Association of Appetite and Related Hormones (Leptin, Ghrelin) with Resting Metabolic Rate of Overweight/ Obese Women: A Case-Control Study

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Abstract

Objective: Low resting metabolic rate (RMR) as a risk factor for weight gain and obesity can be influenced by many factors. Researchers have pointed out the role of appetite and related hormones in obesity and energy intake. The aim of this study was to investigate the relationship between appetite and related hormones in the two groups with normal and impaired resting metabolic rate in overweight or obese Iranian women.

Methods: In this case-control study, 42 healthy female volunteers aged 18-50 years (21 cases,and 21 controls) participated and were evaluated for RMR by indirect calorimetry. Body composition was determined by a body composition analyzer. The Filint questionnaire was used to assess appetite. We also used ELISA kits to assess appetite-related hormones. Finally, the data were analyzed using SPSS software version 25.

Results: The results of the study showed that there is a negative relationship between ghrelin hormone level (p-value = 0.024) and RMR, and there is a positive relationship between insulin hormone level (p-value = 0.001) and RMR. Also, result of the appetite questionnaire showed that in general, both appetite (p-value = 0.044) and hunger index (p-value = 0.043) have a positive relationship with RMR. There was no significant relationship between leptin levels and RMR.

Conclusion: As the results of this study show, it seems that appetite and related hormones have a possible role in promoting RMR.

Introduction

Obesity is one of the most important health problems in the last century and is gradually increasing(1).According to WHO, approximately one billion and three hundred million adults are obese or overweight(2).The etiology of obesity is multifactorial and is caused by various socio-economic factors such as sedentary lifestyle, increased caloric intake, excessive alcohol consumption, and is generally caused by an imbalance between energy intake and energy expenditure leads to accumulation of fat mass and consequently obesity(3). In general, Total daily energy expenditure consists of three main components: resting metabolic rate (RMR) or (REE), diet-induced thermogenesis (DIT) and activity-related energy expenditure (AEE)(4). Resting metabolic rate accounts for the largest share of total daily energy requirements (approximately 60 to 75%) and can be measured at rest and fasting by an indirect calorimetry. Numerous factors affect the level of resting metabolic rate, including age, sex, race, size, body composition, and hormonal status (5-9). Studies have shown that RMR is an important determinant of meal size and energy intake per day(10). RMR is also said to be a predictor of fasting hunger and affects the overall hunger profile (11). So RMR as an energy expenditure component reflects the physiological need for food intake(12).The brain regulates energy homeostasis through neuropeptide signals from adipose tissue and the gastrointestinal tract. For this reason, the gastrointestinal tract is one of the components of the food and appetite control system(13). Many intestinal peptides, including ghrelin, are secreted in this pathway(14). Ghrelin is derived from progerlin 117 amino acid, ghrelin is a 28 amino acid peptide hormone (appetite) that more than 70% of ghrelin is synthesized in the gastrointestinal tract in the fundus of the stomach (15, 16). Ghrelin is available in both acylated and non-acylated forms. Only 10-20% of circulating ghrelin is acylated, and this form is biologically active and plays a very important role in energy regulation and balance (17, 18). Systemic levels of ghrelin in the blood plasma are increased before eating and its secretion is stimulated and enhanced during hunger(19).Ghrelin therefore plays a role in controlling energy balance and increases food intake and reduces energy consumption(20).

Another hormone that affects the energy metabolism is leptin. Leptin is a non-glycosylated peptide hormone with a molecular weight of 16 kDa, encoded by the Obese (Ob) gene (21). This protein contains 167 amino acids, which are involved in regulating metabolic processes (22). It is mainly secreted from adipocytes and its circulating levels are associated with body fat mass (23). Leptin levels are higher in obese people than in normal weight people(24). However, due to the decreased sensitivity of leptin hypothalamic receptors, it is not able to perform actions to consume energy and regulate appetite, and causes a condition called leptin resistance in these patients(25). Leptin is described as a satiety factor that also has stimulating effects on energy consumption and therefore affects both levels of energy balance (26, 27). By reducing food intake and increasing energy consumption, it affects the central nervous system, especially the hypothalamus, and controls energy metabolism in the body(28).

However, studies on the relationship between appetite and the hormones leptin, ghrelin and insulin with energy metabolism reported conflicting results (29-36). We wanted to see how appetite and hormones differed in overweight/obese women with normal and low RMR. To the best of our knowledge, this is the first study of its kind in this field. We also wanted to see if there was an association between appetite and RMR in the people we studied.

Methods

Study population

We designed a case-control study and enrolled 42 women (21 cases and 21 controls) matched for age and BMI, who had been referred to a nutritional laboratory according to their registration in telegram bot we designed. Out of 1300 volunteers registered in telegram bot, 122 people were found suitable to enter the project, and finally 85 people had the final conditions for entry. After a monitoring period of 2-3 months to ensure no medication, supplements were taken, weight fluctuations happened and to check other inclusion criteria, individuals were referred to the Nutrition Laboratory of the Faculty of Nutrition and Dietetics located at the School of Health of Tehran University of Medical Sciences for more detailed evaluations. In order to randomly distribute the subjects in the case and control groups and according to the subject of matching for age and body mass index, individuals were divided into paired blocks in terms of age, body mass index and metabolism level. Each person in the case group (low metabolism) was randomly matched with a person in the control group (normal metabolism) with a difference in maximum age (± 2 years) and maximum body mass index (± 2 units). Volunteers were randomly selected for the study based on the following inclusion criteria (for both cases and controls): Female gender, 25≤ BMI<40 (obesity and overweight), Age over 18 to 50 years, satisfaction to participate in the study. To ensure comparable data, we considered exclusion criteria included: having cardiovascular disease, liver, kidney, thyroid, cancer, diabetes, heart failure and acute or chronic infections based on patient statements and medical history, consumption of drugs and supplements that affect the rate of metabolism, pregnant, lactating, postmenopausal women and professional athletes, history of weight loss surgeries, history of weight loss diet and weight changes during the last 6 months, drug and alcohol use, follow special diets, reluctance to continue reading were excluded. We used the individual's medical history or the person's own statements to check the inclusion and exclusion criteria of the samples.

Participants were told that they had the ability to withdraw themselves or their data from the study at any time. The study protocol was approved by the ethics committee of Tehran University of Medical Sciences (ethics code: (IR.TUMS.MEDICINE.REC.1399.261). All subjects signed written informed consent.

Measurements

Resting metabolic rate

In this study, resting metabolic rate was measured by indirect calorimetry. The MetaLyzer 3B-R3 Cortex Biophysik GmbH spirometer, made in Germany, was used (37).Ventilation and gas exchange were calibrated for each individual before each experiment. The amount of carbon dioxide produced and oxygen consumption per breath was recorded by the device. In this study, a mask designed to inhale and exhale was used and respiratory volume was transferred through a transducer attached to the mask, and gas samples were collected. Resting metabolic rate in the early morning and after 10 to 12 hours fasting was assessed. Participants should refrain from consuming caffeine and exercising vigorously for 24 hours before the test. Subjects were tested in the follicular phase of the menstrual cycle. The measurements were taken with the patients lying down in a supine position. It took 30 minutes and for the calculations, the mid-twentieth minute was taken into account (the first and the last 5 min were ignored). The room was kept at a constant temperature of 22 degrees Celsius.The validation of this device has been confirmed by several studies (38, 39).Out of 47 patients who underwent resting metabolic rate tests and their data were collected, a total of 21 patients were in the case group and 21 patients were in the control group. 3 patients with low resting metabolism (case group) and 2 patients with normal resting metabolism (control group) remained unadapted and were excluded from the study. The criterion for determining low resting metabolism in this study is based on the study of L Flancbaum et al.(40). Subjects were defined as “hypometabolic” when their measured RMR was less than 85 % of the predicted RMR, based on the Harris and Benedict equation, or “normometabolic” when it was within ± 15% of the predicted RMR. PRMR is also calculated based on the formula of Harris-Benedict(41).

Body composition

Body composition including weight, body mass index (BMI), body fat mass (BFM), fat free mass (FFM), visceral fat level, visceral fat area, skeletal muscle mass, body fat percentage (%), waist to hip ratio, waist circumference and soft lean mass were obtained using a body composition analyzer (42).To measure the body composition of all participants in the fasting state, a body analyzer InBody 770 scanner (Inbody Co., Seoul, Korea).Before measuring, according to the instructions of the manufacturer, all people were asked to remove their metal tools, including all jewelry. People were also asked to take off their socks and place their bare feet on the metal plate of the device to place their feet on the metal plate and increase the accuracy of the device. In using this device, how to stand and grab the metal handles of the device was done according to the manufacturer's instructions. After receiving the basic information of each person such as gender, age, height, this device provides the information of body composition from the bioimpedance method and through bioelectrical resistance analysis (BIA).

Dietary assessments

A person's usual dietary intake over the past year was assessed by interview using a semi-quantitative 147-item food frequency questionnaire (FFQ). Based on this questionnaire, the subjects were asked to report the frequency of their food consumption for each food item on a daily, weekly, monthly or yearly basis. The reliability and validity of this questionnaire in Iran had already been confirmed (43).Standard unit sizes and items reported on the household measures were converted to grams using the household measures Guide(44). The energy content of the food items in the feed frequency questionnaire was determined using data from the USDA Food Ingredients Table in the Nutritionist 4 nutrition software database.

Physical activity

In order to assess the physical activity of the participants, the short form of the International Physical Activity Questionnaire (IPAQ) designed by the World Health Organization was used (45).The validity and reliability of this tool have already been evaluated and accepted in Iranian adult women. Scores are calculated according to the frequency and time spent on light, moderate, high, and very high-intensity activities, based on a list of common daily activities.

Appetite:

In this study, Flint appetite questionnaire was used to assess mental feelings about appetite. The questionnaire was developed by Flint et al. In 2000 at the Frederic Berg School of Nutrition in Denmark (46). The amount of appetite is the amount of points that a person obtains in this test. We used paper and pen methods and filled out the appetite questionnaire in the morning after the RMR test, and body composition were taken .In this research, four indicators are included feeling of desire for food, feeling of hunger, feeling of satiety, feeling of consuming future food.So that the horizontal line with a length of 100 mm is drawn between the two options, I am not hungry at all (zero points), I have not been so hungry so far (100 points).The person expresses the feeling of the moment by marking it on this line. In fact, this scale divides appetite into four components, each of which changes independently of the other. This questionnaire has been used in most studies that indirectly measured appetite since 2000. And its reliability in our study was determined by Cronbach's alpha r = 0.80.

Blood sampling

From all participants, 10 cc of fasting blood was taken between 7-10 am and immediately divided. Half was poured into anticoagulant tubes. After storage for 30 minutes at room temperature, a blood clot formed and then centrifuged at 3000 g for 20 minutes. Serums were stored in clean microtubes in a freezer at -80 ° C until the experiment was performed.

Biochemical and hormonal assessments

All hormones were measured by the enzyme-linked immunosorbent assay (ELISA) method. Leptin levels were assessed with an LDN kit (Nordhorn, Germany) with a sensitivity of 0.50 ng/ml, total ghrelin levels were assessed with a sensitivity of 0.01 ng/ml with Crystal Day Christian Day kit, China and insulin levels were assessed with an IBT kit (infinitum biotech, IBT; Netherland) with a sensitivity of 0.11 μU / ml.

Intra- and interassay coefficients of variation (CV) reported by the manufacturer were 3.7– 5% and 5.9–5.8% for leptin, respectively, and CV<8% and CV<10% for total ghrelin, respectively, and 3.7-4.2% and 3.7-4.2% for insulin.

Statistical analysis

Findings of the study were analyzed using SPSS software version 25. Values less than 0.05 were considered significant for all tests. The normality of variable distribution was evaluated using Kolmogorov-Smirnov and Shapiro Wilk tests. Because our data did not show a normal distribution and we used non-parametric tests. Wilcoxon test was used to determine the difference between quantitative variables between case and control groups. Chi-square test or Fischer exact tests was used to determine the distribution of qualitative variables between case and control groups. Linear regression analysis was used to determine the relationship between appetite and related hormones with resting metabolic rate. In the adjusted model, body fat percent was adjusted.

Results

Baseline participant characteristics are presented in (Table-1). The median of age, weight, and BMI were not significantly different among the case and control groups. The results of the median comparison test showed that there was a statistically significant difference between the case and control groups in terms of body fat percentage (P = 0.027). Based on the test of qualitative variables (such as physical activity) between case and control groups, it was found that there is no significant difference between the two groups (is presented in Table-2), and also there was no significant difference in terms of intake of macronutrients, and food groups between the two groups (is presented in Table-3).In (Table-4), the median of studied appetite and hormones are presented. Examination of appetite and leptin, ghrelin, and insulin hormones showed no significant difference between case and control groups (P> 0.05).To find an association between appetite and hormones with RMR, we conducted linear regression in the crude and adjusted model (presented in Table 5). Our crude result found that the insulin hormone levels (β = 0.488 p-value=0.001) are significantly related to resting metabolic rate, and also there is an inverse association between ghrelin hormone levels (β=-0.34, p-value=0.027) and RMR. Besides after adjusting for confounding variables as body fat percentage remained significant. And also in the adjusted model, there is a positive association between appetite (β = 0.323, p-value=0.044) and RMR. In Table 6, we also examined the index of the appetite questionnaire and their relationship with RMR. The results showed that there was a positive significant relationship between the rate of hunger (β = 0.309, p-value=0.047) and RMR, which remained significant after adjusting for the confounder variable.

Discussion

Findings from our case control study showed that there is no significant difference between the median appetite and hormones of leptin, ghrelin and insulin between the two groups with normal metabolism and impaired metabolism. But there is a positive relationship between insulin levels with RMR and there is a negative relationship between ghrelin levels with RMR, there is also a positive relationship between appetite and the rate of hunger with RMR, which remained significant after adjusting for confounder (body fat percentage).

Resting metabolic rate, which is one of the main determinants of energy expenditure (60-70%), can be related to the amount of energy intake per day and eating behaviors. Studies have shown that RMR is an important determinant of meal size and energy intake per day (12). RMR is also said to be a predictor of fasting hunger and affects the overall hunger profile. So RMR as an energy expenditure component reflects the physiological need for food intake. This hypothesis is in line with Edholm's theory that the difference in food intake is due to the difference in energy expenditure (47).

In our study, the results of appetite in the case and control groups indicate a significant direct relationship with RMR. Also, in examining the indicators of the appetite questionnaire(46) with resting metabolic rate, we found that there is a positive relationship between hunger and RMR, which remained significant after adjusting for the confounding variable, which was in line with the results of the study by Caudwell et al. (10). Another point is that there is a paradox that says why in obese and overweight people who have high fat mass and a high amount of energy stored in their body, the tendency to eat and hunger is high, in fact one of the reasons is that, in these people, due to high fat mass, high lean mass (FFM) is also high and FFM is one of the important determinants of RMR, and the higher the RMR level, the higher the rate of hunger and appetite is (10).

In the present study, the hypothesis that the serum level of leptin hormone is associated with resting metabolic rate in the two groups with normal and impaired metabolism was not accepted, which could be due to the low number of samples in the groups. In general, several studies have been conducted to investigate the relationship between leptin and obesity. This indicates that the majority of obese people have higher blood leptin levels than normal people (90%) and the amount of leptin in the blood increases in proportion to the amount of body fat, especially subcutaneous fat, so that there is a direct relationship between the serum level of leptin and its BMI (48). There is evidence to suggest that leptin is involved in regulating energy metabolism. Energy metabolism and body temperature increased in ob/ob mice after leptin injection (49-51).

In our study, the results of leptin in the case and control groups showed no difference between the two groups and no significant association was observed between this hormone and RMR, which was in line with the results of the study by Neuhauser et al.(52). Human studies examining the relationship between leptin hormone and RMR have published conflicting results, some of which have reported no association between RMR and leptin levels in adults (31-33). Some studies also reported a positive association (34, 35), and some a negative association (36). One of the reasons for these contradictory results may be differences in procedure. When we want to study the relationship between leptin and RMR, body composition, FM, FFM is very important and these variables must be considered. While many of these studies reported a positive association, did not pay attention to these variables. In fact, because one of the most important determinants of serum leptin is body fat (34) and in our study, all the samples were obese and overweight, and these two groups were matched based on BMI and age, so it may be the reason for not seeing a difference in leptin levels between the two groups.

We found that there is a negative relationship between serum ghrelin levels and resting metabolic rate in two groups with normal and impaired metabolism. There is evidence to suggest that ghrelin is involved in energy metabolism, especially in regulating food intake (53-60).

In our study, the results indicate a significant inverse relationship of ghrelin hormone with RMR, which is in line with the results of Marzullo et al.(61). The Marzullo study, which investigate 20 obese and 20 lean samples for metabolism and ghrelin levels, found that serum ghrelin levels were 30 percent lower in obese people than in normal people, and with increasing adipose tissue ,there is decrease in leptin and insulin, ghrelin levels. In addition, ghrelin levels decrease less after eating in obese people (62-64). Although an increase in ghrelin levels causes weight gain by increasing food intake and decreasing the energy metabolism and fat catabolism (30, 55, 65).The effect is primarily due to increased calorie intake and the shift of cells from fatty acid oxidation to oxidation of glucose (30, 55).The relationship between ghrelin and energy metabolism levels in obese and overweight people needs further investigation(66). Some studies have shown different results from our research. A study by Ravussin et al. On non-obese identical twins did not show a significant relationship between ghrelin levels and positive and negative energy balance(30). The reason is that ghrelin has two different and contradictory effects on the human body through the somatotropic effect of growth hormone, which leads to a decrease in fat mass and an increase in lean mass, and through the adipogenic effect of ghrelin, leading to an increase in food intake and a decrease in fat oxidation. In fact, people with higher ghrelin levels for the same size and body composition will gain more weight due to overeating and less weight loss due to negative energy balance(30).However, ghrelin is expected to intervene endogenously to improve impaired metabolism (29). In an interventional study conducted in 2018 by Allas et al., They found that injection of non-acylated ghrelin analog (AZP-531) reduced waist circumference and fat mass in humans without changing weight (67).Another human study by Allas et al. in 2016 found that injecting non-acylated ghrelin analogues in obese and overweight adults, decreased weight 2.6 kg and also improved glucose levels without increasing insulin (68). In our study, we found that with the increasing level of ghrelin, carbohydrates per day burned as a substrate for energy (which comes from the result of RMR test) reduces (p-value=0.01). This is in line with a study by Wortley et al.2004, they observed that endogenous ghrelin plays an important role in determining the energy substrate (53) and also conflicting with previous studies which demonstrate that increasing level of ghrelin causes shift of the cells from fatty acid oxidation to oxidation of glucose and ultimately leads to the accumulation of fat in the body (30, 55).Therefore, the possibility that ghrelin intervenes to improve the level of impaired metabolism should be considered.

The present study demonstrates that the serum level of insulin hormone is associated with RMR in two groups with normal and impaired metabolism. In fact, the results showed that in general, the higher the level of insulin hormone, the higher the resting metabolic rate, which is in line with the results of Drabsch et al. (69).Hemostatic regulation of glucose is through the action of the hormone insulin in adipose tissue, muscle and liver tissue. Insulin is an anabolic hormone and is made and stored in the granule cells of the islets of Langerhans. And is secreted in response to an increase in blood glucose concentration (70).The main function of this hormone is to transport glucose into muscle cells and adipose tissue, which causes glycogen synthesis and lipogenesis, and inhibits gluconeogenesis in the liver. In general, one of the main functions of insulin is to focus on tissues that regulate energy metabolism (71).The results of our study demonstrate that insulin hormone in the case and control groups indicate a significant positive relationship with RMR, which is consistent with the results of the study of Ravussin et al. Through the Euglycemic Insulin clamp technique, the thermic effect of insulin and glucose injection can be studied in detail. In this technique, RMR is measured by indirect calorimetry during insulin and glucose injections. The results of several studies have shown that between 50-70% increases in the level of resting metabolism is due to glucose injection and rising insulin levels and conversion of glucose to glycogen (72-74).

Conclusion

The results of this study showed that there is a relationship between ghrelin, insulin, appetite and hunger levels with resting metabolic rate. The higher the level of insulin hormone, the higher the level of RMR and the higher the level of ghrelin, the lower the level of RMR, appetite and hunger index were directly related to the RMR. But in our study, the results of leptin in the case and control groups showed no difference between the two groups and no significant association was observed between this hormone and RMR. Based on the results of some animal intervention studies, it seems that the injection of these hormones through various mechanisms, changes RMR. In this regard, it is recommended to study this relationship by measuring more factors such as acyl and non-acyl ghrelin, insulin sensitivity and other factors related to appetite, especially in the form of clinical trial studies because it is not possible in the form of observational studies of cause and effect relationships.

Abbreviations

RMR, Resting Metabolic Rate; REE, Resting Energy Expenditure; EE, Energy Expenditure; AEE, Activity Energy Expenditure; DIT, Diet Induced Thermogenesis; BFM, Body Fat Mass; FFM, Fat Free Mass. FFQ, food frequency questionnaire; IPAQ, International Physical Activity Questionnaires; CV, coefficients of variation; BIA, Bioelectrical Impedance Analysis; BMI, Body Mass Index

Strengths And Limitations

This study is not able to find the cause and effect relationship due to the case-control design. Furthermore, the study only looked at overweight/obese women, and while we matched cases and controls by age and BMI, there could be some other factors that skewed our results. Considering strengths of the current study, this study for the first time evaluates the relationship between appetite and related hormones with resting metabolic rate in obese/overweight women. RMR was measured by indirect calorimetry which is considered as the gold standard for measuring energy expenditure(4). Also in the present study, the menstrual cycle of women was considered and all of them were examined when they were in the follicular phase. In addition, we measured each participant's dietary intake, body composition, and physical activity.

Declarations

Availability of data and materials

The authors confirm that the data supporting the findings of this systematic review are available within the manuscript and in the included tables.

Author contributions

SH and KM designed the study. SH, HI and SM contributed to the literature searches, data collection and measurements. SY contributed to the statistical analyses and interpretation of the data, SH drafted the manuscript. KM critically revised the manuscript; and agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

Consent for publication

Consent was received from all authors for the publication of this review.

Ethical approval

The study has been approved by the Ethics Committee of Tehran University of Medical Sciences.

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Conflict of interest

The authors declare no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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Tables

Table 1 .Characteristics of the subjects in case and control groups (median and interquartile range)

variables	Normal RMR group (n=21)			Impaired RMR group (n=21)			P value*
	Median,IQR	min	max	Median,IQR	min	max	
Demographic							
Age	35.00,11	25	45	34.00,9	25	47	0.27
Height	163.00,6	154	171	159.00,7	151	168	0.06
weight	80.00,16	62.7	102.1	75.40,13.5	58.8	105.7	0.28
Resting Metabolic rate							
RMR (Kcal/d)	1,541,232.50	1291	1967	1306.00,325.0	830	1716	<0.001
RQ	0.88,0.10	0.83	1.1	0.89,0.08	0.79	1	0.68
Body Composition							
FFM (kg)	46.8,6.10	37.4	57.5	43.10,9.10	34.2	56.7	0.06
FM(kg)	34.00,14.1	21.4	47.2	33.00,9.8	24.2	54.4	0.3
SMM(kg)	25.40,3.9	20.2	31.8	23.30,5.4	18	31.7	0.06
TBW(L)	34.20,3.5	27.4	42.2	32.5,6.8	25.1	41.6	0.08
%PBF	41.40,8.9	30.6	48.3	44.70,5.7	36.1	51.4	**0.027**
WHR	0.93,0.07	0.85	1.4	0.92,0.07	0.86	1.03	0.49
WC(cm)	98.90,17.3	87.1	117.4	93.80,13.3	85.5	120.9	0.54
BMI (kg/m^{2})	29.00,6.9	26.1	38.1	29.10,4.7	25.5	39.8	0.18

Table 2. Description of qualitative data

variable		Normal RMR group (n=21)		Impaired RMR group (n=21)		P-Value*
		N	percentages	N	percentages	
Physical Activity[1]	High	0	0	2	9.5	0.21
	Moderate	12	57.1	14	66.7	
	Low	9	42.9	5	23.8	
Education	Bachelor	18	85.7	18	85.7	0.1
	Associate Degree	2	9.5	1	4.8	
	Diploma	1	4.8	2	9.5	
Occupation	Housewife	3	14.3	9	42.9	0.1
	Employee	18	85.7	11	52.4	
Marriage Status	Married	14	66.7	11	52.4	0.53
	Single	7	33.3	10	47.6	
Economic Status[2]	Weak	1	4.8	2	9.5	0.58
	Medium	9	42.9	8	38.2	
	Good	11	52.4	11	52.4	
BMI[3]	Overweight	11	52.4	13	61.9	0.75
	Obese	10	47.6	8	38.1	

*Obtained from Fisher's exact test

1-Physical activity levels: low: 600MET / Min / week>, medium: 600-3500 MET / Min / week, intense: 3500MET / Min / week <
2-The economic status is graded based on the number of items listed in the general questionnaire: less than 3 weak, 4-6 medium and 7-9 good.
3-Body mass index levels are classified according to WHO criteria. Overweight: 25-29.9 (kg / m 2) Overweight and 30≤ Obesity.

Table 3. Evaluation of food intakes between case and control groups

Variable	Normal RMR group n=21(Median,IQR)	Impaired RMR group n=21(Median,IQR)	P- value*
Energy(kcal)	2103.24,630.44	2279.99,888.25	0.18
Protein(g/d)	81.89,34.65	88.00,30.81	0.84
Carbohydrate(g/d)	289.09,74.74	327.93,115.96	0.14
Fat(g/d)	78.23,24.92	76.58,37.54	0.63
Creal(g/d)	102.55,307.30	351.20,145.55	0.09
Fruites(g/d)	321.00,225.90	261.40,314.50	0.2
Vegetable(g/d)	254.00,277.50	336.80,197.30	0.21
Legumes(g/d)	48.30,47.35	46.50,62.90	0.33
Dairy(g/d)	330.20,232.85	320.20,167.30	0.49
White meat(g/d)	32.30,31.10	50.00,69.25	0.18
Red meat(g/d)	16.90,17.50	21.30,29.50	0.2
Fiber(g/d)	37.92,22.07	36.76,16.67	0.15

Table4.Comparison of the median and interquartile range of the appetite and hormones between case and control

variables	Normal RMR group (n=21)			Impaired RMR group (n=21)			P value*
	Median,IQR	min	max	Median,IQR	min	max	
Appetite Questionnaire							
Appetite	250,88	125	350	225,63	125	300	0.56
Hormones							
Leptin	21.25,6.55	2.21	26.52	20.57,3.99	9.69	26.52	0.9
Ghrelin	1.76,2.68	1.27	10.57	2.11,5.43	1.34	9.23	0.38
Insulin	14.88,6.21	6.97	26.96	13.88,6.42	6.54	35.4	0.43

Table5. Relationship between appetite and hormones with RMR

Variable		Coefficient Beta	Standard Error	*P-Value
Appetite	Crude Model	0.293	0.76	0.06
	Model 1	0.323	0.782	0.044
Leptin	Crude Model	0.063	8.935	0.693
	Model 1	0.022	9.657	0.897
Ghrelin	Crude Model	-0.34	14.309	0.027
	Model 1	-0.349	14.354	0.024
Insulin	Crude Model	0.488	6.177	0.001
	Model 1	0.518	8.087	0.001

Model 1: Modified for body fat percentage (PBF%)

* Obtained from General Linear Model (GLM)

Table6. Relationship between variables of appetite questionnaire with RMR

Variables of appetite Questionnaire		Coefficient Beta	Standard Error	*P-Value
Desire to eat	Crude Model	0.25	2.115	0.11
	Model 1	0.247	2.128	0.117
Hunger	Crude Model	0.309	1.443	**0.047**
	Model 1	0.315	1.448	**0.043**
Fullness	Crude Model	0.028	1.582	0.859
	Model 1	0.033	1.592	0.837
prospective food consumption	Crude Model	0.059	1.834	0.71
	Model 1	0.035	1.891	0.832

Model 1: Modified for body fat percentage (PBF%)

* Obtained from General Linear Model (GLM)