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# Role of *Meda* (Adipocyte) in *Yakrit Vikara* (liver diseases) - Ayurveda prospective

Ashok Kumar Panda<sup>1</sup>, Guru Charan Bhuyan<sup>2</sup>, Krishna Rao<sup>3</sup>, Binitha P<sup>4</sup>, Susmita Otta<sup>5</sup>, Kamala Kanta Parhi<sup>6</sup>

<sup>1-5</sup>Research Officer, Central Ayurveda Research Institute of Hepatobiliary Disorders, Bharatpur, Bhubaneswar, CCRAS, M/O AYUSH, GOI. <sup>6</sup>Assistant Professor, Department of Bio chemistry, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, INDIA.

## ABSTRACT

*Meda Dhatu* (Adipose tissue) was considered as inert tissue that stores fat only but now it is an endocrine gland which controls coagulation, appetite regulation, immunity, glucose and lipid metabolism, reproduction, angiogenesis, fibrinolysis, body weight homeostasis and vascular tone control. *Meda* is the fourth *Dhatu* (stable constituent of body) as per Ayurveda doctrine and resemble with the adipose tissue. *Meda* can create not only *Sthyaulya* (Obesity) in general but also organ specific disorders like - *Medaja Granthi*, *Medaja Masurika*, *Medaja Galaganda*, *Medaja Vridhi* etc. *Yakritmeda* is found in Sanskrit literature. But *Medaja Yakritdalludara* or *Yakrit Vikar* is not enumerated in classical Ayurveda literature. Strong evidences suggested that accumulation of lipids in non-adipose tissues can contribute to cellular dysfunction and cell death, a phenomenon that is called lipotoxicity. Various components of *Meda* and its function found in Ayurveda literature are discussed. Multiple factors hit hypothesis for *Samprapti* (pathogenesis) of *Medaja Yakrut Vikara* (Fatty liver disorders) and its progression with preventive and curative strategies are described with scientific evidences.

**Key words:** Adipose Tissue, Durmeda, Fatty Liver, Medadhatu, Yakritdalludara, Yakrimeda.

## INTRODUCTION

Ayurveda is an experience based knowledge system transformed from *Guru* (Faculty) to *Sisya* (Scholar). Some of the primitive knowledge is in written form as available in different *Samhita* and others were clarified by teachers. This knowledge base is in scattered form. Now a day's Ayurveda is also counted under science. Science has two components, first one is the body knowledge and its process by which the

knowledge is produced and the second component is the way of thinking and knowing about the problem. The scientific process is the way of building knowledge and making prediction about the knowledge gap with sufficient justification and in testable form. Scientists use their intellect with the aid of instruments that extend their sense, reviewing various scientific literatures and careful observation of his hypothesis leads to the invention of new theories. Many times scientists deliberately shared their view with other colleagues through publication in peer review journals.<sup>[1]</sup> Ayurveda has its basic frame work and its own understanding of patho-physiology (*Samprapti*) of diseases.

If any new epidemic outbreak or more prevalent disease came for treatment, then a basic understanding of the symptom of said problem should understood in light of Ayurveda.<sup>[2]</sup> Previously adipose tissue was considered as inert tissue in modern medicine that stores fat only but now it is an endocrine gland as understanding of its role in

### Address for correspondence:

Dr. Ashok Kumar Panda

Research Officer, Central Ayurveda Research Institute of Hepatobiliary Disorders, Bharatpur, Bhubaneswar, Odisha, INDIA.  
E-mail: akpanda\_06@yahoo.co.in

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controls coagulation, appetite regulation, immunity, glucose and lipid metabolism, reproduction, angiogenesis, fibrinolysis, body weight homeostasis and vascular tone control.<sup>[3]</sup> Ayurveda considered *Meda* (adipose tissues) as *Dhatu* (major functional and structural unit). Now a day's fatty liver is common even among obese children. It also found that change in structure and function of adipose tissues have significant systemic and hepatic consequences.<sup>[4]</sup> Previous studies has shown that weight loss more than 7% of BMI have better outcome in fatty liver which points towards the fact that adipose tissue has positive relation in predisposing fatty liver.<sup>[5]</sup> It can also be analysed in Ayurveda point of view.

Ayurveda considered *Dosha Dhatu* and *Mala* as basic component of body and their balanced and imbalanced state of are known as health and disease respectively. *Vata*, *Pitta* and *Kapha* are three humors (*Tridosha*) which functional aspect of living things. *Dhatu*s are seven in number which are structural entity of body. *Malas* (Body waste) are waste product of *Ahara* (diet) and *Dhatu* and their proper excretion is very vital for homeostasis.

*Dhatvagni Paka* (component responsible for tissue metabolism) is a process in which convert the *Dhatu* to *Poshakadhatu* (immobile and storage part) and *Poshya Dhatu* (mobile part). This *Poshya Dhatu* which is the moveable part circulate in its own *Srotas* for the nutrition of successive *Dhatu* whereas *Poshaka* part act as storage and in emergence condition can be utilized as *Poshya Dhatu*. Again *Bhutagni Paka* carried out inside the cell for various nutrients utilised for cellular function. They maintained homeostasis in the principle of *Svabhava Satmya* (immunity), *Samanya* and *Vishesha* (theory of homologous and analogous).<sup>[6]</sup> The Bio energy (*Bala*) is important aspect in Ayurveda for the pathogenesis of any diseases. It provides strength to all *Dhatu*, protect them and *Kostanga* (organ) from *Krimi* (Infection) and *Aghata* (injury) and provide stability of different organ. It works as immune surveillance and maintain homeostasis. *Dhatu Paka* is a condition of

suppuration or destruction of *Dhatu* due to excess *Agni* (heat) or *Srotarodha* (Block of passage) or *Kshaya* (malnutrition). The cardinal sign of *Dhatupaka* are *Nidranasha* (sleeplessness), *Hrudistambha* (heaviness / discomfort of chest), *Vistabha* (constipation), *Gaurabha* (heaviness of body), *Aruchi* (Anorexia), *Arati* (Anxiety or dullness) and *Balahani* (Loss of strength/immunity).<sup>[7]</sup> *Dhatu Rupantara* (Change of architecture of tissues) is a stage where one *Dhatu* is changed to another *Dhatu*, *Upadhatu* or *Mala*, example - *Mamsa Dhatu* changed to *Meda Dhatu* or *Mamsa Dhatu* changed to *Kandara*.

### Meda Dhatu and its components

*Meda* is the fourth *Dhatu* as per Ayurveda doctrine and resemble with the adipose tissue. If the *Meda Dhatvagni* (Digestive power/ adipokines) deregulated than there is a disharmony of distribution of *Baddha Meda* (store in particular site) and *Abaddha Meda* (circulating fat). This *Baddha Meda* can be termed as Visceral fat and *Abaddha Meda* can be understood as circulating lipids. *Durmeda* is another term found in Ayurvedic literature which is nothing but *Ama* of *Meda*. *Durmeda* can be understood as free fatty acid. Excess *Abadhha Meda / Durmeda* are responsible for accumulation in any *Dhatu*, *Srotas*, *Kostanga*, *Sira*, *Granthi* etc. and form *Gara Visha* (lipotoxicity) and disease process initiated. *Meda Dhatu* is nourished from *Sneha* (fatty food) as per *Madhava Nidana*.<sup>[8]</sup> Its distribution in *Mamsa Dhatu* as *Vasa* (subcutaneous fat) *Updhatu* and in small bones as *Sarakta Meda* (red bone marrow). The different components of *Meda* and their function are described and found all are directly or indirectly responsible for *Yakrit Roga* (Table 1). Form this phenomena it can be concluded that *Meda* can create not only as *Sthyaulya* (Obesity) but also organ specific disorders like - *Medaja Granthi*, *Medaja Masurika*, *Medaja Galaganda*, *Medaja Vridhi* etc. But *Medaja Yakritdalludara* or *Yakrit Vikara* is not enumerated in classical Ayurvedic literature. Strong evidence suggested that accumulation of lipids in non-adipose tissues can contribute to cellular dysfunction and cell death, a phenomenon that is called lipotoxicity.<sup>[9]</sup>

Like that due to hypo function of *Jatharagni* and *Medodhatwagni* leads to more production of *Abaddha Meda* and *Durmeda* leading to accumulation in all *Srotas* including *Raktavaha*, *Mamsavaha* and *Medovaha Srotas*. *Sneha Guna* in liver will increase due to accumulation of *Meda* as *Pitta* and *Meda* have *Sneha Guna*. Therefore there is deregulation of *Pitta* production as triggered by *Sneha Guna*. Another events is that more *Kleda* production is initiated due to reduced *Ushna* and more influx of *Rasadhatu*.

*Pitta* is not excreted out properly due to *Srotorodha* (obstruction of channels). This primary situation leads to accumulation of *Durmeda* in *Yakrit* known as *Medaja Yakrit Dalludara* (fatty liver). The further development of the disease involves a variety of mechanisms, including *Sneha Ahara*, hypo function of *Jatharagni*, *Dhatvagni*, *Bhutagni*, *Durmeda Visha* (endotoxins and lipotoxicity), *Sthaulya* (obesity) and *Kapha Prakruiti* (genetic predispositions) for *Dhatu Paka* (necrosis of hepatocyte) and *Dhatu Rupantara* (Fibrosis).

As *Yakrit* is chief organ of *Raktavaha Srotas* and intake of the *Vidahi*, *Snigdha* and *Ushna Annapaana* along with exposure to excessive sunlight and air lead to *Raktavaha Srotodushti*. Again it exposed to various threats of *Krimi* (infection) as it is a *Raktakshaya* and various nutrients of *Ahara Rasa* as literature supports that *Ahara Rasa* is first received by *Jyotisthana* (Liver) which further nourishes the whole body.

Therefore *Bala* (Immunity) played a key role in the pathogenesis of *Yakrit Vikara*. The *Bala* of different components of *Meda*, its *Bhautic* compositions and its strength are stated (Table 2). As *Meda* and *Prakruta Kapha* are same and similar properties, so they have definite role in formation of *Bala*.<sup>[11],[12]</sup>

It is also found that tissue resident macrophages are serving as immune sentinels and they interact with parenchyma cells to boost immunologic well being.<sup>[13]</sup> Adipokine released from fat cells have a definite role on regulatory T cell population, hypertrophy and hyperplasia of adipose tissue.<sup>[14-16]</sup>

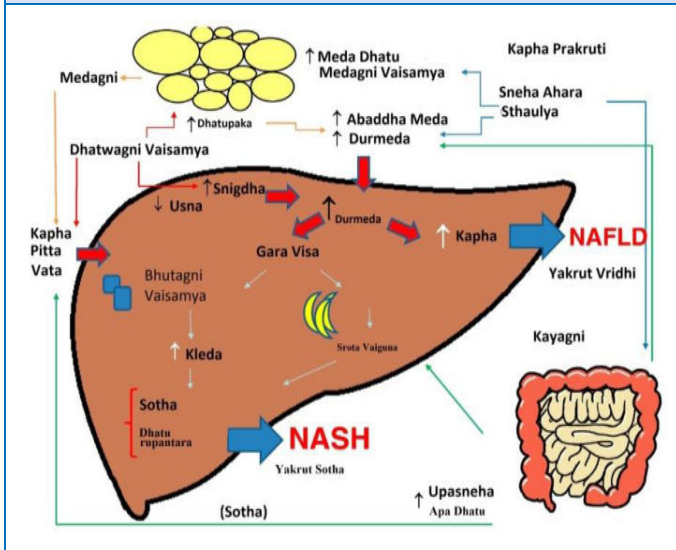
**Table 1: Various component of Meda found in Ayurveda literature and its function.**

Component	Probable Modern interpretation	Function
<i>Baddha Meda</i>	Stored fat / White Adipose tissue	<i>Dhardya</i> (Energy Hoemeostasis), formation of sweat
<i>Abaddha Meda</i>	Circulating lipids (TG)	<i>Srotosanga</i> (Atherogenic)
<i>Durmeda</i>	Free Fatty Acid (FFA)	<i>Ama Visha</i> (lipotoxin)
<i>Sarakta Meda</i>	Myeloid tissue	<i>Asthimpurana</i> and formation of <i>Shukra</i>
<i>Vasa</i>	Subcutaneous fat	Unctuousness
<i>Yakrimeda</i>	Hepatic TG	Store in liver

**Table 2: Major contributors of Bala (Immunity) in Yakrit and its Bhautik composition and level of Bala.**

Component	Bhautik composition	Bala ( Immunity) Level
<i>Meda</i>	<i>Prithivi(+++)</i> , <i>Jala(+)</i> , <i>Agni(+)</i>	Immunity(++)
<i>Kapha</i>	<i>Prithivi(++)</i> , <i>Jala(+)</i> , <i>Agni(+)</i>	Immunity(+++)
<i>Kleda</i>	<i>Prithivi(++)</i> , <i>Jala(++)</i> ,	No Immunity
<i>Rasa</i>	<i>Prithivi(+)</i> , <i>Jala(++)</i>	Immunity(+)
<i>Pitta</i>	<i>Prithivi(+)</i> , <i>Jala(+)</i> , <i>Agni(++)</i>	Immunity(+)
<i>Rakta</i>	<i>Prithivi(+)</i> , <i>Jala(++)</i> , <i>Agni(++)</i>	Immunity(++)
<i>Ojus</i>	<i>Prithivi(+)</i> , <i>Jala(++)</i> , <i>Agni(++)</i>	Immunity(++++)

**Figure 1: Multiple factors hit hypothesis for Samprapti (Pathogenesis) of Medaja Yakrut Roga and its progression.**



### Hypothesis of Medaja Yakrit Sotha and its progression

*Yakrit Dalludara* is the commonest complication of *Udara Roga* (abdominal diseases) where *Yakrit* (Liver) is clearly palpable due to its increase in size. Deposition of *Meda / Yakritmeda* is said to be one of cause of *Yakrit Dalludara*. Nonalcoholic fatty liver disease (NAFLD) encompasses a spectrum of diseases that from simple steatosis (pure NAFLD) can progress to nonalcoholic steatohepatitis (NASH), cirrhosis and hepato-cellular carcinoma. NAFLD progression seems to involve the occurrence of "parallel, multiple-hit" injuries, such as oxidative stress induced mitochondrial dysfunction, endoplasmic reticulum stress, endotoxin-induced, TLR4-dependent release of inflammatory cytokines, and iron overload, among many others. These deleterious factors are responsible for the triggering of a number of signaling cascades leading to inflammation, cell death, and fibrosis, the hallmarks of NASH.<sup>[12]</sup> Hamza El Hadi *et al.* published a multiple parallel hit hypothesis of NAFLD and its progression in figure which is well representation of the pathophysiology of modern medicine. In the same way the samprapti (pathophysiology) hypothesis of *Medaja Yakrit Roga* can be enumerate and explainable.<sup>[17-19]</sup>

Generally *Kaphaja Prakriti* (A type of genetic and epigenetic factor) person are more inclined towards excess intake of fat diet and progressively developed *Sthaula* (obesity). *Sthaula* (obesity) together with *Sneha Ahara* (Fatty dietary habit) and less physical exercise leads to increase *Abaddha Meda* (blood lipid) and vitiate the *Kayagni* first instant then *Medagni Vaisamyam* (alteration of fat metabolism). Dysfunction of *Kayagni* produce more *Durmeda* (FFA) and decrease the power of *Medagni*. It affects the *Dhatwagni* and all three *Doshas* are aggravated and get localized in liver. so *Yakrit Vikara* are *Tridosaja*. There is an increase of *Snigdha Guna* and decrease of *Ushna Guna* triggered to produce more *Kapha* inside Liver. The deposition of *Kapha* and *Durmeda* leads to *Yakruit Vridhi* in first instance where all symptom of *Kapha* are seen and our *Acharya* described as *Kaphaja Udara* so called steatosis (pure NAFLD). Further accumulation of *Durmeda* leads to produce *Kleda*. That *Kleda* along with *Yakrimeda*<sup>[20]</sup> (hepatic FFA) produce *Sopha* (hepatic inflammation) in *Yakrit* and *Dhatu Rupantara* (Parenchymal change to hepatic stellate cells) takes place after *Dhatu Paka*. This condition is relatable to NASH (nonalcoholic steatohepatitis) (Figure 1). *Yakrimeda* (Hepatic FFA) directly block the *Srotas* and *Srotamula* of *Yakrit*, therefore portal hypertension and cholagitis takes place. As a result there is a blockage of intra and extra hepatic duct leads to accumulation of bile and Jaundice. If more *Pitta* accumulated then *Ushna* (Heat) and *Drava* (Liquid) properties of *Pitta* triggered further for *Dhatu Rupantara* (Fibrosis) then *Yakrit Kshaya* (Cirrhosis) takes place in one way and *Yakrutdalludara* (Hepato cellular carcinoma) in other ways or both. Ayurveda literature says all *Udara Roga* (Hepato biliary disorders) converted to *Jalaodara*. If all *Srotas* are involved then various complication like - Portal hypertension, Variceal bleeding, Hepatic encephalopathy, hepato renal syndrome, Ascites etc. takes place.

### Preventive and Curative Strategies

*Sushruta* stated that avoid the etiological factor (*Nidana Parivarjana*) is one of the strategies of prevention and cure for all diseases. As *Sneha* (Fatty

diet) responsible for fatty infiltration of liver, therefore low fat diet as recommended by doctor can prevent further progress and correction *Medaja Yakrit Vikara*. As *Vyayama* (Exercise) increase *Agni* and reduce fat, therefore Physical exercise as recommended by Ayurveda physician should practice in house.<sup>[21],[22]</sup> As *Agni* is one of the causes for *Meda* deposition. *Meda* and *Kaphahara Dravya* is one of the treatment strategies for *Medaja Yakrit Vikara*. *Srotashodhaka* and *Pramathi Drava* can be employed for treatment. So multi modalities treatment as per the *Samprapti Ghataka* (pathogenic factors) can be designed. Fourteen herbs and two metal *Bhasma* are screened from various formulations indicated for *Yakrit Vikara* (Table 3).

**Table 3: Various compound used in Medaja Yakrit Dalludara.**

SN	Name of Dravya	Latin Name	Mode of action	Indication
1.	Ajomada	<i>Trychyspermum roxburghianum</i> (DC)	Deepana, Vidahi	Udara, Gulma, Krimi
2.	Arjuna	<i>Terminalia arjuna</i> (Roxb.)	Kapha Pittahara	Hrudroga, Pandu
3.	Asana	<i>Pterocarpus marsupium</i> Roxb.	Kapha Pittahara,	Kusta, Prameha
4.	Dauharidra	<i>Berberis aristata</i> DC.	Kapha Pittahara,	Vrana, Meha
5.	Maricha	<i>Piper nigrum</i> Linn.	Kapha Medahara	Gulma, Udara
6.	Katuki	<i>Picrorhiza Kurroa</i> Royle	Bhedaniya, Hrudya	Prameha, Dah, Kusta
7.	Hingu	<i>Ferula foetida</i> Regel	Deepana, Pachana	Udara, Krimi
8.	Varuna	<i>Crataeva nurvala</i> Buch-Ham	Deepna, Kapha	Gulma, Asmari
9.	Pipali	<i>Piper longum</i>	Deepana,	Jvara, Kasa,

			Medahara	Swasa
10	Sunthi	<i>Zinziber officinale</i> Rose	Deepana, Kapha	Udara, Kasa
11	Haritaki	<i>Terminalia chebula</i>	Deepana, Rasayana	Rasayana
12	Vidanga	<i>Embelia ribes</i>	Deepana, Krimigna	Udara, Krimi
13	Jeeraka	<i>Carum Carvi</i>	Deepana, Samgrahi	Gulma, Grahani
14	Haridra	<i>Curcuma longa</i>	Leekhaneeya	Visha, Prameha
15	Ela	<i>Elettaria cardamomum</i>	Lekahaneeya	Kasa, Arsha
16	Lauha	Iron Bhasma	Leekhaniya	Pandu, Kamala
17	Tamra	Tamra Bhasma	Leekhaniya	Yakrit, Kamala

## DISCUSSION

Ayurveda considered *Meda* as *Dhatu*, its increase or decrease of quantity and quality may create diseases. *Yakrit Meda*<sup>[24]</sup> word is found in Sanskrit glossary which implies fat in liver or fatty liver. But role of *Meda* in *Yakrit Roga* is not enumerated in Ayurveda classical literatures. As the understanding of pathophysiology of fatty liver increased then it was thought to create the samprapti of *Meda* in *Yakrit Vikara* (diseases of liver). The deposition of *Kapha* and *Durmeda* leads to *Yakruit Vridhi* in first instance where all symptoms of *Kapha* are seen. *Kapha* and *Meda* has similar *Bhautic* composition and properties. Therefore *Kaphaja Udara* is quite similar with fatty liver symptom and many contemporary Ayurveda practitioner treating fatty liver (steatosis and NASH) as *Kaphaja Udara*. It is stated that majority of hepatic lipids in NAFLD are stored in the form of triglycerides. In patients with NAFLD hepatic lipid loading appears to be mainly determined by the availability of FFA from circulation. Hepatic TG is good fat whereas Hepatic FFA is bad fat and there is an alteration of lipid metabolism. Obesity together with dietary

habits and environment factor can lead to raised free fatty acid (FFA) and cholesterol, developed insulin resistance, adipocyte proliferation and worsening adipocyte dysfunction and release of pro-inflammatory adipokines. This is similar to our *Kayagni* and *Meda Dhatvagni Vaisamya*. Similar attempt was made by other scholars also.<sup>[23]</sup> Ayurveda enumerated altered function of *Kayagni* produce *Durmeda* where altered activity of gut microbiome leads to accumulation of triglyceride and toxic level of FFA, free cholesterol and other lipid metabolites causes mitochondrial dysfunction leading oxidative stress and activation of the unfolded protein response (UPR) leading to hepatic inflammation and fibrogenesis which very similar with *Dhatu Paka* and *Dhatu Rupantara*. The listed medicinal plants have *Meda & Kaphahara, Deepana, Pachana, Lekhaniya, Rakta Shodhaka, Srotoshodhaka* and *Pramathi* pharmacological qualities are acting on *Medaja Yarit Vikara* in experimental model and few case and clinical studies.<sup>[24-27]</sup>

## CONCLUSION

*Meda* has a key role for the genesis of *Yakrit Vikara* and its progression from *Yakrit Meda* to *Yakritdalludara*. The medicinal plants having *Meda Kaphahara* pharmacological qualities will act on *Medaja Yarit Vikara*. Further clinical study on *Meda Kaphahara Dravya* in *Yakrit Vikara* is recommended.

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