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A LITERARY REVIEW OF NON-ALCOHOLIC FATTY LIVER DISEASE W.S.R. SAN-TARPANAJANYA VYADHI

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ABSTRACT

Non-Alcoholic Fatty Liver Disease (NAFLD) is a metabolic disorder of the liver characterised by abnormal fat accumulation in liver parenchyma without inflammation in the absence of alcohol consumption. Stages of NAFLD can be classified as Simple Fatty Liver to Non-Alcoholic Steato Hepatitis (NASH). Simple Fatty Liver has a benign prognosis. NASH is associated with Fibrosis and progression to Cirrhosis. So, managing the initial stage can prevent many health hazards in the future. As NAFLD is categorised as a *Santarpanajanya Vyadhi*, therapeutic measures involving *Apatarpana Chikitsa* should be adopted. Detailed information regarding *Santarpanajanya Vyadhi* and its *Chikitsa* is available in different *Samhitas*. ie, *Nidana Parivarjana, Deepana –Pachana, Samshodhana* and *Samsamana*. It is *Kaphapradhana Tridosha Kopa Vikara*. Hence, the selected medicine should possess qualities like *Deepana-Pachana, Srothoshodhana*, *Medhohara, Kaphahara* and *Vatanulomana*. Introducing effective Ayurvedic management after evaluating diseases from an Ayurvedic perspective will benefit society.

Keywords: Non-Alcoholic Fatty Liver Disease, Santarpanajanya Vyadhi

INTRODUCTION

Non-Alcoholic Fatty Liver Disease is a condition defined by excessive fat (>5-10 % of liver weight) accumulation in the form of triglycerides (steatosis) in the liver in the absence of any secondary cause like alcohol or drug use.¹

NAFLD is estimated to have a global prevalence of 24%. A large European study found NAFLD to be present in 94% of obese patients, 67% of overweight patients and 25% of normal-weight patients. The overall prevalence of NAFLD in patients with type 2 Diabetes ranges from 40% to 70%. The frequency of steatosis varies with ethnicity (45% in patients of Hispanic origin, 33% in those of European ancestry and 24% in those of African ancestry) and gender (in those of European descent, 42% male's vs 24% $females)^2$. In India, the overall prevalence of NAFLD in the general population is close to $40\%^3$. Women have a lower risk of NAFLD than men. However, once NAFLD is established, women have a higher risk of advanced fibrosis than men, especially after 50 years.⁴

The main reasons for NAFLD in India are the metabolic risk factors related to a sedentary lifestyle and high-calorie food intake. Obesity, Diabetes Mellitus, Hypertension and Dyslipidemia are the main risk factors for NAFLD, even though some patients may be predisposed genetically. In addition to affecting the liver, NAFLD has become a prevalent risk factor for various extra-hepatic diseases like cardiovascular disease, chronic kidney disease, Bone loss, Obstructive Sleep Apnea and Cancers of various organs. ³

In a study conducted in the United States, it was found that the incidence of NAFLD was 10% higher among overweight individuals compared to lean individuals. Projections suggest that within the next 20 years, NAFLD will become the primary cause of liver-related morbidity and mortality and a leading indication for liver transplantation. Currently, NAFLD ranks as the second most common reason for listing for liver transplantation.⁵

The rationale of the study

Non-Alcoholic Fatty Liver Disease is gaining acceptance as the term for chronic liver disease with histological features similar to those of alcoholrelated liver disease but without significant alcohol intake⁶. Nowadays, the number of Non-Alcoholic Fatty Liver Disease cases is more due to sedentary lifestyles and food habits. The prevalence is higher in those with diabetes and those with metabolic syndrome. In 10- 30% of cases, fatty liver can lead to liver damage. A landmark study conducted in 2018 suggested that the burden of end-stage liver disease due to NAFLD will be doubled in number by the year 2030⁷.

NAFLD is also increasing in incidence in the Kerala population. No established pharmacological treatment is available for NAFLD in modern medicine⁸.

Ayurveda has immense potential for safe and costeffective management of non-communicable diseases, including NAFLD. If this intervention is effective, it will benefit people with sedentary lifestyles. **Aim**

To study and evaluate the *Nidana Panchaka* of NAFLD from an Ayurvedic perspective

Materials and Methods

Classical Ayurvedic texts such as *Charaka Samhita*, *Susrutha Samhita*, *Ashtanga Hridaya*, etc., were analysed to better understand the *Nidana Panchakas* and the *Chikitsa* of the disease.

Non-Alcoholic Fatty Liver Disease in Ayurvedic View

Ayurvedic classics do not directly reference liver disease caused by impaired lipid metabolism due to a sedentary lifestyle and improper dietary habits. Therefore, when understanding such diseases through Ayurveda, we must consider the *Nidana*, *Dosha* and *Dooshya* involved in disease progression. Consequently, NAFLD can be classified under the *Santarpanajanya Vyadhi* described by *Acharya Caraka* in the *Sutrastana* of *Caraka Samhitha*.

The term "*Santarpana*" is derived from the root word "*Trip Preenane*," signifying pleasing and nourishing. *Santarpanam*, in essence, refers to thorough nourishment. Hence, *Santarpanajanya Vyadhis* can be understood as diseases arising from excessive nourishment⁹.

Nidana

Nidana plays an essential role in the onset and management of the disease. Various *Aharaja* and *Viharaja* factors are implicated in this context are:

Aharaja Nidana: Snigdha (Unctious), Madhura (Sweet), Guru (Heavy), Picchila Ahara (Slimy), Navanna (Newly harvested), Nava Madhya (Fresh wine), Anupa and Varija mamsa (Meat of aquatic animals residing in marshy regions), Excessive use of milk and milk products, Goudika Annam (Food prepared with jaggery), Paishtika Ahara (Food prepared from fine wheat), Virudha Ahara¹⁰. Excessive intake of foods that are Guru, Snigdha, Sita, Picchila and Madhura rasa leads to Lepana and Brimhana in the body, as well as Tarpana, resulting in the imbalance of Kapha Dosha¹¹. Consuming too much Dadhi, Navadhanva, and Ksheera (Milk) can cause Sroto-Rodha due to their Abhishyandi and Kledana properties¹². Long-term adherence to such lifestyle practices can vitiate Kapha Dosha, leading to the formation of Ama. These dietary habits can be correlated with modern-day consumption of fried and oily foods, such as cheese, butter, and ghee, which are examples of Snigdha Ahara. Ati Madhura Aharas include white sugars, pastries, sweet beverages, and bakery products like halva, candies, jalebi, and cakes. Pizzas, parathas, biriyani and burgers are Guru Aharas, while Picchila Aharas include curd and fish.

Viharaja Nidana: Cheshta Dwesham, Divaswapna, Saiyya Dosha.

In the modern view, the causes of NAFLD are obesity, Insulin resistance, Hyperglycemia, hypertension, Metabolic syndrome, polycystic ovarian syndrome, Sleep apnea, Hypothyroidism, Hypopituitarism and liver cell damage.

$Rupa^{13}$

The specific symptoms of the disease are not separately mentioned. However, since there is involvement of Jataragni Mandya, Ama and vitiation of Rasa Dhatu, Rakta Dhatu, Mamsa Dhatu and Medo Dhatu along with the Srotas, characteristic features such as Sadam (Malaise), Tandra (Fatigue), Glani (Sleepiness), Alasya (Lethargy), Aruchi (Anorexia), Hrit Daha (Heartburn), Amlodgara (Sour belching), Anannabhilasha (Loss of appetite), Marutamoodata (Belching, Flatulence), Gaurava (Feeling of heaviness), Ati Kshudha (Excessive hunger) and Daurbalya (General debility) may be present.

Additionally, since the Yakrit is affected, symptoms related to Pandu, Kamala and Udara, such as Ayasa Akshamata (Unable to bear physical exercise), Koshta Sula (Right upper quadrant discomfort), Vishtamabha (Abdominal Distension) and Udara Vriddhi (Abdomen enlargement) may also be observed.

In the modern view, the symptoms are often asymptomatic and rarely cause fatigue and right upper quadrant pain. Hepatomegaly, palmar erythema, spider nevi, Anorexia, Ascites, Abdominal collateral vessels, and Encephalopathy are present in advanced stages.

Samprapti

Dosha in NAFLD: Although the disease initially begins with a predominance of *Kapha*. Eventually, the other two *Doshas Vata* and *Pitta* also become involved. *Vata* vitiation occurs due to the *Srotorodha*, which the excessively aggravated *Kapha* and *Ama* cause. This leads to the aggravation of *Vata* in *Koshta*. *Pitta* is affected by the continuous consumption of unctuous *Snigdha Ahara* and indulgence in similar *Vihara*, as *Pitta* possesses a slightly unctuous quality (*Ishat Snigdha Guna*). The *Samprapti* occurs in the *Yakrit*, which is *Raktavaha Sroto Mula*. Due to the *Asraya-Asrayibhava* between the *Rakta Dhatu* and *Pitta Dosha*, *Pitta* also becomes vitiated.

Dhatu Dushti and Sroto Dushti: Rasa Dhatu, Mamsa Dhatu and Medo Dhatu become vitiated due to the imbalance in Kapha caused by Asraya-Asrayibhava. Additionally, the Nidanas lead to Agnimandya, resulting in the formation of improper Rasa Dhatu. As Agnimandya persists and the person continues with the Nidanas, the formation of Uttarotthara Dhatu is affected. Consequently, Rakta Dhatu, Mamsa Dhatu, and Medo Dhatu also become vitiated. The vitiation of these Dhatus further disrupts the Srotas, creating a cycle where the Srotas are also affected. Samprapti: As a result of Aharaja and Viharaja Nidana, Kapha Pradhana Tridosha Kopa and Jataragni Mandya occur. This leads to the formation of Ama. So, the former Rasa Dhatu will be in Sama Rasa condition¹⁴. This Sama Rasa enters the Yakrit through the channels of Rasavaha Srotas, facilitated by Vyana Vata. Subsequently, from the Sama Rasa, Sama Rakta is formed, and there will be Pitta Dushti due to Asraya-Asrayibhava of Rakta and Pitta and the carrier Vyana Vata also gets vitiated. The Yakrit Dushti also will occur as it serves as the Raktavaha Srotomula.

This Sama Rakta leads to the formation of Dooshita Mamsa. Vasa, the Upadhatu of Mamsa, is categorised as 'Sudhamamsasya Sneha'¹⁵. The Dushti of Mamsa Dhatu resulted in the subsequent formation of Dushta Vasa. Given that the Yakrit is regarded as Kalamamsa Vishesha, any impairment in the Mamsa Dhatu leads to the Dushti of Yakri. The presence of Kha Vaigunya in the Yakrit facilitates the accumulation of Dushta Vasa within it, which matches the modern concept of Fatty liver. Continued exposure to Nidana Sevana leads to a progressive increase in fat accumulation within the liver, ultimately developing Cirrhosis and Hepatocellular Carcinoma.



Vasa accumulates in the liver due to Kha Vaigunyata in Yakrit

Fatty liver

Pathogenesis

Both Genetic and environmental factors play roles in the onset and advancement of NAFLD. Day and James proposed a two-hit hypothesis for NAFLD. The first hit involves insulin resistance, which results in the accumulation of triglycerides as fat droplets within hepatocytes, leading to steatosis. Insulin resistance causes an increase in the delivery of free fatty acids and triglycerides to the liver while decreasing their excretion, thereby promoting their accumulation. Insulin resistance leads to dysfunction in adipose tissue, resulting in changes in the production and secretion of adipokines and inflammatory cytokines. Fat accumulation in the liver produces reactive oxygen species and causes endoplasmic reticulum stress and mitochondrial dysfunction. Additionally, excess carbohydrates stimulate fatty acid synthesis in the liver. Non-alcoholic fatty liver disease (NAFLD) impairs glucose and lipid metabolism through two mechanisms: acting as an endocrine organ by releasing various fat-derived cytokines and causing ectopic fat deposition and lipotoxicity due to free fatty acids.

The second hit is multi-factorial, leading to hepatocellular injury and the progression to non-alcoholic steatohepatitis (NASH). The liver becomes more susceptible to injury due to the accumulation of excess fatty acids. This injury is believed to result from peroxisomal fatty acid oxidation, reactive oxygen species (ROS) production from the mitochondrial respiratory chain, microsomal oxidation, and cytochrome P450 metabolism of fatty acids. Obesity also contributes to the second hit, as adipose tissue releases inflammatory mediators such as leptin, tumour necrosis factor-alpha (TNF-alpha), and interleukin-6 (IL-6), which cause hepatocyte damage. Consequently, hepatocytes undergo ballooning, cytoskeletal aggregation, apoptosis, and necrosis.

Samprapthi Ghataka		
Dosha	: Kapha Pradhana	
Tridosha		
	Kapha-	Kledaka
Kapha, Avalmbaka Kapha		
	Pitta	- Pachaka
Pitta, Ranjaka Pitta		
Dooshya	: Dhatu- Rasa, Rakta,	
Mamasa, Meda		
	Upadhatu-Vasa	
Agni	: Jataragni, Medo	
Dhatwagni		
Ama	: Jataragnijanya and	
Dhatwagnijanya Ama		
Srothas	: RasavahaSrothas,	
Raktavaha Srothas, Mamsav	aha	
	Srothas,	Medovaha
Srothas, Annavaha Srothas		
Srotodushti	: Sanga	m, Vimarga
gamanam		
Rogamarga	: Abhyantara	
Utbhava Sthanam	: Amashaya	
Sanchara Sthanam	: Rasayani	
Vyakta Sthanam	: Yakri	it (Dakshina
Parshwa)		

Poorvaroopa

In the initial stage, it is usually asymptomatic *PATHYA-APATHYA Pathya Ahara*

- Deepaniya , Ruksha and Laghu Ahara
- Purana Rakta Sali
- Rakta Prasadana and Kapha Medohara Ahara
- Yava
- Mudga Yusha
- Madhudaga
- Phala Varga

- Shigru, Karavellaka, Patola, Punarnava
- Takra

Pathya Vihara

• Vyayamam

Apathya Ahara

- Ati Sevana of Guru, Snigdha, Madhura, Pichila Ahara
- Virudhahara, Akala and Atimatra Bhojana
- Thila, Masha
- Milk and milk products
- Anupa and Varija Mamsa
- Navannam and Navamadhyam
- Pishta Vaikrita Ahara (deeply fried food)
- Ushna Vidahi and Lavana Atisevana

Apathya Vihara

- Divaswapna
- Vegavarodha
- Avyayama
- Atibhojana
- Shoka
- Krodha
- Bhaya

PROGNOSIS

- Simple steatosis is benign.
- Steatohepatitis is progressive.
- Patients with NASH are at high risk of liver failure and liver cancer.
- NAFLD often coexists with one or more components of the metabolic syndrome, which can contribute to its progression and the development of complications.
- Long-term complications in individuals with simple steatosis typically arise from cardiovascular disease and atherosclerosis, not from liver failure.
- Advanced age, the presence of diabetes, as well as ballooning and fibrosis observed in liver biopsy results, are significant predictors of disease progression.

UPADRAVA

Without proper intervention, the condition may advance to manifestations resembling *Kamala* (Jaundice) and *Udara* (ascites). Complications are ascites, esophageal varices, hepatic encephalopathy, an overactive spleen, leading to a decrease in blood platelet count (hypersplenism), Increased risk of liver cancer, End-stage liver failure, signifying complete liver dysfunction.

CHIKITSA^{16, 17}

As NAFLD is categorised as a *Santarpanajanya Vyadhi*, therapeutic measures involving *Apatarpana Chikitsa* should be adopted. According to *Acharya Caraka*, therapeutic procedures such as *Vamanam* (Emesis), *Virechanam* (Purgation), *Raktamokshanam* (Blood letting therapy), *Vyayamam* (Exercise), *Upavasam* (Fasting), *Dhoomapanam*, *Swedanam*, and *Choorna Pradeha* are recommended for managing *Santarpanajanya Vyadhi*.

The treatment approach should focus on restoring the balance of vitiated *Doshas* and eliminating causative factors. The pathogenesis involves *Agni Vaigunya* and *Kapha Medo Dushti* at the *Mulasthana* of *Raktavaha Srotas*, *Srotorodha* and *Vatakopa*. Consequently, the treatment should target *Agnideepana*, *Amapachana*, *Kapha Medo Anilapaha*, and *Srotoshodhana*, which should align closely with the treatment principles for Medoroga.

If *Dosha* is little, only *Langhana* will be suitable, if the *Madhyama Bala* stage requires treatment through *Langhana* and *Pachana*. This can be achieved using *Laghu*, *Ushna* and *Teekshna Dravya*. These drugs, which are typically *Katu*, *Tiktha* and *Kashaya* in taste and predominantly composed of *Akasha*, *Vayu*, and *Agni Mahabhoota*, contribute to *Langhana* and *Pachana*. If there is more *Dosha*, *Sodhana* is necessary.

Therefore, the recommended treatment approach involves *Nidana Parivarjana*, *Deepana-Pachana*, *Samsodhana* and *Samsamana*.

Nidana Parivarjana

As per Ayurveda classics, the primary treatment approach for any disease is to avoid causative factors. *Kapha* and *Medo Dhushtikara Ahara* and *Vihara* should be avoided to prevent NAFLD.

Deepana-Pachana

Due to *Jataragni* and *Dhatwagni Mandya*, along with the occurrence of *Ama* in the *Samprapti*, the applica-

tion of *Agnideepana* and *Ama Pachana* is beneficial. These measures assist in restoring *Agni* to its normal state, thereby aiding in the proper transformation of *Dhatus*.

Shodhana

Acharya Charaka has mentioned the effectiveness of Shodhana Karma, stating that these therapies cure diseases and restore normal health while also clarifying the sense organs and mind. Among the four Samshuddi procedures of Langhana, Virechana can be selected as the appropriate therapy here since the liver is affected, which is the seat of Pitta and the root of Raktavaha Srotas. Virechana will eliminate not only Dushita Pitta but also Dushita Kapha from the body, promoting the active transformation of Srotas and is indicated for excessive Dosha accumulation.

Samsamana

The drugs of choice for managing NAFLD are those with *Tikta*, *Kashaya Rasa*, *Lekhana*, *Deepana* and *Pachana* properties. These drugs enhance *Ag*-*ni* and reduce *Kapha*, *Meda* and *Ama*, making them effective in the treatment of NAFLD.

Rasayana

Rasayana drugs rectify structural abnormalities in the *Dhatus*, restoring normal function and preventing secondary diseases. Disease formation is significantly influenced by oxidative stress caused by free radicals. Hence, *Rasayana* drugs, with their antioxidant properties, effectively mitigate the biological effects of free radicals, playing a crucial role in disease prevention.

There is currently no specific drug treatment available for NAFLD. However, a combination of therapeutic approaches, such as making lifestyle changes, increasing physical activity, and quitting smoking and alcohol consumption, is thought to be advantageous in managing the condition. Caffeine is a potent antioxidant that can potentially alleviate oxidative stress and inflammation in the liver, offering potential hepatoprotective benefits. A nutritious diet, which includes reducing calorie intake and minimizing the consumption of high-glycemic index (GI) foods, increasing the intake of monounsaturated fatty acids, omega-3 fatty acids, fibre, and specific protein sources like fish and poultry, is recommended for its potential positive impact.

DISCUSSION

NAFLD could not correlate to any disease mentioned in the Ayurvedic text; it can be brought under the Santarpanajanya Vyadhi mentioned by Acharya Caraka. The main factors which are contributing to the pathogenesis of NAFLD are Kapha Medo Vardhaka Ahara and Vihara, and the Samprapti Ghataka involved in NAFLD are Agnimanya, Ama, Kapha Dushti, Rasa Rakta Mamsa Medo Dushti, Sroto Dushti & finally Vasa Dushti. In the initial stage, it is usually asymptomatic and later characteristic features such as Tandra (Fatigue), Aruchi (Anorexia), Anannabhilasha (Loss of appetite), Gaurava (Feeling of heaviness), Daurbalya (General debility) Koshta Sula (Right upper quadrant discomfort) and Vishtambha (Distension of abdomen) may be present. For effective management, a physician should have complete knowledge of the concept of Santarpanajanva Vvadhi, which is available in Samhitas. Therapeutic measures involving Apatarpana Chikitsa should be adopted. According to Acharya Caraka, therapeutic procedures such as Vamanam, Virechanam, Raktamokshanam, Vyayamam, Upavasam, Dhoomapanam, Swedanam and Choornapradeha are recommended for managing Santarpanajanya Vyadhi.

CONCLUSION

NAFLD is a very common condition affecting 25% of the population and can cause significant liver disease in a proportion of patients. Accurate diagnosis and staging are essential in determining the appropriate long-term management for patients with NAFLD. Non-alcoholic fatty Liver Disease (NAFLD) can be categorised as a *Santarpanajanya Vyadhi*, and *Apatarpana Chikitsa* should be implemented. This can be achieved through *Nidana Parivarjanam*, *Deepana–Pachana, Samsodhana* and *Samsamana*. The treatment should focus on *Agnideepana, Amapachana, Srotoshodhana, Lekhana* and *Vatanulomana*.

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