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Review Article

Traditional Chinese Medicine Syndromes for Essential Hypertension: A Literature Analysis of 13,272 Patients

Jie Wang, Xingjiang Xiong, and Wei Liu

Department of Cardiology, Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China

Correspondence should be addressed to Wei Liu; lvzyxxg@163.com

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Background. To simplify traditional Chinese medicine syndrome differentiation and allow researchers to master syndrome differentiation for hypertension, this paper retrospectively studied the literature and analyzed syndrome elements corresponding to hypertension syndromes. Methods. Six databases including PubMed, EMBASE, Chinese Bio-Medical Literature Database, Chinese National Knowledge Infrastructure, Chinese Scientific Journal Database, and Wan-fang Data were searched from 1/January/2003 to 30/October/2013. We included all clinical literature testing hypertension syndromes and retrospectively studied the hypertension literature published from 2003 to 2013. Descriptive statistics calculated frequencies and percentages. Results. 13,272 patients with essential hypertension were included. Clinical features of hypertension could be attributed to 11 kinds of syndrome factors. Among them, seven syndrome factors were excess, while four syndrome factors were deficient. Syndrome targets were mainly in the liver and related to the kidney and spleen. There were 33 combination syndromes. Frequency of single-factor syndromes was 31.77% and frequency of two-factor syndromes was 62.26%. Conclusions. Excess syndrome factors of hypertension patients include yang hyperactivity, blood stasis, phlegm turbidity, internal dampness, and internal fire. Deficient syndrome factors of hypertension patients are yin deficiency and yang deficiency. Yin deficiency with yang hyperactivity, phlegm-dampness retention, and deficiency of both yin and yang were the three most common syndromes in clinical combination.

1. Introduction

Hypertension is an important public health issue worldwide because of its high prevalence and concomitant increase in disease risk [1–3]. It has been estimated that 29% of the world's adult population, or approximately 1.56 billion people, will have hypertension by 2025 [4, 5]. Complementary and alternative medicine (CAM) is becoming increasingly popular [6–13] and numerous interventions are regularly recommended to lower elevated blood pressure (BP) [14–17]. Traditional Chinese medicine (TCM), including herbal medicine and acupuncture, is an important component of CAM therapies [18–21]. Hypertension could be improved by insights from TCM and considerable progress has been made in lowering BP by TCM [22–26].

Syndrome differentiation is a diagnostic and treatment method used in TCM [27, 28]. It plays an important role in the therapeutic process and affects the therapeutic result of certain diseases [29–31]. The syndrome is not only

the basic unit of TCM theory and syndrome differentiation, but also the bridge to associating disease and formula [32-35]. TCM syndrome, which is different from a disease or symptoms, is the abstraction of a major pathogenesis. Syndromes are identified from a comprehensive analysis of all symptoms and signs (including tongue appearance and pulse feeling) from the four main diagnostic TCM methods: observation, listening, questioning, and pulse analyses [36-40]. However, syndromes are the product of speculation in TCM. Therefore, they depend on medical experience, academic origins, and other factors. Therefore, the concept of syndromes is vague and broad, which makes clinical application difficult. Syndrome elements, which are the minimum units of syndromes, contribute to simplifying syndrome differentiation and understanding TCM syndromes. Each element has specific symptoms.

To simplify TCM syndrome differentiation and enable researchers not familiar with Chinese medicine to master the laws of hypertension syndrome differentiation, this paper

retrospectively studied the literature for 13,272 patients with hypertension, published from 2003 to 2013. This study is beneficial to deepening of the understanding of hypertension and providing a basis and reference for clinical treatment using TCM syndrome differentiation.

2. Materials and Methods

2.1. Database and Search Strategies. Six databases including PubMed, EMBASE, Chinese Bio-Medical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), and Wan-fang Data were searched from 1/January/2003 to 30/October/2013. Databases in Chinese were searched to retrieve the maximum possible number of trials of syndrome differentiation for essential hypertension (EH) because syndrome differentiation is mainly used in China. Ongoing registered clinical trials were searched at the International Clinical Trial Registry by the U.S. National Institutes of Health (http://clinicaltrials.gov/). The following search terms were used individually or combined: "hypertension," "blood pressure," "essential hypertension," "syndrome differentiation," "vertigo," "headache," "parting," and "traditional Chinese medicine therapy." The bibliographies of included studies were searched for additional references.

2.2. Inclusion and Exclusion Criteria. Systolic blood pressure (SBP) ≥140 mmHg (1 mmHg = 0.133 kPa) and diastolic blood pressure (DBP) ≥90 mmHg from the literature were based on 1999 WHO-ISH Guidelines for the Management of Hypertension (1999 WHO-ISH GMH), 1998 WHO-ISH Guidelines for the Management of Hypertension (1998 WHO-ISH GMH), 2000 WHO-ISH Guidelines for the Management of Hypertension (2000 WHO-ISH GMH), Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005), China Guidelines on Prevention and Management of High Blood Pressure-2006 (CGPMHBP-2006), and Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). Syndrome differentiation of TCM diagnosis used the Standard of TCM Diagnosis and Curative Effect of Disease-Syndrome, published by the State Administration of Traditional Chinese Medicine in 1994. Standards of dialectical classification used Clinical Research Guiding Principles of New Medicine of Chinese Herbs revised by the State Food and Drug Administration in 2002. Exclusion criteria were secondary hypertension, gestational hypertension, repeated literature, reviews, and literature with no clear classification.

2.3. Classification Criteria of Syndrome Elements. According to the classification criteria of syndrome elements proposed by Wang, statistical analysis was conducted for syndromes included in the cases. The classification criteria of syndrome elements were (1) six-excess external contraction: wind, cold, dampness, dryness, and fire; (2) five endogenous qi: internal wind, internal cold, internal dampness, internal dryness, and internal fire; (3) factors related to gas: qi deficiency, qi

stagnation, qi block, qi counterflow, qi fall, and qi collapse; (4) factors related to blood: blood deficiency, blood stasis, blood collapse, blood dryness, and bleeding; (5) factors related to yin and yang: yin deficiency, yang deficiency, yin exuberance, and yang hyperactivity; (6) others: poison, excessive fluid, and phlegm turbidity.

2.4. Statistical Methods. Two authors conducted the literature search, study selection, and data extraction independently. Disagreements were resolved by discussion and consensus was met through a third party. SPSS 11.5 statistical software was used for data analyses (Chicago, IL, USA). Descriptive statistics procedures calculated frequency and percentage.

3. Results

3.1. Description of Included Literature. After a primary search of the databases, 503 articles were screened. After reading the titles and abstracts, 398 articles were excluded the reasons included; retrospective study that did not match the included criteria of this review (n=42) and duplicated titles (n=356). The full texts of 83 articles [41–123] were retrieved, and 22 articles were excluded for the following reasons: participants not meeting the inclusion criteria (n=11), duplicated data (n=5), patients having other diseases (n=5), and no data for extraction (n=1). In the end, 83 articles [41–123] were included, and all trials were conducted in China (Figure 1). The characteristics of included trials are listed in Table 1.

Overall, 13,272 patients with essential hypertension were included, with an average of 160 per trial, ranging from 23 to 703. Among them, 7075 were men, accounting for 53.3%, while 6197 were women, accounting for 46.7%. There was a wide range in patient age (18–92 years). Sources of cases included 24 provinces and the number of papers in each region is shown in Table 2.

3.2. Extraction of Syndrome Elements of EH. According to the definition of syndrome elements and classification criteria, syndrome elements were obtained and classified from the literature as follows: blood stasis (qi stagnation and blood stasis, qi deficiency with blood stasis, kidney deficiency and blood stasis, stasis blocking channels, phlegm and blood stasis resistance winding); qi stagnation (liver qi stagnation, qi stagnation and blood stasis); phlegm (phlegm turbidity resistance, phlegm-dampness retention); internal fire (intense liver fire, internal harassment of phlegm-heat); internal dampness (spleen deficiency with dampness encumbrance, phlegm-damp retention); internal wind (internal stirring of liver wind, wind-yang interference); qi deficiency (dual deficiency of qi and yin, dual deficiency of qi and blood, and qi deficiency with blood stasis); yang hyperactivity (ascendant hyperactivity of liver yang, yin deficiency with yang hyperactivity); yin deficiency (yin deficiency with yang hyperactivity, liver-kidney yin deficiency, dual deficiency of qi and yin, and deficiency of both yin and yang); yang deficiency (kidney yang deficiency, deficiency of both yin and yang); blood deficiency (dual deficiency of qi and blood).

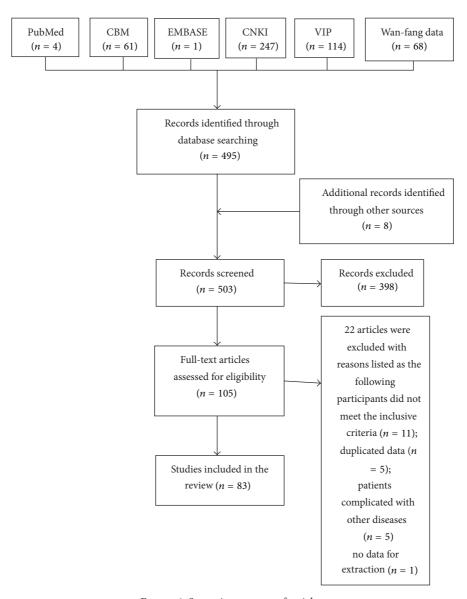


FIGURE 1: Screening process of articles.

As a result, 13,272 cases of hypertension syndrome were classified as 11 syndrome element types, which cover all cases.

3.3. Analysis of Syndrome Elements of EH. Syndrome elements of 13,272 patients with hypertension were divided into excessive syndrome elements and deficient syndrome elements (Table 3, Figure 2). The proportions of excessive syndrome elements are yang hyperactivity (19.08%), phlegm turbidity (13.68%), internal fire (13.21%), internal dampness (11.04%), blood stasis (4.86%), internal wind (1.21%), and qi stagnation (0.78%). The proportion of deficient syndrome elements are yin deficiency (26.27%), yang deficiency (7.89%), qi deficiency (1.80%), and blood deficiency (0.18%). Excessive syndrome elements greater than 10% included yang hyperactivity, phlegm turbidity, internal fire, and internal dampness. Deficient syndrome elements greater

than 10% included yin deficiency. Yang hyperactivity and yin deficiency were the most common syndrome elements of hypertension.

3.4. Targets of Syndrome Elements of EH. The targets of syndrome elements are the disease locations of individual syndrome elements. Disease location of syndrome elements was confirmed according to the five zang-organs and six fuorgans, chi heng fu, and meridians.

As a result, 9091 cases (68.50%) had clear targets of syndrome elements related to liver, kidney, and spleen (Table 4). There were 7789 cases of liver syndromes (85.68%). Among them, there were 2793 cases of internal fire of liver (35.86%), 4033 cases of ascendant hyperactivity of liver yang (51.78%), 543 cases of liver yin deficiency (6.97%), 164 cases of liver qi stagnation (2.11%), and 256 cases of internal stirring of liver wind (3.29%). There were 903 cases of kidney syndromes

TABLE 1: Characteristics of included studies.

Study ID	Sample (M/F)	Age (years)	Diagnosis standard	TCM syndrome differentiation (number of patients)	Region of China
Xu and Chen 2012 [13]	122 (58/64)	60-79	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Phlegm and blood stasis resistance winding (39), yin deficiency with yang hyperactivity (44), and idney deficiency (39)	Beijing
Ferreira and Lopes 2011 [14]	448 (243/205)	M: 62.1 ± 10.9 F: 59.3 ± 8.7	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (284), yin deficiency with yang hyperactivity (43), phlegm-damp retention (74), and deficiency of both yin and yang (47)	Jiangsu
Wang et al. 2013 [15]	99 (50/49)	73 ± 6.1	1999 WHO-ISH GMH	Qi stagnation and blood stasis (99)	Guangdong
Lee et al. 2004 [16]	87 (48/39)	M: 62.7 ± 8.3 F: 58.9 ± 7.5	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Ascendant hyperactivity of liver yang (32), phlegm-damp retention (27), and qi deficiency with blood stasis (28)	Guangdong
Wang et al. 2013 [17]	140 (83/57)	56.5 ± 9.8	Chinese Guidelines for the Management of Hypertension-2010 (CGMH-2010)	Intense liver fire (28), yin deficiency with yang hyperactivity (39), phlegm-damp retention (45), and deficiency of both yin and yang (28)	Heibei
Wang and Xion 2012 [18]	g 76 (38/38)	Not reported	Chinese Guidelines for the Management of Hypertension-2010 (CGMH-2010)	Kidney deficiency and blood stasis (76)	Fujian
Xiong et al. 2013 [19]	395 (228/167)	53 ± 17	Hypertension diagnostic criteria (unclear)	Intense liver fire (54), yin deficiency with yang hyperactivity (177), phlegm-damp retention (62), and deficiency of both yin and yang (102)	Liaoning
Wang et al. 2013 [20]	120 (60/60)	29–62	Hypertension diagnostic criteria (unclear)	Ascendant hyperactivity of liver yang (30), yin deficiency with yang hyperactivity (30), phlegm-damp retention (30), and deficiency of both yin and yang (30)	Hainan
Wang et al. 2013 [21]	184 (83/101)	18-80	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (21), yin deficiency with yang hyperactivity (75), phlegm-damp retention (81), and deficiency of both yin and yang (7)	Jiangsu
Chen 1993 [22]	60 (30/30)	T: 48 ± 8.1 C: 47 ± 6.7	1999 WHO-ISH GMH	Dual deficiency of qi and yin (60)	Guangdong
Wang et al. 2012 [23]	53 (16/37)	40-80	1999 WHO-ISH GMH	Insufficiency of spleen with overabundance of dampness (19), dual deficiency of qi and blood (20), and liver-kidney yin deficiency (14)	Neimenggu
Wang et al. 2013 [24]	112 (83/29)	53.5 ± 11.04	1999 WHO-ISH GMH	Intense liver fire (19), yin deficiency with yang hyperactivity (23), phlegm-damp retention (16), and deficiency of both yin and yang (22)	Jiangxi
Wang and Xion 2012 [25]	61 (M/F not reported)	T: 57.1 ± 6.16 C: 55.67 ± 6.28	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Blood stasis (61)	Guangdong
Chen et al. 2011 [26]	259 (108/151)	65.58 ± 12.17	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (35), yin deficiency with yang hyperactivity (89), phlegm-damp retention (88), and deficiency of both yin and yang (47)	Beijing
Xu and Chen 2011 [27]	81 (53/28)	52.79 ± 12.83	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (42), yin deficiency with yang hyperactivity (18), phlegm-damp retention (14), and deficiency of both yin and yang (7)	Zhejiang

Table 1: Continued.

Study ID	Sample (M/F)	Age (years)	Diagnosis standard	TCM syndrome differentiation (number of patients)	Region of China
Chen et al. 2012 [28]	183 (85/98)	66.81 ± 8.81	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Intense liver fire (28), yin deficiency with yang hyperactivity (53), phlegm-damp retention (57), and deficiency of both yin and yang (45)	Jiangsu
Liu et al. 2011 [29]	89 (45/44)	M: 59.5 ± 10.9 F: 59.3 ± 11.0	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (59), yin deficiency with yang hyperactivity (5), phlegm-damp retention (13), and deficiency of both yin and yang (12)	Jiangsu
Dobos and Tao 2011 [30]	342 (213/129)	M: 59.43 ± 16.76 F: 59.43 ± 11.82	1999 WHO-ISH GMH	Intense liver fire (51), yin deficiency with yang hyperactivity (139), phlegm-damp retention (85), and deficiency of both yin and yang (67)	Guangdong
Xiong et al. 2011 [31]	562 (297/265)	M: 62.1 ± 10.8 F: 58.5 ± 9.1	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (352), yin deficiency with yang hyperactivity (58), phlegm-damp retention (97), and deficiency of both yin and yang (55)	Jiangsu
Wang and Xiong 2012 [32]	398 (199/199)	59.20 ± 9.54	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (88), yin deficiency with yang hyperactivity (196), phlegm-damp retention (89), and deficiency of both yin and yang (25)	Jiangsu
Wang et al. 2013 [33]	178 (81/97)	18-80	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (49), yin deficiency with yang hyperactivity (43), phlegm-damp retention (57), and deficiency of both yin and yang (29)	Shanghai
Tian 2011 [34]	200 (109/91)	30-75	1999 WHO-ISH GMH	Intense liver fire (37), yin deficiency with yang hyperactivity (55), phlegm-damp retention (82), and deficiency of both yin and yang (26)	Tianjin
Wang and Xiong 2012 [35]	120 64/56	T: 62.77 ± 9.18 C: 59.63 ± 8.77	1999 WHO-ISH GMH	Intense liver fire (37), yin deficiency with yang hyperactivity (55), phlegm-damp retention (82), and deficiency of both yin and yang (26)	Hunan
Wang et al. 2012 [36]	494 (264/230)	M: 61.6 ± 10.6 F: 58.3 ± 8.5	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Ascendant hyperactivity of liver yang (313), yin deficiency with yang hyperactivity (52), deficiency of both yin and yang (83), and liver-kidney yin deficiency (46)	Jiangsu
Xu and Chen 2008 [37]	150 (M/F not reported)	Not reported	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (29), randomized stagnation of phlegm (53), dual deficiency of qi and yin (30), and stasis blocking channels (38)	Xinjiang
Cheung 2011 [38]	109 (68/41)	65.6 ± 10.6	1999 WHO-ISH GMH	Intense liver fire (19), yin deficiency with yang hyperactivity (18), phlegm-damp retention (34), and deficiency of both yin and yang (38)	Fujian
Xiong et al. 2013 [39]	102 (58/44)	37–85	1999 WHO-ISH GMH	Intense liver fire (18), yin deficiency with yang hyperactivity (31), phlegm-damp retention (23), and deficiency of both yin and yang (30)	Guizhou
Lu et al. 2004 [40]	40 (23/17)	Not reported	1999 WHO-ISH GMH	Blood stasis (40)	Guangdong
Zhao et al. 2012 [41]	60 (41/19)	T: 62.07 ± 8.88 C: 57.3 ± 9.09	1999 WHO-ISH GMH and Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Blood stasis (60)	Guangdong

Table 1: Continued.

Study ID	Sample (M/F)	Age (years)	Diagnosis standard	TCM syndrome differentiation (number of patients)	Region of China
Liu et al. 2009 [42]	60 (36/24)	T: 53.87 ± 5.92 C: 52.97 ± 5.40	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Phlegm-damp retention (60)	Shanghai
Wang et al. 2012 [43]	82 (49/33)	60-75	1999 WHO-ISH GMH	Liver-kidney yin deficiency (82)	Heilongjiang
Luo et al. 2011 [44]	100 (42/58)	36-81	Hypertension diagnostic criteria (unclear)	Ascendant hyperactivity of liver yang (12), yin deficiency with yang hyperactivity (60), phlegm-damp retention (18), and kidney deficiency (10)	Guangxi
Wang et al. 2012 [45]	80 (48/32)	68.05 ± 5.41	1999 WHO-ISH GMH	Liver-kidney yin deficiency (80)	Guangxi
Wang et al. 2011 [46]	251 (148/103)	55 ± 19	1999 WHO-ISH GMH	Intense liver fire (71), yin deficiency with yang hyperactivity (62), phlegm-damp retention (60), and deficiency of both yin and yang (58)	Liaoning
Bai et al. 2005 [47]	122 (71/51)	T: 44.7 ± 11.6 C: 46.2 ± 9.5	1999 WHO-ISH GMH	Ascendant hyperactivity of liver yang (35), liver-kidney yin deficiency (18), phlegm-damp retention (32), dual deficiency of qi and yin (25), and stasis blocking channels (12)	Hebei
Yang et al. 2005 [48]	80 (41/39)	M: 51.28 ± 6.96 F: 52.71 ± 6.57	1999 WHO-ISH GMH	Ascendant hyperactivity of liver yang (80)	Henan
Xia et al. 2010 [49]	40 (M/F not reported)	T: 55.23 ± 6.01 C: 55.13 ± 6.34	1999 WHO-ISH GMH	Ascendant hyperactivity of liver yang (40)	Gansu
Liu et al. 2003 [50]	60 (43/17)	45-73	Chinese Guidelines for the Management of Hypertension-2009 (CGMH-2009)	Yang hyperactivity (29), phlegm turbidity resistance (31)	Zhejiang
Yin and Liu 2005 [51]	36 (M/F not reported)	40.50 ± 11.51	1999 WHO-ISH GMH	Phlegm-damp retention (36)	Jiangsu
Wu et al. 2010 [52]	90 (41/39)	32–78	1999 WHO-ISH GMH	Ascendant hyperactivity of liver yang and blood stasis (90)	Hebei
Deng 2008 [53]	60 (45/15)	T: 61 ± 4.12 C: 61 ± 4.02	1999 WHO-ISH GMH	Qi deficiency with blood stasis (60)	Hebei
Wu and Xu 2010 [54]	60 (32/28)	Not reported	1999 WHO-ISH GMH	Dual deficiency of qi and yin (60)	Guizhou
Wang et al. 2011 [55]	276 170/106	M: 53.4 ± 21.1 F: 55.6 ± 17.3	1999 WHO-ISH GMH	Wind-yang interference (22), stasis blocking channels (73), yin deficiency with yang hyperactivity (134), and phlegm turbidity resistance (47)	Guangxi
Wu et al. 2010 [56]	156 (79/77)	T: 48 ± 6.9 C: 49 ± 8.2	Hypertension diagnostic criteria (unclear)	Ascendant hyperactivity of liver yang (52), yin deficiency with yang hyperactivity (53), and deficiency of both yin and yang (51)	Zhejiang
Fan and Liu 2010 [57]	395 (203/192)	30-80	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Qi deficiency with blood stasis (65), intense liver fire (91), yin deficiency with yang hyperactivity (63), phlegm-damp retention (57), deficiency of both yin and yang (39), and dual deficiency of qi and blood (18)	Beijing

Table 1: Continued.

Study ID	Sample (M/F)	Age (years)	Diagnosis standard	TCM syndrome differentiation (number of patients)	Region of China
Zhu et al. 2009 [58]	54 (30/24)	61.74 ± 14.89	1999 WHO-ISH GMH	Kidney yang deficiency (24), kidney yin deficiency (30)	Yunnan
Liu et al. 2009 [59]	140 (68/72)	34–79	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (16), yin deficiency with yang hyperactivity (52), phlegm-damp retention (41), and deficiency of both yin and yang (31)	Guangxi
He et al. 2013 [60]	230 (65/165)	43-74	1999 WHO-ISH GMH	Intense liver fire (28), ascendant hyperactivity of liver yang (148), and liver-kidney yin deficiency (54)	Guangdong
Tang et al. 2012 [61]	100 (37/63)	55.1 ± 6.2	1999 WHO-ISH GMH	Intense liver fire (19), yin deficiency with yang hyperactivity (29), deficiency of both yin and yang (20), and liver-kidney yin deficiency (32)	Shanghai
Gong et al. 2010 [62]	120 (60/60)	T: 55.38 ± 8.01 C: 56.80 ± 8.58	1999 WHO-ISH GMH	Intense liver fire (30), yin deficiency with yang hyperactivity (30), phlegm-damp retention (30), and deficiency of both yin and yang (30)	Shandong
Zhang et al. 2005 [63]	60 (32/28)	62.22 ± 6.12	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Intense liver fire (8), yin deficiency with yang hyperactivity (28), phlegm-damp retention (14), and deficiency of both yin and yang (10)	Guangxi
Liu et al. 2009 [64]	200 (105/95)	M: 61.88 ± 11.91 F: 63.07 ± 12.45	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (51), yin deficiency with yang hyperactivity (49), phlegm-damp retention (50), and deficiency of both yin and yang (50)	Guangxi
Wang 2012 [65]	200 (103/94)	46.4 ± 15.46	1999 WHO-ISH GMH	Intense liver fire (96), yin deficiency with yang hyperactivity (46), phlegm-damp retention (18), and deficiency of both yin and yang (37)	Shanxi
Yao and Huang 2007 [66]	47 (22/25)	66.00 ± 12.35	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Intense liver fire (12), yin deficiency with yang hyperactivity (11), phlegm-damp retention (12), and deficiency of both yin and yang (12)	Tianjin
Guo et al. 2002 [67]	120 (62/58)	T: 63.64 ± 9.22 C: 60.30 ± 3.36	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Intense liver fire (30), yin deficiency with yang hyperactivity (30), phlegm-damp retention (30), and deficiency of both yin and yang (30)	Anhui
Zhang et al. 2011 [68]	320 (135/185)	66.40 ± 12.56	2007 WHO-ISH GMH	Intense liver fire (36), yin deficiency with yang hyperactivity (101), phlegm-damp retention (125), and deficiency of both yin and yang (58)	Jiangsu
Liao et al. 2010 [69]	23 (14/9)	T: 65 ± 5 C: 65 ± 8	1999 WHO-ISH GMH	Blood stasis (23)	Fujian
Xiong 2010 [70]	70 (37/33)	53.06 ± 8.62	Hypertension diagnostic criteria (unclear)	Intense liver fire (13), yin deficiency with yang hyperactivity (21), phlegm-damp retention (25), and deficiency of both yin and yang (11)	Heilongjiang
Jiang et al. 2012 [71]	86 (50/36)	36-81	Hypertension diagnostic criteria (unclear)	Yin deficiency with yang hyperactivity (86)	Guangdong
Huang and Wei 2012 [72]	260 (119/141)	65.56 ± 8.42	Chinese Guidelines for the Management of Hypertension-2010 (CGMH-2010)	Intense liver fire (56), yin deficiency with yang hyperactivity (77), phlegm-damp retention (73), and deficiency of both yin and yang (54)	Beijing

Table 1: Continued.

Study ID	Sample (M/F)	Age (years)	Diagnosis standard	TCM syndrome differentiation (number of patients)	Region of China
Lu 2004 [73]	138 (97/41)	61.84 ± 5.25	1999 WHO-ISH GMH	Intense liver fire (16), yin deficiency with yang hyperactivity (43), phlegm-damp retention (45), and deficiency of both yin and yang (34)	Fujian
Sun and Wang 2005 [74]	703 (382/321)	50-79	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Yin deficiency with yang hyperactivity (215), phlegm-damp retention (83), deficiency of both yin and yang (91), ascendant hyperactivity of liver yang (135), liver-kidney yin deficiency (92), yang deficiency (11), qi deficiency (14), dual deficiency of qi and yin (14), blood stasis (11), qi deficiency with blood stasis (3), internal harassment of phlegm-heat (22), internal harassment of phlegm-heat and blood stasis (3), liver-kidney yin deficiency and blood stasis (2), internal harassment of phlegm-heat and qi deficiency (1), deficiency of both yin and yang and internal harassment of phlegm-heat (1), liver-kidney yin deficiency and phlegm-damp retention (1), yin deficiency with yang hyperactivity and blood stasis (1), ascendant hyperactivity of liver yang and internal harassment of phlegm-heat (1), ascendant hyperactivity of liver yang and blood stasis (1), and deficiency of both yin and yang and phlegm-damp retention (1)	Guangdong
Xiang et al. 2012 [75]	125 (75/50)	55–72	Hypertension diagnostic criteria (unclear)	Kidney deficiency and blood stasis (15), internal stirring of liver wind (68), qi deficiency with blood stasis (21), and intermingled phlegm and blood stasis (21)	Guangdong
Zhu 2009 [76]	97 (41/56)	37–79	Hypertension diagnostic criteria (unclear)	Ascendant hyperactivity of liver yang (13), yin deficiency with yang hyperactivity (59), liver-kidney yin deficiency (16), and deficiency of both yin and yang (21)	Shandong
Xu and Wang 2009 [77]	80 (49/31)	40-83	1999 WHO-ISH GMH	Intense liver fire (18), yin deficiency with yang hyperactivity (17), phlegm-damp retention (35), and deficiency of both yin and yang (10)	Xinjiang
Lin and Kang 2012 [78]	69 (37/32)	T: 53.48 ± 10.02 C: 59.20 ± 5.610	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Liver-kidney yin deficiency (69)	Zhejiang
Feng et al. 2013 [79]	60 (60 M)	63.0 ± 7.5	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Ascendant hyperactivity of liver yang (60)	Fujian
Yu and Xing 2010 [80]	168 (108/60)	T: 58 ± 12 C: 54 ± 12	1999 WHO-ISH GMH	Intense liver fire (54), yin deficiency with yang hyperactivity (45), phlegm-damp retention (36), and deficiency of both yin and yang (33)	Beijing
Qiu et al. 2011 [81]	170 (122/48)	54 ± 11.6	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Intense liver fire (43), yin deficiency with yang hyperactivity (40), phlegm-damp retention (38), and deficiency of both yin and yang (49)	Beijing

Table 1: Continued.

Study ID	Sample (M/F)	Age (years)	Diagnosis standard	TCM syndrome differentiation (number of patients)	Region of China
Wu and Xu 2012 [82]	149 (74/75)	61.22 ± 9.36	Hypertension diagnostic criteria (unclear)	Intense liver fire (48), yin deficiency with yang hyperactivity (32), phlegm-damp retention (49), and deficiency of both yin and yang (20)	Hubei
Fang et al. 2007 [83]	220 (128/92)	34-73	1999 WHO-ISH GMH	Intense liver fire (98), yin deficiency with yang hyperactivity (79), phlegm-damp retention (19), and deficiency of both yin and yang (24)	Gansu
Fang et al. 2003 [84]	229 (113/116)	>35	Hypertension diagnostic criteria (unclear)	Liver-kidney yin deficiency (60), yin deficiency with yang hyperactivity (73), phlegm-damp retention (85), and deficiency of both yin and yang (11)	Hangzhou
Peng and Shi 2010 [85]	122 (57/65)	64.62 ± 8.86	1999 WHO-ISH GMH	Qi deficiency with blood stasis (26), intense liver fire (23), yin deficiency with yang hyperactivity (26), phlegm-damp retention (25), and deficiency of both yin and yang (22)	Anhui
Yang et al. 2004 [86]	151 (110/41)	Not reported	Hypertension diagnostic criteria (unclear)	Ascendant hyperactivity of liver yang (151)	Shandong
Shi et al. 2013 [87]	60 (29/31)	52.6 ± 12.3	Clinical research guiding principles of new medicine of Chinese traditional medicine	Phlegm-damp retention (60)	Zhejiang
Han 2004 [88]	377 (182/195)	20-60	Chinese Guidelines for the Management of Hypertension-2005 (CGMH-2005)	Intense liver fire (108), yin deficiency with yang hyperactivity (70), phlegm-damp retention (154), and deficiency of both yin and yang (45)	Anhui
Shen et al. 2008 [89]	79 (40/39)	T: 51.70 ± 4.53 C: 51.67 ± 4.36	Clinical research guiding principles of new medicine of Chinese traditional medicine	Phlegm and blood stasis resistance winding and ascendant hyperactivity of liver yang (79)	Guangzhou
Shen et al. 2005 [90]	290 (120/170)	66.2 ± 1.37	Chinese Guidelines for the Management of Hypertension-2004 (CGMH-2004)	Intense liver fire (34), yin deficiency with yang hyperactivity (99), phlegm-damp retention (114), and deficiency of both yin and yang (43)	Jiangsu
Liu et al. 2009 [91]	240 (120/120)	18-65	Hypertension diagnostic criteria (unclear)	Intense liver fire (240)	Anhui
Lu et al. 2011 [92]	80 (56/24)	T: 66.07 ± 7.15 C: 67.10 ± 7.32	1999 WHO-ISH GMH	Blood stasis (80)	Guangxi
Guo et al. 2006 [93]	60 (30/30)	Not reported	Chinese Guidelines for the Management of Hypertension-2010 (CGMH-2010)	Yin deficiency with yang hyperactivity (60)	Fujian
Zhang et al. 2012 [94]	140 (83/57)	56±10	Chinese Guidelines for the Management of Hypertension-2010 (CGMH-2010)	Ascendant hyperactivity of liver yang (28), yin deficiency with yang hyperactivity (39), phlegm-damp retention (45), and deficiency of both yin and yang (28)	Hebei
Dong et al. 2010 [95]	166 (106/60)	63-82	Hypertension diagnostic criteria (unclear)	Kidney yin deficiency and wind-phlegm (166)	Sichuan

(9.93%). Among them, there were 879 cases of kidney yin deficiency (97.34%) and 24 cases of kidney yang deficiency (2.66%). There were 399 cases of spleen syndromes (4.39%), all of which were spleen qi deficiency.

3.5. Combining Forms of Syndrome Elements of EH. We found that 13,272 cases of hypertension contained 33 syndrome types. According to the definition of syndrome elements, all syndromes were divided into four types: single factor,

Table 2: Number of papers and cases in region.

Region (China)	Provinces	Papers (pieces)	Cases	Male	Female
	Hebei	5	552	323	229
North China	Beijing	6	1374	718	656
North China	Inner Mongolia	1	53	16	37
	Tianjin	2	247	131	116
Northeast	Liaoning	2	646	376	270
Ivortifeast	Heilongjiang	2	152	86	66
	Xinjiang	2	230	124	106
Northwest	Shanxi	1	197	103	94
	Gansu	2	260	148	112
	Henan	2	200	101	99
Central China	Hubei	1	149	74	75
	Hunan	1	120	64	56
	Shandong	3	368	211	157
	Jiangsu	10	3004	1489	1515
	Anhui	4	859	421	438
East China	Zhejiang	6	655	354	301
	Fujian	6	466	307	159
	Jiangxi	1	112	83	29
	Shanghai	3	338	154	184
South China	Guangdong	12	1972	1047	925
South China	Guangxi	7	936	519	417
	Yunnan	1	54	30	24
Southwest China	Guizhou	2	162	90	72
	Sichuan	1	166	106	60
To	tal	83	13272	7075	6197

TABLE 3: Syndrome elements of 13,272 patients with essential hypertension.

Syndrome factors	Frequency	Percentage (%)
Yin deficiency	5554	26.27
Yang hyperactivity	4033	19.08
Phlegm turbidity	2892	13.68
Internal fire	2793	13.21
Internal dampness	2333	11.04
Yang deficiency	1668	7.89
Blood stasis	1027	4.86
Qi deficiency	380	1.80
Internal wind	256	1.21
Qi stagnation	164	0.78
Blood deficiency	38	0.18

two-factor, three-factor, and four-factor syndromes. The statistics of the combined forms of syndrome and their frequency (proportion more than 1%) are shown in Table 5. Internal fire is the most common in the single factor group, while yin deficiency with yang hyperactivity is the most common in the two-factor group. From highest to lowest frequency in the two-factor group are phlegm-damp retention, deficiency of both yin and yang, Liver-kidney

TABLE 4: Targets of syndrome elements.

Target	Percentage (%)
Liver	7789 (85.68)
Kidney	903 (9.93)
Spleen	399 (4.39)
Total	100

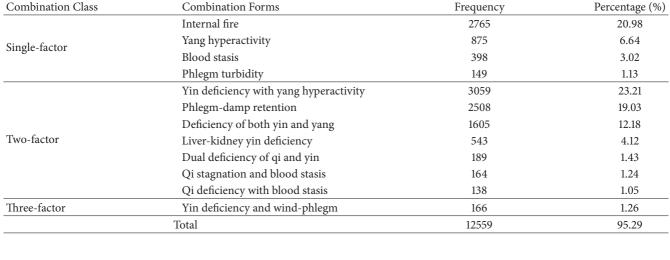
yin deficiency, dual deficiency of qi and yin, qi stagnation and blood stasis, and qi deficiency with blood stasis. The syndrome, yin deficiency and wind-phlegm, is the most common in the three-factor category. There were no four-factor combinations that reached a frequency of greater than 1%.

4. Discussion and Perspectives

4.1. Pathogenesis of Hypertension. Syndrome elements are the expression of pathogenesis of a disease [36]. According to the statistical results of syndrome elements, pathogenesis of EH can be summarized as simultaneous insufficiency and excess. Deficiency syndrome included yin deficiency, yang deficiency, qi deficiency, and blood deficiency. Excess

,	
ation Forms	Frequency
fire	2765
peractivity	875
asis	398

TABLE 5: Combined syndrome forms.



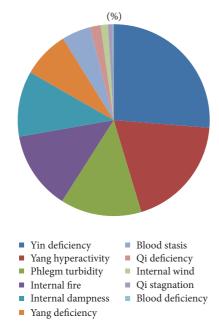


FIGURE 2: Percentage of syndrome factors.

syndrome included blood stasis, phlegm turbidity, qi stagnation, yang hyperactivity, internal fire, internal dampness, and internal wind. Among them, yin deficiency was the most common, followed by yang hyperactivity. Other elements, included in descending order, were phlegm turbidity, internal fire, internal dampness, yang deficiency, blood stasis, qi deficiency, and internal wind. The main disease location is the liver, which is closely related to the kidney and spleen.

4.2. Characteristics of Combined Syndrome Elements of EH. The combined forms of syndrome elements of hypertension have certain characteristics according to the literature, summarized as follows. (1) The combined forms of syndrome elements of hypertension have three forms, single-factor, two-factor, and three-factor forms. (2) Excess syndromes

are more common than deficiency syndromes for singlefactor syndromes, with internal fire, yang hyperactivity, blood stasis, and phlegm turbidity as the main syndrome factors. (3) Deficiency syndrome and excess syndrome was the most common two-factor syndrome, followed by excess syndrome and excess syndrome and deficiency syndrome and deficiency syndrome, respectively. (4) Syndrome of yin deficiency and wind-phlegm was the most common threefactor syndrome.

4.3. Implications for Instructing Clinical Application. The discovery of distributing characteristics of syndrome elements is conducive to instructing clinical application. Several Chinese herbs and classical formulas can lower BP and improve symptoms according to syndrome differentiation (Table 6). First, when aiming to cure internal fire syndrome, use Huanglian Jie Du Tang (detoxicant decoction of Coptis) to clear heat and toxins of the liver [35]. Chinese herbs such as Xiakucao (Prunella vulgaris L.) [123], Huanglian (Coptis chinensis) [124], Huangqin (Scutellaria baicalensis Georgi), Huang-bai (Phellodendron bark), and Zhizi (Gardenia) [125] can lower BP. Second, when aiming to cure yin deficiency with yang hyperactivity, use Tianma Gouteng Yin (decoction of Gastrodia and Uncaria), a famous prescription noted in Za Bing Zheng Zhi Xin Yi (New Meanings in Syndrome and Therapy of Miscellaneous Diseases). Chinese herbs such as Tianma (Gastrodia) [126] and Gouteng (Uncaria) [127] could suppress liver yang hyperactivity. Niuxi (Achyranthes root) [128] and Duzhong (Eucommia ulmoides) [129-131] had antihypertensive effects by nourishing the kidney. Third, when aiming to cure phlegm-damp retention, use Wuling powder [132], Zexie Tang (decoction of Alisma) [133], and Wendantang jiawei decoction (modified decoction for clearing away gallbladder heat). In addition, when aiming at wind-phlegm syndrome, use Banxia Baizhu Tianma Tang (decoction of Pinellia ternata, Atractylodes macrocephala, and Gastrodia elata) to calm the liver, strengthen the spleen, remove dampness, and reduce phlegm [35]. Chinese herbs such as Zexie (Alisma), Fuling (Poria cocos) [134], Zhuling

Table 6: Chinese herbs and classical formulas that lower BP and improve symptoms according to syndrome differentiation.

			4		
Syndrome	Formula	Components	TCM efficacy	Label	Chinese herbs
Internal fire syndrome	Huanglian Jie Du Tang (detoxicant decoction of Coptis)	Rhizoma Coptidis, Radix Scutellariae, Radix et Rhizoma Rhei, and Cortex Phellodendri Chinensis	Clear heat and toxins from liver	Classical prescription of Arcane Essentials from the Imperial Library dispensed by Wang Tao in Tang dynasty	Xiakucao (Prunella vulgaris L.), Huanglian (Coptis chinensis), Huanggin (Scutellaria baicalensis Georgi), Huang-bai (Phellodendron bark), and Zhizi (Gardenia)
Yin deficiency with yang hyperactivity	Tianma Gouteng Yin (decoction of Gastrodia and Uncaria)	Rhizoma Gastrodiae, Ramulus Uncariae cum Uncis, Concha Haliotidis, Cortex Eucommiae, Radix Achyranthis Bidentatae, Herba Taxilli, Fructus Gardeniae, Radix Scutellariae, Herba Leonuri, Sclerotium Poriae Pararadicis, and Caulis	Suppressing liver yang hyperactivity, clearing heat, activating blood, and nourishing the kidney	Classical prescription of New Meanings of Treatment in Miscellaneous Diseases with Traditional Chinese Medicine	Tianma (Gastrodia), Gouteng (Uncaria), Niuxi (Achyranthes root), and Duzhong (Eucommia ulmoides)
	Wuling powder	Alisma, Polyporus, Poria cocos, Ramulus Cinnamomi, Rhizoma Atractylodis Macrocephalae	Dissolving phlegm, draining water-dampness, and warming Yang	Classical prescription of <i>Treatise</i> on Febrile and Miscellaneous Diseases by Zhang Zhongjing in the Eastern Han Dynasty Classical prescription of <i>Treatise</i>	Zexie (Alisma), Zhuling (Polyporus), Fuling (Poria cocos), Banxia (The tube of pinellia),
Dhlam dammass	Zexie Tang (decoction of Alisma)	Alisma, Rhizoma Atractylodis Macrocephalae	Dissolving phlegm and draining water-dampness	on Febrile and Miscellaneous Diseases by Zhang Zhongjing in the Eastern Han Dynasty	ouizhd (Katzona Arackyouis Macrocephalae), Zelan (Herba Lycopi), and Shichangpu (Phiroma Acari Tarackouii)
retention	Wendan Tang jiawei decoction (modified decoction for clearing away gallbladder heat)	Caulis Bambusae in Taenia, Fructus Aurantii Immaturus, Rhizoma Pinelliae, Pericarpium Citri Reticulatae (aged tangerine peel), Poria, Radix et Rhizoma Glycyrrhizae, Radix Codonopsis, Radix Curcumae, and so forth.	Dissolving phlegm and boosting qi	Modified classical prescription of Prescriptions Assigned to the Three Categories of Pathogenic Factors of Diseases	(Nuisonia Acoli tatalittowii)
Wind-phlegm	Banxia Baizhu Tianma Tang (decoction of Pinellia ternata, Atractylodes macrocephala, and Gastrodia elata)	Rhizoma Pinelliae Praeparatum, Rhizoma Gastrodiae, Pericarpium Citri Reticulatae, Poria, and Radix et Rhizoma Glycyrrhizae	Calmed the liver, strengthened the spleen, removed dampness, and reduced phlegm	Classical prescription of <i>Medical</i> Revelations dispensed by Cheng Zhongling in Qing dynasty	Fuling (Poria cocos), Banxia (Pinellia ternata), Baizhu (Rhizoma Pinelliae Praeparatum), Tianma (Rhizoma Gastrodiae), and Chenpi (Pericarpium Citri Reticulatae)

			Table 6: Continued.		
Syndrome	Formula	Components	TCM efficacy	Label	Chinese herbs
Blood stasis	Xuefu Zhuyu Tang	Radix Angelicae Sinensis, Radix Rehmanniae, Semen Pruni Persicae, red flower, Fructus Aurantii, Chinese thorowax root, red peony root, Radix et Rhizoma Glycyrrhizae, Platycodon grandiflorum, Ligusticum chuanxiong Hort, and Radix Achyranthis	Removing blood stasis and promoting Qi	Classical prescription of <i>Yi Lin Gai Cuo</i> (correction of the errors of medical works) by Wang Qingren in the Qing Dynasty	Danggui (Radix Angelicae Sinensis), Chishao (red peony root), Danshen (Salvia miltiorrhiza), Yimucao (Leonurus japonicus), Chuanxiong (Ligusticum chuanxiong Hort), and Shengdi (Radix Rehmanniae)
Liver-kidney yin deficiency	Liu Wei Dihuang Wan (pill of Rehmannia)	Rehmannia glutinosa, Fructus corni, Rhizoma Dioscoreae, Alisma, Poria cocos, and Cortex Moutan Radicis	Replenish liver and kidney yin	Xiaoer Yaozheng Zhijue (Pediatric medicine card straight) by Qianyi in the Song Dynasty	Shanyurou (Fructus corni), Duzhong (Eucommia), Shudi (Rehmannia glutinosa), Gouqizi (Lycium barbarum L.), and Huangjing (Rhizoma Polygonati)
Yang deficiency	Shen qi Wan (kidney qi pill)	Rehmannia glutinosa, Fructus corni, Rhizoma Dioscoreae, Alisma, Poria cocos, Cortex Moutan Radicis, Cortex Cinnamomi, and Radix Aconiti	Recuperate kidney yang	Classical prescription of <i>Treatise</i> on Febrile and Miscellaneous Diseases by Zhang Zhongjing in the Eastern Han Dynasty	Fuzi (Radix Aconiti Carmichaeli), Bajitian (Morinda officinalis), Yinyanghuo (Epimedium), Buguzhi (Psoralea fruits), and Rousongrong (Cistanche)
Qi deficiency	Buzhong yiqi Tang	Codonopsis pilosula, Astragalus membranaceus, Rhizoma Atractylodis Macrocephalae, Tangerine Peel, Rattletop, Radix Bupleuri, Angelica sinensis, and Liquorice	Replenish qi to invigorate the spleen	Classical prescription of <i>Treatise</i> on <i>Spleen and Stomach</i> by Li Dongyuan in the Jin Dynasty	Dangshen (Codonopsis pilosula), Huangqi (Astragalus membranaceus), and Baizhu (Rhizoma Atractylodis Macrocephalae)
Blood deficiency	Danggui siwu Tang	Angelica sinensis, Radix Paeoniae Rubra, Ligusticum chuanxiong Hort, and Rehmannia glutinosa Libosch	Enrich and nourish blood	Classical prescription of <i>Treatise</i> on <i>Febrile and Miscellaneous Diseases</i> by Zhang Zhongjing in the Eastern Han Dynasty	Danggui (Angelica sinensis), Chuanxiong (Ligusticum chuanxiong Hort), Shudihuang (Rehmannia glutinosa Libosch), and Baishao (Radix Paeoniae Rubra)

(Polyporus) [135], and Banxia (The tuber of pinellia) [136] could effectively reduce BP as well. Fourthly, to remove blood stasis, use Xuefu Zhuyu Tang, a famous classical prescription recorded in Yi Lin Gai Cuo (Correction of the Errors of Medical Works) by Wang Qingren in the Qing Dynasty. It is effective in removing blood stasis and promoting Qi. Herbs such as Chishao (red peony root) [137], Danshen (Salvia miltiorrhiza) [138], Yimucao (Leonurus japonicus), and Chuanxiong (Ligusticum chuanxiong Hort) [139] could also lower BP. When aiming to remove qi stagnation and blood stasis, use herbs to promote qi circulation by taking herbs to remove blood stasis. Herbs that promote qi circulation include Chaihu (Chinese thorowax root) [137], Cangzhu (Rhizoma Atractylodis), and Zhiqiao (Fructus Aurantii). Finally, deficiency syndromes including liver-kidney yin deficiency, yang deficiency, qi deficiency, and blood deficiency are common in hypertension. When curing liver-kidney yin deficiency, use Liu Wei Dihuang Wan (pill of Rehmannia) [23]. Liu Wei Dihuang Wan was recorded in Xiaoer Yaozheng Zhijue (Pediatric Medicine Card Straight) by Qianyi in the Song Dynasty, and it can replenish liver and kidney yin. When treating yang deficiency, use Shen qi Wan (kidney qi pill) to recuperate kidney yang. When aiming to treat qi deficiency, use Huangqi (Astragalus membranaceus) [140-142] and Baizhu (Rhizoma Atractylodis Macrocephalae). When aiming to treat blood deficiency, use Danggui (Angelica sinensis) [143], Shengdihuang (Radix Rehmanniae), Chuanxiong (Ligusticum chuanxiong Hort) [144], and Baishao (Radix Paeoniae Rubra).

In summary, the syndrome elements of hypertension are limited and are combined into syndromes. Single and the combined syndrome elements of hypertension are the basis of syndrome differentiation for EH and the key to the standardization of this syndrome. In this paper, we retrospectively confirmed the validity and reliability of the theory of syndrome elements and the combined forms of syndrome elements of hypertension. This study can provide new ideas and methods for the treatment of hypertension by syndrome differentiation, and has laid a foundation for researching syndrome standardization of hypertension.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors' Contribution

Jie Wang and Xingjiang Xiong contributed equally in this paper.

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