





# Explanation of the Concept of Wet Liver Dystemperament (*sue-mizaj*) in Iranian Traditional Medicine (Persian medicine): A Hybrid Concept Analysis

Fatemeh Hakimi<sup>1</sup>, Farideh Yaghmaei<sup>2</sup>, Abbas Alipour<sup>3</sup>, Majid Asghari<sup>4</sup>, Hasan Namdar<sup>5</sup>, Parisa Jafari<sup>6</sup>, Mina Movahhed<sup>7\*</sup>

## Abstract

**Objectives:** The semiology of liver dystemperament can help in predicting susceptibility to some diseases and improving the treatment process of the liver or general disease such as non-alcoholic fatty liver disease (NAFLD). Therefore, the aim of this study was to explain the wet liver dystemperament concept in Iranian traditional medicine (ITM) based on a hybrid concept analysis.

**Materials and Methods:** The literature review of this qualitative study focused on evaluating 11 major academic textbooks from the 3rd to 19th century and some databases. In-depth, semi-structured, and face-to-face interviews were conducted with 16 ITM experts with a minimum of five years of clinical experience and maximum variations in terms of gender, age, and clinical experiences for empirical data gathering. Data were analyzed with MAXQAD10 and conventional content analysis.

**Results:** In this study, wet liver dystemperament was classified into three main themes of systemic, local, and Para-clinical symptoms and 10 categories.

**Conclusions:** This manuscript explains wet liver dystemperament as a disorder in general temperament and determines more important diagnostic criteria.

**Keywords:** Dystemperament, Liver, Concept Analysis, Hybrid Model, Iranian Traditional Medicine, Persian Medicine

## Introduction

Liver is the largest solid organ and performs many essential functions related to digestion, metabolism, immunity, detoxification, and the storage of nutrients within the body. These functions make the liver a vital organ which supports the other organs of the body (1).

Liver disease is a general term that covers all the potential problems when the liver cannot perform its specified functions (2). Investigations show that traditional and complementary medicine [T&CM] provides benefits for liver diseases by improving the quality of life, regulating immunity, controlling disease progression, and prolonging survival (2). Iranian Traditional Medicine (ITM) is a breach of T&CM and is comprehensive in the fields of disease prevention and treatment (3). According to Mojahedi et al (4), ITM is a personalized medicine, and individual differences are presented in the content of temperament (*Mizaj*).

Liver dystemperament in ITM refers to liver dysfunction or liver disease and is considered as one of the basic concepts in diagnosis and treatment (5). ITM scholars believe that each organ of the body has its own temperament for performing its specified functions

effectively. Therefore, if its temperament gets abnormal for any reason, it will be unable to properly perform its functions, and consequently, gradually develops a “complication” called “*Su-e-Mizaj*” or “Dystemperament” (5,6).

ITM is based on humoral medicine, and every humor is a substance made from the digestion and permutation of foodstuffs in the gastrointestinal system (7). Normally, there are four humors in the human body, including “*Phlegm or Balgham, Blood or Dam, Yellow bile or Safra, and Black bile or Sauda*”.

Each of the humors is related to two pairs of qualities or a specific temperament including cold and wet, hot and wet, hot and dry, and cold and dry, respectively (8,9).

The imbalance in body temperament and humors leads to the onset of disease (10). The semiology of liver dystemperament can help predict susceptibility to some diseases and improve the treatment process of the liver or general disease (11). According to his descriptions of illness symptoms in the canon of medicine, Avicenna, as one of the largest ITM scholars, is known as the pioneer of medical sciences in semiology (12). The traditional strategy of the World Health Organization is

Received 10 January 2019, Accepted 7 May 2019, Available online 12 July 2019

<sup>1</sup>Clinical Research Development Unit, Moradi Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. <sup>2</sup>Department of Nursing, Zanzan Branch, Islamic Azad University, Zanzan, Iran. <sup>3</sup>Department of Health and Social Medicine, Mazandaran University of Medical Sciences (MAZUMS), Mazandaran, Iran. <sup>4</sup>Traditional Medicine Research Center, School of Traditional Medicine, Qom University of Medical Sciences, Qom, Iran. <sup>5</sup>Department of Traditional Medicine, School of traditional medicine, Shahed University of Medical Sciences, Tehran, Iran. <sup>6</sup>Department of Persian Medicine, School of Medicine, Zanzan University of Medical Sciences, Zanzan, Iran. <sup>7</sup> Traditional Medicine and Materia Medica Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

\*Corresponding Author: Mina Movahhed, Tel: +98-21-88776027. Email: movahhedm54@gmail.com



## Key Messages

- ▶ This study shows that some traditional diagnostic criteria have not been made applicable today.
- ▶ This paper explains wet and dry liver dystemperament as a disorder in general temperament and determines more important diagnostic criteria

the development of strategies for integrating traditional medicine in the health system based on documented medical studies.

In this regard, providing a practical definition of traditional concepts is necessary based on this strategy (13). Therefore, this study aimed at explaining the concept of wet liver dystemperament based on a hybrid concept analysis.

### Materials and Methods

This study is a qualitative concept analysis, which is a method of research in qualitative studies and is used to provide an applied definition in relation to health and disease concepts (14). In this study, the concept of wet liver dystemperament was analyzed with a hybrid model.

The method of the hybrid model is oriented toward developing concepts through a qualitative investigation using participant observations and interviews of phenomena taking place in situ. The hybrid model is a combination of two theoretical and empirical phases and provides a complete definition of the concept, in this respect, excels in other ways that do not pay attention to experimental data (15). This model consists of theoretical, field work, and final analysis phases.

#### Theoretical Phase

In this phase, some major academic textbooks of Ph.D. students of traditional medicine from the 3rd century to the 19th century (Table 1), namely, the section related to wet liver dystemperament, were reviewed based on the agreement of 60% of the teamwork. This was performed to investigate the nature of the existing knowledge about the concept of wet liver dystemperament and extract a working definition. PubMed and Google scholar databases were reviewed without year limitations using keywords such as *mizaj*, wet/dry, liver, and temperament. Some of the inclusion criteria were full access to the entire article, the relevance of the article, and English or Persian language of the article.

#### Fieldwork Phase

##### Setting and Sample

Purposeful sampling (16) was conducted among 16 ITM experts with the maximum variation in terms of gender, age, and clinical experience, and continued to reach data saturation. An inclusion criterion was having at least five years of clinical experience. To reach the maximum variety, experts were selected from both genders and

different colleges of traditional medicine.

#### Data Collection

In this phase, a questionnaire with open and closed questions was developed based on the results of the theoretical phase. In-depth, semi-structured, and face-to-face interviews were conducted by the researcher, female, and Ph.D. students of ITM.

In addition to individual interviews, the concepts were explained in expert panel sessions consisting of 10-14 experts by focus group methods. In this phase, three main aspects of wet liver dystemperament underwent further investigation:

1. What are the symptoms of the patients with the diagnosis of wet liver dystemperament?
2. What are your most important diagnostic criteria?
3. How much the expressed symptoms in the texts are applicable in the clinic?

#### Data Analysis

Interviews were recorded and transcribed with the consent of the participants using the mp3 player. Reminders were also used in the process of collecting and analyzing data. Moreover, the credibility and confirmability of data were performed to increase the rigor of research. Then, coding was done using MAXQAD10 software, and similar codes were grouped as categories, and the main themes were finally extracted accordingly. For data analysis, the conventional content analysis was used according to the proposed process by Elo and Kyngas (17). This approach consists of preparation, organization, and reporting phases, and when the existing theories or research literature are limited, is often appropriate (18).

#### Final Analytic Phase

The results of the theoretical and field work phases were merged, and similarities and differences were identified as well. Eventually, the functional definition of wet liver dystemperament was extracted and presented in the Expert Panel with the presence of 17 ITM experts and confirmed with an agreement of over 60% by the Delphi method.

### Results

#### Theoretical Phase

In ITM manuscripts, the concept of wet and dry refers to a passive quality or rate of body passivity that can be influenced by various factors. Dry temperament refers to stability and the lack of formation, and wet temperament refers to rapid deformation and the high rate of flexibility in body reactions (6). To the best of our knowledge, this is the first study to clarify the concept of wet liver dystemperament in traditional schools. The working definition of wet liver dystemperament was extracted as follows:

The wet dystemperament of the liver refers to liver

**Table 1.** Ten ITM Important Textbooks Used in This Study

Book Name	English Name	Author	Author's Years of Life	Language
1 Firdous al-Hikmah	Paradise of Wisdom	Ali ibn Raban Tabari	847-861 AD (30)	Arabic
2 The Kitab al-Mansuri	Liber Al-Mansuri, a concise handbook of medical sciences	Razi (Razes)	865-925 AD (31)	Arabic
3 Kamel-al-Sanaat al-Tibbiah	The Perfect Art of Medicine	Majusi Ahwaz (Haly Abbas)	949-982 AD (32)	Arabic
4 Hedayat al mota'allem in fi al-tibb	An educational guide for medical students	Al-Akhawayni Bukhari	?- 983 AD (33)	Persian
5 Al-qanun Fi'l-Tibb	Canon of medicine	Ibn Sina (Avicenna)	980-1037 AD (5)	Arabic
6 Zakhireye Kharazm Shahi	Treasure of Kharazm Shah	Hussain Hussaini Jorjani	1042-1137 AD (34)	Persian
7 Sharh qanon Ibn Sina (Sharh Qarshi)	A commentry on Avicenna's canon	Ibn Nafis	1213-1288 AD (35)	Arabic
8 Sharh-olasbab va alamat	Explaining the causes and signs	Samarghandi-Nafis ibn Avaz Kermani	(15th century) (36)	Arabic
9 Moalejat-e Aghili		Aghili Shirazi	18th century (37)	Persian
10 Teb-e-Akbari	Akbari's Medicine	Mohammad Akbar Arzani (or Akbar Shah)	18th century (38)	Persian
11 Exir-e-Azam	Great Elixir	A'azam khan Chashti	19th century (39)	Persian

Note. ITM: Iranian traditional medicine.

dysfunction and is accompanied by various symptoms. They include the humid and pale tongue, sialorrhea, decreased thirst, creating great thirst in exposure to heat, puffiness or edema of the face and eyelids, weakness of the body, loose body tissue, especially tissues over the liver, drowsiness and lowed sensation, maldigestion, bradycardia, weak pulse, and flexibility in vessel consistency (flexible pulse). In addition, diarrhea, dilute and light urine, paleness, white or light skin, and occasionally oriental complexion or/and improved general condition of the body by eating dry temperament foods are also observed in these patients. Diagram 1 presents the repetitions of symptoms in different texts based on a kind of summative content analysis.

#### Fieldwork Phase

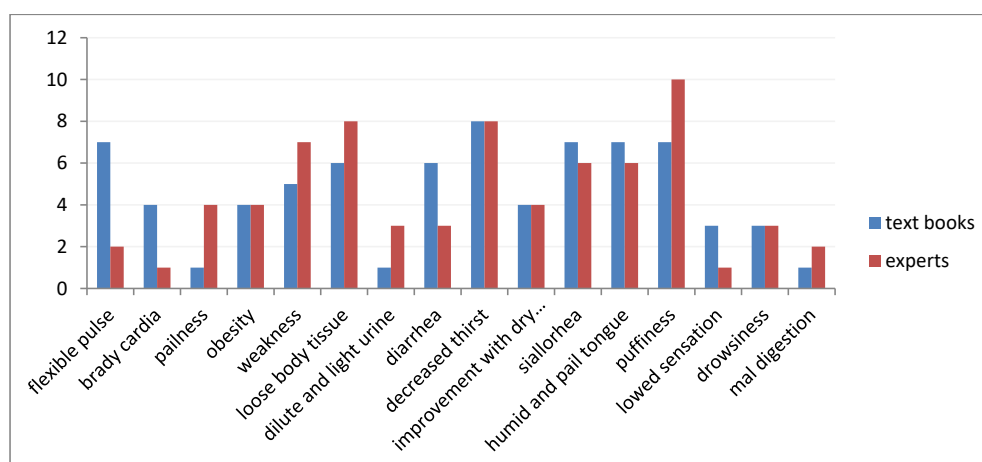
Data saturation was obtained through interviews with 16 interviews. The participants were 11 males and 6

females with an average of 44.5 years old and 15 years of clinical experience from Shahid Beheshti, Tehran, Shahed, Mashhad, Tabriz, Qom, and Babol Universities of Medical Sciences. The interviews were held in sessions of 2-3 hours and a total of 41 hours in their workplace. After analyzing the interviews, some new categories were added to the definition of wet liver dystemperament, which were not mentioned in the texts (Table 2). Figure 1 compares the application of the symptoms in the texts with the clinic.

#### Final Analytical Phase

In the literature review, decreased thirst had the highest score in the diagnosis of wet liver dystemperament. Then, puffiness or edema of the face and eyelids, humid tongue and sialorrhea, and pulse characteristics had the highest citation.

In the interview, puffiness and limb edema, and then decreased thirst, loose body tissue, and weakness or



**Figure 1.** Wet Liver Dystemperament Symptoms Based on a Summative Analysis of Textbooks and Experts

**Table 2.** Sub-categories and Codes of Wet Liver Dystemperament and Semantic Units

Subcategories of Wet Liver Dystemperament	Some Illustrative Quotations
Wide and full pulse	When the moisture exceeds the normal range, the pulse becomes wide, the wide pulse is pathognomonic of wetness. e1 A full pulse can be highly helpful in the diagnosis of wet liver dystemperament. It can be beneficial for the fatty liver or hyperlipidemia. e2
Paleness Whiteness of the lips	In the cold and wet dystemperament of the liver, the skin color becomes pale and white. e4 Whitening of the lips is pathognomonic of cold and/or wet dystemperament of the liver. e3
Obesity talent Abdominal obesity Limb edema	These persons usually have an obesity talent. General obesity without abdominal obesity can differentiate general dystemperament from wet liver dystemperament. e2 Limb edema can be a strong indicator of wet liver dystemperament. e5 Swelling of the hands and feet is pathognomonic of the cold and wet liver dystemperament. e2 I know the morning edema as a cold and wet dystemperament of the liver indicator. e3
Difficulty in starting of physical activity Morning boredom Feeling heaviness Neuropathy Appetite changes Mal digestion	The patient says I feel tired to start work, but when I begin my job, I'll do up to the end. It's hard to find someone who has these characteristics and doesn't have wet liver dystemperament. e6 In the mornings, before he starts working and getting warm, he feels heaviness or he cannot get up easily. e2 Feeling heaviness, numbness, or tingling in the entire right side, especially at the right leg, without any discopathy evidence can be due to liver dystemperament. e7 He says: "I'm eating like before, but I do not enjoy eating like before." e6 In wet liver dystemperament, they are usually looking for something sweet after a meal or tend to have a salty taste. e6 Someone who is always hungry despite eating very much, is strongly in favor of wet liver dystemperament. e6 Belching 3-4 hours after meal. Sensation of heaviness in the stomach even after 12 hours. e6 Sleepiness some hours after a meal can be a sign of weak liver digestion. e8 Bloating permanently, occasionally accompanied by spread or transient pain without any specific gastrointestinal symptoms (e.g., heartburn or stomach pain) is a sign of liver maldigestion. e9
Features in the tongue examination	Severe smooth and thick tongue is observed in wet liver dystemperament. e9 In the side of 2/3 posterior junction of the tongue, a delta line is usually found, which is not a continuous line, and the change of color is observable. In addition, the density or the number of papillae decreases and shows a longer process. e6
Changes in the quality of waste material excretion	Changes are observed in the stool form and defecation pattern, dis-shaped, fatty, or fragmentary stool. e3 Given that moisture affects the nerve, they don't have complete defecation. They feel the stool but cannot excrete the feces or they have incomplete defecation. e3 The diarrhea-predominant IBS can be a feature of wet liver dystemperament. e6 Menstrual pattern changes in each cycle are attributed to the liver dystemperament metabolism. e10
Behavioral characteristics	Rapid psychotic changes. Gets angry or becomes calm very soon. e12 The amount of pleasure from everything comes down. I have a patient that his problem in sexual contact is like that ... he has no other signs except that he does not enjoy anything at all. e6 In wet dystemperament, we have a patient or an indifferent man. e11
Systemic reaction to anything with wet or dry temperament	The patient says, "If I eat yogurt, watermelon or cucumber at night, I will have puffiness tomorrow, or the swelling of my feet increases, my stomach does not get annoyed", and he says that "I'm lethargic, heavy, and drowsy." e12 The sudden onset of allergy symptoms with a slight increase in heat or activity is an indicator of excessive moisture that is diluted. e1

boredom sensation in the body had the most diagnostic application, respectively.

The results showed that the symptoms of liver dystemperament have a large overlap with the symptoms of dystemperament in other organs, and detection based on systemic complications, rejection of the proprietary symptoms of other dystemperaments, and response to treatment have been emphasized in liver dystemperament diagnosis in the interview.

A new definition of wet liver dystemperament was presented in this phase. These symptoms were placed in 10 categories including phenotype, vascular and pulse characteristics, general or gastrointestinal dysfunctions, and the humidity or consistency of the mucus. Other categories were skin and subcutaneous tissue, skin color

disorder, skin and hair problems, sleeping disorders, disrupted waste disposal, behavioral characteristics, and systemic improving or exacerbating reactions to various factors (Table 3).

In the literature review, the value of each sign and symptom is not mentioned, but phenotype, skin color, humidity or consistency of the mucus, skin and subcutaneous tissues, thirst and feeling of boredom, and systemic impressibility speed were the most important diagnostic criteria for the experts.

**Discussion**

The results of this study revealed that some criteria such as pulse and urine indices, which are important in the diagnosis of liver dystemperament in the texts and

**Table 3.** Categories, Sub-categories, and Codes of the Wet Liver Dystemperament Concept

Categories	Codes	
Vascular and pulse characteristics	Flexible pulse, bradycardia, and weak pulse (TEXT) Wide and full pulse (interview)	
Skin and hair problems	Low back and softness of the abdomen or body hair Hair loss	
Skin color disorder	White or light-skin, which is occasionally oriental complexion or olive-skinned **Paleness and whiteness of the lips	
Phenotype	Is not thin, no puffiness or edema of the face and eyelids** Obesity*, obesity talent, abdominal obesity, limb edema**, and morning swelling	
General or gastrointestinal dysfunction	General activity	Weakness of the body**, heavy feeling in the liver place, and lowed sensation Difficulty in starting the activity and reducing feelings of boredom after the start of activity, morning boredom, feeling heaviness, and feeling heaviness or neuropathy in the right half of the body, especially in the right leg
	Appetite	Lack of enjoying food eating, **desire for sweets after meals or salty taste, permanent starvation and lack of satiety, increased appetite, and distaste having breakfast
	Thirst	**Decreased thirst, creating great thirst in exposure to heat
	Digestion	Maldigestion Belching 3-4 hours after meal. A sensation of heaviness in the stomach even after 12 hours, feeling heaviness and pain after a meal in the liver, bloating permanently, occasionally accompanied by spread or transient pain without any specific gastrointestinal symptoms, and weakness or pain in the leg
	Humoral production	Dominance of phlegm/blood concentrations resulting from plasma viscosity and anemia symptoms despite normal hemoglobin
Sleeping disorders	Sleepy/deep sleep and drowsiness	
Behavioral characteristics	Rapid psychotic changes and the lack of enjoyment of various conditions including sexual activity, being patient, or indifferent	
Humidity or consistency of mucus, skin, and subcutaneous tissues	Loose body tissue, especially tissues over the liver Humid skin, sticky moisture on the skin, double chin, layered form, and obese abdomen Humid and pale tongue, sialorrhea, or hypersalivation Sticky saliva, smooth, round, and wide tongue (an increase of thickness and length and width of the tongue), presence of dental effects on the tongue, and decreased density or the number of papillae	
Disrupted waste disposal	Low volume and diluted urine and diarrhea Disorders in urinary defecation and increased urination, dis-shaped, fatty and fragmentary stool, incomplete and delayed defecation, mucus excretion with stool, diarrhea-predominant IBS patterns, excessive sweating, increased volume of semen discharge, and changes in menstrual blood	
Systemic improving or exacerbating reactions to various factors.	*Distaste watery foods, systemic symptoms of exacerbation from fatty or sluggish foods, humid weather, improving in dry weather or with dry temperament foods eating, and sudden onset of allergy symptoms with a little heat or activity	
Para-clinic	Increased volume and dilution of semen in the spermogram, increased interstitial water, fat and low muscles in the in-body measurement. Hyperlipidemia, the existence of dyslipidemia before emerging gastrointestinal symptoms such as bloating and heartburn, gastrointestinal symptoms, along with metabolic syndrome, evidence of fatty liver disease, increased liver enzymes, hormonal disorders (e.g., FSH and estrogen), and lack of mature follicles may be observed in every liver dystemperament	

Note. IBS: Irritable bowel syndrome; FSH: Follicle-stimulating hormone.

\*\* Typical and more agreement between experts; \* is important in some experts opinion.

interviews, have not been made applicable by the experts. It may be due to changes in the general lifestyle, and some of the diagnostic indicators of liver diseases used by ancient scholars are now unusable.

The concept of liver dystemperament has been described based on symptoms and other conceptual aspects such as the mechanism, and changes in the structure of the liver have not been completely explained in any of the texts, literature reviews, or interviews.

In the theoretical phase, diagnosis is based on some scattered symptoms. It should be noted that a new definition of wet liver dystemperament, which has not so far been mentioned, was extracted in this study. Wet liver dystemperament was classified into three main themes

of systemic, local, and para-clinical symptoms and 10 categories.

The categories of wet liver dystemperament are accompanied with the diagnostic symptoms of general temperament in ITM manuscripts as 10 items. Such items included the condition of skin touch, muscle and fat mass, hair condition, skin color, physique, impressibility speed, sleep and wakefulness, physical function, quality of waste matters (i.e., stool, urine, and sweat), and psychic function. Thus, the liver dystemperament can be regarded as a disorder in general temperament. This is a logical consequence of the fact that the liver is the site of the humors, and any dysfunction can affect the whole body (5,19).



In the study by Shahkarami et al, the diagnostic symptoms of liver dystemperament were classified into 10 groups and referred to as local hair on the liver and vein forms (19) which further indicate the intrinsic temperament of the liver compared to liver dystemperament (5). In the assessment of our findings with those of conventional studies on liver dysfunction, obesity has a negative impact on non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome at all aspects and stages of the disease (20). The depletion of adipose tissues and muscle loss are major changes in body composition in patients with advanced cirrhosis (20). The deleterious effects of obesity, including non-alcoholic steatohepatitis, are strongly correlated with visceral adipose tissues (21). Lipolysis from this tissue generates free fatty acids delivered directly to the liver (20).

Patients with chronic liver disease can have a wide spectrum of cutaneous manifestations including xerosis, nail changes, pigmentary changes, hair changes, jaundice, infections, pruritus, and spider angioma (22). Muscle cramp may occur with great frequency and is associated with poor quality of life and sleep disturbance in chronic liver diseases (23). Difficulty with sleep initiation, frequent nocturnal awakening, sleep maintenance insomnia, shortened sleep duration, and poor sleep quality and refreshing sleep are the most common sleep disorders in patients with chronic liver disease or cirrhosis (24). Another investigation reported the accompaniment of fatigue and psychiatric illness such as anxiety or depression with chronic liver disease and NAFLD (25). There is increasing evidence that gut microbiota plays a role in the development of hepatic steatosis (20). Additionally, bile acid excretion and its absorption disorders are important in digestion and induction or treatment of constipation and diarrhea (26). The anemia of diverse etiology is a common complication of chronic liver diseases. The causes of iron anemia include acute or chronic gastrointestinal hemorrhage and hypersplenism secondary to portal hypertension (27). Aplastic anemia may follow the development of hepatitis (27). There is another theory that conjugated bilirubin triggers anemia by inducing erythrocyte death (28). NAFLD is not only liver dysfunction but also an emerging multifaceted systemic disease (29), which is in line with the findings of this study.

### Conclusions

Liver dystemperament is a spectrum of liver dysfunctions and can include some initial symptoms before para-clinic symptoms or complex complications associated with disorders in para-clinic findings.

The explanation of the liver dystemperament concept is the first step toward the development of a therapeutic or diagnostic protocol. It can also be a step toward interventions through lifestyle modifications and herbal medicine complementary therapies. The results of

this study can be used to design a diagnostic wet liver dystemperament tool for the assessment of its relation or prevalence in liver diseases, including NAFLD, to promote diagnostic, therapeutic, and research goals.

Further theoretical and empirical studies are needed to enhance the knowledgebase of liver dystemperament. A definite concept of wet liver dystemperament is required based on its symptoms, conceptual aspects (e.g., physiology), or the mechanisms and changes in the structure of the liver.

There is a need for the development of valid and reliable diagnostic tools, as well as the determination of major and minor diagnostic criteria based on extensive studies on patients with wet liver dystemperament.

### Authors' Contribution

FH and MM: concept and design. FH, MA, HN, PJ and EP: data collection and interpretation of data. FH, FY and AA: performing of the study and writing of the draft. All authors read and approved the study.

### Conflict of Interests

Authors have no conflict of interests.

### Ethical Issues

This study was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (Permission No. 1395-629).

### Acknowledgments

This study is a part of the thesis entitled: Explaining and Item Generation of Diagnostic Tool of the Wet and Dry Dystemperament (*sue-mizaj*) of the Liver in Iranian Traditional medicine (Persian medicine) which was supported by a grant from Shahid Beheshti University of Medical Sciences.

### References

- Mulaikal TA, Emond JC. Physiology and anatomy of the liver. In: Wagener G, ed. *Liver Anesthesiology and Critical Care Medicine*. Cham: Springer; 2018:3-19.
- Guan YS, He Q. A current update on the rule of alternative and complementary medicine in the treatment of liver diseases. *Evid Based Complement Alternat Med*. 2013;2013:321234. doi:10.1155/2013/321234
- Rezadost H, Karimi M, Jafari M. Proteomics of hot-wet and cold-dry temperaments proposed in Iranian traditional medicine: a Network-based Study. *Sci Rep*. 2016;6:30133. doi:10.1038/srep30133
- Mojahedi M, Naseri M, Majdzadeh R, et al. Reliability and validity assessment of Mizaj questionnaire: a novel self-report scale in Iranian traditional medicine. *Iran Red Crescent Med J*. 2014;16(3):e15924. doi:10.5812/ircmj.15924
- Avicenna. *Al-Qanun Fi Al-Tibb [Canon of Medicine]*. 2004.
- Aghili Khorasani Shirazi M. *Kholassat Al-Hekmah (The Principal's of Traditional Iranian Medicine)*. 2006.
- Heydarirad G, Choopani R. "Dry mouth" from the perspective of traditional Persian medicine and comparison with current management. *J Evid Based Complementary Altern Med*. 2015;20(2):137-142. doi:10.1177/2156587214558596
- Pasalar M, Zarshenas MM, Bagheri Lankarani K. Good Digestion is a Key Element for Healthy Hearts: An Appealing Concept from Avicenna's Viewpoint. *Medical Hypothesis, Discovery & Innovation Interdisciplinary Journal*. 2014;1(2):2-4.

9. Emtiazy M, Keshavarz M, Khodadoost M, et al. Relation between body humors and hypercholesterolemia: an Iranian traditional medicine perspective based on the teaching of Avicenna. *Iran Red Crescent Med J.* 2012;14(3):133-138.
10. Rezaeizadeh H, Alizadeh M, Naseri M, Shams Ardakani M. The traditional Iranian medicine point of view on health and disease. *Iran J Public Health.* 2009;38(Suppl 1):169-172.
11. Movahhed M, Mosaddegh M, Mohammadi Farsani G, Abolhasani MH. History of fatty liver in medieval Iranian medicine. *HealthMED.* 2013;7(3):786-792.
12. Erolin C, Shoja MM, Loukas M, et al. What did Avicenna (Ibn Sina, 980-1037A.D.) look like? *Int J Cardiol.* 2013;167(5):1660-1663. doi:10.1016/j.ijcard.2012.09.178
13. World Health Organization (WHO). WHO Traditional Medicine Strategy: 2014-2023. WHO; 2013:1-28.
14. Baldwin MA. Concept analysis as a method of inquiry. *Nurse Res.* 2008;15(2):49-58. doi:10.7748/nr2008.01.15.2.49.c6329
15. Schwartz-Barcott D, Patterson BJ, Lusardi P, Farmer BC. From practice to theory: tightening the link via three fieldwork strategies. *J Adv Nurs.* 2002;39(3):281-289. doi:10.1046/j.1365-2648.2000.02275.x
16. Palinkas LA, Horwitz SM, Green CA, Wisdom JP, Duan N, Hoagwood K. Purposeful sampling for qualitative data collection and analysis in mixed method implementation research. *Adm Policy Ment Health.* 2015;42(5):533-544. doi:10.1007/s10488-013-0528-y
17. Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs.* 2008;62(1):107-115. doi:10.1111/j.1365-2648.2007.04569.x
18. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res.* 2005;15(9):1277-1288. doi:10.1177/1049732305276687
19. Razi (Razes) M. *The Kitab al-Mansuri (Liber Al-Mansuri, a concise handbook of medical sciences).* 2008.
20. Shahkarami E, Minaei B, Dehkordi Jafari E. The Concept of Liver Disease Diagnosis in Avicenna's Canon of Medicine. *Iran J Public Health.* 2013;42(7):785-786.
21. Vajro P, Paolella G, Fasano A. Microbiota and gut-liver axis: their influences on obesity and obesity-related liver disease. *J Pediatr Gastroenterol Nutr.* 2013;56(5):461-468. doi:10.1097/MPG.0b013e318284abb5
22. Kim D, Chung GE, Kwak MS, et al. Body fat distribution and risk of incident and regressed nonalcoholic fatty liver disease. *Clin Gastroenterol Hepatol.* 2016;14(1):132-138.e4. doi:10.1016/j.cgh.2015.07.024
23. Choudhury BN, Jain A, Baruah UD. Dermatological manifestations of chronic liver disease. *Int J Res Dermatol.* 2018;4(2):224-229.
24. Iwasa M, Karino Y, Kawaguchi T, et al. Relationship of muscle cramps to quality of life and sleep disturbance in patients with chronic liver diseases: A nationwide study. *Liver Int.* 2018;38(12):2309-2316. doi:10.1111/liv.13745
25. Formentin C, Garrido M, Montagnese S. Assessment and management of sleep disturbance in cirrhosis. *Curr Hepatol Rep.* 2018;17(1):52-69. doi:10.1007/s11901-018-0390-1
26. Youssef NA, Abdelmalek MF, Binks M, et al. Associations of depression, anxiety and antidepressants with histological severity of nonalcoholic fatty liver disease. *Liver Int.* 2013;33(7):1062-1070. doi:10.1111/liv.12165
27. Rao SSC. Treating constipation with bile: a new target. *Lancet Gastroenterol Hepatol.* 2018;3(8):520-521. doi:10.1016/s2468-1253(18)30166-3
28. Gkamprela E, Deutsch M, Pectasides D. Iron deficiency anemia in chronic liver disease: etiopathogenesis, diagnosis and treatment. *Ann Gastroenterol.* 2017;30(4):405-413. doi:10.20524/aog.2017.0152
29. Lang E, Gatidis S, Freise NF, et al. Conjugated bilirubin triggers anemia by inducing erythrocyte death. *Hepatology.* 2015;61(1):275-284. doi:10.1002/hep.27338
30. Adinolfi LE, Marrone A, Rinaldi L. Non-alcoholic fatty liver disease: beyond the liver is an emerging multifaceted systemic disease. *Hepatobiliary Surg Nutr.* 2018;7(2):143-146. doi:10.21037/hbsn.2018.02.01
31. Tabari A. *Ferdows al-hekmah fi al-tibb (Paradise of wisdom on medicine).* 1928.
32. Ahwazi Arjani A. *Kamel al-Sanaah al-Tibbiyah (The Perfect Art of the Medicine).* 1973.
33. Akhawayni A. *Hedayat al-mota'allemin fi al-tibb (An educational guide for medical students).* 1992.
34. Jorjani I. *Zakhireye Kharazmshahi [Treasure of the Khwarazm Shah].* 1976.
35. Al-Nafiss I. *Sharh qanon Ibn Sina (A commentary on Avicenna's canon).* 1925.
36. Kermani N. *Sharh Al-asbab va Alamat (samarghandi) (Description of causes and symptoms).* 2008.
37. Aghili Khorasani Shirazi SMH. *Moalejate Aghili.* 2009.
38. Arzani M. *Teb-e-Akbari [Akbari's Medicine].* 2008: 805-10.
39. Azam Khan M. *Exir Azam [Great Elixir].* 2008.