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Study of IFN-γ gene Polymorphism and Susceptibility to Diabetes Type 1 in Egyptian Children

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Abstract

Type 1 diabetes T1D is an autoimmune disease resulting from progressive T-cell-mediated, selective destruction of beta cells in the pancreas. Our study aimed to identify the association between IFN-γ gene polymorphism and susceptibility to TID in Egyptian children. This study included 100 Egyptian children with TID and 100 healthy controls. DNA was genotyped for IFN-γ (+874T/A) variant using the (T-ARMS-PCR) approach.

This study found that the presence of the rare alleles of the IFN-γ gene in combination either in homozygous or heterozygous forms was not significant in Egyptian cases with type 1 diabetes compared to controls, there was no relationship between the INFG (+874T/A) gene polymorphism and T1D patients' age, gender, weight, height, and body mass index .No significant difference between the blood pH of D1T cases and the presence of INFG (+874T/A) genotypes Similarly, no further features were associated with the partial pressure of CO2 in arterial blood (pCO2) or blood (HCO3-) bicarbonate levels. There is a significant difference between the random blood sugar (RBS) level of the T1D cases and the presence of INFG (+874T/A) genotypes but no significant difference in hemoglobin A1c percent (HbA1c). No significant difference in blood thyroid function hormones T3, T4, TSH, also the blood creatinine and urea levels of T1D.

Our finding indicated a non-significant association between the presence of the rare alleles of IFN-γ gene polymorphism and susceptibility to diabetes type 1 in Egyptian children.

Keywords: IFN-γ, gene polymorphism; diabetes type 1, Egyptian children.

Introduction

Diabetes mellitus is one of the most prevalent chronic disorders in children. Although a rising incidence of pediatric type 1 diabetes (T1D) has frequently been documented, an over 400-fold variability in incidence has been seen

globally(Cohen et al., 2022) **.**

T1D is a disease characterized by the loss of a kind of cell in the pancreas that produces the hormone insulin, leading to a lifelong dependency on insulin shots. (Felton et al., 2023). T1D is a chronic autoimmune illness marked by insulin insufficiency and subsequent hyperglycemia. Complex interactions between genetic and environmental variables cause autoimmunity to β cell antigens and T1D. (Lloyd et al., 2022).

Diabetes mellitus is a complex condition in which hereditary factors such as cytokines play a significant influence. Cytokines modulate the immune system and have been linked to the development of diabetes mellitus (Khdair et al., 2023).

Diabetes may raise the levels of cytokines in the blood (D'Agostino et al., 2023).

Cytokine-encoding genes are among the risk factors. Cytokines are crucial in cell-mediated immunity, resulting in the death of Beta cells that produce insulin (Daems et al., 2019)**.**

The cytokines Th1 (IFN-γ and IL-2), Th17 (IL-17A), and pro-inflammatory (IL-1β, IL-6, and TNF-α) can all lead to Insulitis. Reduced Th1 and inflammatory responses, such as IL-1Ra, Treg (IL-10 and TGF-β), and Th2 (IL-4) cytokine antagonists, may provide protection. (Wang et al., 2019) Key cytokines include IL-1β, TNF-α, as well as IFN-γ. responsible for inflammation or β-cell death in the islets of Langerhans. (Akil et al., 2021). Single nucleotide polymorphisms SNPs in genes encoding cytokines can alter gene expression and cytokine production, as well as the shape and function of cytokine molecules(Behzadi et al., 2022)**.** Some disorders have been linked to Single nucleotide polymorphisms, according to reports (Elsaid et al., 2021) (Metwally et al., 2023a; Metwally et al., 2023b).

TID patients exhibit increased levels of pro-inflammatory cytokines, such as (TGF-β), interferons (IFNα/β, IFNγ), nitric oxide (NO), The interleukins (IL-1α, IL-1β, IL-10, IL-12) plus tumor necrosis factors (TNFα, TNFβ).

Only type II interferon, IFN-γ, was identified more than 60 years ago. Friedrich Willock was the first to characterize IFN-γ as an interferon inhibitor resulting from phytohemagglutinin generated by activated white blood cells. The IFNG gene codes for the protein IFN-γ, which is made up of two polypeptide chains linked in an antisense manner. (Alspach et al., 2019)

Aim of the study:

This study aimed to identify the association of IFN-γ gene polymorphism and susceptibility to diabetes type 1 in Egyptian children**.**

Methods

Ethical recognition of research

Before participating in the study, all participants provided written informed consent, and blood samples were collected in accordance with methods authorized by the Hospital's Outpatient Clinic's Ethics Committee.

Medical Research Ethics Committee Institutional Review Board (Mansoura Faculty of Medicine Mansoura University), Code Number: R.22.01.1594 . Date: 03/03/2022

Study populations

T1D patients undergo screening and diagnosis between March 2022 and July 2022 in the Genetic Unit of University Children's Hospital. The study includes 100 Egyptian children with T1D from the Endocrine Unit of the University Children's Hospital and a total of one hundred controls**.**

The participants were divided as follows:

This study is a case-control study. The study included (100) patients (54) males (54%) and (46) females (46%). The median (IQR) of age was 11.8 (9.0-13.9) years. Children patients aged between 2 –19 years. The median (IQR) weight was 45.0 (35.0-52.0) kilograms., and the median (IQR) of height was 131.0 (109.3-145.0) centimeters. The median (IQR) of BMI was 27.1 (21.1-34.6) Kg/m2.

Control Studied:

100 healthy children (61) males (61%) and 39 females (39%) aged (3 -19) years. The median (IQR) of the age of controls was 10.0 (8.0-13.0) years. The median (IQR) weight was 30.0 (25.0-39.0) kilograms. The median (IQR) height was 112.0 (98.0-130.0) centimeters. The median (IQR) of BMI was 24.1 (20.3-30.8) Kg/m2.

Sampling

3 milliliters of peripheral blood were drawn from each patient using vacationers. It is placed in test tubes containing an anticoagulant solution, such as EDTA to extract and purify whole blood for DNA analysis (Alexander, 2023; Flynn, 2023). Additionally, peripheral blood samples are obtained to analyze biochemical indicators associated with T1D. such as glucose(Akturk et al., 2024), creatinine, urea, Na, K,CBC,PCO2,HCO3,RBS (Gillery, 2024),HBA1C (Boucsein et al., 2024),T3,T4,TSH,PH, and acetone in urine.

DNA extraction and purification

All participants in this study handled and extracted genomic DNA by applying the generation DNA purification capture column kit (Fermentas,K 0721 Canada). (Tan & Yiap, 2009) .
T-ARMS-PCR was used to amplify and genotype variations of the IFN-Y genes (Medrano & De Oliveira, 2014) **.**

Genetic analysis

Determination of the genotypes Polymorphism of (IFN γ +874A>T) (Lee & Song, 2022) . (Pravica et al., 2000).

The investigation identified an IFN-γ T/A polymorphism with an SNP at +874 location. The SNP typing protocol is described by (Pravica et al., 2000**)**,
A single-stranded oligonucleotide was used to identify T and A polymorphism sequences, covering a 24-base pair area for each allele.
A polymerase chain reaction (PCR) amplification refractory mutation system was carried out in a total volume of 20 µl, comprising 4 µl of generic primer (10 pmol / µl): 5- TCA ACA AAG CTG ATA CTC CA – 3 , with 4 µl of specific A primer (10pmol /µl 5- TTC TTA CAA CAC AAA ATC AAA TCA – 3) or 4 µl of specific T primer (10 pmol / µl). 5- TTC TTA CAA CAC AAA ATC AAA TCT – 3), 10 µl Master Mix (Dream Taq Green PCR Master Mix (2X), Fermentas, USA). and 2 µl of genomic DNA. A thermocycler was used to carry out the ARMS-PCR. ARMS: "PCR amplification results were electrophoresed on 2% agarose gel and under UV light, ethidium bromide was observed (Elmougy et al., 2021) .
A digital camera was used to take a picture of the 262 bp PCR amplified products.
The patient's TA genotype is shown by two bands at 262 bp, one with primer T and the other with primer A.
Conversely, the patient has the TT genotype if there is a band at 262 bp with the T primer and no band with the forward A primer.
The patient has the AA genotype when there is a band at 262 with the A primer and no band with the forward T primer.

Statistical analysis

The data was handled and analyzed using SPSS, version 20 of the Statistical Package for Social Sciences. The quantitative variables were defined by mean and standard deviation and compared using the t-test. On the other hand, A comparison was made between the frequency of the allelic polymorphism under examination and the controls, utilizing the percentage and number of each for testing purposes, using Fisher's exact test and odds ratio (OR) with 95% confidence intervals (CL) to check for positive connection. A p-value of less than 0.05 indicates statistical significance. The link was studied in multiple inheritance models for instance, the dominant model compares the combined homozygous and heterozygous versions of the rare allele against others, whereas the recessive model compares homozygosity for the uncommon allele against others (Elsaid et al., 2012). On the one hand, comparing heterozygous and homozygous variants individually against the wild type of variant revealed the codominant model, however, evaluating the heterozygous variant alone against others revealed the over-dominant model of inheritance. Furthermore, a comparison between the predicted and observed genotypes yielded the Hardy-Weinberg equilibrium (HWE). frequencies associated with the polymorphisms under consideration. A P-value less than 0.05 indicates significance. In silico data analysis was illustrated in **Figure 1.**

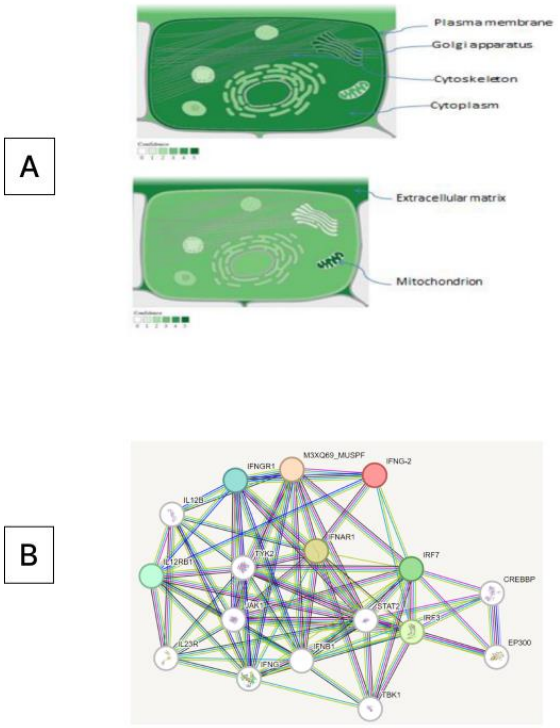

Figure 1: In silico data analysis A) Subcellular localization of IFN-γ protein. Darker color, according to the provided color key, indicates more abundance (data source: https://compartments.jensenlab.org/Search).
B) Functional protein association networks. https://string-db.org/cgi/network?taskId=bSEt83ShLnXhG&sessionId=bPXI7esoMMsk

Results:

In T1D cases, the frequencies of (IFNG) (+874T/A) genotypes and alleles in diabetic patients and healthy controls matched Hardy-Weinberg equilibrium. (HWE). IFNG (+874T/A) genotype frequencies were 51% (TT), 36% (TA), and 13% (AA) in patients with type 1 diabetes (T1D), and 66% (TT), 27% (TA), and 7% (AA) in healthy controls. TID patients had considerably greater frequencies of the A-allele vs T-allele of the IFNG (+874T/A) in comparison to controls.{ (p)= 0.02; OR = 1.74, 95% CI = 1.1-2.75}.
Numerous genetic models were investigated, including recessive, overdominant, dominant, heterozygote, homozygote, and allelic models. Patients with Type 1 diabetes (T1D) did not significantly vary from controls in terms of the frequency of the recessive model (AA) genotype of IFNG (+874T/A) vs (TT+TA). (p = 0.24; OR = 1.99 and 95% CI = 0.76-5.2). Similarly, There was no detectable difference in the frequency of the over-dominant model (TA) genotype vs (TT+AA) between patients with diabetes type 1 (D1T) and controls. (p = 0.22; OR = 1.52 and 95% CI = 0.83-2.77).
In contrast, patients with diabetes type 1 (D1T) had significantly greater frequencies of the dominant model (TA+AA) vs (TT) genotype of the IFNG (+874T/A) than controls (p = 0.04; OR = 1.87 and 95% CI = 1.05-3.29). In patients with DT1, the number of cases of heterozygote genotype (TA) vs (TT) genotype was not much higher than in controls. (p = 0.09; OR = 1.73 and 95% CI = 0.93-3.2). When D1T patients and controls were examined, there was no noticeable difference in the frequency of the homozygote mutant (AA) vs. (TT) genotype (p = 0.09; OR = 2.4, 95% CI = 0.89-6.46).

Table 1. The INFG (+874T/A) gene polymorphism among Egyptian subjects with diabetes type 1 (D1T) compared to controls

***INFG* gene polymorphism**		**DT1 patients (n=100) n (%)**	**Controls (n=100) n (%)**
TT		51 (51%)	66 (66%)
TA		36 (36%)	27 (27%)
AA		13 (13%)	7 (7%)
T-Allele		138 (69%)	159 (79.5%)
A-Allele		62 (31%)	41 (20.5%)
HWE		χ^2= 2.5, *p* = 0.11	χ^2= 2.9, *p* = 0.09
Statistics		OR (95% CI)	*P*
Recessive	AA vs. TT+TA	1.99 (0.76-5.2)	0.24
Over-dominant	TA vs. TT+AA	1.52 (0.83-2.77)	0.22
Dominant	TA + AA vs. TT	1.87 (1.05-3.29)	0.04*
Heterozygote	TA vs. TT	1.73 (0.93-3.2)	0.09
Homozygote	AA vs. TT	2.4 (0.89-6.46)	0.09
Allelic	A vs. T	1.74 (1.1-2.75)	0.02*

TT: homozygous wild-type, TA: heterozygous-genotype, AA: homozygous-mutant, *p*: probability, OR: Odds Ratio, CI: Confidence Intervals, *$p < 0.05$ = significant, **$p < 0.0001$ = highly significant, $p > 0.05$ = non-significant, HWE: Hardy–Weinberg Equilibrium, n = number of cases.

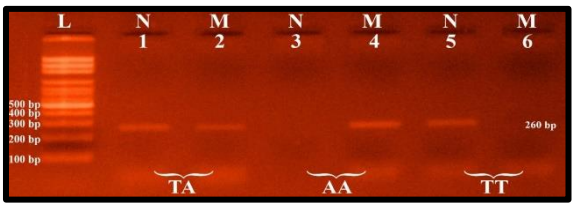

Figure 2. Microphotography of IFNG (+874T/A) (rs2430561) gene polymorphism for DT1 cases and controls using ARMS-PCR.

(N= Normal, M= Mutant, L= 100 bp (base pair) ladder DNA marker)
(TT: homozygous wild-type, TA: heterozygous-genotype, AA: homozygous-mutant).

The INFG (+874T/A) gene polymorphism according to the main demographic characteristics of patients with Type 1 diabetes (T1D) Table 2 classifies the INFG (+874T/A) gene polymorphism in T1D patients according to their age, gender, weight, height, and BMI. This table revealed no statistically significant association between the age, gender, weight, height, and body mass index (BMI) of people with type 1 diabetes and the presence of INFG (+874T/A) genotypes (p)greater than 0.05. This indicates that there was no relationship between the absence or presence of the INFG (+874T/A) gene polymorphism and T1D patients' age, gender, weight, height, and body mass index (BMI).

Table 2. Genotypes of the *INFG* (+874T/A) variant according to the main demographic characteristics &the blood gas analysis of patients with diabetes type 1 (D1T)

Parameter	**DT1 patients(n=100)** *INFG(+874T/A) genotypes* (TA+AA) n=49	TT n=51	***P***
Age(years):Median(IQR)	11 (9.3-13.5)	12(8-14)	0.71
Gender Male(n%) Female (n%)	26(53.1%) 23(46.9%)	28(54.9%) 23(45.1%)	1
Weight (Kg):Median (IQR)	43(33-52.5)	45(35-52)	0.41
Height (Cm): Median(IQR)	130(112-145.5)	132(98-145)	0.78
BMI (Kg/m^2): Median(IQR)	25.6(19.1-35.3)	27.3(23.04-34.3)	
PH; (IQR)Median	7.3 (7.2-7.4)	7.3 (7.2-7.4)	0.75
PCO_2 (mmHg); Median (IQR)	33.1(24.1-40)	36.6 (25.1-42.5)	0.16
HCO_3 (mmole/L) ; Median (IQR)	18.7 (12.2-22.7)		0.27

Ph= Arterial blood pH, pCO_2: Partial pressure of carbon dioxide in arterial blood, HCO_3^-: Bicarbonate level, IQR: Interquartile Range; *p*: probability, $p < 0.05$ = significant, $*p < 0.001$ = highly significant, $p > 0.05$ = non-significant, n = number of DT1 patients.

This table revealed no significant difference between the blood pH of D1T cases and the presence of INFG (+874T/A) genotypes ($p > 0.05$)., Similarly, no further features associated with the partial pressure of CO_2 in arterial blood (pCO2) or blood (HCO3-) bicarbonate levels of D1T cases showed an association with INFG (+874T/A) genotypes (p) greater than 0.05). This demonstrates that there was no link between the absence or presence of the INFG (+874T/A) gene polymorphism with the blood gas analysis of T1D patients.

The INFG (+874T/A) gene variant according to the blood sugar tests and ketones level in urine& the thyroid function tests of patients with Type 1 diabetes (T1D)

Table (3) shows the INFG (+874T/A) gene polymorphism stratified by the blood sugar tests and ketone levels in the urine of D1T patients. This table demonstrated a significant difference between the random blood sugar (RBS) level of the T1D cases and the presence of INFG (+874T/A) genotypes ($p < 0.05$). In contrast, none of the other metrics linked to hemoglobin A1c percent (HbA1c), and ketone levels in the urine of D1T cases showed any correlation with INFG (+874T/A) genotypes ($p > 0.05$). The existence or absence of the INFG (+874T/A) gene polymorphism was related to D1T patients' random blood sugar (RBS) levels. Furthermore, there was no connection between the presence or absence of the INFG (+874T/A) gene polymorphism and the hemoglobin A1c percentage and ketone level in the urine of D1T patients, this table also revealed no significant difference in blood triiodothyronine (T3) levels between D1T cases and those with INFG (+874T/A) genotypes ($p > 0.05$). Similarly, no additional metrics related to blood thyroxine (T4) or thyroid-stimulating hormone (TSH) levels in D1T cases revealed any connection with INFG (+874T/A) genotypes (p greater than 0.05). This indicates that there was no relationship found between the blood T3, T4, and TSH levels of D1T patients and the absence or presence of the INFG (+874T/A) gene polymorphism.

Table 3. Genotypes of the INFG (+874T/A) variant according to the blood sugar tests and ketones level in urine& the thyroid function tests of patients with Type 1 diabetes (T1D)

Parameter	**DT1 patients(n=100)** *INFG(+874T/A) genotypes* (TA+AA) n=49	(TT) n=51	***P***
RBS (mg/dL) ; Median (IQR)	435(399-510)	412 (340-463)	0.016
HbA1C (%) Median) (IQR)	8.5 (7.25-9.5)	8.4 (7.3-9.2)	0.72
Ketones in urine ; n (%) Positive (+) Negative (-)	24 (49%) 25 (51%)	23 (45.1%) 28 (54.9%)	0.42
RBS:Random blood sugar , HbA1C : hemoglobin A1C, n:number of patients IQR: Interquartile Range; *p*: probability, (*p*)< 0.05 = significant,(*p*)< 0.001 = highly significant,(*p*) > 0.05 = non-significant, n = number of DT1 patients			
T3 (ng/mL); (IQR) Median	1.44 (1.04-1.6)	1.4 (1.2-1.76)	0.56
T4 (µg/dL); (IQR)Median	7.6 (6.9-9.3)	7.8 (6.9-8.9)	0.82
TSH (mU/L); (IQR) Median	2.0 (1.6-2.6)	2.1 (1.5-2.4)	0.69
T3= triiodothyronine, T4= thyroxine, TSH=thyroid-stimulating hormone, n: number of patients; IQR: Interquartile Range; *p:* probability, (*p*)< 0.05 = significant,(*p)* < 0.001 = highly significant,(*p*)> 0.05 = non-significant.			

Table 4. D1T patients' kidney function tests were used to stratify the INFG (+874T/A) gene polymorphism. According to this table, the existence of INFG (+874T/A) genotypes and blood creatinine levels in T1D cases did not significantly differ from one another ($p > 0.05$). Corresponding to this, blood urea levels did not significantly differ between INFG (+874T/A) genotype carriers and T1D cases ($p > 0.05$). This implies that the blood creatinine and urea levels of T1D patients were unrelated to the absence or presence of the INFG (+874T/A) gene polymorphism.

Table 4. Genotypes of the INFG (+874T/A) variant according to kidney function tests

Parameter	**DT1 patients (n=100)**		***p***
	INFG (+874T/A) genotypes		
	(TA+AA) (n = 49)	TT (n = 51)	
Creatinine (mg/dL); (IQR) Median	0.6 (0.4-0.7)	0.5 (0.3-0.6)	0.24
Urea (mg/dL); (IQR) Median s=	48.5 (42-52)	45 (41-51)	0.22

n: number of patients; IQR: Interquartile Range; *p:* probability, (*p*)< 0.05 = significant, (*p*) < 0.001 = highly significant,(*p*)> 0.05 = non-significant.

Discussion:

T1D typically begins in people under the age of 30, hence it is sometimes known as juvenile-onset diabetes, despite the fact that it can occur at any age. T1D is a chronic autoimmune illness that is triggered in genetically sensitive individuals by environmental triggers(Al-Husseini, 2020) (Fagbemi et al., 2017; Van Belle et al., 2011) **.** The immune system targets the beta cells in the pancreas islets of Langerhans, killing or injuring them enough to limit, if not eliminate, insulin production. On rare but growing occasions, both T1D and T2D are detected in patients (Ivashkiv, 2018)**.**

To our knowledge, this is the first study to interpret the association of IFN-γ gene polymorphism and susceptibility to diabetes type 1 in Egyptian children.

The involvement of cytokines in the pathogenesis of autoimmune illnesses, notably T1D, has been extensively studied to uncover their potential therapeutic effect.

Screening for cytokines during the early stages of T1D can be beneficial in detecting soluble components relevant to the immune response and better diagnosing and treating the condition (Borilova Linhartova et al., 2019; Cano-Cano et al., 2022)**.**

This study found that Egyptian individuals with type 1 diabetes had considerably greater levels of the unusual alleles of TGF-β1 gene, either homozygous or heterozygous, compared to the control group. There were no significant differences in the IFN-γ gene.

In the current study the genotypes frequencies of the *IFNG* (rs2430561) (+874T/A) showed no significant statistically where $p = 0.09$.

Our results confirmed by previous reports of these polymorphisms are unrelated to T1D (Bazzaz et al., 2014) . Also, our study similar to the report by (Rafinejad et al., 2004) showed a negative relationship between IFN-γ gene polymorphisms and T1D in Iranian patients, indicating that the T allele may be a protective factor against T1D. Moreover, the current study is similar to that conducted by (Yadav et al., 2022)**,** there is no significant difference between tuberculosis (TB) cases and controls P = 0.108.

Our study is supported by the previous study by (Bazzaz et al., 2014; Visentainer et al., 2005)**,** they found no statistically significant change in serum IFN-γ levels when compared to controls. In contrast, two independent investigations have found links between IFN-γ gene polymorphisms in intron 1 and T1D (Jahromi, 2000; Kadowaki et al., 1994)**.**

The current result revealed that the frequency of the IFNG T-allele (+874T/A) is higher in patients and controls than the A allele, The frequency of the A-allele vs the T-allele of the IFNG (+874T/A) was considerably greater in DIT patients compared to controls. ($p = 0.02$; OR = 1.74 and 95% CI = 1.1-2.75). This founding result agreed with Iraqi Children (Hussein et al., 2017)was observed The T allele frequency was found to be higher than that of the A allele in both Type 1 diabetes patients and controls. When Fisher's test was employed, the frequencies of the A allele in the T1D patient sample differed significantly from the control group. The frequencies of the A allele in the T1D patient sample were significantly different from the control sample when Fisher's test was used. Our result in agreement with (Elsaid et al., 2012) for their observation of non-significant in T2D patients and control**.** Also, our study was confirmed by the report of (Malekzadeh et al., 2019)**,** who found an overrepresentation of the IFN-γ +874 polymorphism in I in patients with inflammatory bowel disease (IBD) ($p = 0.020$). Data from the present study contrasted with

(Allam et al., 2018)on Saudi population, who reported The allele IFN-γ +874 is linked to type 1 diabetes (p) less than 0.001. In the Slovak population, other studies did not discover a significant correlation between type 1 diabetes and The polymorphism of IFN-γ+874A/T (Javor et al., 2010) together with the British Caucasian population (Bazzaz et al., 2014). Thus, this previous research is consistent with our study where in both patients with diabetes type 1 (D1T) and healthy controls (p> 0.05). The variance in IFN-γ + 874A/T distributions may be due to race differences in the examined group. Numerous investigations have examined the relationship between protein production and polymorphisms in IFN-γ +874 alleles.. Our results are consistent with reports from (Ivashkiv, 2018)**,** which indicates that these polymorphisms are unrelated to T1DM. They did not show considerable differences between the IFN-γ gene polymorphism at locus +874 genotypes.

(López-Maderuelo et al., 2003)**,** found that individuals with the AA genotype in tuberculosis(TB) produced lower IFN-γ than people with the TT or TA genotypes. Furthermore, tuberculosis susceptibility has been linked to the IFN-γ +874 A allele (Amim et al., 2008) as well as serious respiratory disorders (Chong et al., 2006)**,** T2D (Elsaid et al., 2012) this observation is consistent with our result.

The current study revealed that there was no relationship between the absence or presence of the INFG (+874T/A) gene polymorphism and T1D patients' age, gender, weight, height, and body mass index (BMI) p>0.5, these results are in agreement with (Elsaid et al., 2012) who observed no statistically significant difference was noted comparing the frequencies of TNF-α-308(G/A) and IFN- γ +874 (A/T) genotypes and alleles among various case subgroups regarding age (<40 vs.>40 years), sex (males vs. females), and with (Paine et al., 2012; Salem et al., 2016) .

No significant difference between the blood pH of D1T cases and the presence of INFG (+874T/A) genotypes (p > 0.05), Similarly, no further features were associated with the partial pressure of CO2 in arterial blood (pCO2) or blood (HCO3-) bicarbonate levels of D1T cases.

In our study, there is a significant difference between the random blood sugar (RBS) level of the T1D cases and the presence of INFG (+874T/A) genotypes (p < 0.05). In contrast, none of the other metrics linked to hemoglobin A1c percent (HbA1c), and ketone levels in the urine of D1T cases this result agree with (Snell-Bergeon et al., 2010; Soliman et al., 2002) .

Also, no significant difference in blood triiodothyronine (T3) levels between D1T cases and those with INFG (+874T/A) genotypes (p > 0.05). Similarly, no additional metrics related to blood thyroxine (T4) or thyroid-stimulating hormone (TSH) levels in D1T cases, this result agrees with (Nakkuntod et al., 2006). Moreover, the blood creatinine and urea levels of T1D patients were unrelated to the absence or presence of the INFG (+874T/A) gene polymorphism p> 0.05.

Conclusions

Our finding indicated a non-significant association between the rare alleles of IFN-γ gene polymorphisms and susceptibility to diabetes type 1 in Egyptian children.

Abbreviations

BMI: Body mass index ; DM: Diabetes mellitus; EDTA: Ethylene diamine tetra acetic acid; PCR: Polymerase chain reaction; RBS: Random blood sugar; SNPs: Single nucleotide polymorphisms; T1D: Type 1 diabetes TSH: Thyroid stimulating hormone.

Na:Sodium;K:Potassium; T3: triiodothyronine; T4: thyroxine;HbA1C: hemoglobin A1c; pCO2: Partial pressure of carbon dioxide in arterial blood; HCO3–: Bicarbonate.

pH: Arterial blood PH.

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الملخص العربي

عنوان البحث: دراسة تعدد الشكل الجيني للجين الانترفيرون جاما وارتباطه بمرض السكرى من النوع الأول عند الأطفال المصريين

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يعتبر مرض السكرى من النوع الأول مرض مناعى ناتج عن تحطم الخلايا من النوع بيتا بالبنكرياس ويهدف عملنا الى دراسة مدى ارتباط جين الانترفيرون جاما وعلاقته بالإصابة بمرض السكرى في الأطفال المصريين .وتضمنت الدراسة ١٠٠ من الأطفال المصابين بمرض السكري من النوع الأول و١٠٠ من الكنترول بوحدة الجينات بمستشفى الأطفال الجامعى بالمنصورة . وقد قمنا بقياس مستوى جين الانترفيرون جاما في مصل دم الأطفال المصابين بمرض السكري من النوع الأول باستخدام تفاعل البلمرة المتسلسل وقياس التحاليل مثل السكر الصائم والسكر التراكمي ونسبة الكيتون في البول وهرمونات الغدة الدرقية ووظائف الكلي وتشمل اليوريا والكرياتنين و وقياس غازات الدم وتسجيل الطول والوزن وحساب معامل كتلة الجسم .وأثبتت الدراسة انه لا توجد علاقة بين تعدد الشكل الجيني للجين الانترفيرون جاما وكل من معامل كتلة الجسم والسكر والسكر التراكمي والكيتون ووظائف الكلى وهرمونات الغدة الدرقية وغازات الدم . وأنه لا يوجد ارتباط مؤثر بين تعدد الشكل الجيني للجين انترفيرون جاما وقابلية الإصابة بمرض السكرى من النوع الأول فى الأطفال المصريين.