



ORIGINAL RESEARCH PAPER

Unani

UNDERSTANDING THE METABOLIC RISK FACTOR CLUSTERING: ITS ASSOCIATION WITH OXIDATIVE STRESS AND DIABETES MELLITUS

KEY WORDS: Oxidative Stress, Diabetes Mellitus, Metabolic, Insulin Resistance, CVD.

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ABSTRACT

Metabolic risk factor clustering is the key concept of Insulin resistance and Diabetes Mellitus. Oxidative stress plays an important role in the progression of clustering in the cascade pattern. According to W.H.O. Type 2 Diabetes Mellitus has already reached epidemic proportions currently affecting over 422 million people worldwide and one of the four leading non-communicable diseases highlighted in the targets of the WHO Global Monitoring Framework (2019-20). Oxidative stress from oxidative metabolism had been reported to cause base damage, as well as break strand in genetic level. Oxidative stress is thought to be involved in the development of atherosclerosis (CVD) and had been cited to be of etiological importance in cardiovascular diseases. The present study highlights the various traits of metabolic clustering and its association with reactive oxygen species (ROS).

INTRODUCTION:

According to World Health Organization (WHO), Metabolic syndrome (MetS) definition given in 1999 as MetS is defined using abnormal laboratory results in glucose intolerance, hypertension, lipid profile and atherogenesis.¹ However, the International Diabetes Federation (IDF) suggested a new definition of the MetS in April 2005 as MetS is a cluster of diseases, having biochemical, physiological and clinical factors that directly escalate the menace of T2 Diabetes mellitus and cardiovascular diseases (CVD).^{2,4} the present paper elaborates each traits of metabolic cluster and elucidate its co-relation with oxidative stress and T2 Diabetes.

METABOLIC RISK FACTOR CLUSTERING:

Metabolic risk factor cluster involves five traits such as greater adiposity, decreased High density cholesterol (HDL-C), Elevated triglycerides, Elevated Blood pressure (B.p), and impaired fasting glucose-IFG.⁵

Metabolic Risk Factor Clustering



Fig: 1 showing the traits of the Metabolic cluster

Presence of three or more of these five traits is highly related to Insulin resistance (Diabetes Mellitus) which is known to be metabolic syndrome traits clustered. Presence of 3 or more traits typically leads to tripling of risk of cardiovascular disease (CVD) and 20-fold greater risk for Diabetes mellitus.⁶

⁸The features of each trait are mentioned below:

1. Greater adiposity
2. Decreased High density cholesterol (HDL-C)
3. Elevated triglycerides
4. Elevated Blood pressure (B.p)
5. Impaired fasting glucose-IFG

1. Greater adiposity:

Adiposity is the new non-contagious epidemic, which means the development of fat cells or obesity. In human body, excess energy is reserved as fat in the adipose tissue in order to use in cases of energy deficit. It has been recognized that adipose

tissues has both white and brown adipocytes. The brown adipocytes regulates energy balance and substrate metabolism. The white adipocytes (WAT) are stored in tissues as Triglycerides and mainly responsible for obesity. One of the fundamental causes for greater adiposity is an energy imbalance due to physical inactivity, Unhealthy diet, and family lifestyle, eating habits, metabolism and genetics.⁹⁻¹²

2. Decreased High density cholesterol (HDL-C):

High density lipoprotein (HDL) is the complex class of lipoproteins comprising various subclasses that are different in size, protein, and lipid composition, physiological and patho-physiological significance. HDL-C is inversely related to cardiovascular risk as it is considered to be a main athero-protective function. Metabolic risk factor clustering is characterized by the presence of atherogenic dyslipidemia which includes decreased High density lipoprotein-cholesterol (HDL-C).¹³⁻¹⁵

Individuals with low HDL-C are often insulin resistant and at increased risk of developing T2DM. Several studies showed the association between low HDL-C and increased risks not only of CVD but also T2DM. Metabolic perturbations are mechanistically linked to decreased HDL-C which is already present in prediabetic state and hence an innocent bystander of T2DM.¹⁶⁻¹⁸

3. Elevated triglycerides:

Insulin has pleiotropic effects on lipid metabolism. High production of VLDLs in Insulin resistant state, decreases the stability and levels of HDL-C which is responsible for elevated levels of triglycerides. It is one of the mechanism linking elevated Triglyceride levels with decreased HDL-C levels.^{19,20}

4. Elevated Blood pressure (B.p):

Various studies exhibited that hyperglycemia and hyperinsulinemia are involved in the development of high blood pressure, by triggering the renin angiotensin system and enhancing the action of angiotensin II.²¹ In this condition kidneys start to reabsorb more sodium and increase the vasoconstriction in arteries surrounding heart, which results in increased levels of blood pressure.²²

5. Impaired fasting glucose-IFG:

Impaired fasting glucose is one of the traits in metabolic risk factor cluster. IFG is now defined by an elevated fasting plasma glucose (FPG) concentration (≥ 100 and < 126 mg/dl). IFG was defined in 1997 by the American Diabetes Association as a means of classifying individuals who had

fasting glucose levels between normal and diabetes.²³ It was meant to be analogous to IGT as an intermediate metabolic state between normal and diabetes, IFG is an early stage of developing diabetes and a strong predictor of diabetes.^{24,25} People with isolated IFG predominantly have hepatic insulin resistance and normal muscle insulin sensitivity. It would be preferable to treat the glucose component separately from other components in stratifying diabetes risk.^{26,27}

CHARACTERISTICS OF METABOLIC SYNDROME:

Table: 1

| | |
|-------------------------------|------------------------------|
| High Plasma NEFA | Insulin Resistance |
| Hypertriglyceridemia* | Hyperinsulinemia |
| Profound Postprandial lipemia | Hyperglycemia* |
| Low HDL-C* | Pear-apple anthropomorphism* |
| No HDL-C | Low lipoprotein lipase |
| Small, dense LDL | High hepatic lipase |
| Elevated CETP activity | Hypertension* |

Table: 1 showing the various characteristics of Metabolic syndrome:

CETP-cholesteryl ester transfer protein, NEFA-Non-esterified fatty acid.

Metabolic syndrome according to 2009 joint statement by Albert et al.²³

RELATIONSHIP BETWEEN OXIDATIVE STRESS, DIABETES MELLITUS AND METABOLIC RISK FACTOR CLUSTER:

It is believed that oxidative stress plays important role in the development of vascular complications in diabetes particularly type 2 diabetes mellitus.²⁹ Free radical formation or oxidative stress in diabetes is mainly by non-enzymatic glycation of proteins, glucose oxidation and increased lipid peroxidation leads

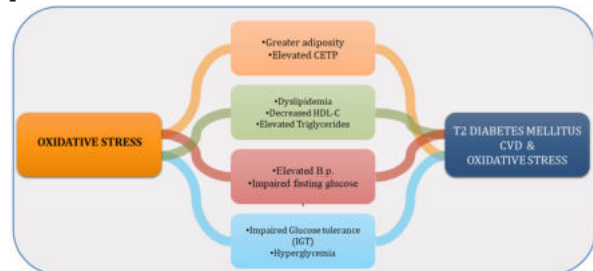


Fig:2 showing inter-relationship between all the traits of metabolic risk factor cluster with oxidative stress and D.M.

to damage of enzymes, cellular machinery and also increased insulin resistance.³⁰ The conceptualization that oxidative stress is the common factor underlying insulin resistance, T2DM, and CVD is cleared here by the above studies. Oxidative stress is taken as the recurrent pathogenic mechanism as precursors as well as fore-runner of linking metabolic risk factors with T2DM and CVD.³¹

CONCLUSION

Metabolic syndrome (MetS) is a cluster of diseases, having biochemical, physiological and clinical factors that directly escalate the menace of T2DM, dyslipidemia, hypertension, insulin resistance, endothelial deterioration and cardiovascular diseases. Alterations in lifestyle remain the main intervention of choice for this syndrome. Modern lifestyle modification therapy combines with specific recommendations on exercise, diet and physical behavioral strategies is recommended. Pharmacotherapy should be considered for those whose risk factors are not reduced with lifestyle changes. A realistic goal for obese individuals should be setup to reduced weight by >8% to 10% over a period of 6 months. Weight reduction should be with a moderate physical activity. Dieto-therapy is to be suggested to low intake of saturated and total fat; reduced usage of sugars and high

glycemic index foods; and increased intakes of vegetables, fruits and whole grains. Well monitoring of Hypertriglyceridemia, High LDL-C and HDL-C. These multiple strategic approaches have positive impact on reducing the metabolic perturbations and improve the human health.

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