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Association of functional dyspepsia with selected dermatology complaints and sleep disturbances based on traditional Persian medicine

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Background: Functional dyspepsia (FD) is a common disorder of the upper gastrointestinal tract. Several documents in conventional medicine claim an association between FD, sleep disturbance, and some dermatological conditions, but there is still debate about these relationships. This study aimed to measure the association between FD and some skin problems and sleep indices based on the attitudes of traditional Persian medicine.

Methods: This study was carried out on patients with the diagnosis of FD and healthy people. The study population consisted of patients who referred to the gastroenterology clinic of Shiraz University of Medical Sciences (Shiraz, Iran) from July to December 2019. To diagnose dyspepsia, we used Rome III criteria. Skin problems and sleep indices were evaluated using a validated researcher-made questionnaire. P-values of ≤ 0.05 were considered significant.

Results: Overall, 160 patients (46 men and 116 women) with FD and 155 healthy individuals (36 men and 119 women) were enrolled in the study. There were significant differences between patients and healthy individuals in terms of dryness of skin (P = 0.001), oily hair, deep sleep, long sleep, insomnia, difficulty sleeping, fatigue after sleeping, and nightmares ($p \leq 0.001$). On the other hand, there were no significant differences between the groups in intermittent sleeping (P = 0.116) and periorbital edema after sleeping (P = 0.195).

Conclusions: According to the results of this study, it seems that there is a positive relationship between FD and some dermatological and sleeping indices based on traditional Persian medicine resources.

Keywords: dyspepsia, sleep, dermatology, traditional medicine

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INTRODUCTION

Dyspepsia is one of the most common digestive disorders, possibly affecting up to 25% of the adult population [1]. About 2-3 percent of the primary visits of general physicians, 30 percent of patients referring to the internal clinics, and 50 percent of patients referring to the gastroenterology clinics suffer from dyspepsia. The prevalence of dyspepsia in western societies and developing countries is relatively conspicuous. This figure reaches 5.8% in Iran [2,3].

Functional dyspepsia (FD) is a biological and psychological disorder caused by impairment in the digestive system, an unhealthy diet, infection with *Helicobacter pylori*, and increased visceral sensitivity [4-6]. FD is a chronic upper gastrointestinal (GI) disorder in the absence of organic disease or biochemical abnormality. Symptoms include epigastric pain and/or upper abdominal pain, postprandial fullness, gastric bloating, early satiety, and nausea [7]. Upper GI tract endoscopy is the standard method to diagnose FD, which is also called dyspepsia without ulcer [8].

Based on the principles of Traditional Persian Medicine (TPM), dyspepsia is the source of several physical disorders, including skin and psychological conditions [9,10]. For example, if a person who has just recovered from an illness shows the symptoms of dyspepsia, it is a serious warning that the illness is going to relapse. While the food enters the stomach, incomplete digestion would happen in the presence of dyspepsia, potentially endangering a person's physical health [7,8,11].

Although the course of FD is not associated with death, it brings a reduced quality of life, huge expenses for treatment and care, and a high burden to society [12]. The cost of care for every patient with dyspepsia is high, including both direct (visits, drugs, laboratory tests, and hospital fees; 80%) and indirect costs (days of unemployment and loss of efficiency; 20%). Hence, the annual cost of dyspepsia in the United States is estimated at more than 8 billion US dollars [12,13].

Nutrition is one of the most important factors associated with skin diseases and mental illnesses [14-16]. It is estimated that 20-50% of patients who are hospitalized acutely have a degree of malnutrition, which leaves several effects on the structure and function of the skin and also affects the brain [17]. For example, malnutrition may alter the structure of the skin and physiological changes including altered pigmentation, atrophy and reduction in the number of hair follicles, hair thinning, and the impaired healing of complex wounds [18]. In addition, malnutrition can have negative effects on mental and psychosocial indices as well as sleep indicators [19-21]. The present study attempted to verify the association of FD with some dermatologic problems and sleep indices.

MATERIALS AND METHODS

Study design and sample size

This was a cross-sectional study with convenience sampling. The study population included all patients with complaints of indigestion or ulcer (persistent and recurrent pain or discomfort in the upper abdomen, early satiety, postprandial fullness, bloating, nausea, and vomiting) who were diagnosed with FD by an experienced gastroenterologist at the Motahari gastroenterology clinic affiliated to Shiraz University of Medical Sciences (Shiraz, Iran) from July to December 2019. Using the two-proportion comparison formula based on the trouble falling asleep percent reported by Lacy *et al.* (43% in patients with FD and 28% in healthy individuals) [22], with a 90% study power and a confidence level of 95%, the minimum sample size was calculated as 155 participants in each group.

The inclusion and exclusion criteria

The simple and available sampling method was performed to enroll the patients into the study. Sampling was continued until attaining enough numbers of patients considering the inclusion and exclusion criteria of the study. The inclusion criteria were patients aged 20-60 years who were confirmed cases of FD according to Rome III criteria, with upper GI tract organic disorders having been ruled out through upper GI tract endoscopy by a gastroenterologist. To minimize the effects of confounding factors, the healthy individuals were selected from the patients' relatives who volunteered to participate in the study given that the patients and their relatives had relatively similar lifestyles and food habits. The participants of the healthy group had no complaint of GI problems and FD according to Rome III criteria in the preceding two years and failed to fulfill the necessary criteria of FD when interviewed by the same physician.

The exclusion criteria included pregnant and lactating women, patients with a positive history of GI tract cancers, GI tract surgeries, treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), or any medications that cause GI disturbances, patients with a history of pancreatitis or systemic hepatobiliary disorders, and known cases of specific skin or psychological disorders.

Data collection

To diagnose FD, the Rome III diagnostic criteria were used. After endoscopic examination, patients without upper GI disorders were enrolled in the study. To assess the sleep and skin complaints of the patients, a researcher-made checklist was used. In this regard, a physician asked the patients about their symptoms concerning selective sleeping and skin conditions.

Characteristics of the researcher-made checklist

The researcher-made checklist consisted of 10 common chief complaints of patients with FD (*Sou-e-hazm* in TPM) according to the textbooks of TPM. The psychometric properties of the checklist were assessed in a pilot study. In this regard, the face validity and content validity of the checklist were approved by a four-member group consisting of two specialists in TPM, a dermatologist, and a psychologist. The dermatologic and sleep complaints were scored by the patient based on a Likert scale from 0 (no symptoms) to 6 (severe symptoms). The complaints included oily hair (a chronic hair condition that is characterized by the continuous development of natural grease on the scalp), dry skin (a distressing condition characterized by scaling, itching, and cracking of the body skin), deep sleep (a type of sleep characterized by feeling refreshed when you wake up in the morning), long sleep (sleeping more than 8 hours per night), insomnia (chronic sleeplessness characterized by sleeping less than 3 hours per night), difficulty sleeping (a type of problem characterized by sleeplessness for more than 2 hours when going to bed), intermittent sleeping (a type of problem characterized by awakening more than 4 times during the sleep period), fatigue after sleep (a type of tiredness characterized by persistent sleepiness and a general lack of energy during daytime), nightmares (a type of disturbing dream characterized by undesirable feelings such as anxiety and fear that awaken the person), and periorbital edema (a condition characterized by swelling around the eyes or eye orbit after awakening). Finally, the mean scores were calculated to evaluate the patients' answers.

Ethics statement

The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (code: IR.SUMS.MED.REC.1397.529). All participants were informed about all aspects of the study and written informed consent was obtained.

Statistical analysis

Statistical analysis was performed using SPSS version 21. To describe quantitative data, the mean and standard deviation (SD) were used; for qualitative data, the chi-squared test was performed. Quantitative data were compared using the independent t-test.

RESULTS

Overall, 160 patients including 46 males (28.75%) and 114 females (71.25%) suffering from FD were enrolled in the case group and 155 healthy individuals including 36 males (23.22%) and 119 females (76.78%) comprised the control group. There were no statistically significant differences between the groups in terms of basic demographic characteristics, except for age and body mass index (BMI). However, according to Cohen's d value, the differences between mean age (d-value = 0.24) and body mass index (d-value = 0.25) between patients and healthy individuals did not disrupt the comparison of other variables. The demographic characteristics of the participants are presented in Table 1.

There were significant differences between patients and controls in the average scores of two considered dermatological indices, namely oily hair and dry skin (Table 2). Furthermore, the results of the study showed that there were significant differences between the groups in all considered sleep indices ($p < 0.001$), except for intermittent sleeping ($P = 0.116$) and periorbital edema after sleeping ($P = 0.195$) (Table 3).

DISCUSSION

The present study showed a significant association between FD and some dermatological and sleep disturbance complaints. In other words, our findings showed that patients with FD suffered

Table 1. Demographic characteristics of the patients with functional dyspepsia and the healthy individuals of the control group

Variables	Functional dyspepsia group	Control group	P-value	Cohen's d value
Age (mean ± SD)	37.92 ± 11.68	35.07 ± 11.16	0.027	0.24
BMI (mean ± SD)	24.38 ± 4.26	25.47 ± 4.50	0.027	0.25
Gender (n)				
Male	46	36	0.264	
Female	114	119		
Marital status				
Married	121	110	0.302	
Single	39	45		
Education level				
Illiterate	19	14	0.449	
Primary school	18	13		
Early secondary school	20	13		
Late secondary school	60	65		
University degree	43	50		
Ethnicity				
Fars	112	118	0.117	
Lor	15	13		
Turk	33	21		
Kurd	0	3		

Table 2. Comparison of patients with functional dyspepsia and the healthy individuals in the control group according to selected dermatology indices based on Traditional Persian Medicine

Skin condition (mean ± SD)	Functional dyspepsia group (n=160)	Control group (n=155)	*P*-value
Oily hair	3.79 ± 1.71	3.22 ± 1.40	< 0.001
Dry skin	3.30 ± 1.68	2.71 ± 1.59	0.001

from selected dermatological and sleep problems significantly more than individuals without FD. Accordingly, the case group (FD) suffered more from oily hair and dry skin than the healthy individuals. Consequently, it can be stated that FD can be associated with some skin and hair problems. The other findings of this study suggested significant differences in the rates of certain sleep disorders between patients with FD and healthy controls. Specifically, patients with FD suffered more from insomnia, difficulty sleeping, fatigue after sleep, and nightmares than healthy individuals. The patients also showed more problems in experiencing deep sleep and long sleep. Hence, FD had a negative effect on the quality of sleep in this group of patients.

Gastrointestinal disorders, especially gastric diseases, are highly important in TPM as it is believed that gastric diseases could be the underlying cause of other diseases [9,23-25]. According to TPM books, most patients with FD suffer from extra-abdominal symptoms including dermatology problems and sleep disturbances [9,26]. The results of this study were largely in line with the concepts of TPM sages about the extra-abdominal symptoms associated with FD. Based on the principles of TPM,

Table 3. Comparison of patients with functional dyspepsia and the healthy individuals in the control group according to selected sleep indices based on Traditional Persian Medicine

Sleep condition (mean ± SD)	Functional dyspepsia group (n=160)	Control group (n=155)	*P*-value
Deep sleep	2.35 ± 1.83	3.03 ± 1.53	< 0.001
Long sleep	1.68 ± 1.17	1.25 ± 0.65	< 0.001
Insomnia	2.27 ± 1.39	1.54 ± 0.96	< 0.001
Difficulty sleeping	2.76 ± 1.59	1.70 ± 1.18	< 0.001
Intermittent sleeping	2.20 ± 1.36	1.99 ± 1.31	0.116
Fatigue after sleeping	2.79 ± 1.46	1.63 ± 1.06	< 0.001
Nightmares	2.81 ± 1.66	1.77 ± 0.85	< 0.001
Periorbital edema after sleeping	1.74 ± 1.18	1.52 ± 1.19	0.195

dyspepsia leads to inappropriate food digestion and production of corrosive humors, which could cause skin and sleep complaints [9,27].

Ismaili *et al.* showed that there was a strong relation between GI manifestations and the severity of acne vulgaris. They found that GI manifestations, including flatulence and constipation, were significantly more prevalent in patients with moderate to high levels of acne than in healthy people [28]. Hong Zhang *et al.* found that there was a relationship between the presence of acne and sebaceous gland diseases and some conditions including halitosis, gastroesophageal reflux, bloating, constipation, frequently eating sweets or spicy foods, and sleeping late at night [29]. These results support the hypothesis of our study, suggesting a relationship between FD and complaints of skin manifestations.

In another study by Szlachcic in Krakow, Poland, rosacea was found to be associated with gastritis, especially in mucosal inflammation of the antral part of the stomach [30]. Besides, according to the literature, elimination of *Helicobacter pylori* leads to improvements of the skin symptoms of rosacea as well as the related GI symptoms [31]. In addition, it is necessary to mention that rosacea can be one of the extra-gastric symptoms of *H. pylori* infection caused by the microbe's cytotoxins and cytokines [32,33]. Furthermore, there is evidence that shows a significant relationship between *H. pylori* infection and idiopathic chronic urticaria [34-36]. In addition, it is necessary to say that *H. pylori* is involved in a variety of diseases outside of the GI tract, but the cause-and-effect relationships remain unclear [37]. Moreover, the evidence showed that high-calorie foods are associated with an increase in serum insulin levels, which causes the proliferation of sebaceous cells, thereby increasing the production of sebum and androgens and decreasing the concentration of sex hormone-binding globulin, all of which contribute to the pathogenesis of acne [38]. In this regard, the results of our study supported the association between patients' complaints of dermatology and GI discomforts.

Based on the principles of TPM, Hair is one of the excretion materials of the body [9,27]. Therefore, the characteristics of the hair can be affected by the quality of food digestion in the stomach. In this concept, poor or inappropriate digestion of foods can give rise to corrosive humor and warm vapors, resulting in several complications including oily hair [23,39,40]. In this setting, the results of our study confirmed the hypothesis of the relationship between FD and oily hair. According to the best of our knowledge, there is no evidence around the association between poor digestion, FD or GI diseases, and oily hair in conventional medicine, but future studies are recommended to find an association between GI diseases such as FD and the patients' complaints concerning their hair.

On the other hand, previous studies have shown that an unhealthy food regime is linked with irregular sleep patterns and shorter sleep lengths. Vegetables, fresh fruits, whole grains as well as low-fat protein diets could bring up a good sleeping pattern due to their macro and micronutrient content [40-42]. There is reliable evidence supporting the effect of the dietary pattern on the quality of sleep.

Yang Li *et al.* revealed the association between sleep disorders and psychological disturbances and FD. They concluded that patients with FD had lower quality of life than healthy individuals. Finally, they suggested that treatment of sleep disorders and psychological disturbances helps in the management of patients with FD [43]. Wang *et al.* and Ali *et al.* showed a relatively high prevalence of sleep disorders in irritable bowel syndrome, gastroesophageal reflux, inflammatory bowel disease, and liver disease patients [43,44]. They indicated that patients with such GI disorders are 2.6 times more likely to experience sleep disorders like insomnia and interrupted sleep [43]. Moreover, according to the study of Lacy BE *et al.*, the quality of sleep in patients with severe and moderate FD is significantly lower than patients with mild FD and individuals without FD [22]. The study of Khanijow *et al.* demonstrated that the quality of sleep improved in response to relieving GI ailments including FD [45]. The findings of our study showed the association between FD and a number of sleep problems conceptualized in TPM including insomnia, fatigue sensation after sleeping, nightmares, and difficulty sleeping. These results were in line with previous studies based on conventional medicine concepts.

It seems that the current study was the first one to evaluate the association of extra-abdominal complaints of patients with FD including sleep disturbances and dermatologic conditions based on TPM knowledge. Therefore, there were some

limitations in the present study. First, there was no previous standard questionnaire or checklist in this setting. So, we designed a researcher-made one. Hence, we recommend developing this checklist to a standardized, valid, and reliable questionnaire based on TPM concepts. Second, the order in which the GI, skin, and sleep complaints developed and the etiological factors involved were not considered; and we only assessed the accompaniment of these symptoms. So, we recommend that future studies focus more to find the cause-and-effect relationship between FD and other extra-abdominal symptoms. Third, the enrolled patients in this study reported data about their selective dermatology problems and sleep disturbances through a structured interview conducted by a physician. So, we indorse that the qualitative dermatology characteristics (such as pH, wetness, sebum, *etc*.) and sleep indices should be measured via specialized medical equipment. Next, we did not consider some probable confounding factors, such as participants' occupation, dietary habits, personal health habits (e.g., bathing), and emotional conditions in the patients and controls. Therefore, we suggest that future studies will be designed with greater control over confounding factors. Finally, it is suggested that the effect of treatment of FD on the improvement of the patients' extra-abdominal symptoms is investigated in future studies.

CONCLUSION

According to the results of this study, there is a relationship between FD and some dermatologic complaints, including skin dryness and oily hair, as well as certain sleep disturbances based on the concepts of TPM. However, in order to achieve more conclusive results, further research is required with larger sample sizes and greater control over the confounding factors.

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Conflict of interest: None declare.

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