



Original Article

Factor analysis of traditional Chinese medicine symptoms for identification of syndrome patterns associated with idiopathic short stature in children

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ABSTRACT

Objectives: Diagnosing idiopathic short stature (ISS) in Traditional Chinese Medicine (TCM) remains challenging partly because the symptoms and syndrome patterns vary among ISS patients and studies. We aimed to use factor analysis of TCM symptoms to identify syndrome patterns associated with ISS in children on the basis of TCM theory. **Materials and Methods:** A cross-sectional study was conducted at Taipei Tzu Chi Hospital, New Taipei City, Taiwan, from October 1, 2014, to February 28, 2016. The study included 957 individuals who were newly diagnosed with ISS through simple random sampling. The outcome measures comprised 34 TCM symptoms related to children's growth, and these symptoms were assessed using a five-level self-report questionnaire, which was completed by children and their parents. A factor analysis was conducted for the extraction of underlying factors. **Results:** A total of 26 symptoms had factor loadings higher than the exact threshold value (0.4), and five factors were extracted. Factor 1, comprising seven symptoms, was interpreted as "yin deficiency and fire hyperactivity of kidney syndrome." Factor 2, which included eight symptoms, was interpreted as "phlegm dampness stagnation of spleen syndrome." Factor 4, which included five symptoms, was interpreted as "liver qi invading the spleen syndrome." Factor 5, which included four symptoms, was interpreted as "spleen-stomach weakness syndrome." Factor 3, which included four symptoms, was uninterpretable. Factors 1–5 accounted for 10%, 9%, 8%, 7%, and 6% of the total variance. **Conclusion:** Four major TCM syndrome patterns, namely, "yin deficiency and fire hyperactivity of kidney syndrome," "phlegm dampness stagnation of spleen syndrome," "Liver qi invading the spleen syndrome," and "spleen–stomach weakness syndrome" were identified and accounted for 40% of the total variance of the 34 TCM symptoms surveyed in children with ISS. Our findings may facilitate the diagnosis of ISS and the optimization of treatment strategies.

KEYWORDS: Children, Idiopathic short stature, Symptoms, Syndrome patterns, Traditional Chinese Medicine

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INTRODUCTION

Idiopathic short stature (ISS) is a condition characterized by a height higher than 2 standard deviations below the corresponding average height for a specific age, sex, and population. This condition is frequently diagnosed when no other abnormalities are detected [1,2]. In Western medicine, ISS is a diagnosis not based on positive findings in the diagnostic workup, but on excluding other recognizable conditions, including nutritional, systemic, endocrinologic, and syndrome/chromosomal abnormalities [3]. The prevalence of children diagnosed with ISS is 23 per 1000 individuals [2].

Moreover, ISS is prevalent in approximately 80% and 40% of children presented with short stature in the Western[3] and Chinese populations [4,5], respectively. Short stature is a common reason for pediatric clinic visits [6,7]. Parents express concern regarding the potential psychological effects of their children's short stature, including low self-esteem, poor school

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performance, or challenges in forming peer relationships [8]. Indeed, short stature is a risk factor for poor quality of life and internalizing problems in children [9,10]. In Western medicine, growth hormone therapy has been effective in increasing the height of some children with ISS, but the cost-benefit ratio remains controversial, and its long-term efficacy remains unclear [2,11]. Thus, the clinical use of traditional Chinese medicine (TCM) in ISS treatment for Asian children is receiving increasing interest [12,13].

The etiology of ISS remains unclear. In theory, TCM believes that the cause of ISS in children is closely related to the dysfunctions of one or more visceral organs, mainly the kidney, spleen, and liver [14,15]. These dysfunctions may lead to various presentations of TCM syndrome patterns, such as spleen deficiency, kidney deficiency, and dual deficiency of spleen-kidney with unbalanced Qi or essence, which are accompanied by a variety of TCM symptoms [14-16]. These clinical signs or symptoms, alongside other indications, are detected and perceived by TCM clinicians to establish the diagnoses of TCM syndrome patterns in individuals with ISS. However, this procedure is primarily based on personal experiences, and the symptoms and syndrome patterns vary among patients with ISS [17-20]. A recent review [16], including 16 studies and summarized TCM symptoms and syndrome patterns related to ISS, reported over 80 TCM symptoms associated with various TCM syndrome patterns in children with ISS. Furthermore, related symptoms varied among studies, even in the same TCM syndrome pattern. Thus, diagnosing syndrome patterns according to TCM symptoms in ISS remains challenging. The study on the modern scientific verification of syndromes and patterns in ISS is still lacking.

In this study, we aimed to use modern statistics to explore TCM symptoms and syndrome patterns associated with ISS in children. A survey questionnaire was used in collecting data, which comprised 34 TCM symptoms self-reported by children and their parents. Factor analysis was used to examine a smaller number of the underlying factors that could explain the variation in large numbers of observed variables (i.e. TCM syndromes) [21,22]. We hypothesized that, through the factor analysis, the TCM syndromes encompassed by underlying factors can then be used for the interpretation of TCM syndrome patterns based on the knowledge of the TCM guidelines [23,24]. The findings of this study may provide valuable information to facilitate the diagnosis of ISS and promote the optimization of treatment strategies.

MATERIALS AND METHODS

Design, setting, and subjects

This study was a cross-sectional investigation using retrospectively analyzed data. From October 1, 2014, and February 28, 2016, children who visited the Children's Growth Clinic at Taipei Tzu Chi Hospital were invited to participate in this study if they had a new diagnosis of short stature (ICD-9: 783.43) without organic pathology. Subjects were not enrolled if children or their parents did not agree to participate in this study. Exclusion criteria were children with short stature caused by known pathological factors such

as tumors, chromosomal defects, or endocrine abnormalities. The study was conducted with the approval of the Institutional Review Board of Taipei Tzu Chi Hospital (IRB approval number: 05-X07-015). Informed consent was obtained from all included participants. This study was conducted in accordance with the Declaration of Helsinki.

Questionnaire and observed variables

We used the Chinese version of "Pediatric Growth TCM Syndrome Questionnaire" for this study. The English version of this questionnaire [Supplementary Table 1] was translated by a professional language expert and validated by two authors. It was based on the Chinese Medicine Diagnosis Guidelines for Pediatric Common Diseases-Precocious Puberty (2012)[25] and was designed by five TCM pediatric experts and one Western medicine pediatrician through a consensus meeting. These experts recommended 34 symptoms potentially related to the growth of children or ISS in the questionnaire, including cold and heat conditions, spontaneous sweating or night sweating, sleep, diet, emotions, and urine and stool problems. This questionnaire also includes basic information such as age, height, weight, body mass index (BMI) value, and parents' height and weight. A subject's symptom response was measured using a five-point Likert scale. To minimize recall bias, we instructed the participants to provide scores of 0-4 on the severity of the symptoms they had experienced during the past month. With the help of explaining the meaning of the content of the questionnaire by nurses, the subjects and their parents completed the questionnaire jointly in the Children's Growth Clinic. The questionnaire usually took no more than 10 min to complete. A total of 957 survey samples were collected, and missing data were filled with the average scores.

Statistical analysis

Factor analysis was conducted to extract underlying factors. For this analysis, we used orthogonal rotation (Varimax), which constrains the factors to be uncorrelated. Before factor extraction, the optimal number of factors to account for variability was determined using a scree plot of eigenvalues and performing parallel analysis. For the scree plot, factors with eigenvalues >1 were selected. For parallel analysis, factors were recomputed according to the random rearrangement of data set eigenvalues, and the new eigenvalues were plotted on the same graph as the scree plot. To distinguish which variables were the major components of each factor, the exact threshold value of the loading value was set at higher than or equal to 0.40. Factors with components <3 variables were not considered. All statistics were carried out with R software (version 3.4.3, Vienna, Austria). The clinical characteristics of the participants are represented as the mean \pm standard deviation. The factor loading in each item and the proportion of variance were analyzed using the "factors" and "psych" packages.

RESULTS

Clinical characteristics

We collected 957 questionnaires: 496 (51.82%) samples from boys and 461 (48.18%) from girls. The clinical characteristics of the subjects are shown in Table 1. The

average age of boys was 11.6 years, the average height and weight were 141.5 cm and 37.5 kg, respectively, and the average BMI was 17.4 kg/m². The average age of girls was 10.5 years, the average height and weight were 136.2 cm and 32.4 kg, respectively, and the average BMI was 17.4 kg/m². The age of the participants ranged from 1.1 years to 19.4 years. The data distribution in the height-for-age chart indicated that the height of most boys [83.9%; Figure 1a] or girls [75.6%; Figure 1b] was below 50%.

Factor analysis

Figure 2 shows the relationship between the number of factors (components) selected and the eigenvalues from the scree plot and parallel analysis. The round dots represent actual values for constructing the scree plot. The triangles represent randomly generated data from parallel analysis. From the intersection between the breakpoints in the scree plot and the randomly generated data, five factors were extracted.

Underlying factors and Traditional Chinese Medicine syndrome patterns

Table 2 shows the factor loading in each of the 34 symptoms surveyed. The respective five extracted factors accounted for 10%, 9%, 8%, 7%, and 6% of the total variance, indicating that the model explained 40% of the total variance. Table 3 shows the symptoms included in four extracted factors in relation to TCM syndrome patterns. “Vexing heat in the chest, palms, and soles,” “tidal heat and sweating,” “night sweating,” “generalized heat,” “dry mouth and thirst,” “profuse dreaming,” and “good appetite,” which were included in factor 1, can be interpreted as the “Yin deficiency and fire hyperactivity of kidney syndrome pattern.” “Bitter taste in the mouth,” “dizziness,” “heavy body,” “fatigue,” “heavy headedness,” “sticky mouth,” “oppression in the chest,” and “stiffness and fullness of the stomach,” which were included in factor 2, can be interpreted as “phlegm dampness stagnation of spleen syndrome pattern.” “Irritability,” “depression,”

“fatigue,” “laziness to speak,” and “like sweets,” which are included in factor 4, can be interpreted as “liver qi invading the spleen syndrome pattern.” “Dry bound stool,” “Poor appetite,” “stiffness and fullness of the stomach,” and “loose stool,” which are included in factor 5, can be interpreted as “spleen-stomach weakness syndrome pattern.” However, “dry eyes,” “red eyes,” “eye pain,” and “crusty eyes,” which were included in factor 3, cannot be assigned to any specific TCM syndrome pattern.

DISCUSSION

We employed factor analysis to explore TCM symptoms and syndrome patterns associated with ISS in children. Based on the self-reported data from the survey questionnaire consisting of 34 potential TCM symptoms, factor analysis revealed five underlying factors encompassing five clusters of TCM symptoms. The extracted factors accounted for 40% of the variance, indicating the proportion of individual differences in measured variables that are accounted for by the extracted factors. As a result, 4 out of 5 extracted factors were eventually interpreted as four major syndrome patterns: factor 1, “yin deficiency and fire hyperactivity of kidney syndrome;” factor 2, “phlegm dampness stagnation of spleen syndrome;” factor 4, “liver qi invading the spleen syndrome;” and factor 5, “spleen–stomach weakness syndrome.”

In this study, the TCM symptoms encompassed by four extracted factors closely resemble those concerning the four syndrome patterns described in guidelines [23,24]. For example, factor 1 included the symptoms “Vexing heat in the chest, palms, and soles,” “tidal heat and sweating,” “night sweating,” “generalized heat,” “dry mouth and thirst,” “profuse dreaming,” and “good appetite.” These symptoms are in line with the most common symptoms of the “kidney yin deficiency and excessive fire pattern,” namely, night sweats, dry mouth and tongue, restlessness, short yellow urine, dry stool, insomnia,

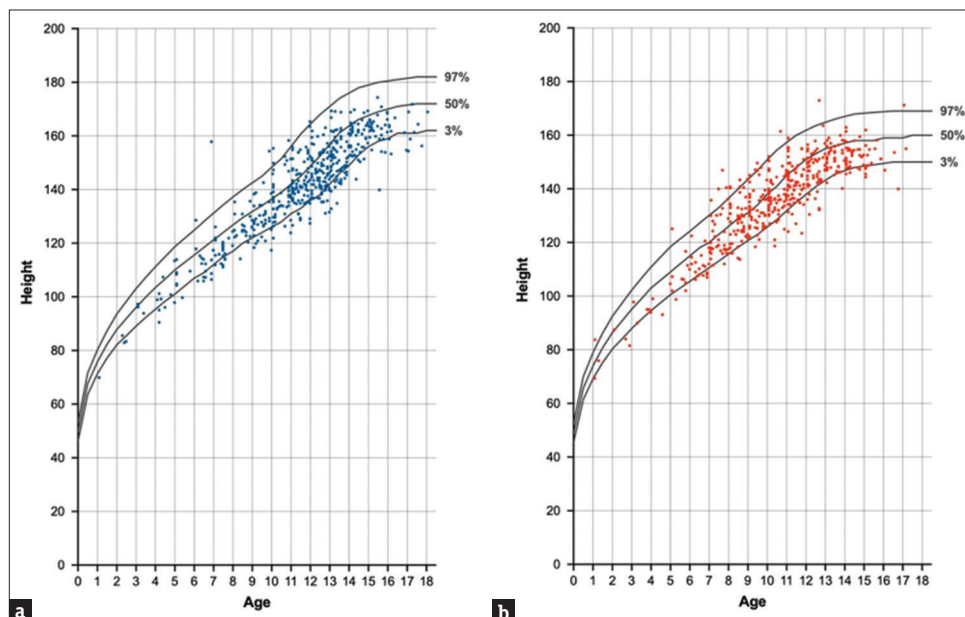


Figure 1: The distribution in the height-for-age chart of the boys (a) and girls (b) in this study

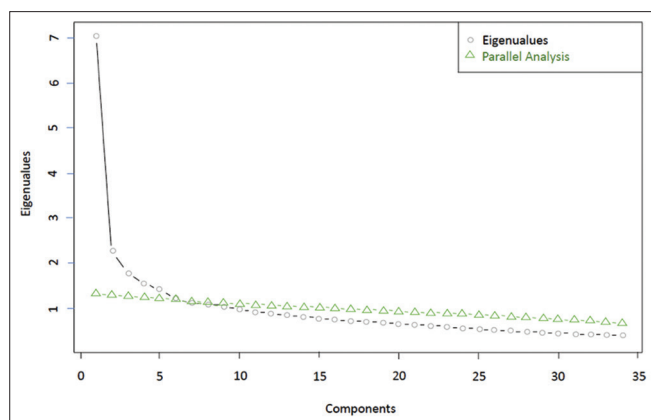


Figure 2: Combined use of the scree plot of eigenvalues and parallel analysis for choosing the appropriate number of factors. For the scree plot, the number of factors was chosen at the point where the eigenvalue was > 1 . For parallel analysis, factors were recomputed, and the new eigenvalues were plotted on the same graph as the scree plot. The elbow of the scree plots and the crossing points between the line from the parallel analysis are six extracted factors

irritability, red tongue with scanty coating, and thready rapid pulse. In addition, factor 2 included the symptoms “Bitter taste in the mouth,” “dizziness,” “heavy body,” “fatigue,” “heavy headedness,” “sticky mouth,” “oppression in the chest,” and “stiffness and fullness of the stomach,” which are in agreement with the most common symptoms of the “phlegm dampness stagnation of spleen pattern,” namely, poor appetite, abdominal distension, loose stools, fatigue, heaviness in the body or head, pale and swollen tongue, and slippery pulse. Furthermore, factor 4 included symptoms of “Irritability,” “depression,” “fatigue,” “laziness to speak,” and “like sweets.” These symptoms are consistent with the most common symptoms of the “liver qi invading the spleen pattern,” namely irritability, depression, sighing, chest or hypochondriac distension, breast tenderness, decreased appetite, and wiry pulse. Moreover, the factor 5 included symptoms of “dry bound stool,” “poor appetite,” “stiffness and fullness of the stomach,” and “loose stool,” which are considered to be the syndrome closest to “spleen–stomach weakness pattern,” namely, poor appetite, fatigue, loose stool, stomach fullness, stomachache, pale tongue or tooth marks, thin white coating, and thin and weak pulse. Unfortunately, we could not refer the symptoms of “dry eyes,” “red eyes,” “eye pain,” and “crusty eyes” included in factor 3 to any specific TCM syndrome patterns. The eye-related symptoms in factor 3 can be grouped into a single extracted factor and may be an indicator for the diagnosis of ISS. Factor analysis is a modern statistical method that can reduce many observed variables (i.e. TCM syndromes) to few underlying factors [22]. TCM symptoms that tend to appear in underlying factors may implicate specific syndrome patterns. This statistical method has been used in exploring symptoms and identifying TCM syndrome patterns associated with several diseases. For example, Gustafson *et al.* [21] conducted a factor analytic approach to identify symptom patterns in dementia and extracted three factors that can explain 35.9% of the total variance of 30 TCM symptoms. Xiong *et al.* [22] performed a factor analysis to identify the symptoms and signs of chronic lower back pain on the basis of TCM theory and extracted four factors that explained 36.9% of the total variance of 31 TCM symptoms.

Table 1: Clinical characteristics of the subjects

	Total (n=957)	Male (n=496)	Female (n=461)
Age (years)	11.0±3.0	11.6±3.0	10.5±2.8
Height (cm)	139.0±17.2	141.5±17.8	136.2±16.2
Weight (kg)	35.0±13.4	37.5±14.8	32.4±11.2
BMI	17.4±3.8	17.4±4.0	17.4±3.6
Birth weight (g)	2978.2±460.1	2983.1±475.9	2973.4±444.7
Height of subject’s father	169.2±6.2	169.4±5.8	169.0±6.6
Height of subject’s mother	156.6±5.0	156.5±5.0	156.6±5.1

BMI: Body mass index

Although the etiology of ISS remains unclear, TCM posits that the dysfunction of one or more visceral organs, mainly the kidney, spleen, and liver, may be involved [14,15]. These dysfunctions may lead to an imbalance in Qi or the essence of the visceral organs resulting in the presentation of a variety of TCM symptoms associated with ISS [14-16]. First, the kidney is responsible for bone marrow production and essence (including growth hormone, estrogen, and testosterone) [26] and plays a crucial role in bone marrow proliferation and skeletal development [27]. Kidney yin deficiency with excessive fire indicates the excessive secretion of the essence, leading to premature growth, accelerated bone age, and early closure of growth plates, which may result in ISS [28]. Indeed, yin deficiency with excessive fire pattern is commonly observed during puberty [29]. Zhou [30] mentioned that early puberty is usually related to yin deficiency. Second, the spleen is responsible for acquiring, digesting, absorbing, and spreading various nutrients needed for life in TCM theory [15]. It is “the source of qi and blood biochemistry” and is crucial to children’s growth and development. However, children often have spleen deficiency, which can result from eating disorders, illness-induced weakness, and impaired digestive functions [31]. Loss of transport in the spleen and stomach leads to anorexia, vomiting, diarrhea, stagnation, or malnutrition in children and to other diseases, eventually resulting in insufficient blood and viscera and affecting the growth and development of children [16,32]. Spleen qi deficiency and stagnation are common syndrome patterns associated with ISS [15,16]. Third, the liver is responsible for storing and regulating blood. Sufficient liver blood nourishes the tendons, resulting in a strong and agile body [28]. Deficient liver blood may lead to slow growth and reduced stamina [33]. Notably, in patients with ISS, emotional factors may affect the function of the liver and lead to liver qi stagnation, which in turn dysregulates the function of the spleen and stomach [34]. Sun *et al.* reported that liver depression and constrain play an important role in ISS [18]. Thus, on the basis of scientific analysis of data from patients’ or parental reports, we were able to assess TCM symptoms and patterns relevant to ISS, which correlated well with the pathophysiology of ISS proposed by TCM experts [14,15]. The four major syndrome patterns identified in this study are related to ISS according to TCM theory.

The diagnosis of ISS in TCM remains challenging partly because symptoms and syndrome patterns vary among

Table 2: Factor loading in every item and the proportion of variance explained by the loading

Symptoms	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Vexing heat in the chest, palms, and soles	0.66	0.12	0.00	0.06	-0.11
Tidal heat and sweating	0.72	0.19	0.09	0.02	-0.02
Night sweating	0.64	0.05	0.17	-0.09	0.22
Dry eyes	0.15	0.18	0.66	0.01	0.04
Generalized heat	0.67	-0.05	0.09	0.21	0.09
Dry mouth and thirst	0.52	0.16	0.17	0.18	0.05
Profuse dreaming	0.45	-0.02	0.23	0.06	0.35
Sleeplessness	0.23	0.00	0.29	0.27	0.30
Dry bound stool	0.21	0.06	-0.01	0.30	0.49
Dark and scant urine	0.30	0.16	0.16	0.28	0.34
Irritability	0.25	-0.01	0.28	0.70	0.12
Depressed	0.11	0.15	0.27	0.70	0.05
Red eyes	0.13	0.14	0.75	0.20	-0.01
Eye pain	0.05	0.14	0.78	0.11	0.01
Crusty eyes	0.21	0.25	0.54	0.13	0.19
Bitter taste in the mouth	0.12	0.41	0.32	0.09	0.04
Rib-side pain	0.03	0.33	0.03	0.02	0.14
Breast tenderness	-0.01	0.04	0.04	0.03	-0.03
Halitosis	0.20	0.31	0.25	0.17	0.09
Dizziness	0.06	0.47	0.28	0.13	0.01
Heavy body	0.07	0.64	0.05	0.14	0.03
Fatigue	0.10	0.57	0.05	0.41	0.07
Laziness to speak	0.00	0.30	0.04	0.58	-0.08
Heavy-headedness	0.03	0.67	0.09	0.02	0.01
Sticky mouth	0.12	0.57	0.17	0.01	0.03
Oppression in the chest	0.09	0.56	0.14	0.04	-0.04
Good appetite	0.53	0.07	-0.06	0.16	-0.33
Poor appetite	-0.16	0.06	0.15	0.13	0.70
Like sweets	0.23	0.07	-0.03	0.45	0.28
Nausea and vomiting	0.11	0.28	0.17	0.20	0.22
Stuffiness and fullness of the stomach	0.16	0.43	0.17	0.00	0.40
Loose stool	0.23	0.30	-0.12	0.09	0.45
Skin rash	0.34	0.08	0.11	0.10	0.10
Acne	0.08	0.28	0.06	0.27	-0.45
Variance (%)	10	9	8	7	6

Bold character numbers signify factor loading ≥ 0.4 , an exact threshold value used in this study

patients with ISS [16]. The identification of syndrome patterns and visceral differentiation are often based on individual physicians' experience [16]. The same symptom can be attributed to different syndrome patterns, and the same syndrome pattern may encompass a variety of symptoms. For example, Jiang *et al.* [17] described five TCM symptoms in cases with dual deficiency of spleen-kidney, whereas Sun *et al.* [18] reported five different TCM symptoms in their cases. Hong [19] described five TCM symptoms in cases with kidney deficiency, whereas Tian and Zeng [20] reported eight different TCM symptoms in their cases. Accordingly, our findings regarding the symptoms and syndrome patterns may provide helpful information for diagnosing ISS in TCM.

The parent factor involving family genes is known to be a determinant of children's height [35]. A recent large-scale study (29,685 men and 32,901 women) surveying anthropometric data reported that adult males and females have an average height of 170 and 158 cm, respectively [36]. The average height of the subjects' father (169 cm) and mother (157 cm) in this study was within the normal range.

Thus, familial short stature is unlikely to be a major issue for our participants. However, the height of most boys (83.9%) or girls (75.6%) was below 50% of the data distribution in the height-for-age charts. The target heights of these boys and girls were expected to be within 162–170 and 150–160 cm, respectively. Accordingly, short stature is a potential problem for some subjects when they become adults. Exploring TCM syndromes and patterns and optimizing treatment strategies may aid in the prevention of this problem.

Several limitations need to be considered. First, this study was a single-center investigation and involved a small sample size. Thus, future multicenter investigations with large sample sizes are warranted to confirm our findings. Second, the symptoms analyzed in this study were self-reported data derived from the subjects' perceptions but were not confirmed by physicians. Future studies may be directed to differences between outcomes of factor analysis using data reported by participants and data defined by physicians. Third, the symptoms surveyed in this study did not encompass all potential symptoms related to ISS. Future studies may

Table 3: Interpretations of traditional Chinese medicine symptoms of underlying factors by traditional Chinese medicine syndrome patterns

Factor	TCM symptoms	TCM syndrome pattern
Factor 1	Vexing heat in the chest, palms, and soles Tidal heat and sweating Night sweating Generalized heat Dry mouth and thirst Profuse dreaming Good appetite	Yin deficiency and fire hyperactivity of kidney syndrome
Factor 2	Bitter taste in the mouth Dizziness Heavy body Fatigue Heavy-headedness Sticky mouth Oppression in the chest Stuffiness and fullness of the stomach	Phlegm dampness stagnation of spleen syndrome
Factor 4	Irritability Depressed Fatigue Laziness to speak Like sweets	Liver qi invading the spleen syndrome
Factor 5	Dry bound stool Poor appetite Stuffiness and fullness of the stomach Loose stool	Spleen-stomach weakness syndrome

The factors were interpreted based on the theory from TCM guidelines: “Clinic Terminology of Traditional Chinese Medical Diagnosis and Treatment-Syndromes” [23] and “Traditional Chinese Medicine Syndrome” [24]. TCM: Traditional Chinese Medicine

incorporate additional symptoms to enrich symptoms’ variety and identify other syndrome patterns.

CONCLUSIONS

Four major TCM syndrome patterns, namely, “yin deficiency and fire hyperactivity of kidney syndrome,” “phlegm dampness stagnation of spleen syndrome,” “Liver qi invading the spleen syndrome,” and “spleen-stomach weakness syndrome” can explain 40% of the variance of the 34 TCM symptoms surveyed in children with newly diagnosed ISS. Our findings may facilitate the diagnosis of ISS and the optimization of treatment strategies.

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Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Cohen P, Rogol AD, Deal CL, Saenger P, Reiter EO, Ross JL, et al. Consensus statement on the diagnosis and treatment of children with idiopathic short stature: A summary of the Growth Hormone research society, the Lawson Wilkins Pediatric Endocrine Society, and the European Society for Paediatric endocrinology workshop. *J Clin Endocrinol Metab* 2008;93:4210-7.
- Cohen LE. Idiopathic short stature: A clinical review. *JAMA* 2014;311:1787-96.
- Wit JM, Clayton PE, Rogol AD, Savage MO, Saenger PH, Cohen P. Idiopathic short stature: Definition, epidemiology, and diagnostic evaluation. *Growth Horm IGF Res* 2008;18:89-110.
- Wu S, Liu QQ, Gu W, Ni SN, Shi X, Zhu ZY. A retrospective analysis of patients with short stature in the South of China between 2007 and 2015. *Biomed Res Int* 2018;2018:5732694.
- Yang CW, Chang YH, Chu CH, Chu SY. The etiology of short stature in children in Eastern Taiwan: A retrospective study. *Tzu Chi Med J* 2010;22:87-9.
- Hitt T, Ginsburg KR, Cousounis P, Lipman TH, Cucchiara AJ, Stallings VA, et al. Concerns and expectations of parents seeking subspecialist care for their child’s short stature. *Horm Res Paediatr* 2019;92:311-8.
- Song KC, Jin SL, Kwon AR, Chae HW, Ahn JM, Kim DH, et al. Etiologies and characteristics of children with chief complaint of short stature. *Ann Pediatr Endocrinol Metab* 2015;20:34-9.
- Murano MC, Feldt MM, Lantos JD. Parental concerns on short stature: A 15-year follow-up. *J Pediatr* 2020;220:237-40.
- Backeljauw P, Cappa M, Kiess W, Law L, Cookson C, Sert C, et al. Impact of short stature on quality of life: A systematic literature review. *Growth Horm IGF Res* 2021;57-58:101392.
- Quitmann JH, Bullinger M, Sommer R, Rohenkohl AC, Bernardino Da Silva NM. Associations between psychological problems and quality of life in pediatric short stature from patients’ and parents’ perspectives. *PLoS One* 2016;11:e0153953.
- Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, et al. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: Growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-i deficiency. *Horm Res Paediatr* 2016;86:361-97.
- Li Y, Chen X, Liu Z, Yang J. Chinese herbal medicine for children with idiopathic short stature (ISS): A systematic review and meta-analysis. *PLoS One* 2022;17:e0270511.
- Lee B, Kwon CY, Jang S. Comparative effectiveness of East Asian traditional medicine for treatment of idiopathic short stature in children: A protocol for systematic review and network meta-analysis. *Medicine (Baltimore)* 2020;99:e22856.
- Zhong Y, Guo Y, Hao Y. Advances in Chinese and Western medicine for idiopathic dwarfism. *MEDS Clin Med* 2022;3:93-100.
- Xia L, Zhang H, Jin X, Ma Y. Discussion on the TCM diagnosis and treatment ideas and methods of short stature from the theory of “spleen-liver-kidney correlation”. *Int J Clin Exp Med Res* 2020;4:248-53.
- Lee B, Kwon CY, Jang S. Analysis of pattern identification and related symptoms on idiopathic short stature – Focusing on traditional Chinese medicine literature. *J Pediatr Korean Med* 2021;35:1-17.

17. Jiang XY, Yan HQ, Wu HQ. Research on the clinical effect of Sijunzi decoction combined with recombinant human growth hormone on idiopathic dwarfism. *Guangming J Chin Med* 2020;35:579-81.
18. Sun FP, Han X, Cui WF, Ge GL. Idiopathic short stature treatment based on syndrome differentiation of liver, kidney, spleen and stomach. *Clin J Chin Med* 2017;9:13-5.
19. Tan KL, He JF, Qu YT, Xie MZ, Lei XM, Dai FY. Observation on therapeutic effect of moxibustion and exercise for children with short stature of deficiency of the kidney essence. *Zhongguo Zhen Jiu* 2009;29:613-5.
20. Chen Q, Xuan GQ. Syndrome differentiation and treatment of short stature. *Mod J Integr Trad Chin West Med* 2005;14:2307-8.
21. Gustafson L, Erikson C, Warkentin S, Brun A, Englund E, Passant U. A factor analytic approach to symptom patterns in dementia. *Int J Alzheimers Dis* 2010;2011:632604.
22. Xiong G, Virasakdi C, Geater A, Zhang Y, Li M, Lerkiatbundit S. Factor analysis on symptoms and signs of chronic low-back pain based on traditional Chinese medicine theory. *J Altern Complement Med* 2011;17:51-5.
23. Wang TF. *Chinese Medicine Diagnostics*. Beijing: People's Medical Press; 2019.
24. Li H. *Traditional Chinese Medicine Syndrome*. Beijing: China Medical Science and Technology Press; 2008.
25. Lin S, Yang W, Yu J. Guideline for clinical diagnosis and treatment of pediatrics of traditional Chinese medicine – Sexual precocity (amendment). *J Pediatr Trad Chin Med* 2016;13:1-5.
26. Xie Q. *Modern Neuroendocrinology*. Shanghai: Fudan University Press; 1999.
27. Li ZG. Theory of modernization traditional Chinese medicine in kidney. *Taipei J Tradit Chin Med* 2011;14:57-64.
28. Juan D. Traditional Chinese medicine clinical treatment of short stature in children. *J Sichuan Tradit Chin Med* 2022;10:34-7.
29. Yu J, Shi Y. Clinical investigation and perspective of traditional Chinese medicine on children with short stature. *Chin Pediatr Integr Trad Western Med* 2015;7:193-5.
30. Zhou F, Hou CG. Clinical study on little girls at early puberty treated with Zhibai Dihuang pill, Da Buyin pill and lysine. *Chin J Tradit Med Sci Technol* 2012;9:204-6.
31. Sun FP, Ge GL, Han X, Cui WF. Clinical observation on 20 cases of idiopathic short stature in preschool children treated with Buzhong Zhuzhang granules. *J Pediatr Tradit Chin Med* 2017;13:57-60.
32. Maciocia G. *Diagnosis in Chinese Medicine: A Comprehensive Guide*. Edinburgh: Elsevier Limited; 2004.
33. Chen Q, Xuan G. The essence of Xuan Guiqi's diagnosis and treatment of idiopathic short stature. *Jiangsu J Tradit Chin Med* 2011;43:17-8.
34. Sun Y, Wang Y, Feng Y. Application of TCM regulating spleen, liver and kidney in the treatment of short stature. *Chin Pediatr Integr Tradit West Med* 2015;7:213-5.
35. Grigoletto V, Occhipinti AA, Pellegrin MC, Sirchia F, Barbi E, Tornese G. Definition and prevalence of familial short stature. *Ital J Pediatr* 2021;47:56.
36. Chen SC, Lin CW, Lee PF, Chen HL, Ho CC. Anthropometric characteristics in Taiwanese adults: Age and gender differences. *Int J Environ Res Public Health* 2021;18:7712.

SUPPLEMENTARY MATERIALS

Supplementary Table 1: Pediatric growth traditional Chinese medicine syndrome questionnaire

Age: _____ Height: _____ Weight: _____

Body mass index: _____ Birth weight (g): _____

Father's height: _____ Mother's height: _____

A. Past history and trauma history: Please tick and indicate the approximate age in brackets

scoliosis fracture ()

trauma (such as falling to the ground, falling down the stairs, car accident, etc.): _____ ()

surgery: _____ ()

other: _____ ()

B. Symptoms: Please answer according to the situation in the past month (please tick)

Number	Symptom	Score 0:	Score 1:	Score 2:	Score 3:	Score 4:
		Disagree	Slightly agree	Moderately agree	Very agree	Extremely agree
1	In situations where the environment is not hot or others do not perceive it as hot, the child may feel that their palms, soles of the feet, or chest are hot. Alternatively, parents may feel that their child's palms or soles of the feet have a higher temperature when touched					
2	In situations where the environment is not hot or others do not perceive it as hot, the child may feel sudden waves of warmth in their head, face, or body. Alternatively, parents may notice that their child doesn't have any particular circumstances but tends to experience intermittent sweating					
3	In a hot environment, the child may feel uncomfortable. Alternatively, even when others feel cool, the child may still say they feel hot					
4	In situations where the environment is not hot or others do not perceive it as hot, the child may experience sweating during sleep but not sweat or have reduced sweating upon waking up					
5	The child is prone to feeling annoyed or angry. Alternatively, parents may perceive that the child is easily impatient or irritable					
6	The child tends to sigh easily					
7	The child feels that they have many dreams and can remember them upon waking up. Alternatively, parents often hear the child talking in their sleep or notice that the child tends to toss and turn or even make movements with their hands and feet during sleep					
8	In a favorable sleep environment, the child has difficulty falling asleep and usually takes >20 min to do so. Additionally, once asleep, the child is easily disturbed and wakes up easily					
9	The child tends to feel a heavy sensation in their body or lower half of the body					
10	The child feels tired or weak and does not feel like moving, or even with slight movement, they feel lacking in strength					
11	The child does not enjoy talking or parents feel that the child is reluctant to speak and often uses nodding or shaking the head instead of answering					
12	The child tends to feel dizzy or lightheaded					
13	The child tends to feel a heavy sensation in the head, as if it is being wrapped or covered by something					
14	The child is prone to redness or bloodshot eyes					
15	The child tends to feel swollen or experience eye pain					
16	The child tends to feel dryness in the eyes					
17	The child often has eye discharge or secretions					
18	The child tends to feel thirsty or have a dry mouth					
19	The child tends to experience a bitter taste in the mouth					
20	Parents often perceive that the child has bad breath					
21	The child tends to feel a sticky sensation in the mouth					
22	The child feels a bloated or stuffy sensation on both sides of the chest (from the armpits to the lower edge of the ribs) or below the rib margin					
23	The child tends to experience breast swelling or breast pain easily					
24	The child easily feels a stuffy sensation in the chest					

- 25 The child has a good appetite and eats more than other children of the same age
 - 26 The child has a poor appetite and eats less than children of the same age, or eats less than before. Alternatively, even without consuming snacks or desserts, the child does not feel hungry during meal times
 - 27 The child enjoys eating sweet or greasy foods
 - 28 The child is prone to nausea, vomiting, or easily producing phlegm and excessive salivation
 - 29 After eating a normal amount of food, the child feels a bloated or distended sensation in the stomach or abdomen
 - 30 The child experiences dry and hard stools or has difficulty passing stools, needing to strain during bowel movements. Alternatively, there may be instances of bleeding after bowel movements. Also, it takes longer for a child to complete a bowel movement without distraction
 - 31 The child's stools are shapeless or not in strips
 - 32 Apart from the first urination in the morning after waking up, the child's urine tends to have a darker color or the volume of urine is often less
 - 33 The child has acne or pimples
 - 34 The child's skin is prone to rashes or bumps
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