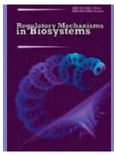

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Association between IL-17A rs2275913 gene polymorphism and the levels of inflammatory markers (NFKB1 and IL-17A) in Iraqi patients with diabetic nephropathy (T2DNP)

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One of the most common complications of chronic kidney disease (CKD) is diabetic nephropathy (T2DNP), which is increasing worldwide. This study aimed to examine the association between IL-17A rs2275913 gene polymorphism and diabetic nephropathy (T2DNP) in Iraqi patients. This study included 150 participants divided into three groups: Control, T2DM (Type 2 diabetes mellitus), and T2DNP. Inflammatory markers (IL-17A) were investigated following the protocol provided with the ELISA kit. Briefly, the enzyme immunoassays known as human NFKB1 and IL-17A were used to quantitatively and specifically identify these cytokines in human serum *in vitro*. The polymerase chain reaction method known as restriction fragment length polymorphism (PCR-RFLP) was used to detect the IL-17A rs2275913 SNP with specific utilization of particular primer sequences. The study found that levels of NFKB1 and IL-17A were significantly higher in the diabetic groups (T2DM and T2DNP) compared to the Control group. The Control group had NFKB1 levels of 1.15 ± 0.28, while the T2DM and T2DNP groups had levels of 4.83 ± 1.49 and 8.56 ± 1.16, respectively. For IL-17A, the Control group showed levels of 19.67 ± 1.85, while T2DM and T2DNP had levels of 43.04 ± 10.32 and 131.81 ± 13.13. The T2DN group exhibited the highest levels for both parameters, with a statistically significant p-value of 0.001 and the multinomial regression analysis examined the association between IL-17A gene polymorphism and T2DM/T2DNP. For the comparison of T2DM versus Control, the AA genotype had an odds ratio (OR) of 5.357, and the AG genotype had an OR of 2.857, both with significant p-values. In the T2DN versus Control comparison, the AA genotype had an OR of 6.562, and the AG genotype had an OR of 3.542, also significant. However, no significant associations were found between IL-17A genotypes and T2DNP compared to T2DM. The study concludes that there is a significant correlation between IL-17A gene polymorphism and diabetic nephropathy (T2DNP) in Iraqi patients, that both T2DM and T2DNP groups had higher levels of the inflammatory markers NFKB1 and IL-17A than the Control group, with the T2DNP group having the highest levels, and that certain IL-17A genotypes are associated with increased odds of developing T2DM and T2DN, but that there were no significant differences between T2DNP and T2DM in terms of IL-17A genotypes. These findings highlight the significance of IL-17A as a potential biomarker and genetic factor in the progression of diabetic nephropathy, suggesting directions for future research and clinical implications in managing diabetic nephropathy as a CKD complication.

Keywords: NFKB1; IL-17A; diabetic nephropathy; rs2275913; SNP.

Introduction

The metabolic condition known as diabetes mellitus (DM) is characterized by abnormally high blood glucose levels. Type 1, type 2, gestational diabetes, neonatal diabetes, maturity-onset diabetes of the young (MODY), and secondary causes resulting from endocrinopathies, steroid use, etc. are among the various types of diabetes mellitus (Sapra & Bhandari, 2023). Type 1 diabetes mellitus (T1DM) and Type 2 diabetes mellitus (T2DM) are the two primary subtypes of DM. T1DM and T2DM are both traditionally caused by impaired insulin production and/or action, respectively (Rajaei et al., 2019). While T2DM is believed to affect middle-aged and older adults who have chronic hyperglycemia as a result of poor lifestyle and nutritional choices, T1DM typically manifests in children or teenagers. Because T1DM and T2DM have very diverse pathophysiologies, each kind has its own etiology, presentation, and treatment (Shim et al., 2019).

Diabetic nephropathy is a microvascular complication that can occur in people with Type 1 diabetes (T1D) or Type 2 diabetes (T2D). Prolonged albuminuria and a steadily declining glomerular filtration rate (GFR) are the condition's hallmarks (Gui et al., 2023). There is strong evidence that intensive, early treatment can stop or slow the disorder's course. Although both T1DM and T2DM can cause diabetic nephropathy, T2DNP accounts for more than 90% of all cases of diabetes and is characterized by insulin resistance (Li et al., 2022). Four causative variables, roughly categorized as metabolic, hemodynamic, growth, and pro-inflammatory or pro-fibrotic factors, originate and sustain the pathogenesis of diabetic nephropathy (Qu et al., 2023). To facilitate discussion, we will characterize the pathogenesis as though each of these elements performed a separate role, despite the fact that there is significant overlap among them as well as variation in their relative contributions over time and among individuals. The glomeruli, tubuli, interstitium, and vasculature are among the renal compartments where these pathogenetic agents cause abnormalities (Umanath et al., 2018).

The progression from the earliest stages of kidney disease to an enlarged kidney with hypertrophy, expanded extracellular matrix (ECM), glomerulosclerosis, vascular hyalinosis, interstitial fibrosis and tubular atrophy, and loss of function leading to end-stage renal disease (ESRD) involves a complex network of molecules, receptors, enzymes, and transcription factors (Młynarska et al., 2024). According to previous research, diabetic nephropathy, which has emerged as a leading cause of death for patients with diabetes, eventually affects more than 20% of them (Zhang et al., 2020). Even though a number of risk factors for diabetic nephropathy have been proposed, including age, race, duration of diabetes, hyperglycemia, dyslipidemia, and hypertension, among others, it is still clinically significant to identify any remaining risk factors for diabetic nephropathy in order to stratify risk and manage the condition (Nowak, 2020; Russo et al., 2020).

One of the main microvascular complications of diabetes that results in end-stage renal disease is diabetic nephropathy (Navarro-González & Mora-Fernández, 2008). By driving mesangial expansion, podocyte destruction, and kidney fibrosis, the pro-inflammatory cytokine interleukin-17 (IL-17) contributes significantly to the pathophysiology of diabetic nephropathy, underscoring the intricate immunological pathways involved in DN (Navarro-González et al., 2009). Renal complications were observed in diabetes patients with the homozygous AA genotype, which carries the A allele of the rs2275913 gene polymorphism matrix metalloproteases and cytokines (Ma et al., 2019). Not only do T helper 17 cells (Th17) produce this cytokine, but other immune cells also emit it. Many intracellular signals are triggered by the IL-17A receptors (IL-17RC/IL-17RA) (Galvan & Danesh, 2016). The nuclear factor-kappa B (NF kappa B) cascade is initiated by IL-17A signaling, which leads to the transcription of pro-fibrotic chemokines [CXCL2 (C-X-C motif) and fibronectin and transforming growth factor beta (TGF-β)] (Sønder et al., 2011). The aim of this study to investigation of the association between IL-17A rs2275913 SNP and the levels of inflammatory markers (NFKB1 and IL-17A) in Iraqi patients with diabetic nephropathy (T2DNP).

Materials and methods

This study included 150 participants divided into three groups: control (n = 50), T2DM (n = 50), and T2DN (n = 50). Blood samples were collected from all participants for biochemical and molecular analyses. The ages of participants ranged from 25 to 70 years, with mean ages of 50.56 ± 8.14 years for the Control group, 54.8 ± 10.63 years for the T2DM group, and 52.86 ± 11.07 years for the T2DNP group. In this cross-sectional study, 50 patients with type 2 diabetes (T2DM), 50 patients with diabetic nephropathy (T2DNP) and 50 subjects as healthy individuals were enrolled.

Inflammatory markers (IL-17A) were investigated following the protocol provided with the ELISA kit. In brief, the enzyme immunoassays known as human NFKB1 and IL-17A were used to quantitatively and specifically identify these cytokines in human serum *in vitro*. The manufacturing company (BT-Lab, China) claims that this test was completed by using Enzyme-Linked Immunosorbent Assay (ELISA). Human IL-17 antibodies were applied to the plate beforehand. To attach to the antibodies coated on the wells, IL-17 from the sample was added. To bind to the IL-17 in the sample, biotinylated human IL-17 antibodies were then added. To attach to the biotinylated IL-17 antibodies, streptavidin-HRP was then added. Color developed in proportion to the quantity of human IL-17 after unbound Streptavidin-HRP was removed during the washing phase during incubation. Substrate solution was then added. After adding an acidic stop solution to stop the reaction, absorbance was measured in a microplate reader at 450 nm in a matter of minutes. The same procedure was performed for estimation of the NFKB1 marker.

Using the Favorgene® (Taiwan) Genomic DNA Purification Kit, the genomic DNA was extracted from the participants' (healthy subjects and patients) peripheral blood. DNA was kept at –20 °C until it was analyzed. 200 µL of the blood was moved to a 1.5 mL microcentrifuge tube once the frozen sample had thawed. After adding 30 µL of proteinase K (10 mg/mL) and quickly mixing, the mixture was incubated for 15 minutes at 60 °C.

The sample was mixed using a vortex mixer after 200 µL of FABG buffer was added. The sample was incubated in a water bath at 70 °C for 15 minutes. Throughout the incubation period, the sample was inverted every three minutes. Five microliters of 10 mg/mL RNase were used to create RNA-free genomic DNA The material was combined with a solution and vortexed before being incubated for five minutes. After adding 250 µL of absolute ethanol, the sample was vortexed for ten seconds. A 2 mL collecting tube was attached to the FABG column. After being moved to an FABG column, the sample mixture was centrifuged for five minutes at maximum speed (10000$^{\times}$ g). The 2 mL collection tube was then removed. The FABG column was put in a fresh 2 mL collection tube.

After washing the FABG column with 400 µL of W1 buffer, the flow-through was discarded after centrifuging the column for one minute at full speed (10000$^{\times}$ g). The FABG column was reinserted into the 2 mL collecting tube. 600 µL of wash buffer was used to clean the FABG column. The FABG column was then centrifuged for one minute at full speed (10000$^{\times}$ g). The FABG column was placed in a fresh 2 mL collection tube and centrifuged for an additional 3 minutes at high speed (10000$^{\times}$ g) to dry the column. One fresh 1.5 mL microcentrifuge tube was used to hold the dry FABG column. After adding 100 µL of hot elution buffer to the membrane center of the FABG column, the column was incubated for 10 minutes at 37 °C. To elute the DNA, the FAGB column was centrifuged for one minute at full speed (10000$^{\times}$ g) and finally the fragment of DNA was stored at –20 °C (Al-Gazally et al., 2016a, 2016b).

The DNA concentration was multiplied by the final volume of the purified sample to determine the total yield. Total Sample Volume (mL) × DNA Concentration (from device) = DNA Yield (µg). 300 µL of blood yields 2–3 µg of DNA in 50 µL of elution buffer. For the following analyses, only DNA samples with sufficient purity ratios (A260/A230 = 1.8–2.1) were employed. The scan drop instrument was used to assess the DNA purity ($A_{260\ nm}/A_{280\ nm}$), as illustrated in Figure 1.

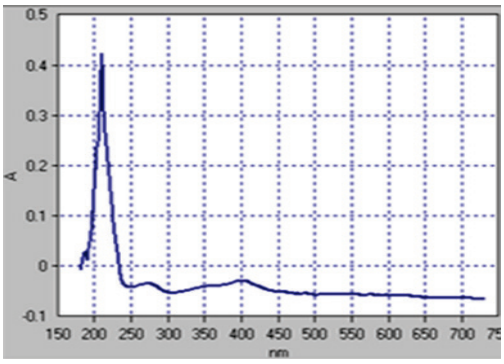

Fig. 1. DNA purity measurement using the scan drop device

For the PCR procedure, certain primers were employed. The Microgen company supplied primer pairs as a lyophilized product with different pico mole concentrations. To create a priming stock, the following steps were taken, per the Microgen company: To achieve 100 pmol/µL (master stock), the appropriate quantity of free nuclease water was supplied in accordance with the manufacturer's instructions. The lyophilized primer was dissolved in the sterile, nuclease-free water after being centrifuged for five minutes at 10,000 rpm. Before the caps were opened, the tubes were spun down. In order to create a master stock that would be utilized once more to create a working stock (final 200 µL working stock), the corporation provided the amount of sterile, 180 µL nuclease-free H_2O to be added to 10 µL for each primer (10 pmol). To equally re-suspend the primers, the tubes were thoroughly stirred by vortexing. The working stock was stored at –20 °C.

The polymerase chain reaction method known as restriction fragment length polymorphism (PCR-RFLP) was used to detect the IL-17A rs2275913 SNP with specific utilization of particular primer sequences as shown in Table 1.

Table 1
The primers' sequence for PCR-RFLP of IL-1A SNP

IL-17A gene	Primer 5'→3'	length	Tm	GC%
rs2275913	F: GCTCAGCTTCTAACAAGTAAG	21	62.6	43
SNP	R: AAGAGCATCGCACGTTAGTG	20	64.5	50

Tables 2 and 3 provide the reaction mixture and PCR conditions for the IL-17A SNP, respectively. Because the generated PCR product contained a cutting site, the enzyme EarI was chosen. The recognition sequence for EarI is CTCTTC. The enzyme will not cut the sequence if the type allele is G because its cutting site is eliminated, leaving only a single 338 bp band. In contrast, the enzyme will cleave the amplicon in the case of variant type allele A resulting in two bands of 259 and 79 bp. By using the agarose gel electrophoresis technique, the PCR product length, PCR reaction specificity, and restricted PCR product were examined.

Table 2
PCR master mix components for amplification of IL-17A SNP

1	DNA	–	10 µL
2	Master mix	2X	20 µL
3	F primer*	10 pmol	2 µL
4	R primer*	10 pmol	2 µL
5	Mgcl$_2$	–	
6	Nucleases free water	–	16 µL
	Final reaction volume	–	50 µL

Table 3
PCR thermo cycler conditions

No	Steps	Temperature, ºC	Time	No. of cycles
1	Initial denaturation	95	7 min	1
2	denaturation	95	40 s	35 cycle
	Annealing	63	30 s	
	polymerization	72	50 s	
3	Final polymerization	73	5 min	1

Statistical analysis was conducted utilizing the Graphpad Prism for Windows statistical software, version 6.0. Data are presented as means ± standard deviation (x ± SD). The impact of treatments was statistically assessed using the one-way analysis of variance (one-way ANOVA) followed by Turkey's post-hoc test to adjust for multiple comparison treatments. Statistical significance was established at the $P < 0.05$ level.

Results

Biochemical analysis. During this study, age, sex, and BMI were among the clinical and demographic traits compared between the Control, T2DM, and T2DNP groups. While there were no discernible changes (matched) in the distribution of sex or age, the study shows substantial differences in BMI status, as shown in Table 4.

Inflammatory markers (NFKB1 and IL-17A) in the studied groups. Table 5 compares the levels of NFKB1 and IL-17A among the control group (n = 50), T2DM (n = 50), and T2DNP (n = 50). The Control group had NFKB1 levels of 1.15 ± 0.28, while the T2DM group had 4.83 ± 1.49 and the T2DNP group had 8.56 ± 1.16 as shown in Figure 4. For IL-17A, the Control group showed levels of 19.67 ± 1.85, compared to 43.04 ± 10.32 in the T2DM group and 131.81 ± 13.13 in the T2DNP group as shown Figure 5. Both NFKB1 and IL-17A levels were significantly higher in the diabetic groups compared to the Control group, with the T2DNP group exhibiting the highest levels. The P-value of 0.001 for both parameters indicates statistically significant differences among the groups. The T2DNP group showed notably elevated levels of both NFKB1 and IL-17A compared to the T2DM group.

Table 4
Demographic and clinical characteristics of the studied groups (control, T2DM, T2DNP)

Characteristics		Groups						χ^2	P-value
		Control, n = 50		T2DM, n = 50		T2DNP, n = 50			
		n	%	n	%	n	%		
Age, year	mean ± SD	50.56 ± 8.14		54.80 ± 10.63		52.86 ± 11.07		–	0.110
Age groups	≤ 45 years	18	36.0	11	22.0	15	30.0	2.380	0.304
	> 45 years	32	64.0	39	78.0	35	70.0		
Sex	male	37	74.0	36	72.0	33	66.0	0.836	0.658
	female	13	26.0	14	28.0	17	34.0		
BMI, kg/m^2	mean ± SD	26.34 ± 3.07		28.07 ± 2.66		25.60 ± 2.60		–	0.003
BMI status	normal weight	22	44.0	10	20.0	29	58.0	15.372	0.004
	overweight	19	38.0	28	56.0	15	30.0		
	obesity	9	18.0	12	24.0	6	12.0		

Table 5
Inflammatory markers in studied groups (n = 50)

Inflammatory markers	Control	T2DM	T2DNP	P-value
NFKB1	1.15 ± 0.28	4.83 ± 1.49	8.56 ± 1.16	0.001*
IL-17A	19.67 ± 1.85	43.04 ± 10.32	131.81 ± 13.13	0.001*

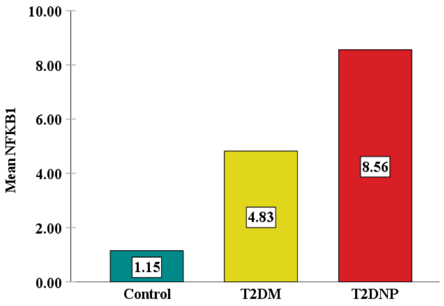

Fig. 2. Comparison of mean NFKB1 levels across Control, T2DM, and T2DNP groups

Frequencies of IL-17A rs2275913 SNP and alleles in the studied groups. The results of analysis of the genotype and allele frequencies of the IL-17A gene polymorphism (IL-17A rs2275913 SNP) in control, T2DM, and T2DNP groups show that significant differences were found in genotype distributions, with the AA genotype more prevalent in T2DM (23.3%) and T2DNP (23.9%) compared to Control (11.4%), and the GG genotype more common in Control (42.9%) than in T2DM (16.3%) and T2DNP (13.6%). The combined AA+AG genotype was also more frequent in T2DM (41.9%) and T2DNP (43.2%) compared to Control (28.6%) can show in Table 6.

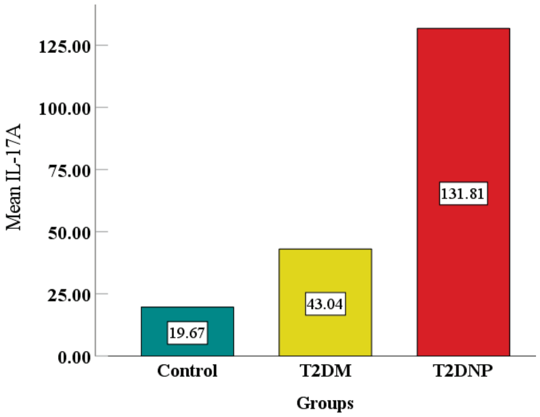

Fig. 3. Comparison of mean levels of IL-17A across Control, T2DM, and T2DNP groups

Allele frequencies showed the A allele was more common in T2DM (56.0%) and T2DNP (59.0%) than in Control (28.0%), while the G allele was more frequent in Control (72.0%) than in T2DM (44.0%) and T2DNP (41.0%). The P-values for genotype and allele frequencies were <0.001, indicating significant differences. Figure 4 shows the gel electrophoresis of amplified gene IL-17.

Table 7 presents the multinomial regression analysis for the association between IL-17A gene polymorphism and T2DM/T2DNP. In the comparison of T2DM vs. Control, the AA genotype had an odds ratio (OR) of 5.357 (95% CI: 1.900–15.106), and the AG genotype had an OR of 2.857 (95% CI: 1.071–7.621), both with significant P-values. In the comparison of T2DN vs. Control, the AA genotype had an OR of 6.562 (95% CI: 2.287–18.832), and the AG genotype had an OR of 3.542 (95% CI: 1.307–9.600), both with significant P-values as shown in Table 7. However, no significant associations were found between IL-17A genotypes and T2DN compared to T2DM.

Table 6
Genotype frequencies of IL-17A gene polymorphism

IL-17A SNP (rs2275913)	Control N	Control %	T2DM N	T2DM %	T2DN N	T2DN %	χ^2	P-value
AA	8	11.4	20	23.3	21	23.9	23.39	<0.001
AG	12	17.1	16	18.6	17	19.3		
GG	30	42.9	14	16.3	12	13.6		
AA+AG/GG	20	28.6	36	41.9	38	43.2		
Alleles								
A	28	28.0	56	56.0	59	59.0	23.48	<0.001
G	72	72.0	44	44.0	41	41.0		

Figures 5 and 6 show the frequencies of IL-17A (rs2275913) genotypes and alleles in the studied groups.

Discussion

The levels of inflammatory markers, NFKB1 and IL-17A were significantly increased in the T2DM and T2DNP groups as compared to the Control group, with peak values in the T2DNP group. These data suggest that chronic inflammation is a common underlying factor in the pathophysiology of diabetes and its complications, particularly in the progression to nephropathy. IL-17A has been implicated in the immune pathogenesis of T2DM through the activation of the NFKB pathway, leading to increased expression of other pro-inflammatory cytokines such as TNF-α and IL-6, which further promote insulin resistance and β-cell dysfunction (Donath & Shoelson, 2011; Qiu et al., 2020).

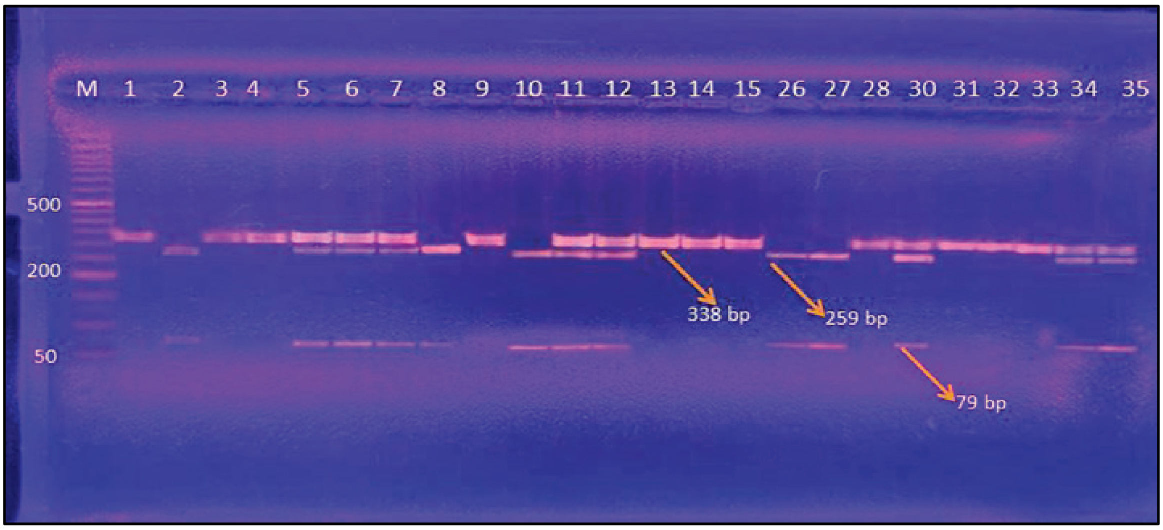

Fig. 4. Gel electrophoresis of amplified IL-17A rs2275913 SNP

Table 7
Multinomial regression analysis of IL-17A gene polymorphism association with T2DM and T2DNP (Control as reference)

Groups	IL-17A/Genotype	P-value	OR	95% CI	
T2DM/ Cont. [a]	AA	0.002	5.357	1.900	15.106
	AG	0.036	2.857	1.071	7.621
	AA+AG/GG	0.002	3.857	1.670	8.911
	GG	Ref.	1	–	–
T2DNP/ Cont. [a]	AA	0.000	6.562	2.287	18.832
	AG	0.013	3.542	1.307	9.600
	AA+AG/GG	<0.001	4.750	2.008	11.236
	GG	Ref.	1	–	–
T2DNP/T2DM [b]	AA	0.686	1.225	0.458	3.279
	AG	0.683	1.240	0.443	3.472
	AA+AG/GG	0.649	1.231	0.503	3.016
	GG	Ref.	1	–	–
	Allele frequencies				
T2DM/Cont.	A	<0.001	3.273	1.817	5.896
	G	Ref.	1	–	–
T2DNP/Cont. [a]	A	0.002	3.700	2.049	6.682
	G	Ref.	1	–	–
T2DNP/T2DM [b]	A	0.668	1.131	0.645	1.981
	G	Ref.	1	–	–

Note: the reference category is [a] – Control, [b] – T2DM; CI – 95% confidence interval; significant differences at $P < 0.05$.

For example, Lontchi-Yimagou et al. (2013) identified IL-17A as one of the top contributors in the development of DNP. Other studies conclude that IL-17A has paradoxical roles during the progression of DN (Afkarian et al., 2013; Lavoz et al., 2020). Besides, complicated diabetes mellitus associated with a high level of IL-17A chronic inflammation supports the hypothesis that inflammatory markers will help elucidate the burden of T2DM and its complications (Navarro-González et al., 2011).

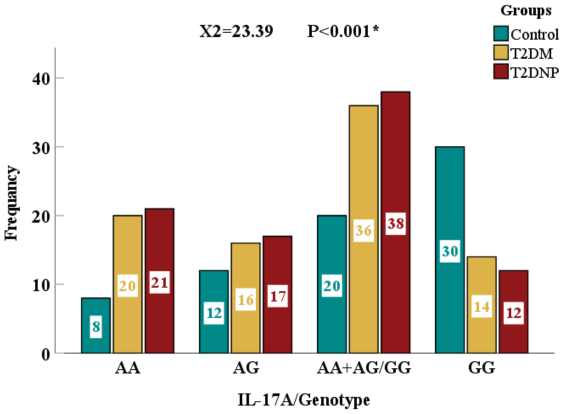

Fig. 5. Frequencies of IL-17A (rs2275913) genotypes

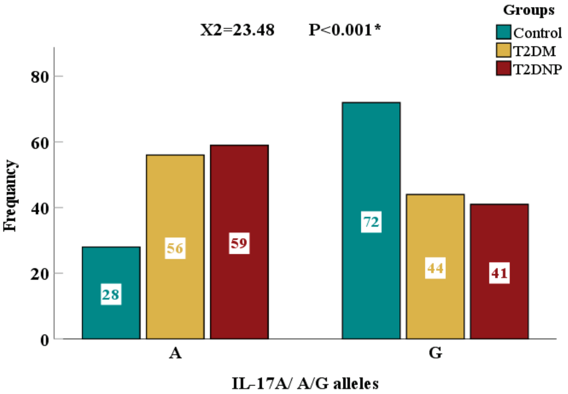

Fig. 6. Frequencies of IL-17A (rs2275913) alleles

Regarding NFKB1, a number of studies have been conducted to explain the role of NFKB1 in the context of T2DM and its complications, including diabetic neuropathy. For instance, one study by Sandireddy et al. (2014) demonstrated that NF-κB activation acts as a major mediator in the development of diabetic complications, which include neuropathy. This study identified that oxidative stress due to hyperglycemia activates NF-κB, which upregulates the expression of multiple pro-inflammatory cytokines, playing a critical role in the pathogenesis of diabetic neuropathy (Sandireddy et al., 2014). Similarly, in another study, Margaryan et al. (2020) discussed the role of NFKB1 in the context of insulin resistance and inflammation in females with T2DM. In the study, it was noted that NFKB1 activation was higher in the adipose tissue of T2DM patients, leading to the release of pro-inflammatory cytokines (Margaryan et al., 2020). These cytokines further exacerbate insulin resistance and further the development of diabetic complications such as neuropathy. Therefore, the investigators may draw the following conclusion . For improving the outcomes in diabetic patients, especially those at risk of nephropathy, intervention is needed at many levels, including insulin resistance, dyslipidemia, and inflammation leading to the release of pro-inflammatory cytokines. These cytokines further exacerbate insulin resistance and further the development of diabetic complications such as neuropathy (Adeyinka & Kondamudi, 2023).

For example, some genotypes of IL-17A have been identified as risk factors for type 2 diabetes mellitus. For instance, Li et al. (2016) reported a significant higher frequency of the AA genotype in diabetics as compared to controls in accordance with the current results (Li et al., 2016). Moreover, Li et al. (2022) indicated that the AA genotype of IL-17A showed a correlation with higher levels of IL-17A and increased inflammation in T2DM patients, suggesting thereby genetic susceptibility for diabetes. The above investigations support the current finding which states that the AA genotype predominantly existed in T2DM and T2DNP groups, thus being a potential risk for diabetes and its complication.

Several studies have analyzed the role of IL-17A genotypes in diabetic complications, such as T2DNP, and found that the AA genotype is associated with increased risk. For instance, Hammad et al. (2016) studied IL-17A polymorphisms in diabetic nephropathy and found that the AA genotype was more frequent in T2DNP patients, which correlated with higher IL-17A levels and disease severity (Hammad et al., 2016). Similarly, Salama-Frisbie et al. (2024) reported that the AA genotype of IL-17A was associated with increased inflammation and progression of diabetic nephropathy, consistent with the present study. The results are in agreement with the present observation that the AA genotype confers a higher risk of diabetic nephropathy, most probably due to its pro-inflammatory effects (Salama-Frisbie et al., 2024).

The GG genotype has also proved to be protective in studies on diabetes and its complications . It was found by Sasi Kumar et al. (2021) that the GG genotype of IL-17A was related to lower levels of IL-17A and diminished inflammation in healthy people, so this may give it a protective effect from diabetes; they also reported that the GG genotype was more frequent in healthy controls and was related to favorable metabolic outcomes in comparison with AA genotype (Sasi Kumar et al., 2021). These studies will support the present observation that the GG genotype is more prevalent in the Control group and may be responsible for protection against diabetes and complications.

Many research studies have associated the alleles of IL-17A with diabetic complications, including nephropathy, with an increased risk due to the A allele. Nazarian et al. (2022), in the study of IL-17A polymorphisms in diabetic nephropathy, found that the A allele was higher among T2DNP patients. Moreover, it is associated with an increased level and severity of IL-17A. Similarly, Lavoz et al. (2019), indicated the association of allele A of IL-17A in inflammation and diabetic nephropathy progression. In conclusion the findings of this study are in concert with the findings of Lavoz et al. (2019), as the result of the current study shows an increased risk related to A allele in diabetic nephropathy ,possibly through proinflammatory activity.

Conclusion

Overall, this study generally reveals the level of metabolic, renal, and inflammatory disturbances in diabetes subjects with even higher levels in their nephropathy equivalents; findings indicating a very real need for a systemic approach including management of blood glucose levels, normalization of lipid profile, and reduction of inflammation to minimize the complication load in these subjects. To the researcher, these findings indicate a complementary approach to the management of diabetes and the prevention of its complications by anti-inflammatory therapies. With this in mind, higher levels of IL-17A and NFKB1 in the T2DNP group may reflect a particular inflammatory pathway to nephropathy that may be further investigated in further studies.

The Department of Physiology at Baghdad University provided an ethical permission letter (No: 200, 10/08/2022) to authorize the conducting of this scientific experiment in the Baghdad hospitals.

Authors declare no conflict of interest recorded in this study.

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