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Research Article

THE RECOMMENDED IRANIAN TRADITIONAL MEDICINE (PERSIAN MEDICINE) DIET IN NON- ALCOHOLIC FATTY LIVER DISEASE

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Abstract:

Non-alcoholic fatty liver disease (NAFLD) is the major cause of chronic liver disease globally. Increasing prevalence of obesity and type 2 diabetes along with NAFLD has made this disease as a main public health problem. Certain treatment is not found yet and lifestyle modification, including physical activity and diet are still the most effective way to keep liver health or treat its ailments. Iranian Traditional Medicine (ITM) is an ancient school of medicine, which can be considered to find a proper diet protocol. From the viewpoint of ITM, liver is a main organ and several diet regimens are prescribed for healing of liver diseases. In this review, we searched the major ITM manuscripts from the 8th to the 19th century and compared with modern studies by searching some databases such as PubMed, Scopus and Google Scholar.

Therapeutic processes in ITM consist of 3 approaches. The first and most important of them is a regimen named Tadabeer that means Instructions for preserving or restoring health and including six essential principles (Setteh-e-Zarourieh). During this phase, in addition to the six essential principles, proper food regimen is recommended to patients, including some abstinence and using beneficial foods (Hepatoprotective in NAFLD).

There are dietary instructions for treating NAFLD and the other diseases of the liver in ITM, which are efficient due to recent studies somehow.

Keywords: Non-alcoholic fatty liver disease, Iranian Traditional Medicine, Persian Medicine, Diet, Hepatoprotective

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INTRODUCTION:

Non-alcoholic fatty liver disease (NAFLD) is rapidly becoming a serious public health problem due to its increased prevalence in accordance to epidemics of obesity, insulin resistance and type 2 diabetes (1–4). NAFLD is the most common cause of chronic liver disease worldwide. It is not a single ailment rather it is a spectrum that covers a range of conditions such as simple steatosis, nonalcoholic steatohepatitis (NASH), fibrosis and cirrhosis (5).

The global incidence of NAFLD is unknown since it depends on the population studied and the methods of diagnosis (6). About 30% of the population in the western world and Asia and 40%-90% of obese cases are affected by this disorder (4,7). The prevalence of NAFLD in Iran is 39.9% (8).

The pathogenesis of NAFLD is complicated and while its exact mechanism remains largely unknown, different genetic factors and/or environmental elements such as dietary habits seem to influence it through a complex network of molecular signals (1,4). The initial accumulation of fat in the liver can occur through several mechanisms; however, the most widely supported models implicate insulin resistance as the key mechanism in primary NAFLD, leading to hepatic steatosis. Insulin resistance is accompanied by an increase in peripheral lipolysis, the liver fatty acids uptake and triglyceride synthesis, which result in fat accumulation in hepatocytes. The progression of steatosis to NASH is not completely understood either (9).

NAFLD is generally an asymptomatic disease, often identified by accident.

Recent data suggest that diet and exercise have beneficial effects on the management of this disease (10).

In addition to therapeutic diets, some types of food, such as those that are rich sources of antioxidants, may help control the derangements found in this disease (10).

Nowadays there is a population's tendency to use traditional and complementary medicine. Iranian traditional medicine (ITM) is an old school of medicine practiced in Iran for centuries ago (11).

In the view of ITM lifestyle management is considered the first step of the approach to any health condition. Lifestyle management in ITM is explained by six essential principles (Setteh-e-Zarourieh).

These rules are related to each other (12). Nutrition's rules are the most important among them. ITM physicians like Rhazes believed that the first step of treatment is nutrition (13).

There is no definite disease matching the symptoms of NAFLD in ITM manuscripts. Depending on the pathogenesis of NAFLD, we consider a range of liver diseases described in the references. This range includes Soo-e-mezaj (change of organ's temperament) especially cold and wet, Ooram (tumefactions), Soddeh (obstruction), and Zaaf (liver weakness) (14,15).

In ITM for liver as a principal organ, there are many therapeutic and health care instructions. One of these instructions is nutrition.

The aim of this review is to investigate nutritional plans suggested by ITM references to protect liver and help managing its diseases.

MATERIALS AND METHODS:

This study is a literature research, investigating major Persian medical and pharmaceutical manuscripts from the 8th to the 18th century AD. We searched the major references of ITM in different century including Ferdows al-Hekmah fi'l-Tibb (The Paradise of Wisdom in Medicine) from Ali Ibn Rabban Tabari (8th), Al-Hawi fi'l-Tibb (Comprehensive Book of Medicine) from Mohammad Ibn Zakariya Razi (Rhazes) (9th), Hidayat al-Muta'allimin fi al-Tibb from Abu Bakr Akhawayni Bukhari (10th), Kamel al-Sanaat al-Tibbeyyah (Complete Book of the Medical Art) from Ali Ibn Abbas Majusi Ahwazi (Haly Abbas) (10th), Al-Qanun fi'l-Tibb (Canon of Medicine) from Hossein Ibn Ali Ibn Sina (Avicenna) (11th), Zakhireh Kharazmshahi (Treasure of Kharazmshah) and Al-Aghraz al-Teb-bieh va al-Mabahes al-Alayieh (Medical Pursuits) from Sayyed Esma'il Jorjani (11th), Tohfat al-Momenin (Rarity of the Faithful) from Hakim Mohammad Momen Tonekaboni (16th), Makhzan al-Adwiah (Drug Treasure) and Kholasato-Al-Hekmah from Mohammad Hussein Aqili Khorasani (18th) and Exir-e-Azam (The Grand Elixir) from Mohammad Azam Khaan (19th). Also we searched databases such as PubMed, Scopus and Google Scholar to found relationship between traditional and modern knowledge.

RESULTS AND DISCUSSION:

NAFLD is becoming a major health care problem worldwide. Coexistence of this disorder with other diseases such as obesity, type 2 diabetes,

hypertension and other cardiovascular diseases make it more important to find a distinct treatment.

NAFLD is defined by liver fat accumulation exceeding 5% of liver weight, in the absence of excessive alcohol intake (6). It is the most common cause of chronic liver disease in the world. NAFLD is a wide spectrum term, encompassing simple hepatic steatosis, hepatic steatosis associated with necroinflammatory lesions, fibrosis and cirrhosis and even hepatocellular carcinoma (HCC) (6,16,17).

There is no obvious symptom in patients and most of them are diagnosed accidentally (9).

Many factors such as signals derive from adipose tissue, muscle, the gut and its microbiota implicate the liver inflammation (5,6). Although liver biopsy is the gold standard method for NAFLD diagnosis, but it is expensive and invasive. Thus, it is used in special conditions. Ultrasonography commonly is used which is simple, non-invasive and safe, but in mild steatosis has low accuracy and operator dependent. Other radiologic techniques include the controlled attenuation parameter (CAP) software on the Fibroscan system and magnetic resonance spectroscopy (MRS) (5,6,18).

In spite of extensive researches to find a decisive treatment, hepatic therapeutic protocols have limited effect on NAFLD. Most of studies have confirmed that the lifestyle modification including diet and exercise are the best strategies for this ailment (4,5,10,18,19).

After searching the major references, we found that there is not an absolute term for NAFLD in ITM manuscripts. In our investigated references, like Canon of Medicine and Exir Azam, 17 liver ailments were described (20). Some of these disorders based on pathogenesis resemble NAFLD. Soo-e-mezaj (change of temperament), Ooram (tumefactions), Soddeh (obstruction or blockage) Zaaf (liver weakness) and Soo-o al qhunieh (precirrhotic phase). Liver in ITM references is a principal organ beside heart and brain (62,63). There are 4 stages for digestion process. The second stage occurs in the liver after ending the first in the stomach. During this stage, the liver produces 4 humors contains sanguine, phlegm, yellow and black bile. The balance in quality and quantity of them have important role in health and disease (64).

Therapeutic protocol in ITM references include:

- 1- Six essential principles (Setteh-e-Zarourieh) modification and Nutritional therapy (Tadabeer bel aghzieh)
- 2- Pharmacotherapy (Tadabeer bel advieh)
- 3- Manual or operative Interference (Aamale Yadaavi) (21)

As stated earlier, the first step in any therapeutic approach such as liver diseases is observing the six essential principles. Following these principles is more effective in health care and prevention of ailments particularly in major organs like liver. The six essential principles contain:

1. Air
2. Sleep and Wakefulness
3. Depletion and Retention
4. Body movement (physical activity) and Repose
5. Mental movement (psychic movement) and Repose
6. Foods and Drinks (12)

Each rule is closely related to other principles. For example, the different seasons and climates affect foods, sleep, wakefulness etc.

1. Air

The first rule named Air includes seasons and climates. In any seasons, foods which are suitable, the time of eating and quantity of food differs. In a particular geographical region, the mountains and sea location, direction of the wind, duration of day and night, temperature and humidity or dryness are considered. Diet, sleep and physical activity must be adjusted. For example, eating foods with long digestion time like animal proteins or heavy physical activities in hot weather can damage liver. In general, all essential rules closely depend on region, weather, humidity and seasons. Air pollution is another factor which can be harmful for the body (12).

2. Sleep and Wakefulness

The duration of sleep depends on personal temperament (Mezaj), but as a rule all people should sleep moderately (more than 6 and less than 10 hours). Excessive wakefulness or sleep can be harmful for health especially liver health. In addition, proper time for sleeping is important. Proper time for sleeping is after the digestion of food (11). Day napping and sleeping too late are not suitable. Sleeping place must have good ventilation, suitable temperature and free of noise. The sleep position also is noticed. Supine position is forbidden. Any excitement (Mental Movement and Repose in general), such as TV watching and anger just before sleeping can induce sleep disorders (22).

3. Depletion and Retention

Excretion of waste materials and retention of beneficial ones is another rule. Generally, there are two main groups of depletion including natural and therapeutic.

Examples of natural depletion are defecation, urination, perspiration, nasal or vaginal discharge, menstruation and ejaculation. Moreover, coughing and sneezing are reflexes which can excrete waste materials. Therapeutic depletion includes purgation, wet cupping (Hijama), phlebotomy (Fasd), enema and emesis. Disorders like constipation, urine retention and menstrual retention cause various diseases including liver problems (11).

4. Body Movement and Repose

The movement rules consist of physical activities. Exercise and massage (Dalk) are also categorized in this section. Duration, intensity and time of physical activities are the most important factors to protect health. Intensive movement after meal, long-term exercise for people with dryness of temperament or prolonged rest influence different organs like liver. On the contrary, long inactivity induce coldness in the body, which is followed by a number of disorders in different organs such as liver. Avicenna in Canon of Medicine emphasizes on exercise. He says: "The best measures is exercise, then nutrition and then sleeping" (14).

5. Mental Movement and Repose

Mental and emotional states like anger, fear, embarrassment, happiness or stress affect the body. Outward and inward movements of pneuma is responsible for this process (12). Hakim Jorjani in Zakhireh Kharazmshahi emphasizes that emotional states' effect on the body is stronger than anything else even nutrition. Chronic fear or stress can induce coldness of temperament which can in turn lead to coldness of liver (23).

6. Food and Drinks

Many scholars consider food and drinks to be the most important principle. As previously mentioned, eating and drinking rules have strong links to other principles in addition to personal habits and temperaments. Food time, quality and quantity depend on the seasons, sleep or physical activities. Although there are many instructions for correct habits such as the number of meals or food qualities (there are four quality contain hot, cold, wet and dry in foods) based on personal temperament, rapid changes are prohibited. Any changes in nutritional habits should be gently (24).

6.1. Time of Eat

The best time to eat is when a person feels hungry that is called "true appetite". Eating before digestion of last meal can be harmful, especially for the liver. Any delay in food intake while having true appetite could have adverse effects. During eating, the environment temperature might not be too hot. Eating duration should be balanced, not too short or too long. Stress, irritability or anger disturbs digestion and any indigestion can cause liver disease. Heavy exercises, intercourse and sleep after eating lead to dyspepsia followed by liver disorders (22).

The foods depending on digestion time are divided into three groups:

- 1- **Thin foods:** they have short digestion time
- 2- **Dense foods:** they have long digestion time
- 3- **Moderate foods:** they have medium digestion time

Eating these three types of foods at the same time is harmful for liver (15).

The digestion process begins with proper food choices and continues with the act of chewing. The following phase is in the stomach thus its health is very necessary (25).

6.2. How to Eat

Chewing well is the most important rule. Chewing should be completed, slowly and calmly. Avoiding to use different foods during a meal because of different digestion time is another rule. Any situation disturbing the body in digesting the foods properly should be avoided such as TV watching. In the other words, the physis (human nature) should be focused on digestion (26). Also standing and moving are not proper positions for eating (22).

6.3. How to Drink

Drinking liquid like water should be limited to 20 minutes before meal and 2 hours after that on the other hand long term thirst, Drinking water, especially cold in the middle of sleep, fasting or after intercourse lead to liver injury (22,24).

6.4. Food Quality

Foodstuffs are categorized in 3 main groups:

- 1- Complete foods like lamb meat, wheat, rice and grapes
- 2- The foodstuffs that possess both nutritive and medicinal qualities but exert their influence mainly through their nutritive quality (nutraceuticals) such as apple, celery and quince.
- 3- The foodstuffs that possess both nutritive and medicinal qualities but exert their influence mainly

through their medicinal quality (phytochemicals) such as ginger, curcumin (Turmeric) and Cinnamon (18).

In addition, foods have various temperaments. Personal temperament and different conditions (health or disease) should be considered for choosing proper food. Ignoring the concordance between the temperament of individual and food, may lead to liver damage regardless of the usefulness of the selected food itself. Another issue is food digestion time. Concurrent use of foods with diverse digestion time during a meal can cause dyspepsia (17).

The next step of managing liver diseases, including NAFLD, is avoidance of harmful foods along with usage of beneficial ones.

Beneficial Foods for Liver

As mentioned earlier, some liver diseases in ITM resemble NAFLD and some kinds of foods are noticed as a liver tonic, hepatoprotective, liver cleanser or obstruction reliever in ITM references. These foods are listed in table 1 with their properties in ITM along with modern research findings. Certain idioms explain the nutrient effectiveness in ITM manuscripts based on the pathogenesis of liver diseases (Nutritional therapy).

Table 1- Beneficial Foods for Liver

	Common name	Scientific name	Traditional name	property	Pharmacological effect in ITM	Pharmacological effect
1	Chickpea	Cicer arietinum L.	Hommas, Nokhod	Hot and dry	Mofatteh ¹ , Monaghi ² (27)	Antihyperlipidemic (28,29)
2	Celery	Apium graveolens	Karafs	Hot and dry	Mofatteh (27)	Hepatoprotective (30), Antioxidant (31)
3	Hazelnut	Corylus avellana	Bondogh, Fandogh	Hot and dry	Moghavi ³	Antioxidant, Anti-inflammatory (32)
4	Barberry	Berberis vulgaris	Zereshk, Ambarbaris	Cold and dry	Mofatteh, Moghavi	Hepatoprotective (33)
5	Currant	Vitis vinifera L.	maveez (munaqqi ¹)	Hot and wet	Moghavi	Hepatoprotective, Antioxidant (34)
6	Quince	Cydonia oblonga Mill.	Safarjal, Beh	Cold and dry	Moghavi	Antidi oxidant, Antihyperglycemic (35)
7	Apple	Malus domestica	Tofaah	Hot and wet	Moghavi	Antioxidant activity, Antihyperlipidemic (36)
8	Fig	Ficus carica	Teen, Anjir	Hot and dry	Mofatteh (14)	Hepatoprotective (37) Antioxidant activity (38)
9	Saffron	Crocus sativus	Zaaferan	Hot and dry	Moghavi Mofatteh (39)	Anti-inflammatory (34), Antioxidant activity (40)
10	Spinach	Spinacia oleracea L.	Esfenaj	Cold and wet	Jaali ⁴	Anti-inflammatory (19), Antioxidant activity (41)
11	Curcumin	Diferuloyl methane	Zardchoobeh, Oroogh-al-sabbaghin	Hot and dry	Jaali	Antihyperlipidemic (42)
12	Carrot	Daucus carota	Jazar, Zardak	Hot and dry	Moghavi, Mofatteh	Antioxidative activity (43)
13	Citron	Citrus medica L.	Balang	Hot and dry	Moghavi ,	Antioxidative activity (44)

Continue.....

¹. Seedless

	Common name	Scientific name	Traditional name	property	Pharmacological effect in ITM	Pharmacological effect
14	Beets	Beta vulgaris	Salgh	Equable ¹	Mofatteh	Antioxidative activity (45)
15	Pomegranate	Punica granatum	Romman, Anar	Cold and wet	Moghavi , Jaali , Mofatteh	Radical scavenger Antioxidant, anti-inflammatory (46,47)
16	Bay Laurel (rand)	Nobilis Laurus	Ghaar	Hot and dry	Mofatteh	Hepatoprotective (48)
17	Common Purslane	Portulaca oleracea	Khorfeh,	Cold and wet	Moghavi	Immunomodulatory effect (49)
18	Melon	Cucumis melo var.inodorus	Betikh, Kharbozeh	Hot and wet	Jaali	Antioxidant, Antihyperlipidemic (50)
19	Iranian Damask Rose	Rosa damascene.Mill	Vard, Gol-e-sorkh	Cold and dry	Moghavi	Radical scavenger Antioxidant (51)
20	Cinnamon	C. zeylanicum	Darsini, Darchin	Hot and dry	Moghavi, Mofatteh	Insulin sensitizer (52) Antioxidant (53)
21	Asparagus	Asparagus officinalis	Helioon	Hot and wet	Mofatteh	Anti-inflammatory (54)
22	Cumin	Cuminum cyminum	Zireh,komun	Hot and dry	Moghavi	Anti-inflammatory (55)
23	Black seed	Nigella Sativa	Siah daneh, shooniz	Hot and dry	Moghavi	Insulin sensitizer, Antihyperlipidemic (56)
24	Almond	Prunus dulcis	Lowzol holw, Badam	Hot and wet	Moghavi	Hepatoprotective, Antihyperlipidemic (18, 19)
25	Ginger	Zingiber officinale	Zanjebil	Hot and dry	Moghavi	Hepatoprotective (57)
26	Radish	Raphanus sativus L.	Fojl	Hot and dry	Liver tonic (20)	Antioxidant, Radical Scavenging Activity (58)
27	Garlic	Allium sativum	Soam,Seer	Hot and dry	Moghavi (27) Mofatteh	Hepatoprotective (59) Antioxidant, Anti-inflammatory (60)
28	Squash	Cucurbita pepo L. Elaeagnus	Ghar'e	Cold and wet	Liver cooling (20), Mofatteh (61)	Antioxidant (62)

1. *Mofatteh*: liver obstruction reliever by the decrement of blood intensity

2. *Monaghi*: cleanses the liver by excretion of waste materials

3. *Moghavi*: protects the organ ailments or injuries, tonic, hepatoprotective

4. *Jaali*: Detergent, cleaner, Scraper (61)

¹ . Balanced in hot, cold, wet and dry

The various abstinences are listed below (14,15).

1. Eating before digestion of last food
2. Eating foods with different digestion times together
3. Drinking cold water especially after exercise, intercourse, in fasting or along with meal
4. Eating sweet desserts
5. Eating in satiety
6. Heavy physical activity after meal
7. Long term thirst
8. Wheat ingredients especially refined flour
9. Some foods such as Beef and veal, Mushroom or rice
10. Cured meat for instance salt-cured
11. Eating with anger, stress or anxiety
12. Very sweet foods
13. Barbecued meat especially raw or burned
14. Excessive use of foods with cold temperament
15. Daytime napping and sleeping immediately after a meal

Pharmacotherapy is the next approach and is correlated to the disorders. In the simple liver dystemperament, medicines with opposite property are used to change temperament and then adjust temperament and finally strengthen. The medicines are used in compound liver dystemperament, which can evacuate the disturbing humor (for example ripener or purgative).

Manual or operative Interference is the last step in therapeutic course and consist of venesection, wet cupping, leech therapy and enema (21). Algorithm of NAFLD treatment in ITM is shown in figure-1.

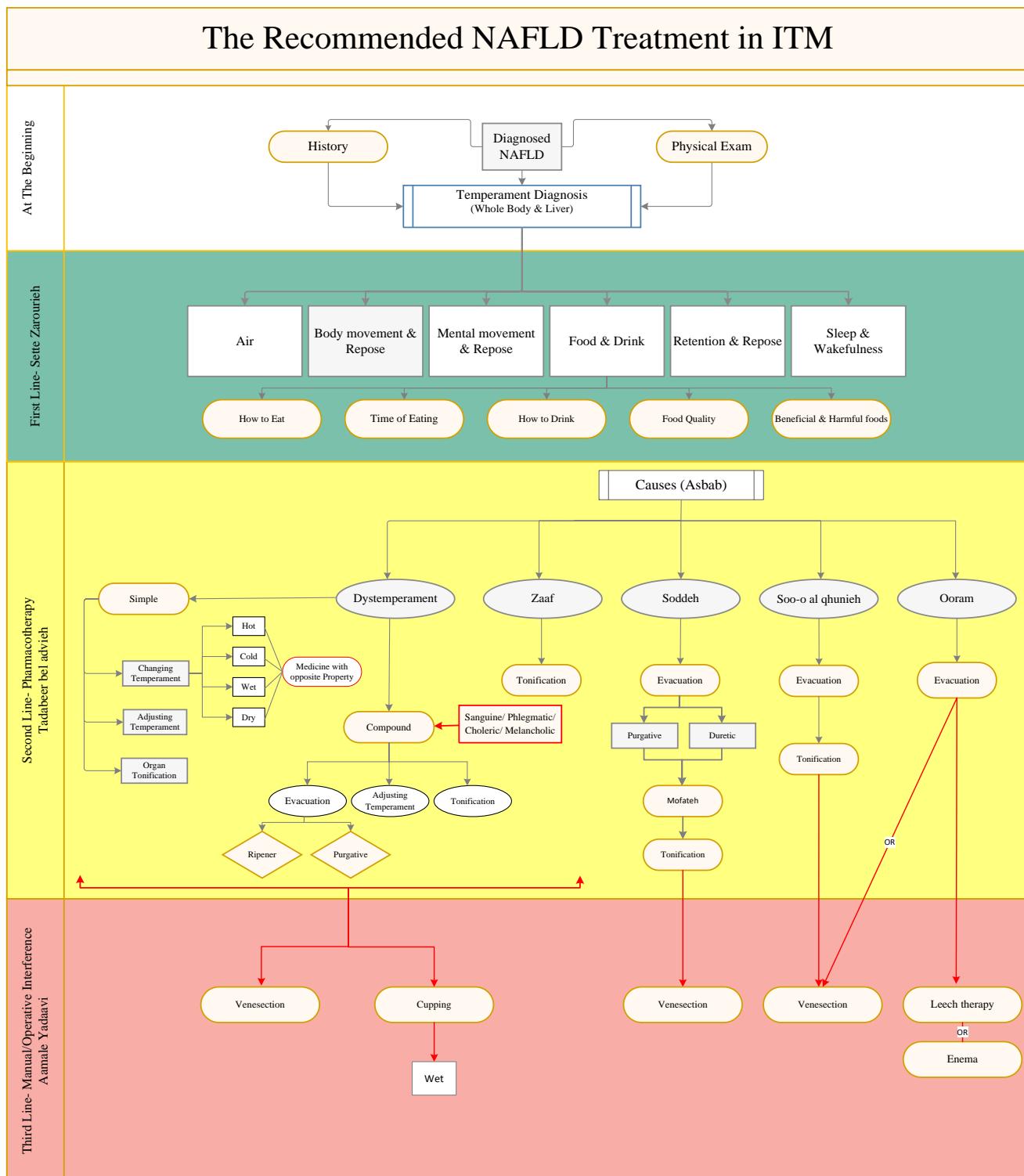
Many researches suggest lifestyle modification as the best protocol in NAFLD treatment. Diet is the most important component in lifestyle. Due to the long process of healing, it is preferred to select a diet that be coordinated with the culture and taste of patients. Many clinical trials have been conducted to find a suitable diet in NAFLD.

Baratta *et al.* in a study on 584 outpatients with HOMA-IR ≥ 3.8 and steatosis showed the reverse relation between adherence to Mediterranean diet and NAFLD prevalence. They implied that greater tendency to Med-diet was accompanied by lower incidence of high grade of hepatic steatosis (63). In a review article, Baselga-Escudero *et al.* showed the effects of the Mediterranean spices and fragrances on NAFLD (64).

In addition, many research articles have been published about hepatoprotective foodstuffs. These studies are consistent with beneficial foods for liver in ITM. Inappropriate patterns of habits of eating including eating too rapidly and eating at night are associated with obesity and NAFLD (65).

Beside diet, the other components in life style such as sleeping, exercise and emotional states affect NAFLD.

Qu *et al.* in 2014 studied on 6998 participants aged 40 to 75 years and showed that longer day napping duration is accompanying with a higher occurrence of NAFLD (66). The similar research by Peng *et al.* in a cross-sectional community-based population study stated that Short sleep duration and long daytime napping correlated with an increasing of NAFLD prevalence (67).

**Fig. 1: Algorithm of NAFLD Treatment in ITM**

The roles of exercise in the treatment of NAFLD were demonstrated in multiple researches. Bae et al. in a cross-sectional analysis showed the relation between regular exercise and reduction in NAFLD risk (68). Regular exercise accompanied by diet regimen have benefits in NAFLD management and insulin resistance reduction (69).

One of the six essential principles in ITM is mental movement and repose. Recent studies demonstrate that emotional states can affect the liver. Macavei et al. in a systematic review showed the role of anxiety and depression in the liver disease progression such as NAFLD (70).

CONCLUSION:

Consistent with the prevalence of obesity and diabetes, NAFLD is increasingly growing. Despite extensive clinical trials, an absolute treatment for NAFLD has not been found so far. Furthermore, medication even herbal drugs have side effects. It seems that lifestyle modification including nutrition and physical activity is the most effective therapeutic strategy although it is difficult to implement, dietary recommendation should be in line with patients' taste and culture. ITM as an old medical school has multiple instructions for treating liver ailments. Nutrition is one of the six essential principles. In addition, nutrition in therapeutic protocol has a major role. Most foodstuffs are listed in ITM references as hepatoprotective approved in modern studies. Further researches on traditional medicine diets needs to be done to show the effectiveness of them to treat NAFLD.

Conflict of interest

None declared.

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