

Original Article

ASSOCIATION OF OBESITY WITH RS1421085 AND RS9939609 POLYMORPHISMS OF FTO GENE WITH T2DM IN EGYPTIAN FEMALES

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ABSTRACT

**Objective:** Obesity has been described as a worldwide increasing health problem and risk factor of various disorders including type 2 diabetes mellitus (T2DM). So, our study aim to determine of common variants of fat mass and obesity associated gene polymorphisms rs1421085 and rs9939609; confers risk of obesity and type 2 diabetic mellitus in Egyptian females.

**Methods:** In this population rs1421085 and rs9939609 polymorphisms of fat mass and obesity (FTO) gene were genotyped in 105 obese patients and 100 healthy controls with ages 14-60 y were collected from Medicine Specialized Hospital, Mansoura University, Egypt during the period between Jul.-Oct. 2016, genotyping of SNPs was performed by restriction fragment length polymorphism (RFLP) assay, fasting blood glucose, homeostasis model assessment of insulin resistance (HOMA IR), body mass index (BMI), waist-to-hip ratio (WHR) lipid profile was determined.

**Results:** There was the significantly higher frequency of the AA compared to controls  $p=0.0001$  of genotypes rs9939609. Also, cases have shown a significantly higher frequency of the C allele,  $p<0.00001$  of rs1421085 genotype polymorphisms increased the risks of obesity. On the other hand, there were no significant correlations between genotypes and obesity-related (anthropometric body composition) parameters. Only the fasting blood glucose was significantly higher in the TA  $p=0.004$ .

**Conclusion:** The FTO rs9939609 and rs1421085 single nucleotide polymorphisms (SNPs) was associated with increased risk of obesity in type 2 diabetic populations on Egyptian females.

**Keywords:** FTO, Polymorphism, Obesity, BMI, Body fat

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INTRODUCTION

FTO gene was assigned to chromosome 16 at position 12.2 [1]. FTO has a total length of 410509 bp and contains nine exons and several nucleotide polymorphisms [2].

The fact that high levels of FTO expression are found in the brain, specifically in the accurate nucleus of the hypothalamus, which is known to play a major role in controlling energy homeostasis and eating behaviour, together with new insights from recent *in vitro* studies indicating a possible role in energy expenditure, provides support for a role of FTO in the explanation of obesity development [3, 4].

Obesity is considered a medical condition involving an accumulation of excess body fat potentially posing a threat to health and life of an individual. The prevalence of obesity is increasing worldwide in both developing and developed countries. It has become a serious epidemic health problem, estimated to be the fifth leading cause of modality at global level [5-9]. On the other hand, studies in Chinese Han [10], Oceanic [11], and African populations [12] failed to confirm rs9939609 variant as a major contributor to obesity and type 2 diabetic (T2D). Studies in Korean, Malay, Japanese, Canadians of South Asian origin, and Chinese populations have reported the association of this SNP with BMI and obesity [13-19]. Despite less frequency of risk allele A in the Chinese population, its effect on BMI was the same as that in the European population [13]. FTO variant associated strongly with T2D but weakly with obesity in Indians [20]. In short, the disease association of the FTO variant varies with ethnicity and populations.

To determine whether FTO gene is a genetic risk factor for developing obesity in Egyptian females, we analyzed rs1421085 and rs9939609 polymorphisms in patients with T2DM, diabetic obesity and healthy controls. Besides, the relationship between FTO gene polymorphisms and obesity is discussed in the manuscript.

MATERIALS AND METHODS

Limitation of the study

This work based on 105 cases (after taking their approved) representing obese cases and obese diabetic cases; 55 cases obese only. Their mean age±SD 36.07±10, range of 14–61 y and 50 cases presenting diabetic obese with mean age±SD 38.94±11 and comparing with 100 healthy control are collecting from the central area of Nile Delta of Egypt from the Department Obesity and Diabetes International Medicine Specialized Hospital, Mansoura University, Egypt, and comparing cases to their complication with length, weight, cholesterol triglycerides, low density liprotein (LDL), high density liprotein (HDL), glycated homoglobulin average of plasma glucose concentration (HbA1c), fasting blood glucose (FBG), Insulin, Homa IR, BMI. For all cases and controls; DNA extraction was carried out followed by PCR detection of their rs 1421085 and 9939609 genetic polymorphism.

Measurement of anthropometric parameters

Body weight, height, waist and hip circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured according to the standard procedures [21]. Body height was measured using a wall-mounted stadiometer, and body weight was measured using a digital scale. BMI of each subject was calculated. Waist circumference was measured just above navel midway between the lower margin of the last rib and iliac crest to the nearest 0.1 cm. Hip circumference was taken as the maximal circumference over the buttocks. Waist-to-hip ratio was calculated from the values of waist and hip circumference. DBP was measured twice from the right arm of the subject in a sitting position using a standard mercury sphygmomanometer.

Measurement of metabolic parameters

Blood samples were drawn after an overnight fast of 8–12 h. Fasting blood glucose (FBG) levels were determined by the glucose oxidase

method using HumaStar 180 chemistry analyzer (Human, Wiesbaden, Germany). Concentrations of plasma insulin, leptin, and leptin receptors were determined by ELISA using the commercial kit with an automated EIA analyzer (Bio-Rad Laboratories, Hercules, CA, USA). FBG and fasting insulin levels were used to measure homeostasis model assessment of insulin resistance (HOMA-IR) calculated by the following formula:  $HOMA-IR = \text{Fasting insulin } (\mu\text{IU/ml}) \times \text{Fasting glucose (mmol/l)} / 22.5$  [22].

#### DNA extraction and genotyping

Genomic DNA was extracted from whole blood using genomic DNA purification kit (Fermentas, USA). Genotyping of rs9939609 polymorphism at FTO locus was carried out by polymerase chain reaction-restriction fragment length polymorphism assay (PCR-RFLP). A DNA fragment containing rs9939609 polymorphism was amplified using specific primers (forward primer sequence: AACTGGCTCT-TGAATGAAATAGGATTCAGA and reverse primer sequence: AGAGTACAGAGACTATCCAAGTGCAGTAC). The PCR was carried out using thermocycler (Icycler 5, BioRad, USA) according to the optimized conditions. In 25  $\mu\text{L}$  reaction, PCR components comprised of 50 ng DNA, 1X Taq buffer, 2 mmol  $\text{MgCl}_2$ , 200  $\mu\text{M}$  of each dNTP, 10  $\rho\text{mol}$  of each primer, and 1U Taq DNA polymerase. Thermal cycling was performed as follows: initial denaturation at 95  $^{\circ}\text{C}$  for 4 min, followed by 35 cycles of denaturation at 94  $^{\circ}\text{C}$  for 30 sec, annealing at 58  $^{\circ}\text{C}$  for 30 sec and extension at 72  $^{\circ}\text{C}$  for 1 min, and then a final extension step at 72  $^{\circ}\text{C}$  for 10 min. Amplified products were digested with Sca1 restriction enzyme (Favorgen, Taiwan) to analyze for polymorphism by RFLP assay polymorphisms of primers of the rs1421085 T>C polymorphism were 5-GGCAGACTTGTAAGGAACAAGA-3 (forward) and 5-AAATTCT-CATCAGACACTTAATCGAT-3 (reverse) which generated the 127-bp fragment. For the rs1421085 T>C variant, the expected fragment sizes were 101- and 26-bp for the *ECO32I* restriction site. The PCR profile for the rs1421085 T>C polymorphism consisted of an initial melting step of 95  $^{\circ}\text{C}$  for 5 min; 35 cycles of 95  $^{\circ}\text{C}$  for 30s, 51  $^{\circ}\text{C}$  for 40s and 72  $^{\circ}\text{C}$  for 40s and a final step of 72  $^{\circ}\text{C}$  for 10 min.

#### Statistical analysis

The data were analyzed using Statistical Package for Social Sciences (SPSS Inc. Chicago, IL, USA, version 17.0). Quantitative variables

were expressed as mean  $\pm$  standard error (SE). Student's *t*-test was applied to observe the differences between case and control groups. The whole data were stratified according to age in subgroups. Hardy Weinberg equilibrium test (HWE) was applied to determine the variation in distribution of alleles and genotypes within the concerned population. Allelic frequencies were calculated by gene counting. Chi-square ( $\chi^2$ ) test was used to determine the significant differences of genotype and allelic frequencies between obese and nonobese groups. Association of rs9939609 and the rs1421085 variant with obesity was determined by Pearson Chi-square using codominant, dominant and recessive models. Odds ratio (OR) and 95% confidence interval (CI) were calculated to determine the risk of obesity associated with the risk allele. The association of FTO rs9939609 variant with anthropometric and metabolic traits was determined using General Linear Model (GLM) assuming codominant, dominant, and recessive genetic models. The genotypes were coded as (0, 1, 2) in codominant model, (0, 1) in dominant model and (1, 0) in recessive model corresponding to the number of copies of risk allele.

#### RESULTS

By comparing demographic and laboratory data of obese cases compared to controls (table 1) shows demographic and laboratory data of obese cases compared to controls. All parameters showed significant higher values in cases compared to controls ( $p < 0.05$ ) except for the waist hip ratio (WHR). On the other hand, the demographic and laboratory data of obese diabetic cases compared to controls (table 1) shows demographic and laboratory data of obese diabetic cases compared to controls. All parameters showed significant higher values in cases compared to controls ( $p < 0.05$ ) except for the waist-hip ratio and LDL levels ( $p > 0.05$ ).

The demographic and laboratory data of obese non-diabetic cases compared to controls shows demographic and laboratory data of obese non-diabetic cases compared to controls. Values corresponding to length, weight, cholesterol, triglycerides, LDL, insulin, Homa IR, waist, hip and BMI were significantly higher in cases compared to controls ( $p < 0.05$ ); whereas both groups showed no significant difference regarding their age, waist-hip ratio, FBG and HbA1C ( $p > 0.05$ ).

**Table 1: Demographic and laboratory data of obese and obese diabetic cases compared to controls**

	Controls*		Obese**		p	Obese Diabetic***		
	Mean	$\pm$ SD	Mean	$\pm$ SD		Mean	$\pm$ SD	p
Age	31.88	11.066	36.07	10.870	.007*	38.94	11.083	.000**
Length	165.14	10.956	159.38	6.077	.000**	158.36	7.631	.000**
Weight	72.20	56.719	105.47	13.024	.000**	108.20	9.282	.000**
Cholesterol	171.98	12.367	202.71	43.770	.000**	202.18	41.621	.000**
Triglyceride	82.12	20.873	137.33	52.406	.000**	151.40	47.398	.000**
HDL	41.64	5.268	44.43	12.413	.039*	49.66	14.349	.000**
LDL	119.70	19.414	133.77	42.481	.003*	120.99	39.190	.787
HbA1c	5.10	.518	7.15	4.931	.000**	8.05	1.515	.000**
FBG	95.43	7.175	119.44	32.136	.000**	146.56	26.038	.000**
Insulin	5.42	1.585	22.39	4.627	.000**	19.95	4.942	.000**
Homa IR	1.15	.390	5.73	1.127	.000**	6.35	1.239	.000**
Waist	66.04	9.147	102.48	7.941	.000**	103.68	6.747	.000**
Hip	79.04	8.888	112.29	8.092	.000**	113.72	6.725	.000**
WHR	.95	1.169	.91	.014	.717	.91	.006	.798
BMI**	24.32	1.606	41.66	5.739	.000**	43.42	5.639	.000**

\*n = 100, \*\*n = 55, \*\*\*n = 50, \* = p-value < 0.05, \*\* = p-value < 0.001, \*\*\*BMI: body mass index (%). Data presented mean  $\pm$  SD.

The frequency of FTO rs9939609 polymorphic forms in total obese cases compared to controls adjusted by age (table 2) shows the frequency of FTO rs9939609 polymorphic genotypes in total obese cases compared to controls adjusted by age. Obese cases showed significantly higher frequency of the AA genotype compared to controls in the codominant model (21.9% vs. 4%,  $p = 0.0001$ ). Also, observed in the recessive model ( $p = 0.0001$ ). However, cases showed a significantly lower frequency of TA genotype in the overdominant model (35.2% vs. 60%,  $p = 0.00026$ ).

The Frequency of FTO rs9939609 polymorphic forms in total obese cases compared to controls adjusted by diabetes and age (table 2) shows the frequency of FTO rs9939609 polymorphic genotypes in total obese cases compared to controls adjusted by age and diabetes. Obese cases still, showed significantly higher frequency of the AA genotype compared to controls in the codominant model (21.9% vs. 4%,  $p = 0.012$ ). This was also observed in the recessive model ( $p = 0.0039$ ).

The results of FTO rs9939609 exact test for Hardy-Weinberg equilibrium shows exact test for Hardy-Weinberg equilibrium in

all studied subjects as well as each separate group. Regarding the groups of all participants, the test showed the non-significant difference between the observed and expected frequencies for polymorphic genotypes i.e. coping with the genetic equilibrium.

On the contrary, regarding each individual group of controls and cases, each was significantly departing from the equilibrium probably due to the high values of AA in cases and TA in controls.

**Table 2: Frequency of FTO rs9939609 polymorphic forms in total obese cases compared to controls adjusted by diabetes and age**

Model	Genotype	Controls <sup>+</sup>	Obese	Obese cases <sup>++</sup>		Obese-diabetic cases <sup>+++</sup>	
				OR (95% CI)	p-value	OR (95% CI)	p-value
Codominant	T/T	36 (36%)	45 (42.9%)	1.00	0.0001**	1.00	0.0001**
	T/A	60 (60%)	37 (35.2%)	0.58 (0.31-1.07)		0.58 (0.31-1.07)	
	A/A	4 (4%)	23 (21.9%)	4.99 (1.55-16.06)		4.99 (1.55-16.06)	
Dominant	T/T	36 (36%)	45 (42.9%)	1.00	0.65	1.00	0.65
	T/A-A/A	64 (64%)	60 (57.1%)	0.87 (0.49-1.57)		0.87 (0.49-1.57)	
Recessive	T/T-T/A	96 (96%)	82 (78.1%)	1.00	0.0001**	1.00	0.0001**
	A/A	4 (4%)	23 (21.9%)	6.80 (2.22-20.90)		6.80 (2.22-20.90)	
Over dominant	T/T-A/A	40 (40%)	68 (64.8%)	1.00	0.0026*	1.00	0.0026*
	T/A	60 (60%)	37 (35.2%)	0.41 (0.23-0.74)		0.41 (0.23-0.74)	
Alleles	T	132 (66%)	127 (60%)	1.27 (0.8-1.9)	0.29	1.27 (0.8-1.9)	0.29
	A	68 (34%)	83 (40%)				

<sup>+</sup>n = 100, <sup>++</sup>n = 55 and <sup>+++</sup>n = 50.

On the other hand, the frequency of FTO rs1421085 polymorphic genotypes in total obese cases compared to controls adjusted by age shows the frequency of FTO rs1421085 polymorphic genotypes in total obese cases compared to controls adjusted by age. Obese cases showed significantly higher frequency of the CC genotype compared to controls (29.5% vs. 3%,  $p < 0.0001$ ). This was also observed but to a lesser degree for the CT genotype (37.1% vs. 29%,  $p = 0.0001$ ) in the codominant model. This was also observed in the recessive model for the CC genotype ( $p = 0.0001$ ) and in the dominant model for the CT+CC genotypes (66.7% vs. 32%,  $p = 0.0001$ ). Cases have also shown a significantly higher frequency of the C allele (48% vs. 18%,  $OR = 4.37$ ,  $95\%CI = 2.8-6.8$ ,  $p < 0.00001$ ).

The Frequency of FTO rs1421085 polymorphic forms in total obese cases compared to controls adjusted by diabetes and age shows the frequency of FTO rs1421085 polymorphic genotypes in total obese cases compared to controls adjusted by age and diabetes. Obese cases showed significantly higher frequency of the CC genotype compared to controls (29.5% vs. 3%,  $p < 0.0001$ ). This was also observed but to a lesser degree for the CT genotype (37.1% vs. 29%,  $p = 0.0001$ ) in the codominant model. The same was also observed in the recessive model for the CC genotype ( $p = 0.0001$ ) and in the dominant model for the CT+CC genotypes (66.7% vs. 32%,  $p = 0.0001$ ). Cases have also shown a significantly higher frequency of the C allele (48% vs. 18%,  $p < 0.00001$ ).

Hardy-Weinberg equilibrium in all studied subjects as well as each separate group, regarding the control group, the test showed non-significant difference between the rs1421085 exact tests for Hardy-Weinberg equilibrium shows exact test for observed and expected frequencies for polymorphic genotypes i.e. coping with the genetic equilibrium. On the contrary, regarding the group of cases and in all participants, the test was significantly departing from the equilibrium probably due to the high values of CC and CT in cases.

Significantly, higher frequency of the FTO rs9939609 A and rs1421085 C haplotype compared to controls (22.1% vs. 6.11%,  $OR = 4.40$ ,  $95\% CI = 2.09-9.3$ ,  $p = 0.0001$  adjusted by age,  $OR = 4.70$ ,  $95\% CI = 2.02-10.93$ ,  $p = 0.0004$  adjusted by age and diabetes).

The laboratory parameters related to lipid profile (table 3) and blood sugar in all obese cases regarding their FTO rs9939609 gene polymorphic types shows laboratory parameters related to lipid profile and blood sugar in all obese cases regarding their FTO rs9939609 gene polymorphic types. Cases showed no significant difference for all values of lipid profile (cholesterols, triglycerides, HDL and LDL) as well as laboratory tests of diabetes (HbA1c, FBG, insulin and Homa IR) related to their polymorphic genotypes, also no significant BMI and WHR related to their polymorphic genotypes.

**Table 3: Parameters related to lipid profile and blood sugar in all obese cases regarding their FTO rs9939609 and rs1421085 gene polymorphism**

	rs9939609					rs1421085				
	Genotype	N	Mean	±SD	P (TT vs TA)	Genotype	N	Mean	±SD	P (TT vs TC)
Cholesterol	T/T	24	206.92	43.411	.955	T/T	35	200.17	39.212	.941
	T/A	12	206.08	36.592		T/C	39	199.51	37.572	
	A/A	14	190.71	43.187		C/C	31	209.61	55.143	
Triglycerides	T/T	24	155.29	53.179	.435	T/T	35	144.46	58.506	.723
	T/A	12	141.83	35.680		T/C	39	139.92	51.175	
	A/A	14	152.93	47.671		C/C	31	126.02	46.085	
HDL	T/T	24	51.25	15.840	.858	T/T	35	42.83	11.703	.313
	T/A	12	50.33	10.790		T/C	39	45.67	12.233	
	A/A	14	46.36	14.726		C/C	31	44.68	13.578	
LDL	T/T	24	126.46	41.455	.391	T/T	35	137.03	53.139	.542
	T/A	12	113.95	39.048		T/C	39	130.55	37.144	
	A/A	14	117.64	36.679		C/C	31	134.13	35.808	
HbA1c	T/T	24	8.03	1.336	.759	T/T	35	6.55	1.533	.441
	T/A	12	8.18	1.557		T/C	39	6.86	1.875	
	A/A	14	7.99	1.851		C/C	31	8.18	8.691	
FBG	T/T	24	139.50	15.795	.004*	T/T	35	117.03	31.831	.291
	T/A	12	165.25	35.327		T/C	39	124.97	32.360	
	A/A	14	142.64	25.040		C/C	31	115.19	32.252	

Insulin	T/T	24	20.45	4.949	.093	T/T	35	23.47	4.915	.091
	T/A	12	17.46	4.823		T/C	39	21.67	4.114	
	A/A	14	21.21	4.598		C/C	31	22.10	4.826	
Homa IR	T/T	24	6.34	1.448	.671	T/T	35	5.91	1.268	.670
	T/A	12	6.14	.898		T/C	39	5.80	.960	
	A/A	14	6.55	1.144		C/C	31	5.44	1.130	
BMI	T/T	24	43.54	4.850	.984	T/T	35	40.52	3.632	.228
	T/A	12	43.59	8.774		T/C	39	41.67	4.408	
	A/A	14	43.06	3.595		C/C	31	42.93	8.452	
WHR	T/T	24	.91	.005	.233	T/T	35	.92	.022	.177
	T/A	12	.91	.008		T/C	39	.91	.007	
	A/A	14	.91	.004		C/C	31	.91	.007	

N = number of cases. Data presented mean±SD. \* = p-value.

The laboratory parameters related to lipid profile and blood sugar in all (table 3) obese diabetic cases regarding their FTO rs9939609 gene polymorphic type's shows laboratory parameters related to lipid profile and blood sugar in all obese diabetic cases regarding their FTO rs9939609 gene polymorphic types. Cases showed no significant difference for all values of lipid profile (cholesterols, triglycerides, HDL and LDL) as well as laboratory tests of diabetes (HbA1c, insulin and Homa IR) related to their polymorphic genotypes. Only the fasting blood glucose was significantly higher in the TA genotype than that of the TT genotype.

On the other hand, Laboratory parameters related to lipid profile and blood sugar in all obese cases regarding their FTO rs1421085 gene polymorphic types shows laboratory parameters related to lipid profile and blood sugar in all obese cases regarding their FTO rs1421085 gene polymorphic types. Cases showed no significant difference for all values of lipid profile (cholesterols, triglycerides, HDL and LDL) as well as laboratory tests of diabetes (HbA1c, FBG, insulin and Homa IR) related to their polymorphic genotypes.

Finally, the laboratory parameters related to lipid profile and blood sugar in all obese diabetic cases regarding their FTO rs1421085 gene polymorphic types shows laboratory parameters related to lipid profile and blood sugar in all obese diabetic cases regarding their FTO rs1421085 gene polymorphic types. Cases showed no significant difference for all values of lipid profile (cholesterols, triglycerides, HDL and LDL) as well as laboratory tests of diabetes (HbA1c, FBG, insulin and Homa IR) related to their polymorphic genotypes.

## DISCUSSION

The first FTO polymorphisms associated with obesity were identified through a genome-wide association (GWA) study searching for novel genes associated with type-2 diabetes in diabetic cases and population controls from the Welcome Trust Case Control Consortium in the United Kingdom [23, 24]. Our study aims mainly to check for the association of FTO gene rs 1421085 and rs 9939609 genes on obesity cases and diabetic obeses (T2DM) cases in Egyptian female.

In the first part of our study we have compared of FTO rs 9939609 polymorphic forms in total obese cases compared to controls and adjusted by age we showed significantly higher frequency of the AA genotype compared to controls ( $p = 0.0001$ ).

Also, it is found a strong association in total obese cases compared to control adjusted by diabetes and age was showed significantly frequency of AA genotype compared with controls ( $p = 0.012$ ).

On the other hand, our study did not appear to influence any lipid parameter in the subject tested include (cholesterol, Trighcerds HDL and LDL) as well as laboratory tests of diabetes (HbA1C, FBG, insulin and Homa IR) in all obese cases of FTO rs 9939609 gene. Only rs FTO 9939609 gene showed fasting blood glucose was significantly higher in TT genotype than TA genotype,  $p = 0.04\%$ . Therefore, our study reported that strong association of FTO rs 9939609 and T2DM. Also, there is no significant of BMI and WHR in this study of FTO rs 9939609 gene polymorphism in obesas and obesas diabetic case adjusted by age. Our data are in agreement with [25] reported that spatial analysis and meta-analysis showed an association between genetic polymorphism FTO 9939609 and T2DM. Also, showed that

rs 9939609 was associated with T2DM risk somewhat independent BMI in East and South Asia population.

On the other hand, our study did not in agreement with Europe and the American population for FTO rs 9939609 polymorphism and there was an association between genetic polymorphism T2DM risks somewhat dependent BMI.

Our data showed not in agreement within the Chinese population [10] showed that FTO rs 9939609 genotype was not found to be associated with obesity overweight BMI, circumference or body fat. This is may be due to limited lifestyle or age.

Also, in adult Pakistan female population, [26] reported that association of rs 9939609 polymorphism variant of FTO gene in adult Pakistan female with BMI and obesity with measure of body fat distribution such as waist circumference, but our data in accordance with suggest the role of this polymorphism in fat deposition and predisposing factor for obesity, association of rs 9939609 variant of FTO gene with higher fasting blood sugar predispose to T2DM.

There was no increased risk of obesity in term of rs 9939609 polymorphism on their study on Cobort of Swedish men born 1920-1924 [27].

Additionally, [28] noted that the FTO rs 9939609 variant was associated with increase BMI adjusted for age beside Aalle of rs 9939609 polymorphism has been associated with increased risk to best-developing obesity.

Also, [29] note find an association of rs 9939609 with neither birth weight nor weight again in very low birth weight infant.

Our study similarly within Pakistan population Our study similarly [30] reported that FTO9939609 gene is associated with obesity and showed for the first time in Pakistan with cornary artery disease to influence any lipid parameter in the subject tested, however, show a consistent association with blood glucose level. Therefore, it might play a role in progression to cornary artery disease through effecting plasma glucose metabolism.

This is according with a recent meta-analysis which reported that this variant has no correlation with serum lipid chemistry and is associated with glucose [31].

Other studies have found an interaction between the FTO rs 9939609 genotype and physical activity and reported that physically interactive homozygous risk. Allel carries has a  $1.95 \pm 0.3$  kg/m<sup>2</sup> increase in BMI compared with homozygous T allel and obesity. This is related to quantitative trails such as body weight waist circumference, fat mass was significantly with allel carrier [32].

On the other hand our data also noted by comparing of FTO rs 1421085 polymorphic forms in total obese cases compared to controls adjusted by diabetic and age. We showed significantly higher frequency of the CC genotype compared with controls ( $p < 0.0001$ ).

Also, all cases shown significantly higher frequency of C allel ( $p < 0.00001$ ) of FTO rs 1421085 polymorphic form in total cases compared to controls adjusted by diabetes and age was increase risk of obesity and T2DM BMI and WHR independently.

Also, we have compared of lipid profile and blood sugar in all obese cases to their FTO rs 1421085 polymorphic gene type. Our data showed parameter related to lipid profile there was no significant difference as well as testes of diabetes (HbA1c, FBG, insulin and Homa IR).

Our studies showed no significant difference by comparing lipid profile and blood sugar in all obese diabetic cases to their FTO rs 1421085 gene polymorphism.

In addition to that our study found an association of FTO gene 1421085 polymorphism and high lights the possible role of obesity and T2DM type 2 diabetes and its correlation with higher fasting glucose independently from BMI and WHR on Egyptian female. This is may be due to limited lifestyle or age. The 1421085 C allele was significantly associated with increase BMI was reported in Korean population [15].

Our data showed in agreement with Tunisian population [33] reported the association of FTO gene 1421085 polymorphism and high lights the possible role gene as a predictor of cardiovascular disease and T2DM and its correlation with higher fasting glucose independently from BMI. Other studies have shown in the Chinese population [34] say there no significant association between FTO variant of rs 1421085 genotype and obesity and level TC, TG, HDL and LDL were not found to be significantly associated with obesity.

Also, our data showed not agreement with European population, [11] reported that no significant association between FTO polymorphism includes 1421085 and BMI.

Our data also showed not in agreement with European population, [25] reported that spatial analysis showed studies on rs 1421085 in scarce and have limited regional coverage, lack of association due to smaller sample size and less studies.

There was no significant relationship has been reported between FTO gene polymorphism rs 9939609 and rs 1421085 and BMI in Turkey population [35], similarly rs 9939609 polymorphism and obesity was not associated with obesity [36].

Also, protuyuses children population, [37] found a significant association of rs9939609 and rs 1421085 polymorphism with weight, BMI, BMI 2-score waist circumference and hip circumference.

## CONCLUSION

Finally, the present study was the first that reports the association of FTO gene polymorphism with obesity and T2DM and its correlation with higher fasting blood glucose also shown significant higher frequency of C allele which increases the risk of obesity. On the other hand, there was no significant correlation between genotype and obesity-related (anthropometric body composition) parameter.

The authors are glad to identify their contributions in the present work; Prof. Nassar A, was a principle investigator, research plan, supervision of the induction process and follow up steps of investigation and interpretation of final data. Also, Prof. Wafaa A was followed up results and had the supervision of Veterinary work and interpretation of final data. Finally, Prof. El Baz RA and EL ZEKRED AS were carried out the laboratory research investigations.

## AUTHORS CONTRIBUTIONS

All the author have contributed equally

## CONFLICT OF INTERESTS

Declared none

## REFERENCES

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