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# Correlation of ACE (I/D) gene polymorphisms with type 2 diabetes mellitus and post-recovery from Covid-19 in Iraqi patients: A case-control investigation

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## *Abstract*

**Objective**

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder. This disorder causes elevated blood sugar levels due to either insulin resistance, decreased pancreatic beta cell function, or both. SARS-CoV-2 is also a pathogenic respiratory virus that causes COVID-19. The aim of this study was to study the correlation between the levels of FBS, HbA1c, WBC, lymphocyte percentage, T3, T4, TSH, CRP, D-dimer, LDH, and ferritin parameters and ACE gene polymorphism (I/D) in patients with type 2 diabetes (G2) and recovered COVID-19 (G3) compared to the control group (G1).

**Materials and methods**

This study included 60 patients with type 2 diabetes (G2), 60 recovered patients from COVID-19 (G3), and 60 ethnically matched controls (G1). All subjects were between 30 and 45 years of age. All subjects were referred to Diwaniyah Teaching Hospital in Diwaniyah Province, Iraq. Biochemical parameters FBS, HbA1c, WBC, lymphocyte percentage, T3, T4, TSH, CRP, D-dimer, LDH, and ferritin were calculated. PCR was also used to amplify and examine the ACE(I/D) gene polymorphism.

**Results**

The study found a significant relation among the parameters (FBS, HbA1c, WBC, Lymphocyte%, T3, T4, TSH, CRP, D-dimer, LDH, and ferritin) and ACE gene polymorphisms. The results showed that there was a significant difference ($P < 0.05$) between genotypes II and ID compared to genotype DD in patients at high risk of developing type 2 diabetes in COVID-19 recoveries. Genotypes II and ID had a higher incidence of type 2 diabetes in Iraqi individuals who recovered from COVID-19.

**Conclusion**

The findings of this study showed that the ACE gene polymorphism (I/D) was significantly associated with changes in biochemical parameters in patients with type 2 diabetes and recovered patients from COVID-19. The risk of developing or worsening type 2 diabetes, especially in recovered patients from COVID-19, was higher for genotypes II and ID than for genotype DD. These results indicate that the genetic composition of the renin-angiotensin system may play a role in metabolic susceptibility after SARS-CoV-2 infection. Therefore, it may be used as a potential indicator in screening, prevention, and better management of patients at risk. However, larger studies in larger populations are needed to confirm these findings.

**Keywords**: ACE, Covid-19, type 2 diabetes mellitus disease, T2DM

**Paper Type:** Research Paper.

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## Introduction

One of the chronic metabolic disorders is type 2 diabetes mellitus (T2DM). One of its symptoms is blood sugar. One of its causes is insulin resistance. In this case, the target cells respond less to insulin. Another cause is the gradual decline in the function of pancreatic beta cells. This leads to insufficient insulin production. Sometimes a combination of the two above is the cause (Ahmad et al., 2022). Macrovascular complications such as atherosclerosis are one of

the consequences of this disorder and can lead to stroke and myocardial infarction. The next consequence is microvascular complications such as retinopathy, nephropathy, and neuropathy. There are several laboratory methods to diagnose it (Sandoval & Patti, 2023). For example, in the oral glucose tolerance test (OGTT), blood sugar is measured two hours after consumption and must be 200 mg/dL (11.1 mmol/L) or more. Or glycosylated hemoglobin (HbA1c) should be equal to or greater than 6.5%. Another method is to measure fasting blood sugar on two separate occasions, which should be equal to or greater than 126 mg/dL (7.0 mmol/L). In addition, if there are classic symptoms of high blood sugar, it is better to measure blood sugar randomLy to confirm the diagnosis. In this case, it should be 200 mg/dL (11.1 mmol/L) or more (Bellary et al., 2021). There are also many ways to treat it. The use of metformin is the first option. Because it both reduces hepatic glucose production and increases insulin sensitivity. In more advanced cases, sulfonylureas (to increase insulin secretion), thiazolidinediones (to increase insulin sensitivity), GLP-1 receptor agonists (to enhance glucose-dependent secretion and slow gastric emptying), SGLT2 inhibitors (to increase renal glucose excretion) are used. The last option is insulin therapy to supplement or replace endogenous insulin production (Galicia-Garcia et al., 2020). On the other hand, COVID-19 is a highly contagious respiratory infection. Its causative agent is the SARS-CoV-2 virus. This virus mainly targets the angiotensin-converting enzyme 2 (ACE2) receptors, allowing the virus to enter cells, especially respiratory epithelial cells, and replicate. Complications include coagulation disorders, myocarditis, acute respiratory distress syndrome (ARDS), and neurological problems such as encephalitis and Guillain-Barré syndrome (Shi et al., 2020). One way to identify it is through genetic identification, which is performed by performing an RT-PCR test on nasopharyngeal or pharyngeal swab. Serological tests such as ELISA are also used to detect IgM and IgG antibodies to confirm previous infection or immune response (Yuki et al., 2020). Evaluation of supportive options such as oxygen therapy and mechanical ventilation is also recommended in severe cases. Antiviral drugs such as remdesivir are also used. These drugs inhibit the viral RNA-dependent RNA polymerase. Immunomodulatory drugs such as dexamethasone reduce the hyperactive inflammatory response. Meanwhile, monoclonal antibodies targeting the viral spike protein are used to prevent disease progression (Yang et al., 2020). A crucial component of the RAS is a peptide that is encoded by the ACE gene. It is the system in charge of inflammation, fluid balance, and blood pressure. Compared to the ACE I allele, the ACE D allele is linked to increased ACE activity (Khurana & Goswami, 2022). Findings from genetic association studies indicate that the DD genotype-related higher ACE activity may increase the risk of T2DM possibly by influencing insulin sensitivity and pancreatic beta-cell function. Furthermore, since local RAS affects renal function, the DD genotype is linked to the development of diabetic nephropathy and retinopathy, retinal fibrosis and inflammation (Hussain et al., 2020). ACE I/D polymorphisms are relevant to COVID-19, as the virus needs to enter the cell using ACE receptor. Angiotensin-converting enzyme (ACE) inhibitors, which block the function of ACE, are commonly given to patients with hypertension and heart disease, both

of which are risk factors for severe COVID-19 (Sriram et al., 2020). The I/D polymorphism of the ACE gene might disrupt the balance of the RAS system, possibly changing ACE activity or expression levels; this could in turn affect the rate of viral entry and symptomatology. ACE may be affected by the varying expression / shedding in subjects with DD genotype (with increased ACE activity) (Pigeyre et al., 2020). That has the potential to impact the amount of virus in the body and how an individual responds to virus caused by SARS-CoV-2. Some studies imply that the DD genotype may be related to a more severe course of COVID-19 either as a consequence of an intensifying inflammatory response or changed vascular permeability mediated by the RAS (Shirbhate et al., 2021). Moreover, genetic variety is crucial for promoting the development of more sophisticated genes, safeguarding existing populations, advancing evolutionary processes, and enabling adaptation to changing conditions in the natural environment (Mohammadabadi et al., 2021a). Conversely, the identification of gene polymorphisms is crucial in the process of detecting and treatment of diseases (Mohammadabadi, 2016; Saadatabadi et al., 2023). Moreover, the study of populations and breeds, using molecular techniques is very important and useful for their characterizing (Mohammadifar and Mohammadabadi, 2017; Noori et al., 2017). Conservation of genetic diversity requires the proper performance of conservation superiorities and sustainable handling plans that should be based on universal information on population structures, including genetic diversity resources among and between populations and breeds (Mohammadifar & Mohammadabadi, 2018; Mohammadabadi et al., 2024a). Genetic diversity is an essential element for genetic improvement, preserving populations, evolution and adapting to variable environmental situations (Sulimova et al., 2007; Mohammadabadi et al., 2024b). On the other hands, determination of gene polymorphism is important in characterizing of various populations (Mohammadabadi et al., 2010; Mohammadabadi et al., 2024c) in order to define genotypes of individuals and their associations with immune system, resistance or susceptibility to diseases (Mohammadabadi et al., 2021b). The accurate description of ACE (I/D) allele frequencies throughout the Iraqi population and their potential correlation with susceptibility to T2DM and the severity or recovery outcomes of COVID-19 still lacks important information. The association between the incidence of type 2 diabetes and the ACE gene polymorphism (I/D) has been reported by various studies. However, the results of these reports have been contradictory. For example, some studies have even shown that the D allele can be a potential risk factor. The effect of ACE gene polymorphisms on the course of the disease has also been investigated in studies related to COVID-19. However, these findings cannot be generalized to the whole world. Because there is a lot of genetic and ethnic diversity in the world. Therefore, the aim of this study was to investigate the ACE gene polymorphisms (I/D) in patients with type 2 diabetes and COVID-19 in the Iraqi population.

**Materials and methods**

In the present study, 180 individuals were tested. Their ages ranged from 30 to 45 years. The number of men and women in each group was equal, and there were 60 individuals in each group. The first group or G1 were all healthy (control group), the second group or G2 were type 2 diabetics, and the third group or G3 were COVID-19 patients who had recovered. All individuals did not have any other diseases and did not smoke. This was done to increase accuracy, specificity, and eliminate the effect of comorbidities on biomarkers and ACE gene polymorphisms. This can make the research results more reliable and accurate. 5 mL of venous blood was collected from each individual. All steps from sampling to performing all related clinical tests were carried out at Al-Diwaniyah Teaching Hospital in Al-Diwaniyah Governorate, Iraq, between 18/5/2024 and 27/6/2025. 2 mL of blood were placed in Na-EDTA tubes to be used for DNA extraction, and the remaining 3 mL were placed in a gel tube for the purpose of good separation of the blood by centrifuge. The serum was then spun in a centrifuge at room temperature for about ten minutes to separate it (4000 x g). The complete blood and serum were kept at -20 °C until they were needed for other tests. The laboratory study was conducted in two parts. The first part included the estimation of biomarkers (FBS, HbA1c, WBC, Lymphocyte%, T3, T4, TSH, CRP, D-dimer, LDH, and ferritin). Ferritin concentration was estimated using Fluorecare Instrument (Microprofit, china). WBC and Lymphocyte% were estimated using Hemolyzer® 3 NG instrument (STERILAB, UK). FBS was estimated using Spectrophotometer instrument (ERBA, Germany). Quo-Test® instrument (EKF Diagnosis, USA) was used to estimate HbA1c. CRP was estimated using the turbidity method by means of the Cobas e 411 device (HITACHI, Germany). T3, T4, TSH, and D-dimer were measured using the Elisa assay by means of Vidas method and the BIOBASE device (BIOBASE, China). LDH was estimated using the Architect plus C400 device (Abbott, America). Part two of the study involved a PCR test to measure the amplification of the ACE (I/D) gene for DNA samples. Genomic DNA was extracted from whole blood using a AddPrep DNA Extraction Kit (Bioneer/Korea). Then, DNA concentration was measured using a Nanodrop instrument (absorbance at 260-280 nm) and DNA purity was estimated using a Quantus Fluorometer. Evaluation of the DNA samples was performed using Quantus techniques. Concentration ranged from 10 to 65 ng/μL and purity ranged from 1.7–1.9. Process approach was used to analyze DNA Integrity Number (DIN) before and after processing. An Agilent 2100 Bioanalyzer was used to separate DNA fragments via capillary electrophoresis. The signal intensity axis of an electropherogram shows DNA fragment peaks. The prominence and ratio of important DNA peaks are used by a unique DIN algorithm to identify and evaluate this electropherogram. Then reducing degradation by augmenting the ratio of these peaks to the DNA area. Microscale degradation products are recorded as “abnormalities” in the electropherogram. The algorithm then assigns a DIN score to the computer by evaluating the rapid and post-trace features on a scale from 1 (very degraded) to 10 (healthy and intact). Based on the DNA Integrity Number (DIN) of 8.2 to 8.5, the samples were high-quality and suitable for genetic investigation. PCR Amplification for extracted DNA was performed using specific forward 5'-

CTGGAGACCACTCCCATCCTTTCT-'3 and reverse 5'-GATGTGGCC ATCACATTCGTCAGA -'3 primers for ACE (I/D) gene (Joung et al., 2006). PCR products were electrophoresed on 1% agarose gel. 3µL of loading dye (New Biolabs, England) was combined with 7µL of DNA for genomic DNA analysis electrophoresis. After the samples were properly placed into each gel well, the electrical power was switched on at 50 V for one to two hours. After migrating from the cathode (-) to the anode (+) pole, the DNA band is stained using the gel's green safe dye. In order to record the observed bands, the gel's safe stained bands were photographed using a gel documentation system and viewed using a UV transilluminator set to 365 nm. The heterogeneous fragments included homozygous II genotypes (490 bp), homozygous DD genotypes (190 bp), and heterozygous I/D genotypes (490 & 190 bp).

**Ethics approval:** This research has been approved by the Ethical Approval Committee of College of Education (Reference No., 318, 7/4/2024) at the University of Al-Qadisiyah, Iraq.

**Statistical analysis:** Descriptive statistics and One-Way ANOVA (P-value < 0.05) were employed using SPSS version 27 (SPSS Inc., Chicago, IL, USA) to validate the statistical analysis of genotype distributions and allele frequencies of the ACE (I/D). Gene polymorphisms across the study groups (G1, G2, and G3), were estimated by calculating the odds ratio (OR), with 95% confidence interval (CI), and $\chi 2$ values. The present study's results are shown as percentages or as mean ± standard deviation (SD). A P-value of less than 0.05 indicates that the 95% CI is statistically significant (Pakkir Shah et al., 2025). GraphPad Prism version 9 (San Diego, CA, USA) was used for statistical analyses to compare groups for biochemical and immunochemical tests. A significant difference was defined as a p value of less than 0.05 using One-Way ANOVA (Analysis of Variance). The data was presented as mean ± standard deviation (SD), with a significance criterion of $P < 0.05$. With the Student's t-test, the mean ± standard deviation may be examined. A p-value of less than 0.05 is considered statistically significant (Le Berre et al., 2022).

## Results

**Clinical characteristics and biomedical indicators in the studied groups G1, G2, and G3:** The results of parametric tests for the control group (G1), patients with type 2 diabetes (G2), and patients recovered from COVID-19 (G3) are given in Table 1. Data differences were considered statistically significant when P values were less than 0.05. In this study, age matching was used to minimize the differences caused by large age differences.

**Examination of the association between ACE (I/D) gene polymorphisms and the risk of T2DM (G2) and Covid-19 (G3) in comparison to the control group (G1):** Table 2 shows the ACE gene polymorphisms (I/D) in the control group (G1), patients with type 2 diabetes (G2), and patients recovered from COVID-19 (G3). A comparison of the ACE gene gel electrophoresis results for groups G1 and G2 is presented in Figure 1, while this comparison is reported for groups G2 and G3 in Figure 2. The gene and genotypic frequencies of the ACE gene for the three studied groups are reported in Figures 3 and 4, respectively.

**Table 1. Biomedical indicators in the studied groups G1, G2, and G3**

| Parameters | Groups | | | T-test | P-value |
|---|---|---|---|---|---|
| | G1-control Mean ± SD | G2-T2DM Mean ± SD | G3- Covid-19 patients recovered Mean ± SD | | |
| **FBS (mg/dl)** | 95.86 ± 10.64 | 316.42 ± 22.19 | 177.9 ± 42.68 | 37.53 | 0.001 |
| **HbA1c (mmol/mol)** | 5.46 ± 0.69 | 11.17 ± 2.56 | 7.38 ± 1.8 | 10.31 | 0.02 |
| **WBC (µL)** | 6.30 ± 1.48 | 8.59 ± 1.46 | 8.16 ± 2.71 | 8.046 | 0.018 |
| **Lymphocyte%** | 7.75 ± 1.97 | 4.58 ± 0.43 | 17.44 ± 3.64 | 13.81 | 0.031 |
| **T3 (nmol/L)** | 1.29 ± 0.4 | 0.93 ± 0.18 | 0.83 ± 0.16 | 0.620 | 0.043 |
| **T4 (nmol/L)** | 7.91 ± 0.97 | 11.95 ± 2.45 | 8.63 ± 13.6 | 9.653 | 0.026 |
| **TSH (µIU/L)** | 2.98 ± 0.94 | 4.28 ± 1.29 | 0.98 ± 0.17 | 2.844 | 0.01 |
| **CRP (mg/L)** | 2.39 ± 0.74 | 38.95 ± 9.48 | 81.39 ± 8.14 | 24.56 | 0.003 |
| **D-dimer (ng/mL)** | 277.84 ± 38.2 | 617.14 ± 39.85 | 397.1 ± 42.36 | 38.94 | 0.0001 |
| **LDH (U/L)** | 192.8 ± 33.5 | 326.8 ± 51.68 | 594.6 ± 62.8 | 31.72 | 0.001 |
| **Ferritin (ng/mL)** | 87.58 ± 11.49 | 267.9 ± 47.1 | 419.29 ± 63.4 | 35.78 | 0.0001 |

**Fasting blood sugar = FBS, glycosylated hemoglobin = HbA1c, white blood cells = WBC, triiodothyronine = T3, thyroxine = T4, thyroid stimulating hormone = TSH, C-reactive protein = CRP, and lactate dehydrogenase = LDH. Data are presented as mean ± standard deviation (SD). Based on the t-test, P values less than 0.05 were considered significant.**

**Table 2. The ACE (I/D) polymorphism genotypes and allele distribution in G1 (Control), G2 (T2DM), and G3 (Covid-19 patients recovered) were examined**

| Polymorphisms ACE (I/D) | G1 (Control) N=60 (%) | G2 (T2DM) N=60 (%) | G3 (Covid-19 patients recovered) N=60 (%) | $X.^2$ | OR (95%CI) | P-value |
|---|---|---|---|---|---|---|
| **II genotype** | 10 (16.7%) | 8 (13.3%) | 4 (6.7%) | 10.635 | $1.0^{ref}$ ($1.0^{ref}$) 0.319 (0.098-0.965) 0.576 (0.187-1.789) | 0.024* |
| **ID genotype** | 15 (25%) | 34 (56.7%) | 32 (53.3%) | | | |
| **DD genotype** | 35 (58.3%) | 18 (30%) | 24 (40%) | | | |
| **I allele** | 35 (58.3%) | 42 (70%) | 40 (66.7%) | 5.264 | $1.0^{ref}$ ($1.0^{ref}$) 0.894 (0.584-1.367) | 0.182 |
| **D allele** | 25 (41.7%) | 18 (30%) | 20 (33.3%) | | | |
| **II genotype** | 10 | 8 | 4 | 3.568 | $1.0^{ref}$ ($1.0^{ref}$) 0.436 (0.148-1.2831) | 0.379 |
| **ID&DD genotypes** | 50 | 52 | 56 | | | |
| **DD genotype** | 35 | 18 | 24 | 6.385 | $1.0^{ref}$ ($1.0^{ref}$) 1.563 (0.895-2.7371) | 0.041* |
| **ID&II genotypes** | 25 | 42 | 36 | | | |

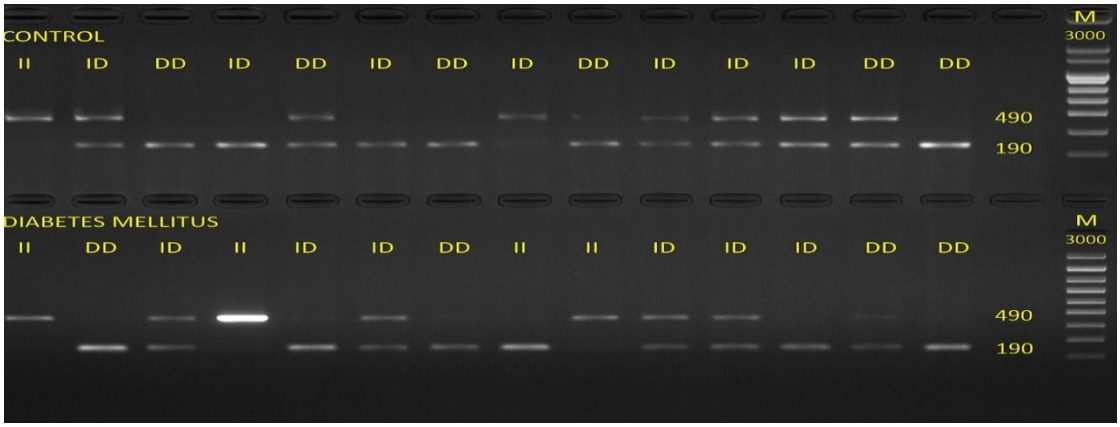


**Figure 1. Comparison of amplified fragments for the ACE gene on gel electrophoresis for groups G1 and G2**

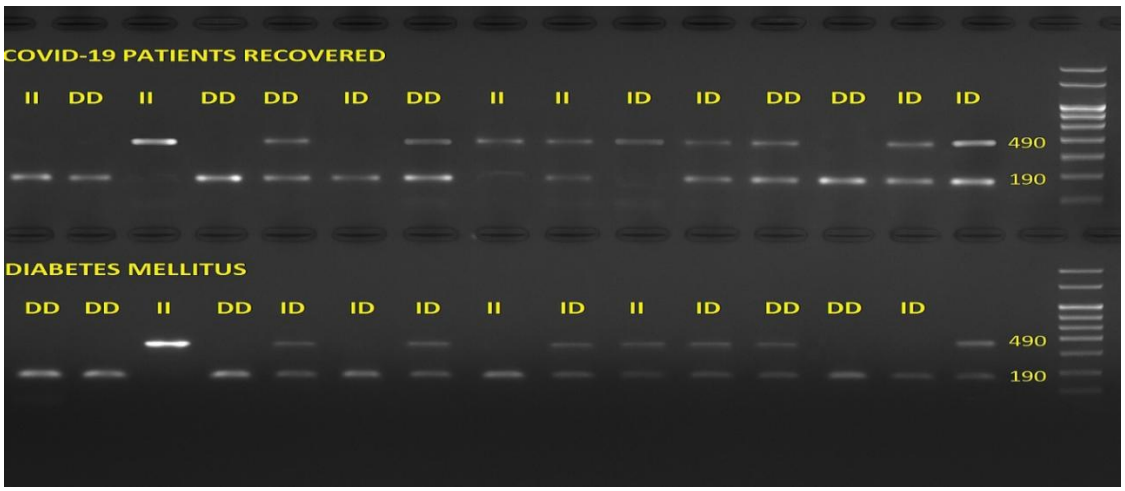


**Figure 2. Comparison of amplified fragments for the ACE gene on gel electrophoresis for groups G2 and G3**

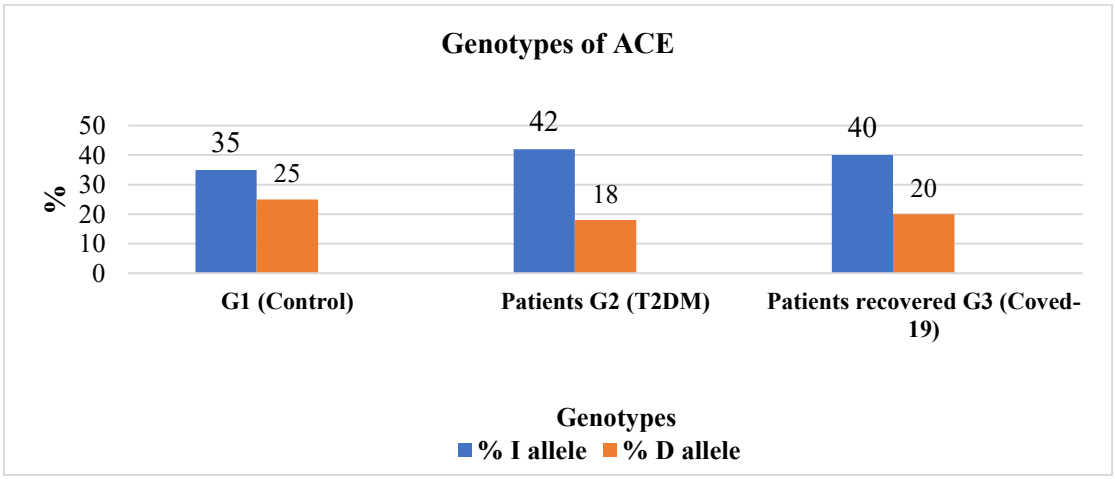


**Figure 3. Percentage of I and D alleles of the ACE gene in control, patients with type 2 diabetes, and patients who recovered from COVID-19 groups**

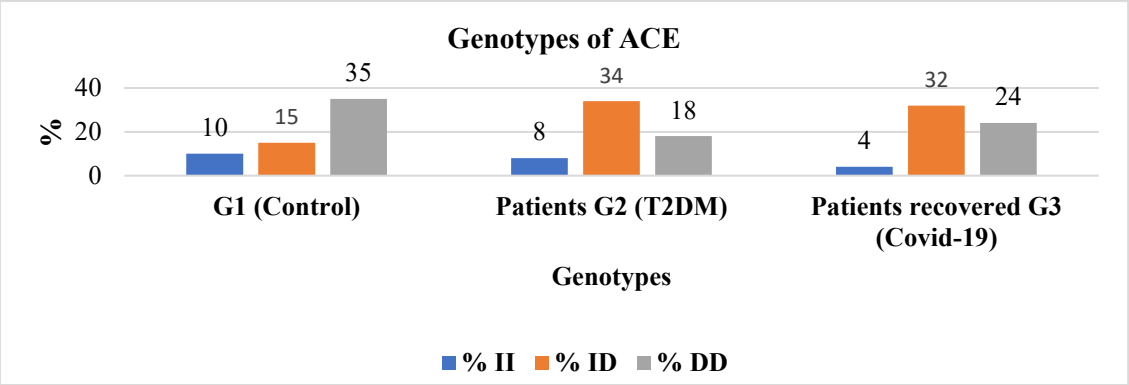


**Figure 4. Percentage of II, ID, and DD genotypes of the ACE gene in control, patients with type 2 diabetes, and patients who recovered from COVID-19 groups**

## Discussion

The one-way ANOVA approach was used for statistical analysis to compare the levels of biomedical parameters (FBS, HbA1c, WBC, Lymphocyte%, T3, T4, TSH, CRP, D-dimer, LDH, and ferritin) between the studied groups (G1, G2 and G3). Table 1 displays the findings of the statistical study. The result of the statistical analysis showed an effective relationship between the levels of biomedical parameters in the studied groups. This relationship was significant ($p< 0.05$). The results of this study showed that metabolic and inflammatory disorders persist in patients with type 2 diabetes (T2DM) and recovered patients from COVID-19 after the acute phase of the disease. Fasting blood sugar (FBS) is expected to be significantly increased in T2DM patients. This is indicative of poor glucose control. However, increased FBS was observed in many recovered patients from COVID-19, even in the absence of a history of diabetes. This could indicate that SARS-CoV-2 infection can independently cause dysglycemia. This disorder could possibly be due to direct damage to pancreatic beta cells, or systemic inflammation, or induction of insulin resistance, or a combination of these factors. The results of this study are consistent with the results of a study by Yones et al. (2024) who compared FBS levels in T2DM patients and COVID-19 patients with healthy controls. High HbA1c levels in T2DM patients indicate that chronic hyperglycemia is present and that the average blood sugar has increased over the past 2–3 months. In addition, evidence from this study suggests that COVID-19 can impair glycemic control in recovered individuals and cause an increase in HbA1c. This phenomenon is observed in both patients with underlying diabetes and some individuals without a history of diabetes. These findings are consistent with the results of Prattichizzo et al. (2022). This could be due to the detrimental effects of the virus on pancreatic function, persistent inflammation, metabolic stress due to severe illness, and corticosteroid use. The interactions between these pathways could lead to disruption of glucose homeostasis and persistence of dysglycemia after recovery from COVID-19 (Matviichuk et al., 2024). Increased white blood cell (WBC) counts in T2DM patients and COVID-19 recoveries may indicate persistent inflammation. Mild chronic inflammation is a hallmark of type 2 diabetes. This inflammation can exacerbate insulin resistance, microvascular abnormalities, and increased neutrophil counts. Anurag et al. (2020) reported that WBCs are

increased in T2DM patients and COVID-19 patients compared to healthy controls, which supports the results of the present study. In COVID-19 survivors, sustained immune activation and increased lymphocytes and neutrophils occur. This may indicate immune reconstitution and long-term inflammatory consequences, and has been reported as a feature of both diseases in previous reports (Wu & Gao, 2020). The percentage of lymphocytes was reduced in T2DM patients. This may indicate immune dysfunction due to adverse metabolic status and chronic inflammation. In contrast, lymphocyte counts increased in COVID-19 recovered individuals. This could also be due to intense immune activation and the formation of immune memory cells. These differences suggest a complex interplay between metabolic health, viral immune response, and immune cell migration in different organs. The present findings are consistent with the results of Cheng et al. (2021) comparing the percentage of lymphocytes between T2DM patients with COVID-19 and healthy individuals. Triiodothyronine (T3) levels were decreased in T2DM patients and COVID-19 recovered individuals. This could also be due to low T3 syndrome or sick euthyroid syndrome. This condition is related to a common physiological response to chronic diseases and systemic stress. This syndrome is characterized by a decreased peripheral conversion of thyroxine (T4) to T3, a possible increase in reverse T3, and an inhibition of deiodinase enzyme activity. These results are consistent with those of Zhao et al. (2023), who reported a decrease in T3 levels in patients with type 2 diabetes and COVID-19 compared to healthy controls. The decrease in T3 in COVID-19 survivors is likely due to the post-acute phase of the patient's euthyroid syndrome. This is an adaptive phase during which the body facilitates the recovery process from the inflammatory and catabolic stress caused by the viral infection by reducing energy expenditure and metabolic rate. Severe COVID-19 can directly disrupt the activity of deiodinase enzymes and thyroid hormone transport by inducing systemic inflammation and cytokine storm. This results in a decrease in T3 and an increase in rT3. This adaptive response may be a protective mechanism to reduce energy expenditure during the recovery period (Pal and Banerjee, 2020). The results of this study suggest that COVID-19 and type 2 diabetes can have long-term effects on glucose homeostasis, immune function, and the thyroid axis. They can do this through common inflammatory, metabolic, and hormonal pathways. Therefore, it is necessary to closely monitor metabolic, inflammatory, and hormonal markers in T2DM patients and COVID-19 survivors, even after clinical recovery. A common phenomenon in patients with type 2 diabetes mellitus (T2DM) and those recovering from COVID-19 is that their thyroxine (T4) levels increase. This increase is more indicative of changes in thyroid hormone metabolism and may not necessarily indicate true hyperthyroidism. In T2DM patients, chronic inflammation and insulin resistance can disrupt thyroid hormone-binding proteins. This disruption also leads to an increase in total T4 without a corresponding increase in free and physiologically active T4. In addition, researchers have shown that type 2 diabetes can affect the peripheral conversion of T4 to triiodothyronine (T3) or the binding of thyroid hormones to carrier proteins such as TBG. Du et al. (2023) compared T4 levels in patients with COVID-19 and T2DM with those of healthy subjects, and their results confirmed the findings of this study. Ilera et al., (2022) reported that in COVID-19 survivors, the initial systemic inflammatory response may have lasting consequences on the hypothalamic-pituitary-thyroid axis. Transient thyrotoxicosis or hyperthyroidism are

subclinical thyroid disorders after COVID-19 and can be caused by thyroiditis or stress-induced release of thyroid hormones. Inflammation, metabolic dysregulation, and immune responses can temporarily or permanently alter thyroid hormone levels. Therefore, careful clinical assessment and monitoring of thyroid function is essential. Lisco et al. (2021) reported that these elevations can indicate a sick euthyroid syndrome or a non-thyroid disease. In this state, the body adapts to stressful conditions. Several metabolic factors and physiological stresses affect thyroid-stimulating hormone (TSH) levels. In T2DM patients, insulin resistance and chronic inflammation can disrupt thyroid hormone metabolism and TSH secretion. Therefore, it can lead to an increase in TSH, even within the normal range. In contrast, in patients with COVID-19, factors such as systemic inflammation, direct effects of the virus on the thyroid gland, or acute medication use may cause a temporary decrease in TSH and create a transient euthyroid state in the patient. Rossini et al. (2023) compared TSH levels in COVID-19 and T2DM patients with healthy subjects, and their results are consistent with the results of this study. On the other hand, increased lactate dehydrogenase (LDH) levels in T2DM patients and COVID-19 survivors can indicate cellular damage and metabolic disorders. In type 2 diabetes, tissue damage caused by chronic hyperglycemia and oxidative stress increases the release of LDH from damaged cells. This may reflect impaired glucose metabolism and microvascular problems. The results of this study are in line with the findings of Li et al. (2020). They compared LDH levels in COVID-19 and T2DM patients with healthy controls. In addition, several other factors, including chronic inflammation, organ damage (e.g., lung and heart), and endothelial dysfunction after recovery from COVID-19, can lead to continued cell lysis and increased LDH levels. This could indicate active tissue repair processes or persistent disease (Yan et al., 2021). CRP levels are higher in T2DM and COVID-19 patients due to persistent low-grade inflammation and acute inflammation after SARS-CoV-2 infection. Chronic low-grade systemic inflammation associated with T2DM may raise baseline CRP. Additionally, COVID-19 begins a powerful inflammatory cascade that may cause a "cytokine storm" of pro-inflammatory cytokines that boost hepatic CRP synthesis, resulting in CRP concentrations more than three times higher than typical. Debi et al. (2022) examined CRP levels in T2DM and COVID-19 patients with healthy controls. The results of the current study are in line with their results. Increased D-dimer values in T2DM and COVID-19 individuals indicate hypercoagulability and fibrinolysis activation. In T2DM, persistent low-grade inflammation and functional impairment to the vascular endothelium cause high D-dimer levels, indicating microvascular and macrovascular problems. Post-COVID-19 endothelium damage and inflammation may extend D-dimer rise beyond viral clearance, increasing the risk of thrombi and consequences. Current findings support Pangaribuan and Pase (2021) study that compared D-dimer levels in T2DM and COVID-19 patients to healthy controls. Ferritin levels are often elevated in patients with type 2 diabetes mellitus (T2DM) and in individuals with or recovering from COVID-19. This may be due to chronic inflammation and dysregulation of iron metabolism. In T2DM patients, elevated ferritin may indicate oxidative damage and insulin resistance. This may contribute to disease progression. One factor that may exacerbate post-acute outcomes is that after COVID-19, higher ferritin levels are associated with cytokine storm and chronic systemic inflammation. Therefore, careful monitoring of ferritin status in both patient

groups appears essential. Liani et al. (2022) studied ferritin levels in T2DM and COVID-19 patients with healthy controls. The current research supports their results. Table 2 shows the genetic and allele frequencies of the ACE(I/D) in controls (G1), T2DM patients (G2), and restored Covid-19 patients (G3). Data revealed a correlated association of ACE (I/D) alleles with T2DM among Covid-19 recovered patients which significantly coincide with the results of Sieńko et al., (2020). The results of statistical analysis showed that compared to the DD genotype, the I/D polymorphism was statistically significantly different from the ID and II genotypes ($P = 0.041 < 0.05$). These findings are consistent with the results reported by Bandyopadhyay et al. (2020). The ACE (I/D) polymorphism is involved in the pathophysiology of both type 2 diabetes mellitus (T2DM) and COVID-19 and is of particular importance in the interaction between these two diseases. ACE2 is known as the cellular receptor for SARS-CoV-2 and is a key component of the renin-angiotensin system (RAS). Over activity of the renin–angiotensin system (RAS) is frequently observed in patients with T2DM, including hyperactivity of ACE and decreased ACE II expression or activity. Such imbalance in diabetic patients can predispose them to quality infection by SARS-CoV-2 and towards a more severe disease. When the virus binds to the ACEII enzyme, it is taken into the cells, and its surface expression is down-regulated (Dhumad et al., 2020). The reduced functional ACE II contributes to an RAS imbalance favoring angiotensin II - a potent vasoconstrictor and pro-inflammatory peptide whilst reducing the opposing effects of angiotensin-(1-7). As a result, this can aggravate inflammation, endothelial dysfunction, and possibly higher mortality from ARDS and other complications of severe COVID-19 in people with T2DM. The precise pathways by which T2DM impacts ACE (I/D) expression and function, and how COVID-19 modifies this, are complex and will be explored, but include mechanisms including hyperglycemia-associated oxidative stress and inflammation (Elfowiris et al., 2022). Consequently, the relationship shared by T2DM, COVID-19 and the ACE I/D polymorphism is truly intricate. The angiotensin-converting enzyme (ACE) gene is located on chromosome 17. This locus has a common polymorphism caused by an insertion [I (289 bp)] or deletion [D (287 bp)] of an Alu repeat sequence in intron 16. This polymorphism has a significant effect on ACE levels. Studies have shown that individuals who are homozygous for DD have the highest ACE activity, homozygous for II have the lowest activity, and heterozygotes for ID have intermediate activity of the enzyme (Pati et al., 2020). In the case of T2DM, an increase of ACE activity, which is associated with DD genotype, has been attributed to the pathogenesis and progression of other diabetic complications such as nephropathy and cardiovascular disease (CVD). A central component of the renin-angiotensin-aldosterone system (RAAS) is the enzyme ACE. This enzyme converts angiotensin I to angiotensin II. Angiotensin II is a potent vasoconstrictor molecule with profibrotic effects. Therefore, this enzyme plays an important role in regulating blood pressure (Sandooja et al., 2020). Increased ACE activity in patients with type 2 diabetes can exacerbate insulin resistance and impair endothelial function. Therefore, this condition can increase the complexity of the disease state. The causative agent of COVID-19, the SARS-CoV-2 virus, uses the ACE2 receptor to enter cells. ACE and ACE2 are separate and non-homologous enzymes. However, they are functionally related. Their interaction and balance play a key role in regulating vascular, inflammatory, and metabolic responses. Angiotensin Converting Enzyme

inhibitors (ACE inhibitors), often given for hypertension or for diabetic nephropathy, may affect expression of ACE II (Deepashree et al., 2021). ACE I/D polymorphism may play a modifying role in the severity and progression of COVID-19, especially among patients with T2DM. In fact, some studies have proposed that the DD genotype, endowed with higher ACE activity, may exhibit changes in ACE2 expression or function that could affect SARS-CoV-2 viral entry or the inflammatory response to SARS-CoV-2 infection. Nevertheless, the exact mechanisms and full effect of ACE I/D polymorphism on COVID-19 risk and severity in T2DM individuals remain to be determined since with divergent results have been reported by using different populations and study designs (Taha et al., 2023). ACE I/D, T2DM, and COVID-19, act quasi-synergistically, at the clinical level, challenging and calling for personalized approaches to management.

**Conclusion:** The results of this study indicate that type 2 diabetes (T2DM) and COVID-19 are associated. They mediated this association through common metabolic, inflammatory, and hormonal pathways. The abnormalities in glycemic control, increased inflammatory markers, and changes in thyroid function observed in T2DM patients and COVID-19 survivors may indicate that these two diseases have persistent effects on metabolic homeostasis and immunity. Thyroid hormone changes are mainly associated with the patient's euthyroid syndrome and may not necessarily indicate primary thyroid disease. From a genetic perspective, the ACE (I/D) polymorphism plays an important role in the interaction between T2DM and COVID-19. The significant difference between the ID and II genotypes compared to DD, together with the pivotal role of the ACE/ACE2 pathway in the renin-angiotensin system, indicates that this pathway should be considered and emphasized in the pathophysiology of the two diseases. Therefore, it is necessary to carefully monitor metabolic and inflammatory markers in diabetic patients and COVID-19 survivors to prevent late complications.

## Author Contributions

THM and HHKA: Conceptualization, methodology, software, validation, formal analysis, investigation, resources, and data curation. RSAA and YHA: writing-original draft preparation, writing-review, visualization, and funding acquisition.

## Data Availability Statement

Data are available from the authors upon reasonable request.

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## Ethical Considerations

This research has been approved by the Ethical Approval Committee of College of Education (Reference No., 318, 7/4/2024) at the University of Al-Qadisiyah, Iraq. Moreover, the study was carried out with integrity, with no fabrication, falsification, plagiarism, or any scientific misconduct.

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**Conflict of interest**

The authors declare that they have no conflict of interest.

**References**

Ahmad, E., Lim, S., Lamptey, R., Webb, D. R., & Davies, M. J. (2022). Type 2 diabetes. *The Lancet*, *400*(10365), 1803–1820. https://doi.org/10.1016/S0140-6736(22)01655-5

Anurag, A., Jha, P. K., & Kumar, A. (2020). Differential white blood cell counts in COVID-19: A cross-sectional study of 148 patients. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, *14*(6), 2099–2102. https://doi.org/10.1016/j.dsx.2020.10.029

Bandyopadhyay, A. R. (2020). COVID-19: An epidemiological and host genetics appraisal. *Asian Journal of Medical Sciences*, *11*(5), 116–117. https://doi.org/10.71152/ajms.v11i3.3496

Bellary, S., Kyrou, I., Brown, J. E., & Bailey, C. J. (2021). Type 2 diabetes mellitus in older adults: Clinical considerations and management. *Nature Reviews Endocrinology*, *17*(9), 534–548. https://doi.org/10.1038/s41574-021-00512-2

Cheng, Y., Yue, L., Wang, Z., Zhang, J., & Xiang, G. (2021). Hyperglycemia associated with lymphopenia and disease severity of COVID-19 in type 2 diabetes mellitus. *Journal of Diabetes and Its Complications*, *35*(2), Article 107809. https://doi.org/10.1016/j.jdiacomp.2020.107809

Debi, H., Itu, Z. T., Amin, M. T., Hussain, F., & Hossain, M. S. (2022). Association of serum C-reactive protein (CRP) and D-dimer concentration on the severity of COVID-19 cases with or without diabetes: A systematic review and meta-analysis. *Expert Review of Endocrinology & Metabolism*, *17*(1), 83–93. https://doi.org/10.1080/17446651.2022.2002146

Deepashree, G. A., Ramprasad, E., Jayakumar, M., Solomon, F. D., & Gnanasambandan, R. (2021). ACE ID gene polymorphism contributes to chronic kidney disease progression but not NOS3 gene among type 2 diabetes with nephropathy patients. *Endocrinology and Metabolism Science*, *4*, Article 100100. https://doi.org/10.1016/j.endmts.2021.100100

Dhumad, M. M., Hamdan, F. B., & Al-Mayah, Q. S. (2020). Angiotensin-converting enzyme insertion/deletion (I/D) gene polymorphism in Iraqi type 2 diabetic patients: Association with the risk of cardiac autonomic neuropathy. *Egyptian Journal of Medical Human Genetics*, *21*, Article 20. https://doi.org/10.1186/s43042-020-00062-8

Du, J., Zhao, X., Xu, X., Zhang, Z., & Zhang, X. (2023). Association between thyroid parameters and subclinical atherosclerosis in hospitalized euthyroid patients with type 2 diabetes mellitus. *Diabetes, Metabolic Syndrome and Obesity*, *16*, 3163–3171. https://doi.org/10.2147/DMSO.S429941

Elfowiris, A., & Banigesh, A. (2022). Evaluation of antioxidant therapeutic value of ACE inhibitor as adjunct therapy on type 2 diabetes mellitus patients with cardiovascular disease.

*ACS Pharmacology & Translational Science*, *5*(6), 413–418. https://doi.org/10.1021/acsptsci.1c00269

Galicia-García, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of type 2 diabetes mellitus. *International Journal of Molecular Sciences*, *21*(17), Article 6275. https://doi.org/10.3390/ijms21176275

Hussain, M., Abbas, S., Bilal, A., Aslam, M. N., & Awan, F. R. (2020). Association of ACE I/D polymorphism with risk of diabetes in cardiovascular disease patients. *Experimental and Clinical Endocrinology & Diabetes*, *128*(2), 82–88. https://doi.org/10.1055/a-0824-6515

Ilera, V., Delfino, L. C., Zunino, A., Glikman, P., Drnovsek, M., Reyes, A., Dios, A., Toibaro, J., Pachioli, V., Lannes, N., Guida, A., & Gauna, A. (2021). Correlation between inflammatory parameters and pituitary-thyroid axis in patients with COVID-19. *Endocrine*, *74*(3), 455–460. https://doi.org/10.1007/s12020-021-02863-2

Joung, C. I., Park, Y. W., Kim, S. K., Uhm, W. S., Kim, T. H., & Yoo, D. H. (2006). Angiotensin-converting enzyme gene insertion/deletion polymorphism in Korean patients with systemic sclerosis. Journal of Korean Medical Science, 21(2), 329–332. https://doi.org/10.3346/jkms.2006.21.2.329

Khurana, V., & Goswami, B. (2022). Angiotensin-converting enzyme (ACE). *Clinica Chimica Acta*, *524*, 113–122. https://doi.org/10.1016/j.cca.2021.10.029

Le Berre, M., Gerlach, J. Q., Dziembała, I., & Kilcoyne, M. (2022). Calculating half maximal inhibitory concentration (IC50) values from glycomics microarray data using GraphPad Prism. In M. Kilcoyne & J. Q. Gerlach (Eds.), *Glycan microarrays* (Methods in Molecular Biology: Vol. 2460, pp. 89–111). Humana. https://doi.org/10.1007/978-1-0716-2148-6_6

Li, C., Ye, J., Chen, Q., Hu, W., Wang, L., Fan, Y., Lu, Z., Chen, J., Chen, Z., Chen, S., Tong, J., Xiao, W., Mei, J., & Lu, H. (2020). Elevated lactate dehydrogenase (LDH) level as an independent risk factor for the severity and mortality of COVID-19. *Aging*, *12*(15), 15670–15681. https://doi.org/10.18632/aging.103770

Liani, F. N., Widjanarko, S. W., & Novida, H. (2022). The role of serum ferritin level and disease severity in COVID-19 with type 2 diabetes mellitus patients. *Bali Medical Journal*, *11*(3), 1805–1810. https://doi.org/10.15562/bmj.v11i3.3818

Lisco, G., De Tullio, A., Jirillo, E., Giagulli, V. A., De Pergola, G., Guastamacchia, E., & Triggiani, V. (2021). Thyroid and COVID-19: A review on pathophysiological, clinical and organizational aspects. *Journal of Endocrinological Investigation*, *44*(9), 1801–1814. https://doi.org/10.1007/s40618-021-01554-z

Matviichuk, A., Yerokhovych, V., Ilkiv, Y., Krasnienkov, D., Korcheva, V., Gurbych, O., Shcherbakova, A., Botsun, P., Falalyeyeva, T., Sulaieva, O., & Kobyliak, N. (2024). HbA1c and leukocyte mtDNA levels as major factors associated with post-COVID-19 syndrome in type 2 diabetes patients. *Scientific Reports*, *14*(1), Article 25533. https://doi.org/10.1038/s41598-024-77496-2

Mohammadabadi, M. (2016). Inter-simple sequence repeat loci associations with predicted breeding values of body weight in Kermani sheep. *Genetics in the Third Millennium*, *14*(4), 4386–4393. https://sciexplore.ir/Documents/Details/472-591-539-924

Mohammadabadi, M. R., Torabi, A., Tahmourespoor, M., & Baghizadeh, A. (2010). Analysis of bovine growth hormone gene polymorphism of local and Holstein cattle breeds in Kerman province of Iran using polymerase chain reaction restriction fragment length. *African Journal of Biotechnology*, *9*(41), 6848–6852. https://www.ajol.info/index.php/ajb/article/view/130242

Mohammadabadi, M., Akhtarpoor, A., Khezri, A., Babenko, O., Stavetska, R. V., Tytarenko, I., Ievstafiieva, Y., Buchkovska, V., Slynko, V., & Afanasenko, V. (2024a). The role and diverse applications of machine learning in genetics, breeding, and biotechnology of livestock and poultry. *Agricultural Biotechnology Journal*, *16*(4), 413–442. https://doi.org/10.22103/jab.2025.24662.1644

Mohammadabadi, M., Babenko Ivanivna, O., Borshch, O., Kalashnyk, O., Ievstafiieva, Y., & Buchkovska, V. (2024c). Measuring the relative expression pattern of the UCP2 gene in different tissues of the Raini Cashmere goat. *Agricultural Biotechnology Journal*, *16*(3), 317–332. https://doi.org/10.22103/jab.2024.24337.1627

Mohammadabadi, M., Kheyrodin, H., Afanasenko, V., Babenko Ivanivna, O., Klopenko, N., Kalashnyk, O., Ievstafiieva, Y., & Buchkovska, V. (2024b). The role of artificial intelligence in genomics. *Agricultural Biotechnology Journal*, *16*(2), 195–279. https://doi.org/10.22103/jab.2024.23558.1575

Mohammadabadi, M., Meymandi, M. G., Montazeri, M., Afanasenko, V., & Kalashnyk, O. (2021a). Molecular characterization of Iranian dromedaries using microsatellite markers. *Acta Agronomica*, *69*(4), 321–330. https://api.semanticscholar.org/CorpusID:249364533

Mohammadabadi, M., Oleshko, V., Oleshko, O., Heiko, L., Starostenko, I., Kunovskii, J., Bazaeva, A., & Roudbari, Z. (2021b). Using inter simple sequence repeat multi-loci markers for studying genetic diversity in guppy fish. *Turkish Journal of Fisheries and Aquatic Sciences*, *21*(12), 603–613. https://doi.org/10.4194/1303-2712-v21_12_03

Mohammadifar, A., & Mohammadabadi, M. (2018). Melanocortin-3 receptor (MC3R) gene association with growth and egg production traits in Fars indigenous chicken. *Malaysian Applied Biology*, *47*(3), 85–90.

Mohammadifar, A., & Mohammadabadi, M. R. (2017). The effect of uncoupling protein polymorphisms on growth, breeding value of growth, and reproductive traits in the Fars indigenous chicken. *Iranian Journal of Applied Animal Science*, *7*(4), 679–685. https://journals.iau.ir/article_535799.htmL

Noori, A. N., Behzadi, M. R. B., & Mohammadabadi, M. R. (2017). Expression pattern of Rheb gene in Jabal Barez Red goat. *Indian Journal of Animal Sciences*, *87*(11), 1375–1378. https://doi.org/10.56093/ijans.v87i11.75890

Pakkir Shah, A. K., Walter, A., Ottosson, F., Russo, F., Navarro-Díaz, M., Boldt, J., Kalinski, J. J., Kontou, E. E., & Petras, D. (2025). Statistical analysis of feature-based molecular

networking results from non-targeted metabolomics data. *Nature Protocols*, *20*(1), 92–162. https://doi.org/10.1038/s41596-024-01046-3

Pal, R., & Banerjee, M. (2020). COVID-19 and the endocrine system: Exploring the unexplored. *Journal of Endocrinological Investigation*, *43*(7), 1027–1031. https://doi.org/10.1007/s40618-020-01276-8

Pangaribuan, J. P., & Pase, M. A. (2021). Correlation between HbA1c and D-dimer in type 2 diabetic with COVID-19 patients. *Journal of Endocrinology, Tropical Medicine and Infectious Disease*, *3*(4), 145–151. https://doi.org/10.32734/jetromi.v3i4.7529

Pati, A., Mahto, H., Padhi, S., & Panda, A. K. (2020). ACE deletion allele is associated with susceptibility to SARS-CoV-2 infection and mortality rate: An epidemiological study in the Asian population. *Clinica Chimica Acta*, *510*, 455–458. https://doi.org/10.1016/j.cca.2020.08.008

Pigeyre, M., Sjaarda, J., Chong, M., Hess, S., Bosch, J., Yusuf, S., Gerstein, H., & Paré, G. (2020). ACE and type 2 diabetes risk: A Mendelian randomization study. *Diabetes Care*, *43*(4), 835–842. https://doi.org/10.2337/dc19-1973

Prattichizzo, F., de Candia, P., Nicolucci, A., & Ceriello, A. (2022). Elevated HbA1c levels in pre-COVID-19 infection increase the risk of mortality: A systematic review and meta-analysis. *Diabetes/Metabolism Research and Reviews*, *38*(1), Article e3476. https://doi.org/10.1002/dmrr.3476

Rossini, A., Cassibba, S., Perticone, F., Benatti, S. V., Venturelli, S., Carioli, G., Ghirardi, A., Rizzi, M., Barbui, T., Trevisan, R., & Ippolito, S. (2023). Increased prevalence of autoimmune thyroid disease after COVID-19: A single-center, prospective study. *Frontiers in Endocrinology*, *14*, Article 1126683. https://doi.org/10.3389/fendo.2023.1126683

Saadatabadi, L. M., Mohammadabadi, M., Nanaei, H. A., Ghanatsaman, Z. A., Stavetska, R. V., Kalashnyk, O., Kochuk-Yashchenko, O. A., & Kucher, D. M. (2023). Unraveling candidate genes related to heat tolerance and immune response traits in some native sheep using whole genome sequencing data. *Small Ruminant Research*, *225*, Article 107018. https://doi.org/10.1016/j.smallrumres.2023.107018

Sandooja, R., Vura, N. V. R. K., & Morocco, M. (2020). Heightened ACE activity and unfavorable consequences in COVID-19 diabetic subjects. *International Journal of Endocrinology*, *2020*, Article 7847526. https://doi.org/10.1155/2020/7847526

Sandoval, D. A., & Patti, M. E. (2023). Glucose metabolism after bariatric surgery: Implications for T2DM remission and hypoglycaemia. *Nature Reviews Endocrinology*, *19*(3), 164–176. https://doi.org/10.1038/s41574-022-00757-5

Shi, Y., Wang, G., Cai, X.-P., Deng, J.-W., Zheng, L., Zhu, H.-H., Zheng, M., Yang, B., & Chen, Z. (2020). An overview of COVID-19. *Journal of Zhejiang University Science B*, *21*(5), 343–360. https://doi.org/10.1631/jzus.B2000083

Shirbhate, E., Pandey, J., Patel, V. K., Kamal, M., Jawaid, T., Gorain, B., Kesharwani, P., & Rajak, H. (2021). Understanding the role of ACE-2 receptor in pathogenesis of COVID-19 disease: A potential approach for therapeutic intervention. *Pharmacological Reports*, *73*(6), 1539–1550. https://doi.org/10.1007/s43440-021-00303-6

Sieńko, J., Kotowski, M., Bogacz, A., Lechowicz, K., Drożdżal, S., Rosik, J., Sietnicki, M., Sieńko, M., & Kotfis, K. (2020). COVID-19: The influence of ACE genotype and ACE-I and ARBs on the course of SARS-CoV-2 infection in elderly patients. *Clinical Interventions in Aging*, *15*, 1231–1240. https://doi.org/10.2147/CIA.S261516

Sriram, K., & Insel, P. A. (2020). Risks of ACE inhibitor and ARB usage in COVID-19: Evaluating the evidence. *Clinical Pharmacology & Therapeutics*, *108*(2), 236–241. https://doi.org/10.1002/cpt.1863

Sulimova, G. E., Azari, M. A., Rostamzadeh, J., Mohammadabadi, M. R., & Lazebny, O. E. (2007). κ-casein gene (CSN3) allelic polymorphism in Russian cattle breeds and its information value as a genetic marker. *Russian Journal of Genetics*, *43*(1), 73–79. https://doi.org/10.1134/S1022795407010115

Taha, M. M., Mahdy-Abdallah, H., Shahy, E. M., Helmy, M. A., & ElLaithy, L. S. (2023). Diagnostic efficacy of cystatin C in association with different ACE genes predicting renal insufficiency in T2DM. *Scientific Reports*, *13*(1), Article 5288. https://doi.org/10.1038/s41598-023-32012-w

Wu, D., & Gao, S. (2020). Analysis of the lymphocyte count in type 2 diabetic patients with coronavirus disease (COVID-19): A retrospective study in a centralized treatment center. *Diabetes Research and Clinical Practice*, *166*, Article 108340. https://doi.org/10.1016/j.diabres.2020.108340

Yan, H., Vijay, A., Jiang, F., Zheng, N., Hu, Y., Ye, H., Ollivere, B., Cai, T., Valdes, A. M., & Aithal, G. P. (2021). Serum glucose, lactate dehydrogenase and hypertension are mediators of the effect of body mass index on severity of COVID-19. *Endocrinology, Diabetes & Metabolism*, *4*(2), Article e00215. https://doi.org/10.1002/edm2.215

Yang, L., Liu, S., Liu, J., Zhang, Z., Wan, X., Huang, B., Chen, Y., & Zhang, Y. (2020). COVID-19: Immunopathogenesis and immunotherapeutics. *Signal Transduction and Targeted Therapy*, *5*, Article 128. https://doi.org/10.1038/s41392-020-00243-2

Yones, M. S., Al-Wasiti, E., Al Qaseer, A. H., & Al-Rubaiawi, H. K. (2024). The effect of severe COVID-19 infection on biochemical markers (FBS, HbA1c, FA, INS, C-Pep) in diabetic patients. *Anaesthesia, Pain & Intensive Care*, *28*(5), 804–808. https://doi.org/10.35975/apic.v28i5.2553

Yuki, K., Fujiogi, M., & Koutsogiannaki, S. (2020). COVID-19 pathophysiology: A review. *Clinical Immunology*, *215*, Article 108427. https://doi.org/10.1016/j.clim.2020.108427

Zhao, X., Sun, J., Xin, S., & Zhang, X. (2023). Predictive effects of FT3/FT4 on diabetic kidney disease: An exploratory study on hospitalized euthyroid patients with T2DM in China. *Biomedicines*, *11*(8), Article 2211. https://doi.org/10.3390/biomedicines11082211

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# همبستگی پلی‌مورفیسم ژن ACE (I/D) با دیابت نوع ۲ و دوره پس از بهبودی از کووید-۱۹ در بیماران عراقی: یک مطالعه موردی-شاهدی

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## چکیده

**هدف:** دیابت نوع ۲ (T2DM) یک اختلال متابولیک مزمن است که با افزایش سطح قند خون به‌دلیل مقاومت به انسولین، کاهش عملکرد سلول‌های بتای پانکراس یا هر دو مشخص می‌شود. ویروس SARS-CoV-2 نیز یک عامل بیماری‌زای تنفسی است که موجب بیماری کووید-۱۹ می‌گردد. هدف از این مطالعه، بررسی ارتباط بین سطوح پارامترهای FBS، HbA1c، WBC، درصد لنفوسیت‌ها، T3، T4، TSH، CRP، D-dimer، LDH و فریتین با پلی‌مورفیسم ژن ACE (I/D) در بیماران مبتلا به دیابت نوع ۲ (G2) و افراد بهبودیافته از کووید-۱۹ (G3) در مقایسه با گروه کنترل (G1) بود.

**مواد و روش‌ها:** در این مطالعه، ۶۰ بیمار مبتلا به دیابت نوع ۲(G2) ، ۶۰ بیمار بهبودیافته از کووید-۱۹ (G3) و ۶۰ فرد سالم هم‌نژاد به‌عنوان گروه کنترل (G1) شرکت داشتند. سن تمامی شرکت‌کنندگان بین ۳۰ تا ۴۵ سال بود و همگی به بیمارستان آموزشی دیوانیه در استان دیوانیه عراق مراجعه کرده بودند. پارامترهای بیوشیمیایی شامل FBS، HbA1c، WBC، درصد لنفوسیت‌ها، T3، T4، TSH، CRP، D-dimer، LDH و فریتین اندازه‌گیری شد. همچنین، پلی‌مورفیسم ژن ACE (I/D) با استفاده از روش PCR تکثیر و بررسی گردید.

**نتایج:** نتایج مطالعه نشان داد که بین پارامترهای بیوشیمیایی مورد بررسی و پلی‌مورفیسم ژن ACE ارتباط معناداری وجود دارد. اختلاف آماری معنی‌داری ($P < 0.05$) بین ژنوتیپ‌های II و ID در مقایسه با ژنوتیپ DD در بیمارانی که در معرض خطر بالای ابتلا به دیابت نوع ۲ پس از بهبودی از کووید-۱۹ قرار داشتند، مشاهده شد. ژنوتیپ‌های II و ID با بروز بالاتر دیابت نوع ۲ در افراد عراقی بهبودیافته از کووید-۱۹ همراه بودند.

**نتیجه‌گیری:** نتایج این مطالعه نشان می‌دهد که پلی‌مورفیسم ژن ACE (I/D) به‌طور معناداری با تغییرات پارامترهای بیوشیمیایی در بیماران مبتلا به دیابت نوع ۲ و افراد بهبودیافته از کووید-۱۹ مرتبط است. خطر بروز یا تشدید دیابت نوع ۲، به‌ویژه در بازماندگان کووید-۱۹، در حاملان ژنوتیپ‌های II و ID بیشتر از ژنوتیپ DD بود. این نتایج بیانگر آن است که ترکیب ژنتیکی سیستم رنین-آنژیوتانسین می‌تواند در حساسیت متابولیک پس از عفونت SARS-CoV-2 نقش داشته باشد و به‌عنوان یک شاخص بالقوه در غربالگری، پیشگیری و مدیریت بهتر بیماران پرخطر مورد استفاده قرار گیرد. با این حال، انجام مطالعات گسترده‌تر در جمعیت‌های بزرگ‌تر برای تأیید این یافته‌ها ضروری است.

**کلمات کلیدی:** دیابت نوع ۲، کووید-۱۹، ACE، T2DM

**نوع مقاله:** پژوهشی

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