

Cardiometabolic Syndrome : An Emerging Global Health Issue

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Abstract

Cardio metabolic syndrome (CMS) is a combination of metabolic dysfunctions characterized by insulin resistance, impaired glucose tolerance, dyslipidemia, hypertension and central obesity. CMS is recognized as a disease entity by the World Health Organization (WHO) and American Society of Endocrinology. CMS represents a constellation of metabolic abnormalities that are risk factors for cardiovascular diseases. These cardiovascular and metabolic derangements individually and interdependently lead to increases in cerebrovascular disease (CVD) morbidity and mortality, making the CMS an established and strong risk factor for premature CVD. Data found that the prevalence of cardiometabolic syndrome (CMS) is increasing in all age groups, both in men and women from the latest National Health and

Nutritional Examination Survey (NHANES). Alteration in fatty acid metabolism, such as excessive fatty acid release in the plasma is likely to contribute to these metabolic abnormalities.

There is an established and proven benefits in reversing abnormal responses and decreasing cardiovascular risks by the treatment strategies including moderate physical activity, weight reduction, rigorous blood pressure control, correction of dyslipidemia and glycaemic control.

Keywords: Cardio metabolic syndrome (CMS), Cerebrovascular disease (CVD).

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Introduction

Cardio metabolic syndrome (CMS) is a constellation of metabolic dysfunctions characterized by insulin resistance and impaired glucose tolerance, atherogenic dyslipidemia, hypertension and intra-abdominal adiposity (IAA).¹ The disorder has received multiple names, including syndrome X,

dysmetabolic syndrome, plurimetabolic syndrome, insulin resistance syndrome, and finally, CMS¹. CMS is now recognized as a disease entity by the American Society of Endocrinology (ASE), National Cholesterol Education Program (NCEP), and World Health Organization (WHO).² These cardiovascular and metabolic derangements individually and interdependently lead to a substantial increase in cardiovascular disease morbidity and mortality, making the CMS an established and strong risk factor for premature and severe CVD and stroke. The risk of chronic heart disease (CHD), myocardial infarction (MI) and stroke is much higher in persons who have CMS than in those without the syndrome.²

The most widely used clinical criteria for diagnosing the CMS are those proposed by the WHO and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).²

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	NCEP ATP III	WHO
Fasting blood glucose	≥100 mg D dL	Impaired Fasting Glucose (IFG) D Impaired Glucose Tolerance (IGT) D Type 2 Diabetes Mellitus (T2DM)
Abdominal obesity		
Men	>102 cm. Waist Circumference (WC)	Waist-to-hip ratio >0.90 (or body mass index ≥30 kg D m ²)
Women	>88 cm. Waist Circumference (WC)	Waist-to-hip ratio >0.85 (or body mass index ≥30 kg D m ²)
Triglycerides	≥150 mg D dL	≥1.7 mmol/L
HDL Cholesterol		
Men	<40 mg D dL	<0.9 mmol/L
Women	<50 mg D dL	<1.0 mmol/L
Blood pressure	≥130 D 85 mm Hg	≥140 D 90 mm Hg
Microalbuminuria	-	Yes

Metabolic syndrome is defined as having at least 3 of 5 components; visceral obesity (elevated waist circumference (WC)>102 cm for male and >88 cm for female).Elevated fasting plasma glucose >100mg/dl, hypertension (>130/85 mmHg, high triglycerides(>150 mg/dl),high density lipoprotein (HDL) cholesterol (<40mg/dl for male, <50mg/dl for female).²

Waist circumference is a more sensitive indicator than body mass index (BMI) for prediction of cardiovascular risk. A new body index known as a body shape index (ABSI) proposed by Krakauer and Krakauer taking into consideration waist circumference, height and weight which predicts premature mortality.³

Prevalence: Data from the Third National Health and Nutritional Examination Survey (NHANES III)(1988 - 1994)found that the overall age adjusted prevalence of CMS was 24% in the US adult population.² The prevalence of CMS increases linearly with age from approximately 7% in those who are 20-29 years old to approximately 45% in those who are more than 60-year of age. The prevalence of metabolic syndrome in Bangladesh is 32% in female and 28% in male.⁴Pooled prevalence is 30% which was higher than the prevalence estimated around the world 20 – 25%.⁴ In an African study it was found that cardiometabolic risk factors were increased among Ghanaian urban settlers than rural people due to sedentary life style and unhealthy food habit and there was a association between obesity and

type 2 diabetes mellitus (T2DM).⁵ Nearly42.7% of T2DM patients were suffering from CMS. Female sex, divorced ladies and increased body roundness index(BRI) were influencing CMS. BRI could be integrated as a routine screening to detect CMS among patients diagnosed asT2DM.⁶ The frequency of CMS increases dramatically in both sexes between the third and the sixth decades of life and appears to plateau thereafter.²

Pathophysiology

At the cellular level, visceral obesity is the result of imbalance between energy intake and expenditure. Both abdominal adiposity and fatty liver are correlated with CMS, but the relationship is stronger with visceral adiposity. Visceral fat is metabolically active tissue that produces various pro-inflammatory and prothrombotic cytokines. Defective oxidative metabolism mainly impaired mitochondrial function is involved in visceral fat gain and the development of insulin resistance. Various studies have shown that the alterations in number or density of mitochondria and its oxidative metabolism are associated with development and progression of metabolic syndrome. Similarly, insulin resistance seems to be associated with a decrease in the mitochondria to nuclear Deoxyribonucleic Acid (DNA) ratio in adolescents.⁷

Adiponectin, a hormone from adipose tissue has shown to possess cardioprotective effects. It has anti-inflammatory and anti-atherogenic properties. The

hypothesis is that hypoadiponectinaemia may explain the pathophysiology of metabolic syndrome. Low level of adiponectin has been found in patients with diabetes, dyslipidemia and obesity.⁷

Insulin resistance in adipose tissue stimulate an increase in lipolysis and free fatty acids release in bloodstream. Increased fatty acids can i) impair insulin action in skeletal muscle and liver leading to increased blood glucose concentration, ii) stimulates hepatic Very-low-density lipoprotein (VLDL) production leading to increased serum triglyceride and decreased HDL.³ Among the CMS risk factors, the relation between insulin resistance and Hypertension (HTN) is well established. Several different mechanisms are proposed. First, insulin is a vasodilator when given intravenously to people of normal weight with secondary effects on sodium reabsorption in the kidneys. In the setting of insulin resistance the vasodilatory effect of insulin can be lost, while the renal effect on sodium reabsorption is preserved. Hyperinsulinaemia may result in increased sympathetic nervous system activity and contribute to the development of HTN, a risk factor for CMS.⁸

Disease progression

CMS begins with high cholesterol starting as early as 20 years, being increasingly overweight, especially around the middle, having high blood pressure, showing symptoms of insulin resistance followed by having a heart attack or a stroke.¹ Epidemiological survey in Georgia showed one in three and one in two adults are at risk of or have metabolic syndrome: obesity rose 9% in adults between 2011 – 2019. Heart disease and diabetes together are the leading cause of premature death in Georgia more than 150000 of potential lives are lost per year as a result of these two diseases costing about 9 billion dollars a year and 600 million missed days at work was lost.²

Cardiometabolic risk factors

Nine risk factors were identified that accounted for 90% of population attributable risk of MI in men and 94% in women.

They are: 1) Abnormal lipids, 2) Smoking, 3) Hypertension, 4) Diabetes, 5) Abdominal obesity, 6) Psychosocial stress, 7) Lack of consumption of fruits and vegetables, 8) lack of moderate alcohol

consumption and 9) Lack of physical activity. Men with one risk factor 10 times and females are 5 times likely to die from cardiac cause or stroke. If a person has two or more risk factors at the age of 50 years – for male 14 times and for female 8 times more chance of dying from myocardial infarction or stroke than those who does not have risk factors.⁹

Treatment challenges

The current approach to the treatment of CMS includes aggressive control of classical risk factors, including dyslipidaemia, hypertension, diabetes and smoking. However there is a major clinical need to address cluster risk factors which include high plasma insulin, intra-abdominal obesity, prothrombotic and proinflammatory cytokines.¹⁰

Public Health Approach

1. Public education
2. Screening for at risk individuals:
 - Body habitus/activity
 - Family history
 - Smokers
 - Blood pressure
 - Blood sugar/ hemoglobin A1C (HbA1c)
 - Lipid profile
3. Exercise:
 - Improves cardiovascular fitness
 - Weight control
 - Increases insulin sensitivity
 - Reduces incidence of diabetes mellitus (DM)

Loss of body weight

Weight loss of 7% body weight will improve lipids, Insulin sensitivity, control blood pressure and reduces incidence of diabetes. Brisk walking - 30 min./day will reduce 10% body weight. Healthy lifestyle changes can help prevent or delay serious health problems.

Healthy diet

Healthy eating plans, dietary approaches to stop hypertension (DASH) diet, Mediterranean diet, emphasizing eating vegetation, fruits, high fiber whole grains and lean protein are some examples of healthy diet. Reducing or managing stress, physical activity, meditation, yoga and other programs can help to handle stress and improve emotional and physical health.

Smoking cessation

Both passive and active exposures are harmful and major risk factors for insulin resistance and metabolic syndrome, macrovascular disease (peripheral vascular disease, MI, Stroke), microvascular complications of diabetes and pulmonary disease. Consider group therapy and medication support (nicotine replacement, bupropion, varenicline)

Pharmacological interventions

BP Control:

Target goal is <130/80. It is conclusively proven that long-term sustained hypertension is an increased risk of cardiovascular disease. It has been seen that there is 40% reduction in stroke with control of hypertension. For optimal blood pressure control, initiate behavioral changes like regular exercise, improve diet quality including salt restrictions.

If target blood pressure is not achieved after behavioral changes, consider pharmacotherapy.

Diabetes control

For every 1% rise in HbA1c there is an 18% rise in risk of cardiovascular events and a 28% increase in peripheral arterial disease. Evidence is accumulating to show that tight blood sugar control in both type 1 and type 2 diabetes mellitus reduces risk of cardiovascular disease. If 1% reduction of HbA1C is achieved, one can expect a reduction in risk of 21% of any diabetes related end point complications, 37% for micro vascular complications and 14% myocardial infarction. For optimal plasma glucose control, initiate behavioral changes, regular exercise, improve diet quality. If HbA1c <6.5% is not achieved after behavioral changes, consider pharmacotherapy.

Lipid Control

Target goal is HDL > 40mg%, LDL < 100 mg/dl and TG < 150mg%. Studies shows 24-37% reduction of CVD risks with the use of statins and fibrates. Initiate behavioral changes first with regular exercise and improve diet quality, then pharmacotherapy if necessary.

Pharmacotherapy for high risk: initiate statin treatment immediately. For intermediate risk, if LDL-C > 3.5mmol/L, initiate statin treatment. If multiple cardiometabolic risk factors, initiate statin treatment. For low risk observe and if LDL-C > 5.0 mmol/L, initiate statin treatment.

Weight loss surgery

The use of weight loss surgery in the clinical management of T2DM in severely obese persons has been recommended^{11,12}. Some clinicians believe it is better to use surgery very early in the course of the disease in order to anticipate clinical deterioration. Others suggest a delayed approach to surgery only in patients not adequately controlled pharmacologically. Obesity management strategy can be challenging and it is now generally believed that behavioral modification, dietary macronutrient composition and physical activity are key components that affect CMS management.

Conclusion

CMS is a key driver of cardiovascular events. Owing to the high prevalence of cardio metabolic risk factors, prompt assessments with appropriate treatment in primary care are needed to help reduce future complications. Addressing comprehensive medication review is not only about counseling patients but rather targeting health promotion efforts to prevent disease. The key treatments involve behavior change, exercise programme, vascular protective measures such as pharmacotherapy and bariatric surgery for weight reduction might be needed for patients at high risk.

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