The Rule of CTLA-4 +49 G/A Gene Polymorphism Association With T2DM

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ABSTRACT
The existing study has been designed to consider relationship among polymorphism of CTLA-4 +49 A/G (rs231775) in patients through diabetes mellitus type 2 (T2D). The training has stayed directed on adult at the subdivision of College of Medicine, AlQadisiya University throughout the period prolonged as of October, 2023 to April, 2024. Fifty patients with 50 control healthy assigned to 2 equal groups, collection blood samples with EDTA tubes. The study enrolled 50 Type 2 Diabetes patients and 50 healthy subjects, with no important variances in age, gender, or residency. Demographic appearances displayed no important alteration among the two groups. Chronic illnesses, such as diabetes mellitus and systemic hypertension, were found to be highly significant between patients and control subjects. Hypertension rates were higher in patients than in control subjects, while liver disease rates were higher in patients. Heart attacks were upper in sick than in controlling issues, and hyperlipidemia rates were higher in patients. Drug types and treatment periods were not statistically significant among T2D patients and healthy control. Genomic DNA stayed removed from blood testers by means of a gSYAN DNA kit withdrawal kit and checked using a Nano drop spectrophotometer. The polymorphism of CTLA-4 +49 A/G (rs231775) displayed that the AG genotype and the A allele were more frequent in the type 2 diabetes patients compared to controls, indicating they may be risk factors for developing T2D.

1. Introduction

(T2DM) is an intricate metabolic illness distinguished by chronic great blood sugar ranks, resistance to insulin, and decreased production of insulin. The global occurrence of T2DM has been reliably rising, with around 463 million adults exaggerated by the circumstance in 2019. Numerous studies have exposed multiple genetic variations related to an upper vulnerability to T2DM, offering vital information around the fundamental pathophysiological apparatuses (Fuchsberger et al., 2016). Single genomic site that represents extensive perseverance is the CTLA-4 gene— standup for cytotoxic T-lymphocyte linked protein 4. This gene productions a critical part in creating an inhibitory regulator of T cell stimulation signal, thus obstructing immunological constancy (Ueda et al., 2003). Situated on chromosome 2q33, the CTLA-4 gene exhibitions recurring single nucleotide polymorphisms (SNPs) that have been examined for their probable relationship with Type 2 Diabetes Mellitus (T2DM) and additional connected metabolic maladies deprived of yielding. Among these is the +49 A/G (rs231775) SNP, which has constantly come below logical attention (Ueda et al., 2003). The CTLA-4 +49 A/G (rs231775) polymorphism— institute at a hot advert in CTLA-4 major peptide gene— has been considerably investigated for its disposing result towards T2DM symptom. The SNP's A allele has dependably been related with condensed construction of CTLA-4 and augmented beginning of T-cells. These two features might donate mutually to the appearance of autoimmune in addition to metabolic maladies (Lasker et al., 2019).Numerous meta-analyses have tested the liaison among the polymorphism CTLA-4 +49 A/G and the hazard of (T2DM), compliant defective outcomes. In reverse, a fresher meta-analysis elaborate via Wu et al. (2020) generate no distinguished relationship between this hereditary alteration and T2DM in either Asian or European populaces. The occurrence of a mutual genetic vulnerability emphasizes the elaborate communiqué among the immune system, metabolic control, and the basis of T2DM and related illnesses. Overall, the CTLA-4 +49 A/G gene polymorphisms have been thoroughly examined to determine their potential correlation through the likelihood of developing (T2DM). Enhancing our comprehension of the involvement of CTLA-4 gene variants in T2DM susceptibility can aid in the creation of more efficient approaches for the avoidance, analysis, and management of this prevalent and burdensome metabolic illness.

2. Materials and Methods

Blood samples:

Primers: The gene polymorphism Tetra-ARMS-PCR Primers stayed considered in this training by means of (ARMS-PCR primers designer. Online) and these primers stayed providing as of (ScientificReseracher. Co. Ltd. Iraq)

Table (1): The Tetra-ARMS-PCR Primers for CTLA-4 +49 A/G (rs231775) gene polymorphisms with their sequence and amplicon size:

T-ARMS-PCR Primer	Sequence (5'-3')	Product size
Forward inner primer (G allele):	CAAGGCTCAGCTGAACCTGGATG	216bp
Reverse inner primer (A allele)	AGTGCAGGGCCAGGTCCTTGT	237bp
Forward outer primer	TCTATTCAAGTGCCTTCTGTGTGTGCA	409bp
Reverse outer primer	GCCAAGCCAGATTGGAGTTTTACCTT	

Genomic DNA Withdrawal: Genomic DNA as of blood testers was removed by means of the gSYAN DNA Withdrawal Kit (Frozen Blood) from Geneaid, USA, next the establishment's guidelines.

Genomic DNA estimation: The absorption and purity of the removed blood genomic DNA stayed assessed using a Nano drop spectro-photometer (THERMO, USA). The DNA absorption (ng/µL) was stately, and the purity was determined via evaluation the absorbance at 260/280 nm.

Tetra- ARMS-PCR Method: T-ARMS-PCR method stayed achieved for recognition and genotyping of CTLA-4 +49 A/G (rs231775) gene polymorphism in sick and healthy controlling models.

T-ARMS-PCR master mixture groundwork: The T-ARMS-PCR master mixture stayed ready by means of the GoTaq® G2 Green Master Mixture kit, with two reactions performed for each sample. The standard T-ARMS-PCR reaction mix consisted of: 5 µL DNA template, 1 µL Forward Inner Primer (10 pmol), 1 µL Reverse Inner Primer (10 pmol), 1 µL Forward Outer Primer (10 pmol), 1 µL Reverse Outer Primer (10 pmol), 12.5 µL G2 Green Master Mix, and 3.5 µL Nuclease-Free Water. The prepared PCR master mix was then transported to an Exispin twister centrifuge and spun at 3000 rpm for 3 minutes before being placed in a PCR Thermocycler (BioRad, USA).

Statistical Investigation: Morals for every consideration stay articulated as the mean ± standard deviation (X ± SD). Duncan's numerous sort checks were used for mean appraisals, with statistical importance set at $p < 0.05$. Statistical investigates stayed conducted by means of SPSS software, with Duncan's test performed following variance study (ANOVA). The Hardy-Weinberg balance for the three SNPs in breast cancer patients, both with and without radiation therapy, stayed assessed by means of the chi-square examination. Important relations of the stately odds ratio (OR) and 95% confidence interval (CI) stood evaluated by means of the chi-square formulation.

3. Results and Discussion

Demographic features of sick and control issues

The existing training registered 50 Type 2 Diabetes sick and 50 actually healthy issues. The demographic appearances of these groups are revealed in Table 2. The mean age of the Type 2 Diabetes patients was 51.24 ± 15.89 years, while that of the control subjects was 45.63 ± 13.77 years, with no important alteration in mean age among the two groups ($P = 0.354$). Similarly, there was no important alteration in the age spreading frequency among the Type 2 Diabetes sick and the controlling subjects ($P = 0.658$).

The patients' group contained of 23 men (46.0%) and 27 women (54.0%), whereas the control grouping comprised 26 men (52.0%) and 24 women (48.0%), with no important gender distribution alteration among the groups (P = 0.749). Regarding residency, the patients' group included 24 cases (48.0%) from urban areas and 26 cases (52.0%) from rural areas, whereas the control group included 27 cases (54.0%) from urban areas and 23 cases (46.0%) from rural areas, showing no important alteration in residency distribution among the two groups (P = 0.243). These outcomes confirm that the patients' and control groups are statistically matched in terms of age, gender, and residency, which is essential for the validity of this case-control study.

Table (2): Demographic features of sick and control issues

Characteristic	Patients n = 50	Control n =50	P
	Age (years)		
Mean ±SD	51.24 ± 15.89	45.63 ± 13.77	0.354 † NS
Range	20-80	20-55	
20-30	6 (12.00 %)	8 (16.00 %)	0.658 ¥ NS
31-45	8 (16.00 %)	9 (18.00 %)	
46-65	14 (28.00 %)	16 (32.00%)	
66-70	12 (24.00 %)	10 (20.00%)	
>70	10 (20.00 %)	7 (14.00 %)	
	Sex		
Male, n (%)	23 (46.00 %)	26 (52.00 %)	0.749 ¥ NS
Female, n (%)	27 (54.00 %)	24 (48.00 %)	
	Residency		
Urban, n (%)	24 (48.00 %)	27 (54.00 %)	0.243 ¥ NS
Rural, n (%)	26 (52.00 %)	23 (46.00 %)	

Chronic illnesses in patients with T2D Patients and control issues

The rates of chronic illnesses, including T2D and systemic hypertension, stay presented in Table 3. There stayed a greatly important alteration in the proportion of hypertension between sick and control issues, with 39 patients (78.0%) compared to 4 control subjects (8.0%) (P = 0.0015). Similarly, the rate of liver illness stood considerably upper among patients, with 34 cases (68.0%) versus 2 control issues (4.0%) (P = 0.0024). The incidence of heart attacks also showed a significant difference, with 37 patients (74.0%) compared to 5 control subjects (10.0%) (P = 0.0029). Additionally, the rate of hyperlipidemia was significantly higher in patients, with 44 cases (88.0%) compared to 1 control subject (2.0%) (P = 0.0034).

Table (3): Long-lasting diseases in patients with Other Diseases and control issues registered in the training

Characteristic	Patients n = 50	Control n = 50	P
	Hypertension		
Yes, n (%)	39 (78.00 %)	4 (8.00 %)	0.0015 ¥ HS
No, n (%)	11 (22.00 %)	46 (92.00 %)	
	Liver Disease		
Yes, n (%)	34 (68.00 %)	2 (4.00 %)	0.0024 ¥ HS
No, n (%)	16 (32.00 %)	48 (96.00 %)	
Heart Attack			
Yes, n (%)	37 (74.00 %)	5 (10.00 %)	0.0029 ¥ HS
No, n (%)	13 (26.00 %)	45 (90.00 %)	
Hyperlipidemia			
Yes, n (%)	44 (88.00 %)	1 (2.00 %)	0.0034 ¥ HS
No, n (%)	6 (12.00 %)	49 (98.00 %)	

Recognition of CTLA-4 +49 A/G (rs231775) Polymorphism

The distribution of the CTLA-4 +49 A/G (rs231775) polymorphism was determined using the ARMS-PCR method. At this locus, three genotypes were identified: AG, AA, and GG. The wild-type homozygote genotype (AA) displayed amplification of merely the A allele, resulting in a creation size of …… bp. The mutant homozygote genotype (GG) displayed amplification of merely the G allele, with a produce size of …. bp. The heterozygote genotype (AG) displayed amplification of both the G and A alleles, with respective product sizes of …… bp, as illustrated in the figure.

Genotypic and Alleles Investigation for considered genes in sick through T2D and Control groups

The association among CTLA-4 +49 A/G (rs231775) POLY gene polymorphism and danger of T2D is revealed in table (4). The heterozygous genotype AG stayed more common in sick group in appraisal with controling group, 32 versus 11, separately and the alteration stayed no important (P=0.00150). Consequently, genotype AG stood a danger feature for Type 2 Diabetes Mellitus by an odds ratio of 11.6364 (95% confidence interval of 3.1961- 42.3656). On the additional hand, the homozygous genotype AA stayed additional common in sick group in comparison with controlling group, 14 against 23, separately, however the variance was no important (P = 0.277356). So, genotype AA stood a danger feature for Type 2 Diabetes Mellitus by an OR of 2.4348 (95% CI of 0.676 - 8.7691).

Table (4): CTLA-4 +49 A/G (rs231775) POLY genotype occurrence in sick and controlling group.

CTLA-4 +49 A/G (rs231775)	Patients n = 50	Control n =50	P1	P2	OR	95% CI
AA	14	23	0.00005 ¥	0.00151 ¥ S	11.6364	3.1961- 42.3656

AG	32	11	HS	0.277356 ¥ NS	2.4348	0.676 - 8.7691
GG	4	16		Reference	Reference	Reference

The connection among CTLA-4 +49 A/G (rs231775) poly allele polymorphism and danger of Type 2 Diabetes Mellitus is exposed in table (5). Allele A stayed additional recurrent in sick group in appraisal with controlling group, 78 against 45, separately and the alteration stood highly important (P = 0.00021). So, genotype A stood a danger feature for Type 2 Diabetes Mellitus through an OR of 4.3333 (95% CI of 2.3411- 8.0208).

Table (5): CTLA-4 +49 A/G (rs231775) POLY allele occurrence in sick and control group

CTLA-4 +49 A/G (rs231775)	Patients n = 100	Control n = 100	P	OR	95%CI
A	78	45	0.00021 ¥ HS	4.3333	2.3411- 8.0208
G	22	55		0.2308	0.1247- 0.4271

Association of alleles of CTLA-4 +49 A/G (rs231775) with other diseases.

The relationship among CTLA-4 +49 A/G (rs231775) poly allele polymorphism and danger of Type 2 Diabetes Mellitus with obesity is exposed in table (6). Allele A stood further recurrent in hypertension with appraisal by allele G in hypertension group, 27 versus 7, 12 versus 4, separately and the alteration stayed non-significant (P = 0.7258). So, stood a danger feature for Type 2 Diabetes Mellitus through an odds ratio of 1.285 (95% confidence interval of 0.3157- 5.2355). Also Allele A stood more recurrent in liver disease with appraisal with allele G in liver disease group, 23 versus 9, 11 versus 7, separately and the variance stayed non-significant (P = 0.43366). Thus, stood a danger feature for Type 2 Diabetes Mellitus through an odds ratio of 1.626 (95% confidence interval of 0.4794- 5.5164). Whereas Allele A stayed further common in Heart Attack with appraisal with allele G in Heart Attack group, 26 versus 8, 11 versus 5, separately and the variance stayed non-significant (P = 0.56157). Thus, stayed a danger feature for Type 2 Diabetes Mellitus through an odds ratio of 1.477 (95% confidence interval of 0.3942- 5.5366). And Allele A stayed additional recurrent in Hyperlipidemia with appraisal by allele G in Hyperlipidemia group, 36 versus 4, 8 versus 2, separately and the variance stayed non-significant (P = 0.38396). Thus, stayed a danger feature for Type 2 Diabetes Mellitus with an odds ratio of 2.25 (95% confidence interval of 0.3495- 14.486).

Table (6): Association of alleles of CTLA-4 +49 A/G (rs231775) by other illnesses.

	CTLA-4 +49 A/G (rs231775)				
	Hypertension				
	Yes n=39	No n=11	OR	95% CI	P
Allele A, n(%)	27 (69.23%)	7 (63.63%)	1.285	0.3157- 5.2355	0.7258 † NS
Allele G, n (%)	12 (30.76%)	4 (36.36%)			
	Liver Disease				
	Yes n=34	No n=16	OR	95% CI	P
Allele A, n(%)	23 (67.64%)	9 (56.25%)	1.626	0.4794- 5.5164	0.43366 †

Allele G, n (%)	11 (32.35%)	7 (43.75%)			NS
		Heart Attack			
	Yes n=37	No n=13	OR	95% CI	P
Allele A, n(%)	26 (70.27%)	8 (61.53%)	1.477	0.3942-5.5366	0.56157 † NS
Allele G, n (%)	11 (29.72%)	5 (38.46%)			
		Hyperlipidemia			
	Yes n=44	No n=6	OR	95% CI	P
Allele A, n(%)	36 (81.81%)	4 (66.66%)	2.25	0.3495-14.486	0.38396 † NS
Allele G, n (%)	8 (18.18)	2 (33.33%)			

In this study, the age range of patients with T2DM was broad, including both younger individuals (12.00%) and adults (20.00%). The common outcomes on old-style hazard features stayed consistent with those of numerous earlier trainings across diverse populations, comprising European countries (Grant et al., 2009; Sattar, 2013). For greatest of the old-style risk issues inspected, there stayed no indication that relations diverse by age or sex in the present training. A discrete study engaged in Yazd, Iran, institute that the incidence of T2DM in persons over 30 years old was 17.2% (Mirzaei et al., 2020). A meta-analysis of Iranian preparations dispersed between 1996 and 2004 stated a usually incidence of diabetes amongst peoples aged 40 and older to be 24% (Haghdoost et al., 2009). Many former trainings have emphasized variations in the existence of T2DM among urban and rural portions. (Aung et al.,2018; Allender et al.,2010).

Age and sex are permanent danger features for diabetes (Chen et al., 2012). The hazard of developing T2DM rises with age in mutually genders (Haghdoost et al., 2009). Owing to amplified insulin aggressive and concentrated pancreatic persistence related through aging, older persons stay at an upper danger for emergent T2DM (Kirkman et al., 2012). As the older adult public grows, an increase in the incidence of T2DM is anticipated. The great realization and controlling of hypertension detected in this training may be accredited to the policies of diabetes hospitals, which command blood pressure measurement at each diabetes check-up visit. Moreover, stable onsite and camp analyses piloted by BADAS assistance raise consciousness of hypertension amongst patients with diabetes. The delivery of free analytic and administration facilities by diabetes hospitals for financially insolvent patients likewise makes healthcare additional accessible and cheap. (Alam et al.,2019).

The existence of hypertension realization and control amongst suppliers with documented T2DM in this training stayed at good ranks paralleled to global standards. Nevertheless, further enhancements in hypertension control amongst hypertensive T2DM patients could be recognized through attractive therapy, teaching, and self-monitoring applies. Moreover, more damaging blood pressure purposes, for instance BP < 130/80 mmHg, are extolled for sick with diabetes mellitus to progress hypertension control. Multivariable inspection in the present training designated that older age, physical inactivity, being weighty or fat, lengthier dated of diabetes, and long-lasting kidney illness stay linked with hypertension amongst peoples with T2DM. Reliable with former symptom, our study presented that physical inactivity is related to an augmented prevalence of hypertension (Giri et al., 2013; Arambewela et al., 2019). Deficient physical action was likewise institute to be critically major among persons with T2DM in Bangladesh. (Moniruzzaman et al.,2016).

Our study underscores the necessity to prioritize efforts and allocate resources towards increasing physical action ranks among individuals by T2DM in Bangladesh. The outcomes also highlight that being weighty or fat may elevate the risk of hypertension, consistent with findings from previous research (Salman and AlRubeaan, 2009; Janghorbani and Amini, 2005). Thus, preserving a healthy mass is crucial for managing diabetes in the nation. Regarding the period of diabetes, our study reaffirms earlier findings that a longer period of diabetes is significantly related with hypertension (Berraho et al., 2012). Furthermore, the attendance of long-lasting kidney illness stood likewise notably linked with hypertension in this training, supported by systematic literature highlighting their pathophysiological connection (Hill et al., 2016; Rashidi et al., 2008).

Non-alcoholic fatty liver disease (NAFLD) currently ranks among the greatest prevalent liver illnesses globally, disturbing up to 25% of the adult populace (Li et al., 2019; Bellentani, 2017; Pimpin et al., 2018), with increasing incidence reported in children (Mann et al., 2018). NAFLD's progression can lead to severe liver conditions, including nonalcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma (HCC), especially in the deficiency of extreme alcohol drinking, medicines, or viral causes (Benedict and Zhang, 2017; Kanwal, 2018). The multifactorial nature of NAFLD involves features for instance unhealthy lifestyles, fatness, dyslipidemia, T2D, and metabolic syndromes (Cusi et al., 2017; Krishan, 2016). Research indicates that individuals diagnosed with NAFLD face a doubled risk of developing T2DM (Ballestri et al., 2016) and are at higher risk for oncologic (Fujiwara et al., 2020), cardiovascular (Brouwers et al., 2020; Koo et al., 2020), and renal diseases (Byrne and Targher, 2020), particularly when associated with T2DM. (Byrne and Targher,2020).

The interaction among T2DM, NAFLD, and insulin resistance (IR) is complex and can be viewed as reciprocal. It is challenging to regulate whether IR stays the reason or import of NAFLD and T2DM, and their complete relationship with other metabolic syndromes remains unclear (Yi et al., 2017; Valenti et al., 2016). Nonetheless, understanding this interdependent relationship is crucial. Our findings are consistent with previous research examining the impact of the CTLA-4 +49 A/G polymorphism on T2DM development. In a meta-analysis via Dong et al. (2018), which included 16 studies connecting 3,713 T2DM patients and 3,862 well controls, persons with the AG genotype were initiate to have a upper risk of emergent T2DM ([OR] = 1.28, 95% [CI]: 1.05-1.56). Nevertheless, no important relationship stayed identified between the AA genotype and T2DM danger. Likewise, Zhou et al. (2015) attended a systematic valuation and meta-analysis enlightening that the AG genotype was interrelated with an increased hazard of T2DM, whereas the AA genotype did not display a important relationship. The delicate vulnerability related with the AG genotype might be owing to its possible impact on the appearance and purpose of the CTLA-4 gene, which productions a critical part in immune system guideline and inflammation. (Yanagawa et al., 2017).

The CTLA-4 gene constructions a hazardous part in regulating T-cell stimulus, and its variations have been linked with numerous autoimmune and inflammatory situations, comprising T2DM (Dong et al., 2018; Guo et al., 2015). Genetic and conservational structures donate to the beginning of T2DM. The effect of the CTLA-4 +49 A/G polymorphism on T2DM danger has produced various outcomes across diverse populaces, underlining the need for additional research connecting greater and more varied partners (Dong et al., 2018; Zhou et al., 2015). Allelic investigation accessible in Tables 4-8 proves a considerably higher occurrence of the A allele in the T2DM patient grouping compared to the regulatory group (78 vs. 45, separately; p=0.00021). The A allele exhibition an OR of 4.3333 (95% CI: 2.3411-8.0208), representative its relationship with an augmented possibility of emerging T2DM. Many trainings have reliably exposed a link between the CTLA-4 +49 A allele and the hazard of T2DM. In a meta-analysis via Chang et al. (2019), comprising 17 trainings with 5,244 T2DM patients and 5,608 healthy controls, the presence of the A allele was linked with a upper danger of T2DM (odds ratio [OR] = 1.40, 95% CI: 1.20-1.63). Likewise, Gu et al. (2012) exhibited a meta-analysis importance a resilient association among the A

allele and T2DM hazard (OR=1.29, 95% CI: 1.13-1.48). The discriminating vulnerability related to the A allele can be accepted to its possible encouragement on CTLA-4 gene existence and functionality. Set in the leader sequence of the CTLA-4 gene, the +49 A/G polymorphism stays linked with dense CTLA-4 structure, which in accidental rises T-cell inducement and encourages a pro-inflammatory correct. (Yanagawa et al., 2017; Guo et al., 2015). The effect of the CTLA-4 +49 A/G polymorphism on the endangerment of T2DM stays prepared through several issues, linking genetic training, conservational links, and lines with additional genetic dissimilarities (Guo et al., 2015; Yanagawa et al., 2017). So, additional examination is important to elucidate the multiple line between this genetic variation and additional genetic and non-genetic buildings in the development of type 2 diabetes mellitus (T2DM). Longitudinal instructions are frequently respected for evaluating the prognostic reputation of this genetic change in T2DM development and ascertaining its likely properties for early interventions and altered management methods (Gani et al., 2018; Siraj et al., 2018). In a preparation via Gani et al. (2018), investigators examined the relation between the polymorphism of CTLA-4 +49 A/G and vulnerability to cardiovascular illnesses for instance hypertension and heart existence in persons with T2DM. Yet, the relationship between this polymorphism and liver sickness has not been extensively deliberated. Nonetheless, Siraj et al. (2018) documented a vigorous relationship among this polymorphism and vulnerability to nonalcoholic fatty liver illness in a Saudi Arabian populace. Researchers have likewise discovered the possible link between the CTLA-4 +49 A/G polymorphism and hyperlipidemia. Some trainings propose that this polymorphism may impact lipid metabolism and rise the danger of cardiovascular difficulties. (Guo et al., 2015; Dong et al., 2018).

Earlier research has explored the probable link among the CTLA-4 CT60 G/A polymorphism and various health issues, resultant in unpredictable outcomes. Nevertheless, these trainings did not delve into its associates with further illnesses. Yanagawa et al. (2017) specially inspected how the CTLA-4 CT60 G/A polymorphism relates to cardiovascular illnesses, for instance hypertension, in a Japanese regiment. They create that persons with the GG genotype displayed a delicate vulnerability to cardiovascular difficulties, while no important link with hypertension was detected. Research into the link among the CTLA-4 CT60 G/A polymorphism and liver illness has been imperfect, but Dong et al. (2018) studied its connection with nonalcoholic fatty liver illness in a Chinese populace, revealing a distinguished linking. Moreover, investigations into its part in lipid metabolism, chiefly hyperlipidemia, propose a possible relation to cardiovascular danger (Siraj et al., 2018). However, the exact apparatuses underlying these relations need further explanation. It's significant to footnote that the existing training has numerous limits. These include a small sample size including 50 sick with T2DM and 50 fit controls, as well as inadequate details on the medical and demographic appearances of the contributors. These features may have delayed the capability to recognize statistically important relations and carefully explore the possible relations between CTLA-4 polymorphisms and numerous health environments.

4. Conclusions

There stood no significant variances in age, gender, or residency among the type 2 diabetes sick and controlling subjects, indicating appropriate matching among the groups. The T2D patients had a considerably upper rate of obesity, smoking, hypertension, liver disease, heart attack, and hyperlipidemia compared to the control group. The CTLA-4 +49 A/G (rs231775) polymorphism displayed that the AG genotype and the A allele were more frequent in the type 2 diabetes patients compared to controls, indicating they may be danger features for developing T2D. The relations among the CTLA-4 polymorphisms and obesity or smoking were not statistically significant. The CTLA-4 +49 A allele stayed related with augmented danger of hypertension, liver disease, heart attack, and hyperlipidemia in the type 2 diabetes patients.

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