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Inflammation as an Integral Part of Medoroga w.s.r. to Metabolic Syndrome – A Conceptual Analysis

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ABSTRACT

Santarpanottha vikaras are the results of indulgence in the factors where energy consumption is high with minimal utilization. High calorie diets with minimal physical activity, sedentary life style lead to metabolic error of *Medo Dhatu* and results into *Medoroga* - Metabolic Syndrome. The term Metabolic Syndrome refers to a group of symptoms composed of altered fasting glucose, central obesity, hypertension and impaired lipid metabolism. The factors involved in metabolic syndrome are associated with sedentary lifestyle, increased central deposition of adipose tissue, reduced HDL cholesterol, and raised triglycerides, high blood pressure, and altered glucose in genetically susceptible persons. Abnormal metabolism of fat predisposes the process of inflammation and inflammation in turn becomes precipitating factor of establishing pathology of various conditions like dyslipidemia, insulin resistance, hyperglycemia, hypertension, atherosclerosis, CAD, cancer and so on. The article highlights about the role of diet, physical activity in altered metabolism and inflammation as key process in establishing the disorders of metabolic error with their Ayurvedic perspective.

KEYWORDS

Santarpanottha vikara, Medo dhatu, Medo roga, Metabolic Syndrome, Inflammation

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INTRODUCTION

The concept of *Medoroga* is well discussed topic in the *Brihatrayees* under the umbrella heading of *Santarpana janya vyadhis*. ***Medorogah – Medo dhatu dushti janya rogah[1].*** *Medoroga* means the set of disorders manifested as a sequence of altered metabolism of *Medodhatu*. It is so mentioned in the classics that the *Srotas* that represents or carries *Medodhatu* gets vitiated due to the following factors like *Avyayama, Divaswapna, Medya ahara ati bhakshana* and also *Varuni madya sevana*[2]. The disorders in metabolism of various body factors especially due to excessive nourishment are considered as *Santarpana janya vikaras*[3]. *Medoroga* is one such disorder established as a result of *Santarpana.*

Metabolic syndrome is a group of disorders due to errors of metabolism. These metabolic errors may include insulin resistance, hypertension, dyslipidemia, and an increased risk of clotting of blood. Affected individuals are usually obese or overweight. The excess amount of accumulated visceral fat associated with chronic inflammation leads to the development of arteriosclerosis, dyslipidemia, insulin resistance and also associated with fatty liver disease often. Lack of physical activity, sedentary life style, lowered endurance, erratic eating habits, physical and mental stress, hormonal inductions and altered sleep wake cycle are considered to be the common factors that induce metabolic errors.

AIMS AND OBJECTIVES

In the article, an attempt is made to analyze the altered state of metabolism of *Medodhatu* that leads to manifestation of various resultant disorders.

A critical review of the metabolically deranged *Medo dhatu* leading to inflammation and further manifesting into Metabolic Syndrome is done.

A diligent review and analysis of the literature and research outcomes are attempted to state the fact that Inflammation in *Meda dhatu* is an integral part of manifestation of metabolic syndrome and other related disorders.

ALTERED METABOLISM OF MEDA DHATU IN METABOLIC SYNDROME:

1. Analysis of Etio - pathogenesis-

The *dhatu roopi* medas gets increased when the person indulges in the following *nidanas*[4]. -

- *Ati Sampooranat* – Food consumption in excess quantity.
- *Ati Guru, snigdha madhura sheeta ahara Upayogat* – Excessive intake of food which is

heavy to digest, unctuous, sweet, cold potential

- *Avyayamat* – Lack of exercise.
- *Avyavayat* – Lack of sexual activity.
- *Divaswapnat* – Sleeping during day time.
- *Harsha-nityatvat* – Always being happy / not bothering for any thing
- *Achintanat* – Free from tensions and worries.
- *Beejaswabhavat* – Genetical predisposition.
- *Sleshmala Ahara – Kapha dosha vardhaka Ahara.*
- *Adhyashana* – Consuming of food before digestion of previously consumed food.
- *Shayya asana sukha* – comforts and sophistications

The food that are rich in *Snigdha Madhura Guru Pichchila gunas, Navanna Navamadya*, aquatic foods, Milk products, products of jaggery and sugar, sleeping in day time, physically less active and sedentary life style, are the identifiable factors that contribute to impaired metabolism. Life style happens to be a major contributing factor to cause metabolic impairments and related disorders[5]. The daily habits of an individual and his inappropriate relation to the environment accounts to the diseases caused due to incorrect life-style.

Among the dietary habits, 3 major patterns are identified[6]:

1. The healthy dietary pattern (HDP) – HDP means consumption of food composed of vegetables, legumes and nuts, fruits, low-fat food, less of dairy, meat, and olives.

2. The Western dietary pattern (WDP) - The western pattern of diet includes fast food, drinks and beverages of high energy, sweets, condiments, cereals, snacks, mayonnaise.

3. The Unhealthy dietary pattern (UNHDP) - This comprises of consumption of high fatty diet, dairy products, meat- especially red meat, brain liver kidney etc. repeated consumption of coffee or tea and a less consumption of liquid oil. This pattern of diet is largely composed of hydrogenated fats and meat which leads to establish the link between the dietary pattern and altered metabolism of fat and the MUH phenotype.

Varuni madya sevana[7]**-** *Madya* has a role in establishing the pathological process of *Dosha prakopa* and *Avarana*. Among the chronic alcoholics 2/3 of them are affected with Chronic alcoholic myopathy which is characterized by selective atrophy of Type II fibers (glycolytic, fast-twitch, anaerobic) Alcohol increases the concentration of cholesterol hydroperoxides – which is nothing but *Saama meda*. Alcohol affecting the fat metabolism and liver function is an established fact. *Varuni madya* is prepared out of *Punarnava, Shalipishta, Taala*, and

Kharjura rasa. This *Varuni madya* is *Laghu* and more watery in nature. It helps to increase the *Jaleeyamsha* in the body thus establishing *medodushti* by increasing *Klinnata* in the body.

The formation of the *Dhatu* is complete from the 4 types of *Ahara* when the *Dhatu ushma*, *Maruta* and *Srotas* are in optimal levels. *Agni* at all 3 levels namely *Jatharagni*, *Dhatvagni* and *Bhutagni* is the prime factor that aids to attain the complete formation of *Dhatus* and all the metabolic processes. After being acted upon by all these 3 *Agnis*, the *Annarasa* turns into *Dhatu* of two different *Avastha* namely *Sthayi dhatu* and *Asthayidhatu.* These *Asthayi dhatu* are the precursors of *Sthayi dhatu* which keep circulating throughout the body before getting converted into *Sthayi dhatu*. According to the principle of *Dhatavo dhatvaharah* the *Asthayi medo dhatu* is the *Poshaka bhava* for the *Sthayi medo dhatu*. In other words, the circulating lipids are the precursors of the adipose tissue. More the amount of circulating lipids more is the deposition of the adipose tissue as per the rule of *Samanya siddhanta*. And also it is to be noted that, the hypo functioning of the *Agni* leads to reduction in the metabolic activity and vice versa. Hypo functioning of *Medo dhatwagni* leads to declined metabolic activity in *Medodhatu* and favours deposition of excess *Medodhatu*. Hyper functioning of *Medo dhatwagni* or otherwise, leads to enhanced metabolic activity resulting in declined deposition of adipose tissue and thereby reducing body fat.

Clinical implications that could be observed in an individual with altered metabolism of fat are[8]-

1. Ayushohrasa-

There could be an ambiguity in stating this. But it is sensible that various complications resulted by *Medo dhatu vriddhi* are life risks. As a result of nourishment of *Meda dhatu* alone in excess, the *Poshana* of other *Dhatu bhaga* declines leading to *Oja kshaya* also. Inappropriate *Poshana* of the *Dhatus* with excess *Meda* and *Ojakshya* risks the tissue components and could involve life risking manifestations.

2. Javoparodha-

Java means energy/ endurance/ potential of tissue components. Excess fat deposition and established metabolic error leads to fatigability in the tissues.

3. Kruchra vyavayata-

Sexual intercourse is an act which demands physical and mental involvement. *Sankalpa* (mental preparedness) is an effort which prepares the person for the act of sexual intercourse. Due to malfunctioning of the *Dhatu* components and heavy body mass, lack of mental preparedness for the act of sexual intercourse leads to difficulty in

initiation and performance. Due to declined levels of *Shukra dhatu* resulted due to *Margavarana* caused as a result of *Meda dhatu upalepa* in the *Srotas*, the sexual drive and fertility are also affected.

4. Daurbalya-

Fatigability is due to improper *Poshana* of *Dhatus* and also lack of endurance.

5. Daurgandhya-

In *Sthoulya, Vikruta kapha dosha* is mixed with *Meda dhatu* in the form of *Kleda*. Because of the tendency of the *Abaddha, amayukta meda dhatu* the bad body odour is resulted. *Gandha* (odour) is the main characteristic of *Prithvi Mahabhuta*. *Meda dhatu* is composed of mainly *Prithvi* and *Aap Mahabhutas*. Altered composition and metabolism in these two basic elements of the body makes the sweat which is *Meda dhatu mala* turning out to be *Visra Gandhi* (foul smelling). This bad odour is observed in mouth, body parts, urine, faeces, sweat etc.

6. *Swedabadha-*

Sweda is mala of *Meda dhatu*. Excessive perspiration is observed in *Sthoulya* as a result *of Ama abaddha klinna meda dhatu (kapha sansarga, vishyanditva, guruta and vyayama asahatva)* which develops tendency of emitting *Visragandhi sweda*.

7. *Ati ksudha and 8. Ati pipasa-*

Enhanced appetite and voracious eating are seen as a result of *Koshta gata vata*. The *Margavarana* to *Vata dosha* in the *koshta* leads to *Vigunata* of *Samana vata*, thereby does *Agni Sandhukshana*. Thus the person develops huge appetite and tends to eat more. *Agni* has *Urdhva mukhitva*. The excess *Agni* in the *Koshta* creates excess thirst.

METABOLIC SYNDROME

The term Metabolic Syndrome refers to a cluster of associated symptoms composed of impaired fasting glucose, abdominal obesity, hypertension and dyslipidemia[9]. The WHO (1999) criteria for diagnosis of Metabolic Syndrome requires[10]

Presence of any one of these - (i) diabetes mellitus, (ii) impaired glucose tolerance, (iii) impaired fasting glucose or insulin resistance, and two of the following criteria defined below:

- Blood pressure: > 140/90 mmHg
- Dyslipidemia: triglycerides (TG): > 1.695 mmol/L and high density lipoprotein cholesterol (HDL-C) < 0.9 mmol/L (male), < 1.0 mmol/L (female)
- Central obesity: in male waist: hip ratio > 0.90m; in female waist: hip ratio > 0.85m, or body mass index > 30 kg/m2
- Microalbuminuria: urinary albumin excretion ratio >20 µg/min or albumin: creatinine ratio > 30 mg/g

DISCUSSION:

ABNORMAL METABOLISM AS PREDISPOSER TO INFLAMMATION:

Lack of body exercise, no botheration for anything, not undergoing *Shodhana karma* will tend the person to accumulate excess amount of *Kapha*, *Pitta*, *Meda* and *Mamsa dhatu*[11].

The important factors that contribute to lifestyle disorders include wrong food habits, physical inactiveness, inappropriate body posture and largely affected biological clock. Physical inactivity is a major predictor of cardio vascular diseases and the related high risk of death. The components that diagnose the metabolic syndrome comprise of sedentary lifestyle, excessive fat tissue deposition which is predominantly central type, reduced HDL cholesterol, and increased level of triglycerides and glucose, high blood pressure in genetically susceptible persons. Metabolic syndrome can exist with obesity which is commonly a visceral deposition, dyslipidemia that leads to atherogenesis, insulin resistance, genetic susceptibility, dysfunctioning of the endothelial layer, high blood pressure, increased coagulating tendency and high levels of physical and mental stress. All these factors predispose the process of inflammation which is identifiable by presence of abnormal adipocytokines such as TNF (tumor necrosis factor) - α, interleukin-1 (IL-1), IL-6, leptin, and adiponectin. The clinical phenotype along with the biological phenotype interact together to initiate the pro- inflammatory state and later become chronic inflammation leading to inflammation in the arteries and further resulting in phenomenon of atherosclerosis.

THE PROCESS OF INFLAMMATION

The free radicals of oxygen are produced in the human body through various metabolic processes. These free radicals affect the important tissue components causing cell injury and disturbing cellular well-being and homeostasis. These free radicals target mainly the lipid tissue, nucleic acids and protein molecules which accumulate as age advances in the individual. Chronic damage by free radicals causes two major causes of death - Cancer and Atherosclerosis mainly and also it is found that free radicals cause severe muscular damage in due course. Thus one can learn that it is oxidative stress that makes a major contribution to inflammatory diseases.

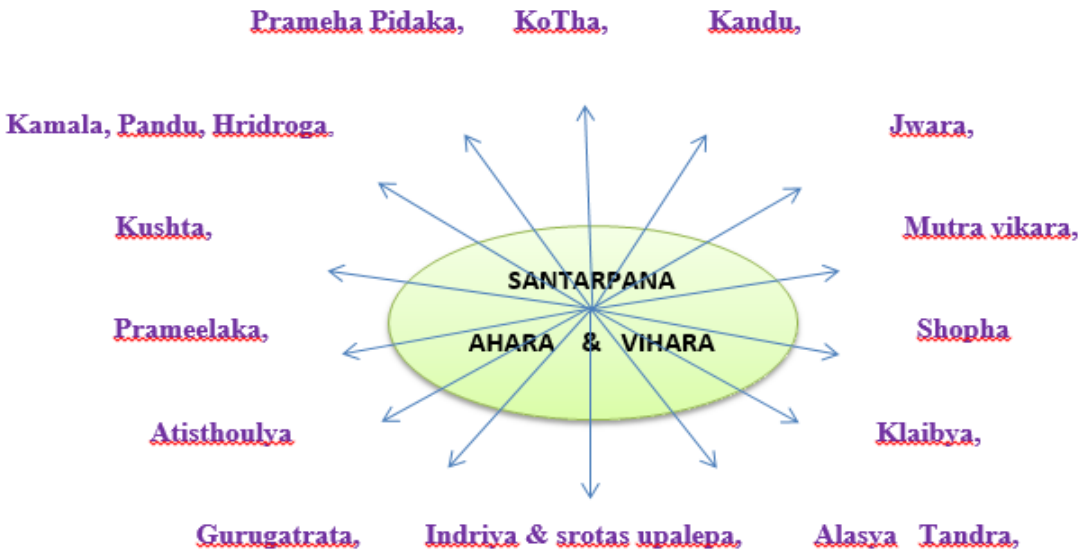
Muscular damage is caused by atherosclerosis as result of relative ischemia and it is found that atherosclerosis is caused due to the free radical reactions involving the lipids in the intima of the arteries and the circulating plasma which is derived of diet that yields peroxides and other relative substances *(Saama Meda)*. Cellular damage

in the endothelium and arteritis are resulted due to release of these substances when associated with retained LDL compounds. Thus retention of LDL and other substances as a result of oxidative stress that manifests into inflammatory process can be termed as ***Kha vaigunya*** caused by the *Hetu sevana* in specific *Srotas.*

Production of C - reactive protein is an important outcome of acute inflammatory process, infection and cellular damage. Though CRP is not a diagnostic criterion independently, it is an important tool in the management, being an important clinical parameter.

CLINICAL IMPLICATIONS DUE TO THE PROCESS OF INFLAMMATION:

As a result of *Santarpana Ahara* and *Vihara* the person tends to become abode of various disorders of metabolism as shown in the figure below. If these disorders are cautiously observed they seem to fall under one major pathological process – ***INFLAMMATION.***



➢ ***Prameha pidaka, Prameelaka-***

Prameha, Prameha pidaka, Prameelaka, Madhumeha are well known diseases caused due to *Santarpana* and altered metabolism of *Medodhatu.* The most accepted and unifying hypothesis to describe the pathophysiology of the metabolic syndrome is insulin resistance that is believed to be caused by defective action of insulin. The insulin resistance is manifested initially as postprandial hyperinsulinemia, followed by fasting hyperinsulinemia and finally leading to established hyperglycemia.

➢ ***Pandvamaya, Kamala, Hridroga-***

Panduroga in broad spectrum if considered, one can notice that the disease is not just pertaining to that of blood: rather it is of entire cardio vascular system. It is mentioned that *Panduroga* is *Rasa pradoshajanya vikara* and a *Santarpanottha vyadhi*. Altered metabolism of *Dhatus* is invariably present in *Pandu roga*. Apart from this the *Sroto upalepa* and *Medo dhatu upachaya* causes *Hridroga lakshanas* initially with *Kapha bahulata* and later on due to *Margavarodha* it leads to *Vataja hridroga* manifestation. The metabolic syndrome is known to increase overall cardiovascular mortality by a factor of 1.5-2.5. It is found that higher levels of triglycerides associated with increased waist circumference leads to higher risk of cardiac abnormalities as mentioned with a ratio of 2.40 in men and of 3.84 in women for CAD. When compared to the other influencing factors, it is excess visceral fat that has been found the strongest to cause hypertension.

The link that establishes pathophysiology between visceral fat deposition and cardiovascular disease is a multifactorial phenomenon[12]. One of those mechanisms could be thought as the accumulation of visceral fat and ectopic fat that happens to be fatty degeneration of cardiac cells. Visceral fat accumulation is found to be the strongest predictor of excess deposition of epicardial and pericardial fat. Accumulation of pericardial fat leads to vascular deposition, vascular calcification, and relative cardiovascular manifestations. Epicardial fat in particular, accounts to have relation with the presence of atrial fibrillation as the most critical factor for causing stroke. Thus visceral fat deposition facilitates epicardial and pericardial fat accumulation, arteriosclerosis and hypertension catering into an increased risk of Cardio Vascular Diseases[13].

➢ ***Atisthoulya, Gurugatrata-***

The four fold key factors of Metabolic Syndrome are - Visceral obesity, insulin resistance, oxidative stress and inflammation[14]. The "platinum standard" described by IDF for additional measurements includes pro-inflammatory state with presence of IL-6 and TNF-alpha, adipocytokines with presence of leptin and adiponectin, HOMA-IR, elevated levels of free fatty acid, markers of endothelial dysfunction and prothrombotic state with PAI-1and fibrinogen, and also raised levels of hormones of pituitary-adrenal axis[15]. Low intensity inflammation in adipose tissue is caused by macrophages and adipocytes of visceral adipose tissue that release inflammatory mediators[16]. Significant positive association with Metabolic Syndrome components is shown by Leptin, PAI-1 and hsCRP[17]. Deposition

of triglycerides in the adipocytes causes macrophageal activation and increased production of proinflammatory cytokines and also disregulation of adipocytokines.

➢ ***Shopha***

The seriousness of the condition is established by the activation of inflammatory pathways that is used normally as host defence. Inflammatory process is initiated by more than a single triggering factor. A vicious cycle may be established involving several stress reactions initiated by overloaded metabolic impairments such as, oxidative and inflammatory stress, organelle overgrowth and cellular hypertrophy. Hypertrophy of the adipocytes through the inflammatory pathway facilitates cell injury which evokes the inflammatory process. Incompetence in the adipose tissue to take up the huge fat load results in deposition of the fat in other organs like liver mainly, which in turn begins the consequential hyperinsulinemia and Insulin Resistance. Excessive ingestion of fatty and energy rich food stuffs without addition of anti-oxidant compensation contributes largely to inflammation. Oxidative stress / Inflammation are also resulted due to the interaction of microbiota with food and obesity, disturbances in the circadian rhythm of biological components[18].

➢ ***KoTha, Mutra vikara, Jwara-***

The triggers of inflammation in adipose tissue are identified as adipocytes hypertrophy, hypoxia of the local tissue and some of microorganisms like Cytomegalovirus, C. Pneumoniae and H. pylori[19]. The Pro inflammatory stimuli get evoked by the mediation of Toll – Like receptors (TLR) which are originally the innate immunity receptors. The process gets activated after binding of free fatty acids or bacterial lipopolysaccharides and the byproducts of lipids degradation and also the nuclear factor -kB translocation into the nucleus thus initiating transcription of Interleukin-6, TNF-alpha, resistin, various chemokines and adipokines[20]. NF-kB regulates activity of more than 125 genes, most of which are identified as proinflammatory[21].

Metabolic Syndrome evokes six specific different risk factors of developing cancer where in Insulin resistance, hyper insulinemia and chronic subclinical inflammation which promote cellular differentiation and thus triggering genesis of tumour directly or indirectly. Stimulation of cell survival with enhanced cellular proliferation and angiogenesis facilitate cancer progression[22].

Hyper insulinemia, which is the most common finding in Metabolic Syndrome, might aggravate and lead to rapid growth of cancers especially colorectal and pancreatic

carcinoma, liver cancer because insulin acts as a growth factor during cell proliferation. Adipocytes secrete adipokines which are actually the proinflammatory cytokines and also growth factors such as insulin-like growth factor 1 or vascular endothelial growth factor together which represent a central mediator of the inflammatory response in obese individuals. P13K signalling that regulate cell survival, cell proliferation, and cell migration is stimulated through these growth factors. Thus, chronic inflammation in adipose tissue promotes hyperplasia, tumour genesis and metastasis formation. Abdominal obesity can also induce significant changes in stem cells of abdominal adipose tissue which may initiate breast cancer formation through estrogen-dependent pathways[23].

➢ ***Vatarakta-***

In recent years, hyperuricemia has also been considered as a part of Metabolic Syndrome[24], since high serum uric acid is clearly correlated with the prevalence of with the same. It is found that, increased levels of serum uric acid is directly proportional to the risk of future type 2 diabetes and are associated with several components of Metabolic Syndrome such as IR, hypertension, and arteriosclerosis[25]. Atherogenic effects are probably mediated by higher activity of pro-oxidant in comparison to antioxidant forms of xanthine oxidoreductase[26]. Increased vascular inflammation may result from this alteration.

➢ ***Indriya upalepa and srotas upalepa-***

Impaired blood clotting[27] has been observed in Metabolic Syndrome, which increases the risk for cardiovascular events. Beside atherothrombotic cardiovascular events, there is also a higher rate of thromboembolism. Both are provoked by reduced activity of vasodilators and an increased expression of vasoconstrictors as consequential manifestation of endothelial damage. This dysfunction appears to result from chronic inflammation, dyslipidemia, and hypertension. Apart from these, there is enhanced coagulating activity by platelets, heralded by increased levels of fibrinogen and plasminogen activator inhibitor. Enhanced coagulation activity could be result of increased production of coagulation factors and proinflammatory cytokines by the liver because of hepatic IR. Several adipokines, such as leptin and adiponectin, are also found to influence the function of platelet leading to hypercoagulation.

➢ ***Atisthoulya-***

The link between hypercortisolism[28] and Metabolic Syndrome was recognized based on similar clinical manifestations. In particular, subclinical hypercortisolism,

which is defined as disturbed hypothalamus-pituitary-adrenal (HPA) axis activity without symptoms of an overt Cushing's syndrome or presence of an adrenal incidentaloma, has been linked to Metabolic Syndrome. On the contrary, it has also been hypothesized that there is an association of hyperactivity of HPA axis with Metabolic Syndrome.

➢ ***Klaibya***

Polycystic ovary syndrome[29] (PCOS) is one of the most common disorders of endocrine in young women in their reproductive age and it is related closely to Metabolic Syndrome. The incidence of visceral obesity in women detected with PCOS varies between 61 and 76%[29]. As in Metabolic Syndrome, the visceral/central obesity in PCOS is associated with elevated levels of triglycerides, LDL and cholesterol as well as lowered levels of HDL and results in an increased risk of arteriosclerosis. Clearly, PCOS is related to an impaired homeostasis of metabolism and as a sequence brings the elevated risk of cardiovascular ailments.

Apart from physiological causes, *Klaibya* is also manifested due to *Manasika* factors many times. Psychological upsets and serious psychiatric conditions influence the libido and fertility of the individual. Depressive disorders are often associated with metabolic disturbances like hypertension, increased cardiovascular risk, chronic inflammation, and altered insulin signalling. The incidence of Metabolic Syndrome is threefold higher in patients with psychiatric disorders compared to the general population which includes depression, bipolar disorders, and schizophrenia[30]. The underlying mechanisms for causing vascular changes, altered hormonal secretions like hypercortisolism and failure of the body to develop coping strategies are being discussed to arrive at conclusion.

CONCLUSION

Metabolic Syndrome is group of disorders that are caused due to excessive nourishment which come under the general heading of *Santarpana janya vikara. Medoroga* is a disorder that is resulted due to *Santarpana* and altered metabolism of *Meda dhatu*. It becomes clear from the diligent study of literature and research outcomes that, all the pathological manifestations resulted due to metabolic error are predisposed with a major setback-Inflammation. Adipose tissue, arteries, pericardial region, mesentery, peri- renal area, nervous system, hormonal secretion… every system is affected by the process of inflammation. Thus it is well understood that for all the disorders and their relative

complications and implications, Inflammation plays an integral and invariable role.

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