Prevalence of Coronary Atherosclerotic Heart Disease in Metabolic Syndrome Patients

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Abstract:

Aim & objectives:
This review discusses association between CoronaryAtherosclerotic heart disease(CAD) and metabolic syndrome(MS) and also evaluates conventional and emerging risk factors.

Background:
Metabolic syndrome affects approximately one quarter of the population in developed countries.Metabolic Syndrome is a cluster of disease condition.The major features of the Metabolic Syndrome include central obesity,hypertriglyceridemia,low levels of high density lipoprotein(HDL-c)cholesterol,hyperglycemia and hypertension.Cardio vascular disease is the leading cause of death globally,major risk factors of Coronary Atherosclerotic heart Disease are smoking,alcohol,diabetes.The cardiovascular disease arising from different component of MS is not uniform.Each component is a independent risk factor of CoronaryAtherosclerotic heart disease and they all interact synergistically further increasing risk.

Reason:
By diagnosing metabolic syndrome patients in early stage,we can prevent coronary atherosclerotic heart disease.

Key words:Heart disease,hypertension,metabolic syndrome,cardio atherosclerotic heart disease,obesity.

INTRODUCTION:-

Metabolic Syndrome (MS) is a cluster of clinical characteristics that is associated with enhanced coronary risk.[1]According to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, metabolic syndrome is associated with a greater risk of atherosclerotic disease than any of its individual components.[1]It has been studied that individuals with MS are at increased risk for Coronary Artery Disease (CAD).[2]Insulin resistance is a central pathophysiological process associated with MS.[3]Presence of MS increases the risk of Coronary Artery Disease (CAD) by 7.3 times in male and 10.2 times in female patients.[4]NCEP ATP III identified CAD as the primary clinical outcome of the MS.[5]According to NCEP ATP III, underlying risk factors for CAD are obesity (especially abdominal obesity), physical inactivity and atherogenic diet other than the major risk factors, which are cigarette smoking, hypertension, elevated Low Density Lipoproteins (LDL) cholesterol, low High Density Lipoproteins (HDL) cholesterol and family history of premature Coronary Artery Disease (CAD). Other risk factors include elevated triglycerides, chylomicrons, insulin resistance, glucose intolerance, pro-inflammatory state and pro-thrombotic state.[6,7]Majority of these factors can be identified and modified.

DEFINITIONS AND DIAGNOSTIC CRITERIA FOR METABOLIC SYNDROME:-

There are currently two major definitions for metabolic syndrome provided by the International Diabetes Federation and the revised National Cholesterol Education Program,respectively.

INTERNATIONAL DIABETES FEDERATION(IDF)[8]

Central Adiposity & Two or more of the following

- Fasting Triglycerides >150mg/dl or on specific medication.
- HDL Cholesterol <40mg/dl and <50mg/dl for men and women respectively,or on specific medication.
- Blood pressure >130mm systolic or >85mm diastolic or previous diagnosis or on specific medication.
- Fasting plasma glucose >=100mg/dl or previously diagnosed Type 2 diabetes.

Criteria for central adiposity:-

MEN	WOMEN	ETHNICITY
>=94cm	>=80cm	Europoid,Sub-Saharan African,Eastern & Middle Eastern
>=90cm	>=80cm	South Asian,Chinese,&Ethnic South &Central American
>=85cm	>=90cm	Japanese

National Cholesterol Education Program And Adult Treatment Panel III(NCEP:ATPIII)[8]

Three or more of the following.

- Central obesity
  Waist circumference >102cm (M), >88cm (F)
- Hypertriglyceridemia
  Triglycerides>=150mg/dl or specific medication
- Low HDL cholesterol<40 mg/dl and <50 mg/dl for men and women,respectively,or on specific medication.
- Hypertension
  Blood pressure >=130mm systolic or >=85mm diastolic or on specific medication.
- Fasting plasma glucose
  >=100 mg/dl or on specific medication previously diagnosed Type 2 diabetes.

The major differences between IDF and NCEP:ATP III criteria were According to IDF,Metabolic syndrome patients should have central adiposity and use geography-specifity cut points for waist circumference.

According to NCEP, ATP III,Metabolic syndrome patients may have or may not have central adiposity and use only one set of cut points for waist circumference,regardless of geography.

COMPONENTS OF METABOLIC SYNDROME:-

ATP III identified 6 components of the metabolic syndrome[9]

- Abdominal obesity
- Atherogenic dyslipidemia
- Raised blood pressure
- Insulin resistance +/-glucose intolerance
- Proinflammatory state
- Prothrombotic state

All these components are major and emerging risk factors for the metabolic syndrome.

PATHOGENESIS OF METABOLIC SYNDROME:-

The metabolic syndrome seems to have 3 potential etiological categories : obesity and disorders of adipose tissue; insulin resistance; and a constellation of in dependant factors (eg: molecules of hepatic, vascular, and immunologic origin) that mediate specific components of the metabolic syndrome. Other factors – ageing, pro inflammatory state, and hormonal changes have been implicated as contributors as well. [9]

Obesity is rampant in the United States sand is becoming increasingly common worldwide. The increase in obesity prevalence is due to two major factors, plentiful supplies of inexpensive foods and sedentary jobs.[10] The foremost physical consequence of obesity is atherosclerotic cardiovascular diseases (ACVD) [11], The ASCVD include the major risk factors and emerging risk factors. The major risk factors are hypercholestrolemia, hypertension, and hyperglycaemia. The emerging risk factors are arty ergogenic dyslipidemia , insulin resistance , proinflammatory state, and prothrombotic state. The relationship of obesity to these risk factors varies, depending on the genetic and acquired characteristics of individuals. The majority of obese persons who develop ASCVD typically have a clustering of these risk factors (metabolic syndrome). The constellation of major and emerging risk factors that make up the metabolic syndrome can be called metabolic risk factors. [12]

Obesity can be defined as an excess of body fat which is determined by weight (kilograms) divided by height squared (square meters). In clinical terms, a BMI of 25-29 kg/m ^{2} is called overweight ; higher BMIs ($>=$30 kg/m^2) are called obesity. The best way to estimate obesity in clinical practice is to measure waist circumference. The advantage of measuring waist circumference is that an excess abdominal fat is correlated more closely with the presence of metabolic risk factors than total body fat.[13]

In obesity, multiple products are released from adipocytes in abnormal amounts. One of them is non esterified fatty acids(NEFAs).[10] Obese persons release increased amounts of NEFAs into the circulation.

Increased plasma free fatty acid concentrations are the main cause of insulin resistance.[14][15] Insulin resistance is defined as decreased biological response to normal concentration of circulating Insulin. It is one of the major components of metabolic syndrome.[16]

Normally, insulin promotes FFA uptake into the adipocyte by stimulating the LPL-mediated release of FFA from lipoprotein triglyceride.Fatty acids enter the adipocyte both by diffusion down a concentration gradient as well as by facilitated transport.Insulin regulation of fatty acid transports such as FAT/CD36,FABPs,and/orFATP is not known.Insulin stimulates glucose transport into the adipocyte,thereby increasing the availability of glycerol-3 phosphate(Glycerol-3P) for triglyceride (TG) synthesis.Insulin may have a direct stimulatory effect on lipogenic enzymes such as DGAT.By inhibiting HSL,it reduces the intracellular lipolysis of cytosolic triglycerides,thereby promoting adipocyte triglyceride storage[17] But in obese,due to insulin resistance,there is diminished suppressive effect on HSL,leading to increased formation of FFA in adipocytes.FFA esterification in fat cells is dependent on the supply of glycerol-3-phosphate derived from insulin-mediated glucose uptake and glycolysis in the adipocyte.The insulin mediated glucose uptake is diminished in insulin resistance.So,there is increased release of NEFAs in circulation.

A number of studies have indicated that elevated plasm FFA and high fat diets can increase post absorptive hepatic glucose production and induce hepatic insulin resistance i.e., reduce the ability of insulin to suppress hepatic glucose production). Increased plasma FFA , by mass action augments FFA uptake by hepatocytes, leading to accelerated lipid oxidation and accumulation of acetyl CoA.

1. Increased acetyl CoA stimulates pyruvate carboxylate and phosphoenolpyruvate carboxykinase, the rate-limiting enzymes in gluconeogenesis as well as glucose-6-phosphatase, the rate controlling enzyme for glucose release from the hepatocyte
2. Increased FFA production provides a source of energy (in the form of ATP) and the reduced nucleotides (NADH) to drive gluconeogenesis .
3. Elevated plasma FFA induces hepatic insulin resistance by inhibiting the insulin signal transduction system. [18]

Increased FFA in the liver leads to increased triglyceride synthesise and subsequently increased hepatic VLDL apo-100 secretion. Because of hepatic insulin resistance, insulin is not able to inhibit either triglyceride synthesis or VLDL apoB-100 secretion. Elevation of the triglyceride rich VLDL increases the activity of cholesterol ester transfer protein (CETP). So there is increased transfer of triglyceride from VLDL to LDL in exchange for cholesterol. These triglyceride enriched lipoproteins are good substrate for the enzymatic hepatic lipase, which by hydrolysing the triglyceride causes;

1. increased clearance of HDL cholesterol from the blood , so HDL level is reduced
2. formation of highly atherogenic small dense LDL. Thus promotes development of atherogenic dyslipidemia .[19]

   Other products released by adipose tissue are adipocytokines. Adipocytokines include adiponectin, leptin, angiotensinogen, tumour necrosis factor alpha, interleukin 6, plasminogen activator-inhibitor 1, resistin.

These proteins are increased (with the exception of adiponectin, which decreases) in obesity. All these cause insulin resistance in peripheral tissue especially muscle and liver.[20]

CONCLUSION:-

All these factors which are obesity , insulin resistance , dyslipidemia (increased triglycerides, low HDL, & increased LDL) leads to impaired glucose tolerance (IGT), diabetes mellitus, hypertension, proinflammatory & prothrombotic state. All these components are together called metabolic syndrome . So patients with metabolic syndrome are more prone for atherosclerotic cardiovascular diseases.

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