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METABOLIC SYNDROME : A LOOMING RISK

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ABSTRACT

The etiology of metabolic syndrome is not clear. However, it is thought that obesity, adipose tissue disorders and insulin resistance have important effects on the physiopathology of dyslipidemia, glucose intolerance, chronic subclinical inflammation and hypertension. Although the prevalence of metabolic syndrome differ according to diagnostic criteria and study populations, prevalence rates have rapidly increased during the recent years. In the physiopathology of metabolic syndrome, environmental factors as well as genetic factors play an important role. In parallel to this fact, the main aim of treatment provided for patients, diagnosed with metabolic syndrome is regulating life style habits and in this way, treating the underlying causes. Thus adopting healthy life style behaviors, educating the patient and his/her family is of paramount importance. In this review, metabolic syndrome, its diagnostic criteria, main components and treatment approaches are addressed in the light of the current literature.

Keywords: *Metabolic Syndrome, Cardiovascular Diseases, Type II Diabetes, Treatment Approaches for Metabolic Syndrome*

INTRODUCTION

Metabolic syndrome (MetS) is defined as a condition involving the coexistence of abdominal obesity, lipid metabolism disorders, hypertension and insulin resistance (deteriorated glucose tolerance / Type II diabetes) (Sarti and Gallagher, 2006). In other words, MetS is a disorder of metabolic origin and contains risk factors related to the development of cardiovascular diseases (CVD) and Type II diabetes (Dağdelen, Yıldırım and Erbaş, 2008; Alberti *et al*., 2009; Alphan, 2008).

The etiology of metabolic syndrome is not clear, however, it is thought that obesity, adipose tissue disorders and insulin resistance have important effects on the physiopathology of dyslipidemia, glucose intolerance, chronic subclinical inflammation and hypertension. Abdominal obesity and insulin resistance, which are accepted to be key components, play an important role in the physiopathology of MetS (Singh *et al*., 2009; Mehta and Reilly, 2004). In the development of MetS, it is known that genetic factors are effective as well as environmental risk factors (Kitiş *et al*., 2010; Chichlowska *et al*., 2009).

The Prevalence of Metabolic Syndrome

In the last two decades, it has been observed that the number of MetS cases have significantly increased throughout the world (İkinci and Atak, 2010; Onat *et al*., 2006). Although the prevalence of metabolic syndrome differ according to diagnostic criteria and study populations (Ritchie and Connell, 2007; Tamsma *et al*., 2005), prevalence rates have rapidly increased during the recent years. It has been estimated that, in parallel to the expected increase in Type II diabetes and obesity, the number of people with MetS will rapidly increase in the coming years (Ritchie and Connell, 2007; Evangelista and McLaughlin, 2009).

Based on the Adult Treatment Panel (ATP) III diagnostic criteria, the prevalence of MetS according to the National Health and Nutrition Examination Survey (NHANES) III data was reported to be 34% between the years 2003 and 2006 among American adults. While no significant difference has been reported to exist between females and males, it has been determined that the prevalence of MetS increased with Body Mass Index (BMI) and age. Moreover the prevalence rates differ across ethnic groups (Ervin, 2009). In a study it was found that the prevalence MetS was 26.7% in the American population aged 20 or more and it differed across ethnic groups. In the same study, the prevalence of MetS was found to be 22.9% in males and 30.1% in females (Jordan *et al*., 2012).

The most comprehensive MetS prevalence study conducted in Turkey is the Turkish Metabolic Syndrome Research (METSAR). A METSAR study was conducted for determining the MetS prevalence in the Turkish population by using the ATP III diagnostic criteria and recruiting 4259 people. It was reported that the prevalence of MetS was 33.9% in the adult population. In this study, the MetS prevalence was determined to be 39.6% in females and 28% in males. The study results showed that the prevalence of MetS increased in both genders with age and that prevalence rates did not differ between urban and rural areas (Kozan *et al*., 2007). In the KARDIYOMETRE study conducted by the Metabolic Syndrome Association, in order to represent the Turkish population, data obtained from individuals living in 14 different cities, aged over 20 years was evaluated. According to the study results, the MetS prevalence in Turkey was found to be 35% according to the ATP III diagnostic criteria. It was underlined that the MetS prevalence in males was 32.9% and 36% in females (Oguz *et al*., 2008).

According to the 2012 report of the Cardiovascular Diseases and Risk Factors among Turkish Adults Study (TEKHARF), which comprised MetS prevalence rates in various regions and MetS prevalence changes during the last decade, the prevalence in Turkish adults aged 40 or more was found to be 53%. The data was obtained from 1754 people aged between 45 and 74 who were examined twice, and who had a median age of 46 at the beginning. The 22 years follow-up study of the complete cohort revealed that the prevalence of MetS increased by 1.3% every year for the last 12 years. The MetS prevalence in Turkey increased mostly in the Southeastern Anatolia and Mediterrian regions. On the other hand, the prevalence rates decreased in the Marmara region (Onat *et al*., 2013).

Diagnostic Criteria of Metabolic Syndrome

The first official definition of MetS was provided by the World Health Organization (WHO) Study Group. In this definition, patients with glucose regulation disorder symptoms, were in the high risk group for Type II diabetes. Later, the WHO criteria were regulated and it became possible to detect MetS diagnosis among people with normal glucose tolerance (Uzunlulu and Oguz, 2007). According to the 1998 diagnostic criteria of MetS provided by WHO, in addition to insulin resistance, at least two of the following must exist: Obesity, hypertension, hypertriglyceridemia, low HDL-K levels and microalbuminuria (Falentin, 2010).

The most widely used MetS definition was provided by the National Cholesterol Education Program (NCEP) ATP III in 2001. The diagnostics criteria was based on the waist circumference values recommended in the 2005 guideline of the International Diabetes Federation (IDF) for determining abdominal obesity in European people. The existence of at least 3 criteria out of 5, like, increased waist circumference (abdominal obesity), hypertension, low HDL-K value, increased plasma triglyceride and increased fasting blood glucose (hyperglycemia), is diagnosed as MetS (Alberti *et al*., 2009) (Table 1).

Table 1. NCEP-ATP III Diagnostic Criteria for Metabolic Syndrome*

Criterion	Limit value	
Abdominal obesity	NCEP description	M:102cm
(Waist circumference)		F: 88cm
	IDF description	M: 94cm
	(For Europeans)	F:80cm
Low HDL - K**	M: 40 mg/dl	
	F: 50 mg/dl	
Hyperglycemia**	100 mg/dl	
Hypertriglyceridemia**	150 mg/dl	
High blood pressure**	130/85 mm7Hg	

*For the diagnosis of Metabolic Syndrome, 3 criteria out of 5 must exist.
**This criterion value is normal, but drugs are used for controlling it.
American National Cholesterol Education Program-Adult Treatment Panel = NCEP-ATP
International Diabetes Federation = IDF

MAIN COMPONENTS OF METABOLIC SYNDROME

Abdominal obesity

Adipose tissue is not only a source of energy, but is also an active organ which can secrete many cytokines and peptides of fat tissue. Although it has been predicted that the discovered adipocytokins contribute to obesity and MetS, the complex network of relations in its pathogenesis cannot be clearly explained (Altaş, Gürsu and Gülcü Bulmuş, 2011). Waist circumference, which is an objective indicator of the increase in fat tissue located around the intra-abdominal organs (Oğuz *et al*., 2008; Ritchie and Connell, 2007), is crucial for the early diagnosis of MetS or for detecting individuals carrying MetS risk (Appel, Jones and Kennedy-Malone, 2004).

A field survey was conducted by the Turkish Diabetes, Hypertension, Obesity and Endocrinological Diseases Prevalence Study (TURDEP) II. The study recruited adults aged 20 or more and was conducted between January 2010-June 2010 in 15 cities and 540 centers. According to the TURDEP II report, the prevalence of obesity was 32% in Turkey. It was also reported that being overweight was more prevalent among males, whereas obesity was more prevalent in females. In 12 years following TURDEP I, it was determined that body weight increased by 6 kg, waist circumference by 6 cm and hip circumference by 7cm in female adults; whereas body weight increased by 8 kg, waist circumference by 7 cm, and hip circumference by 2cm in males (Satman *et al*., 2013).

Hyperglycemia

Type II diabetes is a case which emerges after insulin resistance and is a chronic disease which is closely related to the increase in fat tissue and to fat metabolism disorder. Insulin resistance identifies the non-responsiveness of the organism to insulin effects. Insulin resistance in MetS develops after insulin binding to receptors and after intracellular deterioration (Oguz, 2008).

According to the TURDEP-I results, the diabetes prevalence in Turkish adults aged 20 or more is 6.2% in males and 8% in females (general average 7.2%). On the other hand, according to the TURDEP-II results, the general average was 13.7% (12.4% in males and 14.6% in females). In TURDEP-II, it was also reported that a significant increase in the prevalence of diabetes occurred in 12 years (Satman *et al.*, 2013).

Insulin resistance, dyslipidemia, high HbA1c and high blood pressure are important risk factors for CVDs. All of these criteria are strongly related to nutrition habits, sedentary life style and genetic factors. People with Type II diabetes carry CVD risk 3.2 times greater than those that do not have Type II diabetes (Karmally *et al*., 2012).

Dyslipidemia

In the TEKHARF study, which was conducted in Turkey, it was determined that abdominal obesity has a negative effect mostly on HDL-K values in Turkish adults (Onat *et al*., 2004). Dyslipidemia studies show that HDL-K levels are genetically low in the Turkish population and that triglyceride and LDL-K levels are within normal limits. Compared to the American and European populations, HDL-K levels are 10%–15mg/dl lower in the Turkish population. Low HDL-K value is a major risk factor and each 1mg/dl decrease in HDL-K increases CVD risk by 2.4% (Bersot, Palaoğlu and Mahley, 2002).

High triglyceride and low HDL-K values are of paramount importance in means of insulin resistance and CVD risk (Singh *et al*., 2009). Today, coronary artery disease is among the most important conditions. The most important modifiable risk factor that plays a role in the etiology of coronary artery disease is dyslipidemia. In addition, all components of MetS is atherogenic and they increase CVD risk (Grundy *et al*., 2004; Tatli, 2010).

Hypertension

Hypertension is defined as increase in blood pressure and is a condition where the systolic/diastolic blood pressure measure result is higher than 140/90 mm/Hg. More than 50% of hypertensive patients were presented with insulin resistance. Insulin resistance or hypereinsulinemia and dyslipidemia are more frequent in hypertensive people compared to those without hypertensitivity. Therefore, since insulin resistance, dyslipidemia and hypertension coexist in people diagnosed with MetS, these patients should be carefully treated in clinics (Singh *et al*., 2009).

According to the TURDEP II report, the rate of hypertension is 25.6% in Turkey. Similar to the TURDEP I study, the hypertension rate is approximately 30% and does not differ according to gender or due to rural or urban environment (Satman *et al*., 2013).

A study examined the presence of prehypertension and hypertension along with related risk indicators in overweight and fat females. A total of 5272 overweight and fat females were recruited and 323 females of normal weight comprised the control group. According to the study results, people with normal weight had higher rates of normal blood pressure, overweight people had higher rates of prehypertension and obese people had higher rates of hypertension. In the same study, it was determined that age, body weight, body fat ratio and waist circumference values increased with blood pressure (Celik, 2008).

Treatment Approaches for Metabolic Syndrome

In the physiopathology of MetS, environmental factors as well as genetic factors play an important role (Berra, 2003). In parallel with this fact, the main aim of treatment provided for patients diagnosed with MetS involved regulation of life style habits and in this way, treating the underlying cause (Berra, 2003; Hall *et al*., 2006). The fundamental treatment strategies regarding life style regulations include controlling the risk factors that cause insulin resistance via life style changes and initiating drug therapy in order to reach clinical goals. There is no single agent which can treat MetS except for life style changes. The most appropriate treatment method involves weight control via weight loss, healthy nutrition, promoting life style changes in order to acquire regular exercise habits and smoking cessation (Grundy *et al*., 2004).

In a prospective study by Onat *et al*. (2007), the protective effect of physical activity against cardiometabolic disorders was examined among Turkish adults and it was found that the risk of developing diabetes, hypertension and MetS is 25-30% lower in the active group compared to the inactive group.

Life style changes including diet, exercise, and weight control form an important step in MetS treatment. Regarding multifactorial life style changes, patient's motivation sources should be carefully determined and life style choices must be considered (Fappa *et al*., 2008; Stramiello, 2009). The first step of planned changes is evaluating the individual's current life style habits. In this way, the individual should be assisted in recognizing negative behaviors and relevant decisions should be made in collaboration with the individual with MetS (Akbulut and Rakıcıoğlu, 2010). In the management of MetS, the first year goal is to decrease body weight by at least 10% (McClendon *et al*., 2010).

Smoking and alcohol consumption increases CVD risk in people with MetS. Therefore, patients' habits should be considered while planning life style changes. In a study which investigated the triggering factors in MetS among healthy people aged between 18 and 39, the participants were grouped according to smoking status and their cardiovascular and metabolic conditions were scored. At the end of the study, it was found that males have more MetS risk factors compared to females (Corwin *et al*., 2006).

Problems encountered during the application of adopted healthy life style behaviors or the insufficiency of life style changes in treatment necessitate the use of pharmacological agents by regulating their use according to the patient's characteristics (Büyüktuncer, 2008; Berra, 2003; Hall *et al*., 2006).

The sole use of life style changes may not be sufficient in case of dyslipidemia, hypertension or diabetes. Statins are the first drug of choice in the treatment of dyslipidemia. Statins decrease LDL-K levels and increase HDL-K levels (Brown *et al*., 2008; Miller and Mitchell, 2006).

In hypertension control, angiotensin converting enzyme inhibitors (ACE) and/or angiotensin receptor blockers (ARB) is a group of pharmacological agents which are primarily recommended (Roseson, 2005; Hall *et al*., 2006).

In the treatment of insulin resistance, pharmacological agents which increase insulin sensitivity, namely Metformin and Glitazones are used (Rosenson, 2005). In the treatment of patients diagnosed with Type II diabetes, oral antidiabetic drugs (OAD) and/or insulin treatment is used (Erbas, 2006).

In addition, in patients diagnosed with MetS, it is known that the level of coagulation factors such as proinflammatory cytokins, CRP and fibrinogens is elevated. In this context, Aspirin use of 75-100 gm/day is recommended for MetS patients who have a high atherosclerotic CVD risk in order to prevent atherotrombotic complications (Brown *et al*., 2008; Hall *et al*., 2006).

CONCLUSION

In conclusion it can be said that in order to raise awareness regarding MetS and related health problems via training activities, it is necessary to detect excessive weight, obesity and unhealthy life style behaviors in early ages. Awareness is also necessary to solve possible health issues encountered in the early period of the lifecycle. Educating the patient and his/her family is crucial for promoting healthy life style behaviors in the course of MetS treatment (Fappa *et al*., 2008; Hacıhasanoğlu, 2009; Brown *et al*., 2008). In this stage, doctors, nurses and other health personnel should be in collaboration for the spread of this awareness programme. Moreover, it would be beneficial for the MetS patient and his/her family to receive regular training provided by health professionals.

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