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Review Article

Metabolic Syndrome and Its Management: A Brief Review

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ABSTRACT

Metabolic syndrome is referred to as the clustered metabolic conditions that can cause heart disease, diabetes and all cause mortality. The presence of equal to or more than three components including larger waist circumference, exalted triglyceride levels, lower levels of HDL-cholesterol, hypertension and exalted levels of fasting blood glucose is necessary for the diagnosis of the syndrome. A rapid increase of obesity and metabolic syndrome prevalence is being reported in India as well as other South Asian countries causing greater morbidity and mortality rates as a result of type 2 diabetes and cardiovascular disease. Obesity along with insulin resistance is contemplated as the fundamental cause of metabolic syndrome. It is also contributed by many other factors specifically by ageing, life expectancy, sedentary lifestyle and inadequate nutrition. Diagnosis and treatment of the syndrome on time is necessary to prevent further consequent risks of diseases. Lifestyle modification including weight loss, exercise and diet with decreased intake of fat, simple sugars and consuming higher amounts of fiber like fruits and vegetables, whole grains and legumes is primarily required in managing the syndrome. Pharmacological treatment is necessary to be provided to those in whom lifestyle modification solely is not enough to manage the metabolic syndrome. Nutraceuticals due to their functional roles can be beneficial in treatment of metabolic syndrome along with reduced risk of cardiovascular disease.

Keywords: Metabolic syndrome, Insulin resistance, Cardiovascular disease, Lifestyle modification, Pharmacological treatment, Nutraceuticals.

INTRODUCTION

Metabolic syndrome (MetS) refers to the accumulation of interrelated physiological, biochemical, clinical and metabolic factors straightaway leading to the increased risk of atherosclerotic cardiovascular disease (CVD). [1] MetS is represented as a number of metabolism related anomalies clustered together. These comprise central obesity along with hypertension, resistance to insulin and atherogenic dyslipidemia. These are vigorously allied to the augmented peril to develop diabetes and both atherosclerotic and nonatherosclerotic CVD. [2] Although several criteria and definitions have been used to diagnose metabolic syndrome, [3-5] it is in general approved that the presence of 3 or greater than that of these constituents is essential: larger waist circumference (greater than or equal to 90 cm in men and greater than or equal to 80 cm in women), elevated triglyceride levels (greater than or equal to 150 mg/dl), lower HDL-cholesterol level (less than 40 mg/dl in males and less than 50 mg/dl in females), hypertension based on systolic blood pressure (SBP) and diastolic blood pressure (DBP) (SBP is greater than or equal to130 mmHg and/or DBP is greater than or equal to 85 mmHg or medication going on for hypertension), and raised fasting blood glucose level (fasting

blood sugar is greater than or equal to 100 mg/dl or medication going on for diabetes mellitus). [3,6,7]

1. Prevalence of metabolic syndrome

Around twenty to twenty five percent of the adult populace all over the world is estimated of having MetS. They are two times expected to die from and thrice expected to have a stroke or heart attack in comparison to those not having MetS. Additionally, they have five times greater risk to develop type 2 diabetes. [8] The prevalence of MetS ranges from <10 percent to about 84 percent all over the world depending upon the region of the study population, rural environment or urban environment and age, sex, race and ethnicity of the study population. It also depends on the definition of MetS used. [9,10] A rapidly increased obesity and MetS prevalence is being observed in India as well as other South Asian countries causing increase in mortality and morbidity as a result of cardiovascular disease and type 2 diabetes. [11,12] MetS is estimated to be present in about one third of urban South Asians. [13] About thirty percent of Asian Indian children and adolescents were observed of having insulin resistance and a lot of of them exhibited the characteristics of syndrome. [14] CVD is predicted to be the greatest cause of disability and death in India by the year 2020. About 2.6 million of Indian population's death is estimated to be because of CVD. [15] Indian urban population reported of having MetS is from $1/4^{th}$ to $1/3^{rd}$. Additionally, women have one and half to two times higher prevalence in comparison to men. [16]

2. Pathogenesis of metabolic syndrome

Metabolic syndrome is a condition of substandard inflammation that results due to multifaceted interaction among the genetic and environmental components. The numerous components constituting the syndrome include resistance to insulin, visceral adiposity and atherogenic dyslipidemia. The other components include endothelial dysfunction, genetic predisposition, raised SBP and/or DBP, hypercoagulable state and chronic stress. [1] Visceral adiposity caused majorly by the larger intake of high calorie foods is reported to chiefly trigger the majority of pathways involved in the syndrome. [17] Insulin resistance, neurohormonal activation and chronic inflammation emerge out as the leading reported mechanisms in the instigation, progress and evolution of metabolic syndrome to cardiovascular disease. [2] Insulin resistance mediating the increased circulation of free fatty acids (FFAs) has an essential contribution in the pathogenesis of MetS. Protein kinase activation by FFAs is inhibited in the muscles causing decreased uptake of glucose, whilst increased in the liver promoting gluconeogenesis in addition to lipogenesis. The clear result is a hyperinsulinemic state formation essential to sustain euglycemia, sooner or later causing decrease in the secretion of insulin. [18] Insulin resistance also plays a role in developing hypertension as a result of FFAs causing deprivation of insulin's vasodilation together with vasoconstriction. [19] Additionally, insulin resistance results in increased serum viscosity, prothrombotic state initiation, and pro-inflammatory cytokines release out of the adipose tissue contributing to the greater CVD risk. [20] Insulin resistance is contributed by deposition of visceral fat as compared to subcutaneous fat due to the visceral lipolysis causing increase in the supply of FFAs towards the liver by splanchnic circulation. [2] Increased FFAs towards liver causes upsurge in the very low density lipoproteins (VLDL) produced and increased synthesis of hepatic triglyceride. Thus, hypertriglyceridaemia being one of the vital diagnostic criteria for MetS is also an excellent reflection of insulin resistance. [21]

3. Etiology

Although the fundamental cause of MetS remains a challenge between the experts, insulin resistance together with central obesity are examined as noteworthy aspects. Added factors too such as genetics, being physically inactive, ageing, a

proinflammatory state and changes related to hormones might contribute to the syndrome but their effect may differ based on the ethnic group. Obesity shows a contributing effect on hypertension, higher levels of cholesterol in serum, reduced HDL cholesterol and hyperglycemia and has an independent association with increased risk of cardiovascular disease. [8] Positive family history, smoking, increasing age, obesity, low socioeconomic status, postmenopausal status, physical inactivity, sugary drink and soft drink consumption, too much alcohol consumption, western dietary patterns, reduced cardiorespiratory fitness, needless television watching, usage of antiretroviral drugs in human immunodeficiency virus infection, atypical antipsychotic drug utilization (e.g. clozapine) are identified as the factors at risk for metabolic syndrome. [22] Increased prevalence of MetS in adults is reported due to number of factors like ageing of the population, increased life expectancy and obesity, sedentary lifestyle and inadequate nutrition. Increase in the prevalence of MetS and related risk factors of CVD are being observed among people having low socioeconomic status additionally to being migrated from rural areas to the urban and are living in urban slum areas. The major causes are associated to rapidly occurring changes related to nutrition, lifestyle changes and socioeconomic changeovers, consequential to extending prosperity, urbanization, mechanization, and migration from rural areas to the urban. [23] Metabolic syndrome is also found to be related to additional medical disorders including hepatic steatosis, cholesterol cholelithiasis, obstructive sleep apnea, gouty arthritis, major depressive disorder, musculoskeletal disorders and polycystic ovary syndrome. [5]

4. Management

Metabolic syndrome is a state of persisting substandard inflammation accompanied by the reflective systemic effects on kidney, liver, skin, eyes, sleep, reproductive system, cardiovascular system and cancer. [1] Identifying the patients having MetS clinically and their management are necessary to commence efforts to effectively execute the treatments for reducing their subsequent diseases' risk. [24] Effectual approaches for prevention comprise changes related to lifestyle, primarily losing weight, dietary modification and exercise and the treating the MetS includes proper utilization of pharmacological agents for reducing the definite factors at risk. Consideration of the pharmacological management is essential for them in whom risk factors are not effectually lessened with the pre-emptive measurements and changes related to lifestyle. [25] Healthy lifestyle is considered as the primary management for MetS including moderate restriction of calories (to attain a five percent to ten percent weight reduction of the body in the beginning year), moderately increased physical activity and alterations in dietetic composition, whilst secondary intervention includes drug therapy which is required in those people in whom lifestyle changes are not sufficient and are considered at a higher risk for cardiovascular disease. [8] The difficulty is faced in clinical management of metabolic syndrome because of absence of any recognized method for the prevention or improvement of the whole syndrome. As a result, many of the physicians treat every component of MetS separately. Emphasis is laid particularly on the components which are effortlessly acquiescent towards the treatment through drugs. [1] Recent National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) recommendations for treating the MetS patients promote therapies that can decrease LDL-c along with triglycerides and increase HDL-c. Intervention of patients at primary level usually includes treating through statins for improving the lipid profiles of these patients. Though, current researches put forward the potential of recently acknowledged drugs that include thiazolidinediones, GLP-1 agonists, and DPP-4 inhibitors which appear very much beneficial in decreasing the development of

MetS associated disorders. [26]

Role of Diet

Diet being one of the major environmental factors increasing the metabolic syndrome among the people can provide protective effects by bringing changes in dietary patterns. The western diet including the consumption of meat that is processed meat, refined grains, fried meat and desserts based on sugars is straight away related to increased risk of MetS, [27] while Mediterranean diet has been related with its reduced risk. [28] Dietary pattern involving the consumption of vegetables, fruits, legumes, whole grains, fiber rich foods, fish, lean meat, poultry and dairy products that are fat free is reported to protect the population from MetS. [29,30] Diet related strategies are supposed to emphasize the necessity of sticking to diets being used traditionally and restricting the intake of sugared beverages, food products having greater saturated and trans fat contents. Snacking in between the main mealtimes needs to be avoided. Consuming dairy foods with lower fat contents need to be increased. Salted and processed foods should essentially be avoided for the prevention of hypertension. Increased intake of dietary fiber, green leafy vegetables and fruits is essential for the prevention of obesity. There can be influential effect of nourishment all through perinatal period and early childhood on insulin resistance and metabolic syndrome in later life. Thus, both undernutrition and excessive nutrition of mothers having detrimental effects on children is essential to be evaded. [31] A variety of natural compounds termed as nutraceuticals, derivative of plant extracts, spices, herbs, and essential oils have definite beneficial roles in managing patients of MetS. Nutraceuticals are the dietary supplements providing health benefits along with basic nutritional value. Turmeric, garlic, cinnamon, *Rhizoma coptidis*, neem, Bergamot orange, cumin, fenugreek, cardamom, ginger, grapes, onions, fish oils and broccoli are reported to be beneficial in treatment of the MetS. These therapies are yet not recommended to replace pharmacotherapies due to the beneficial roles of the nutraceuticals still being investigated. [2] A number of nutraceuticals utilized in clinical practices are found to control the pathogenesis of diabetes mellitus, MetS and related complicating issues. They also auspiciously restrain several biochemical and clinical consequences. These nutraceuticals are vitamins having antioxidant potential like vitamin C and vitamin E, flavonoids, vitamin D, conjugated linoleic acid, omega-3 fatty acids, minerals like chromium and magnesium, α-lipoic acid, phytoestrogens, and dietary fibers. [32] Nutraceuticals can be an effective alternatives for difficult to handle drug treatments. Functional foods, especially plant proteins have shown positive effects by improving insulin resistance and reducing triglyeride secretion. Probiotics and prebiotics have the ability of amending intestinal microbiome, decreasing absorption of particular nutrients and improving the metabolic management of energy rich foods. Certain nutraceuticals particularly, red-yeast rice, berberine, curcumin and vitamin D have reported to provide beneficial roles by improving lipid handling by the liver and improving insulin resistance. [33] Some plants including *Lagenaria siceraria* (bottle gourd), *Trigonella foenum-graecum* (fenugreek), Curcuma longa (turmeric), *Vigna mungo* (black gram or black lentil), *Camellia sinensis* (green tea), *Emblica officinalis* (amla) and *Murraya koenigii* are reported of having excellent remedial properties to cure hypertension, obesity, diabetes and hypercholesterolemia. [34]

CONCLUSION

Metabolic syndrome is a worldwide epidemic causing increased risk of CVD, type 2 diabetes mellitus and all cause mortality. MetS is being recognized as a rising threat in the upcoming years. Insulin resistance and obesity are measured as the leading causative factors of the syndrome. Other contributing factors identified are

notably ageing of the population, increased life expectancy, sedentary lifestyle and inadequate nutrition. An increase in each component of MetS results in its development accompanied with greater risk of CVD. Thus, decrease in one or two components of MetS can result in reduced risk of the diseases caused by the syndrome. Precise and well-timed diagnosis and treatment of MetS is therefore essential to prevent the further risk of diseases. Lifestyle modification can be the initial option for the populace. Modernized lifestyle modification therapy includes particular suggestions on diet and exercise with behavior related approaches. Treating MetS pharmacologically must be recommended to them in whom risk factors are not sufficiently abridged through lifestyle modification. Weight reduction of >7% to 10% in time span of 6 months to 12 months of overweight/obese people, daily moderately intense physical activity of minimum thirty minutes and nutritional therapy including reduced consumption of saturated fat and total fat, decreased intake of foods containing simple sugars and having high glycemic index and higher intake of fruits, vegetables, legumes and whole grains can tackle various components of metabolic syndrome. Many nutraceuticals are gaining importance as are found to have beneficial roles in managing MetS. Thus, prevention and treatment of MetS through nutraceuticals which are readily available and have minimum side effects may show beneficial effects in lowering the consequent disease risks.

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