

Assessment of Causal Relationship Between Type 2 Diabetes Mellitus and Hypothyroidism: A Bidirectional Two-sample Mendelian Randomization Study

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) and hypothyroidism are two common endocrine disorders that frequently co-occur in clinical practice. Observational studies have suggested a potential association between T2DM and hypothyroidism, but the magnitude of the causal relationship remains unclear. **Objective:** The current investigation was to assess the possible causal relationship between T2DM and hypothyroidism through the application of a bidirectional two-sample Mendelian Randomization (2SMR) analysis. **Methods:** We performed bidirectional 2SMR analysis to investigate the causal relationship between T2DM and hypothyroidism in European population by the publicly accessible genome-wide association studies (GWASs) summary datasets. The total sample size were extracted from the IEU Open GWAS Project database. Causal estimate was based on inverse-variance weighted (IVW) method, and additional sensitivity tests to evaluate the validity of the causal direction. IVW and MR-Egger were used for heterogeneity testing, and MR-Egger was also used for pleiotropy testing. Leave-one-SNP-out analysis was used to identify potential impact of single nucleotide polymorphisms (SNPs). IVW (random effects) were performed to further validate the reliability of results. **Results:** Our results showed that there have significant association between genetically predicted T2DM and hypothyroidism risk: (OR=1.060, 95% confidence interval (CI): 1.018-1.104, P=0.005); or between genetically predicted hypothyroidism and T2DM risk: OR= 1.060, 95% CI: 1.018-1.104, P=0.005). **Conclusions:** These findings suggested that T2DM and hypothyroidism have a complex bidirectional causal inference using the 2SMR analysis of GWAS datasets. The findings are only relevant for genetic predisposition; thus, further research are needed to determine the impact of non-genetic predispositions.

Keywords

Type 2 Diabetes Mellitus, Hypothyroidism, Mendelian Randomization, Causal Relationship, GWAS