# Impact of tumor necrosis factor-α and interleukin 6 polymorphisms on type 2 diabetes mellitus Sudanese patients

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## ABSTRACT

Extensive studies in humans over the last decades have shown the significant functions of cytokines in diabetes development. The present study aimed to assess the impact of tumor necrosis factor (TNF)-α and interleukin (IL) 6 polymorphisms on type 2 diabetes mellitus (T2DM). The study involved 450 participants; 200 individuals were included in the control group, and 250 individuals represented T2DM patients. The polymerase chain reaction-restriction fragment length polymorphism technique was used to identify the genotypes and alleles of the TNF-α 308G/A variants rs1800629 and IL-6 (-174 C→G) variants rs1800629, while amplification refractory mutation system polymerase chain reaction is used to identify genetic variations of IL-6 (-174 C→G). The result revealed a statistically significant (p=0.0028) difference in the frequency of the AA genotype of the TNF-α rs1800629 variant between the study group and the control group. Interestingly, the findings also showed a significant difference (p=0.0001) in the frequency of the CC genotype of the IL-6-rs1800795 variant between the study and control groups. The TNF-α gene (308G/A) and the IL-6 (-174 C→G) polymorphism were found to be strongly related to an elevated risk of T2DM in the Sudanese population.

## Introduction

Type 2 diabetes mellitus (T2DM) is a complex set of metabolic illnesses characterized by chronic hyperglycemia.[1,2] The International Diabetes Federation estimates that 536.6 million adults worldwide currently suffer from diabetes mellitus in 2024, and this is expected to rise to 783.2 million by 2045.[2,3] T2DM is defined by decreased insulin production from pancreatic β-cells and insulin resistance.[1-4] Diabetes mellitus is a chronic condition that significantly lowers the quality of life. It is regarded as one of the most significant and prevalent conditions seen in medical clinics, and because of the numerous complications and comorbidities associated with this pathology, it currently poses a serious risk to the entire world.

Over time, it may cause damage to the kidneys, heart, blood vessels, eyes, nerves, and heart.[5,6]

The pathogenicity of insulin resistance and T2DM has been related to the immune system. The pathogenicity of insulin resistance and T2DM has been related to immune system activation and subclinical chronic inflammation; several authors suggested that inflammatory cytokines like interleukin (IL) 6 and tumor necrosis factor (TNF) may be important mediators in the pathophysiology of T2DM, linking the disease to several other frequently occurring disorders believed to have inflammatory causes.[3,6-11] Several studies have demonstrated that TNF-α plays a crucial role in the development of insulin resistance and T2DM by inhibiting intracellular signaling from the insulin receptor.[12-15] Trapali *et al.* stated that TNF-α is essential in the development of insulin resistance and T2DM.[11] Furthermore, several polymorphisms in the IL-6 gene have been associated with an increased risk of T2DM, according to Jamil *et al*.[16] Numerous other studies have shown that IL-6 is probably required to maintain glucose homeostasis.[16-19]

Nonetheless, Sudan was included as one of the nations with a diabetes prevalence of more than 12% in the 2019 International Diabetes Federation's diabetes atlas.[11] This is in line with a previous study conducted in Sudan that found that the prevalence rates of uncontrolled T2DM and T2DM were comparatively higher at 80.0% and 20.8%, respectively.[5]

Most of the published data about diabetes mellitus in Sudan were epidemiological studies, few studies determined the genetic aspect. The present work aimed to determine the association between TNF-α and IL-6 polymorphisms with T2DM among Sudanese patients.

## Materials and Methods

### Study population and sampling

The current work is a case-control study, carried out at Fedail Specialist Hospital in Khartoum, Sudan, over 3 years (2019-2022). The purpose of the research was explained to the study population, and the blood samples were collected from those who agreed and signed the consent form. The ethical clearance (AAU-MLT-DCC-25489) was obtained from the ethical committee of Medical Laboratory Sciences, Alzaiem Alazhari University, Sudan.

The study population involved 450 individuals with fasting glucose levels <100 mg/dL without the use of glucose-lowering drugs; 200 of them did not have a history of diabetes nor a diagnosis as diabetic patients, and they were represented as a control group. The remaining 250 participants were T2DM patients, and they were represented in the study group. Both groups were matched, and they were free of bacterial or viral infections, cancer, cardiovascular disease, arthritis, renal, hepatic, or endocrine disorders, and other conditions at the time of the sample.

### Assay of biochemical markers

The following biochemical markers were measured using the Cobas C311 clinical chemistry auto-analyzer (Roche Diagnostics, Mannheim, Germany): cholesterol, glycated hemoglobin (HbA1c), fasting plasma glucose, triglycerides, total low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol.

### Genotyping analysis of tumor necrosis factor-α

The genomic DNA was isolated from the peripheral blood leukocytes for each participant using the Promega-USA DNA Purification Kit (Madison, USA). The polymerase chain reaction (PCR)-restriction fragment length polymorphism test was used to identify the genotypes and alleles of the TNF-α 308G/A variants rs1800629 and IL-6 (-174 C→G) variants rs1800629.[20] The genomic region containing the TNF-α 308G>A variant was amplified using a specific set of primers (forward primer: AGGCAATAGGTTTTGAGGGCCAT, reverse primer: TCCTCCCTGCTCCGATTCCG). The PCR program was done according to the following conditions: denaturation for 10 minutes at 94°C, followed by 35 cycles, each consisting of 30 seconds of denaturation at 94°C, 30 seconds of annealing at 62°C, 35 seconds of extension at 72°C, and 10 minutes of final extension at 72°C. The products of the PCR for rs1800629 G>A (107 bp) were digested by Nico1 into 87 bp and 20 bp. The reaction mixture included 10 µL (0.2 µg) of PCR products, 1 µL of restriction enzymes with 17 µL of nuclease-free water, and 2.0 µL of 10XNE buffer. This cocktail was incubated at 37°C for 5 hours. The digested PCR products were loaded into a 3.0% agarose gel electrophoresis and visualized using an ultraviolet transilluminator.

### Detection of interleukin 6 (-174 C→G) gene polymorphisms

The amplification-refractory mutation system (ARMS) PCR is applied in this study to identify genetic variations of IL-6 (-174 C→G). The Primer 3 software was used to create ARMS primers (Fo-outer primer: CGATGGAGTCAGAGGAAACTCA, Ro-outer primer: GGAGATAGAGCTTCTCTTTCGTTCCCG, F I-G-inner primer: TTTTCCC CCTAGTTGTGTCTTGCC, and R I-C-inner primer: GACCAA TGTGACGTCCTTTAGCATC). The reaction was carried out using 20 µL of a reaction mixture (Microgen Inc, Sejong, Korea) that contained 10 µL of Master, 2.0 µL of DNA, and 2.0 µL of each primer comprising 25 pmol. The thermocycling process involved denaturation at 94°C for 10 minutes, followed by 35 cycles of denaturation at 94°C, 35 s of annealing at 63°C, and a final extension at 72°C for 5 minutes. An ultraviolet transilluminator was used to observe the PCR results after they had been analyzed using 2.0% agarose gel electrophoresis.

### Statistical analysis

The analyses have been managed using SPSS version 22 (IBM, Chicago, IL, USA), a statistical software for the social sciences. The continuous variables are categorized using the mean ± standard deviation. An independent *t*-test was used in the study to compare continuous variables and evaluate group differences. A chi-square test was used to categorize variables that were grouped by frequency and percentage. The genes that were linked to one another were identified using odds ratios and 95% confidence intervals. Chi-square testing was utilized to look at the genotype frequency values' Hardy-Weinberg equilibrium. For statistical significance, a two-tailed $p<0.05$ threshold was established.

## Results

Biochemical analyses presented in Table 1 indicated elevated levels of HbA1c and fasting blood glucose (FBG) in the study group compared to the control group, with values of 9.6±2.3% *vs.* 5.6±0.40% and 200±71 mg/dL *vs.* 88.1±11 mg/dL, respectively, highlighting typical clinical features of T2DM in the study group. The study group's fasting plasma glucose, LDL, HDL, total cholesterol, triglycerides, and HbA1c values were found to be significantly correlated with the control group.

FBG, HbA1c, and genotype distribution in control individuals and T2DM patients were shown to be extremely significantly correlated with single-nucleotide polymorphism (SNP) rs1800629 GG/AA, with the exception of FBG and HbA1c (Table 2). FBG and HbA1c levels were greater in T2DM patients with GG genotypes than in those with GA and AA genotypes (p=0.002, 003).

SNP rs180795 showed similar significant results. In both the control group and T2DM patients, a GG/CC connection was seen between genotype distribution, FBG, and HbA1c, except for FBG and HbA1c (Table 3). FBG and HbA1c levels were greater in T2DM patients with GG genotypes than in those with GC and CC genotypes (p=0.040, 003) (Table 4).

According to Table 4, there was a statistically significant (p=0.0028) difference in the frequency of the AA genotype (rs1800629 variation) between the study group and the control group. Similar results were obtained for the frequency of the A allele, which was detected in 20.7% of the study group and 32.2% of the control group. There was a significant variation in frequency (p=0.0003). Additionally, Table 4 shows that the association was found to be valid under the additive (p=0.0028), recessive (p=0.0099), and dominant (p=0.0003) genetic models.

Table 5 shows that there was a significant difference (p=0.0001) in the frequency of the CC genotype (rs1800795 variation) between the study group and the control group. The rates were 5% and 18%, respectively. The frequency of the C allele, which was found to be 21% in the control group and 34.4% in the study group, and the prevalence of the G allele, which was found in 79% of the control group and 65.4% of the study group, also showed notable variations and were both statistically significant (p=0.0001). Furthermore, it was observed that the link held under the additive (p=0.0001), recessive (p=0.0001), and dominant (p=0.0036) genetic models (Table 5).

**Table 1.** Comparative results of biochemical markers in obese type 2 diabetes mellitus patients and healthy subjects.

| Variables | Patient (n=250) | Control (n=250) | p |
|---|---|---|---|
| Gender (male/female) | 130/120 | 132/118 | 0.7900 |
| Age (years) | 58±15 | 56±14 | 0.7600 |
| BMI (kg/m$^2$) | 28.5±1.2 | 23.2±1.1 | 0.0001 |
| Fasting plasma glucose (mg/dL) | 200±71 | 88±11 | <0.0010 |
| Total Cholesterol (mg/dL) | 207±45 | 170±24 | <0.0010 |
| Triglyceride (mg/dL) | 155±36 | 124±31 | <0.0010 |
| LDL-C (mg/dL) | 111±31 | 77.8±26 | 0.0035 |
| HDL-C (mg/dL) | 39±8.10 | 46±17 | 0.0030 |
| Heamoglobin A1c (%) | 9.6±2.30 | 5.6±0.40 | <0.0010 |

Comparisons were performed by independent samples t-test; data are mean±standard deviation; p<0.05 is statistically significant; n, number of individuals; BMI, body mass index; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

**Table 2.** Statistical analysis of clinical parameters in association with genotype distribution of rs1800629 GG/AA in 450 subjects (250 type 2 diabetes mellitus cases and 200 control subjects).

| Parameters | Subjects | GG | GA | AA | p |
|---|---|---|---|---|---|
| BMI (kg/m$^2$) | T2DM | 26.7±0.9 | 27.4±0.83 | 27.7±0.74 | 0.785 |
| | Controls | 24.6±1.80 | 24.7±0.80 | 25.4±0.80 | 0.150 |
| FBG (mg/dL) | T2DM | 144±33.50 | 202±61.5 | 273±49.0 | 0.002 |
| | Controls | 88.0±10.45 | 89.0±9.40 | 88.0±9.52 | 0.790 |
| HbA1c (%) | T2DM | 8.50±1.30 | 10.3±0.24 | 11.2±0.30 | 0.003 |
| | Controls | 5.67±0.53 | 5.73±0.44 | 5.76±0.56 | 0.854 |
| TG (mg/dL) | T2DM | 154±40.0 | 161±35.0 | 148±38.0 | 0.952 |
| | Controls | 126±31.5 | 124±26.0 | 131±35.40 | 0.536 |
| HDL-C (mg/dL) | T2DM | 41.4±8.65 | 42.2±9.40 | 31.0±7.10 | 0.743 |
| | Controls | 48.75±6.8 | 45±7.84 | 44.7±6.0 | 0.524 |
| LDL-C (mg/dL) | T2DM | 109±32.5 | 112±33.6 | 108±31.2 | 0.965 |
| | Controls | 80±26.0 | 78±24.7 | 82±26.8 | 0.832 |
| Total chl (mg/dL) | T2DM | 197±40.7 | 213±46.0 | 203±46.2 | 0.843 |
| | Controls | 171±27.4 | 176±23.2 | 183±23.3 | 0.700 |

Data is shown as mean±standard deviation; p<0.05 is statistically significant; BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; TG, triglyceride; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; chl, cholesterol; T2DM, type 2 diabetes mellitus.

**Table 3.** Statistical analysis of clinical parameters in association with genotype distribution of rs1800795 GG/CC in 450 subjects (250 type 2 diabetes mellitus cases and 200 control subjects).

| Parameters | Subjects | GG | GC | CC | p |
|---|---|---|---|---|---|
| BMI (kg/m$^2$) | T2DM | 26.75±0.93 | 26.41±0.92 | 27.88±0.85 | 0.963 |
| | Controls | 24.50±1.65 | 24.60±0.87 | 24.70±1.20 | 0.404 |
| FBG (mg/dL) | T2DM | 156.7±36.8 | 262.0±61.5 | 270.6±51.4 | 0.040 |
| | Controls | 88.5±9.75 | 89.0±9.50 | 89.5±9.8 | 0.950 |
| HbA1c (%) | T2DM | 8.70±1.68 | 11.40±2.5 | 11.62±2.84 | 0.002 |
| | Controls | 5.80±0.50 | 5.78±0.45 | 5.67±0.44 | 0.740 |
| TG (mg/dL) | T2DM | 157±30.34 | 156±31.00 | 148±45.58 | 0.779 |
| | Controls | 125±30.00 | 124±31.85 | 126±36.71 | 0.664 |
| HDL-C (mg/dL) | T2DM | 41.90±8.74 | 35.97±7.60 | 41.10±9.23 | 0.524 |
| | Controls | 45.64±6.75 | 45.34±7.85 | 45.81±5.92 | 0.830 |
| LDL-C (mg/dL) | T2DM | 109.5±33.3 | 113.3±31.5 | 108±32.1 | 0.623 |
| | Controls | 79.0±26.54 | 80.0±27.53 | 79.2±18.10 | 0.150 |
| Total Chl (mg/dL) | T2DM | 203±40.54 | 213±49.02 | 188±43.44 | 0.488 |
| | Controls | 173±26.90 | 178±23.82 | 183±16.42 | 0.295 |

Data is shown as mean±standard deviation; p<0.05 is statistically significant; BMI, body mass index; FBG, fasting blood glucose; HbA1c, glycated hemoglobin; TG, triglyceride; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; chl, cholesterol; T2DM, type 2 diabetes mellitus.

**Table 4.** Genotypes distribution, allele frequency, and genetic models of the tumor necrosis factor G308A gene rs1800629 variant among the study population.

| Variant rs1800629 | | | Controls group (n=200) | | Patients group (n=250) | | OR (95% CI) | p |
|---|---|---|---|---|---|---|---|---|
| | | | Frequency | % | Frequency | % | | |
| Genotypes[a] | | GG | 120 | 60 | 107 | 42.8 | | |
| | | GA | 77 | 38.5 | 125 | 50 | 1.82(1.23-2.67) | 0.0023 |
| | | AA | 3 | 1.5 | 18 | 7.2 | 6.72(1.92-23.48) | 0.0028 |
| Alleles[b] | | G | 317 | 79.3 | 349 | 67.8 | 1.76(1.29-2.39) | 0.0003 |
| | | A | 83 | 20.7 | 161 | 32.2 | | |
| Genetic model[c] | Additive | GG | 120 | 60 | 107 | 42.8 | 6.72(1.92-23.48) | 0.0028 |
| | | AA | 3 | 1.5 | 18 | 7.2 | | |
| | Recessive | AA | 3 | 1.5 | 18 | 7.2 | 0.20(0.10-0.67) | 0.0099 |
| | | GG+GA | 197 | 98.5 | 232 | 92.8 | | |
| | Dominant | GG | 120 | 60 | 107 | 42.8 | 2.00(1.37-2.92) | 0.0003 |
| | | GG | 120 | 60 | 107 | 42.8 | | |

Comparisons were performed by the chi-square test (X2); CI, confidence interval; OR, odds ratio; data is represented as number and %; [a]Genotypes GA *vs.* AA, GG *vs.* AA; [b]G alleles *vs.* A alleles; [c]additive model (AA *vs.* GG), recessive model (AA *vs.* GG+GA), and dominant model (GG *vs.* +GA+ AA).

**Table 5.** Genotype distribution, allele frequency and genetic models of the interleukin 6 gene rs1800795 variant among the study population

| Variant (rs1800795) | | | Controls group (n=200) | | Patients group (n=250) | | OR (95% CI) | p |
|---|---|---|---|---|---|---|---|---|
| | | | Frequency | % | Frequency | % | | |
| Genotypes[a] | | GG | 126 | 63 | 123 | 49.2 | | |
| | | CG | 64 | 32 | 82 | 32.8 | 1.30 (0.80-2.00) | 0.1943 |
| | | CC | 10 | 5 | 45 | 18 | 4.6 (2.20-9.60) | 0.0001 |
| Alleles[b] | | G | 316 | 79 | 328 | 65.6 | 2.00(1.50-2.70) | 0.0001 |
| | | C | 84 | 21 | 172 | 34.4 | | |
| Genetic model[c] | Additive | GG | 126 | 63 | 123 | 49.2 | 4.60 (2.20-9.60) | 0.0001 |
| | | CC | 10 | 5 | 45 | 18 | | |
| | Recessive | CC | 10 | 5 | 45 | 18 | 0.30 (0.12-0.49) | 0.0001 |
| | | GG+GC | 190 | 95 | 205 | 82 | | |
| | Dominant | GG | 126 | 63 | 123 | 49.2 | 1.75 (1.20-2.60) | 0.0036 |
| | | GC+CC | 74 | 27 | 127 | 50.8 | | |

Comparisons were performed by the chi-square test (X2); CI, confidence interval; OR, odds ratio; the data is represented as number and %; [a]Genotypes GC *vs.* CC, GG *vs.* CC; [b]G alleles *vs.* C alleles; [c]additive model (CC *vs.* GG), recessive model (CC *vs.* GG+GC), and dominant model (GG *vs.* +GC+ CC).

## Discussion

Diabetes mellitus is a metabolic disease that is characterized by elevated plasma glucose levels, which over time, leads to cell damage in the eyes, nerves, heart, blood vessels, and renal. Statistical data show that the amount of frequency of diabetes mellitus cases has been gradually growing over time. However, T2DM is supposed to be a polygenic disease that occurs due to complex interactions between numerous environmental factors and genes.[20-23]

The present study aimed to determine the impact of TNF-α and IL-6 polymorphisms on T2DM Sudanese patients. According to the best of our knowledge, this is the first molecular-based study carried out in Sudan that discussed the relationship between TNF-α and IL-6 polymorphisms in T2DM.

Our results showed significant increases (p=0.0001) in body mass index (BMI) among the study group (T2DM), with a mean of 28.5±1.2 *vs*. 23.2±1.1. This finding suggested that BMI is a risk factor for T2DM among the Sudanese population. Similar findings were pointed out by several authors.[10,13] Moreover, the study group showed high levels of HbA1C and FBG compared to the control group (9.6±2.3 *vs*. 5.6±0.40 and 200±71.0 *vs*. 88±11); these findings indicate uncontrolled T2DM. Also, the study group showed abnormal lipid profiles, which included excessive triglycerides, cholesterol, and LDL with low HDL, which may reflect the impact of diabetes mellitus. Moreover, the current study showed a strong correlation between the study group and BMI, HbA1c, triglycerides, total cholesterol, LDL, and HDL, since these are the common clinical signs of diabetes mellitus, the findings were consistent with many previous publications.[7,10,24]

Our results revealed noteworthy correlations between the study group (T2DM) and both rs1800795 and rs1800629 variations; the A and C alleles were more prevalent among the study group. Numerous studies have indicated that polymorphisms in TNF-α (rs1800629) and IL-6 (rs180795) enhance the risk of developing T2DM, which is consistent with our findings.[3,6,8,13-15]

Similarly, Martinez *et al*. examined the association between the polymorphisms for TNF-α (rs180629), IL-6 (rs1800795), and T2DM; they reported a substantial rise in the chance of developing T2DM.[10] Other authors, such as Rodrigues *et al*., disagreed with our findings, claiming that TNF-α (rs1800629) and T2DM are unrelated.[7] Jamil *et al.* stated the same report concerning the relation between T2DM and polymorphisms in rs1800629.[16] This inconsistency in the results may be owing to the different study populations.[15,16]

Liju *et al*.,[24] Abdellatif *et al*.,[25] Khdair *et al*.,[26], Huang *et al*.,[27] and Shi *et al.*[28] reported that the precise genetic risk factors linked to T2DM may vary depending on the ethnicity and genetic composition of the population in question. While Obirikorang *et al.* highlight that various groups and ethnicities generated diverse results.[29] Our findings demonstrated that T2DM patients (study group) had a significantly higher prevalence of the A/A genotype of the TNF-G308A gene, particularly rs1800629, compared to the control group (7.2% *vs*. 1.5%, p<0.0028). Martinez *et al*. reported that T2DM patients had significantly higher frequencies of the A/A genotype (p=0.004) than the control groups, which is consistent with our finding.[10]

According to our findings, T2DM patients had significantly higher frequencies (p=0.0001) of the homozygous C alleles of the IL-6 (rs1800795) mutation than healthy controls. These results agreed with those of Obirikorang *et al*., who found that the C allele was significantly more common in T2DM patients than in control groups (p=0.0010).[29] Our findings demonstrated that, across all genetic models, both the RS1800629 and RS1800795 polymorphisms were significantly associated with T2DM in Sudanese. These results are consistent with recent research that was carried out in different demographic areas.[3,21,22,28,30]

## Conclusions

The TNF-α gene (308G/A) and the IL-6 (-174 C→G) polymorphism were found to be strongly related to an elevated risk of T2DM in the Sudanese population.

## References


1. Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest-growing global public health concern: early detection should be focused. Health Sci Rep 2024;7: e2004.
2. Darogha SN. Serum levels of TNF-a and IFN-g gene polymorphism in type 2 diabetes mellitus in Kurdish patients. Cell Mol Biol 2021;67:171-7.
3. Mohamed AH, El-Sayed ZH, Megahed A, et al. Association of IL-10 and IL-6 gene polymorphisms with type 2 diabetes mellitus among Egyptian patients. Eur J Gen Med 2013;10:158-62.
4. Stavros S, Mavrogianni D, Papamentzelopoulou M, et al. Association of tumor necrosis factor-α -308G>A, -238G>A, and -376G>A polymorphism with recurrent pregnancy loss risk in the Greek population. Fertil Res Pract 2021;7:9.
5. Omar SM, Musa IR, Idrees MB, et al. Prevalence and associated factors of erectile dysfunction in men with type 2 diabetes mellitus in eastern Sudan. BMC Endocr Disord 2022;22:141.
6. Cheng Z, Zhang C, Mi Y. IL-6 gene rs1800795 polymorphism and diabetes mellitus: a comprehensive analysis involving 42,150 participants from a meta-analysis. Diabetol Metab Syndr 2022;14:95.
7. Rodrigues KF, Pietrani NT, Bosco AA, et al. IL-6, TNF-α, and IL-10 levels/polymorphisms and their association with type 2 diabetes mellitus and obesity in Brazilian individuals. Arch Endocrinol Metab 2017;61:438-46.
8. Ayelign B, Negash M, Andualem H, et al. Association of IL-10 (-1082 A/G) and IL-6 (-174 G/C) gene polymorphism with type 2 diabetes mellitus in the Ethiopian population. BMC Endocr Disord 2021;21:70.
9. Pickup JC, Mattock MB, Chusney GD, Burt D. NIDDM as a disease of the innate immune system: association of acute-phase reactants and interleukin-6 with metabolic syndrome -X. Diabetologia 1997;40:1286-92.
10. Martínez-Ramírez OC, Salazar-Piña DA, de Lorena RM, et al. Association of NFκβ, TNFα, IL-6, IL-1β, and LPL polymorphisms with type 2 diabetes mellitus and biochemical parameters in a Mexican population. Biochem Genet 2021;59:940-65.
11. Trapali M, Houhoula D, Batrinou A, et al. Association of

TNF-α 308G/A and LEPR Gln223Arg polymorphisms with the risk of type 2 diabetes mellitus. Genes 2021;13:59.
12. Tayel MY, Nazir A, Abdelhamid IM, et al. TNF-α-308 G> A and IL10-1082A> G polymorphisms as potential risk factors for lymphoproliferative disorders in autoimmune rheumatic diseases. Egypt J Med Hum Genet 2020;21:2.
13. Ayelign B, Genetu M, Wondmagegn T, et al. TNF-α (-308) gene polymorphism and type 2 diabetes mellitus in Ethiopian diabetes patients. Diabetes Metab Syndr Obes 2019;12:2453-9.
14. Luna GI, Silva ICR da, Sanchez MN. Association between -308G/A TNFA polymorphism and susceptibility to type 2 diabetes mellitus: a systematic review. J Diabetes Res 2016;2016:6309484..
15. Feng RN, Zhao C, Sun CH, Li Y. Meta-analysis of TNF 308 G/A polymorphism and type 2 diabetes mellitus. PLoS One 2011;6:e18480.
16. Jamil K, Jayaraman A, Ahmad J, et al. TNF-alpha -308G/A and -238G/A polymorphisms and its protein network associated with type 2 diabetes mellitus. Saudi J Biol Sci 2017;24:1195-203.
17. Vijay J, Gauthier MF, Biswell RL, et al. Single-cell analysis of human adipose tissue identifies depot and disease-specific cell types. Nat Metab 2020;2:97-109.
18. Qi L, van Dam RM, Meigs JB, et al. Genetic variation in the IL6 gene and type 2 diabetes: tagging-SNP haplotype analysis in a large-scale case-control study and meta-analysis. Hum Mol Genet 2006;15:1914-20.
19. Pradhan AD, Manson JE, Rifai N, et al. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA 2001;286:327-34.
20. Elssaig EH, Ahmed-Abakur EH, Alnour TMS, et al. Significant association between genetic polymorphism of insulin-like growth factor-2 mRNA binding protein-2 and type 2 diabetes mellitus: a population-based case-control study. J Clin Lab Anal 2025:e25147.
21. Elssaig EH, Ahmed-Abakur EH, Alnour TMS, et al. Significant association between insulin-like growth factor 2 mRNA-binding protein 2, interleukin-6 polymorphisms, and type 2 diabetes mellitus. J Res Med Sci 2024;29:71.
22. Karadeniz M, Erdogan M, Berdeli A, Yilmaz C. Association of interleukin-6-174 G>C promoter polymorphism with increased risk of type 2 diabetes mellitus patients with diabetic nephropathy in Turkey. Genet Test Mol Biomarkers 2014;18:62-5.
23. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2021. Diabetes Care 2021;44:S15-33. Erratum in: Diabetes Care 2021;44:2182.
24. Liju S, Chidambaram M, Mohan V, Radha V. Impact of type 2 diabetes variants identified through genome-wide association studies in early-onset type 2 diabetes from the South Indian population. Genomics Inform 2020;18:e27.
25. Abdellatif HM, Binshabaib MS, Shawky HA, ALHarthi SS. Association between periodontitis and genetic polymorphisms in interleukins among patients with diabetes mellitus. Dent J 2021;9:45.
26. Khdair SI, Al-Naimat OS, Jarrar W, et al. The Influence of TNF-α, IL-6, TGF-β1, IFN-γ, IL-10 polymorphisms on predisposition to diabetes mellitus among Jordanian patients. Endocr Metab Immune Disord Drug Targets 2023;23:681-91.
27. Huang Q, Wang Y, Gu B, Xu Y. Whether the risk of gestational diabetes mellitus is affected by TNF-α, IL-6, IL-10 or ADIPOQ polymorphisms: a meta-analysis. Diabetol Metab Syndr. 2020;12:81.
28. Shi LX, Zhang L, Zhang DL, et al. Association between TNF-α G-308A (rs1800629) polymorphism and susceptibility to chronic periodontitis and type 2 diabetes mellitus: a meta-analysis. J Periodontal Res 2021;56:226-35.
29. Obirikorang C, Lokpo SY, Owiredu WKBA, et al. Association between interleukin-6 gene polymorphism (rs1800795 and rs1800796) and type 2 diabetes mellitus in a Ghanaian population: a case-control study in the Ho Municipality. Biomed Res Int 2024;2024:3610879.
30. Wei Q, Chen X, Chen H. Association of single nucleotide polymorphisms of the IL-6, IL-10, and TNF-α genes with susceptibility to gestational diabetes mellitus. Genet Test Mol Biomarkers 2020;24:390-8.