RESISTIN GENE POLYMORPHISM IN OFFSPRING OF PATIENTS WITH TYPE 2 DIABETES MELLITUS

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OBJECTIVES

Background: Resistin is a hormone that potentially links obesity to T2DM. Several Single Nucleotide Polymorphisms (SNPs) have been identified in the Resistin Gene (RETN). Polymorphism of RETN +299 (G>A) may contribute to increased resistin levels, which may be involved in the pathogenesis of T2DM [1].

Aim of work: To study the association between resistin gene +299 polymorphism and insulin resistance in non-diabetic offspring of T2DM.

METHODS

Methods: This case control study included 60 volunteers divided into 2 groups:

Group A: Control group including 30 healthy individuals with negative family history of DM.
Group B: Offspring of patients with T2DM including 30 non-diabetic individuals with positive family history of DM. The latter group was further classified after OGTT into:
Group B1: 15 individuals with normal glucose tolerance.
Group B2: 15 individuals with impaired glucose tolerance.

All individuals had an estimation of serum resistin level by ELISA and RETN+299 polymorphism by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (***PCR-RFLP***) (Table 1).

Table (1): Comparison of the mean values ±SD of the demographic and chemical parameters among different subgroups of the study by Anova test.

	Group A	Group B1	Group B2	F	P
Age	35.967 ± 9.121	34.8 ±7.839	38.5 ±6.739	0.762	0.476 (NS)
Gender Male/ female	16/14	7/8	10/5	X^2=1.279	0.521 (NS)
BMI (Kg / m²)	22.4±1.7	23.1±3.1	23.92±1.9	1.2	0.812 (NS)
Fasting blood glucose (mg/dl)	84.43±7.5	88.87±6.3	111.87±7.12 a,b	79.604	0.001 (HS)
2 h post prandial blood glucose (mg/dl)	110.07±10.45	114.933±10.52	165.2±11.56 a,b	139.234	0.001 (HS)
Fasting insulin (µIu/ml)	3.4±1.03	6.7±1.38 a	12.76±3.993 a,b	89.014	0.001 (HS)
Serum resistin (ng/ml)	1.315±0.18	1.37±0.2	4.46±0.843 a,b	274.2	0.001 (HS)
HOMA-IR	0.7±0.217	1.458±0.28 a	3.54±1.16 a,b	108.372	0.001 (HS)

HS=Highly Statistical Significance. NS=None Statistical Significance.
a=Significant as compared with control. b=Significant as compared with normal glucose tolerance.

Table (2): Comparison of the frequency and percentage of different genotypes and alleles in different subgroups of the study by X^2 test.

	Group A		Group B1		Group B2		X^2	P
	N	%	N	%	N	%		
AA	3	10%	4	26.667%	7	46.667%	10.24	0.0376 (S)
GA	12	40%	9	60%	6	40%		
GG	15	50%	2	13.333%	2	13.333%		
AA+GA	15	50%	13	86.7%	13	86.7%	7.93	0.018 (S)
GG	15	50%	2	13.3%	2	13.3%		
A	18	30%	17	56.7%	20	66.7%	8.221	0.016 (S)
G	42	70%	13	43.3%	10	33.3%		

S=Statistical Significance.

Table (3): Comparison of the mean values ±SD of different biochemical parameters in relation to the different genotypes in group B2 by Anova test.

	AA	GA	GG	F	P
Fasting blood glucose (mg/dl)	119.174±2.62	110.5±8.1 a	104.5±3.5 a,b	7.671	0.007 (HS)
2 h post prandial blood glucose (mg/dl)	175.143±4.95	160.67±4.32 a	145±2.01 a,b	40.746	0.001 (HS)
Fasting insulin (µIu/ml)	14.13±2.11	11.22±1.113 a	7.1±0.77 a,b	15.193	0.001 (HS)
Serum resistin (ng/ml)	5.044±0.73	4.15±0.523 a	2.5±1.09 a,b	10.829	0.002 (HS)
HOMA-IR	4.18±0.61	3.06±1.19 a	1.8±0.262 a,b	19.549	0.02 (HS)

HS=Highly Statistical Significance.
a=Significant as compared with AA. b=Significant as compared with GA.

Table (4): Correlation coefficient between serum resistin level (ng/ml) versus different biochemical parameters of the study in group B2.

	Fasting blood glucose (mg/dl)		2 h post prandial blood glucose (mg/dl)		Fasting insulin (µIu/ml)		HOMA-IR	
	r	P	r	P	r	P	r	P
Serum resistin	0.606	0.01 (S)	0.683	0.03 (S)	0.719	0.03 (S)	0.737	0.02 (S)

S=Statistical Significance.

RESULTS

Results: We found a statistically significant increase of serum resistin (AA genotype and combined GA+AA genotypes), decrease in GG genotype, increase of A allele ($P<0.03$) and increase in the indices of insulin resistance in the impaired glucose tolerant offspring as compared to the control individuals as well as normal glucose tolerant offspring (Table 2).

There was also a statistically significant association between hyperglycemia and resistin gene polymorphism at positions +299 (G>A) (Table 3).

Moreover, a significant positive correlation was found between serum resistin level and insulin resistance in impaired glucose tolerant offspring (Table 4).

CONCLUSIONS

Conclusions: The present study support that RETN+299 G>A SNP and increase in serum resistin may have contributed to increased insulin resistance with subsequent susceptibility to T2DM in offspring of type 2 diabetic patients. Those carrying AA and combined GA+AA genotypes are more at risk.

References

[1] ***Khalil O, Alnahal A, Ghonium M. et al., (2014):*** *Does Resistin Gene Polymorphisms +299 (G>A) Participate in Insulin Resistance in Egyptian non-Obese Type 2 Diabetes? Int J Genomic Med ; 2: 117-123.*