AN AGADATANTRA PERSPECTIVE OF NON-ALCOHOLIC FATTY LIVER DISEASE- A CRITICAL REVIEW

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ABSTRACT

Visha(poison) is something which is toxic to bodies. The exposure to a toxic environment is unavoidable in the present era. Based on the origin of toxicity and its effect on the body, *visha* is divided into various types. *Dooshivishas*(cumulative toxins) are those toxic compounds which are not able to produce the acute symptoms and which partially undergoes biotransformation and accumulated in the body for long term producing various symptoms. The Liver, a primary site of metabolism, is the major organ affected by fat metabolism. The improper metabolism leads to fatty infiltration of the liver which later affects the normal functions leading to a metabolic rearrangement in the body. NAFLD(Non-alcoholic fatty liver disease) represents a spectrum of illness with stages of hepatic steatosis, steatohepatitis, fibrosis and cirrhosis. In NAFLD, due to chronic use of *virudhaaharavihara*(in-compatible food and regimens), *dooshivisha* vitiates *dhatus(rasa raktamamsa and medas)*(tissues of the body such as plasma, blood, muscle, fat)and due to *kaphadoshaavarana*, defective digestion *(agnimandya)* and defective metabolism *(dhatwagnimandhya)* occur. *Agnimandhya* reflects as *bhootagnimandhya* and *dhatvagnimandya*. When *dhatvagnimandya* occurs the mostly affected *agni* is *medodhatvagni* (defective metabolism of fat) as the *nidanas* (causes) are favourable for its *dushti* (vitiation) and due to *kaphaavarana* of *dooshivisha*. *Medodhatvagnimandhya* (defective metabolism of fat) leads to the formation of *samamedas* (fat globules). The *samamedas* (fat globules) reaches the *yakrut* (liver), *sthanasamsraya* occurs at *yakrut* (liver) and impairs the functions of *yakrut* (liver). The pathology of NAFLD coincides with that of *dooshivisha.*

KEYWORDS – *Visha, Dooshivisha,* NAFLD.

INTRODUCTION

The concepts of Ayurveda about etiological and Pathological basis of diseases are different from the current concept in modern medicine. Hence while considering the diseases, Ayurveda gives more emphasis to the physiological homeostasis of the body.

The term *visha*(poison) means that which produces '*vishada*'(sadness) [1]**.** A human being's cannot avoid contact with toxic compounds; however, it takes more than contact alone to produce adverse effects

in an organism. The human body cannot get rid of them completely by their excretory capacity. As a result, these toxins accumulate in our body and create serious health problems and also the aetiology of many diseases is not known, here comes the concept of *Dooshivisha* (cumulative toxins).

The term *Dooshivisha* originated from the root word *"dosha"* means that which cause dusk of *dhatus(*tissues of the body), ie, which brings about Pathological imbalance, *visha* means any substances that enter the body and vitiates normal functioning of *rasadi dhatus* (bodily Humor) [2]. In short, it is an attenuated or denatured poison which functions as a latent toxin in the body. According to the classics causative factors for *Dooshivisha* are in-animate, animal and artificial poisons that are not eliminated from the body [3]. From the traditional *VishaVaidyaGrantha*, we get references that incompatible food, indigestion, suppressing natural urges and mental factors act as causative factors for *Dooshivisha* [4]

Different opinions about *DooshiVisha*

Susrutha:

Visha that vitiates *rasadidhatus* '*vishamhidooshivishaytamupaiti', visha* itself with lower potency that becomes or gets the term *dooshivisha*. Any poison whether animal, vegetable or chemical in origin not eliminated from the body, the left out portions of *visha* partially nullified by anti poisonous drugs, the natural provoking factors like fire, wind, sun etc will cause the substance to establish their symptoms[3]

"Dooshitham desa kalanna diwaswapnaurabheeshanasa

Yasmath dooshyate Dhatun thasmath dooshivisham smritam"[5]

Dalhana :

Any poison that is devoid of natural properties of *visha*, incapable of producing acute symptoms of poisoning.

Even though it is having low potency, it should not be neglected, because it continues to exist in the body for many years getting enveloped by *Kapha*(one among bodily Humor). The retarded potency of all the ten qualities of *visha* is said to be responsible for delayed action and cumulative toxicity on the body. [6]

Charaka :

It vitiates *raktadhatu* (blood) and causes skin lesions such as *kitibha*(psoriasis), *Koda*(hives). [7]

Chakrapani :

That *visha* which express its toxic effect in the body after long intervals, i.e., it may be inactive for long periods and its chronic nature can extend for years. [8]. He defines *dooshivisha* as

"kalantharaprakopivishamDooshivisham" (that gets vitiated after a long time) [8]. Because of the enveloping (*avarana*) action by *kapha*, this low potency poison is retained in the body for a long period without producing any grave or fatal symptoms.

Vagbhata:

Jeernam (partially metabolized), *Vishagnaoushadhibhihatam* (incompletely inactivated by antitoxic drugs), *Davagni Vataatapa shoshitam* (becomes low potency by the effect of water, fire, air, sun etc), *Swabhavato swagunair na yuktam*(naturally losing its actual property) is *dooshi visham*.[9]

Yogaratnakara classified *kritrimavisha* (artificial poison) as

Savisha – Dooshivisha (by mixing toxic components)

Avisha- Garavisha (by mixing non-toxic components)[10]

KasyapaSamhitha: Two types of *samyogajavisha (*a combination of toxic components)

Savisha – Dooshivisha

Avisha – Gara visha [11]

NON-ALCOHOLIC FATTY LIVER DISEASE- NAFLD

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of liver disease encompassing simple fatty infiltration (steatosis), fat and inflammation (nonalcoholic steatohepatitis, NASH) and cirrhosis, in the absence of excessive alcohol consumption (typically a threshold of < 20 g/day for women and < 30 g/day for men is adopted). While simple steatosis has not been associated with liver-related morbidity, NASH is linked with progressive liver fibrosis, cirrhosis and liver cancer, as well as increased cardiovascular risk. Non-alcoholic fatty liver disease (NAFLD) is rapidly becoming the most common liver disease worldwide. About 2-3% of the general population is estimated to have non-alcoholic steatohepatitis (NASH), which may progress to liver cirrhosis and hepatocarcinoma. As a rule, the prevalence of NAFLD is higher in males and increases with increasing age, and it is influenced by the diagnostic method and the characteristics of the population, especially lifestyle habits. [12]

The primary risk factors of NAFLD are obesity, type II diabetes, and the metabolic syndrome including dyslipidemia and hypertension. However, diseases other than the metabolic syndrome can be associated with hepatic fat, and these might enter into the differential diagnosis of fatty liver disease of the usual type. [13] The pathogenesis of NASH was based on a '2-hit hypothesis'. The 'first hit', hepatic triglyceride accumulation, or steatosis, increases the susceptibility of the liver to injury mediated by 'second hits', such as inflammatory cytokines/adipokines, mitochondrial dysfunction and oxidative stress, which in turn lead to steatohepatitis and/or fibrosis. Free fatty acids (FFA) play an important role in directly promoting liver injury, which has led to the

modification of this theory. In obesity and insulin resistance (IR) there is an increased influx of FFA to the liver. This FFA either undergo β-oxidation or are esterified with glycerol to form triglycerides and cause hepatic fat accumulation. There is now substantial evidence that FFA can directly cause toxicity by increasing oxidative stress and by activation of inflammatory pathways, therefore hepatic triglyceride accumulation may be a protective mechanism by preventing the toxic effects of unesterified FFA. Additionally, a 'third-hit' has been added to reflect inadequate hepatocyte proliferation. In the healthy liver, cell death stimulates replication of mature hepatocytes which replace the dead cells and reconstitute normal tissue function. However oxidative stress, a central feature of NAFLD pathogenesis, inhibits the replication of mature hepatocytes which results in expansion of the hepatic progenitor cell (oval cell) population. These cells can differentiate into hepatocyte-like cells, and both oval cell and intermediate hepatocyte-like cell numbers are strongly correlated with fibrosis stage, suggesting that cumulative hepatocyte loss promotes both accumulation of progenitor cells and their differentiation towards hepatocytes. Activation of these cells has also been implicated in hepatocellular carcinogenesis. In chronic liver injury, the development of fibrosis/cirrhosis is dependent on the efficacy of hepatocyte regeneration, and therefore cell death with an impaired proliferation of hepatocyte progenitors represents the proposed 'third hit' in NAFLD pathogenesis. [14] Most subjects with NAFLD are asymptomatic. In such cases, the diagnosis is often made when the person is discovered to have either abnormal liver enzymes or features of a fatty liver on an imaging study performed for unrelated reasons. When symptoms occur, the most common ones to bring NAFLD patients to clinical attention include Malaise, Fatigue, Right upper quadrant discomfort, Sleepiness during the day, Disturbed sleep patterns, Lethargy etc. [15]

In Ayurveda view, etiological factors of NAFLD like recently emerging liver disorders can be concluded as due to incompatible food and regimens. Most of the modern food items contain colouring materials, preservatives etc which act as cumulative toxins (*dooshivisha*) in our body. According to "Two hit hypothesis" the production of reactive O2 species and endotoxins results in non-alcoholic steatohepatitis from NAFLD. Since the liver is the organ of detoxification, etiopathogenesis can be well explained based on *dooshivisha*.

In NAFLD due to the continuous use of *virudhaharavihara* (in-compatible food and regimens), *dooshivisha* vitiates *dhatus ie, rasa rakta mamsa and medas* (tissues of the body such as plasma, blood, muscle, fat) and impairs the normal metabolism of the body."*Kaphavrutam"* (enveloping by *kapha*) as *Kaphenamandeekrtaushnadigunam*, which means *ushna , sukshma, rooksha* etc properties of *visha* are retarded by *Kapha*. *Varshaganubandhi* means " *Kaphena anger mandyaditwat apakat chirasthayi".* ie, due to *kaphadoshaavarana*, (enveloping by *kapha*) defective digestion (agnimandya) and defective metabolism (dhatwagnimandya) occur, which in turn leads to *apakata* (indigestive nature) of *Dooshivisha*.[16]Due to above said factors defective digestion (*agnimandya*) and defective metabolism (*dhatwagnimandya* especially in *medhodhatwagni*) occur, as the nidanas (causes) are favourable for this. In addition to this "***dehadasheshamyatanirgatam tat jeernam***" is *Dooshivisha*. Which means that the poisons which are not eliminated from the body and which do not produce any acute symptom, but in the long term due to continuous

exposure (accumulation) when they reach at a specific toxic dose at a specific site they tent to produce their toxic signs and symptom. [17]. In NAFLD the accumulation is specifically, *yakrut* (liver)

Thus pathophysiology of NAFLD is

Dooshivisha

⇩

Rasadushti bcoz of jataragnimandyam (defective digestion*)*

⇩

Formation of *samarasa*

⇩

Reaches *yakrut*(liver) and cause *Yakrutdushti*

⇩

Ranchakapitha and *bhootagni vitiation*

⇩

Impairs *dhatuparinama* and *dhatwagnimanda (medhodhatwagni*)

⇩

Faulty formation of *sthoolabhaga* and *kitta*

⇩

Formation of *samamedas*

⇩

Samamedas reaches the *yakrit*,*sthansamsraya* occurs and impairs its function

DISCUSSION

The Liver, a primary site of metabolism, is the major organ affected by fat metabolism. The improper metabolism leads to fatty infiltration of the liver which later affects the normal functions leading to a metabolic derangement in the body. NAFLD represents a spectrum of illness with stages of hepatic steatosis, steatohepatitis, fibrosis and cirrhosis. NAFLD is strongly associated with obesity, Dyslipidemia, Type 2 (Non-insulin dependent) diabetes mellitus and so may be considered to be the hepatic manifestation of the metabolic syndrome. [18]

Nowadays we are leading a sedentary life with improper food habits, unwanted use of long term medications, suppressing natural urges etc and these will lead to a condition termed as *dooshivisha*, by partial biotransformation of accumulated toxins.

Fatty liver may be considered as a type of cytotoxicity. The accumulation of fat is a common cellular response to toxic compounds which are normally reversible. Usually, it is triglycerides which accumulate, Steatosis is particularly common in the liver as this organ has a major role in lipid metabolism. The lipid may appear in the cell as many small droplets or as one large droplet, [19]

In NAFLD, due to chronic use of *virudhaaharavihara*, *dooshivisha* vitiates *dhatus(rasa raktamamsa and medas)* and due to *kaphadoshaavarana*, defective digestion *(agnimandya)* and defective metabolism *(dhatwagnimandhya)* occur. *Agnimandhya* reflects as *bhootagnimandhya* and *dhatvagnimandya.* When *dhatvagnimandya* occurs the mostly affected *agni* is *medodhatvagni* as the *nidanas* are favourable for its *dushti* and due to *kaphaavarana* of *dooshivisha. Medodhatvagnimandhya* leads to the formation of *samamedas* (fat globules). The *samamedas* reaches the *yakrut*(liver), *sthanasamsrāya* occurs at *yakrut* and impairs the functions of *yakrut* which can be compared with the cytotoxicity produced by the accumulation of fat due to the common cellular response to toxic compounds. While discussing the *Vyapthi* of *dooshivisha* by *charaka*. It is clear that when *dooshivisha* affects *medodhatu, tantra, alasya, nidra* etc are the symptoms which can also be correlated with the symptoms of NAFLD

CONCLUSION

Nowadays human being's are leading a sedentary life with improper food habits, unwanted use of long term medications, suppressing natural urges etc. All these will lead to the condition termed as *Dooshivisha*, by partial biotransformation of accumulated toxins. By the influence of certain provoking factors, this *Dooshivisha* will lead the path to various disorders including *yakrutvikaras*(liver disorders). NAFLD cannot be exactly correlated to a single disease mentioned in Ayurveda but covers the spectrum of diseases in which dooshivisha with medodushti, impaired metabolism and in the later stage *kamala,udara* etc are present. The risk factors for the aetiology of NAFLD includes *virudhaahara* and *vihara* which results in the formation of *dooshivisha* and exerts its influence in *rasa, raktha, mamsa* and *medodhatus.* Moreover, Concept of *Dooshivisha* should be incorporated into the treatment of other chronic and challenged diseases, where the conventional system of medicine fails to achieve the required result

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