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Article Review

SNP rs11196205 transcription factor 7 like 2 (TCF7L2) as a metabolic disorder genetic marker

Elsa Badriyya[1*], Siti Fatimah Putri Hasyul[2]

[1] Faculty of Pharmacy, Universitas Andalas, 25163, Padang, Sumatera Barat, Indonesia

[2] Faculty of Pharmacy, Universitas of Garut, Garut, Jawa Barat

[*]**Corresponding author(s):** badriyyaelsa25@gmail.com; +6281363017199

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Abstract

TCF7L2 is a gene that is closely related to type 2 diabetes mellitus. Examining the link between the TCF7L2 gene and type 2 diabetes mellitus, researchers often linked it to the variant, namely single nucleotide polymorphism. This review article focuses on SNP rs11196205 TCF7L2. This review article presents the impact of SNP rs11196205 TCF7L2 on T2DM in several ethnic groups.

Review articles are written using the "Preferred Reporting Items for Systematic Reviews and Meta-analyses" (PRISMA) method. Search for SNP rs11196205 TCF7L2 polymorphism on PubMed and Science direct. The keywords used are TCF7L2 combined with diabetes mellitus type 2 and SNP rs11196205. Articles selected for research will be published from 2013-2023.

The results of the literature search and article selection process found three thousand eight hundred and fifty-six articles obtained based on searches in PubMed and Science Direct. One thousand nine articles were found in PubMed and two thousand eight hundred and forty seven articles were obtained from Science Direct. The screening results obtained 1250 articles based on exclusion criteria (review articles, book chapters and encyclopedia). There were 71 articles that matched the topic of the review article, namely SNP rs11196205 TCF7L2. Finally, 8 articles were obtained which were analyzed using the 2019-2023 publication criteria.

No significant association was found in the study between amygdalar volume and the TCF7L2 SNP rs11196205 in an elderly Jewish population with psychiatric disorders and type 2 diabetes mellitus. Pregnant women with the rs11196205-GC genotype had a significantly higher risk of GDM, based on age, BMI before pregnancy, and family history of T2DM. When participants carry the rs11196205-GC genotype, the risk of GDM is 3.51 times compared to participants without the rs11196205-GC genotype. There were no significant differences for the allele and genotype frequencies of TCF7L2 rs11196205. In the TCF7L2 rs11196205 examination based on the CC genotype, the risk of GDM was 1.92 times compared to participants without the rs11196205 genotype in a population in south western Iran.

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Introduction

Type 2 Diabetes Mellitus (T2DM) is a metabolic disorder caused by many genes (polygenic) (Syamsurizal, S., Kadri, 2018). The CAPN10 gene was the first T2DM candidate gene identified through genome screening, and among all the genes identified to date, the TCF7L2 gene shows the most association with T2DM (Gravand, Foroughmand, & Boroujeni, 2018). The TCF7L2 gene variant (repetitive sequence/rs) has been identified as the strongest genetic risk factor for T2DM. The TCF7L2 gene has many repetitive sequences/rs) which can be used as marker genes, one of which is rs11196205 (Cai et al., 2019).

SNP rs11196205 in the TCF7L2 gene is located in intron 4. The TCF7L2 gene is located on chromosome 10q25.3. The TCF7L2 gene contains 215,863 bases, has 17 exons, which code for 596 amino acids (Xue, Cao, Ma, Zhou, & Wang, 2021a). The TCF7L2 gene, which influences insulin secretion and glucose production, is expressed in many tissues including fat, liver, and pancreatic islets of Langerhans. It has been shown that the TCF7L2 gene plays a central role in coordinating proinsulin expression and its subsequent processing to form mature insulin (Syamsurizal et al., 2014). The protein encoded by the TCF7L2 gene is a transcription factor, which is involved in the WNT/ β-catenin signaling pathway, which plays a role in cell proliferation and differentiation (Ganmore et al., 2019).

Common variants in the TCF7L2 gene have been identified as the strongest genetic risk factor for T2DM in various ethnic groups. There is a strong relationship between TCF7L2 and T2DM in Icelandic society. The distribution of genotypes for each SNP conformed to Hardy-Weinberg equilibrium (Syamsurizal, 2016).

This meta-analysis aims to explore the relationship between Single Nucleotide Polymorphisms (SNP) rs11196205 TCF7L2 and T2DM (Xi & Ma, 2020).

Method

Search Strategy

The review article was written using the "Preferred Reporting Items for Systematic Reviews and Meta-analyses" (PRISMA) method (Oxman et al., 1994). Search for SNP rs11196205 TCF7L2 polymorphism on PubMed and Science direct. The keywords used are TCF7L2 combined with diabetes mellitus type 2 and SNP rs11196205. Articles selected for research will be published in 2013-2023. Reference lists are created based on the suitability of the article topic and are then reviewed.

Data extraction

The review study was carried out by three independent reviewers who extracted based on: author's name, year of publication, region of study, race/ethnicity of research subjects, age of respondents, allele frequency distribution, and p-value Hardy-Weinberg Equilibrium (HWE) test. Disagreements regarding inclusion/exclusion of studies or risk estimates were resolved through focus group discussions.

Results and Discussion

Article selection

Research analysis uses the "Preferred Reporting Items for Systematic Reviews and Meta-analyses" (PRISMA) method, see table 1 and the genetics association review article SNP rs11196205 TCF7L2 (table 2). Results of literature search and article selection process Figure 1. Three thousand

eight hundred and fifty-six articles were obtained based on searches in PubMed and Science Direct. One thousand nine articles were found in PubMed and two thousand eight hundred and forty seven articles were obtained from Science Direct. The screening results obtained 1250 articles based on exclusion criteria (review articles, book chapters and encyclopedia). There were 71 articles that matched the topic of the review article, namely SNP rs11196205 TCF7L2. Finally, 8 articles were obtained which were analyzed using the 2019-2023 publication criteria. Figure 1.

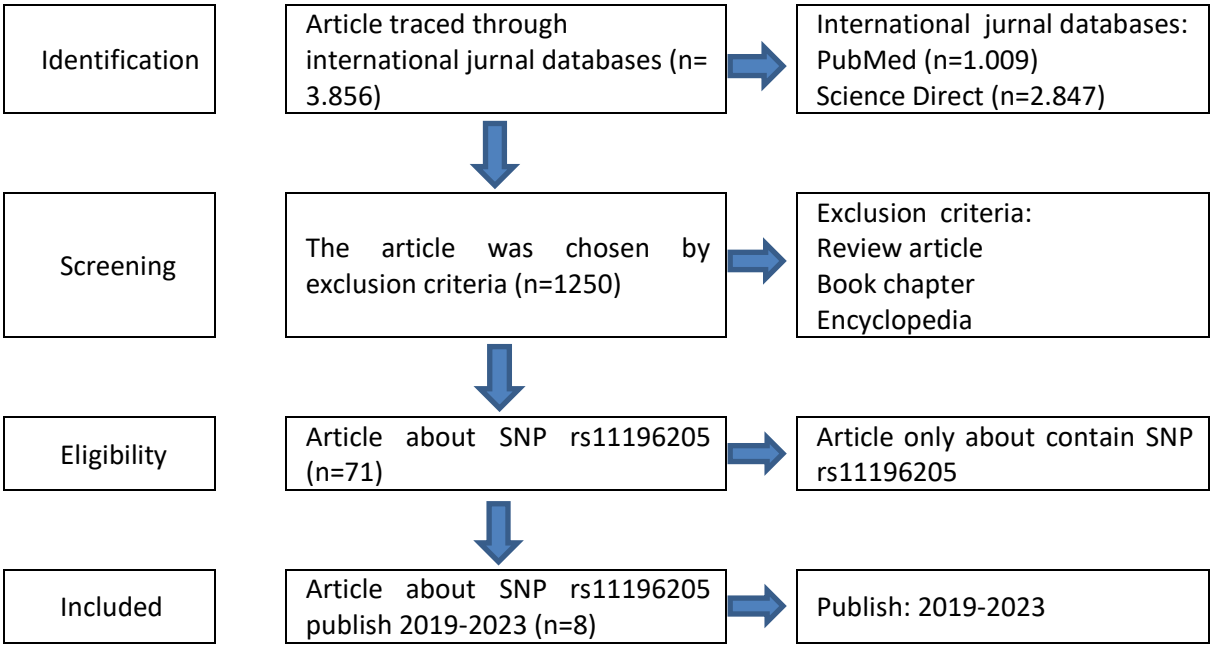

Figure 1. PRISMA flow diagram of the literature review process for study on SNP rs11196205 Transcription Factor 7 Like 2 (TCF7L2) as a metabolic disorder genetic marker

SNPs in TCF7L2 are associated with psychiatric disorders, such as schizophrenia and bipolar disorder. Greater atrophy of the amygdala and hippocampus has been associated not only with T2D, but also with high plasma glucose levels within the normal range (Ganmore et al., 2019). However, the etiology underlying brain volume differences in T2D remains unknown. We examined the association of four TCF7L2 SNPs with WMH, gray matter, and amygdala regional volumes obtained from structural brain magnetic resonance imaging in elderly Jewish T2D patients.

The amygdala is the area of the brain responsible for defining and controlling emotions. Generally, the emotional reaction to stress that occurs when a person is unable to regulate their emotions is known as an amygdala hijack. Further examination of the left and right amygdala separately, revealed that the relationship was derived primarily due to left amygdala volume versus right amygdala volume. In conditional analysis, it was found that the association of SNPs rs7901695, rs12255372 or rs7903146 with amygdalar volume was not independent of the most significant SNP rs11196205, and therefore only one association signal was detected in this region. WMH volumes with TCF7L2 SNPs were robust to Bonferroni adjustment for multiple testing correction. The researcher's sample size is considered small in the context of genetic association studies.

No significant association was found in this study between amygdalar volume and TCF7L2 SNPs rs7901695, rs7903146, and rs12255372. Although rs11196205 was not tested directly in ENIGMA GWAS. Several explanations for these differences in results are plausible besides different genetic

models, including that the observed association between TCF7L2 and amygdalar volume is specific to the Jewish population, for individuals affected by T2D (Ganmore et al., 2019).

Gestational diabetes mellitus (GDM) is one of the most common complications during pregnancy, presenting with varying degrees of abnormal glucose tolerance. GDM in Asian populations is higher than 20%. The prevalence of GDM in the Chinese population has increased in recent years. In the long term, the risk of type 2 diabetes mellitus increases (Zhang et al., 2022).

Pregnant women with the rs4506565-AT, rs7895340 GA, rs7901695-TC, and rs11196205-GC genotypes had a significantly higher risk of GDM, based on age, pre-pregnancy BMI, and family history of T2DM. Cumulative effect analysis further concluded that when participants carried these four risk genotypes, the risk of GDM was 3.51 times that of participants without any risk genotype.

Common variations in the TCF7L2 gene have been identified as a strong predictor of T2DM risk. In a North Indian population, the researchers concluded that rs7901695 heterozygosity and mutant genotypes were associated with increased risk of T2DM. In recent years, GDM has raised widespread concern among researchers about the correlation between TCF7L2 polymorphism and GDM. A total of 1,820 pregnant women were included in this study. All participants were enrolled during 24~30 weeks of gestation immediately after the 75 g oral glucose tolerance test.

FPG, OGTT-1h, and OGTT-2h levels according to different genotypes are shown in Figure 1. There were no significant differences in FPG levels between genotypes for each SNP. Pregnant women with the rs7895340 GA genotype and the rs11196205-GC genotype had significantly higher OGTT-1h levels than the wild type. At the OGTT-2h level, carriers with heterozygous genotypes were significantly higher than carriers with homozygous primary alleles in all four SNPs (S. Sun, Huang, Huang, Zhang, & Sun, 2021).

A study on the association of TCF7L2 rs11196205 (C/G) and CAPN10 rs3792267 (G/A) polymorphisms with type 2 diabetes mellitus in the South West of Iran. The PCR results of TETRA ARMS-PCR products for TCF7L2 rs11196205 and PCR amplification of the CAPN10 gene as well as the results of PCR product digestion are shown in Fig. To determine the association of TCF7L2 rs11196205 and CAPN10 rs3792267 polymorphisms with T2DM, we analyzed the allele and genotype frequency distribution between patients and healthy controls for both SNPs and our results showed that there were no statistically significant differences for the allele and genotype frequencies of TCF7L2 rs11196205 or CAPN10 rs3792267 polymorphism between subjects with T2DM and non-diabetic subjects. The allele and genotype frequencies of TCF7L2 rs11196205 are shown in Tables 2 and 3.

By general comparison between the genotype frequencies of cases and controls, significant differences were seen. So, there is no significant difference between the two groups. The allele and genotype frequencies of CAPN10 rs3792267 are shown in Tables 4 and 5. T2DM patients for GG, GA, and AA, respectively. In a general comparison between the genotype frequencies of cases and controls, the differences were not significant.

Conclusion

No significant association was found in the study between amygdalar volume and the TCF7L2 SNP rs11196205 in an elderly Jewish population with psychiatric disorders and type 2 diabetes mellitus. Pregnant women with the rs11196205-GC genotype had a significantly higher risk of GDM, based on age, BMI before pregnancy, and family history of T2DM. When participants carry the rs11196205-GC genotype, the risk of GDM is 3.51 times compared to participants without the rs11196205-GC genotype. There were no significant differences for the allele and genotype

frequencies of TCF7L2 rs11196205. In the TCF7L2 rs11196205 examination based on the CC genotype, the risk of GDM was 1.92 times compared to participants without the rs11196205 genotype in a population in south western Iran.

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