DOI: https://doi.org/10.54393/pbmj.v4i2.124

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
Volume 4, Issue 2 (Jul-Dec 2021)

Reciew Article

Metabolic Syndrome & Its Dietary Management; A Review

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ARTICLE INFO

Key Words:
Metabolic Syndrome, Syndrome X, Mediterranean Diet, Nutraceuticals

How to Cite:
Aslam, M., Shahroz, R. A., Ramzan, S. ., Ali, S. ., Shehzad, F. ., Shafi, A. ., Ajmal, K. ., Rehman, N. ., Iqbal, S. ., Tanveer, S. ., & Fatima, E. . (2021). METABOLIC SYNDROME & ITS DIETARY MANAGEMENT; A REVIEW. Pakistan BioMedical Journal, 4(2). https://doi.org/10.54393/pbmj.v4i2.124

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ABSTRACT

Metabolic Syndrome or MetS is a multifactorial disease consisting of obesity, hypertension, dyslipidemia, and hyperglycemia. It's common in 25% of the general population in the Northern US and Western Europe. In Pakistan, the statistics of MetS are unknown, however, it is expected to be twice that of the US. The middle age group and the geriatrics population have the highest number of MetS cases with risk factors such as obesity, s dentary lifestyle, alcohol, inadequate, inadequate sleep, and a non-vegetarian diet. The complications of MetS include obesity, diabetes, and cardiovascular events. A Meditteranean diet rich in fruits and vegetables, whole grains, and olive oil as the source of fat is considered to be the only effective dietary management in MetS. Moreover, a high lean protein, low and complex carbohydrate and moderate unsaturated fats have also shown positive progress in MetS, especially with long-term weight reduction. Micronutrient's requirements also increase in MetS. Fulfilling these increased requirements has been shown to regulate and improve the metabolism of fats and carbohydrates. Vitamin C and E, flavonoids, vitamin D, conjugated linoleic acid, omega-3 fatty acids, minerals such as magnesium and chromium, α-lipoic acid, phytoestrogens, and dietary fiber all have been studied to support the treatment of MetS along with aloe vera and other herbal products, yoga and aerobic exercises.

INTRODUCTION

Metabolic syndrome (MetS) or syndrome X has become a huge challenge for health professionals around the world. Factors such as urbanization, high caloric intake (mostly refined and processed foods), increasing obesity, and diabetes mellitus [1]. During the past decade, the definition of MetS has been evolving. Currently, the diagnostic criteria for MetS are mentioned in Table1.1.

Criteria	Definition (Consensual criteria) [1]	Other non-consensual criteria
Central obesity	Abdominal waist [2] Men: >102 cm (US) or 94 cm (EU) Women: > 88 cm (US) or 80 cm (Europe)	Different cutoff values of BMI ≥ 28 or ≥ 28.8 or ≥ 30 kg/m^2
Dyslipide-mia	Triglyceride ≥ 150 mg/dL (1.7mmol/L) HDL cholesterol Men: <40 mg/dL (1.03 mmol/L) Women: <50 mg/dL (1.29 mmol/L)	Statin or fenofibrate medication [3]
Hypertension	> 135/85 mmHg	Any Antihypertensive Therapy 3
Glucose Intolerance	Hyperglycemia Fasting Glucose ≥ 110 mg/dL, or Type 2 Diabetes	Any anti-diabetes therapy (oral or insulin)

[1] Diagnosis of metabolic syndrome (MetS) necessitates at least 3 out of 5 criteria;
[2] Other cut off values have been established for Asians and Latin Americans;
[3] These treatments can be taken into account for the diagnosis of MetS unless if given for a preemptive purpose.

Table 1: Diagnostic criteria of MetS

3 out of 5 criteria are the minimum requirement from the table above are needed to define MetS [2]. These criteria are

not the cause but biomarkers of metabolic syndrome, can also occur in a lean person with a healthy BMI and normal waist circumference [3]. Fatty liver disease (usually NAFLD and NASH) is also marked in individuals with MetS with isolated diabetes mellitus, hypertriglyceridemia and obesity [4]. Moreover, MetS is linked with 2 times rise in cardiovascular outcomes and 1.5 times rise in all-cause mortality [5]. The prevalence of MetS is not known in the general population of Pakistan. However, a study conducted in 2012 highlights the prevalence of MetS was 63.7% among the studied patients. The results also marked that the most common risk factor present among the cases of MetS was the weight/height ratio or BMI over 25, which was seen in 70.3% of the cases [6]. From the results, it is estimated that MetS occurrence in Pakistan is almost 2x in comparison to the United [7]. Recent studies have confirmed that pediatric nutrition is linked with disorders like MetS, obesity, and diabetes in the later age groups. Both conditions including maternal undernutrition and overnutrition are the reasons for infant underweight and overweight and changed postnatal growth(for example quick catch-up growth among LBW infants) leads to obesity and MetS later in life, most probably adulthood [7]. LBW is related to decreased muscle mass during fetal development and adulthood. Thus, it subsequently elevates the risks of MetS, Type 2 DM, and CVD later in life. This is because skeletal muscle is important to maintain resting energy expenditure (REE) as well as the complete body insulin sensitivity. Furthermore, apart from these, infections and growth restriction as a result of inadequate calories and inflammation can also contribute to CVDs and metabolic disorders such as MetS [8]. Although, it is known that weaning and complementary feeding introduction can affect the future health of infants, overconsumption of high-calorie beverages during infancy is linked with obesity in childhood. Even though there's evidence that infants who were provided fish oil supplements in infancy had improved blood pressure. A high intake of salt during weaning may also increase blood pressure, elevating the chances of hypertension and developing a liking to salt and salty foods [9]. Metabolic Syndrome induces hyperglycemia contributing to insulin resistance which is the same cause for Type 2 Diabetes Mellitus [10]. Diabetes itself leads to microvascular complications. Diabetic Nephropathy is one of these microvascular complications [11]. Directories of clinical inflammation, such as elevated hsCRP, are connected with the incidence of T2DM and MetS [12]. Among the macrovascular complications of metabolic syndrome and diabetes mellitus type 2, peripheral artery disease is one of the most common complications and comorbidity [13]. Due to dyslipidemia in Metabolic syndrome, hypertension and cardiovascular complications are common in subjects. The most common cardiovascular complication is atherosclerosis [14]. Atherosclerosis can be defined as the progressive thickening and hardening of the walls of arteries due to fat accumulation on their inside layer. This further leads to diseases such as coronary artery disease and many strokes [15].

Dietary Management Of Metabolic Syndrome: Diet plays an important role in the management and curing of MetS. Certain diets, macronutrient, and micronutrient composition, complementary foods, herbs, and nutraceuticals are used for the treatment and prevention of MetS.

Diet Trends / Plans: A diet that can drastically reduce and normalize the levels of hyperglycemia and dyslipidemia is the first approach for the treatment of MetS. The diet must also be low in sodium and saturated fats, meanwhile high in antioxidants. Mediterranean Diet (MD) is the only diet that has shown positive results in patients with MetS. The diet dates back to ancient times in the Mediterranean regions. Based on olive oil (as the primary source of added fat), plant foods (fruits, vegetables, legumes, tree nuts, seeds, and cereals), modest intake of seafood (mostly fish), dairy, and low-to-moderate alcohol (typically red wine), balanced by comparatively limited use of red meat and other meat products defines this diet. Until recently, the Mediterranean diet gains the attention of medical professionals by proving a wide range of health benefits. The first reports discovered cardiovascular protection of the Mediterranean diet, as numerous large-scale clinical studies, exhibited a significantly marked reduction of atherosclerotic clinical events (a CVD complication of MetS) in populations following a Mediterranean diet plan. Succeeding clinical trials also confirmed promising effects on the risk for metabolic syndrome, obesity, T2DM, cancer, and neurodegenerative diseases [16]. Olive oil is a monounsaturated fatty acid (MUFA) that has a cardioprotective, anti-oxidative, and anti-inflammatory effect. Numerous prospective clinical studies conducted showed that the Mediterranean diet was linked with a reduced risk of MetS [17].

Macronutrients Distribution: The macronutrients distribution designed for Metabolic Syndrome aims to avoid and treat obesity by changing the caloric content (total calories), macronutrient distribution marking at 15% protein, lipids at 30%, and carbohydrates to 50-55%. Decreasing dietary fat and increasing fiber are also done. Even though this distribution appears to work for decreasing caloric density and helping short-term weight loss, however, for longer periods its adherence is not possible due to the low levels of satiety [18]. Many experiments and studies have been done on macronutrient composition to find the best approach in weight reduction for the treatment of obesity and overweight. One recent nutritional intervention

research did a comparison of the effect of 4 weight-loss diets with different percentages of fat, protein, and carbohydrates. Researchers checked the difference in body weight after two years, doing a comparison of low vs. high-fat diet, average vs. high protein diet, and the highest vs. lowest carbs composition diet. The test subjects lost seven percent of their primary bodyweight with no group differences after 6 months; however, weight regaining was seen in all groups after 12 months. Finally, after 12 months, the weight difference was not that much visible in the groups. In conclusion, the study commented that no major nutrient affected weight loss. However, one of the findings in the study stated that choosing a high protein or low-fat diet was linked to improving weight loss [19,20]. Multicenter intervention research examined the comparison of a low caloric, low-fat diet versus a low caloric, moderately high-fat diet for the management of overweight and obesity. The weight-loss period was 10-week, and after that period, the low-fat diet had a similar average weight loss in comparison to the high-fat diet, however, there were lesser dropouts and more patients lost 10% of their weight in the low-fat diet when compared to the high-fat diet [21]. In a review article, the researchers examined low-fat diets for obesity and found that fat-limited diets and calorie-restricted diets both had the same result for getting stable weight loss in overweight or obese individuals. One more recent trial did a comparison of 3 diet effects on weight maintenance after a starting 8% weight loss. The dietary composition included different carbohydrates and fat types. One was a monounsaturated fatty acid diet with a composition of 35–45% fat, in which the MUFA content was 20%. The second diet was a low-fat diet with a composition of 20–30%. The third was a control diet with a 35% fat composition. The protein content was the same composition (10–20%) in all three of the diets. After 6 months, there was not a major effect on weight regain prevention from all three diets; however, both the low-fat diet and MUFA diet ended in comparatively less body fat regaining in contrast to the control diet [30] Several intervention studies concluded that a high protein diet showed beneficial effects and much improved results in comparison to a normal protein diet when it comes to weight loss and maintaining that weight. So, keeping the same fat intake, a high protein diet increases 24 hours satiety, body temperature, sleeping energy expenditure, protein balance, and fat oxidation which were responsible for weight loss and maintenance [22]. In another weight loss research, a comparison was done on the variations in body weight and composition after short-term weight loss which was 4 months, followed by eight months of weight maintenance follow-up time by consuming two types of diets. One was a moderate-protein diet with a composition of 30% of calories from protein, 40% carbohydrates, and 30% fat. The second was a conventional high-carb diet consisting of 15% protein, 55% carbohydrates, and 30% fat. The result concluded that the moderate protein diet with 30% protein showed positive results both in the starting weight loss and long-term weight maintenance [23]. Evidence is generating over time that the recommended daily allowance (RDA) for protein is not enough to preserve muscle mass in adults during calories restriction for weight loss. [24] It should be noted that the current RDA of protein for the maintenance of muscle mass is based on adequate caloric intake. Moreover, there are not enough carbs and fats to exhibit a protein-sparing action as well. Thus, a moderate-protein diet with a composition of 30 to 35% is expected to be one of the best strategies to decrease weight and maintain that weight in a long run. However, this diet should also come with the warning that it is not applicable to renal patients who need limited protein intake. It should be noted that even though a calorie deficit is the most important factor for weight loss, but the macronutrient percentage distribution affects body composition changes and long-term reliability. More studies are required in this scenario to establish higher protein recommendations in a calorie deficit diet to further improve weight loss and weight maintenance in a long run. For patients with MetS, an energy deficit, high proteins (30 to 35%, especially lean and high BV proteins), low fat (20 to 30%, high in MUFA and low in saturated and trans-fat), and normal carb (40 to 50%, complex and low GI) diet is the best approach. During a weight decreasing diet, the quantity of protein needed to retain muscle mass is also increased due to the caloric restriction [25,26].

Micronutrients Distribution: Similar to the macronutrient's distribution, micronutrients are also important in MetS to decrease hyperlipidemia, hyperglycemia, hypertension and induce weight reduction. The primary goal is similar to the macronutrients distribution which is weight reduction to treat obesity and overweight. Incomplete vitamin and mineral intake are recognized among patients with obesity but is unidentified among long-term weight-loss patients. A new study found the dietary quality and micronutrient adequacy among weight-loss maintainers. It was a comparison between the weight loss maintainers and the controlled group. Weight loss maintainers had a 10.1 point higher Healthy Eating Index score and greater chances of meeting recommendations for minerals and vitamins including copper, magnesium, potassium, vitamin A, vitamin B6, and vitamin C. Weight loss maintainers, in comparison to the controlled group, also reported increased percentages of calories from carbohydrates and protein and lower calories from fat. [27] Numerous individuals with overweight or obesity surpass caloric requirements but fail to meet vitamin and mineral requirements. Numerous

micronutrient deficiencies are a risk factor for an obese individual. Such micronutrients include minerals like iron, calcium, magnesium, zinc, copper, folate, and vitamins like vitamins A, B12, C, D, and E [28]. The contributory factors for the incomplete micronutrient's intake include poor diet quality, energy-dense, and low nutritive value food overconsumption, limited fruits and vegetables in the diet in the US [29]. These factors with micronutrients deficiencies increase the risk of numerous chronic diseases, including MetS, cancer, CVDs, T2DM, and osteoporosis. These diseases are further linked with symptoms such as increased fatigue, lower immune response, and impaired cognitive function (i.e., attention, memory, and mood) [30]. Low levels of fat-soluble vitamins such as carotenoids, vitamin A, D, and E have been related to Metabolic Syndrome. These vitamins are both antioxidative and anti-inflammatory and even have an important role as hormone regulators and/or lipid metabolism and glucose homeostasis sensors. Studies show that providing a diet rich in fat-soluble vitamins can drastically decrease complications of metabolic syndrome such as dyslipidemia and Diabetes Mellitus Type 2 [31,32]

Nutraceuticals: Metabolic syndrome elevates the risk factors linked with an increased risk of T2DM and CVDs. Clinical inflammation, platelet activation, and varied oxidative stress are common in MetS. Even the combination of multiple interventions such as appropriate diet and reaching a healthy weight, regular exercise, and timely intake of prescription drugs, are being used, epidemiological data still indicates an increase in MetS cases at an alarming rate representing both the multifactorial nature of these diseases and rare acquiescence of individuals to make strategies. Multiple nutraceuticals have shown positive effects in managing the pathogenesis and regular a series of clinical and biochemical reactions. These nutraceuticals consist of antioxidant vitamins which are water-soluble antioxidants (vitamins C and E), plant-based antioxidants (flavonoids), fat-soluble antioxidants (vitamin D, conjugated linoleic acid, omega-3 fatty acids), antioxidative minerals (magnesium and chromium), and others including α-lipoic acid, phytoestrogens, and dietary fibers. [33] Numerous researches emphasized on the use of alternative medications for the treatment and management of MetS such as, traditional Chinese herbs, including ginseng, berberine, and bitter gourd, that have shown positive metabolic effects. [34] Herbal supplements, including, berberine, bitter melon, nigella sativa, and Gymnema sylvestre, are also used for the management of MetS and other metabolic diseases [35]. Several studies done on animal subjects indicate that the use of dietary antioxidants can delay and possibly prevent diabetes complications which include diabetic nephropathy and neuropathy. The way these antioxidants do so is by protecting against oxidative stress [36]. Vitamin C also known as ascorbic acid has a chain-breaking antioxidant, killing reactive oxygen species directly, and preventing the initiation of chain reactions that would instead lead to a decrease in protein glycation. Research on animal trial has proven that, vitamin C due to its antioxidative effect also decreases diabetes-induced sorbitol buildup and lipid peroxides in erythrocytes[37]. Vitamin E is also known as α-tocopherol also plays a role in protecting cell membranes from oxidative degradation of lipids. A decrease in Vitamin E resulting in deficiency is linked with an elevated level of aldehydes and peroxides in many tissues [38].

The lower risk of CVDs is linked with an increased intake of antioxidants via diet or supplements in a prospective cohort study [39]. These antioxidants include water-soluble vitamins A, C, and E as well as β-carotene, folic acid, niacin, and two minerals called zinc and selenium. High intake of Vitamin B was also associated with a faster decline in glomerular filtration rate [40]. Vitamin D, a fat-soluble vitamin with its anti-inflammatory and immune system changing property is found to be able to control the inflammatory pathway in T1DM, decreasing the inflammation in pancreatic islets and reducing autoimmune insulitis. Moreover, a reduction in insulin resistance and increase in the production and secretion of insulin is also linked to Vitamin D supplementation. It is often seen that a deficiency in Vitamin D is common in obese and T2DM patients because Vitamin D is pre deposited in such fat storages where it becomes less available. Hyperparathyroidism is often seen in diabetic patients due to irregular increases in calcium ions [41]. Omega-3 fatty acids (a monounsaturated fatty acid or MUFA) intake is linked to greatly lowering the levels of bad cholesterol (including VLDL and triglycerides) in T2DM, lowering blood pressure, and inflammation. Omega-3 can also prevent insulin sensitivity doesn't show any improvement in glycemic control or fasting insulin [42] Flavonoids are polyphenols compounds found in numerous food including fruits, vegetables, tea, herbs, and red wine. Citrus fruits and other food sources mentioned below have a huge amount of flavonoids prevented in them and are regularly consumed as a part of the diet in most countries. Flavonoids have been linked to improving inflammation via their anti-inflammatory effect and can be used in diseases with clinical inflammation marked [43]. Polyphenol is an antioxidant with ROS scavenging properties. It is also involved in controlling the components taking part in thrombosis. Flavonoids have been reported to have a reverse relationship with CVD stated by numerous prospective studies [44]. One of the trace elements 'Chromium' is said to be lower than usual in diabetic

individuals resulting in chromium deficiency. With the intake of chromium supplements, it is seen that insulin sensitivity is also improved along with glucose tolerance in T2DM [45]. Magnesium is also supposed to lower the risk of diabetes with an inverse relationship between magnesium intake and fasting insulin levels indicating improving insulin sensitivity. [46] α-Lipoic acid exhibits a Reactive Oxygen Species (ROS) killing effect because of its natural antioxidative property. Regeneration of other antioxidants such as Vitamin C, E, and glutathione as well as chelation of transition metals are shown by the combined use of α-Lipoic acid and dihydrolipoic. Furthermore, an 18–20% increase in insulin sensitivity has been shown in T2DM individuals when given α-Lipoic acid [47]. Soy has the most isoflavones which are a class of phytoestrogens, in comparison to any other plant. Phytoestrogens and estradiol are structurally similar and thus both of them exhibit similar effects. A lot of attention has been given to soy and phytoestrogen thanks to its recent health benefits . Soy and phytoestrogens have been shown to effectively improve glucose uptake and lower adipose tissue in recent animal studies. However, when it comes to studies on humans, there's no clear evidence that supports this statement [48]. Dietary fibers consist of a mixture obtained naturally from food sources, a by-product from processed grains, and even commercial supplements. Complex carbs such as polysaccharides, oligosaccharides, and nonedible compounds such as lignin, and associated plant substances are found in fiber. According to numerous studies, the general requirement of fiber is not being fulfilled by the US population. Some observational studies also conclude that there's an inverse relationship between dietary fiber and CVDs. Such fibers which are found from sources such as whole grain and cereals have a cardioprotective role [49] Fiber with different types has been used for the management and treatment of MetS as a complementary or alternative food. It is found to have a reverse relation with weight. Dietary fiber (soluble) has a thick and gel-like property which is linked with increased insulin sensitivity and lower glucose level in T2DM patients after eating. But soluble dietary fiber intake did not lower the risk of T2DM. In comparison, the consumption of insoluble fibers demonstrated the strongest relations with decreased risk of diabetes. In terms of insoluble fiber, this glucose-lowering effect was minimal. With the cereal dietary fiber increased consumption, it drastically reduced diabetes risk. A 21% reduced diabetes risk is assumed if there are 2 servings of whole grains per day, as concluded by 6 prospective studies [50] Studies have also shown that interventions that rises physical activity levels and improve aerobic fitness cause a decrease in MetS risk. In a randomized clinical trial, combined resistance and aerobic exercise effectively lessened metabolic syndrome [51]. Doing yoga regularly has been shown to reduce waist circumference and systolic blood pressure in individuals with metabolic syndrome who are not using a conventional form of exercise [52].

CONCLUSION

Metabolic Syndrome is a multifactorial disorder often confused with other disorders and diseases. With the criteria set for a case to be defined as MetS, a rise in several cases has been started to be reported worldwide. However, a developing country like Pakistan still needs to consider these criteria and report cases to know the prevalence of MetS in the country. Likely, extensive studies have been conducted to support the positive outcomes of nutritional management in MetS. A well-balanced diet and regular physical activity can be incorporated to prevent consequences associated with metabolic syndrome.

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