

METABOLIC SYNDROME; AN APPROACH TO ITS ETIO-PATHOGENESIS IN AYURVEDIC PARLANCE

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ABSTRACT

Metabolic Syndrome (MS) is a Life threatening metabolic disorder affecting millions of people not only in India but all over the world. Insulin resistance and abdominal obesity are the major hazardous etiological factors which play key role in the genesis of complex biological mechanism of MS at gross as well as subtle level. MS is also associated with other associated risk factors such as CVD, CKD, PCOD and NAFLD etc. In this perspective Ayurveda the science of life describe the two major concepts of diseases first one which is related to outcome of over-nutrition and second one related to under-nutrition. The disease MS is supposed to be the outcome of over nutrition due to defective metabolic process at gross as well as at cellular level. The present article is an effort to understand the etio-pathogenesis of MS in ayurvedic parlance and it may enlighten the path for future researchers to cope with MS and its life threatening hazardous side effects.

KEYWORDS: CKD, CVD, Diabetes Mellitus, Insulin Resistance, Metabolic Syndrome, NAFLD, PCOD

INTRODUCTION

The metabolic syndrome consists of a constellation of metabolic abnormalities that confer increased risk of Cardio Vascular disease (CVD) and Diabetes Mellitus (DM). MS is also known as Syndrome X or Insulin Resistance syndrome. The criteria for the MS have evolved since the original definition by the World Health Organization in 1998. The major features of MS include Central obesity, Hypertriglyceridemia, Decrease High density lipoprotein (HDL), Hyperglycaemia and Hypertension. The latest definition of MS is given by the National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III) in 2004 by the presence of 3 or more, out of these 5 criteria's-

- **Waist circumference** >102 cm in males
>88 cm in females
- **Hyper Triglyceridemia;** Triglyceride >150 mg/dl or specific medication.
- **Low HDL cholesterol;** <40 mg/dl in males
<50 mg/dl in females or specific medication.
- **Hypertension;** Blood pressure>130/85 mm/Hg or specific medication.
- **Fasting plasma glucose** >100 mg/dl or specific medication or previously diagnosed Type2 DM.

Ayurvedic Aspect

Obesity and Lipid disorders have been vividly conceived in Ayurveda with context of Medoroga (Dyslipidemia) and Prameha (Diabetes). The classical Ayurvedic texts have vividly described Santarpajanya Vikaras (Comprise of diseases due to over nutrition and defective tissue metabolism). Ayurveda is very much concerned about conservation of health rather than eradication of disease. It presumes that improper dietary habits and deranged functions of different sets of Agni (Metabolic fire) give rise to formation of Ama (reactive antigenic factor). Since last few decades, the conventional system of medicine is focusing on the concept of metabolic syndrome, which seems very similar to the concept of Santarpajanya Vikaras of Ayurveda.

The production of Medadhatu (Lipids) is disturbed by variety of etiological factors including Medodhatvagni (Lipid metabolic process). Side by side the quantity (amount and proportion) and quality (contents) of Medadhatu (Lipids) are also disturbed by the same. When Medadhatu (Lipids) interacts with preformed form of Ama (reactive antigenic factor), it changes and alters the quality and quality of fatty tissues including cholesterol. The interaction of Ama (reactive antigenic factor) with fatty tissues is known as Sama Medadhatu, which is the main cause of Medoroga (Dyslipidemia), and it is the liver (Yakrata), which is responsible for qualitative derangement of lipids and cholesterol. This form of Ama (reactive antigenic factor), when circulates all over the body may lead to blockade of micro-channels and precipitate antigenic reactions and generate series of inflammatory events in the body. If such categories of Ama (reactive antigenic factor) interact with Medadhatu (Lipids), it may lead to a variety of metabolic disorders.

Sthana (Place) and Swarupa (Form) of Meda Dhatu (Lipids) in the Pathogenesis of Ms

The most of Medadhatu resides in Medodhara Kala (3rd kala) i.e greater and lesser omentum. Other sites are Udara (abdomen), Sphika (gluteal region), Stana (thorax) and Gala (neck and clavicular region). Medas is present in the body in two main forms i.e Posaka and Posya.

Posaka (Mobile in nature)	Posya (Immobile in nature)
↓	↓
Which is circulated in whole body along with Rasa (Plasma and lymph) and Rakta (blood) for nourishing the Posya Medadhatu.	Which is stored in Medodhara Kala (3 rd kala) i.e greater and lesser omentum and in its sites like Udara (abdomen), Sphika (gluteal region), Stana (thorax) and Gala (neck and clavicular region)
↓	↓
According to Modern science, it can be correlated with cholesterol and lipids, which are present in circulating blood.	According to Modern science, it can be correlated with adipose tissues/fat.

This concept refers that, Defective Posaka Medadhatu is the triggering factor, which causes accumulation of abnormal Posya Medadhatu which finally causes excessive fat deposition (Adiposity) in Viscera (Visceral Adiposity) as well as in subcutaneous tissues (Subcutaneous Adiposity).In the pathogenesis of MS, Posya Medadhatu increases inordinately and at the expenses of other dhatu (tissues). In other words, while Posya Medadhatu is increasing, all other

dhatu (tissues) undergo wasting/depletion on account of lack of proper nourishment.

Probable Pathogenesis of Metabolic Syndrome

In the pathogenesis of MS, key factors are Central adiposity and Insulin resistance. Central (Visceral) adipose tissue has tendency to direct the FFAs directly to the liver. These FFAs causes release of several pro-inflammatory mediators (i.e. adiponectin, leptin, CRP etc.), from the liver which are then directed to the systemic circulation and gives rise to other consequences of MS. Ayurveda believes that obesity and asthenia depends chiefly upon the quality of Rasa dhatu (the first post digestive essence from food) which is source of nourishment for the entire body. That is also the source of deranged Medodhatu in terms of Medodhatu vridhi (adiposity).

According to Ayurveda classics there are three sets of Agnivyapara (Metabolic process) viz.

- Jatharagni level (Main Digestive/Metabolic Fire)
- Bhutagni level (Metabolism at gross level)
- Dhatvagni level (Metabolism at tissue/cellular level)

All type of Ahara (Food taken) ingested undergoes Jatharagnipaka (Metabolic process) at the level of Amasaya (stomach) and Pachyamanasaya (small intestine). The nature of Jatharagnipaka (Metabolic process) is Sanghatbheda (disintegration of macromolecule of food into smaller one) to make it fit for digestion and absorption. This entire phenomenon of digestion takes place in three Avasthapaka (digestion at different levels) at different level in G.I. tract viz-

- Madhura avasthapaka (Salivary digestion)
- Amla avasthapaka (Gastric digestion)
- Katu avasthapaka (Intestinal digestion)

This Anna rasa is absorbed via Rasa and Raktavaha srotasa (Circulatory channels) and reached towards the liver. The same idea is also conceived in modern physiology and opines that both diet and drug after absorption through G.I tract primarily metabolize at the level of liver through its subsequent metabolic enzymes. The metabolic enzymes and associates of liver are comparable to Rasagni of Ayurveda. This Rasagni proper metabolize the Ahara *rasa* and make it convenient for respective Dhatu. The formed nutrient pool at the site of liver, reaches towards the heart through Rasa and Raktavaha srotasa (Circulatory channels). Now these forms of metabolic components of diet are transported all over the body.

After seeing the above concept, it is clear that in Adiposity, although Jatharagni is in its normal level but due to hyper-functioning of anabolic set of Dhatvagni, remaining Dhatus properly not utilized the nutrient for their growth so there is excessive formation of Medadhatu (adipose tissue) which ultimately leads to Medovridhi (adiposity).

It is presumed that following etiological factors contribute a lot in the genesis of adiposity viz.

- Nature, quality and quantity of diet and lifestyle errors.
- Metabolic tendency governed by genetics.
- Obstruction of body channels by accumulated metabolic wastes, un-metabolized & un-utilized nutrients and other reactive agents in the life process of metabolism.

Process of Pathogenesis of Metabolic Syndrome through Ayurveda

- **Sanchaya (Stage of Accumulation)**

Due to excessive indulgence in Adhyasana (repeated and over eating behavior) Madhura, sita, Snigdha ahara (i.e intake of excessive sweet, cold and fatty diet) and lack of physical exercise, Avyavaya, Divasvapna etc. (sedentary life styles) with and without presence of Bijadosa (genetic predisposition), there is aggravation of all the three dosas (specially Kapha dosas). This form of Kapha have physical similarity with Ama and Medadhātu, which get accumulated over immovable part of the body in vicious manner and finally the whole nutritional pool is shifted towards strengthening of Medadhātu.

- **Prakopa (Stage of Aggregation)**

The increase of Kapha in quantity and quality is responsible for the disturbance in the functions of Agni (Metabolic fire) at different level in the body especially at the level of Bhutagni and Medodhatvagni. The deranged functions of Agni may lead to formation of Ama (reactive antigenic factor). Because Kapha and Meda are of same nature that's why Ama formed at Medodhatvagni level gets mixed with circulating Annarasa / Ahararasa (nutritional pool) and causes blockage of micro channels (Srotosanga). This blockage of micro channels (Srotosanga) can be compared with the downstream signaling of the Insulin receptors due to excess formation of Free Fatty Acids i.e. FFA (Ama).

- **Prasara (Stage of Scattering)**

If a person is still consuming Fatty and high calorie diet and following sedentary life style, this preformed and newly formed FFAs (mainly from the Visceral adipose tissue) circulated all over the body in the form of Ama rasa.

- **Sthana-Samsharya (Stage of Localisation/Prodromal Symptoms Appearance)**

The circulating Ama rasa (FFAs from the visceral adipose tissue) gets localized at different places in the body. FFAs which are directed to the liver stimulate, release of different pro inflammatory mediators. In due course of time these inflammatory mediators play a key role in the pathogenesis of atherosclerosis. Most of the FFAs occupy the insulin receptors by molecular mimicry, may lead to Insulin resistance.

Beside this, Insulin resistance causes an imbalance between production of NO and secretion of endothelin-I, leading to decrease blood flow and activation of sympathetic system which may lead to develop Hypertension.

- **Vyakta (Stage of Expression / Appearance of Signs and Symptoms)**

If the whole process is continuously going on, it causes downstream signaling of the insulin receptors due to occupancy by the circulating FFAs, which causes Insulin resistance and the condition known as Hyperinsulinemia. Initially this stage represents as postprandial hyperglycemia, then fasting hyperglycemia and finally as the Hyperglycemia or Type 2 DM.

FFAs which are directed to the liver are associated with increased production of apo-B containing triglyceride rich very low density lipoproteins (VLDLs). In the presence of hypertriglyceridemia, a decrease in the cholesterol content of HDL is a consequence of reduced cholesteryl ester of the lipoprotein core in combination with cholesteryl ester transfer protein mediated alteration in triglyceride, making the particle small and dense i.e increase in LDL concentration. Small dense LDLs are thought to be more atherogenic. They may be toxic to the endothelium, and they are able to transmit

through the endothelial basement membrane and adhere to glycosaminoglycans and results in atherosclerosis and Hypertension.

- **Bheda (Stage of Complications)**

The manifestation of the Upadrava (complications) of MS such as Atherosclerosis, Cardio vascular diseases (CVDs), Non alcoholic Fatty liver disease (NAFLDs) and Poly cystic ovarian disease (PCODs) etc. can be considered as the Bheda stage of MS.

THE SUMMARY OF WHOLE PROCESS OF PATHOGENESIS OF MS THROUGH AYURVEDA

Dosas	Predomonantly Kapha (Mainly Kledaka) Pitta (Mainly Pacaka) Vata (Mainly Samana and Vyana)
Dusya	Rasa, Rakta, Mamsa, Meda, Majja, sukra and Oja (Mainly Meda)
Agni	Medodhatu agnimandya
Srotasa	Rasavaha, Raktavaha, Mamsavaha, Medovaha, Majjavaha and sukravaha (Mainly Medovaha)
Srotodusti	Saaga Vimarga gamana Atipravritti
Adhisthana	Sarva sarira
Udbhavasthana	Amasaya
Ama	Dhatvagni Mandata Janya

Role of Agni (Metabolic / Digestive Fire) in the Pathogenesis of Ms

As long as life in man, every tissue, organ and cell has to undergo process of constant changes to meet their survival and needs. This constant process of change either for yielding energy (Catabolic) or synthesize the tissue (Anabolic) is termed as Agni (Metabolic fire) in Ayurveda. Agni (Metabolic fire) maintains organism integrity and vitality by converting the food consumed in various ways and also to provide energy necessary for proceeding innumerable vital activities through the Pakadi karmas i.e. biophysical and biochemical process. Agni (Metabolic fire) participates and regulates the course of digestion and metabolism or any transformation in the tissues.

In the pathogenesis of MS, Agni (Metabolic fire) plays a very important role since beginning to the end. In the cases of MS, Agni mandata (Defective metabolic process) is especially at the level of Medadhatu (Lipids). Agni (Metabolic fire) is the root cause of MS. According to Ayurvedic classics Dhatvagni (Metabolism at tissue/cellular level) are seven in numbers. Each one is located in its specific dhatu (Tissue/cells) to permits its moieties from the circulating substances derived after bhutagni paka (Metabolism at gross level), to form its own tissue.

Dhatvagni functions mainly are of two types-

- Synthesis of new proteins
- To yield energy for the functions of tissues

If Dhatvagni is impaired, both these functions will impair. In the view of modern physiology also, that the tissue of the body are being reformed as rapidly as they are destroyed in the course of metabolism. Energy is obtained by the organism by the process of oxidation. No oxidation can proceed unless there is a simultaneous reduction of some other compound. The materials with which the tissue cells are synthesized are derived from food sources, which are suitable, processed during the course of their digestion and metabolism.

MS is caused by the excessive intake of madhura (sweet) Ahara, snigdha (Fatty) Ahara, adhyasana (repeated / over eating) and sedentary life style etc. Due to these nidana (causes), as Ahara taken is not properly digested. This may lead to formation of Ama i.e. reactive antigenic factor. This form of Ama is distributed all over the body with Ahara *rasa* and mainly increases the Sama Medadhatu (Visceral Adiposity) because of its excessive unctuous and sweet nature. This Ama formation suggests that there is Dhatvagni mandata (defective metabolism) at the level of Medadhatu (Lipids).

Modern Concept of Dhatvagni Paka

- According to modern physiology the “First step of a hormone’s action is to bind a specific receptor at the target cell. Cells that lack receptors for the hormones, do not respond. Receptors for some hormones are located in target cell membrane, whereas other hormone receptors are located in the cytoplasm or nucleus. When this hormone combines with its receptors, this usually initiates a cascade of reaction in the cell, with each stage becoming more powerfully activated.
- A type of hormone will act on a particular tissue. The target tissues that are affected by a hormone are those that contain its specific receptors. Similarly each Dhatvagni has a specific action at its own dhatu. Though all the Agneyansas (Minute part of metabolic fire) are in circulation, a specific Agneyansas will have action on a specific dhatu (Tissue).
- Insulin is an important hormone which is crucial for normal metabolism of carbohydrates, fats and proteins. The role of Rasagni (type of metabolic fire) is to convert the received material in liver into micro forms to nourish all the dhatus to perform their functions. Similarly insulin activity is associated with energy abundance from energy giving food in the diet and it plays an important role in storing the excess energy.
- Without insulin no cell membrane permits glucose molecule to transport inside the cell. Insulin increases glucose transport and usage by most of the cells of the body in the same way that it affects glucose transport and usage in the muscle. Hence Insulin resistance can be compared with Medodhatvagni mandata (defective metabolism) which ultimately leads to Hyperglycemia, Hypertriglyceridemia and other components of MS.
- Insulin also promotes fat synthesis and storage. Insulin activates Lipo-protein lipase in the capillary walls of the adipose tissue, which splits the triglyceride into the fatty acids. Thus Insulin resistance plays the role of Medodhatvagni mandata on which medodhatu vridhi (Adiposity) and ksaya of other dhatus (Immune-deficiency) are obtained.
- The number of receptors in a target cell (Pacakansa in dhatu) usually does not remain constant from day to day or even from minute to minute. The receptors dhatus themselves are often inactivated or destroyed during the course of their function and at other times they are reactivated or new ones are manufactured by their respective Dhatvagni.
- When dhatus are possessing laghu guna (micro form), they easily respond to the Agneyansas since their receptors are sensitive and undergo metabolic changes. If they possess guru guna (macro form) due to involvement of Ama, they will not respond much to Dhatvagni, leading to Dhatvagni mandata. Dhatvagni condition or igniting capacity depends upon the state of dhatu receptors on which it is acting upon.
- Hence the Dhatvagni are the chemical or hormonal factors essential for changing the sequences of bases at DNA up to formation of functional protein for the purpose of synthesis of its tissue (anabolic) and enzymatic factors

essential to yield energy for tissue functions (catabolism).

- Under Dhatvagni starting from mitochondria (Power house of the cell), all enzymatic, co-enzymatic factors and catalytic factors participating in the chain reactions in the tissue to yield energy and the anabolic steroids, responsible for growth are also to be considered as same.
- All endocrine, exocrine and paracrine including intercellular and intracellular enzymes are can be considered as the Dhatvagni ansas (part of metabolic fire).

CONCLUSIONS

The etio-genesis and management of MS in conventional system of medicine is still not satisfactory and warranting newer strategies from other resources. It seems to explore an Ayurveda based process of pathogenesis and line of management for treating MS.

From the present research work it can be concluded that Metabolic syndrome is well defined and still evolving etio-pathogenesis in biomedical sciences, is as such not described in Ayurvedic classics, but it may be considered as the Meda (Lipids) dominant disorder and having strong resemblance with Santarpanjanya vikaras (diseases due to over nutrition). The management of MS in modern medical sciences is still not satisfactory and the current strategy of prevention and treatment of metabolic syndrome is rapidly changing. Hence many researchers in the field are inclined to understand scientific study of its complex etio-pathogenesis and treatment development from Ayurvedic resources. The present research work has been under taken with the same perspective

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