The Metabolic Syndrome Latest Medical and Biochemical Trends

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Received: 12 April 2015 Accepted: 30 April 2015 Published: 15 May 2015

Abstract

The world population is noting an increasing trend towards development of particular diseases like Obesity, hypertension, diabetes mellitus. Some of them are turning into modern epidemics. These diseases can occur in isolation. Recent trends suggest the interlink age of the disease patterns leading to development of syndromes. One such syndrome is the Metabolic Syndrome. The Metabo1ic Syndrome is one of the major public health issues of this century. It is constellation of physical conditions and metabolic abnormalities commonly found in association with increased risk for development of Type 2 diabetes mellitus , Cardiovascular disease and other medical conditions. The article Deals with the Medical and Biochemical events occurring as a result of this developing medical Illness.

Index terms— diabetes, insulin, hypertension, obesity, resistance, panel, metabolic, lipoprotein.

1 I. Introduction

The prevalence of the metabolic syndrome depends on age, ethnic background, and gender. It rises linearly from 20 to 50 years and plateaus thereafter. Looking at various studies around the world, which included population samples, aged from 20 to 25 and upwards, the prevalence varies from 8% (India) to 24% (United States) in men and from 7% (France) to 46% (India) in women. 5 T Obesity, insulin resistance, physical inactivity, advanced age and hormonal imbalance have been suggested as the underlying risk factors for the development of metabolic syndrome. Thyroid hormones play an important role in regulating energy homeostasis, glucose and lipid metabolism. The metabolic syndrome. 1 was first described in the 1920 by Kylin, a Swedish physician, as the association of high blood pressure (hypertension), high blood glucose. (hyperglycemia) and gout. The. link between the syndrome features and cardiovascular disease was made as early as the 1960s by Welborn and by Camus, the latter coining the term "Tri syndrome Metabolique". 2 Advances in the 1970s and early 1980s expanded our understanding of the link of these to coronary heart disease, even in the absence of diabetes, and linked the metabolic risk factors to atherosclerosis. 3

2 II. Components of Metabolic Syndrome a) Abdominal Obesity

The genetic and environmental factors play a major role in metabolic and cardiovascular of obesity. Abdominal obesity is related, to greater risk of cardiovascular events and Type 2 DM. Waistcircumference is a general index of central fat mass and it reflects both abdominal subcutaneous adipose tissue (SAT) and abdominal visceral adipose tissue (VAT) and is major determinant of metabolic and cardiovascular complication of obesity 6 . Visceral obesity may partly be a marker of a dysmetabolic state and partly a cause of the metabolic syndrome . Although waist circumference is a better marker of abdominal fat accumulation than the body mass index, an elevated waistline alone is not sufficient to diagnose visceral obesity and have proposed that an elevated fasting triglyceride concentration could represent, when waist circumference is increased, a simple clinical marker of excess visceral/ectopic fat. 7 Abdominal obesity, due to intra-abdominaI adiposity, drives the progression of multiple cardiometabolic risk factors independently of body mass index. This occurs both through altered

secretion of adipocyte-derived biologically active substances (adipokines), including free fatty acids, adiponectin. interleukin-6. tumour necrosis factor alpha. and plasminogen activator inhibitor-I, and through exacerbation of insulin resistance and associated cardiometabolic risk factors. 8

3 b) Increased Triglycerides

Dyslipidemia is widely established as an independent risk factor for CVD. Low HDL Cholesterol and hypertriglyceridimia have been found to be independent and significantly related to myocardial infarction and stroke in patient with Metabolic Syndrome. The dyslipidemia may be caused by combination of overproduction of very low density lipoprotein (VLDL), apoB-100, decreased catabolism of apo B containing particle and increased catabolism of HDL apo-Al particle. In Type 2 DM, insulin resistance and obesity combine to cause hypertriglyceridemia and low HDL-C, due to over production of VLDL. Plasma LDL-C levels are normal in Metabolic Syndrome though LDL particles are smaller and denser than normal which may be associated with increased cardiovascular risk. 9 The effects of low HDL-C and high triglyceride levels., are related to greater risk of coronary disease due to variety Of environmental and genetic factors. The genetic variants of lipoprotein lipase, hepatic lipase, cholesterol ester transfer protein and peroxisome proliferator-activated receptors have effects on HDL-C and TG levels in population which contributes to the development of Metabolic syndrome.

The primary defect is probably focused in the inability to incorporate the Free fatty acids to triglycerides (TGs) by the adipose tissue (inadequate esterification) **??**7 . This result is reduced fatty acid trapping and consequent retention by the adipose tissue. The insulin resistance also causes reduced retention of FFA by adipocytes. Both these abnormalities lead to the increased flux of FFA back in the liver. Adipose tissue is a prominent source of cholesteryl ester transfer protein. 10 Cholesteryl ester transfer protein is an important determinant of lipoprotein composition because of its capacity to mediate the transfer of cholesteryl esters from cholesteryl ester rich lipoproteins to TG rich lipoproteins in exchange for TGs. 11 In obese subjects, cholesteryl ester transfer protein activity and mass are increased. 12

4 c) Low Hdl-Cholesterol

Low HDL-Cholesterol in patient with Metabolic syndrome is often considered as secondary to raised TG. 13 Lipid exchange is taking place between LDL & LDL particles mediated by cholesterol ester transport protein (CETP). These TG rich but cholesterol depleted HDLC is more prone to be catabolized. They undergo hydrolysis of their TGs components and dissociation of their protein component apo-A (the main protein of HDL). 14 There is circumstantial evidence that low HDL-C contributes to increase risk of atherosclerosis in this Condition. 15

5 d) Blood Pressure

There is tendency of weight gain in middle age, which is positively correlated with blood pressure levels and highly related to the prevalence and incidence of hypertension in the population. 16 The reduction of blood pressure to level <130/85 mm Hg in patients suffering with diabetes mellitus or at high risk of cardiovascular disease in effective. This fact helped to incorporate blood pressure as part of Metabolic Syndrome. The blood pressure measured in sitting posture and at rest if it is >130/85 mm Hg is a part of Metabolic Syndrome. Most of the affected person having Metabolic syndrome are overweight or obese hence to reduce the blood pressure specific attention towards weight reduction is given; diet restriction-active lifestyle and exercises and if required pharmacological agents are given. The relation between insulin resistance and hypertension 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 kidney. In the setting of insulin resistance, the vasodilatory effect of insulin can be lost, but the renal effect on sodium reabsorption preserved. Fatty acids themselves can mediate relative vasoconstriction. Hyperinsulinaemia The Metabolic Syndrome Latest Medical and Biochemical Trends Increased flux of FFA from periphery to the liver in increasing resistance state stimulates hepatic TG synthesis which in turn promotes the assembly & secretion of TG containing VLDL" as well as apo B production in liver. may result in increased sympathetic nervous system activity and contribute to the development of hypertension.

6 e) Impaired Fasting Glucose

It is believed that insulin resistance is the pathophysiological process that underlying the cardiovascular risk factor in Metabolic syndrome. Indices of insulin resistance predicts atherosclerosis and cardiovascular events independent other risk factors including fasting glucose and lipid levels. Impaired fasting glucose is diagnosed when fasting levels are 110 to 126 mg/dl on two occasions according to criteria of the American Diabetes Association. At a given level of obesity, an individual may have normal glucose tolerance, impaired glucose tolerance, on type 2 diabetes mellitus. The factors that determine the degree of impairment of glucose metabolism are insulin sensitivity and beta cell reserve capacity Insulin sensitivity in normal individuals varies by approximately 3-fold. In insulin resistance individuals, the pancreatic ? cells must secrete more insulin to maintain euglycemia. However, prolonged hyperfunction can lead to ? cell exhaustion. The biochemical/molecular basis of ? cell exhaustion have yet to be elucidated. Blood glucose levels then begin to rise, manifested first as impaired glucose tolerance and later as type 2 diabetes mellitus. 17

7 III. Conclusion

With the increasing evidence in increasing development of Metabolic syndrome throughout the world both in developed world as well as developing world and the presence of factors which increase the risks of significant morbidity and mortality as a result of metabolic syndrome, basic biochemical alterations occurring need to be properly understood so as to frame a therapeutic schedule for all the major factors which play an important role in the development of the syndrome and to evolve effective pharmacotherapy on the basis of biochemical alterations occurring in the disease. [1]

Figure 1: he

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Hypertension	Raised arterial pressure (140/90 mmHg)	or antihypertensive medication
Dyslipidemia	Raised plasma triglyceride(>1.7 mmol/L) or low HDL cholesterol (<0.9 mmol/L) in men and (<1.0mml/L) in women	
Central or general obesity	Waist to hip ratio >0.90 in men: >0.85	in womenor BMI>30Kg/m2
Microalbuminuria	Urinary albumin excretion rate >20ug/min or albumin: creatinine ratio>30 mg/g	

Figure 2: Table 1 :

2

	Cholesterol education program (NCEP) Adult Treatment Panel III (ATPIII)
Risk factors	Defining levels*
Abdominal obesity (waist circumference)	
Men	>102 cm(> 40 inch)
Women	>88cm (> 35 inches)
Triglycerides	>150 mg/dl
HDL Cholesterol	
Men	<40mg/dl
Women	<50mg/dl
Blood Pressure	>130/85 mm Hg
Fasting Glucose	>110 mg/dl

*Metabolic syndrome: diagnosis is established when >3 of these risk factors are present

Figure 3: Table 2 :

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