**ROLE OF TRANSCRIPTION FACTOR 7 LIKE RS7903146 AND RS12255372 GENE POLYMORPHISMS AND SELECTIVE BIOCHEMICAL TESTS IN TYPE II IRAQI DIABETIC PATIENTS**

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**Abstract**

Recent studies have related to see whether the TCF7L2 gene polymorphisms rs7903146 (C/T) and rs12255372 (G/T) are linked to the risk of developing T2DM in the Iraqi population. In this study, biochemical and genetic parameters. Real-time PCR was used to genotype the samples. In both patients and controls, the frequency of genotypes, alleles, anthropometric measurements, glycemia, and glycated hemoglobin (HbA1c) was measured. As result, The TCF7L2 SNPs rs7903146 and rs12255372 had genotyping success rates of 98.55 and 97.42 percent, respectively. For both SNPs, the allele and genotype frequencies were in Hardy-Weinberg equilibrium. Between patients and controls, the genotype and allele frequencies for (TCF7L2 SNP rs7903146) allele were not substantially different. The frequency of the (rs7903146 T) allele in the controls was 29 percent, whereas it was 28 percent in the patients (P = 0.61). The TCF7L2 SNP rs12255372 genotypic and allelic frequencies did not vary substantially between patients and controls. In controls, (rs12255372 T) allele frequency was 21%, but in patients, it was 27% (P = 0.42).

**Keywords:** Type 2 diabetes, Genetic association, Transcription factor 7-like 2 (TCF7L2), Polymorphism

1. **Introduction**

Hyperglycemia is the primary symptom of type 2 diabetes, which is a metabolic illness with several contributing factors. Inadequate insulin production or resistance to insulin that has been secreted both play critical roles in the pathogenesis of type two diabetes (1,2). In addition to this, it may lead to a number of consequences, the most common of which are cardiovascular and endothelial illnesses (3,4). An examination of the whole genome indicated that numerous genes have a role in the etiology of type two diabetes (5). In particular, the transcription factor (7-like 2), or TCF7L2, gene is recognized as the best potential gene involved in everything from the impairment of insulin synthesis to the development of type 2 diabetes (5). The transcription factor 7 like 2 (TCF7L2) gene is an essential component of the Wnt signaling pathway. It is an entero-endocrine transcription factor that is located on chromosome 10q (6). Following this, stimulation of Wnt catenin promotes the assembly of -catenin with BCL9, which is then followed by translocation, into the nucleus and the formation of an active form with (TCF7L2) (7).

1. **Materials and Methods** 
   1. **Materials**: Primers (rs7903146, rs 12255372), 100 bp DNA ladder, 50 bp DNA lader, Restriction enzymes (Rsal enzyme, 2U Tsp509I enzyme).
   2. **Methods:** Genomic DNA extraction

Genomic DNA Profiling

RFLP-PCR Technique

PCR master mix preparation

PCR Program

1. **Result and discussion**

**3.1 The Genotype and allele frequencies of the (TCF7L2 SNPs rs7903146) gene polymorphism**

There was no discernible difference between the patients and the controls with regard to the genotype or allele frequencies for (TCF7L2 SNP rs7903146 allele). In the healthy control, the frequency of the (rs7903146) T allele was 28 percent, whereas in the sick population, it was only 29 percent. The rs7903146 C allele frequency for the controls was 72 %, whereas it was 71% in the patients (P = 0.61). The frequencies of the T/T, C/C, and C/T genotypes were 54, 36, and 10 percent, respectively, for the controls, while the rates were 49, 44, and 7 percent, straight, for the patients (P = 0.30). (Table 4.2).

Table 4.2 Genotype and allele frequencies of the (TCF7L2 SNPs rs7903146) gene polymorphism in with diabetic patients and healthy control group

|  |  |  |  |
| --- | --- | --- | --- |
| **TCF7L2 SNPs rs7903146** | **PATIENTS (N=100)** | **HEALTHY (N=100)** | **P.VALUE** |
| Genotypes | - | - | - |
| CC | 49(49%) | 54(54%) | 0.32 |
| CT | 44(44%) | 36(36%) |
| TT | 7(7%) | 10(10%) |
| Alleles | - | - | - |
| C | 142(71%) | 144(72 | 0.61 |
| T | 58(29%) | 56(28%) |
| P = ˂0.05, N= Number of persons | | | |

**3.2 The Genotype and allele frequencies of the(TCF7L2 SNPs Rs 12255372 polymorphism**

In terms of genotypic and allelic frequencies for the TCF7L2 SNP rs12255372, there was no significant difference between patients and controls. The frequency of the rs12255372 T allele was 21 percent in the control group, but it was 27 percent in the sick group (P = 0.42). The frequency of the rs12255372 G allele was 79 percent in the normal group, and it was 73 percent in the patient group (P = 0.51). The T/T, G/G, and G/T genotype frequencies were, respectively, 63, 32, and 5% for the controls. However, they were, respectively, 52, 42, and 6% for the patients (P = 0.31); this indicates that the T/T, G/T, and G/G genotype frequencies were significantly lower in the patients. (Table 4.3).

Table 4.3 Genotype and allele frequencies of the(TCF7L2 SNPs Rs 12255372 polymorphism in with diabetic patients and healthy control group

|  |  |  |  |
| --- | --- | --- | --- |
| **TCF7L2 SNPs Rs 12255372 gene** | **PATIENTS (N=100)** | **HEALTHY (N=100)** | **P.VALUE** |
| Genotypes | - | - | - |
| GG | 52 (52%) | 63 (63%) | 0.31 |
| GT | 42 (42%) | 32 (32%) | 0.31 |
| TT | 6 (6%) | 5 (5%) | 0.31 |
| +Alleles | - | - | - |
| G | 146 (73%) | 158 (79%) | 0.51 |
| T | 54 (27%) | 42 (21%) | 0.42 |
| P = ˂0.05, N= Number of persons | | | |

1. **Conclusion**

This is the first study to investigate at the TCF7L2 SNPs rs7903146 and rs12255372 in Type 2 Diabetes patients from a racially mixed community in Iraq. The results that are given here are just incomplete. Despite the fact that allele frequencies and the genotype in the patient groups as well as the control group, were equal (P > 0.05) for each variants, the patient group had a significantly higher frequency of both variations, Given the limited number of people that participated in the study, we cannot say for certain that the results we obtained are accurate, because we cannot rule out the possibility that our findings are skewed due to the small sample size. Alternately, such results might be ascribed to unique ethnic effects due to the fact that the majority of the previously reported connections were established in research with populations that were mostly European.

1. **References**

**1.** Lin, Y. and Sun, Z. 2010. Current views on type 2 diabetes. The Journal of endocrinology., 204(1): 1.

**2.** Kyrou, I. and Kumar, S. 2010. Weight management in overweight and obese patients with type 2 diabetes mellitus. The British Journal of Diabetes and Vascular Disease., 10(6): 274-283.

**3.** Ali, R., Mzayek, F., Rastam, S., Fouad, F. M., O’Flaherty, M., Capewell, S. and Maziak, W. 2013. Forecasting future prevalence of type 2 diabetes mellitus in Syria. BMC Public Health., 13(1): 1-7.

**4.** DeSouza, C. and Fonseca, V. 2009. Therapeutic targets to reduce cardiovascular disease in type 2 diabetes. Nature Reviews Drug Discovery., 8(5): 361-367.

**5.** Elbein, S. C. 2009. Genetics factors contributing to type 2 diabetes across ethnicities. Journal of diabetes science and technology., 3(4): 685-689.

**6.** Castrop, J., van Norren, K. and Clevers, H. 1992. A gene family of HMG-box transcription factors with homology to TCF-1. Nucleic acids research., 20(3): 611.

**7.** Yi, F., Brubaker, P. L. and Jin, T. 2005. TCF-4 mediates cell type-specific regulation of proglucagon gene expression by β-catenin and glycogen synthase kinase-3β. Journal of Biological Chemistry., 280(2): 1457-1464.