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Association of transcription factor 7-like 2 (TCF7L2) gene polymorphism with type 2 diabetes mellitus in Chinese Korean ethnicity population

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Abstract

Presently, data on the type 2 diabetes mellitus (T2DM) in Chinese Korean ethnicity are very scarce. This study aimed to explore the relationship between the transcription factor 7-like 2 (TCF7L2) and T2DM in Chinese Korean ethnicity population. This case-control study involved 43 T2DM Chinese Korean ethnicity patients (T2DM group) and 43 healthy Chinese Korean ethnicity normoglycemic subjects as controls (Control group). All included participants aged from 40 to 75 years old. Clinical and biological data were collected to determine the phenotypic traits. The restriction fragment length polymorphism-polymerase chain reaction was used to analyze the TCF7L2 by genotyping for rs7903146 (C/T). Spectrophotometer with Chronolab kits was used to conduct the biochemical analyses. TCF7L2 was associated with T2DM in the Chinese Korean ethnicity population ($P < .01$ for alleles, and $P < .05$ for genotypes). Significant differences were found 2 groups regarding the T allele (37.2% T2DM patients vs 15.1% healthy subjects, $P < .01$), and G allele (62.8% T2DM patients vs 84.9% healthy subjects, $P < .01$). The risk genotypes were GG (83.7% T2DM patients, vs 44.2% healthy control, $P < .01$), GT (4.7% T2DM patients, vs 20.9% healthy control, $P = .04$), and TT (11.6% T2DM patients, vs 34.9% healthy control, $P = .01$). The results of this study demonstrated that TCF7L2 is associated with T2DM in the Chinese Korean ethnicity population, which is an important risk factor for T2DM in this population.

Abbreviations: BMI = body mass index, DM = diabetes mellitus, HDL = high-density lipoprotein, LDL = low-density lipoprotein, OR = ratio risk, RFLP-PCR = restriction fragment length polymorphism-polymerase chain reaction, SPSS = statistical package for the social sciences, T2DM = type 2 diabetes mellitus, TCF7L2 = transcription factor 7-like 2.

Keywords: Chinese Korean ethnicity population, transcription factor 7-like 2, type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the most types of diabetes. It is a metabolic disease and is characterized by chronic hyperglycemia and disturbances in carbohydrates.[1] It has confirmed that T2DM results from the insulin secretion impaired, insulin resistance in peripheral tissues and hepatic glucose output increase.[1] Previous studies also confirmed that it can cause significant morbidity, disability, and early mortality, and is also associated with a huge economic burden for both family and the society.[2,3] It has reported that about 381.8 million adults suffered from diabetes mellitus (DM) in 2013 around the world. This number will expand by 55% in 2035, which means 591.9 million adults will be affected with DM.[2]

T2DM interacts between genetic and environmental factors. It associated with several susceptibility genes, identified by the high throughput genome-wide association studies.[4–9] One of the most important factors is the transcription factor 7-like 2 (TCF7L2), which involves in insulin secretion.[10–13] Previous studies have also confirmed that TCF7L2 association is highly reproducible in various ethnic populations with T2DM.[10–21]

The association between the TCF7L2 and T2DM has not been studied in Chinese Korean ethnicity population in China till date. The aim of this study was to investigate the association between the TCF7L2 rs11196205 (G/T) gene polymorphism and T2DM in Chinese Korean ethnicity population.

2. Methods

2.1. Ethics statement

This study was approved by the ethics committee of First Affiliated Hospital of Jiamusi University and was conducted in accordance with the Helsinki Declaration. All the participants were required to provide the written informed consent.

2.2. Study population

This case-control study included 43 T2DM Chinese Korean ethnicity patients (T2DM group) and 43 healthy Chinese Korean ethnicity normoglycemic participants as controls (Control group). All included participants aged from 40 to 75 years old. In addition, all T2DM patients were diagnosed according to

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the International Diabetes Federation criteria.[22] All participants including both T2DM patients and healthy subjects, who were tested negative for diabetes, were recruited from the First Affiliated Hospital of Jiamusi University. The data were collected from all participants from both groups. These data included sex, age, height, waist, and hip circumference to the nearest 0.5 cm, weight in light close to the nearest 0.1 kg, body mass index (BMI), waist-to-hip ratio, and blood. In addition, blood samples were also collected for testing the biochemical and molecular assays.

2.3. Biochemical assays

Fasting plasma glucose, serum cholesterol and triglycerides, high-density lipoprotein (HDL)-cholesterol, and low-density lipoprotein (LDL)-cholesterol were measured. Chronolab kits (Tiangen Biochemical Technology Co, Ltd, Beijing, China) were used to test and collect the above data by a spectrophotometer (8000 UV–Vis). Friedwald formula was used to calculate the LDL cholesterol.[23]

2.4. DNA extraction and genotyping

The Chelex method was used to extract DNA from blood samples on filter paper, and then stored at −20°C. The TCF7L2 rs11196205 (G/T) polymorphism was genotyped using the following primers: Forward 5'-GAA AGT TCT CAA CAT TTA TAA CTT CG-3', Reverse 5'-TTT GCC CAA TAA TAT GCC ATG AAA -3' (Great Wall Biotechnology Engineering Co, Ltd, Shanghai, China). The final reaction volume of 25 μL was used for polymerase chain reaction (PCR) perform. It consisted of 0.1 μL genomic DNA, 1.5 μL each primer, 2.5 μL $MgCl_2$ of PCR buffer, 2 μL deoxynucleotide triphosphate, 5 μL Hot Start Taq DNA polymerase (QIAGEN) and 16.9 μL nuclease-free water. The PCR was conducted on a BIOMETRA T3 Thermal Cycler under the following conditions: 95°C for 2 minutes, followed by 35 cycles of 95°C for 30 seconds, 58°C for 30 seconds, 72°C for 30 seconds, and a final extension of 72°C for 5 minutes. The amplicons were digested with Helicobacter pylori CH4 III (Hpy-CH4III) restriction enzyme at 65°C for 3 hours. The electrophoresis on a 2% agarose gel was used to separate the products, which were visualized under a UV transilluminator.

2.5. Sample size calculation

The sample size was calculated based on the disease variant with a ratio risk (OR) of 10 and an expected allele frequency of 0.10 in the general population by using the Power and Sample Size Calculation software.[24] The minimum size of each group was estimated at 36 participants with $\alpha = 0.5$, $\beta = 0.8$. Assuming a 20% drop-out rate, therefore, the required sample size of this study was estimated to be 86 participants, with 43 assigned to each group.

2.6. Statistical analysis

The data of allele and genotype frequencies were analyzed and performed by using Statistical Package for the Social Sciences (SPSS) software (v.17.0, SPSS, Chicago, IL). The Mann–Whitney *U* test was used to analyze the quantitative data. The Chi-square test or Fisher exact test was used to analyze the qualitative variables. The statistical significance level was set at $P < .05$.

3. Results

The characteristics are summarized in Table 1. No significant differences of age, sex, BMI, systolic blood pressure, diastolic blood pressure, and triglycerides were detected between 2 groups. However, there were significant differences of waist-to-hip ratio ($P < .01$), fasting plasma glucose ($P < .01$), total cholesterol ($P < .01$), HDL cholesterol ($P < .01$), and LDL cholesterol ($P < .01$) between 2 groups.

Table 1

Characteristics of the study population between 2 groups.

Characteristics	T2DM group (n = 43)	Control group (n = 43)	*P* value
Mean age, yr	56.9 (10.7)	58.2 (11.1)	.58
Sex			
Male	20 (46.5)	18 (41.9)	.66
Female	23 (53.5)	25 (58.1)	.66
BMI, kg/m^2	27.9 (3.5)	28.1 (3.7)	.80
WHR	0.9 (0.1)	1.0 (0.1)	<.001
SBP, mm Hg	129.4 (15.1)	132.8 (16.3)	.32
DBP, mm Hg	79.2 (6.8)	80.1 (7.3)	.55
FPG, g/L	1.6 (0.4)	1.0 (0.1)	<.01
TC, mg/dL	154.4 (14.2)	198.6 18.5)	<.01
HDL-C, mg/dL	45.8 (5.5)	50.2 (5.6)	<.01
LDL-C, mg/dL	83.3 (8.7)	114.0 (18.9)	<.01
TG, mg/dL	138.7 (16.6)	144.3 (17.4)	.13

Data are present as mean ± standard deviation or number (%).
BMI = body mass index, DBP = diastolic blood pressure, FPG = fasting plasma glucose, HDL = high density lipoprotein cholesterol, LDL = low density lipoprotein cholesterol, SBP = systolic blood pressure, TC = total cholesterol, TG = triglycerides, WHR = waist-to-hip ratio.

All findings were showed in Table 2. The results of this study demonstrated that TCF7L2 rs7903146 (C/T) was associated with T2DM ($P < .01$ for alleles, and $P < .05$ for genotypes). The minor allele was T and the major allele was G. The T allele was determined to be the risk allele (37.2% T2DM patients vs 15.1% healthy subjects, $P < .01$), while the G allele was determined to be the protective allele (62.8% T2DM patients vs 84.9% healthy subjects, $P < .01$) (Table 2). The frequencies of the genotypes were as follows with GG genotype (83.7% T2DM group, vs 44.2% control group, $P < .01$), GT genotype (4.7% T2DM group, vs 20.9% control group, $P = .04$), and TT genotype (11.6% T2DM group, vs 34.9% control group, $P = .01$) (Table 2).

4. Discussion

It is reported that a variety of population who suffered from the T2DM.[24] However, the epidemiological data of T2DM are limited, especially on its genetic determinants. This study aimed to explore the association between the TCF7L2

Table 2

Association between the TCF7L2 and T2DM.

TCF7L2 rs11196205 (G/T)	T2DM group (n = 43)	Control group (n = 43)	OR (95% CI)	*P* value
Alleles				
G	54 (62.8)	73 (84.9)	0.30 (0.14, 0.63)	<.01
T	32 (37.2)	13 (15.1)	3.33 (1.60, 6.94)	<.01
Total (2N)	86 (100.0)	86 (100.0)	–	–
Genotypes				
GG	36 (83.7)	19 (44.2)	6.50 (2.37, 17.82)	<.01
GT	2 (4.7)	9 (20.9)	0.18 (0.04, 0.91)	.04
TT	5 (11.6)	15 (34.9)	0.25 (0.08, 0.76)	.01
Total (N)	43 (100.0)	43 (100.0)	–	–

Data are present as number (%).
OR = odd ratio, T2DM = type 2 diabetes mellitus, TCF7L2 = transcription factor 7-like 2.

rs11196205 (G/T) polymorphism and T2DM in Chinese Korean ethnicity population in China. It has been found that the frequency of the minor T allele was 30%, which was comparable to the 30.15% in the Czech population,[25] 34.45% in the Iranian population[26] and 36.15% in the Arab population.[27] The variation of the T allele frequency among the different population could account for the genetic diversity among those different ethnic groups,[14,15,17,18,20] with a significant association of OR 3.92 (95% CI 2.04–7.67, $P < .01$). The result of the present study is consistent with the previous studies in diverse ethnic populations[14,15] with a strong association between TCF7L2 and the risk of T2DM.

The results of this study showed an association between the rs11196205 (G/T) polymorphism of the TCF7L2 gene and T2DM in Chinese Korean ethnicity population in China. Presently, although the pathophysiology of T2DM remains unclear, such substantial evidence still suggests that the TCF7L2 gene can help to predict the development of TD2M in several ethnic populations. Thus, it is also can be considered as a very important tool to identify the Chinese Korean ethnicity population at risk. In addition, the confirmed association between TCF7L2 and T2DM in an independent population can also provide evidence for the further study of TCF7L2 and its related molecules and pathways as potential therapeutic targets for T2DM.

Although the association between the TCF7L2 and T2DM in Chinese Korean ethnicity population was confirmed, this study still suffered from several limitations. First, the sample size was pretty small, which may lead to the deviation from Hardy–Weinberg equilibrium in this study. Thus, a larger sample size studies are needed to verify this results in the future. Second, healthy participants in the control groups should also be carefully selected in order to avoid confounding by population stratification. Third, lacking of randomization, allocation, and blinding may result in high risk of selection.

5. Conclusion

The rs11196205 (G/T) polymorphism of the TCF7L2 gene is associated with T2DM in Chinese Korean ethnicity population. Thus, it can help clinical genetic test to predict the occurrence of T2DM in Chinese Korean ethnicity population.

Author contributions

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