Polymorphism of 8-oxoguanine DNA glycosylase -1(OGG1)in Iraqi Patients with Type2 Diabetes Mellitus

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KEYWORDS

Polymorphism, Polymorphism, Diabetes Mellitus

ABSTRACT

Chronic hyperglycemia in type 2 diabetes mellitus leads to elevated oxidative stress. As a consequence , the accumulation of reactive oxygen species (ROS)may cause additional damage to various biological macromolecules, including DNA. Several studies have demonstrated that oxidative stress plays an important role in the pathogenesis of type2 diabetes mellitus. The aim of this study is to investigate the association of polymorphisms of 8- oxoguanine DNA glycosylase-1(OGG1) repair gene polymorphism to the susceptibility of type 2 DM in an Iraqi population with T2DM patients from Wasit Province. All samples were collected from the local community of Wasit province, Iraq. Forty five type 2 diabetes mellitus patients (22 males and 23 females) and 35 healthy controls (17 males and 18 females) were genotyped for 8-oxoguanine DNA glycosylase-1(OGG1) using PCR- RFLP technique. In both patients and control groups, the distribution frequencies of genotypes and alleles of 8-oxoguanine DNA glycosylase-1(OGG1) A/G was inconsistent with the Hardy-Weinberg equilibrium in T2DM patients($\chi2$=49.542,P=(0.00001); $\chi2$=82.0185,P=(0.0001) respectively. The Cys/Cys(mt/mt) OGG1 genotype was significantly higher in patients than controls(mt/mt;33(37%)vs,0.00 in controls. The Ser/Cys (wt/mt) was 7(16%) and 6(17%) in patients and controls respectively and Ser/Ser genotypes wt/wt; decreased significantly in patients 5(11%) vs,29(83%) in controls. The wt and mt allele frequencies of OGG1were highly significant between the two groups P=0.00001. The wt allele was the major one in control group with a percent of (90.28) vs. (18.89) in patients group. Whereas the mt the frequent allele in patients with a percent of (81.11) vs. (18.89).This further analysis showed that the individuals carrying the homozygous Cys/Cys(mt/mt) genotype were more likely to have increased the risk of T2DM very significantly with OR= 190.02800 (CI95% 10.8329 to 3342.2603) ,P=0.0003. The genotypes Ser/Ser(wt/wt) and Ser/Cys(wt/mt) decrease the association with T2DM with OR=0.0259 (CI95% 0.0072 to 0.0930), and 0.8904 (CI95% 0.2701 to 2.9347)respectively, P= 0.0001 and 0.08486 for each genotype respectively, These results suggest that mt allele may be considered as risk allele of T2DM whereas the wt allele is protective agent T2DM.Association analysis showed that the type2 diabetes mellitus risk of females with OGG1 gene Cys/Cys(mt/mt) genotype was highly significant 81.4000 fold higher than that in controls OR= 81.4000 (CI 95% 4.3089 to 1537.7322), P= 0.0033.Ser/Cys(wt/mt) genotype increase the probability of the disease with OR = 1.7647 (CI 95% 0.3745 to 8.3154), P = 0.4727.Similary,Ser/Ser(wt/wt) genotype decrease the association with T2DM with OR= 0.0091 (CI95% 0.0009 to 0.0959), P = 0.0001.Type2 diabetes mellitus patients particularly with Cys/Cys(mt/mt) genotype increases the association about more than 111 times in males patients than that in controls OR= 111.3636 (CI95% 5.7135 to2170.6226), P = 0.0019 While, genotypes Ser/Cys(wt/mt) and Ser/Ser (wt/wt) reduce the likelihood of T2DM with OR= 0.2222 (CI95% 0.0209 to 2.3585),P = 0.2120 and 0.0476(CI95% 0.0091 to 0.2484), P= 0.0003 respectively. the genetic model for OGG1 in comparison between T2DM patients and controls . The dominant model indicated that patients and controls of (wt/mt+mt/mt) genotype increased significantly the association with T2DM in patients: (5/7 and 33) comparing with control (29/6 and 0.00) with OR (38.666),P=0.0001.The recessive model revealed that patients carrier the genotype (wt/wt+wt/mt) declined significantly the association with the disease :(33/5 and 7) in patients versus (0.00/29 and 6) in controls,OR=0.0053,P=0.0003.The Over-dominant model showed that patients with the genotype (wt/wt+mt/mt) in creased non-significantly the association with the disease when compare patients (7/5 and 33) with controls(6/29 and 0.00) ,OR=1.123,P=0.848

1. Introduction

Type 2 diabetes mellitus is a metabolic disorder characterized by hyperglycemia and insulin resistance. One of the key factors contributing to the pathogenesis of type 2 diabetes is oxidative stress, which leads to DNA damage. Studies have shown that type 2 diabetic patients exhibit elevated levels of oxidative DNA damage, as evidenced by increased levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) (Al-Aubaidy and Jelinek, 2011). This oxidative DNA damage is primarily repaired through the base excision repair pathway, with 8-oxoguanine DNA glycosylase-1 (OGG1) playing a crucial role in initiating the repair process (Pan etal., 2016). OGG1 is an enzyme that specifically recognizes and excises 8-oxoguanine (8-oxoG), one of the most abundant base lesions induced by oxidative stress in DNA (Visnes etal., 2018). The repair of 8-oxoG by OGG1 is essential for maintaining genomic integrity and preventing mutagenesis. Studies have indicated that OGG1 deficiency can exacerbate

DNA damage and lead to various pathological conditions, such as cardiac dysfunction (Anene-Nzelu etal., 2022). Furthermore, research has highlighted the association between oxidative DNA damage and diabetic complications, such as nephropathy and retinopathy (Goodarzi etal., 2010). The extent of DNA damage in diabetic patients has been evaluated using various assays, including the Comet assay, which measures DNA strand breaks as a marker of oxidative stress (Nithya etal., 2017). Additionally, the evaluation of DNA damage in diabetic patients with and without peripheral neuropathy has been studied, emphasizing the importance of understanding the impact of DNA damage on diabetic complications (Prasad etal., 2015). Moreover, the role of OGG1 polymorphisms in cancer susceptibility has been investigated, suggesting that variations in the OGG1 gene may influence an individual's risk of developing cancer (Karahalil etal., 2012). This highlights the significance of understanding the genetic factors that modulate DNA repair mechanisms in the context of disease development. In conclusion, the evaluation of DNA damage in type 2 diabetic patients and its correlation with OGG1 repair gene polymorphisms is crucial for elucidating the mechanisms underlying diabetic complications and potential therapeutic targets. Understanding the interplay between oxidative DNA damage, OGG1 function, and disease pathogenesis can provide valuable insights into the development of personalized treatment strategies for diabetic patients.The aim of this study is to investigate the association of polymorphisms of 8- oxoguanine DNA glycosylase-1(OGG1) repair gene polymorphism to the susceptibility of type 2 DM an Iraqi population with T2DM patients.

2. Methodology

This is a case-control study that was carried out on the 10th of October 2023 to the 29th of April 2024, at the College of Education for Pure Sciences / Department biology / University of Wasit. There were eighty people that took part in the study. The people were split up into two groups:

1 .The patient group, which included 22 male and 23 female participants from Wasit province, Iraq, with a mean age ± SD of 57.38 ± 7.67 years and a median age of 57 years, included 45 persons with DMT2.

2 .The control group, consisting of 35 individuals (17 male and 18 female), had an age range of 40 to 78 years. The average age was 57.38 years with a standard deviation of 7.67 years, and the median age was 57 years. All participants in the control group appeared to be in good health. They made their selection from the local Wasit province, Iraqi community.

Five ml of venous blood was harvested using a vacuum blood collection tube. The blood was put into ethylenediaminetetraacetic acid –k3 (EDTA) tubes, labeled, and stored at-20^{0}C until DNA extraction and genotyping. Using Quick-DNATM Blood MiniPrep (Zymo, USA) kit Catalogue Nos. D3024 and D3025, genomic DNA was isolated from whole blood. Genotyping identification of 8-Oxoguanine DNA glycosylase-1 Ser326Cys was carried out using Restriction Fragment of Genotype Length Polymorphism (REFLP) – Polymerase Chian Reaction (PCR). Two Primers were used to detect the SNP of gene OGG1. The sequence of these primers is shown in table1.

Table 1 : The specific primers of *OGG1*gene

Forward primer	5'- ACTGTCACTAGTCTCAC CAG-3'	47.2	47.1	201 base pair
Reverse primer	5'- GGAAGGTGCTTGG GGAAT-3’	55.1	55.6	

The digestion reactions were **carried out using restriction enzyme *Fnu4HI* (*BioLabs*).**

Statistical Analysis

ANOVA analysis frequencies for SNP_s were calculated directed counting method. Hardy-Weinberg equilibrium (HWE) for each SNP was investigated. Statistically significant when less than 0.05

3. Result and Discussion

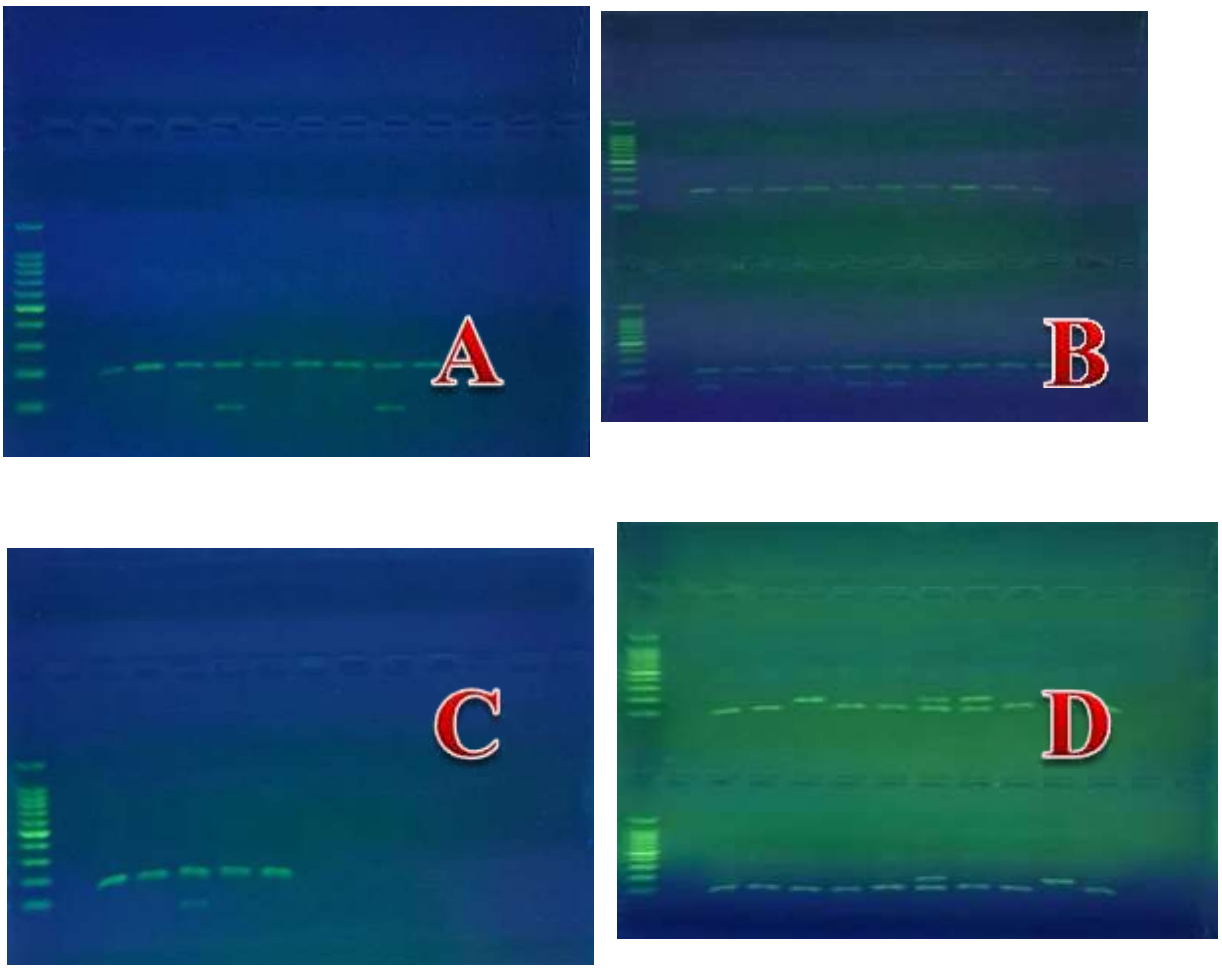
Genotypes and allele frequencies of *8-oxoguanine DNA glycosylase-1(OGG1)* in patients and controls

Forty five type2 diabetic mellitus patients (22 males and 23 females) and 35 healthy controls (17 males and 18 females) were genotyped for *8-oxoguanine DNA glycosylase-1(OGG1)*. In both patients and control groups, the distribution frequencies of genotypes and alleles of *8-oxoguanine DNA glycosylase-1(OGG1) A/G* was inconsistent with the Hardy-Weinberg equilibrium in T2DM patients(χ^2=49.542,*P*=(0.00001); χ^2=82.0185,*P*=(0.0001) respectively. These results indicate that distributions are not in equilibrium. The allele and genotype frequencies of *OGG1 A/G* gene polymorphisms were used to estimate the odds ratio (OR), confidence intervals (95% CIs), χ 2, and *P*-value. PCR products of *8-oxoguaninebDNA glycosylase-1(OGG1)* A/G bands sizes were 201 base pair. The results of enzyme digestion using *Fnu4HI* produced several fragments grouped into 3 types of fragments:

1-ACA (serine) /AGA(cysteine),wt/wt 200bp/100bp

2-ACA(serine) /ACA(serine),wt/wt 200bp

3-AGA(cysteine) /AGA(cysteine),mt/mt 100bp figure1



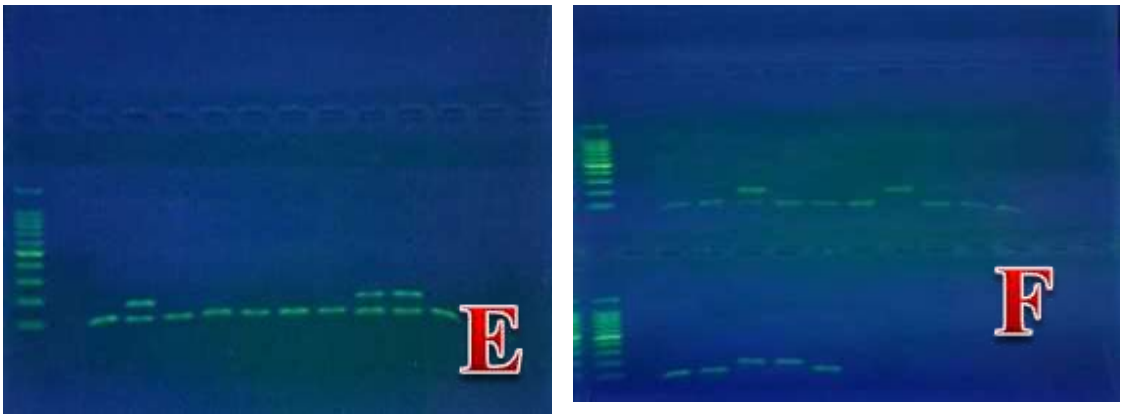


Figure1:Electrophoresis pattern of PCR products digested with *Fnu4HI* restriction enzyme(2.5% agarose gel 5volt/cm^2): DNA molecular marker 100bp size.A:sample1-10controls,B:sample 11-30 controls,C:samples 31-35 controls,D:sample 36-55 patients,E:sample 56-65 patients,F:sample 66-80 patients.

The result for the effect of *OGG1* polymorphism on T2DM has been summarized in table3.1.The Cys/Cys(mt/mt) *OGG1* genotype was significantly higher in patients than controls(mt/mt;33(37%)vs,0.00 in controls. The Ser/Cys (wt/mt) was 7(16%) and 6(17%) in patients and controls respectively and Ser/Ser genotypes wt/wt;decreased significantly in patients 5(11%) vs,29(83%) in controls.The wt and mt allele frequencies of OGG1were highly significant between the two groups *P*=0.00001. The wt allele was the major one in control group with a percent of (90.28) vs. (18.89) in patients group. Whereas the mt the freguent allele in patients with apercent of (81.11) vs. (18.89

Table1: Distribution of genotypes and allele frequencies of *OGG1* in T2DM patients and controls

Groups	**GenotypeNO.(%)**			**Allele frequency (%) NO.**	
	wt/wt	**wt/mt**	**mt/mt**	**wt**	**mt**
Control	29(83)	6(17)	0.00(0.00)	(90.28) 46	9.72) (6
Patients	5(11)	7(16)	33(73)	18.89) (17	(81.11) 72
Chi square χ^2	**49.542**			**82.0185**	
***P*-value**	**0.00001**			**0.00001**	
Significance level	**Sig[1].**				

P Significant at Sig1.

wt/mt : ACA(serine) / AGA (cysteine)

wt/wt : ACA(serine) /ACA (serine)

mt/mt : AGA(cysteine) / AGA (cysteine)

Susceptibility Analysis of 8-oxoguanine DNA glycosylase-1 polymorphism to Type2 Diabetes Mellitus

Table 2 shows the association of each genotype of *8-oxoguanine DNA glycosylase-1* susceptibility to T2DM. This further analysis showed that the individuals carrying the homozygous Cys/Cys(mt/mt)

genotype were more likely to have increased the risk of T2DM very significantly with OR= 190.02800 (CI95% 10.8329 to 3342.2603) ,*P*=0.0003. The genotypes Ser/Ser(wt/wt) and Ser/Cys(wt/mt) decrease the association with T2DM with OR=0.0259 (CI95% 0.0072 to 0.0930), and 0.8904 (CI95% 0.2701 to 2.9347)respectively, *P*= 0.0001 and 0.08486 for each genotype respectively, These results suggest that mt allele may be considered as risk allele of T2DM whereas the wt allele is protective agent T2DM.

Table:2 Odds ratio(95% confident intervals) for T2DM in relation to *OGG1* genotypes

Genotypes	Controls NO	Patients NO	OR	OR95%CI	*p*-value	Significance level
wt/wt	29	5	**0.0259**	**0.0072 to 0.0930**	**0.0001**	Sig.[1]
wt/mt	6	7	**0.8904**	**0.2701 to 2.9347**	**0.8486**	Ns.
mt/mt	0.00	33	190.2800	10.8329 to 3342.2603	0.0003	Sig.[2]

Ns.non-significant *P*>0.05

Sig.[1] : *P* < 0.01

Sig.2 : *P* < 0.05

The odds ratio(confident intervals 95%)for T2DM in relation to *of 8-oxoguanine DNA glycosylase-1* among females in studied groups

Association analysis showed that the type2 diabetes mellitus risk of females with *OGG1* gene Cys/Cys(mt/mt) genotype was highly significant 81.4000 fold higher than that in controls OR= 81.4000 (CI 95% 4.3089 to 1537.7322), *P*= 0.0033 table 3.3.Ser/Cys(wt/mt) genotype increase the probability of the disease with OR = 1.7647 (CI 95% 0.3745 to 8.3154), *P* = 0.4727.Similary,Ser/Ser(wt/wt) genotype decrease the association with T2DM with OR= 0.0091 (CI95% 0.0009 to 0.0959), *P* = 0.0001.

Table:3 Odds ratio(95%confident intervals)for T2DM in relation *OGG1* genotype of female patients and control

Genotypes	Controls NO	Patients NO	OR	OR95%CI	*P* value		Significance level
wt/wt	15	1	0.0091	0.0009 to 0.0959	0.0001		Sig.[1]
wt/mt	3	6	1.7647	0.3745 to 8.3154	0.4727		Ns.
mt/mt	0.00	16	81.4000	4.3089 to 1537.7322	0.0033		Sig.[2]

Ns.non-significant *P*>0.05

Sig.[1] : *P* < 0.01

Sig.[2] : *P* < 0.05

The odds ratio(confident intervals 95%) for T2DM in relation to *8-oxoguanine DNA glycosylase-1* among males in studied groups

Type2 diabetes mellitus patients particularly with Cys/Cys(mt/mt) genotype increases the association about more than 111 times in males patients than that in controls OR= 111.3636 (CI95% 5.7135 to2170.6226), *P* = 0.0019 While, genotypes Ser/Cys(wt/mt) and Ser/Ser (wt/wt) reduce the likelihood of T2DM with OR= 0.2222 (CI95% 0.0209 to 2.3585),*P*= 0.2120 and 0.0476(CI95% 0.0091 to 0.2484), *P*= 0.0003 respectively.

Table4: Odds ratio (95% confident intervals)for T2DM in relation *OGG1* of male patients and controls

Genotypes	Controls NO	Patients NO	OR	OR95%CI	*P* value	*Significant level*
wt/wt	14	4	0.0476	0.0091 to 0.2484	0.0003	Sig[1].
wt/mt	3	1	0.2222	0.0209 to 2.3585	0.2120	Ns.
mt/mt	0.00	17	111.3636	5.7135 to 2170.6226	0.0019	Sig[2].

Ns.non-significant *P*>0.05

Sig.[1] : *P* < 0.01

Sig.[2] : *P* < 0.05

Genetic model for *OGG1* polymorphisms in patients with T2DM compared with controls

Table 5 represented the genetic model for *OGG1* in comparison between T2DM patients and controls . The dominant model indicated that patients and controls of (wt/mt+mt/mt) genotype increased significantly the association with T2DM in patients: (5/7 and 33) comparing with control (29/6 and 0.00) with OR (38.666),*P*=0.0001.The recessive model revealed that patients carrier the genotype (wt/wt+wt/mt) declined significantly the association with the disease :(33/5 and 7) in patients versus (0.00/29 and 6) in controls,OR=0.0053,*P*=0.0003.The Over-dominant model showed that patients with the genotype (wt/wt+mt/mt) in creased non-significantly the association with the disease when compare patients (7/5 and 33) with controls(6/29 and 0.00) ,OR=1.123,*P*=0.848

Table 5:Genetic model of *OGG1* Polymorphisms in T2DM patients compared with controls

Genetic model	Genotype	Controls NO	Patients NO	OR	OR95%CI	*P* value	Significance level
Dominant	**wt/mt+mt/mt wt/wt(Ref.)**	**0.006/29**	**7/335**	**38.6667**	10.7563 to 138.9992	0.0001	**Sig[1].**
Recessive	**wt/wt+wt/mt mt/mt(Ref.)**	**29/6 0.00**	**5/7 33**	**0.0053**	**0.0003 to 0.0923**	0.0003	**Sig[1].**
Over-dominant	**wt/wt+mt/mt wt/mt(Ref.)**	**29/0.00 6**	**5/33 7**	**1.1232**	0.3408 to 3.7020	0.8486	**Ns.**

Ns.non-significant *P*>0.05

Sig.[1] : *P* <0.01

Sig[1] : *P* <0.01

Discussion:

It is widely accepted that chronic hyperglycemia induces DNA oxidative damage in type 2 diabetes, but little is known about the effect of hyperglycemia on the DNA repair system which plays a critical role in the maintenance of genomic DNA stability in diabetes (Pang *etal*.,2012). Peripheral blood cells are often used for comet assay to detect DNA strand break while urine and serum samples are commonly used for 8-OHdG quantification. The *OGG1* gene is one of the important genes that has recently received a lot of attention to investigate the relationship between its Ser326Cys polymorphism and the predisposition to type 2 diabetes.DNA lesions caused by reactive oxygen species(ROS) and other free radicals have been implicated in the etiology of many diseases including diabetes(Hadjivassiliou *etal*.,1998). One of the oxidatively induced pro mutagenic bases is 8-OHdG. Diabetic patients have higher concentrations of 8-OHdG in urine (Malin *etal*.,1999), blood cells (Dandona *etal*.,1996), muscle (Suzuki *etal*.,1999),and pancreas(Sakuraba *etal*.,2002;Ku *etal*.,2009).In previous studies that have investigated the association of polymorphisms of several factors among patients with type2 DM from Wasit province,Balal and Ghali,2021 revealed that IL-10 is a major contributor to the onset of type 2 diabetes mellitus and there may be a correlation between low levels of interleukin-10 and type two diabetes. Al-Sarray and Ahmed ,2021 found that may be a correlation between high levels of TNF-α and type 2 diabetes mellitus . Shamkhi and Ahmed, 2021 displayed that levels of SIRT1 may be not associated with type2 diabetes mellitus.Furthermore, the cell free mitochondrial DNA increases significantly in patients with type2 diabetes mellitus(Hussein and Ghali,2022). COX-1 is a major contributor to the onset of type 2 diabetes and there may be an association between low levels of cyclooxygenase-1and type 2 diabetes(Jebil and Ghali2021). The association analysis of IL-17AG197A gene polymorphism with T2DM displayed that heterozygous AG genotype of IL-17AG197A showed a risk association among T2DM with OR=1.24 CI95% (0.31 - 5.01) p-value =1.00 and the G allele was associated with an increased risk ofT2DM Khadhum and Ahmed ,2022). Mahmood and Ghali,2022a revealed that there was an association between the polymorphism of Osteoprotegerin (OPG) polymorphism and susceptibility to type2 diabetes mellitus. Mahmood and Ghali,2022 b found also that there may be a correlation between high levels of OPG and T2DM.Thamer etal.,2020 found that IL-4 concentrations had a non-significant difference when compared patients with type-2 diabetes mellitus with the control while patients with T2DM revealed elevated serum levels of IL-6 compared to control group.Ahmed and Ghali,2019 found that different transversion and transition mutations at IL-6-174 (G/C) gene are associated with type-2 diabetes mellitus.Alwan and Ghali,2023a revealed that The polymorphism of telomerase reverse transcriptase(TERT) rs 2736100 variant A <C are associated with the susceptibility of type2 diabetes mellitus. The association analysis of (TERT) rs2853669 with susceptibility to type2 diabetes mellitus showed that the individuals carrying the heterozygous AG genotype and homozygous AA genotypes were more likely to have a significantly increased risk of type2 diabetes mellitus(Alwan and Ghali,2023 b).The human insulin receptor gene rs1366600 has possible roles in type2 diabetes mellitus susceptibility (Foad and Ahmed ,2023a). A SNPs located within miRNA-binding sites:acyl-CoA synthetase 1 rs2292899 have possible roles in type2 diabetes mellitus susceptibility. (Foad and Ahmed ,2023 b) The homozygous GG genotype of acyl-CoA synthetase 1 rs2292899 is associated with type2 DM. In the current study, the distribution frequencies of genotypes and alleles of *8-oxoguanine DNA glycosylase-1(OGG1)* A/G was inconsistent with the Hardy-Weinberg equilibrium in T2DM patients . These results indicate that distributions are not in equilibrium. The Cys/Cys(mt/mt) OGG1 genotype was significantly higher in patients than controls. The Ser/Cys (wt/mt) was similar in patients and controls and Ser/Ser genotypes wt/wt decreased significantly in patients .The wt and mt allele frequencies of *OGG1*were highly significant between the two groups. The wt allele was the major one in control group with a percent of in patients group. Whereas the mt the frequent allele in patients with a controls.These results are consistent with (Das *etal*.,2018) in relation to distribution of genotypes and allele frequencies in patients with T2DM from a northeastern Indian population.Their results also demonstrated a slight increase in the risk for T2DM among individuals with OGG1 Ser/Cys and Cys/ Cys genotype by 1.3- and 1.6-fold respectively. These results were of the current study (Hassan *etal.*,2015) who compared

the distribution of genotypes of DNA repair genes *OGG1*between type 2 diabetic patients and non-diabetic subjects in an Iraqi population .Their results revealed that frequency of *OGG1* ser/ser (homozygous) genotype showed (26.67%) in patients and (70 %) in control .The differences were significant (P≤0.01). While ser/cys genotype showed higher significantly in diabetes mellitus Type2 (70%) compared to controls (30%). The differences were significant. *OGG1* cys/cys genotype frequency showed significantly elevated in the diabetes mellitus type2(3.33%) comprising to controls (0.00%).Moreover, a report by(Kasznicki *etal*.,2009) revealed no association of the *OGG1* Ser326Cys polymorphism with the risk for T2DM in a Polish population. In another study by (Thameem *etal*.,2010) it was suggested that *OGG1* could play an important role in the pathogenesis of T2DM. Thus, gene-gene and gene-environment interactions may increase the risk for T2DM among individuals with this DNA repair gene polymorphism. However, in some of the sub group analysis ,results were contradictory , the sample number was relatively low. The association of the Ser326Cys polymorphism of the *8-oxoguanine glycosylase 1 (OGG1)* gene with type 2 diabetes was examined using a Japanese population .HbA1c levels and frequency of diabetic subjects were significantly higher in subjects with genotypes with Cys allele than in those without (p = 0.032 and 0.037, respectively). Multiple logistic regression analysis showed that genotypes with Cys allele were significantly associated with diabetes (OR: 1.32, p = 0.0289) , (Daimon *etal*.,2009). In Turkish population, T2DM patients with OGG1 Ser326Cys polymorphism were compared with patients with a wild genotype, a 2–3 times statistically significant increase has been observed (OR 1.858, 95% CI = 1.099–3.141, p = 0.021), Gönül *etal*.,2012). Caliskan *etal*.,2022 found that the *OGG1* Ser326Cys genotypes distribution in Bulgarian subjects was consistent with the Hardy–Weinberg equilibrium. The *OGG1* Ser326Cys genotypes distribution (p >0.05) andallele (p >0.05) frequencies between patients and control subjects (p >0.05)did not reach statistical significance. The further analysis of the current study showed that the individuals carrying the homozygous Cys/Cys(mt/mt) genotype were more likely to have increased the risk of T2DM very significantly with OR= 190.02800 (CI95% 10.8329 to 3342.2603) ,P=0.0003. The genotypes Ser/Ser(wt/wt) and Ser/Cys(wt/mt) decrease the association with T2DM with OR=0.0259 (CI95% 0.0072 to 0.0930), and 0.8904 (CI95% 0.2701 to 2.9347)respectively, P= 0.0001 and 0.08486 for each genotype respectively, These results suggest that mt allele may be considered as risk allele of T2DM whereas the wt allele is protective against T2DM.Similar findings were observed among males patients with T2DM. Among females, Association analysis showed that the type2 diabetes mellitus risk of females with OGG1 gene Cys/Cys(mt/mt) genotype and Ser/Cys(wt/mt,whereas,Ser /Ser(wt/wt) genotype decrease also the association with T2DM. Genetic modeling revealed that the dominant model indicated that patients and controls of (wt/mt+mt/mt) genotype increased significantly the association with T2DM in patients. The recessive model revealed that patients carrier the genotype (wt/wt+wt/mt) declined significantly the association with the disease .The Over-dominant model showed that patients with the genotype (wt/wt+mt/mt) increased non-significantly the association with the disease. The results of the current study clearly indicates that repair of oxidative DNA damage is diminished in patients with T2DM. Subjects with the *OGG1* Cys326/Cys326 genotype were found to have a higher expression level of *OGG1* mRNA than wild-type allele carriers (Lotte *etal*.,2008). There are many studies indicating that *OGG1* Ser326Cys polymorphism is linked with the diminished repair activity of *OGG1* (Kershaw *etal*.,2012). Although opposite data is alsoavailable (Kohno *etal*.,1998) A positive association between *OGG1* Ser326Cys polymorphism andinsulin sensitivity, diabetes or diabetic complications are reported by severalgroups (Daimon *etal*.,2009;Sun *etal*.,2010) In the previous studies, *OGG1* Ser326Cys polymorphism wasexamined as a risk factor for the development of diabetes. However, the data about the effect of *OGG1* Ser326Cys polymorphism on the repair of the 8-OHdGlesion is limited. (Wu *etal*., 2015) determined that *OGG1* mRNA is lower and plasma 8-OHdG level is higher in T2DM patients carrying the Cys/Cys geno-type; *OGG1* Ser326Cys polymorphism shows a correlation with coronary arterylesions in T2DM patients. Genetic alterations in *OGG1* are thought to influence the development of oxidative stress and thus contribute to the pathophysiology of many diseases including cancer. While many sequence variants within the *OGG1* gene have been identified, the main focus has been on the Ser(326)-Cys variant, since several

epidemiological studies have associated the Ser(326)Cys polymorphism with many types of cancer including kidney, colon and lung cancer .(Kahn,2001; Farook Thameem, 2010) .Carriers of Cys/Cys were found to have lower *OGG1* activity and impaired ability to repair 8-OHdG than the carriers of Ser/Ser allele, thus contributing to the cancer risk.(Lee *etal*.,2005;Shamsa,2012) the Ser(326)Cys variant was reported to be associated with decreased insulin sensitivity in subjects with normal glucose tolerance suggesting that genetic alterations in *OGG1* may contribute to insulin resistance and potentially T2DM (Wang *etal*.,2006;Maglani *etal*.,2021).(Miglani *etal*.,2021)found that *OGG1* polymorphisms are significantly related to oxidative and genotoxic damage, and mutant type genotype presented higher levels of DNA damage. These results are similar to findings of (Chen *etal*.,2003) who showed higher repair activity of *OGG1* Ser/Ser for 8-OHdG than the *OGG1* Cys/Cys. Also, (Aka *etal*.,2004) and(Pawlowska *etal*.,2009) observed that Cys/Cys and Ser/Cys *OGG1* genotypes had less DNA repair capacity compared to the Ser/Ser *OGG1* genotype.*OGG1* DNA Repair Gene Polymorphism As a Biomarker of Oxidative and Genotoxic DNA Damage.There are a number of clinical studies, indicating that the mutant genotypes of *OGG1* have higher DNA damage and lower repair capacity of 8-OHdG than wild-type genotype(Wei *etal*.,1996;Paz-Elizer *etal*.,2003), which is associated with the risk of lung cancer(Wei *etal*.,1996), type 2 diabetes(Chen *etal*.,2011), breast cancer(Synowiec *etal*.,2008) and nasopharyngeal carcinoma(Cho *etal*.,2003). Some previous researchers have deduced that the reduced DNA repair capacity of mutant *OGG1* genotypes may result from either the loss of a putative regulatory serine phosphorylation site or the introduction of a redox-sensitive cysteine amino acid at position 326(Smart *etal*.,2006).

4. Conclusion and future scope

The potential.

Potential for Future Development

The healthcare data.

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Funding

Lorem ipsum dolor sit amer

Conflict of Interest

Lorem ipsum dolor sit amet

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