Research Article

Study of TNF α gene polymorphism in Type 2 Diabetes

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Abstract

DM is one of the five principal causes of death universally. It is a growing heath problem of multifactorial origin, understanding its genetic background might help in early detection and disease prevention. Obesity, especially visceral adiposity, and physical inactivity are major risk factors for diabetes in Egypt. A 2010 World Health Organization (WHO) report indicated that 30.3% of Egyptian adults are obese. Egypt currently has the third highest prevalence of obesity in the Middle East and North Africa (MENA) region, after Saudi Arabia and United Arab Emirates. It has been reported that genetic variations in the promoter region regulate tumor necrosis factor-α (TNFα) production and transcription and, they influence susceptibility to inflammatory related diseases. Single nucleotide polymorphism studies in the promoter region of TNFα (_238) have suggested its role in increased insulin resistance. This is a prospective case control study aimed at detecting the impact of TNF α 238 G/A rs 361525 gene polymorphisms in T2DM in Egyptian population. It included 40 diabetic patients, and 40 apparently healthy unrelated volunteers. We underwent history taking, clinical examination with detection of BMI and W/H ratio, laboratory investigations, (finger prick test, 75 gram oral glucose tolerance test, HA1C, fasting and 2hPP blood glucose, and detection of TNF -238G/A gene polymorphisms that was performed by using PCR/RFLP method. In respect to the distribution of TNFα 238 G/A polymorphism genotypes: In patients with T2DM it was (GG genotype: 75%, AA genotype 5%, and GA genotype: 20%). In control it was (GG genotype: 90%, AA genotype: 2.5%, and GA genotype: 7.5%).

Key words: TNFα G/A 238 gene polymorphism, Type2 Diabetes, obesity, insulin resistance.

Introduction

TNF-α plays a central role in the pathogenesis of obesity-induced insulin resistance as evidenced by the augmented levels of TNF-α in systemic circulation, liver and adipocytes[1,2,3,4] The TNF-α-induced insulin resistance is dependent on the intracellular and molecular mechanisms that involve the activation of stress-related protein kinasis [5].

Subjects and Methods

The study was carried out from June 2013 to November 2017.The subjects were collected from both Internal medicine and Diabetes outpatient clinics in Minia University Hospital. The genetic analysis of this study was carried out in Biochemistry Department, Faculty of Medicine, Minia University. Written informed consent was obtained from all the study participants. The study was approved by local committee.

Inclusion criteria:

The study included two groups:

Group 1: included 40 diabetic patients.

Group 2: included 40 apparently healthy unrelated volunteers. The diagnosis was according to ADA (2013) criteria.

Exclusion criteria:

Subjects taking drugs (steroids, metformin, oral contraceptive pills, oral hypoglycemic agents, antiepileptics, beta blockers, and thiazides). Pregnant women, Patients with coronary artery disease, chronic liver or kidney diseases, cerebral vascular disease, malignancy, and thyroid disease.

All patients and healthy volunteers were subjected to the following:
History taking, clinical examination, laboratory investigations (Finger prick test, 75 Gram oral glucose tolerance test HA1C, fasting and 2 HPP blood glucose, lipid profile, and detection of both TNF-238G/Ars(361525) gene polymerphisms.

Statistical analyses

All of the analyses were performed with version 21 of Statistical Package of Social Science (SPSS).

Table (1): Comparison Of The Study Groups As Regard Demographic And Anthropometric Characteristics

Variables	Group 1 Diabetics No=40	Group 2 Control No=40	P value
BMI (kg/m^2) (mean±SD) Rang / median	36.8±6.3 (27-51)/34	25.2±2.9 (17-31)/25	0.0001*
Waist circumference in cm (mean±SD) Rang/ median	110.6±8.6 (91-124)/109	92.8±14.5 (70-117)/85.5	0.0001*
Hip circumference in cm (mean±SD) Rang / median	124.7±11.1 (110-147)/	109.1±11.4 (90-129)/	0.0001*
W/H Ratio (mean±SD) Rang/ median	0.88 ± 0.07 (0.80-1.09)/0.86	0.84 ±0.07 (0.7-1)/0.85	0.01*

Continuous data are expressed as mean ± standard deviation and comparisons were done by student's t test while qualitative variables are expressed as frequency and compared by $\chi 2$ test. BMI=body mass index, W/H= waist / hip ratio, FH= family history. *= statistically significant results.

As shown in table 1, when we compared the two groups by student's t test we found that diabetics had higher BMI, waist circumference, hip circumference and W/H ratio than control and this had a statistical significance.

Table 2: Comparison Of The Study Groups As Regard Family History Of Diabetes And Some Clinical Characteristics

Variables	Group 1 Diabetics No=40	Group 2 Control No=40	P value
Positive FH of DM: no (%)	25(62.5%)	0	0.007*
SBP(mmHg)(mean±SD) Rang/ median	137.25±11.2 (120-160)/140	108.25±9.8 (100-130)/105	0.0001*
DBP(mmHg)(mean±SD) Rang/ median	85.75±10.4 (70-110)/80	69.75±6.5 (60-80)/70	0.0001*
Pulse(b/m) (mean±SD) Rang/ median	77.05±4.6 (70-85)/75	73.38±5.5 (65-85)/72	0.002*

Continuous data are expressed as mean ± standard deviation and comparisons were done by student's t test while qualitative variables are expressed as frequency and compared by $\chi 2$ test. *= statistically significant results.

Table 2**,** shows that the frequency of family history of T2DM was statistically higher when we compared diabetics with control (p=0.007).As regard SBP, DBP and pulse they were higher in diabetics than control (p=0.0001 for SBP and DBP, for pulse p=0.002).

Table (3): Comparison Of Glycemic Indices Of The Study Groups:

Variables	Group1 Diabetics No=40	Group2 Control No=40	P value
FBG(mg/dl) (mean±SD) Rang/ median	169.80±37.4 (84-280)/167.5	82.65±7. 6 (70-95)/ 84.5	0.0001*
2HBG (mg/dl) (mean±SD) Rang/ median	275.08±42.5 (200-400)/280	115.10±3.5 (110-123)/115	0.0001*
HA1C(%) (mean±SD) Rang/ median	9.8±2.2 (6.7-15)/9.2	4.9±0.4 (4.1-5.6)/5.1	0.0001*

Continuous data are expressed as mean ± standard deviation and comparisons were done by student's t test. FBG=fasting blood glucose, 2HBG= two hour post prandial blood glucose, HA1C=glycosylated haemoglobin.*= statistically significant results.

Table 3**,** shows that by using student's t test, we found that FBG, 2HBG and HA1C were higher in diabetics than controls and this had a statistical significance (p=0.0001, for each).

TNFα 238 G/A Polymorphism Genotypes Distribution Among The Study Groups:

Genotypes and alleles	Group1 Diabetics No =40	Group 2 Control No =40	p -value between each 2 groups
Homozygous AA no (%)	2(5%)	1(2.5%)	0.2
Wild type GG no (%)	30(75%)	36(90%)	
Heterozygous GA no (%)	8(20%)	3(7.5%)	
A allele	12(15%)	5(6.2%)	0.07
G allele	68(85%)	75(93.8%)	

*= statistically significant results.

Table 4, shows that in our study we found that, in patients with T2DM (GG genotype: 75% of, AA genotype: 5%, and GA genotype: 20%). In the healthy volunteers (GG genotype: 90%, AA genotype 2.5%, and GA genotype: 7.5%).

Discussion

In our study among the risk factors for diabetes, obesity (measured with BMI, Waist circumference, and W/H ratio) was found to have significant association with the occurrence of diabetes. The mean of BMI in diabetic patients it was 36.84. While in the control group it was 25.22. Similarly, the mean of waist circumference in diabetic patients it was 110.63. While in the control group it was 92.83. The mean of W/H ratio in diabetic patients it was 0.88. While in the control group it was 0.84.This finding was similar to previous studies[6].

Similarly, in a previous study by Meisinger et al., (2014), persons with newly diagnosed diabetes, had higher BMI and waist circumference, as well as a higher systolic and diastolic blood pressure, and more often suffered from hypertension[7].

In our study we found that, in patients with T2DM (GG genotype: 75% of, AA genotype: 5%, and GA genotype: 20%). In the healthy volunteers (GG genotype: 90%, AA genotype 2.5%, and GA genotype: 7.5%), but this did not have a statistical significance similar to previous study[6].

Conclusion

We concluded that TNFαG/A gene polymorphism had a role in type 2 DM, by affecting mainly insulin resistance; also, we concluded that type 2 DM can be prevented or at least delayed by regular exercises and keeping ideal body weight.

References

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