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ORIGINAL ARTICLES

Cross-sectional study about nutritional risk factors of metabolically unhealthy obesity

RYM BEN OTHMAN,[1] OLFA BERRİCHE[2], AMEL GAMOUDİ[2], RAMLA MİZOURİ[1], DONİA JERAB[2], NADİA BEN AMOR[2], FATEN MAHJOUB[2], HENDA JAMOUSSİ[2]

[1]University of Tunis El Manar, Faculty of Medicine of Tunis
[2]National Institute of Nutrition and Food Technology Service A, Tunis

Abbreviation list:

MS: metabolic syndrome
IDF: International Diabetes Federation
T2dm: type 2 diabetes mellitus
WHO: World Health Organization
MHO: metabolically healthy obese

Introduction: A substantial proportion of obese subjects are metabolically healthy and free from metabolic complications. Many mechanisms that could explain the existence of the metabolically healthy obese phenotype have been suggested, involving in particular a healthy lifestyle and diet. The aim of this study was to study the anthropometric, nutritional and biological profile of two groups: obese with metabolic syndrome (MS+) and obese without metabolic syndrome (MS-).

Methods: It is a cross-sectional study, conducted between January 2022 and 15 March 2022. We recruited 90 obese MS+ and 82 obese MS-. Both groups were matched for age and sex. The glycemia, triglycerides (TG), total cholesterol (TC), HDL-C, LDL-C were measured as well as the body composition and anthropometric data. The diet was determined by the 24-hour recalls. Eating disorders, sleep disorders (PSS4 scale) and depression (HADS) were also searched.

Results: In MS+ group we noticed: higher BMI, waist circumference, more caloric diet, elevated consumption of saccharides. This group had more eating disorders such as night eating syndrome and bulimia and sleeping disorders (sleep onset and total insomnia). MS+ group was more stressed and depressed. The MS- group had a Mediterranean diet and more intake of: EPA, DHA, olive oil, green tea, oleaginous fruits, linseed, vegetables and whole grains. They also practiced more fasting.

Conclusions: It is important to know the protective nutritional factors of the metabolic syndrome in order to be able to focus on them during education sessions and thus protect the obese from metabolic complications.

Key words: obesity, Mediterranean diet, metabolic syndrome, sleep disorder, olive oil.

INTRODUCTION

The prevalence of obesity has increased worldwide. Indeed, according to a study carried out by the WHO in 2019, the prevalence of overweight in the world concerned 39% of adults worldwide, i.e. more than 1.9 billion adults, including 650 million obese [1]. As for Tunisia, the Tunisian Health Examination Survey carried out in 2019 showed that the prevalence of obesity among Tunisian adults reached 26.2% [2].

The importance and interest in Metabolic syndrome (MS) with obesity lies in its association with many metabolic diseases such as type 2 diabetes mellitus (T2DM) and coronary heart disease

However, this link between overweight, visceral obesity and the appearance of metabolic disorders is not an absolute rule, because not all obese people systematically develop the metabolic abnormalities described above. Indeed, the literature describes a phenotype of obese subjects and who do not present any metabolic complication. They are called “metabolically healthy obese” (MHO) [3].

Numerous studies suggest that a healthy diet (Mediterranean diet) coupled with a healthy lifestyle would prevent the onset of metabolic complications in obese subjects [4] and reduce the risk of onset of the metabolic syndrome [5, 6]. This type of diet characterristically uses olive oil, fish, wheat, olives, and grapes.

This is why we have chosen in this end-of-studies project to focus on this theme, and to focus our study on the comparison between the nutritional profiles of obese people with or without metabolic syndrome.

Thus, the objectives of our study were to compare the anthropometric, nutritional and biological profiles of two groups: obese with metabolic syndrome (MS+) and obese without metabolic syndrome (MS–), and to identify the factors associated with the presence of metabolic syndrome in obese subjects.

MATERIAL AND METHODS

We recruited consecutively all obese subjects who consulted the obesity unit at the national institute of nutrition of Tunis, between January and March 2022: there were 172 obese adults attending this outpatient unit in this period. They were subdivided into 2 groups:

1st group: 90 obese with Mets (**MS+**)

2nd group: 82 obese without Mets (**MS-**)

These two groups were matched for sex, age and body mass index (BMI).

We included in our study obese patients who volunteered or who gave their consent, aged over 18 and with a BMI ≥ 30 kg/m^2 according to the WHO classification [7].

We have not included: Patients who have not given their consent to participate in the study, BMI < 30, Patients under the age of 18, pregnant and breastfeeding women, on long-term corticosteroid therapy, patients with a history of pathologies that may influence their eating behavior such as psychiatric, neurological or neoplastic disorders, patients with thyroid disorders and patients with renal insufficiency. Syndromic, genetic, endocrine or iatrogenic obesity were not included. Patients with a disturbed renal assessment and missing medical reports were excluded.

We assessed the presence of the following eating disorders:

– Prandial hyperphagia: Excess calorie consumption at mealtimes.

– Snacking: Frequent and repeated ingestion of various foods between meals without hunger feeling.

– Night eating syndrome: Nocturnal hyperphagia.

– Binge eating disorder: Recurrent episodes of binge eating, but without resorting to the inappropriate compensatory behaviors characteristic of bulimia.

– Food compulsions: Consumption of food following a sudden impulse and which often occurs between meals.

Psychological profile (stress, sleep quality, depression and anxiety)

All patients benefited from an interview including food survey, stress questionnaire (Cunji), sleep questionnaire (Epworth), symptoms of depression and anxiety (HADS).

For the evaluation of stress, we used the brief stress evaluation scale, this is the scale of Cungi 1997 [8]. This scale is made up of 11 items, and for each the response is from 1 to 6.

The evaluation of the quality of sleep was carried out using the Epworth Sleepiness Scale [9], this questionnaire assesses the level of daytime sleepiness of the patient. It is composed of 8 items, and for each situation the patient must select an answer from (0 to 3). The interpretation is as follows:

– A total of less than 10 suggests that there is no excessive daytime sleepiness

– A total of 10 and above suggests excessive daytime sleepiness.

To assess the depressive state of the patients, we used the "HAD" scale (Hospital Anxiety and Depression Scale) [10]. This is a structured questionnaire of 14 items. This questionnaire consists of two subscales each having 7 items, one for anxiety, the other for depression. Each item is rated on a 4-point scale, i.e. from 0 to 3, evaluating the intensity of symptoms over the past week. The scores therefore range from 0 to 21 and the highest scores correspond to the presence of more severe symptoms. The addition of the scores obtained for each item allows the following interpretation:

- Less than 7 points: no symptoms of depression.
- 8 to 10 points: doubtful symptomatology.
- 11 and over: certain symptomatology.

To distinguish our two groups (MS+ and MS-) we based on the definition adopted by the IDF [11]: a waist circumference ≥ 94 cm in men and ≥ 80cm in women, fasting triglyceridemia ≥ 1.50 g/l (1.7 mmol/L) or treatment, HDL cholesterol < 0.4 g/l (1.03 mmol/l) in men and < 0.5 g/l (1.29 mmol/L) in women, blood pressure ≥ 130/85 mm Hg or treatment or fasting blood glucose ≥ 1 g/l (5.6 mmol/l) or treatment. Three criteria are needed for the diagnosis.

This research was conducted in accordance with the Declaration of Helsinki, for research involving human subjects. Ethical approval was obtained from the Ethics Committee at the national institute of nutrition of Tunis. Written consent was given by all participants.

Clinical history was obtained and a complete examination was carried out for all participants. Weight, height, calculated BMI and waist circumference. Fat mass and lean body mass were measured using bioelectrical impedance TANITA scale.

A lab test was performed fasting including: glycaemia, HbA1C, uric acid; AST, ALT, cholesterol, triglycerides, HDL and Low-density lipoprotein cholesterol (LDL-C) levels were calculated using the Friedewald formula. Venous blood samples were immediately processed in the laboratory of the national institute of nutrition.

The calorie intake was provided by the computer software NUTRILOG, which was validated in Tunisia and contains Tunisian food data. Using this software, the calorie content as well as the macro- and micronutrient content of the diets of patients was determined based on their 24-hour recalls entries. We used a questionnaire from the PREDIMED study to seek the adherence of our sample to the Mediterranean diet [12]. It is a validated questionnaire of 14 questions, allocating 1 point for each validated unit and making it possible to establish a final score of adherence to the Mediterranean diet [13–15].

Physical activity was measured using the short version of the International Physical Activity Questionnaire (IPAQ), in French version [16–17]. It is a validated questionnaire allowing to estimate the physical activity carried out during the last 7 days, by relating to its frequency, its duration and its intensity. The IPAQ score was obtained using an online computer application [18]. It made it possible to define three levels of physical activity: high, moderate and low.

Paired Student's t-test was used for dependent samples to compare the anthropometric, biochemical, and dietary variables in both groups. Data analysis was performed using the SPSS version 22 Package.

RESULTS

At the beginning of the recruitment, no statistically significant differences were found in age, gender and BMI, indicating that the study population was homogenously distributed in both groups, as can be observed in Table 1.

In the MS+ group: 40.4% of patients already had known and treated hypertension, 57.4% of patients presented with pathological systolic BP (p=0.001) and 25.5% of patients presented with pathological diastolic BP (p=0.01).

In the MS+ group there were 36.2% of diabetics against 5.90% in the MS- group. The majority of patients in the MS+ group (57.4 %) were in the prediabetes stage, while the majority of patients in the MS- group (55.9 %) had normal glycemic status (p=0.0001).

The MS+ group had an average triglyceride dosage very significantly higher than the MS- group, of which 41.3% of MS+ patients had a pathological triglyceride dosage, against 0% of MS- patients (p=0.0001). The MS+ group had an average HDL dosage very significantly lower than the MS- group of which 70.2% of MS+ patients had an HDL dosage pathological, against 36.4% of MS- patients (p=0.03).

The level of physical activity (using IPAQ score) did not differ significantly between the two groups (p=0.35) and Mets/min was lower in MS+ group without a significant difference (712.81 vs 844.83, p=0.82).

We searched in our populations for several disorders related to MS such as: depression, stress, sleeping disorders and eating disorders. Results are present in Table 2. PSS4 stress scale showed that MS+ group was more stressed than MS- group (8.23 versus 5.38 p=0.02).

Diet comparison between groups is shown in Table 3.

The MS– group had a significant intake in the consumption of MUFA, EPA and DHA ($p < 0.05$); No significant difference was identified for SFA, PUFA, vitamin C, and vitamin E.

We have completed the food survey by a frequency questionnaire; the distribution of patients according to their frequency of consumption of certain foods is shown in Table 4.

After calculating the points obtained by each group for the 14 units of the questionnaire, the mean score for adherence to the Mediterranean diet was significantly higher in the MS- group than in the MS+ group (7.49 *versus* 6, p=0.003). So the MS- group adhered more to the Mediterranean diet.

The level of physical activity did not differ significantly between the two groups. Indeed, 61.7% of the MS+ group had a moderate physical activity versus 73% in MS- group; p= 0.35.

Table 1

General characteristics of the population

	MS+	MS-	p
Mean age (years)	46.85	44.95	0.44
Women (%)	91.5	97.3	0.37
Married (%)	72.3	64.9	0.13
Weight (kg)	108.17	98.54	**0.01**
Height (cm)	162.57	160.08	0.11
BMI (kg/m²)	40.12	38.53	0.28
Waist circumference (cm)	120.52	114.67	**0.01**
Fat mass (kg)	50.98	45.63	**0.05**
Lean mass (kg)	56.77	53.01	**0.03**
Fasting glucose level (mmol/l)	7.59	5.42	**0.0001**

Table 1 (continued)

HbA1C (%)	6.64	5.65	**0.0001**
Past medical history of hypertension (%)	40.4	10.8	**0.003**
Past medical history of DM (%)	27.7	13.9	0.13
Past medical history of dyslipidemia (%)	34	13.9	**0.03**
Mean systolic BP (mmHg)	13.75	12.19	**0.0001**
Mean diastolic BP (mmHg)	8.21	7.01	**0.0001**
TG (mmol/l)	1.7	1.01	**0.0001**
TC (mmol/l)	5.05	4.98	0.78
HDL (mmol/l)	1.17	1.4	**0.0001**
Calculated LDL-C (g/l)	1.26	1.2	0.5
Creatinin (µmol/L)	59.43	55.44	0.22
Uric acid (µmol/L)	310.00	297.58	0.47
AST (UI/L)	21.96	22.03	0.96
ALT (UI/L)	21.33	18.45	0.16

Table 2
Association between SM and different disorders

	MS+ (%)	MS- (%)	p
Hyperphagia	78.7	61.6	0.09
Snacking	61.7	61	0.7
Night eating syndrom	46	22	**0.02**
Bulimia	60.2	34	**0.04**
Compulsion	74.2	63.2	0.15
Regular eating pattern	23.6	48.2	**0.01**
Constantly meals in front of screens	44.7	35.1	0.48
Regular fasting outside the month of Ramadan	12.8	40.5	**0.004**
Sleep onset insomnia	66	43.2	**0.04**
Total insomnia	29.8	10.8	**0.05**
Epworth normal	57.4	75.7	0.29
HADS>10 (certain depression)	10.6	2.7	**0.01**

HADS: hospital anxiety and depression scale

Table3
Diet comparison between groups

	MS+	MS-	p
Calories (kcal)	3145	2553	**0.001**
Calorie surplus (calories-daily energy requirements) (Kcal)	1181	608	**0.001**
Fiber (g)	26.8	29.25	0.24
Cholesterol (mg)	314.17	252.14	0.08
Carbohydrates (g)	381.93	291.73	**0.0001**
Carbohydrates (g/kg of ideal body weight)	6.6	5.2	**0.01**
Proteins (g/d)	98.1	86.78	**0.02**
Proteins (g/kg of ideal body weight)	1.6	1.5	0.07
Lipids (g)	123.98	106.92	**0.03**
SFA (%)	8.5	8.4	0.9
MUFA (%)	14.25	16.46	**0.001**
PUFA (%)	10.19	12.11	0.42
Sodium (mg)	2499.6	2088	**0.04**
Potassium (mg)	3208.79	2888.58	0.09
Vitamin c (mg)	123.37	120.92	0.88
Vitamin E (mg)	28	26.39	0.44
Linoleic acid (g)	32.06	23.45	**0.003**
Alpha linolenic acid (g)	1.61	1.1	**0.0001**
Omega 6/ omega 3	21.44	22.19	0.72
EPA (mg)	107	207	**0.001**
DHA (mg)	127	249	**0.002**
Fructose (g)	59.15	42.19	**0.008**
Sugars (g)	114.27	85.01	**0.005**

KCal: calories

d: day

SFA: saturated fatty acids

MUFA: monounsaturated fatty acids

PUFA: polyunsaturated fatty acids

EPA: eicosapentaenoic acid

DHA: docosahexaenoic acid

Table 4
Food consumption frequencies of the population

Frequency of consumption	Mean		p
	MS+	**MS-**	
Olive oil (frequency/week)	4.80	5.87	**0.04**
Corn oil (frequency/week)	2.83	3.7	0.24
Combined vegetable oil (frequency/week)	3.57	1.86	**0.01**
Butter (frequency/week)	0.52	0.35	0.52
Margarine (frequency/week)	0.65	0.13	**0.02**
Fries (frequency/week)	1.85	1.36	0.23
Grean tea (frequency/week)	3.21	4.64	**0.03**
Coffee (frequency/day)	1.53	1.62	0.74
Nuts (frequency/week)	1.23	2.58	**0.02**
Flaxseed (frequency/week)	0.096	1.3	**0.001**
Added sucrose (g/day)	19.5	11.6	**0.04**
Soda (frequency/week)	2.48	1.72	0.24
Fruits (portion/d)	1.98	2.09	0.74
Vegetables (g/d)	207.98	309.46	**0.0001**
Whole grains (frequency/week)	0.67	2.79	**0.0001**
Fishs (frequency/week)	1.57	1.51	0.45
Eggs (frequency/week)	7.28	5.56	0.06

DISCUSSION

The results of the present study demonstrate differences in food consumption and psychological profile between the two groups. Indeed the MS+ group had a waist circumference and a BMI more important but also their food comsuption was more caloric, rich in glucose and fructose, butter and oil and they had also eating disorder and sleep insomnia. They were more stressed and depressed than MS- group. In the other hand, MS- group had Mediteraneen diet, with an intake of olive oil, green tea, seed, vegetables, flaxseeeating disorderd and whole grains more frequent. They had a more regular eating pattern and they practiced fasting more frequently.

The benefits of a Mediterranean diet on health, cardiovascular disease prevention, and other aliments have been shown in adult populations with obesity [19]. Even though adherence to the Mediterranean diet is important, other factors also influence obesity prevention, such as eating habits, depression, stress, sleeping disorders and eating disorders [20]. Thus, it is necessary to strengthen adherence to the Mediterranean diet while also addressing other factors that contribute to obesity and metabolic alterations.

Since hypertension, glycemic disorders, tryglicerides and HDL values are part of the components of the diagnosis of the metabolic syndrome, results showed in Table 1 are therefore expected.

Eating disorders (bulimia and night eating syndrome) more frequent in the MS+ group. Indeed, according to a recent study by Hudson *et al.*, binge eating shows a strong association with MS. Importantly, this association appears to be related not only to increased body weight, but also to other independent factors that remain poorly understood [21]. According to another study by Hudson *et al.*, binge eating may confer a risk of developing metabolic disorders that are part of the components of MS, beyond the risk attributable to obesity alone [22]. Similarly for McCuen *et al.* [23], where it is the food choice of patients during night eating (fatty and carbohydrate-rich foods) that explains the appearance of metabolic disorders.

The practice of fasting outside the Ramadan period is much more frequent in patients in the MS– group. A study conducted by Eljaafari showed that the caloric restriction resulting from the practice of fasting could protect against inflammation and the metabolic syndrome associated with obesity. Indeed, the infiltration of immune cells within adipose tissue in obese people contributes to the establishment of an environment of chronic low-grade inflammation, leading to the installation of tissue resistance to insulin. Thus, according to this study, the practice of fasting demonstrated beneficial effects in reducing obesity associated with the metabolic syndrome, thanks to the reduction of inflammation in adipose tissue [24]. Also, a large number of studies support the effects of fasting on reducing the risk of obesity and improving cardio-metabolic parameters [25, 26].

In our study, patients in the MS+ group had more depressive symptoms according to HADS than in the MS- group. Indeed, a review of the literature and meta-analysis, studied the relationship between MS and depression, showed that there was a significant relationship between depression and MS [27]. Depression can also lead to the development of MS by inducing unhealthy behaviors such as alcohol consumption, smoking, poor quality diet, sedentary lifestyle and sleep disturbances [28].

In our study, patients in the MS+ group were more stressed. Indeed, a prospective study on the association between work stress and MS and including 10,308 participants aged 35 to 55 years, revealed a dose-response association between exposure to work stress and the MS. Indeed, employees with chronic job stress were more likely to develop MS than those without job stress [29]. Chronic stress leads to the activation of central nerve pathways and prolonged stimulation of the adrenal glands, leading to an increase in the secretion of glucocorticoids. This mechanism would lead to the appearance of insulin resistance and MS [30].

Our results showed a significantly higher consumption of green tea in the MS- group. Green tea is characterized by the presence of a high concentration of polyphenolic compounds called catechins, which are an important source of dietary antioxidants in humans. Epigallocatechin-3-gallate being the most abundant and the most studied [31]. Thus, the beneficial effects of epigallocatechin-3-gallate on health are attributed to its great antioxidant function [32]. Studies have suggested that epigallocatechin-3-gallate causes a reduction in fasting blood sugar levels through altered expression of the GLUT4 gene, increased insulin sensitivity, and facilitates the entry of glucose into blood cells [33]; In addition, it would reduce the rate of cholesterol absorption by affecting the micellar solubilization of cholesterol in the digestive tract [34].

Association between sucrose and MS was well studied in the literature. An experimental study by Andres-Hernando *et al*. showed that overconsumption of sucrose led to the onset of obesity and MS in mice [35]. According to the prospective cohort study SUN, an increase in the consumption of sugar-sweetened beverages was associated with a higher risk of onset of SM and the onset of other metabolic disorders [36]. Another review of the literature, including 24 studies and 93,095 participants, highlighted a dose-response association between the consumption of sugary and artificially sweetened beverages and the risk of SM onset [37].

The mean score for adherence to the Mediterranean diet was significantly higher in the MS- group than in the MS+ group (7.49 versus 6, p=0.003). The Mediterranean diet is characterized by a higher consumption of vegetables, fruits, legumes, whole grains, nuts, olive oil and fish, with a moderate consumption of dairy products and wine and a low consumption of red meat [38]. This joint consumption of healthy foods causes synergistic effects between the different bioactive components of the Mediterranean diet. Thus beneficially influencing several metabolic pathways at the origin of type 2 diabetes and MS. The SUN Cohort is a prospective cohort study that found an inverse relationship between adherence to a Mediterranean diet and the incidence of MS [39]. Another study also reported an inverse association between adherence to the Mediterranean diet and waist circumference, blood pressure, and low HDL levels [40]. But still, the PREDIMED study also demonstrated that participants' adherence to a Mediterranean diet for a period of 4.8 years were 1.35 times more likely to reverse MS compared to a control group [41]. Based on the evidence presented above, Mediterranean diet may protect against metabolic diseases linked to chronic inflammation and overproduction of reactive oxygen species.

Consuming enough fruits and vegetables is a main feature of most healthy diets, such as the Mediterranean diet. This group of foods contains significant amounts of fiber, vitamins with antioxidant power (vitamin C, vitamin E, beta-carotene), minerals and polyphenols, such as flavonoids. Indeed, it seems that their ability to reduce oxidative stress and inflammation [42], to lower blood pressure [43] and to prevent weight gain [44] would be the main arguments in favor of their beneficial effects. Other studies have also shown a trend towards a lower risk of developing MS with higher consumption of fruits and vegetables [45, 46].

Limitation: small size and the design of the study.

In conclusion, our study showed differences between the nutritional profiles of obese subjects with or without metabolic syndrome and revealed the presence of nutritional, dietary, biological, psychic and anthropometric factors associated with metabolic syndrome in obese subjects. A healthy lifestyle and a healthy Mediterranean-type diet may be recommended for all obese subjects in order to prevent them from metabolic complications.

Introducere: *O proporție crescută de pacienți obezi au o formă metabolic sănătoasă a obezității caracterizată prin lipsa sindromului metabolic. Multe mecanisme care ar putea explica apariția acestui fenotip au fost sugerate, în principal, făcându-se referire la stilul de viață sănătos și la dietă. Scopul acestui studiu fost să caracterizeze profilul antropometric, nutrițional și biologic a două grupuri: obezi cu sindrom metabolic (MS+) și obezi fără sindrom metabolic (MS-).*

Metode: *Este un studiu transversal, desfășurat între 22 ianuarie și 15 martie 2022. Au fost recrutați 90 obezi MS+ și 82 obezi MS-. Ambele grupuri au fost echilibrate ca vârstă și sex. Glicemia, trigliceridele, colesterolul total, HDL-C și LDL-C au fost măsurate și au fost adunate datele antropometrice și cele corespunzătoare compoziției corporale. Dieta subiecților a fost notată conform metodei amintirii alimentelor ingerate în ultimele 24 ore. Totodată a fost investigată și prezența tulburărilor de alimentație, tulburărilor de somn (scala PSS4) și a depresiei (HADS).*

Rezultate: *În grupul MS+ s-a observat: BMI și circumferința taliei semnificativ mai mari, dietă mai bogată caloric cu consum crescut al carbohidraților. În acest grup s-au obiectivat tulburări de alimentație, precum sindromul alimentației nocturne și bulimia, precum și tulburări de somn (insomnie de inducție, precum și insomnie atât de inducție, cât și de menținere). Subiecții din grupul MS+ au avut niveluri mai mari de stres și erau mai depresivi.*

În ceea ce privește grupul MS- aceștia urmau o dietă mediteraneeană și aveau aport mai mare de EPA, DHA, ulei de măsline, ceai verde, fructe oleaginoase, semințe de in, legume verzi și cereale integrale. Totodată, aceștia aveau perioade mai lungi de fasting.

Concluzii: *Este important să cunoaștem factorii nutriționali protectori față de sindromul metabolic, astfel încât să ne putem concentra asupra lor în educația pacienților, urmând ca aceștia să fie astfel protejați de complicațiile sindromului metabolic.*

Correspondence to: Rym Ben Othman, M.D,University of Tunis El Manar, Faculty of Medicine of Tunis, 11 rue Jbal Lakhdhar 1029 Bab Saadoun Tunis
Mail: benothmanr@gmail.com
Phone: +21652262806

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