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Comparing of Metabolic Syndrome Components, Inflammation, Cortisol Level, and Psychological Distress in Obese/Overweight and Normal Weight Women

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ABSTRACT

Background: High levels of stress in obese people, hypothalamic-pituitary-adrenal (HPA) axis disorder, and social pressures can increase cortisol level and lead to psychological disorders. The aim of this study is to compare psychological distress, biochemical parameters, and metabolic syndrome components between normal-weight and overweight (OW)/obese women. **Methods:** This was an analytical cross-sectional study conducted on 75 women aged 18 to 60; they were divided into three groups: obese and OW on diet (obese/OW on diet), obese and OW without diet (obese/OW without diet), and normal-weight. The components of metabolic syndrome, serum cortisol, and high sensitive C-reactive protein (hs-CRP) levels were measured. General health questionnaire-28 (GHQ-28) was also completed to assess psychological distress. **Result:** The results revealed that there was a significant difference between normal weight and the other two groups regarding metabolic syndrome components, which included waist circumference (WC), fasting blood sugar (FBS), systolic blood-pressure (SBP), and hs-CRP (P<0.05). Serum cortisol level was significantly higher in obese/OW on diet compared with the other two groups (P<0.001). Moreover, the total-GHQ score was significantly lower in normal weight compared with the group of obese/OW on diet and the group without diet (P=0.001). **Conclusion:** Being on a diet may expose a person to stress and increase the serum cortisol level. Elevated psychological distress, metabolic syndrome components, and inflammation were apparent in obese and OW women compared to normal-weight ones.

Keywords: *Obesity; Metabolic syndrome; Inflammation; Psychological distress; Diet; Non-communicable diseases*

Introduction

Obesity, as a chronic multifactorial disease, results from a positive balance of energy and excess fat accumulation throughout life. Obesity leads to structural abnormalities, physiological damage, and functional disorders when left untreated (Jastreboff *et al.*, 2019). According to the World Health Organization (WHO), overweight and obesity are among the top five causes of

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mortality in the world (World Health Organization, 2009). Moreover, it has been shown that obesity can lead to many complications including Type-2 diabetes (T2D), cardiovascular disease, insulin resistance (Barazzoni *et al.*, 2018), metabolic syndrome (Expert Panel on Detection, 2001, Segula, 2014) and psychological problems (Gortmaker *et al.*, 1993, Segula, 2014).

Since obesity is considered a chronic stressor for body and creates the stigma of being obese, it can stimulate hypothalamic-pituitary-adrenal (HPA) axis. It has been suggested that a prolonged period of HPA-axis stimulation to chronic obesity stress disrupts HPA-axis regulatory mechanisms (Hillman *et al.*, 2012, Vinstrup *et al.*, 2021). Studies have shown that HPA-axis, which plays an important role in fat metabolism and distribution, makes a great contribution to the development of obesity by over-stimulation in response to increased stress (Hillman *et al.*, 2012, Morita *et al.*, 2016). Moreover, there has always been a reciprocal connection between cortisol levels and obesity to the extent that one can stimulate the other and vice versa. Accordingly, any stimulus that targets either of these two seems to be able to affect the other and change the course of treatment (van Rossum, 2017). Cortisol, known as one of the most important glucocorticoids, increases glucose production in liver cells and develops hyperglycemia. Elevated cortisol level inhibits insulin secretion from pancreatic beta cells. This inhibition is associated with impaired glucose tolerance and insulin resistance (Amatruda *et al.*, 1985, Gulliford *et al.*, 2006). Cortisol also increases plasma-free fatty acids by stimulating the breakdown of stored triglycerides (TG) in adipose tissue (Björntorp and Rosmond, 2000). Some previous reports have shown that there is an objective link between cortisol and obesity or cortisol and metabolic syndrome (Abraham *et al.*, 2013).

As previously mentioned, one of the complications caused by obesity is mental problems, where psychological distress assumes great significance. Psychological distress refers to a distressing emotional state experienced by an individual in response to a particular stressful situation which inflicts temporary or permanent harm to the individual (Ridner, 2004). The most common symptoms of psychological distress include anxiety, depression, and loss of emotional/behavioral control (Veit and Ware, 1983). Given that mental disorders affect all physiological systems of the body; researchers have focused on the role of this phenomenon in the pathophysiology of non-communicable diseases. Some of these psychological problems, like depression and anxiety, are associated with chronic metabolic disorders such as insulin resistance, type 2 diabetes, and dyslipidemia. The relationship between obesity and mental health is a complex issue comprised of physical, social, and psychological factors (Gatineau and Dent, 2011). In addition, this relationship is a two-way route; that is, obesity lowers the quality of life, which return, increases mental disorders. People suffer from mental problems due to different causes such as drugs side effects, bulimia nervosa, being OW or obese, etc. (Taylor *et al.*, 2013). Another factor that mediates the relationship between body mass index (BMI) and psychological distress is the stigma of obesity. It means that inappropriate labels on obese people in society, along with discrimination and prejudice in their treatment, lead to symptoms of psychological distress, especially anxiety and depression (Alimoradi *et al.*, 2020, Lin *et al.*, 2020). This is why psychological distress is considered both the cause and effect of obesity since it is the result of social pressures on obese people. Moreover, the resulting physiological changes can complicate the process of obesity. On the other hand, with regard to the people who undergo weight-loss treatment, decreased self-esteem resulting from the stigma of being overweight is among the main causes of treatment failure, suggesting the effect of psychological factors on the outcome of treatment (Petroni *et al.*, 2007). This study aims to compare physical and biochemical parameters, metabolic syndrome components, and psychological distress between overweight or obese women referred to diet therapy clinics for weight loss for more than

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three consecutive periods, overweight/obese women who were referred to the clinics for the first time, and normal weight women.

Materials and Methods

Study design and participants: All the participants in this study were selected from women referred to Imam Reza Nutrition and Diet Therapy Clinic affiliated with Shiraz University of Medical Sciences (SUMS), Shiraz, Iran from November 2019 to October 2020.

Eligible participants were 18 to 60-year-old women with BMI ≥ 25. Pregnant and lactating women; subjects with a history of hospitalization in psychiatric clinics, drug addiction, smoking, use of sleeping pills and glucocorticoids; those with connective tissue disease, tumors, diabetes, any inflammatory diseases, and recent viral infection; use of any medication for hypertension, dyslipidemia, and diabetes; and those who used other methods of weight reduction like surgery or special medications were excluded from this study. Furthermore, the participants were not under a medical condition or took no medications that could affect pituitary and adrenal glands functioning.

In the first group of the study, the participants were required to have more than three consecutive visits to the SUMS Imam Reza Nutrition and Diet Therapy Clinics regarding weight loss diet. Meanwhile, in the second group, the participants had the same inclusion criteria and it was their first visit to the clinics. The third group also had the same inclusion criteria, with the exception of having a normal weight (BMI= 18.5-24.9 kg/m^2).

Moreover, participants who had followed a weight loss diet during three months prior to the onset of the study were not included in the second and third groups of the study.

The sample size of this study was calculated based on multiplying the number of independent variables by 10 (Bujang *et al.*, 2017). Independent variables in this study were the level of blood pressure, TG, waist circumference (WC), fasting blood sugar (FBS), HDL-Cholesterol, hs-CRP, serum cortisol, psychological distress, BMI, fat mass, muscle mass and being on diet. Accordingly, the sample size was decided to include 120 (12×10) participants. 90 participants were assigned to the first and second groups of the study (45 participants in each group) and 30 participants to the third group. However, this study was conducted at the beginning of Covid-19 pandemic period, and since then, many clients avoided going to diet therapy clinics during the pandemic. The size of the sample was based on the last existing files and the files that would be collected in a one-year period.

In this cross-sectional-analytical study, 300 clinical weight loss files were collected from clients who were referred to SUMS diet therapy clinic, Eventually, 25 women who met the inclusion criteria agreed to participate in this study (group1, obese/OW on diet) (**Figure 1**).

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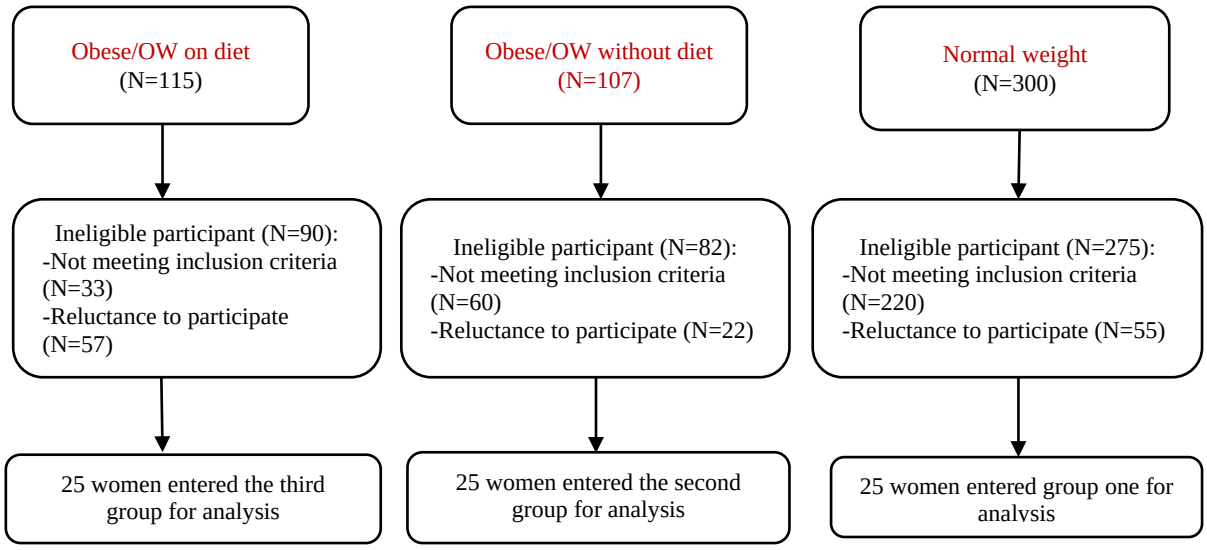

Figure 1. Flowchart of the study.

In addition, 25 OW/obese women, who met inclusion criteria and went to diet therapy clinic for the first time, agreed to take part in the second group of the study (group 2, obese/OW without diet). 25 women in the third group were selected through convenience sampling from healthy people with normal weight who referred to the SUMS clinics and agreed to participate in the study (group 3, normal weight).

After explaining the study protocol over the phone by the staff of the clinic, the eligible clients came to the clinic on separate days and times to complete the consent form. The required information including dietary intake, demographic and anthropometric information, and psychological distress questionnaire were completed, and they went to the designated laboratory for blood sampling.

Measurements: Three-day dietary records checklist was given to the participants and they were asked to record their food intake on two week days and one day on weekend according to the educational brochure. Meanwhile, the participants were contacted and their questions were answered by an expert nutritionist. Then, the daily energy intake of the participants was computed by Nutritionist-4 software (first data bank, San Bruno, CA, USA) which was modified for Iranian foods. Moreover, the participants' physical activity level was recorded by metabolic equivalents (MET) questionnaire with MET/h/day which included nine questions and was validated for Iranian population (Aadahl and Jørgensen, 2003). At the beginning of the study, a demographic questionnaire addressing the participants' age, level of education, and marital and employment status was completed by all the participants.

Weight (kg) and height (cm) of all the participants were measured at the beginning of the study by Seca scale (to the nearest 0.1kg and 0.1cm, respectively). BMI of all the groups was calculated based on weight (kg)/height (m)^2. WC was measured between the iliac crest and lower ribs by a flexible meter.

The participants' fat mass, lean mass, and water body weightwere also measured using a bioelectric impedance analysis device (BIA, BC-418) in a standing position. Fifteen minutes before the analysis, the participants were asked to remain in a standing position and perform body composition analysis on an empty stomach before any physical activity (Mialich *et al.*, 2014).

Five-milliliter venous blood sample was collected after 10-12 hours of fasting at 8 am from each participant to measure biochemical data. Blood samples were centrifuged at 2000g/min for 10 minutes to separate the serum which was stored at −70 °C until further analysis.

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FBS, TG, and high-density lipoprotein cholesterol (HDL-C) serum levels were measured using an autoanalyzer (Biotecnica Instrument, BT1500) via commercial kits (Parsazmun, IRAN). Serum levels of cortisol and hs-CRP were measured by ELISA kits (Diametra and LDN, respectively).

GHQ-28 was completed by the participants to measure psychological distress. This questionnaire assesses their mental health status during the previous weeks. The 28-items GHQ consists of four subscales to evaluate somatic symptoms (questions 1 to 7), anxiety and insomnia (questions 8 to 14), social dysfunction (questions 15 to 21) and severe depression (questions 22 to 28). A point Likert scale was used which ranged from 0 for "never", 1 for "usually", 2 for "rather more than usual", and 3 for "much more than usual" (Momenan *et al.*, 2012). 0 is the minimum score of GHQ-28, and 84 is the highest one. Lower GHQ-28 scores represent lower levels of psychological distress (Goldberg and Hillier, 1979).

Taghavi confirmed the reliability and validity of Iranian version of GHQ-28 questionnaire in their study (Taghavi, 2002). Based on Hmwe et al.'s suggestion, the subjects with a total score of ≤ 23 may be classified as having normal mental health, and those with scores >23 were categorized as psychiatric (Hmwe *et al.*, 2015).

Ethical considerations: The protocol of this study was reviewed and approved by the local ethics committee of Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.REC.1398.758). This protocol was described for the participants and informed consent form was obtained from them.

Data analysis: SPSS3 was used to perform statistical analysis. Data were reported as median (IQR) or mean±SD according to the normal/abnormal distribution determined by the Shapiro-Wilk test. A chi-square test was used to describe qualitative variables of the study. To compare the groups, ANOVA test and Tukey's post-hoc test were used for normally distributed data, and Kruskal-Wallis test was used to compare skewed data. Moreover, a multivariate linear regression test was used to predict psychological distress, and Spearman correlation test was used to determine the correlation. P-value was statistically significant at ≤0.05.

Results

Seventy five women with a mean age of 36.8±9.5 participated in the study. **Table 1** shows the participants' demographic characteristics. The three groups of the study did not differ significantly in terms of age, educational level, and marital status, but the employment status was significantly different (P=0.007).

Table 2 shows the participants' anthropometric measurements, physical activity level, and calorie intake. The three groups did not differ significantly in terms of physical activity level. However, there was a significant difference in weight, BMI, fat mass, muscle mass, and body's water weight regarding the three groups of the study (P<0.001 in all cases).

Post-hoc analysis demonstrated that the groups of normal weight, obese/OW on diet groups, and the obese/OW without diet were significantly different in body weight, fat mass, muscle mass, and body water weight (P<0.001). Moreover, the groups significantly differed in their amount of calorie intake (P<0.001).

Table 3 shows the participants' metabolic syndrome, serum level of cortisol, and hs-CRP. As this Table shows, WC was significantly different in the three groups (P<0.001), the reason of which might be due to the significant difference between the obese/OW on diet and normal weight groups, and between the normal weight and the obese/OW without diet groups (P<0.001). In addition, FBS level was different in the three groups (P=0.004), which is shown to be due to the significant difference between the groups of normal weight and obese/OW on diet (P=0.03), and normal weight and obese/OW without diet (P=0.005). Additionally, the serum TG level was significantly different in the three groups (P=0.01); moreover, Tukey's post-hoc test showed a significant difference between the groups of normal weight and obese/OW without (P<0.007). Regarding SBP, a significant difference

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was observed in the three groups (*P*=0.001) which was due to the significant difference between normal weight and obese/OW on diet cases (*P*=0.009) and normal weight and obese/OW without diet ones (*P*=0.002). DBP and serum levels of HDL-C were not significant in all the groups.

Table 1. Demographic characteristics of the participants regarding the three groups.

Variables	Obese/OW on diet n=25	Obese/OW without diet n=25	Normal weight n=25	P-value[a]
Age(y)				0.33
20-30	4(16)[b]	8(32)	9(36)	
31-40	12(48)	14(56)	9(36)	
41-50	6(24)	3(12)	5(20)	
51-60	3(12)	0	2(8)	
Level of education				0.17
Illiterate	1(4)	0	0	
Belo high school diploma	2(8)	0	2(8)	
High school diploma	10(40)	5(20)	4(16)	
Associate degree	5(20)	3(12)	5(20)	
Bachelor's degree	11(44)	9(36)	11(44)	
Master's degree	2(8)	8(32)	3(12)	
Employment status				
Unemployed /housewife	21(84)	11(44)	18(72)	
Rank 3 job[c]	0	1(4)	1(4)	0.007
Rank 2 job[d]	4(16)	13(52)	3(12)	
Rank 1 job[e]	0	0	3(12)	
Marital status				0.22
Single	4(16)	8(32)	8(32)	
Married	20(80)	15(60)	13(52)	
Widowed /divorced	1(4)	2(8)	4(16)	

[a]: Chi-square test; [b]: n(%); [c:] Apprentice shop, laborer, driver, simple clerk; [d:] Business owner, skilled clerk, military service members; [e:] Managers and bosses, top-level military, physician, dentist, university professor.

Table 2. Comparison of anthropometric indicates, physical activity, and calorie intake in the three groups.

Variables	Obese/OW on diet n=25	Obese/OW without diet n=25	Normal weight n=25	P-value[a]
Weight(kg)	84.4(69.5-114.9)[b]	76.7 (65-105)	58.3 (49-68)	<0.001
Body mass index(kg/m²)	31.8 (26.1-41.2)	29.5 (25-40.5)	22.2 (18.88-24.89)	<0.001
Fat mass(kg)	31.4 (24.30-59.90)	28.0 (19.90-48.7)	18.1 (12.6-.23.1)	<0.001
Muscle mass(kg)	46.0 (37.3-54)	45.5 (39.7-56.3)	39.7 (33.6-42.6)	<0.001
Body water weight(kg)	36.2 (33.8-38.3)	34.3 (32.6-36.1)	30.9 (29.7-31.9)	<0.001
Physical activity (MET.h/day)	36.3 (32.8-39.4)	33.9 (30.5-39.6)	38.8 (32-45.1)	0.12
Calorie intake(kcal)	1347.0±367.5	2635.0±364.5	1248.9±274.4	<0.001

[a]: Kruskal-wallis test was used to compare the groups except calorie intake (one-way ANOVA); [b]: All the data were presented as median (IQR) except calorie intake mean±SD.

Furthermore, the cortisol level was significantly different in the groups (*P*<0.001). Based on post-hoc test, the serum cortisol level in obese/OW on diet group was significantly higher than normal weight (*P*<0.001) and the obese/OW without diet groups (*P*=0.004). The serum level of hs-CRP was also significantly different between the three groups (*P*<0.001), the reason of which was the significant difference between the normal weight and obese/OW on diet groups (*P*=0.001) and between normal weight and obese/OW without diet groups (*P*<0.001).

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Table 3. The comparison of metabolic syndrome components and biochemical parameters in the three groups.

Variables	Obese/OW on diet N=25	Obese/OW without diet N=25	Normal weight N=25	P-value[a]
Circumference waist(cm)	105.1 (91-132)	100.3 (87-115)	84.4 (71-101)	<0.001
Fasting blood sugar(mg/dl)	99.3 (80-205)	97.1 (75-148)	86.2(71-102)	0.004
Triglyceride(mg/dl)	148.0(73-322)	161.8(91-444)	114.4(58-180)	0.01
Systolic blood pressure(mmHg)	115.4 (80-140)	116.6 (90-140)	107.0 (80-120)	0.001
Diastolic blood pressure(mmHg)	70.9(60-100)	79.2(60-95)	77.8(65-90)	0.7
High density lipoprotein(mg/dl)	42.7±6.7	45.1±3.3	48±9.0	0.13
Serum cortisol(ng/ml	257.8 (115.1-398.1)	176.9 (101.1-410)	163.9 (93.9-301.2)	<0.001
C-reactive protein(ng/ml)	8.2 (1.0-14.9)	5.8 (0.8-13.2)	1.8 (0.1-5.9)	<0.001

[a]: All data except High density lipoprotein (HDL-C) were analyzed by Kruskal-Wallis test, and the values were reported as median (IQR) and HDL-C data were analyzed using one-way ANOVA, and the values were reported as mean±SD.

Table 4 shows the scores of psychological distress and their subscales among the three groups of the study. The scores for GHQ-total, anxiety/insomnia, social dysfunction, and severe depression symptoms were significantly different in all three groups (*P*=0.001, *P*=0.007, *P*=0.002 and *P*=0.003, respectively). The post-hoc test also showed that GHQ-total and severe depression scale were significantly different between the normal weight and obese/OW on diet participants (*P*=0.01, *P*=0.004, respectively) as well as normal weight and obese/OW without diet ones (*P*=0.001, *P*=0.02, respectively). The post-hoc analysis also revealed that there was a significant difference between normal weight and obese/OW without diet groups regarding anxiety/insomnia and social dysfunction scales (*P*=0.005, *P*=0.002, respectively). In addition, the prevalence of psychological distress was 28% in the obese/OW on diet group, and %36 in the obese/OW without diet group; there was no psychological distress in the normal weight group.

Table 4. Scores of general health questionnaire regarding the groups

Variables	Obese/OW on diet n=25	Obese/OW without diet n=25	Normal weight n=25	P-value[b]
GHQ-total[a]	19.08 (5-38)	21.44 (9-48)	12.36 (1-21)	0.001
Somatic symptom	5.72 (2-13)	5.76 (1-15)	4.20 (1-9)	0.15
Anxiety/insomnia	5.08 (0-13)	6.60 (1-12)	3.52 (0-8)	0.007
Social dysfunction	6.24 (2-12)	7.20 (3-14)	4.44 (0-7)	0.002
Severe depression	2.04 (0-11)	1.88 (0-13)	0.20(0-3)	0.003

[a]: General health questionnaire-total; [b]: All data were analyzed using Kruskal-Wallis test and the values were reported as median (IQR) (25^{th} percentile and 75^{th} percentile)

To evaluate the likelihood of psychological distress, hs-CRP, daily calorie intake, serum cortisol, and BMI of all the study groups were included in the model. The results of the model showed that none of the mentioned variables were related to the probability of psychological distress and that they were not predictive of it.

The average number of the sessions in which the obese/OW women participated regarding the first group visiting the dietitian at diet therapy clinic was 4.9±2.0 times, and their average weight during diet therapy sessions was 5.6±4.6 kg (5.9±3.6 percent of initial weight). On the other hand, the correlation between weight loss and cortisol was weak and direct (r=0.25, *P*=0.22), yet the correlation between weight loss and hs-CRP was weak and inverse (r=-0.23, *P*=0.26), and weight loss had no significant correlation with GHQ-total (r=0.0, *P*=0.72).

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Discussion

In this study, the authors simultaneously compared the components of metabolic syndrome, inflammation, cortisol, and psychological distress in the three groups of obese/OW women on diet, the obese/OW without diet, and normal-weight women. WC, FBS, and SBP were higher in the obese/OW without diet and on diet groups compared to the normal-weight one. Moreover, given the role of obesity in the formation of toxic adipose tissue, cytokines, inflammation, and increased insulin resistance, it Interfere with the homeostatic regulation of blood sugar and liver function and increases FBS, along with TGs and blood pressure, all of which collectively lead to metabolic syndrome (Akter *et al.*, 2017, Marchesini *et al.*, 2001). Many studies have reported a positive association between obesity and the components of metabolic syndrome (Saleh *et al.*, 2017, Walatara *et al.*, 2016, Zampetti *et al.*, 2018). However, in this study, no significant difference was observed between the three groups of the study regarding DBP. As a cardio metabolic risk factor, obesity is associated with accelerating aortic stiffness, which increases SBP, compared to DBP (Zampetti *et al.*, 2018).

On the other hand, the rate of weight loss in the obese/OW on diet did not contribute to a significant difference regarding the mean components of metabolic syndrome compared to the obese/OW without diet. Nonetheless, previous studies revealed the impact of weight loss on the components of metabolic syndrome, but it is noteworthy that the obese/OW on diet did not achieve the ideal weight, and the average weight loss was 4.6±6.5 kg (Harvie *et al.*, 2011, Phelan *et al.*, 2007). This discrepancy in findings could be the reason for the lack of significant difference between the obese/OW on diet and without diet groups. In a study conducted on obese people with diabetes, Wing et al. reported a slight decrease in serum levels of fasting blood glucose in people with a weight loss of less than 6.9 kg (Wing *et al.*, 1987). Based on the rate of their weight loss, Wing *et al.* divided the participants into four groups: with a weight loss of 0 to 2.3, 2.4 to 6.8, 6.9 to 13.6, and more than 13.6 kg. In addition to examining fasting glucose, their study showed that in order to reduce the serum level of TG and increase HDL-C, it is necessary to lose more than 13.6 kg (Wing *et al.*, 1987). In another study conducted by Poorolajal *et al.*, the rate of weight loss affecting blood pressure was reported to be 24-40% in OW cases and 54-40% in obese ones (Poorolajal *et al.*, 2017). Meanwhile, the mean percentage of weight loss in the obese/OW on diet group in this study was only 5.9±3.6.

Findings related to hs-CRP showed higher inflammation in both the obese/OW women on diet and without diet, compared to the normal-weight group. Several studies supported the association between inflammation and hs-CRP, on the one hand, and obesity, on the other (Ellulu *et al.*, 2016, Lavanya *et al.*, 2017, Monteiro and Azevedo, 2010). Adipose tissue, as an endocrine gland, produces proinflammatory adipocytokines (e.g. IL-1, IL-2, IL-6 and…), which stimulates the production and release of C-reactive protein from liver. Therefore, with the increase in body fat mass, along with weight gain, the production of inflammatory cytokines in the body such as CRP also increases (Black *et al.*, 2004). Nevertheless, the identified mechanisms include abnormalities in fatty acid homeostasis, increased fat cell size, local hypoxia, and mitochondrial dysfunction (Heilbronn and Liu, 2014, Reilly and Saltiel, 2017). These mechanisms function as a link between excess calories and chronic inflammation or are the factors that may perpetuate chronic tissue inflammation (Burhans *et al.*, 2018).

In this study, the level of hs-CRP was not significantly different between the obese/OW on diet and without diet. A systematic review study reported that for every kilogram of weight loss achieved through any type of intervention, 0.13 mg/dl C-reactive protein was reduced (Selvin *et al.*, 2007).

In this study, despite the average weight loss of 6.4±6.5 kg in the obese/OW on diet group, hs-CRP level was not significantly different regarding the two obese/OW groups of the study. Due to the researchers' lack of knowledge

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regarding the amount of hs-CRP before starting diet in the obese/OW on diet, it is likely that the mean level of hs-CRP before the start of the diet was higher, which decreased after weight loss; however, its serum level is still higher than that of the group without diet. On the other hand, different studies have reported different weight losses for reduced hs-CRP levels. Madsen et al. suggested a weight loss of more than 10% to improve hs-CRP levels and inflammatory factors (Madsen *et al.*, 2008). However, a clinical trial study showed that a weight loss of more than 5% obtained from a calorie-restricted diet would reduce the serum level of hs-CRP (Imayama *et al.*, 2012). Thus, it is suggested that more studies should be performed in the future.

Comparing serum cortisol levels indicated that, contrary to the authors' expectations, the level of serum cortisol was higher in the obese/OW on diet group compared with the obese/OW without diet. Since the difference in the mean weight regarding the two groups was not statistically significant, and the level of serum cortisol in women on diet was not significantly correlated with the rate of weight loss (r=0.22, *P*=0.25), higher cortisol in women on diet might be the result of weight loss treatment and energy deficiencies, regardless of reduced weight. In line with this study, Tomiyama *et al.* found that dietary monitoring increased psychological distress, and calorie restriction increased plasma cortisol levels (Tomiyama *et al.*, 2010). Likewise, another study on the relationship between the level of serum cortisol and calorie restriction corroborated the effect of calorie restriction on increasing cortisol levels (Nakamura *et al.*, 2016).

The reason for this increased cortisol is not only a rise in psychological distress, but also the release of cortisol to maintain energy reserves when calorie restriction is less than 1200 (Nakamura *et al.*, 2016, Tomiyama *et al.*, 2010).

Conversely, in this study, the cortisol levels were significantly higher in both obese/OW women compared with normal-weight women. This finding was supported by numerous previous studies regarding increased cortisol levels in hair and serum samples of obese men and women (Al-Safi *et al.*, 2018, Chan *et al.*, 2014, Hu *et al.*, 2017). In a cross-sectional study, Morita *et al.* showed that decreased concentration of cortisol in morning saliva had a significant relationship with BMI, WC, waist to hip ratio, and skinfold ratio of the triceps to the scapula (Morita *et al.*, 2016). To justify the discrepancy between this study and those mentioned earlier, the difference in the way cortisol was measured differently in the samples of saliva and hair can be taken into consideration. On the other hand, the cortisol included in Morita's study was measured at 6, 10, and 11 o'clock in the morning, and due to changes in the cortisol cycle at different times of the day, the difference in the time when cortisol was measured might be the reason for this discrepancy in various studies.

Cortisol can lead to obesity in a number of ways. Activation of hypothalamic-pituitary-adrenal (HPA) axis under stressful conditions begins with the release of circulating corticotropin-releasing hormone, which stimulates the anterior pituitary gland, and with the release of Adrenocorticotropic hormone (ACTH), cortisol is synthesized in zona fasciculata/zona reticularis of the adrenal cortex cells. A long-term increase in cortisol leads to continuous production of glucose and an increase in blood sugar (Lovallo and Buchanan, 2017, Sapolsky *et al.*, 2000). The continuous high blood glucose level through insulin suppression leads to insufficient glucose transfer to the cells. These energy-deprived cells send hunger signals to brain, which can lead to overeating (Porte and Woods, 1981). Another mechanism which explains the role of cortisol in weight gain is the storage of TGs as visceral fat in abdominal cavity by mobilizing fatty acids (Björntorp, 1996). Cortisol is also involved in the conversion of immature fat cells to adult fat cells. The reason is higher levels of 11-β-hydroxysteroid dehydrogenase, which causes cortisone to be converted to cortisol in adipose tissue (Draper and Stewart, 2005).

In this study, the scores of total psychological distress and severe depression subgroup in normal-weight women was lower than obese/OW women without diet and those on diet; Moreover, the

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scores of anxiety/insomnia and social disorders subgroup in the normal-weight group was lower than non-treated obese/OW group. The findings related to the frequency of psychological distress indicated that the number of people with psychological distress in normal-weight group was less than both obese/OW women on and without diet. This shows a positive relationship between anxiety and OW/obesity. In line with our this study, Rouhvaza's research confirmed the association between psychological distress and central obesity in men and women over 19 (Roohafza *et al.*, 2014). Others have reported a positive association between obesity and psychological distress in adolescents and women (Kubzansky *et al.*, 2012, Martín-López *et al.*, 2011). Psychological distress through behavioral and physiological changes such as reduced quality of life (Kolotkin and Andersen, 2017), sleep disorders, overeating to suppress negative emotions, mental health problems, stress, inflammation, increased appetite, and possibly decreased metabolism led to obesity and OW (Hemmingsson, 2014).

In contrast to this study, Martinez found no significant difference in the level of psychological distress between obese and underweight people (Martínez *et al.*, 2014). According to Atlantis' study, the way an individual feels about his/her weight accounts for the relationship between psychological distress and weight, suggesting that feelings of dissatisfaction with weight can lead to psychological distress in both underweight and OW groups (Atlantis and Ball, 2008). Given that various psychological and social factors can influence the relationship between obesity and distress, drawing definitive conclusions about the positive relationship between weight and psychological distress is difficult, as it is necessary to control distorting factors and conduct further comprehensive studies .In yet another study by Fredman *et al.*, weight-related self-stigma and insomnia were the mediators of the relationship between weight and psychological distress (Friedman *et al.*, 2002). A case study revealed that weight and psychological distress were mostly associated with countries where the public opinion was more inclined towards controlling obesity, and the reason is that obese people are likely to be labeled, thereby experiencing more social stress and psychological distress (Chen and Tan, 2018). This can also be considered an important factor for differences in the score of psychological distress and its relationship with obesity in studies of different countries.

In this study, there was no significant difference between the prevalence of psychological distress, the score of total-GHQ, and its subgroups in obese/OW treated and untreated women. It should be noted that some studies have considered obesity treatment a risk factor for increased psychological distress, regardless of weight and type of treatment (Dreber *et al.*, 2017, Goldsmith *et al.*, 1992). In the present study, both groups were somehow seeking weight-loss treatment. Accordingly, the participants in group 2 were selected from those who referred to clinics with the aim of receiving a diet, while still not undergoing diet therapy, which can increase psychological distress in both groups to the same extent; the reason is the lack of significant difference in psychological distress between the two groups.

An examination of psychological distress probability model illustrated that none of the variables, i.e. hs-CRP, daily caloric intake, serum cortisol, BMI, and the group of the study, predicted the likelihood of psychological distress. Although the present study can be considered a comprehensive and thorough survey addressing physical and psychological aspects of obesity and OW, it had some limitations too; the participants' diet types were not examined. On the other hand, self-reporting of distress assessment tool (GHQ questionnaire) and the coincidence of sampling time with the outbreak of COVID-19 might have affected distress score and other psychological aspects of this study. Therefore, it is suggested to conduct more studies with greater number of regarding the effect of diet therapy on mental disorders in future.

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Conclusion

Going on a diet, irrespective of weight changes, might expose a person to stress and increase the serum cortisol levels; a significant weight loss was probably required to improve the components of metabolic syndrome and inflammation. It was also found that psychological distress, metabolic syndrome components and inflammation were higher in obese and OW cases compared with normal-weight ones.

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Conflict of interests

The authors declared no conflict of interest.

Authors' Contribution

Soltani E, Hejazi N, Sohrabi Z and Gordali M wrote and reviewed the manuscript; Soltani E was involved with the research method, ; Hejazi N was the managed the project, and Gordali M analyzed data. All the authors approved the final manuscript.

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