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ORIGINAL ARTICLE

The association between Uncoupling proteins (UCP2) gene expression and obesity.

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ABSTRACT

Background: Medically, obesity is a condition in which there is excessive body fat accumulation that affecting health negatively. People are considered obese when their body mass index (BMI) exceeds 30 kg/m^2. Uncoupling proteins (UCPs) are mitochondrial proteins that disperse the inter-membrane electrochemical potential as heat.

Objectives: To examine the association between Uncoupling proteins (UCP2) gene expression and obesity.

Methods: Analysis of UCP2 gene expression, done by Real Time Polymerase Chain Reaction (RT-PCR) in two groups with a total of 62 participants. The 1st group included 31 obese patients and the 2nd included 31 (age-matched) healthy unrelated volunteers as a control group.

Results: A significant association of UCP2 gene expression among obese group was shown when compared with the control group ($p<0.001$). There was no significant association when compared according to gender, Chi-square (X2) was 2.38 and ($p=0.304$). Our results showed negative significant correlation between UCP2 gene expression and BMI for obese group ($p<0.05$).

Conclusions: These results suggested that the uncoupling proteins (UCP2) gene expression might play a significant role as a risk factor of obesity.

Keywords: obesity, Uncoupling protein 2 gene expression, Real-Time polymerase chain reaction (RT-PCR).

INTRODUCTION

Obesity is defined as abnormal fat accumulation in adipose tissue, which may lead to health impairment [1]. People are generally considered obese when their body mass index (BMI) is over 30 kg/m^2 [2]. It is characterized by a disrupted regulation in energy balance, which lead to excessive body fat accumulation. Its increasing prevalence poses a major public health concern because it is a risk factor for a host of additional chronic conditions, including chronic kidney diseases, type II diabetes, hypertension, cardiovascular disease and Cancer [3].

Uncoupling proteins (UCPs) are mitochondrial proteins that disperse the inter-membrane electrochemical potential as heat (energy homeostasis) [4]. They are of three types: UCP1, 2 and 3. UCP2 is considered of highly importance genes for regulating intracellular adenosine triphosphate (ATP). The human UCP2 gene is on chromosome 11. The loci of the UCP2 gene on these chromosomes are in regions that display linkage to obesity [5].

Because of its role in changing the rate of metabolism and increasing body mass index (BMI), comes the important role of UCP2 gene expression in some metabolic diseases [3]. It causes an imbalance of the ratio between intake and expenditure of energy that can lead to obesity [6]. On the basis of the central role of the UCP2 gene expression in obesity, it was hypothesized that UCP2 gene expression is a risk factor for obesity.

Methods

The current study was done in Zagazig University - Faculty of medicine, Medical Biochemistry and Internal medicine departments. Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association

(Declaration of Helsinki) for studies involving humans.

Thirty-one patients diagnosed as obese patients and thirty-one (age-matched) healthy unrelated volunteers were taken as a control group. None of the cases had any other disease that may interfere with the study parameters or were deteriorated cases.

The cases included 31 patients diagnosed as obese patients, 16 males and 15 females and their ages ranged from 42 to 65 with mean ± SD (55.2±6.3) years. Anthropometric measurement including height, weight and waist circumference (abdominal circumference at the level of iliac crest) and clinical details including blood pressure measurement were obtained from the case report.

BMI was calculated from the ratio of body weight in kg to height in square meters and expressed as kg/m^2 units. They were diagnosed as obese in accordance to their body mass index, their BMI ranged from 30.2 to 36.3 with mean ± SD (33.99± 1.4). All patients and healthy individuals gave their written consent before blood sample collection. In addition to a full history and clinical examination, routine investigations including X-ray for chest, liver function, kidney function, serum uric acid, fasting blood sugar analysis were performed to all cases to exclude factors that could influence measurements.

Collection of blood samples

Four ml of blood sample was taken from every participant under complete aseptic condition. The whole blood was collected in sterile EDTA (solute form) containing tubes and kept frozen at -20◦C till analysis.

RNA Extraction

RNA was isolated using Simply P Total RNA Extraction kit from Qiagen, Germany, catalogue No: Bsc52 S1. As per manufacturer's instructions, measurement of UCP2 gene expression RNA was converted into cDNA by reverse transcription (RT) using Real time reverse transcriptase polymerase chain reaction (RT-PCR) at 75°C for 5 min, 60°C for 60 min and 90°C for 5 min. (Maxime RT Premix kit catalogue no: 25081).

Quantitative Real-Time PCR was performed using real-time cycler (DTlite 4 DNA-TECHNOLOGY. PCR was performed in a final volume of 20 µL containing 7µL of H2O, 1 µL of template DNA, 1 µL of each primer (1 µM), and 10µL of 2X PCR Master mix solution (Qiagen, Germany).

We ran all samples in duplicate. The same set-up was used for the negative control, with one exception of cancellation of adding cDNA sample. There was no detection of PCR product in control conditions. Briefly, amplification of β actin and UCP2 mRNA was done in separate wells at 95°C for 10 minutes, then 55 cycles comprised at 95°C for 15 seconds and 60°C for one minuet for extension and annealing steps.

statistical analysis

We conducted statistical analysis using (SPSS) version 23 of the statistical package for Windows, considering a p-value of < 0.05 statistically significant.

RESULTS

The cases included 31 patients diagnosed as obese patients, 16 males and 15 females and their ages ranged from between 42 to 65 with mean± SD (55.2±6.3) years Table 1.

The results of the present study showed that there was a significant association of UCP2 gene expression among obese group when compared with the control group ($p<0.001$). And there was no significant association when compared according to gender Chi-square (X2) was 2.38and ($p=0.304$). Our results show negative significant correlation between UCP2 gene expression and BMI for obese group ($p<0.05$) Table 2.

Thirty-one patients in the obese group UCP2 gene expression was decreased with mean value of 0.2 while its mean value among control group is 0.95. There was a significant association when compared with the control group ($p <0.001$)) Table 3**.**

Table (1): Socio-demographic characteristics of studied groups

	Control group (N = 31)	**Obese group (N = 31)**	**Test of sig.**	**P**
Age per year Mean ±SD Median (min-max)	 52.7 ± 2.5 53(47-57)	 55.2 ± 6.3 55(42-65)	 F=2.1	 0.13
Sex no. (%) Male Female	 10(32.3) 21(67.7)	 16(51.6) 15(48.4)	 $\chi 2$ = 2.38	 0.304

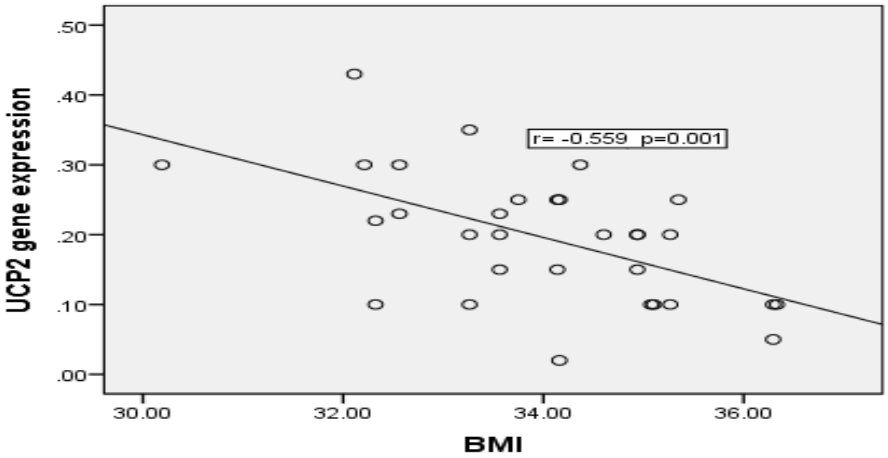
Table (2): Comparison between control group, and obese group regarding anthropometrics measures (each group n=31)

	Control group (N = 31)	Obese group (N = 31)	F test	P value	p-value between group
Weight/kg Mean ±SD Median (range)	75.29±5.1 74 (65-85)	100.5±8.4 97 (88-115)	178.9	<0.001	<0.001
Height/cm Mean ±SD Median (range)	181±6.5 181 (169-191)	171.8±5 170 (165-182)	23.9	<0.001	<0.001
BMI Mean ±SD Median (range)	22.9±0.98 23.2 (21.9-24.4)	33.99±1.4 34 (30.2-36.3)	919.9	<0.001	<0.001

Table (3): Comparison between control group and obese group regarding UCP2 gene expression (each group n=31)

	Control group (N = 31)	Obese group (N = 31)	F test	P value	p-value between group
UCP2 gene expression Mean ±SD Median (range)	0.997±0.25 0.95 (0.42:1.53)	0.196±0.093 0.2 (0.02: 0.43)	158.6	<0.001	<0.001

Figure (1): Scatter plot define the negative correlation between UCP2 gene expression and BMI for obese group r=-0.559.



DISCUSSION

Obesity is a major health problem for most countries in the world and is influenced by environmental and some genetic factors [7]. Obesity is abnormal fat accumulation in adipose tissue, which may lead to health impairment. People are generally considered obese when their body mass index (BMI) is over 30 kg/m^2, and considered as overweight when (BMI) ranges (25 to < 30) kg/m^2 [2].

Approximately 118 candidate genes are associated with obesity. Some of them are genes encoding leptins (LEP), leptin receptor (LEPR), uncoupling proteins (UCP), and insulin receptor (INCR) gene. The stability and regulation of body weight depends on energy expenditure, and adiposeness as well as the importantly food intake [8].

Uncoupling proteins (UCPs) are mitochondrial proteins that disperse the inter-membrane electrochemical potential as heat (energy homeostasis) [4,9]. UCP2 is considered as

mitochondrial membrane transporter expressed in white adipose tissue and is involved in energy balance regulation [10].

Uncoupler Protein (UCP2) gene consists of three hundred nine amino acids, it is located on chromosome 11q13, it consists of 8 exons and 7 introns, with 8174 base pair (bp) length. Disturbance of UCP2 expression in adipose tissue can lead to obesity [11].

To explore the possibility of Uncoupler Protein gene role in obesity, we examined the depot specific comparison of UCP2 gene expression in different metabolic states in our study.

We found a significant association of UCP2 gene expression among obese group when compared with the control group ($p<0.001$). And there was no significant association when compared according to gender Chi-square (X2) was 2.38and ($p=0.304$). Our results show negative significant correlation between UCP2 gene expression and BMI for obese group ($p<0.05$).

Similar to our finding, *Oliveira et al* found that UCP2 gene expression is downregulated in patients with obesity. *Brandao et al* also emphasized our results as they reported that UCP2 expression is lower in obese subjects when compared with normal weight subjects. The reduction in UCP2 expression could induce less active thermogenesis and adipose tissue fat accumulation [12,13].

Margaryan et al reported that all participants who had metabolic disorders had lower expression of UCP2 mRNA in comparison to the controls [14].

In agreement with our results was *Oberkofler et al* and *Sujata et al* who reported that UCP2 gene expression decreased in obese subjects in comparison to the control group [11,15].

The negative significant correlation between UCP2 gene expression and BMI for obese group is also proved by Pedersen et al as they experienced that the UCP-2 mRNA expression was inversely correlated with the amount of adipose tissue ($r = -0.53$, $p < 0.001$) [16].

Putting these findings together, indicate that status of UCP2 gene expression is likely to play a critical role in obesity.

CONCLUSION

These results suggested that UCP2 gene expression might be useful genetic biomarkers of obesity in Egyptian patients.

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