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Design and Validation of Mizaj Identification Questionnaire in Persian Medicine

Hossein Salmannezhad [1], Morteza Mojahedi [2,3,*], Abbas Ebadi [4], Seyyed Ali Mozaffarpur [2], Abbas Alipoor [5], Roshanak Saghebi [2] and Ali Montazeri [6]

[1]Department of Persian Medicine, School of Persian Medicine, 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 History of Medical Sciences, School of Persian Medicine, Babol University of Medical Sciences, Babol, Iran
[4]Behavioral Sciences Research Center, Nursing Faculty, Baqiyatallah University of Medical Sciences, Tehran, Iran
[5]Thalassemia Research Center, Mazandaran University of Medical Sciences, Sari, Iran
[6]Population Health Research Group, Health Metrics Research Center, Iranian Institute for Health Sciences Research, ACECR, Tehran, Iran

[*]*Corresponding author*: Babol University of Medical Sciences, Gangafrooz St., Babol, Iran. Tel: +98-1132194728-30, Fax: +98-1132194728, E-mail: mortazamojahedy@gmail.com

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Abstract

Background: Paying attention to individual differences in presenting health directives is the most important properties of Persian Medicine (PM). Accordingly, individuals in each society are divided into nine Mizaj groups. Access to the standard diagnostic scale is one of the research priorities of PM.
Objectives: The present study aimed at designing a preliminary self-administered Mizaj questionnaire, and assessed its reliability and validity.
Materials and methods: For this exploratory sequential study, Mizaj identification indices were extracted using PM references, and people and PM experts' interviews. The preliminary questionnaire was designed and the validity and reliability of the questionnaire were evaluated using weighted Kappa statistics (> 0.4), ICC and ROC curve, and determining the sensitivity and specificity of cut-off points.
Results: Overall, 15 PM experts, and 221 volunteers participated in various stages of this study. Among 119 designed questions for 30 Mizaj identification indices, 60 items had acceptable reliability. The final questionnaire containing 20 items was extracted after the validity assessment. The sensitivity and specificity of this questionnaire at the specified cut-off points were 71% and 68% for warmness, 63% and 71% for temperance in warmness-coldness, 80% and 57% for coldness, 74% and 58% for wetness, 71% and 69% for temperance in wetness-dryness, and 78% and 85% for dryness, respectively.
Conclusions: This is the first standard Mizaj identification questionnaire, which includes more dimensions of Mizaj identification and can be used for individuals aged 20 to 60 years old. This questionnaire is recommended for Mizaj identification researches and as a supplementary diagnostic scale for clinical activities of Persian Medicine practitioners.

Keywords: Precision Medicine, Questionnaires, Reproducibility of Results, Temperament, Validation Studies

1. Background

In recent years, a variety of activates by research and educational centers have created awareness and a platform to introduce and promote Persian medicine to the world (1). The World Health Organization (WHO) has demanded more significant attention to traditional medicines for various reasons, including dissatisfaction of patients with treatments in some areas of modern medicine and the lack of access to modern health services for a large number of people in some parts of the world (2). Persian Medicine (PM) has evolved over many years, and it has been used through centuries as the common medicine in many countries (3). Based on the teachings of the PM, maintaining health should precede treatment (4). Furthermore, PM known as Mizaj Medicine has its basic diagnostic and therapeutic focus on the theory of Mizaj and the balance of humors (5). The model adopted by PM in explaining the concept of Mizaj is very similar to Personalized Medicine because, in both perspectives, individual differences are considered as the most important part of diagnostic measures and therapeutic interventions (6). According to the theory of Mizaj, each creature is created from the mixture of four elements of air, fire, water, and earth, the qualities of which are warm and wet, warm and dry, cold and wet, and cold and dry, respectively (7, 8). The reaction between these el-

ements and the effect of their qualities on each other results in a unique combination of qualities that is specific to each individual, named Mizaj (9). Considering the mixture of the four mentioned qualities, nine general Mizaj categories can be considered. These Mizajes will be a mixture of warmness, temperance, and coldness on one hand, and wetness, temperance and dryness on the other (10). In PM, various indices have been used to identify Mizaj, which are categorized to ten groups called "ten criteria of Mizaj identification" (Ajnas-e-ashareh), which include several physical, physiological, and psychological characteristics of individuals (7, 10). These criteria include the characteristics of touch, muscle and fat mass, hair, skin color, physique, the speed of impressibilities, sleep and wakefulness, physical functions, waste matter, and mental functions (3, 10).

It was only in the recent decades that the approach to the unique characteristics of individuals in diagnosing and responding to treatment has been the focus of attention of many scholars of Modern medicine, whereas individual differences have already been the main focus of health and medical approaches of old medical schools, including PM for a very long time (10, 11). Today, modern medicine is looking for specific ways to diagnose and treat each individual through different approaches (12), such as "Nutrigenomics", "Pharmacogenomics", "Precision Medicine", and "Personalized Medicine" so that by choosing the best medicine and dose for each individual, he or she will get the best treatment results with minimum side effects (13-15).

In PM, health and therapeutic instructions are different from one person to another (16), and therefore, the recognition of each person's Mizaj plays a pivotal role in the pursuit of health and disease (3).

Considering the importance of Mizaj identification in PM and the abundance of its indices, a major concern of PM experts is to provide proper Mizaj identification scales (17). The presence of such scale, besides being used clinically, can be very useful in research projects that need to identify the Mizaj of the participants (3, 16). Most studies that investigated the relationship between Mizaj and physiological characteristics or diseases have usually not used standard methods of Mizaj identification, which can be a disadvantage to research in PM (18). Only in one study entitled "Hot and Cold Natures and Some Parameters of Neuroendocrine and Immune Systems in Traditional Iranian Medicine", Shahabi et al. claimed that warmness or coldness of the subjects was identified using a standard questionnaire. However, the researchers did not mention the source of the questionnaire in their work or if the questionnaire was designed by them, they did not report the standardization procedure (18). The only reliable Mizaj identification scale is self-reported "Mojahedi's Ten-Item Mizaj Questionnaire" (MMQ), which was designed and validated in 2014 (10). Despite the ease of use and clarity of scoring in MMQ, the absence of some Mizaj indices, lack of sufficient sample size and low sensitivity and specificity for wetness-dryness are among the limitations of the mentioned study; furthermore, this Questionnaire was validated by participation of 20- to 40-year-old volunteers, which is a limited age range and can be extended in future surveys. The aim of this study was to design a self-reported scale for Mizaj identification among 20- to 60-year-old individuals.

2. Methods

This study was conducted between 2015 and 2016, in Babol, Iran, and the Ethical code was received on 24th of April 2015 (Mubabol.rec.1394.99). This research was an exploratory sequential study, which was carried out in two stages of production and reduction of items. In the first phase, a qualitative method was applied to produce items and in the second phase, a quantitative cross-sectional method was used for psychometric analysis of the scale (19).

2.1. Item Generation

2.1.1. Qualitative Study

This section aimed at determining the dimensions and characteristics of Mizaj based on PM literature, the opinion of experts, as well as the determination of terms in folk literature vocabulary.

In the first step, all of the properties related to ten criteria of Mizaj identification were extracted by reviewing selected PM texts, including Al-Qanun fi al-Tibb (The Canon of Medicine), Kamil al-Sinaa al Tibbiyah, Kholasat al-Hikmah, and Exir-e-Azam, as well as articles written in the recent years by PM scholars in the area of Mizaj.

In the second step, by conducting a semi-structural interview with PM professors with more than ten years of clinical experience, their experiments and clinical practices on Mizaj definition were gathered.

In the third step, different groups of people aged 20 to 60 years in Babol city were selected from both genders with different social and educational backgrounds using purposive sampling. They were assessed through semi-structural interviews to explain their personal properties about ten Mizaj identification criteria.

2.1.2. Item Pool Generation

Selected phrases from written sources and interviews were associated with one of the ten criteria of Mizaj identification. Words and sentences with higher frequency and clarity were selected to design the questionnaire.

In this step, a team of five researchers, including three PM experts and two psychometrics with more than five years of clinical or research experience, designed the item pool. This collection included all items related to areas of Mizaj identification with a five-dimensional Likert scale that covered a spectrum of coldness-warmness or wetness-dryness of Mizaj identification indices.

2.2. Primary Validity Assessment

2.2.1. Qualitative Face Validity

The initially designed questionnaire was given to 40 volunteers of both genders, including PM specialists, students and other strata of people with different ages (20 to 60 year). They were asked to comment on the clarity, simplicity, and semantic understanding of items and related options and offer their suggestions; then the necessary corrections were made for the best clarity and simplicity.

2.2.2. Content Validity

Fifteen professors and faculty members working at schools of PM with more than five years educational research and clinical experience were invited. The content validity of the questionnaire was carried out in two phases:

In the first phase, a questionnaire was prepared to set up the Content Validity Ratio (CVR) and options related to determining the necessity of using the item, including "necessary, useful but not necessary, and not necessary" were presented for each item. The experts were asked to choose one of the options and comment on the necessity of the items (20).

In the second phase, the Content Validity Index (CVI) was investigated in two steps. First, the Bausell and Waltz method was used to specify the Item Content Validity Index (I-CVI). For this purpose, the extracted questionnaire from the first phase was sent to experts, and they were asked to allocate a score of four to one to each option (completely relevant, relevant, relatively relevant, and not relevant), regarding the relevance of each item to the field (15, 21, 22).

2.3. Reliability Assessment

The reliability of the questionnaire was measured using the test-retest method. In this step, four health centers in different regions of Babol, Northern Iran, were randomly selected and 30 families were randomly extracted from each center. All members from mentioned families, who met the desired inclusion and exclusion criteria, were invited for different stages of the study. The inclusion criteria included voluntary participation and age range of 20 to 60 years. The exclusion criteria included chronic disease, pregnancy and menstrual period, continuous use of medications, drug or alcohol addiction, and withdrawal from voluntary participation. After explaining the objectives and methodology of the research by the researchers and signing the written consent form, they were also assured that their information would remain confidential. The participants were asked to complete the questionnaire extracted from the content validity step. The questionnaire was re-completed two weeks later (23).

2.4. Secondary Validity Assessment

A team of three PM experts with at least ten years of clinical experience in Mizaj identification were invited to collaborate, and they visited the volunteers one by one at one time in an examination room. According to the expert agreement, the Mizaj of each volunteer was determined in two categories of coldness-warmness (cold, temperate, and warm) and wetness-dryness (wet, temperate, and dry). At the same time, the volunteers completed the questionnaire from the reliability stage. The sample size required for this step was estimated as three to ten volunteers per item (24).

To evaluate the weight of the items in the identification of coldness-warmness or wetness-dryness, the options of the items as well as the diagnosis of experts were transformed into binary states. Therefore, six binary state models were created for Mizaj identification (cold, temperate, warm and wet, temperate, and dry). For example, to assess the weight of items in the coldness model, volunteers, whose Mizaj was identified by experts to be cold, were labeled one and others were labeled zero. On the other hand, in each item, volunteers, who chose the first and second options (which expressed the coldness or wetness) were labeled one and the volunteers, who chose other options were labeled zero, and so on. In the next step, the correlation between each item and the experts' diagnosis was assessed by Binary Logistic Regression method, and the Odds Ratio (OR) was calculated for each of the states in each item (experts diagnosis was considered as the standard). Considering the resulting values, each item was labeled with coldness-warmness or wetness-dryness. As a result of this step, questions that had an acceptable OR ($OR > 1$) were selected at least in one of the six models (coldness, temperance, warmness and wetness, temperance, and dryness) and were kept for the next step while others were deleted.

In the second step, questions related to the same area (coldness-warmness or wetness-dryness) were placed in one subscale, and again by Binary Logistic Regression method, the OR of items was calculated in the model. Similar items in each subscale were determined and those that had the highest OR in the model were selected, and others were deleted. Eventually, a model with a specified number of items was extracted to determine the warmness-coldness, named warm/cold subscale, and another model

with a specified number of items was used to determine wetness-dryness, named wet/dry subscale.

In the third step, Receiver Operating Characteristic (ROC) Curve was used to determine the cut-off points of the two warm/cold and wet/dry subscales of the final questionnaire (experts diagnosis was the gold standard and the questionnaire was used as a test). After selecting the best cut-off points in the six states of coldness, temperance, warmness and wetness, temperance and dryness, their sensitivity and specificity were calculated as the final step of the survey.

2.5. Statistical Analysis

For content validity assessment, the following formula was used to determine the CVR value:

$CVR = \frac{ne - N/2}{N/2}$

ne: number of experts, who had chosen the "necessary" option, N: total number of experts.

Based on the number of experts, the approved Lawshe table of items was selected for the second phase, using the suggested percentage (20).

Item Content Validity Index (I-CVI) was calculated by dividing the number of experts, who agreed (rank three or four for each item), by the total number of experts (15). In this method, items with a score higher than 0.79 were appropriate, between 0.70 and 0.79 needed modification, and less than 0.70 were considered unacceptable (21).

In order to calculate the total score of the Scale-Content Validity Index (S-CVI), the sum of I-CVI of the approved questions was divided by the total number. An acceptable cut-off point for the total score was considered 0.8 (22).

For reliability assessment, Weighted Kappa statistics (WK $>$ 0.4) was used for each item. Cronbach's alpha coefficient was used to assess internal consistency, and the Interclass Correlation Coefficient (ICC $>$ 0.7) was used to assess the stability of total score (23).

For secondary validity assessment several statistical analysis were used, binary logistic regression method for extraction of the best model of final questionnaire, and ROC curve to determine the best cut-off points of the two warm/cold and wet/dry subscales of final questionnaire. All processes of the analysis were done with the IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA).

3. Results

3.1. Item Generation

Overall, 30 indices, which were extracted based on reliable PM references and interviews, were categorized into ten groups called "ten criteria of Mizaj identification." The research team designed two to six questions with appropriate options for each criteria, as the item pool. The initiative 119-item questionnaire was the result of this step (Table 1).

3.2. Primary Validity Assessment

Among 40 invited volunteers, 35 volunteers commented on the 119-item initial questionnaire for face validity assessment. Seven items that did not have adequate clarity and fluency, according to the opinion of most volunteers, were omitted and some items were modified. Then, the 112-item questionnaire was again given to the same volunteers for second assessment, and all the 112 items remained unchanged due to the lack of a new suggestion.

In order to perform the content validity stage, of 20 qualified PM experts, who were invited from five academic centers, 15 experts, six (40%) female and nine (60%) male, who were on average 45 $\pm$ 7 years old and had 12 $\pm$ 2 years of clinical experience in PM Medicine completed the forms. The place of their work was Tehran, Babol, Mashhad, Esfahan, and Shiraz University of Medical Sciences. The CVR and CVI values were calculated for each item. According to the Lawshe table, the minimum score for 15 experts in CVR was 0.49, and the questions that did not meet this minimum level were eliminated (25). In case of I-CVI, questions with a content validity index of less than 0.7 were omitted and seven items, which had a score from 0.7 to 0.79 were edited; the modified forms were sent to experts for the second time and final I-CVI values were calculated. Finally, 38 items, which did not meet the designed requirements (CVR $<$ 0.49 or I-CVI $<$ 0.79) were omitted and 74 questions remained as the final result of this stage (Table 1). The S-CVI value was found to be 0.93 for the 74-item questionnaire.

3.3. Reliability Assessment

In order to perform a reliability assessment of the questionnaire, 105 twenty- to sixty-year-old volunteers were invited from both genders. Of these, nine volunteers refused to participate in the study, 12 volunteers were excluded from the study due to a chronic disease, and 11 volunteers could not finish the second phase of the questionnaire completion on time. Finally, 73 volunteers completed the questionnaire in two test and retest stages with a two-week interval. Cronbach's alpha for test and retest stages was 0.77 and 0.80, respectively.

The calculated ICC for the 74-item questionnaire final score was 0.88 (0.82 to 0.93). According to the Weighted Kappa (WK) assessment, 14 items, which had a WK less than 0.4 were omitted (26) and the number of items reached 60 (supplementary file. Appendix 1).

The Cronbach's Alpha of the remaining 60 questions at the test and retest stages was 0.69 and 0.74, respectively,

Table 1. The Number of Items for Each of the Ten Mizaj Identification Criteria and Their Decreasing Trend in Various Steps of Validity and Reliability

Mizaj Identification Criteria, Indices of Criterion	Number of Items After Each Step				
	Item Generation	Face Validity	Content Validity	Reliability	Validity Assessment
Touch					
Warm - cold	5	5	4	3	1
Wet - dry	4	4	2	1	0
Nail	2	1	0	0	0
Muscle and fat mass	6	6	3	3	2
Hair					
Growth	2	2	1	1	0
Color	2	2	1	1	0
Amount	1	1	1	1	1
Diameter	1	1	1	1	0
Hairstyle	4	3	2	2	0
Skin color	2	2	2	2	1
Physique	11	10	6	6	3
Impressibility speed					
Temperature	9	8	7	7	1
Food	3	3	3	2	1
Humidity	2	2	0	0	0
Sleep and wakefulness	5	5	4	4	1
Physical functions					
Somatic	16	16	10	6	3
Verbal	6	6	4	4	2
Quality of waste matter					
Sweat	2	2	1	1	0
Stool	1	1	0	0	0
Urine	2	1	1	0	0
Psychic function					
Learning speed	2	2	1	0	0
Self confidence	10	9	6	4	2
Irritability	4	4	4	2	0
Speed of anger	3	3	3	2	0
Memory	2	2	2	2	0
Optimism	2	2	0	0	0
Happiness	3	3	1	1	1
Community relations	6	5	3	3	1
Excitement	1	1	1	1	0
Total	119	112	74	60	20

and the ICC of total scores of the two stages was 0.901 (0.841 to 0.938).

3.4. Secondary Validity Assessment

Among 240 volunteers visited by the team of experts, nine were excluded due to the exclusion criteria and ten volunteers were excluded due to a lack of final agreement among the experts in Mizaj identification. Finally, the Mizaj of 221 volunteers was confirmed by a team of three PM experts and at the same time, they completed the 60-item questionnaire. The mean of the experts' age was 39 $\pm$ 4.3 years old. One of them was female and they had 10 $\pm$ 2.5 years of clinical experience. According to the results of Binary Logistic Regression analysis, 38 items, which had a significant relationship between the answers of the volunteers in one or more options and the view of experts (OR $>$ 1), were kept, and 22 items with low OR (OR $\leq$ 1) were omitted. Then, the items that measured a common index in

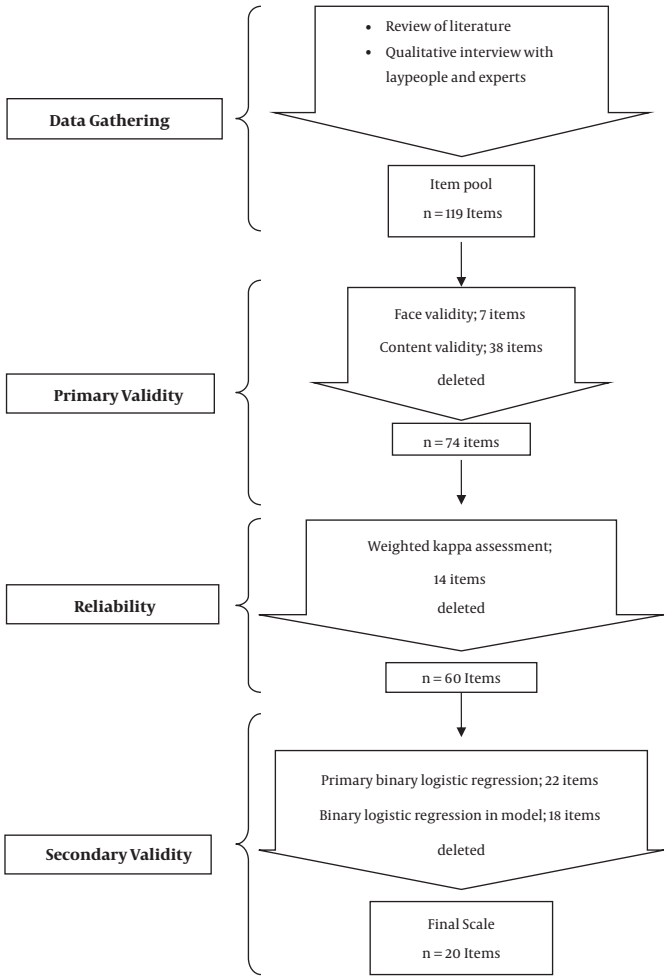

Figure 1. Flowchart of outline of the study protocol

each area (warm, temperate, cold and wet, temperate, and dry) were defined in six separate models and again binary logistic regression was performed. Finally, 18 items were omitted and 15 items, which obtained the highest Odds Ratio in the three models of coldness, temperance and warmness, were named cold-warm subscale, and five items in the three wetness, temperance and dryness models, were named wet-dry subscale. The final questionnaire with 20 items was prepared for the scoring phase (supplementary file. Appendix 2).

3.5. Scoring

The ROC curve was plotted to determine cut-off points based on experts Mizaj identification. Best cut-off points according to the area under curve selected, and sensitivity and specificity of the cut-off points, were extracted. As respected, each item score ranged from one to five; the score for the 15-item cold-warm subscale was considered to be 15 to 75, and for the five-item wet dry subscale, this was 5 to 25. The results showed that the effect of the ceiling and floor in this study was zero. The specified cut-off points and calculated sensitivity and specificity are shown in Table 2.

4. Discussion

This study was conducted to design and validate the second standard instrument in Mizaj identification after MMQ and the first scale for Mizaj identification in 20- to 60-old-year people. According to PM principles, Mizaj identification is one of the most important prerequisites for the

Table 2. Subscales of Mizaj Questionnaire and Specific Cut-Off Points

Subscales, Domain	Score	Sensitivity, %	Specificity, %
Warm-cold			
Coldness	≤ 46	80	57
Temperance	47 - 49	63	71
Warmness	≥ 50	71	68
Wet-dry			
Wetness	≤ 14	74	58
Temperance	15 - 16	71	69
Dryness	≥ 17	78	85

diagnosis of health status and illness (6, 10). From this perspective, therapeutic intervention and dietary recommendations are incomplete without Mizaj identification (3, 27). In recent years, efforts have been made to design and validate Mizaj identification questionnaires, for example, Ahmadi et al. in 2014 reported that they designed a scale to identify innate Mizaj (28), while Roshandel et al. in 2015 reported that they designed a scale to identify innate Mizaj and health Mizaj (29). Unfortunately, both of these studies lacked a gold standard for Mizaj identification and some of the validation steps, such as content validity process and reliability, were not properly performed. In addition, the questions of these questionnaires were not clear and the scoring method was not specified. Instead, in Mojahedi et al.'s study, 10 PM professors collaborated to determine the content validity, and besides, the consensus of the expert panel was used to identify the Mizaj of volunteers as a gold standard (30). Hence, the current study could only be compared with Mojahedi's survey. In the current study, 15 experts participated to assess the content validity, and a significant increase was observed in sample size (221 subjects compared with 52). Considering all Mizaj identification indices, 119 questions were designed as an item pool in the first step, which is much more than the number of initial questions in Mojahedi's survey. After the initial validation phase, 60 questions remained, which was 21 questions more than Mojahedi's study.

In reliability assessment, the number of items with acceptable reliability in this study was higher than Mojahedi's study (60 items versus 39 items). The highest number of questions in both studies was related to psychic and physical functions. Sleep-related items had the lowest Kappa in Mojahedi's study, while in the current study, four sleep-related items showed acceptable Kappa, which can be attributed to the subject of questions and their design.

According to the final questionnaire resulting from this study (supplementary file. Appendix 2), 20 extracted questions cover nine areas of ten criteria of Mizaj identification, while MMQ covers six areas. The highest number of questions in both of the questionnaires is related to physical function, and none of the two questionnaires cover waste matter indices. In addition, MMQ was standardized with 20- to 40-year-old participants, while the present questionnaire was designed and standardized with 20- to 60-year-old volunteers. Another point of this study was that the sensitivity of warm, cold, dry and wet cut-off points and so the specificity of the dry cut-off point were higher than MMQ. On the other hand, the specificity of MMQ in its warm, cold, and wet cut-off points was higher than the current study, therefore, this questionnaire can be more efficient in screening MMQ for diagnostic studies (30). Another achievement of this study was the assessment of the sensitivity and specificity of temperance cut-off points in warmness coldness and so wetness dryness compared with Mojahedi's survey, which is because the low sample size of temperate volunteers was not enough to calculate the sensitivity and specificity of their cut-off points.

The current study had some limitations and weaknesses that should be considered in the future. The first limitation was the exclusion of some indices of ten Mizaj identification criteria. Although there were considerable related questions in the initial questionnaire, they were eliminated at different stages of validation due to a lack of desired coefficients. Since these results were similar to the results of Mojahedi's survey, it is suggested that in the future, the metric relationship between these indices should be considered, especially those related to skin temperature, anthropometric indices, skin color, and hair indices. The other limitation was the lack of access to the weight of each criterion in Mizaj identification. Since some of these ten criteria, such as psychic and physical functions, which include several indices according to PM literature, have more items in the initial questionnaire and remained in the final version, the weight of these criteria increased in the current questionnaire. However, this alone does not indicate the greater role of these criteria in Mizaj identification. The strengths of this study were a larger sample size, and the usage of ordinary people's opinions to produce clear sentences in the questions. More specific studies need to assess the weight of each criterion in Mizaj identification. Furthermore, since the aim of this survey was ease of use for researchers in Mizaj identification, it did not compute the impact of each item according to its OR in final questionnaire. It is suggested for future studies to assess the exact impact of ten criteria and their indices for Mizaj identification.

4.1. Conclusion

The present questionnaire passed through all steps of design, reliability, and validation assessment of a standard diagnostic scale in medicine. After MMQ, this questionnaire can be used as the second scale for Mizaj identification by therapists as a supplementary scale for Mizaj identification. It can also be a standard scale for Mizaj identification in Mizaj-related researches. According to the current results, the cut-off points in coldness, wetness, and dryness of the present questionnaire had higher sensitivity than MMQ, despite MMQ cut-off points having higher specificity. Therefore, the researchers recommend this questionnaire for screening Mizaj studies and MMQ for diagnostic Mizaj surveys in PM.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

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Footnotes

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