D-risk by 5.8-fold compared to individuals with normal weight. The independent effects of high (vs. low) genetic risk and unfavourable (vs. favourable) lifestyle were relatively modest by comparison, with the highest genetic risk group having a 2-fold increased risk of developing T2D compared with the lowest group; and unfavourable lifestyle was associated with a 20% increased risk of developing T2D compared with favourable lifestyle.

The authors conclude: "The effect of obesity on type 2 diabetes risk is dominant over other risk factors, highlighting the importance of weight management in type 2 diabetes prevention."

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