Review Article

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Metabolic Syndrome in Women: An Evidence-Based Review

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ABSTRACT

Background: Metabolic syndrome (MetS) is a group of metabolic abnormalities that significantly increase the risk of cardiovascular diseases (CVDs), Type 2 diabetes mellitus (T2DM), and pre-mature death. In women, risk of developing metabolic syndrome increases during the menopausal transition. This review aims to assess the impact of MetS in middle aged women, especially during the transition period.

Methods: This review was conducted using a full search strategy of potentially relevant literatures on MetS across all included database. The collected data were organized, summarized, and presented in a logical, descriptive manner.

Results: The synthesized evidence indicates an increased prevalence of MetS among women undergoing the menopausal transition.

Conclusion: Increased prevalence of MetS among menopausal women is signaling an elevated risk of cardiovascular diseases, Type 2 diabetes mellitus among these females indicating the need for proper screening and preventive strategies for middle-aged women.

***Keywords:** Metabolic syndrome, women, cardiovascular diseases, menopause*

INTRODUCTION

Non-communicable diseases (NCDs) such as CVDs, cancers and T2DM have emerged as a leading cause of pre-mature morbidity and mortality and have become major public health concerns worldwide including Nepal. [1] MetS is a common condition that increases peoples' risk of future development of T2DM and CVDs. It is estimated that about 20–25 % of the world's population have the MetS and are three times more likely to die from heart attack or stroke compared with people without it. [2]

MetS is a metabolic abnormality that has become dramatically more common, creating a significant health burden worldwide.[3] It is a group of interconnected health conditions characterized by the co-occurrence of hyperglycemia, dyslipidemia, hypertension, and central obesity. [4,5,6] Also known as syndrome X and insulin resistance syndrome, MetS directly increases the risk of CVDs, T2DM, and other chronic conditions globally.[7]

According to the International Diabetes Federation (IDF), a MetS diagnosis requires; central obesity {waist circumference of ≥ 94 cm (men) and ≥ 80 cm (women)} and any two of the following: triglycerides (≥ 150 mg/dL), HDL cholesterol (< 40 mg/dL) (males) and < 50 mg/dL (females), hypertension (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg) and fasting glucose (≥ 100 mg/dL).[8] Among the varying definitions proposed by various international regulatory bodies, most studies agree that individuals having ≥3 of the listed factors qualifies as having MetS.[9]

MetS has increased worldwide including South Asia, influenced by socioeconomic changes, sedentary lifestyle and rural to urban migration.[10] Globally, men have a higher overall rate of CVDs, while, women's risk for CVDs and T2DM increases during the middle age. In Nepal, CVDs, cancers and chronic respiratory disease account for over half of all deaths.[1] MetS is common in Nepal, particularly among those with T2DM, with a rate of 80.3%.[9] This review aimed to determine the prevalence and impact of MetS in middle aged women, especially during menopausal transition.

SEARCH STRATEGY

The search strategy included terminologies and keywords in previous similar articles on metabolic syndrome. The articles that were published in MEDLINE/PubMed, Google scholar, and Web of Science databases were

included in the search strategy (inception of the database up to 2023). The keywords that were used to search consisted of "metabolic syndrome", "metabolic syndrome in women", "menopausal women and metabolic symptoms", and "cardiovascular disease." Literatures in English were included. The reference lists of identified articles were also searched for further papers. The reviewed data were organized, summarized, and presented in a logical, and descriptive manner. To avoid the duplication of the content, this review is structured around the different sections. For the title and abstract screening, articles were excluded if they were not conducted in humans, not focused on women-specific aspects, articles peripheral to the review's central themes, were editorials or case reports. Likewise, full -text articles of all articles that passed the title/abstract screening were thoroughly examined for quality assessment. Reviewer herself extracted data from the included studies focusing on the key information such as study designs, participants characteristics, and outcome of the studies. For the data synthesis, selected studies were categorized by primary outcome i.e., prevalence estimates and impact of MetS in women and used textual description to summarize the management and preventive strategies. All data supporting the conclusions of this review are available within this manuscript.

PREVALENCE OF METABOLIC SYNDROME IN WOMEN

The prevalence of MetS increases with increasing age and increasing glucose intolerance. The prevalence of the syndrome differs greatly in different populations. MetS is prevalent in 20% to 30% in middle-aged women and has been linked to the development of CVD and T2DM.[11] Amongst pre-and postmenopausal women it ranges from 13.8% to more than 60.0%.[2] In Brazil, the estimated prevalence of the syndrome among Brazilian pre-and postmenopausal women was 24.0% and 44.4% according to National Cholesterol Education Program's Adult Treatment Panel (NCEP ATP) III criterion.[12] In India, the prevalence of MetS was found to be 64% among the menopausal women.[13]

A study done at Tribhuvan University Teaching Hospital of Kathmandu, Nepal also reported higher prevalence of MetS in post-menopausal women (57.8%) in comparison to pre-menopausal women (20%). As per study, 13.3% were diabetic, 23.3% were hypertensive, 82.2% had abdominal obesity (waist circumference (WC)>80 cm), 43.3% were overweight (BMI 25-29.99 Kg/m2) and 13.3 % were obese (BMI≥30 Kg/m2). WC, BMI and systolic blood pressure (SBP) were significantly higher in post-menopausal group.[14]

Changing dietary patterns such as high-calorie intake, high fat consumption, and low consumption of dietary fiber foods, and other behavioral factors like sedentary lifestyles, increase in tobacco use, and excessive alcohol consumption could be directly related to the rising prevalence of MetS.[15,16] In particular, excess visceral fat and physical inactivity are the two main lifestyle factors causing alteration in insulin action.[17] A Brazilian study reported obesity (73.5%) reduced high-density lipoprotein level (63.0%) and elevated blood pressure (60.9%) as the most prevalent indicators of MetS.[18]

Studies around the world have shown that alterations in lipid metabolism due to estrogen deficiency is thought to be a significant component of CVD risk in post-menopausal women. These factors contribute to an increased prevalence of the MetS in post-menopausal women compared with pre-menopausal women.[11,14,19]

IMPACTS OF THE METABOLIC SYNDROME IN WOMEN

The MetS is now considered to be driving the twin global epidemics of T2DM and CVDs.[14] Abdominal obesity, a key component of metabolic syndrome, is quite prevalent in women of every country. In men, it increases continuously to the 50s and then decreases. In contrast, it increases rapidly in the 50s among women especially after the menopause due to decreased protective effect of estrogens in adipose tissue distribution.[20]

During menopausal transition, the reduced level of estrogen and alteration in the testosterone-to- estrogen ratio leads to a significant metabolic transition such as redistribution of fat from the gluteal-femoral region to central abdominal depots. The deficiency of estrogen contributes to endothelial dysfunction and a pro-inflammatory state. Concurrently, post-menopausal women exhibit a more atherogenic lipid profile, marked be elevated total cholesterol, low density lipoprotein, triglycerides and reduced high density lipoprotein. These combined factors substantially lead to metabolic abnormalities, dyslipidemia, hyperglycemia leading to MetS and elevate the risk of CVDs in women than men.[13,19, 21, 22]

Due to rapid onset of changes in lives of middle-aged women, they show not only physical, but also psychological and emotional symptoms such as depression, anxiety, and valuelessness, which bring about a variety of health problems. Middle-aged woman's

decreased physical activities, along with the overall degeneration of the body functions through menopause further accelerates the onset of MetS and its negative effects.[20] Several cross-sectional studies have linked MetS and poorer physical performance, especially those with abdominal obesity, are at greater risk for developing self-reported functional impairments.[23]

Along with several health problems occurring during mid-life, emergence of MetS is of particular significance because it is a risk factor for progression, and mortality due to CVDs and other chronic health problems in middle adults.[24] Thus, timely identification of middle-aged women at high risk for MetS has important implications for the reduction of CVD burden, both nationally and internationally.

PREVENTION AND MANAGEMENT OF METABOLIC SYNDROME

The most effective initial strategy for addressing each component of MetS and improving CVD prognosis is through comprehensive lifestyle changes. According to American Heart Association (AHA) guidelines for CVD prevention in women, lifestyle interventions include weight reduction in overweight and increasing physical activity, healthy eating pattern and stress management. [22] Evidence from a systematic review of randomized clinical trials indicated that weight loss interventions led to significant reduction in systolic and diastolic Blood Pressure, LDL-cholesterol, triglycerides, fasting plasma glucose, and hemoglobin A1C within 6–12-month timeframe. [21]

Dietary recommendations for the prevention and treatment of the MetS include consumption of whole grains, prioritizing high dietary fiber, fruit, and vegetable sources, healthy protein (mainly plants, fish and seafood), low intake of saturated and trans-unsaturated fat in addition to limiting foods with high added sugar and salt contents, alcohol and ultra-processed beverages.[25] The high concentration of beneficial nutrients - including dietary fiber, omega fatty acids, antioxidants, minerals - in balanced diet can affect MetS components. These contents can modulate the gut microbiota and inhibition of Nuclear factor Kappa-light-chain (NF-kB) signaling, which reduces oxidative stress and inflammation. As a result, this may enhance insulin sensitivity, improve lipid metabolism, and lower blood pressure.[21]

Physical activity is part of a healthy lifestyle and has many benefits in the treatment of MetS. Current guidelines recommend that combined physical activities (both aerobic and resistance) are the most effective measures in improving MetS parameters. Therefore, brisk walking for at least 30 min daily is recommended as the principal form of physical activity and more vigorous physical exercises should be considered if there are no contraindication.[26] The contemporary clinical guidelines advise an initial weight reduction of 7% to 10% from baseline body weight over 12month period, facilitated by a caloric deficit and regular physical activity. The long-term goal is maintenance of a body mass index (BMI) of less than 25 kg/m^2. [27]

The prime emphasis in management of the MetS is to mitigate the modifiable, underlying risk factors (obesity, physical inactivity and atherogenic diet). There is no single pharmacological therapy of MetS. The priority of drug therapy is for person with elevation of LDL cholesterol, serum glucose and BP. Management requires an individualized strategy that addresses each component and its related comorbidities separately. This includes antihypertensive drugs, hypoglycemic agents, statins and antiplatelets for the high-risk persons as per the current guidelines. [28,] The blood pressure target is set at <140/90mmHg. Lowering of BP effectively reduces risk of CVD in women. Also, women with history of gestational diabetes may also require intervention targeting the MetS. [29]

Moreover, social support and the management of psychosocial stresses are also significant for the maintenance of a healthy lifestyle among the people with MetS. [27] To conclude, the maintenance of a healthy lifestyle is facilitated by individualized lifestyle modification as per the age, and availability of resources among the women with MetS.

CONCLUSION

Metabolic Syndrome is a multifaceted syndrome affecting people globally that is responsible for increasing the risk of morbidity and mortality due to CVDs and T2DM. Advancing age is thought to predispose women, especially during the menopausal transition, to the development of MetS. The higher prevalence of the MetS in post-menopausal women is an indication that they are at risk of developing CVDs and T2DM. Therefore, women in that group should be advised about the importance of screening MetS earlier in the midlife and to adopt healthy lifestyles to minimize the incidence of these conditions to prevent pre-mature mortality and disability associated with the chronic conditions.

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