

ORIGINAL RESEARCH

Relationship Between Gout And Constitution of Traditional Chinese Medicine

Ye Yuan, MD; Jingguo Zhou, MM; Wenguang Xie, MM; Fuchao Cheng, PhD; Haiyan Jiang, MM

ABSTRACT

Objective • The objective of this study was to explore common TCM constitutions among gout patients and investigate the potential relationship between traditional Chinese medicine's (TCM) constitution and clinical parameters.

Methods • A total of 219 gout patients with 195 participants were included in this study. All participants completed a baseline questionnaire on demographic characteristics, including age, weight, and family history. The biased constitution of TCM was identified by questionnaires surveyed with a TCM constitution table.

Results • Of 195 patients with gout, phlegm-damp accounted for the majority of TCM constitution classifications, followed by Qi-deficiency, damp-heat, and

Yang-deficiency constitutions. Besides, patients with these four constitutions have a higher BMI, blood sugar, and homocysteine.

Conclusion • The major types of constitution among these gout patients were phlegm-damp, Yang-deficiency, Qi-deficiency, and damp-heat. Gout symptoms with TCM constitutional theory may contribute to provide new insights into more rapid diagnosis and treatment for the effective prevention or therapy of gout. It is necessary to design more case-control studies and high-quality cohort in the future researches to provide a more helpful evidence-based basis for evaluating the relationship between TCM constitution and gout patients. (*Altern Ther Health Med*. 2024;30(7):162-167).

Ye Yuan, MD, Associate chief physician, Department of Geriatrics, Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu, China. **Jingguo Zhou, MM**, Chief physician; **Haiyan Jiang, MM**, Attending doctor; ²Department of Rheumatology and immunology, The First Affiliated Hospital of Chengdu Medical College, Chengdu, China. **Wenguang Xie, MM**, Chief physician, Department of Science and Technology, The First Affiliated Hospital of Chengdu Medical College, Chengdu, China. **Fuchao Cheng, PhD**, School of Computer, Chengdu University, Chengdu, China.

Corresponding author: Jingguo Zhou, MM
E-mail: yuanye202020@163.com

INTRODUCTION

Gout is an autoinflammatory disease partly due to an aging population and unhealthy lifestyle habits.^{1,2} A typical gout attack is caused by the formation of monosodium urate crystals in the joints (usually the peripheral joints of the feet) due to high levels of urate in the blood and causes joint dysfunction.³ Without lowering urate, gout attacks tend to be more frequent and may develop into a chronic inflammatory and painful state known as chronic gouty arthritis.⁴ The increased mortality of gout patients is largely related to hypertension, hyperlipidemia, obesity,

chronic kidney disease, and diabetes.⁵ Gout adversely affects the healthy quality of life.⁶ Although preventive medication is available, inexpensive, and effective, only a small proportion of people with gout receive adequate medication.^{7,8} Therefore, it is very important for the preventive treatment of gout, which may improve the care and treatment of gout patients.

The constitution of traditional Chinese medicine (TCM) is a medical system embedded in a complicated conceptual framework that can be used to understand various aspects of life, including physical well-being.⁹ In TCM, the relatively stable characteristics of human individuals in life, which are determined by genetic and acquired factors, are called constitution, manifested in morphological structure, physiological function, and psychological activity. According to the classical theory of TCM and modern research, the currently accepted method is to divide people's constitution into nine basic types: Yang-deficiency, Yin-deficiency, Qi-deficiency, phlegm-damp, damp-heat, blood-stasis, special diathesis, Qi-stagnation, and gentleness constitution,¹⁰ and this theory has been widely used in the TCM system to guide clinical practice. According to TCM theory, congenital and acquired factors can affect an individual's TCM constitution, thereby determining an individual's disease development and susceptibility.¹¹ To ensure the consistency and objectivity of

TCM constitution in research applications, standardized questionnaires have been designed to serve this purpose, such as the TCM Constitution Questionnaire (CCMQ) and the Constitutional Questionnaire (BCQ).^{11,12} “Constitution can be classified”, “Disease is associated with the constitution” and “Constitution can be adjusted” are three key scientific problems in the study of TCM constitution. Most of the research on TCM constitution focuses on these three problems.

Research into the constitution of TCM can guide individual treatment and prevention of diseases and can also judge the prognosis and susceptibility of diseases.¹³ Studies have shown that patients with the different constitutions will show completely different clinical characteristics in some diseases, that is, the theory of “Disease is associated with the constitution”. This theory has been verified in patients with diabetes, gastrointestinal cancer, lung cancer and other diseases,¹⁴⁻¹⁶ which analyze the constitutions of patients with different diseases contributing to decrease the incidence based on adjustment of the constitution. Some typical herbal formulas have significant prophylactic and therapeutic effects on gout.¹⁷ In addition, the effect of clearing heat and removing dampness medicine in the treatment of gout is slightly better than that of Western medicine.¹⁷ Gout is a heterogeneous disease with genetic tendency; however, there are rare reports on the clinical characteristics of gout patients with different constitutions.

This study aims to obtain the association of TCM constitution with the severity in gout patients achieved by questionnaires according to the TCM theory, and to provide new insights into the pathogenesis of gout for the effective prevention and therapy of gout.

MATERIALS AND METHODS

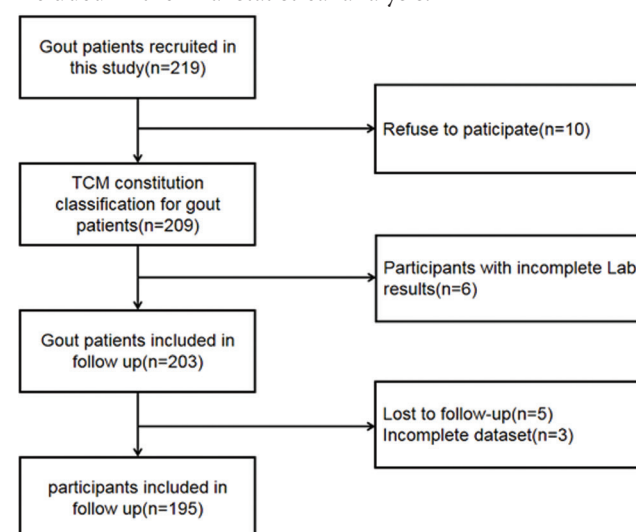
General information

A total of 219 patients diagnosed with primary gout (males and females, range 27-78 years, disease duration 1-17 years) were recruited between January 2021 to January 2022 from the Hospital of Chengdu University of Traditional Chinese Medicine and The First Affiliated Hospital of Chengdu Medical College in this study. The flowchart of the participant recruitment is shown in Figure 1. A total of 195 patients were included. Inclusion criteria: a) Meet the diagnostic criteria of gout and TCM syndrome differentiation criteria; b) Within 48 h of acute attack; c) Those who have relapsed or chronic recurrent disease for the first time. Exclusion criteria: a) Patients with serious diseases such as the heart, liver, kidney, lung, and endocrine system; b) Those who have been treated with hormones for a long time; c) Those who have secondary gout secondary to other diseases; d) Those who have taken pain before the onset of symptoms. This study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of our hospital. Written informed consent was obtained from all patients.

TCM constitution classification standard

According to the standard of “Classification and Judgment of Constitution of Traditional Chinese Medicine,” the TCM constitution bias of the above-mentioned patients

Figure 1. Participant recruitment flowchart. A total of 219 patients with primary gout were recruited, and 195 were included in the final statistical analysis.



who met the inclusion criteria was determined by a questionnaire survey using the TCM constitution table (ZYYXH/T157-2009) published by the Chinese Association of Traditional Chinese Medicine in 2009.¹³ We calculated the original score and recorded corresponding conversion score. The scores of each choice of “TCM Constitution Classification and Judgment Self-Test Table” in every question option ranges from “no” to “often” as 1 to 5 points, respectively. According to the standard, the constitution types are divided into Yang-deficiency, Yin-deficiency, Qi-deficiency, phlegm-damp, damp-heat, blood-stasis, special diathesis, Qi-stagnation, and gentleness constitution (balanced constitution). Among of them, conversion score ≥ 60 points were considered as balanced constitution and all biased constitution type’s conversion score were < 30 points.

Physical Examination

All patients received a routine examination during admission, including routine blood tests, biochemical tests, blood glucose, blood lipids, homocysteine, creatinine, and uric acid. Blood routine tests were performed by the blood biochemical analyzer, including white blood cells, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). The automatic biochemical analyzer detected creatinine, blood glucose, blood lipids, homocysteine, urea, and uric acid.

Statistical analysis

Statistical data was analyzed by using Statistical Product and Service Solutions (SPSS) 26.0 software (IBM, Armonk, NY, USA). Quantitative data conforming to normal distribution are presented as the mean \pm SD, and comparisons between groups were performed using Student’s *t* test. Qualitative data is represented by (n (%)), and the difference between two or multiple groups was determined by the Chi-squared test. *P* < .05 was considered significant.

Table 1. TCM constitution evaluation of 195 participants

TCM constitution	Age	Male (%)	Weight (kg)	Course of disease
Yang-deficiency				
Yes (53)	45 ± 12	50 (94.3%)	78.0 ± 22.1	11.6 ± 9.6
No (142)	39 ± 15	106 (74.6%)	70.2 ± 18.6	5.7 ± 3.7
P value	.0096	.0022	.014	<.0001
Yin-deficiency				
Yes (33)	43 ± 38	30 (90.9%)	83.2 ± 33.6	10.4 ± 11.3
No (162)	45 ± 15	157 (96.9%)	73.0 ± 16.3	7.3 ± 5.0
P value	.61	.11	.0089	.013
Qi-deficiency				
Yes (69)	47 ± 14	60 (87.0%)	65.4 ± 11.5	19.7 ± 16.5
No (126)	43 ± 16	85 (67.5%)	73.7 ± 23.0	6.4 ± 4.8
P value	.083	.21	.0055	<.0001
phlegm-damp				
Yes (72)	55 ± 15	66 (91.7%)	72.2 ± 11.2	11.9 ± 9.4
No (123)	49 ± 16	95 (77.2%)	74.6 ± 20.7	4.9 ± 3.8
P value	.011	.010	.36	<.0001
Damp-heat				
Yes (56)	49 ± 19	51 (91.1%)	80.5 ± 29.7	10.3 ± 10.4
No (139)	43 ± 15	117 (84.2%)	72.6 ± 14.4	7.0 ± 4.8
P value	.021	.21	.013	.0028
Blood-stasis				
Yes (50)	59 ± 21	46 (92.0%)	75.5 ± 19.6	21.0 ± 11.3
No (145)	48 ± 16	120 (82.8%)	68.5 ± 10.8	6.5 ± 4.9
P value	.0002	.11	.0019	<.0001
special diathesis				
Yes (25)	32 ± 4	20 (80.0%)	80.5 ± 26.9	5.3 ± 2.0
No (170)	45 ± 16	156 (91.8%)	73.2 ± 18.5	7.8 ± 7.3
P value	.0001	.064	.086	.091
Qi-stagnation				
Yes (16)	41 ± 21	12 (75.0%)	66.0 ± 13.2	17.0 ± 12.0
No (179)	46 ± 15	170 (95.0%)	75.5 ± 17.7	6.2 ± 4.3
P value	.22	.0022	.038	<.0001
Gentleness				
Yes (50)	46 ± 14	42 (84.0%)	74.5 ± 15.9	5.0 ± 3.4
No (145)	43 ± 16	135 (93.1%)	73.6 ± 19.2	9.3 ± 8.0
P value	.24	.056	.77	.0003

Note: TCM, traditional Chinese medicine. Yes, the corresponding TCM constitution. No, healthy controls with corresponding TCM constitution. Data are presented as the mean ± SD; $P < .05$ was considered significant.

RESULTS

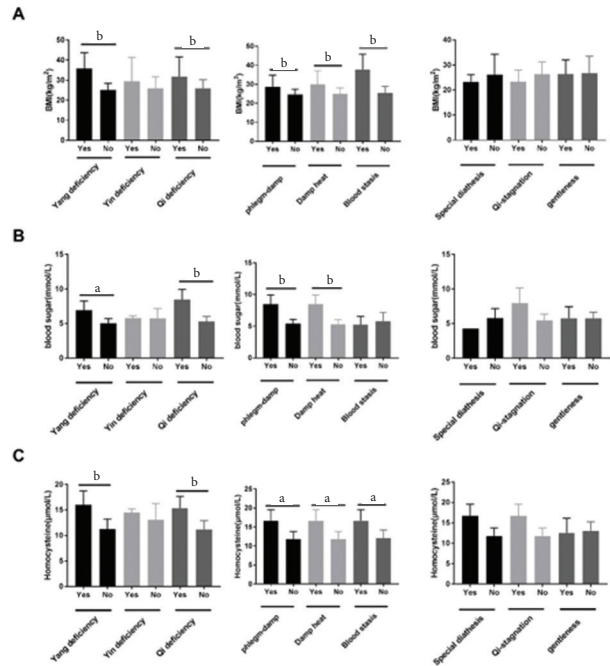
TCM constitution assessment

According to the standard of “Classification and Determination of Constitution of Traditional Chinese Medicine”, the enrolled gout patients mainly manifested the constitutions of phlegm-damp (72), Qi-deficiency (69), damp-heat (56), and Yang-deficiency (53). The constitutions of Yin deficiency (33 patients), blood stasis (50 patients), special diathesis (25 patients), Qi-stagnation (16 patients), and gentleness (50 patients) were also observed in patients with gout (Table 1). These data showed that phlegm-damp, Qi-deficiency, damp-heat, and Yang-deficiency constitutions accounted for the majority of TCM constitution classifications of gout patients.

Relationships between TCM constitution and BMI/blood sugar/homocysteine

Patients with Yang deficiency, Qi deficiency, phlegm-damp, damp-heat, and blood stasis have a higher BMI (Figure 2A, $P < .01$). Blood sugar levels were elevated in patients with Yang deficiency, Qi deficiency, phlegm-damp, and damp-heat (Figure 2B, $P < .05$). In patients with Yang-deficiency, Qi-deficiency, phlegm-damp, damp-heat, and blood stasis, homocysteine level was significantly increased (Figure 2C, $P < .05$). There were no significant differences between patients with Yin deficiency, special diathesis, Qi-stagnation, or gentleness constitution with BMI, blood sugar, and homocysteine. The results showed that patients with Yang deficiency, Qi deficiency, phlegm-damp, and damp-heat had a higher BMI, blood sugar, and homocysteine.

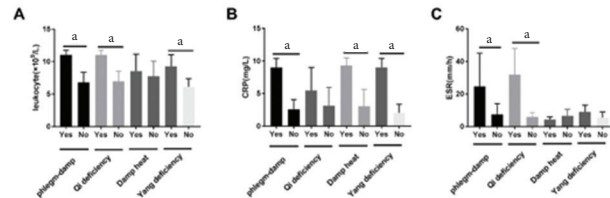
Figure 2. Relationship between BMI, blood sugar, and homocysteine and TCM constitution. (A) Body mass index (BMI) of respondents with 9 TCM constitutions; (B) Blood glucose of respondents with 9 TCM constitutions; (C) Homocysteine of respondents with 9 TCM constitutions.



^a $P < .05$
^b $P < .01$, vs. Yes group.

Note: Yes, the corresponding TCM constitution. No, healthy controls with corresponding TCM constitution.

Figure 3. The relationship between four TCM constitutions and blood routine. (A) The number of leukocytes in patients with four TCM constitutions; (B) CRP levels in patients with four TCM constitutions; (C) ESR in patients with four TCM constitutions.



^a $P < 0.01$, vs. Yes group.

The relationship between four TCM constitutions and blood routine

According to clinical observations and previous data, we mainly study the first four constitutions: phlegm-damp, Qi-deficiency, damp-heat, and Yang-deficiency. Patients with Yang deficiency, Qi-deficiency, or phlegm-damp have higher levels of leukocytes (Figure 3A, $P < .01$). The levels of CRP were up-regulated in patients with Yang deficiency, phlegm-damp, and damp heat (Figure 3B, $P < .01$). In addition, ESR was significantly increased in patients with phlegm-damp and Qi deficiency (Figure 3C, $P < .01$). The results revealed

Figure 4. Relationship between TCM constitution and renal function in gout patients. (A) Urea content of respondents with 4 TCM constitutions; (B) Creatinine levels of respondents with 4 TCM constitutions; (C) 24 h uric acid of respondents with 4 TCM constitutions.

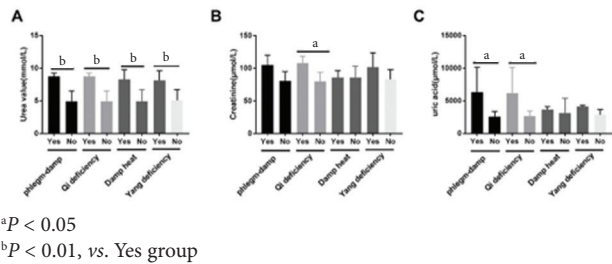


Figure 5. Comparison of blood uric acid and blood lipids among 4 TCM constitutions. (A) Blood uric acid levels of respondents with 4 TCM constitutions. (B) The levels of blood lipid were detected in 4 TCM constitutions. (C) Number of gout attacks in 4 TCM constitutions.

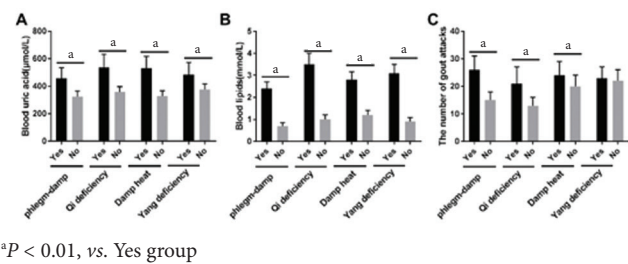


Table 2. Distribution of different constitution types in TCM syndrome types

TCM constitution	TCM Syndrome Type (n)				total	χ^2	P value
	Spleen deficiency and dampness syndrome	damp-heat stasis syndrome	Phlegm and blood stasis syndrome	Qi and blood deficiency syndrome			
Phlegm-damp	36	21	10	5	72	17.21	.046
Qi deficiency	33	24	6	6	69		
Damp heat	39	15	2	0	56		
Yang deficiency	37	11	4	1	53		
total	145	71	22	12	250		

Note: TCM, traditional Chinese medicine. $P < .05$ was considered significant.

Table 3. Patients with gout have two or more constitution-related distributions (n)

TCM constitution 1	TCM constitution 2	total
phlegm-damp	Qi-deficiency	28
phlegm-damp	Damp heat	21
phlegm-damp	Yang-deficiency	16
Qi-deficiency	Damp heat	20
Qi-deficiency	Yang-deficiency	13
Damp heat	Yang-deficiency	12
phlegm-damp; Qi-deficiency	Damp heat; Yang-deficiency	4
phlegm-damp; Damp heat	Qi-deficiency; Yang-deficiency	1

that these four TCM constitutions have a correlation with blood routine.

Relationship between TCM constitution and renal function in gout patients

The urea content of the patients with Yang-deficiency, Qi-deficiency, damp-heat, or phlegm-damp constitutions were all elevated (Figure 4A, $P < .01$). Patients with a

Qi-deficiency constitution have high levels of creatinine (Figure 4B, $P < .05$). In addition, patients with Qi-deficiency and phlegm-damp constitutions have high levels of uric acid (Figure 4C, $P < .05$), suggesting there is a correlation between TCM constitution and renal function.

Comparison of blood uric acid and blood lipids among 4 TCM constitutions

As shown in Figure 5, patients with phlegm-damp, Qi-deficiency, Yang-deficiency, or damp-heat have higher levels of blood uric acid and blood lipid (Figure 5A-B, $P < .01$). Gout attacks increased in patients with phlegm-damp, Qi-deficiency, and damp-heat constitutions (Figure 5C, $P < .01$).

Distribution of different constitution types in TCM syndrome types

There were 36 patients in phlegm-damp group, 33 in Qi-deficiency group, 39 in damp-heat group, and 37 in Yang-deficiency group presented with spleen deficiency and dampness syndrome. There were 21, 24, 15, and 11 patients with damp-heat stasis syndrome in phlegm-damp, Qi-deficiency, damp-heat, and Yang-deficiency groups, respectively. There were 10, 6, 2, and 4 patients presented with phlegm and blood stasis syndrome in four different groups, respectively. In addition, 5 patients presented with Qi and blood deficiency syndrome in phlegm-damp group, 6 patients in Qi-deficiency, and 1 patient in Yang-deficiency group. There was a significant difference in TCM constitution between different TCM syndrome types (Table 2, $F = 17.21$, $P = .046$).

Patients with gout have two or more constitution-related distributions.

As shown in Table 3, 28 gout patients showed phlegm-damp accompanied by Qi deficiency, 21 patients showed phlegm-damp accompanied by damp-heat, and 16 patients presented with phlegm-damp accompanied by Yang-deficiency. There were 20 and 13 patients with Qi-deficiency accompanied by damp-heat or Yang-deficiency, respectively. 12 patients showed damp-heat accompanied by Yang-deficiency. Furthermore, other constitutional types (a combination of 4 constitutions) accounted for less than 5%.

DISCUSSION

Epidemiological evidence shows that both the incidence and prevalence of gout are on the rise.^{18,19} The gout diagnosis largely depends on higher serum urate concentrations.²⁰ At present, the specific pathogenesis of gout is not fully understood. This study used phlegm-damp, Yang-deficiency, Qi-deficiency, and damp-heat as the common constitution types of gout patients. Patients with these four constitutions have a higher BMI, blood sugar, and homocysteine, suggesting that we should identify and focus on the people with these constitution as soon as possible and take appropriate intervention measures like exercise, diet, and so on, to help the return of balanced constitution.

Previous studies have reported the association of TCM constitution with various diseases, such as diabetes, hypertension, obesity, and cancer-related fatigue in cancer patients.^{14,15,21-23} Furthermore, a clinical study on the relationship between TCM constitution types and various diseases (such as hypertension and diabetes) provides evidence for supporting the use of TCM constitutions for health maintenance and disease prevention.²⁴ For example, 86 studies have reported that the proportion of phlegm-damp constitution in diabetes patients is 17%, the proportion of Qi-deficiency constitution is 13%, and the proportion of Yin-deficiency constitution is 18%, which are the most frequent types of the constitution in diabetes patients.¹⁴ The proportion of patients with constitutional deviation in the hypertensive group is higher, and Yin-deficiency and blood stasis constitutions are related to essential hypertension.²¹ In addition, phlegm wetness, Qi-deficiency, blood stasis, and Yin-deficiency have different effects on the prevalence of hypertension.²⁵ TCM syndrome differentiation intervention improves blood pressure and plasma glucose, and is effective for hypertensive patients with diabetes.²⁶ Although TCM constitution has been extensively studied in many diseases, few studies have focused on gout patients. Agents isolated from some herbaceous herbs have a curative effect on treating gout.²⁷ Similarly, in this study, we explored the correlation between TCM constitution and gout patients. Our results showed that TCM constitution was closely related to gout, and patients with gout are mainly characterized by phlegm-damp, Qi-deficiency, damp-heat, and Yang-deficiency. Taken together, we found that patients with hypertension, diabetes and gout were in common features of phlegm-damp, Qi-deficiency, while hypertension and diabetes patients mainly have Yin-deficiency constitution and gout Yang-deficiency. The TCM constitution theory analyzes the pathological characteristics of people with different constitution types, analyzes the disease state, lesion nature, and development trend, and conducts treatment according to TCM syndrome differentiation.²⁸ Therefore, we suggested that TCM syndrome differentiation intervention may contribute to improve gout patients.

The final product of purine and protein metabolism in the human body is uric acid, and excessive serum uric acid may precipitate uric acid crystals.^{29,30} This study evaluated the relationship between high levels of uric acid and different TCM constitutions. We found that phlegm-damp and Qi-deficiency were associated with high uric acid content. Studies have reported that patients with gout presented a higher percentage of glucose, uric acid, cholesterol, triglycerides, and creatinine compared with normal individuals.³¹ Our results showed that patients with Qi-deficiency have high creatinine, and high levels of uric acid in gout patients were significantly correlated with Qi-deficiency and phlegm-damp constitution. Patients with Yang-deficiency, Qi-deficiency, phlegm-damp, and damp-heat have high levels of urea, blood uric acid, and blood lipids. Homocysteine, blood sugar, and BMI were increased in patients with Yang-

deficiency, Qi-deficiency, phlegm-damp, and damp-heat. Studies have shown that there is a strong correlation between TCM constitution and physical examination indicators, including renal function, liver function, blood routine, and urine routine.³² Similarly, in this study, results showed that different TCM constitutions have different degrees of correlation with blood routine and renal function. In addition, gout patients have two or more TCM constitutions, and the distribution of four TCM constitution types among TCM syndrome types is statistically significant. Our results indicated that blood lipids, blood sugar, homocysteine, creatinine, uric acid, and urea may be the relevant factors for gout.

Based on the Constitution of TCM, human beings' constitution is stable and adjustable in a certain period. Therefore, through regulating the constitution it can achieve the purpose of preventing the occurrence and development of the disease, regulating the pathological state of the patient, and improving the prognosis.³³ Furthermore, it can improve and regulate the biased constitution related to gout/hyperuricemia and develop ideas and methods for the prevention and treatment of gout by diet therapy and TCM decoction so as to prevent diseases before occurrence, prevent the transmission of a disease after its onset, and prevent the recurrence after recovery.³⁴ In this study, the distribution of biased constitution types in patients with gout was Yang-deficiency, phlegm-damp, damp-heat, and Qi-deficiency in the highest proportion. Four TCM constitution types (Yang-deficiency, phlegm-damp, damp heat, and Qi-deficiency) may be potential risk factors for gout patients. Our results may provide new insights into the pathogenesis of gout and benefit the prevention and therapy of gout.

Despite our research on the relationship between age, sex, weight, and course of disease, the incomplete information and individual differences of the included subjects increased the heterogeneity and a certain risk of deviation in the result. Therefore, it is necessary to design more case-control studies and high-quality cohort to provide a more helpful evidence-based basis for evaluating the relationship between TCM constitution and gout patients.

FUNDING

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

This study has been approved by the ethics committee of The First Affiliated Hospital of Chengdu Medical College (No. 2021CYFYIRB-BA-36-F01) in compliance with the Declaration of Helsinki. All the OC cases have signed written informed consent.

AUTHORS' CONTRIBUTIONS

YY and JGZ: conception, design and analysis of data, performed the data analyses and wrote the manuscript; WGX, FCC and HYJ: contributed to the conception of the study; wrote the manuscript; All authors have read and approved the manuscript.

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