



A Review of Cold-Wet Mizaj and Phlegm Dominance Indices in Persian Medicine

Payam Dolatshahi¹, Reihaneh Moeini², Roshanak Mokabberinejad³, Farooq Ahmad Dar⁴, Mostafa Alizadeh¹, Morteza Mojahedi^{5,*}

¹ Student Research Committee, Babol University of Medical Sciences, Babol, Iran

² Traditional Medicine and History of Medical Sciences Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran

³ Department of Traditional Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁴ Department of Tashreeh wa Munafeul Aza, Faculty of Unani Medicine, Aligarh Muslim University, Aligarh, India

⁵ Department of History of Medicine, School of Traditional Iranian Medicine, Babol University of Medical Sciences, Babol, Iran

* Corresponding author: Department of History of Medicine, School of Traditional Iranian Medicine, Babol University of Medical Sciences, Babol, Iran. Email: mortazamojahedy@gmail.com

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Abstract

Background: Personalized medicine, an emerging approach, considers individual differences to tailor treatments optimally. Persian medicine (PM) incorporates individual differences through Mizāj (temperament). A comprehensive understanding of each Mizaj type's characteristics is essential in designing standardized diagnostic tools.

Objectives: This study aims to explore the attributes of one of the most significant Mizaj groups, namely cold-wet Mizaj, and its subtypes, including cold-wet Su-e-Mizaj (dystemperament), as well as phlegm dominance in PM sources.

Methods: Persian medicine literature, including the Canon of Medicine, was reviewed for relevant concepts. Reliable scientific databases, including PubMed, Scopus, and MagIran, were searched using keywords such as Mizaj, temperament, Su-e-Mizaj, dystemperament, cold-wet dystemperament, phlegm, and Balgham. The obtained results were studied and categorized.

Results: Out of the 196 articles obtained related to Mizaj, 16 investigated indices. No studies were found on the indices of cold-wet Mizaj and phlegm dominance separately. PM sources exhibit high congruence in describing the characteristics of cold-wet Mizaj. Specifically, emphasis is placed on characteristics such as coldness and softness of the skin to the touch, high fat mass, pale and white complexion, excessive body secretions, weakness and slowness of physical and physiological actions, low vitality, timidity, poor memory, and slow-wittedness. In cold-wet dystemperament, symptoms are more severe, and in the presence of phlegm, a feeling of heaviness is also mentioned as a specific symptom.

Conclusions: By compiling indices of cold-wet Mizaj/dystemperament and phlegm dominance, this study can contribute to the development of standardized PM questionnaires, facilitating a personalized approach to the diagnosis and treatment of diseases.

Keywords: Persian Medicine, Personalized Medicine, Mizaj, Temperament, Phlegm

1. Background

Various quantitative and qualitative biological indices have been used in conventional medicine to determine health status and diseases (1). Although attempts were made to designate biological indices within a normal range until a few decades ago, there has been a recent emphasis on individual differences, especially susceptibility to diseases and treatment methods (2-5). Using this personalized approach, it is

possible to determine the most effective treatment with the least risk of side effects for each individual using genomics and omics technology (3, 6-9). Thus, the development of personalized medicine in the future is expected to lead to cost-effective use of healthcare resources (10, 11). This is while individual differences in biological indices have been a fundamental part of diagnosis and treatment in many ancient medical systems (12-15).

Persian medicine (PM) or Iranian traditional medicine (ITM) is a holistic medical school. In this school, Persian scholars preserved the scientific recommendations of Greece and Rome and expanded upon them with their own experiences, making them comprehensive, improved, and expanded (16, 17). According to PM, every individual has specific physical, physiological, and psychological characteristics, collectively referred to as Mizaj (15, 18-20). Considering that biological and behavioral differences largely depend on omics and gene expression, categorization patterns based on phenotype, as specified in traditional medicines including PM, can potentially be used as a practical clinical arm of personalized medicine (9, 18, 21, 22).

The type of Mizaj plays an essential role in recommendations for health maintenance as well as the diagnosis and treatment of diseases (14, 23, 24). Although each person has a unique Mizaj, Persian scholars have categorized this concept according to certain criteria and indices to facilitate health management (15, 25, 26).

Based on the theory of Mizaj, healthy individuals are classified according to indices related to two pairs of qualities, namely hotness/coldness and wetness/dryness (14, 27, 28). Hence, healthy individuals are divided into nine Mizaj groups, including one moderate, four single (hot, cold, wet, dry), and four compound (hot-wet, hot-dry, cold-wet, cold-dry) groups. Deviation from the normal range of each of these groups results in a *Su-e-Mizaj* (dystemperament) of that type (15, 25, 29), which may in turn lead to a variety of diseases (30-32). These diseases are categorized into 16 groups, including eight simple dystemperaments (cold, wet, dry, hot, hot-dry, hot-wet, cold-dry, cold-wet) and eight dystemperaments accompanied by substance (humor) dominance. Among these conditions, hot-wet (sanguine dominance), hot-dry (yellow bile dominance), cold-wet (phlegm dominance), and cold-dry (black bile dominance) are among the most common dystemperaments. Substance-dominant dystemperaments occur when the amount of one of the four humors increases beyond the normal ratio or the quality deviates from a healthy normal state (15, 24, 32).

Individuals with cold-wet Mizaj or the related cold-wet dystemperament are prone to diseases such as joint pain and inflammation, headaches, sinusitis, infectious and febrile diseases, lung disorders, digestive disorders and weakness, weight gain (leading to conditions like cardiovascular disorders, fatty liver, and diabetes), dysmenorrhea, infertility, and mental disorders (30, 33-41). Moreover, many symptoms of this dystemperament

are consistent with conditions of unknown etiology in conventional medicine, including weakness and fatigue. PM sources recommend practical measures to correct cold-wet dystemperament or to treat related diseases, supported by primary evidence (42, 43). Diagnosing cold-wet Mizaj in individuals and recommending preventive measures accordingly will help reduce the occurrence of diseases associated with cold-wet Mizaj (27, 35, 42-46).

PM sources have specified several indices to determine types of Mizaj and dystemperament, including cold-wet Mizaj/dystemperament and phlegm dominance (24, 27, 28). Other schools of traditional medicine have also presented similar models of categorization. For instance, some disease classifications in Traditional Chinese Medicine (TCM) are relatively similar to Mizaj classifications in PM. In this regard, a large group of TCM diseases is known as phlegm pattern diseases (47, 48). The indices specified for diagnosis of this pattern are very similar to those of cold-wet dystemperament and phlegm dominance in PM (13, 47). TCM researchers have developed standard questionnaires to detect phlegm patterns, with research and clinical applications (47, 49).

Indices of cold-wet Mizaj, cold-wet dystemperament, and phlegm dominance are scattered in PM sources, posing challenges in research and clinical application of data (25, 26, 45). Extraction and classification of data to facilitate subsequent design and standardization of diagnostic tools are one of the solutions to this issue (15, 28, 45).

Although preliminary studies have endeavored to standardize Mizaj indices and some types of dystemperament in healthy individuals, no study has been conducted to extract and standardize indices of general types of dystemperament, including cold-wet Mizaj disorders and phlegm dominance (27, 30, 35, 50-52).

2. Objectives

The purpose of this study is to extract the diagnostic criteria of cold-wet Mizaj and its related pathological conditions, i.e., cold-wet dystemperament and phlegm dominance from PM sources as a prelude to designing standard diagnostic tools.

3. Methods

In this qualitative review, authentic PM sources, including al-Mansouri fil Tibb (Rhazes; 865-925 AD), Qanoon fi al-Teb (Avicenna; 980-1037 AD), Kamel al-Sana'ah al-Tebiyah (Haly Abbas; 949-982 AD), Zakhira-e-

Khwarzamshehi (Ismaeil Jorjani; 1042-1137 AD), and Exire Azam (Mohammad Azam Khan; 19th century), were studied to extract indices of cold-wet Mizaj/Su-e-Mizaj and phlegm dominance. Each source was reviewed for emphasized words and sentences and their repetition. Furthermore, keywords such as "Mezaj," "Mizaj," "cold-wet," "Balgham," "Su-e-Mizaj," "Dystemperament," "Temperament," and "Phlegm" were searched in scientific databases including ScienceDirect, PubMed, Scopus, MagIran, SID, IranMedex, and Google Scholar search engine. The related findings were collected, and indices of cold-wet Mizaj and Su-e-Mizaj, and phlegm dominance were categorized.

4. Results

4.1. Scientific Databases

A total of 196 articles related to Mizaj were obtained, among which 19 had endeavored to extract Mizaj and dystemperament indices in PM. No article was found on indices of general cold-wet Mizaj, dystemperament, or phlegm dominance. Several articles related to phlegm patterns in oriental medicine were found, some of which were devoted to the extraction of diagnostic indices and development of standard questionnaires.

4.2. Authentic PM Sources

4.2.1. Cold-Wet Mizaj

The compound cold-wet Mizaj is a result of dominance of cold and wet qualities (15, 24, 50). In a healthy state, an individual with cold-wet Mizaj is said to have a healthy cold-wet Mizaj. Under such conditions, there are no symptoms of any disease, and the person is healthy and in balance. When characteristics of a Mizaj type are intensified in such a way that body functions are disturbed, a cold-wet dystemperament develops (15, 26). Simple cold-wet dystemperament occurs when there is an increase in cold-wet symptoms for a limited period of time, partially relieved by a warm environment and consumption of hot-natured foods. In the presence of symptoms of phlegm dominance, this dystemperament is called substance-dominant cold-wet dystemperament or phlegmatic dystemperament. This increase in phlegm results from certain lifestyle and nutritional habits and individual susceptibility (15, 24, 26, 53).

4.2.2. Mizaj Indices

Most written PM sources have clearly specified cold-wet Mizaj/dystemperament indices, with Avicenna's Canon of Medicine containing the most detailed classification. Ten groups of physical and behavioral characteristics have been proposed as Mizaj indices in PM sources, called "Ajnas-e Ashareh". They include characteristics of the skin in palpation, muscle and fat mass, hair condition, skin color, sleep, physique, physical and physiological functions, reaction of the body to external factors, mental and emotional states, and body excretions (15, 26, 27). Characteristics of each feature based on the Mizaj type are explained differently in PM sources. In the present study, the aforementioned characteristics are presented in three groups: Physical, physiological, and psychological indices.

The most important indices of cold-wet Mizaj in PM literature include:

(1) Physical indices: Cold and soft skin to touch, fair complexion, overweightness with a dominance of fat mass, small bone frame, non-prominent joints and vessels, and weak and slow pulse;

(2) Physiological indices: Slow physical movements, abundant nasopharyngeal secretions, digestive symptoms such as poor digestion, flatulence, and dyspepsia; and

(3) Psychological indices: Low vitality, timidity, poor memory, and dullness. In addition, each of the mentioned symptoms is intensified in cold-wet dystemperament and can lead to several diseases (24, 54, 55).

The important indices of cold-wet Mizaj, simple cold-wet dystemperament (without substance), and cold-wet dystemperament with substance (phlegm) dominance are listed in Table 1.

4.3. Physical Indices

- Tactile examination (Malmas): Individuals with a cold-wet Mizaj have cold and soft skin. This feature is present and may intensify in cold-wet dystemperament and phlegmatic dystemperament (23, 24, 54-56).

- Hair: Sparse hair, baldness, lank hair, and light-colored or gray hair are mentioned as signs of cold-wet Mizaj. Graying of the hair is also pointed out as a sign of phlegm dominance (23, 24, 55, 56).

- Skin Color: Light-colored skin tone is a sign of cold-wet Mizaj and dystemperament (23, 55, 56). Phlegmatic dystemperament is also associated with a whitish skin tone in most PM sources (23, 24).

- Physique: This index includes bone structure, the condition of superficial veins, and pulse (24, 28). Among these, only the pulse has been mentioned in simple

Table 1. Cold-wet Mizaj/Dystemperament and Phlegm Dominance Indices in Persian Medicine ^a

Domain	Index	Characteristic	Healthy Cold-Wet Mizaj	Simple Cold-Wet Dystemperament	Phlegmatic Dystemperament
Physical	Tactile exam	Cold skin	++	+	++
		Soft skin	++	+	++
		Soft nails	+	-	-
	Skin color	Light-colored skin tone	+	+	++
		Leadens face, eyes, and tongue	-	-	+
		Scanty	++	-	-
	Hair condition	Slow growth	+	-	-
		Delayed baldness	+	-	-
		Thin	+	-	-
		Soft and straight	++	-	-
		Blond, Gray, or White	++	-	+
	Physique	Small chest	++	-	-
		Small palms and soles (coldness)	+	-	-
		Short, thick fingers	+	-	-
		Narrow non-prominent veins	++	-	-
		Non-prominent joints	+	-	-
		Tiny pulse (short, narrow, and low-set)	++	-	+
		Soft pulse (flexible)	+	-	++
		Slow pulse	+	+	++
		Low pulse rate	+	+	++
		Wide pulse	-	-	+
	Soft tissue	Overweightness (excessive fat)	++	-	++
		Flaccidity of soft tissues and muscles	+	+	++
		Joint laxity	+	+	+
		Puffiness of the eyes	-	+	+
		Swelling of the hands and feet	-	+	+
	Physiological	Sleep	Swelling of the face and body	-	-
Increasing the duration and depth of sleep			+	+	++
Drowsiness			-	+	+
Body excretions		Dream of water, snow, coldness	-	-	++
		Abundant mucosal secretions	+	+	++
		Viscous saliva	-	-	++
		Odorless sweat and urine	+	+	-
		Light-colored urine	+	+	++
		Cloudy urine	-	-	+
Reaction to external factors		Soft stools	+	+	-
		Easily influenced by coldness and cold-natured foods	+	-	-
		Annoyed by cold/cold-wet climate	-	+	-
		Annoyed by cold and wet-natured foods	-	+	-
		Benefit from warmth and warm-natured foods	+	+	-
		Annoyed by wetness	+	+	-
Other functions		Benefit from dryness	+	+	-
		Slow movements	+	-	-
	Slowness of speech	+	-	-	
	Fatigue	+	+	++	
	Weakness	-	+	+	
	Feeling of heaviness	-	+	++	
	Low libido	+	+	+	
	Low appetite	+	-	+	
Psychological	Weak digestion	+	+	++	
	Sour belching	+	-	++	
	Low thirst	+	+	++	
	Timidity	++	+	-	
	Mild anger	+	+	-	
	Forgetfulness	+	+	+	
Mental and emotional states	Low vitality	+	+	++	
	Influenced by the smallest issues	+	-	-	
	Rapid disappearance of Reactions	+	-	-	

^a Out of the total five PM literature: ++: Mentioned in three or more references; +: Mentioned in less than three references.

cold-wet dystemperament and phlegmatic dystemperament, while the rest of the features are only mentioned in healthy cold-wet Mizaj. A small chest, non-prominent superficial veins, and weak pulse are regarded as signs of coldness-wetness, with more emphasis on coldness. Additionally, short-thick fingers, small joints, and a soft pulse are considered factors favoring the diagnosis of cold-wet Mizaj. Some sources also consider slowness and differences in the pulse as characteristics of cold Mizaj/dystemperament and phlegm dominance (24, 54, 56).

Soft tissue: In all PM sources, an increase in the amount of muscle and body fat is a sign of wetness, with increased body fat being a specific sign of coldness and wetness. Thus, obesity and fat accumulation are one of the important characteristics of cold-wet Mizaj, especially phlegmatic dystemperament (23, 24, 55, 56). Some literature points to flaccidity and flabbiness of soft tissues in all three cold-wet Mizaj groups (23, 24, 56). The two types of cold-wet dystemperament are accompanied by swelling of the hands, feet, and eyelids, although flaccidity of body tissues is a more emphasized symptom. In general, flaccidity is mostly due to an

increase in wetness, and the higher the ratio of wetness to coldness, the more severe this symptom is (23, 24, 55-57).

4.4. Physiological Indices

Slowness and weakness of physical and physiological body functions are signs of coldness. In some PM texts, an increase in the duration and depth of sleep, being influenced by wet and cold weather and foods, increased body excretions, slowness of movements, fatigue, low appetite, weak digestion, and low libido are signs of cold-wet Mizaj (23, 24, 54-56). Fatigue and weakness are emphasized as symptoms of simple cold dystemperament, but more specifically of phlegmatic dystemperament. A feeling of heaviness, accompanied by weakness, is also mentioned as a specific index of substance-dominant dystemperament. Weak digestion and sour belching are also indicative of phlegmatic dystemperament (23, 24, 54-57). Among physiological indices, the following indices have received more attention in this regard.

Sleep: Among the various characteristics of sleep, the duration and depth of sleep as well as dream content are the most important characteristics of Mizaj diagnosis. The duration and depth of sleep are increased in all three groups (23, 24, 55, 56). Drowsiness and dozing are other symptoms of cold-wet dystemperament. Dreaming of snow, white objects, cold, rain, lightning, water, and the sea have also been proposed as a specific indicator of phlegmatic dystemperament (23, 24, 54-57).

The reaction of the body to external factors: The response of individuals with a healthy cold-wet Mizaj to environmental qualities was not mentioned in any of the reviewed literature. In some sources, the speed of becoming cold when exposed to a cold environment has been noted as a sign of cold Mizaj, while discomfort in moist weather and preference for dry weather are indications of wet Mizaj (24, 54). Moreover, benefiting from hot-natured foods, experiencing adverse effects from cold-natured foods, and not feeling healthy in winter have been mentioned as signs of cold Mizaj (24, 54). Symptoms of phlegm dominance have not been mentioned under this index. Some PM sources consider a lack of or little thirst as a symptom of phlegmatic dystemperament (23, 25, 55, 56).

Body Excretions: Abundance and dilution of body secretions are signs of coldness and wetness. For instance, excessive nasopharyngeal secretions are a sign of coldness-wetness, while dilute secretions especially indicate wetness (55). Regarding types of dystemperament, drooling and rhinorrhea, and soft

stools are signs of cold-wet dystemperament (24, 54). Light-colored, odorless urine and sweat are signs of coldness (23, 24). Abundant viscous oral secretions and white, turbid urine are indicative of phlegmatic dystemperament (23, 24, 55, 56).

4.5. Psychological Symptoms

Mental and emotional states such as fear, forgetfulness, low-wittedness, dullness of the senses, being good-tempered, being influenced by the smallest issues, and slowness of speech favor cold-wet Mizaj (23, 24, 55, 56). Rapid resolution of situation-induced emotional states is a sign of wet Mizaj. Moreover, fear and lack of imagination are mentioned as symptoms of cold dystemperament (23, 24, 55, 56), while excessive forgetfulness is considered a sign of wet Su-e-Mizaj (24). Symptoms such as low-wittedness, dullness, and forgetfulness have been emphasized as signs of phlegmatic dystemperament (23, 24, 55, 56).

4.6. Underlying Factors

Persian scholars used various signs for the diagnosis of phlegmatic dystemperament, which can also be considered as underlying or predisposing factors to phlegmatic dystemperament. They include childhood and old age, lifestyle habits such as inactivity and overeating (especially cold-wet-natured foods like fish and yogurt that produce phlegm), bathing, occupation, winter, living in cold-wet climates, prolonged illness, and a history of phlegmatic diseases (23, 24, 55, 56).

5. Discussion

Today, the development of personalized medicine has been accompanied by a surge of studies examining the costs and benefits of this approach (3-5, 10, 11). The World Health Organization has set the expansion of complementary medicine as one of its important strategies to increase efficiency and reduce the costs of treatment (56-58). As one of the schools of complementary medicine, PM has dealt with individual differences via the concept of Mizaj to provide personalized lifestyle recommendations and treatments (15, 18, 19, 26).

This study was conducted to extract scattered indices of cold-wet Mizaj/dystemperament and phlegm dominance in PM literature. Precise diagnosis of cold-wet Mizaj/dystemperament relies on standardizing these indices. The results of the present study are the first step to the design of standard diagnostic tools such as questionnaires and checklists.

In 2014, Mojahedi et al. reported the cold-wet Mizaj indices based on PM literature, but they did not mention cold-wet dystemperament indices (28), while in the present study, cold-wet Mizaj/dystemperament and phlegmatic dystemperament were presented for the first time in a comparative manner in three axes of physical, physiological, and psychological indices.

Several studies have investigated the association between indices and Mizaj types. Although some findings are in line with PM theories, more studies are needed to prove these theories (19, 59-63).

Dr. Mojahedi's questionnaire effectively identifies the nine Mizaj types in a standardized manner, significantly aiding in the execution of interdisciplinary research projects thus far. However, for a more precise diagnosis of particular Mizaj/dystemperaments and to screen individuals for susceptibility to or early signs of Mizaj-related illnesses, the development and standardization of specific questionnaires across various axes of Mizaj/dystemperaments are essential.

Several studies have demonstrated connections between cold-wet dystemperament/phlegm dominance and associated conditions such as joint inflammation, depression, oligomenorrhea/amenorrhea, obesity, metabolic disorders, and chronic ailments characterized by weakness and fatigue (37, 38, 64, 65). The results from these studies suggest an association between the parameters examined in the PM sources and cold-wet dystemperament. A prevalent limitation in many of the mentioned studies was the absence of standardized diagnostic instruments, diminishing result validity and underscoring the importance of creating standardized tools in this domain. Backed by evidence, this methodology could enhance obtaining a comprehensive perspective and consequently, optimal treatment through Mizaj modification. Substantiating this hypothesis relies on the availability of standardized instruments for diagnosing cold-wet Mizaj or phlegm dominance. With the comprehensive features outlined for the range of cold-wet Mizaj, the outcomes of our research can serve as a basis for crafting pertinent standardized diagnostic instruments.

As summarized in Table 1, symptoms such as a small chest, narrow superficial veins, and short fingers are mentioned merely as symptoms of a healthy cold-wet Mizaj, and not of simple or substance-dominant dystemperament. Most of such indices are related to physical body structure and normal Mizaj and seem to be intended to determine primary Mizaj rather than being as useful in dystemperament. Theoretically, individuals with a basic cold-wet Mizaj are more vulnerable to cold-wet diseases when exposed to factors

that increase coldness and wetness (22, 52-55). Therefore, it is suggested that the aforementioned indices be considered as predisposing factors or minor criteria in diagnosing cold-wet dystemperament.

Phlegm dominance is also discussed in other medical schools, especially oriental medicine. An instance is phlegm patterns in TCM, which are similar to phlegm disorder in PM in terms of name and some characteristics. The common indices of phlegmatic disorders in PM and TCM include phlegmatic post-nasal discharge, nervous system disorders such as headache and sleepiness, digestive disorders such as indigestion, poor appetite, stomach fullness, and mucous stool, feeling of heaviness or weakness in the limbs, fatigue, and joint pain (13, 45-47). Considering the importance of diagnosis and the association between phlegm patterns and various diseases including cardiovascular disorders, TCM researchers have developed standard diagnostic questionnaires (13, 47).

There are many similarities between some syndromes in TCM and disease symptoms in PM, which need more comparative studies in this field. According to TCM, yin and yang balance brings about health, and an imbalance between them indicates unhealthiness. In TCM, there are various syndromes, each of which indicates a specific physiological or pathological status. Among them, symptoms of yang deficiency syndrome have similarities with simple cold-wet dystemperament, and symptoms of phlegmatic syndrome are similar to substance-dominant cold-wet dystemperament in PM (15, 24, 66).

Evaluating the points of agreement and differences between diagnostic indices of phlegmatic disorders in TCM and PM, and other similar syndromes can help find commonalities between the two ancient schools of medicine and use the potential capacities of these medical schools along with modern medicine in personalized diagnosis and treatment.

The fundamentals of Ayurvedic medicine share several similarities with PM, including the use of lifestyle modifications in disease prevention and treatment, as well as the consideration of physical, physiological, and psychological characteristics in assessing the body's state. Ayurveda proposes the tri-dosha theory, wherein the characteristics of Vata, Pitta, and Kapha in an individual's body are determined based on various indicators. However, close resemblances between cold-wet dystemperament in PM and Ayurvedic definitions were not found.

On the other hand, some similarities have been observed between the symptoms of certain diseases in modern medicine and the indices of cold-wet

dystemperament in PM. In 2019, Fatemi Tekieh et al. identified similarities between symptoms of hypothyroidism and cold dystemperament, including fatigue, increased cold sensitivity, a puffy face, unexplained weight gain, arthritis, and depression. Based on these findings, the authors proposed clinical studies to explore the correlation between thyroid-related factors and cold dystemperament in PM (67).

While some symptoms of PM's dystemperament and certain diseases in modern medicine may resemble each other, these similarities cannot fully explain the similarity of illnesses between these two medical schools. Integrative medicine could utilize this finding as a guiding principle.

5.1. Conclusions

This study reports the classification and relative importance of each indicator of cold-wet Mizaj and dystemperament. The results serve as a foundation for the standardization of diagnostic indices for cold-wet Mizaj and dystemperament, an important Mizaj group in PM.

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Footnotes

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