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Original Article

The characteristics and prescription patterns of Chinese herbal medicine in clinical practice for the treatment of anemia

Wei-Di Chen [a], Hung-Sen Huang [a, b, c], Yuan-Chih Su [b, d], Shen-Chieh Chou [e], Wen-Chao Ho [f], Ming-Ching Kao [g], Hung-Jen Lin [a, b], Sheng-Teng Huang [a, b, c, *]

[a] Department of Chinese Medicine, China Medical University Hospital, Taichung, Taiwan
[b] School of Chinese Medicine, China Medical University, No.91, Hsueh-Shih Road, Taichung 40447, Taiwan
[c] Cancer Research Center for Traditional Chinese Medicine, Department of Medical Research, China Medical University Hospital, Taichung, Taiwan
[d] Management Office for Health Data, China Medical University Hospital, Taichung, Taiwan
[e] Department of Pharmacy School of Pharmacy, China Medical University, Taichung, Taiwan
[f] Department of Public Health, China Medical University, Taichung, Taiwan
[g] Department of Biological Science and Technology, College of Biopharmaceutical and Food Science, China Medical University, Taichung, Taiwan

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ABSTRACT

Objective: Chinese herbal medicine (CHM) is frequently applied to patients to improve the symptoms and signs associated with anemia. The aim of this study is to use the claims data from the National Health Insurance Research Database (NHIRD) in Taiwan to analyze CHM prescription patterns and to identify the frequency and combinations of CHM commonly used to treat anemia.
Materials and methods: A total of 41,028 patients were diagnosed with anemia in Taiwan within the defined study period. After randomly equal matching for age and sex, data from 7682 patients characterized as CHM users and non-users were analyzed. Network analyses of the 30 most frequently applied herbs and formulas were used to indicate CHM combinations in patients with anemia.
Results: Those patients with anemia who were older, office workers, and lived in central areas of Taiwan had higher tendencies toward CHM usage. Based on considerations of comorbidities, anemia patients associated with chronic kidney diseases, diabetes mellitus, and hypertensive diseases preferred Western medical management and demonstrated a lesser likelihood of combining treatment with CHM; by contrast, those with coronary artery disease demonstrated a higher tendency for CHM use. Notably, *Astragalus membranaceus* (AM) and Gui-Pi-Tang (GPT) were the most commonly prescribed CHM single herb and formula, respectively. The core prescription pattern consisted of AM, *Salvia miltiorrhiza* (SM), *Angelica sinensis* (AS), GPT, and Si-Wu-Tang (SWT), as indicated by the associations and frequency of CHM utilization by traditional Chinese medicine (TCM) physicians.
Conclusion: This study demonstrates that CHM may be applied as an integral element of treatment for patients with anemia. It also provides insight regarding individual therapy and common clinical practices of TCM physicians in the treatment of anemia. Further research is required to explore potential interactions and possible mechanisms at play with CHM management of anemia.

Introduction

Anemia is a significant public health issue affecting people of all ages, particularly pregnant women and young children. According to research, 41.8% of pregnant women and 47.4% of preschool children are affected by this condition globally [1]. In 2010, global anemia incidence was estimated to be approximately 32.9%, with 68.36 million years lived with disability [2]. Anemia has significant health implications, and is characterized by signs of pallor, fatigue, dizziness, shortness of breath, and weakness; it is further associated with low hemoglobin and ferritin levels [3]. It may also lead to decreased cognitive abilities, weaker immune function, and increased rates of mortality without effective management.

According to the American Society of Hematology, there are several types of anemia, classified as iron-deficiency anemia (IDA),

* Corresponding author. Department of Chinese Medicine, China Medical University Hospital; School of Chinese Medicine, China Medical University, No. 2, Yude Rd, North District, Taichung 40447, Taiwan.
E-mail address: sheng.teng@yahoo.com (S.-T. Huang).

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vitamin-deficiency anemia, aplastic anemia, hemolytic anemia, sickle cell anemia, and anemia caused by other diseases; of which IDA accounts for more than half of all cases [4]. While trauma and gastrointestinal bleeding are two other major causes of blood loss, the decreased production and uptake of iron and vitamins will induce iron-deficiency anemia and vitamin-deficiency anemia. Some forms are caused by increased breakdown associated with genetic disorders, these include aplastic anemia, sickle cell anemia, and anemia associated with certain autoimmune diseases. Anemia in elders or individuals associated with chronic diseases such as chronic kidney diseases, inflammatory bowel diseases, and chronic heart failure may lead to an increased risk of death, requiring increased supervision by physicians [5].

In terms of treatment, the blood transfusion is a common and effective method used to relieve signs and symptoms efficiently, based on hemoglobin levels. Meanwhile, there are two forms of pharmacotherapy iron supplementation. The oral form of ferrotherapy is a convenient, inexpensive, and effective option; however, there are side-effects which cannot be ignored, including gastrointestinal upset, muscle pain, and hives. The other form of ferrotherapy is through parenteral administration, administered based on considerations of oral ferrotherapy ineffectiveness, or inhibited absorption. However, long-term iron administration via the parenteral route will induce hemosiderin in various organs, and skin hyperpigmentation. Of concern, despite the advantages of iron supplementation, the long-term biologic effects of iron include the activating the generation of oxygen radicals leading to an increase of infectious disease morbidity [6]. Therefore, based on the limitations of Western medical treatments, finding an adjunct ferrotherapy to enable the reduction of the iron dose in traditional therapy is a challenge facing the health care community that needs to be addressed.

The National Health Insurance (NHI) system in Taiwan is well-organized, and recruits' data pertaining to both conventional Western medicine and TCM therapies. It has been become an important part of the health care system, and has provided valuable insight into the treatment of various diseases, including chronic myeloid leukemia [7], allergic rhinitis [8], heart disease [9,10], pulmonary disease [11], diabetes mellitus [12], hypertension [13], and precocious puberty [14]. Depending on the diagnostic pattern, TCM physicians will advise one or more herbal formulas combined with several single herbs for each prescription. In this study, we analyzed a cohort of one million beneficiaries from the NHIRD from 2001 to 2012 to evaluate and compare characteristics and prescription patterns between CHM users and non-users in patients with anemia.

The usage of CHM granules is covered by the NHI in Taiwan. These Chinese herbal products, including single Chinese herbs and multi-herbal Chinese formulas are permitted to be prescribed by TCM practitioners. All of the CMH granules covered by the NHI program are manufactured by Good Manufacturing Practice (GMP)-certified pharmaceutical companies. The actual daily CMH granule prescriptions in clinical practice are recorded in the NHI database. The specific purpose of this study is to investigate CHM utilization and prescription patterns in patients with anemia. We conducted a population-based retrospective cohort study of the NHI database to evaluate demographic differences, common prescriptions, and relevant single herb and formula combinations which offers insightful information regarding the use of CHM as a complementary and alternative option for the treatment of patients with anemia.

Patients and methods

This study used the Longitudinal Health Insurance Dataset of 2000 (LHID2000) as a data source. LHID2000 is a sampling dataset of the NHIRD which randomly selects 1 million beneficiaries from total beneficiaries, and contains all medical records of those one million subjects from 1996 to 2013. The demographic characteristics between the LHID2000 and the general NHIRD showed no difference after Chi-square test ($\chi 2 = 1.74$, df = 1, p-value = 0.187). With a 99% coverage rate, the NHIRD records many criteria of beneficiary data, including basic individual information (sex, date of birth, living area, insurance type, etc.), ambulatory care data, inpatient data, detailed drug information, and other relative medical data on an annual basis. Both ambulatory care data and inpatient data included disease diagnosis code in accordance with the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). A disease diagnosis without valid clinical findings may be considered a medical fraud by the NHI with a penalty of a 100-fold payment as claimed by the treating physician or hospital. Detailed drug information recruited the scientific and/or commercial name, number of drugs, dosages and drug use duration. Before release for research, each beneficiary identification code in the NHIRD was transformed into a set of dummy numbers, in order to avoid exposure of beneficiary personal information.

The study cohort with anemia was identified by ICD-9-CM code: 280–285, including only those subjects diagnosed with anemia at least twice (n = 58,597). After the exclusion criteria, there were 41,028 subjects with anemia included in this study. Of those subjects, 27,558 were classified as CHM users after been diagnosed with anemia; among them, 4741 subjects used CHM specifically for the treatment of anemia (anemia CHM users). This study matched CHM users and non-CHM users by 1:1 frequency matching. There were in total 3841 subjects included in each group, identified as CHM users and non-CHM users. All steps of the study population selection are shown in Fig. 1.

The demographic characteristics of the study population included sex, age, job type and area of residence. The population was further sorted into four age groups: < 20, 20–39, 40–59, ≥60. In accordance with insurance type, employment was classified as office worker, manual worker, or other. The four areas of residence were classified as northern Taiwan, central Taiwan, southern Taiwan, and eastern Taiwan and offshore islands, respectively. Comorbidities with anemia were included as follows: coronary artery disease (ICD-9-CM: 410–413, 414.01–414.05, 414.8, 414.9), congestive heart failure (ICD-9-CM: 398.91, 402.01, 402.11, 402.91, and 428), chronic liver disease and cirrhosis (ICD-9-CM: 571), chronic kidney disease (ICD-9-CM: 250.4, 403.XX, 404.XX, 585, 586), chronic obstructive pulmonary disease and allied conditions (ICD-9-CM: 491, 492, 493, 496), diabetes mellitus (ICD-9-CM: 250, A181), and hypertensive disease (ICD-9-CM: 401–405, A260, A269). All comorbidities were required to have been diagnosed at least twice to be included in this study.

As for statistical analysis applied in this study, Chi-square test was used to evaluate the association between CHM and non-CHM cohorts for identification of demographic characteristics and comorbidities. Differences of average age between CHM users and non-CHM users were tested by two-sample student's t-tests. Odds ratio (OR) and 95% confidence interval (95% CI) were calculated by univariate analysis and multivariable logistic regression. The combination patterns of Chinese herbal products were demonstrated by network analysis. The significance level was set at $\alpha = 0.05$. All statistical analyses were processed by applying the statistical software package, SAS, version 9.4 (SAS Institute, Inc., Cary, NC). The network analysis was carried out by open-sourced freeware NodeXL (http://nodexl.codeplex.com/). The spot indicates the frequency of each herb or formula use. The line bar indicates the association between each two connections with different thickness. The thicker of spot and line are concomitant with the higher frequency and association.

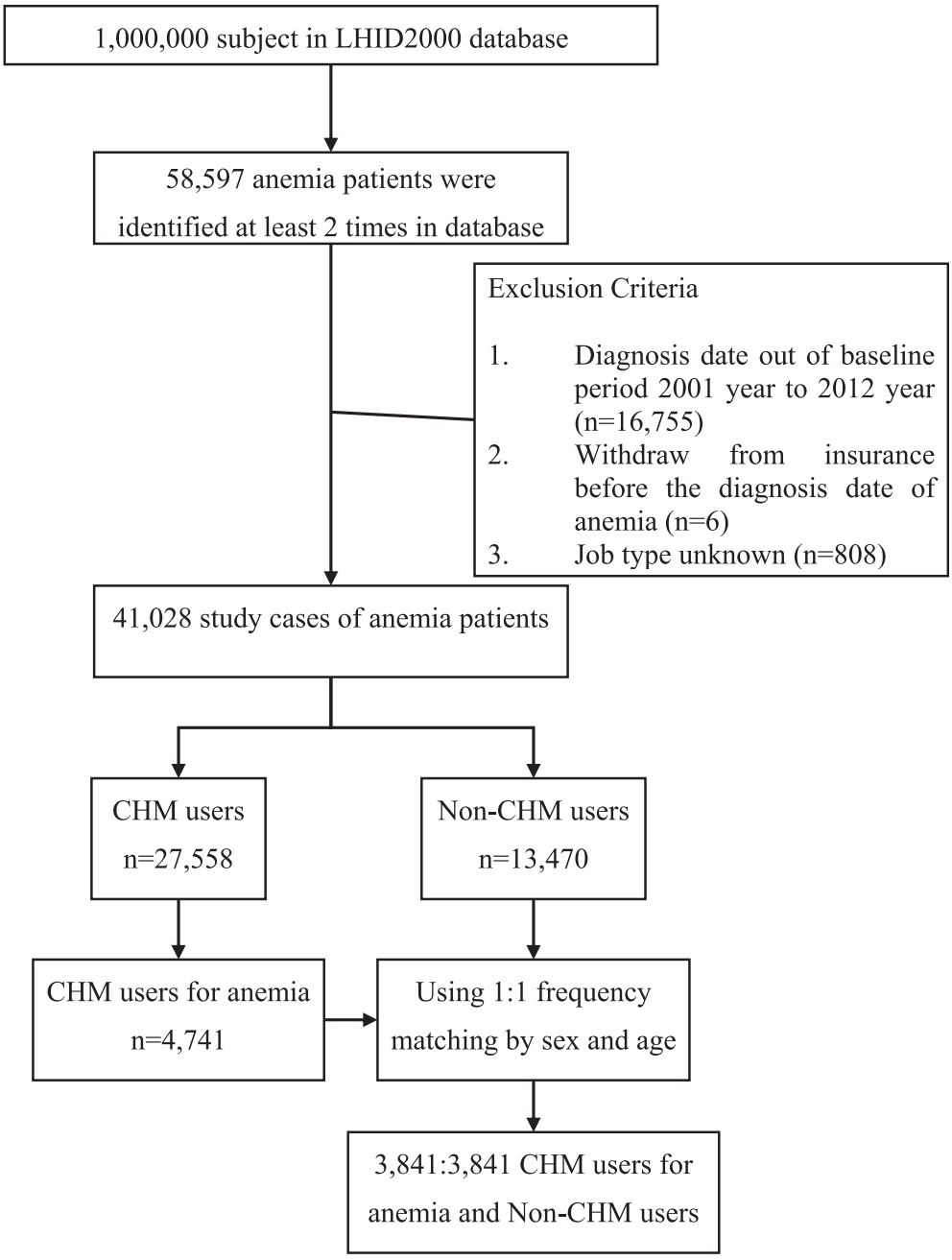

Fig. 1. Flow chart of study cases (Chinese herbal medicine, CHM) from Longitudinal Health Insurance Database (LHID2000) in Taiwan during 2001–2012.

Results

Among the CHM users cohort, 86.54% of subjects were female. The adjusted OR showed no significant odds differences of CHM use between female and male subjects (adjusted OR = 1.08, 95% CI: 0.94–1.24; shown in Table 1). Approximately 80% of users with anemia using CHM treatment for management were between 20 and 59 years of age; while the population greater than 60 years of age were more likely to use CHM for the treatment of anemia (adjusted OR = 1.7, 95% CI: 1.35–2.14). The mean age between the CHM user and non-CHM cohorts showed no significant difference (p value = 0.7661). Over half of the CHM users with anemia were office workers; whereas manual workers were less likely to use CHM for the treatment of anemia. In terms of area of residence, the highest percentage of anemia CHM users was located in northern Taiwan; while the patients residing in central Taiwan displayed the highest numbers of CHM use for anemia management, associated with adjusted odds ratio 1.19 with 95% CI 1.07–1.34. In contrast, the patients living in eastern Taiwan and offshore islands showed the lowest percentage of using CHM for treatment of anemia. Only subjects with comorbidity of coronary artery disease indicated higher utilization rates of CHM for anemia (adjusted OR = 1.26, 95% CI: 1.02–1.57). Subjects with comorbidities of chronic kidney disease, diabetes mellitus, and hypertensive disease had significantly low odds ratios, indicating a lower rate of CHM use among these three groups. As illustration, patients suffering from diabetes mellitus displayed the lowest adjusted odds ratio, 0.49 with 95% CI 0.38–0.63.

Table 1
Demographic characteristics and odds ratio with 95% confidence interval estimated by logistic regression of patients diagnosed with anemia in Taiwan during the period of 2001–2012.

Variable	Non-CHM		CHM		p value*	OR (95% CI)	
	N = 3841		N = 3841				
	50.00%		50.00%				
	n	%	n	%		Crude	Adjusted
Sex					1		
Female	3324	86.54	3324	86.54		1	1
Male	517	13.46	517	13.46		1 (0.88–1.14)	1.08 (0.94–1.24)
Age at baseline					1		
<20	390	10.15	390	10.15		1	1
20–39	1473	38.35	1473	38.35		1 (0.85–1.17)	1 (0.85–1.18)
40–59	1534	39.94	1534	39.94		1 (0.85–1.17)	1.11 (0.94–1.31)
≥60	444	11.56	444	11.56		1 (0.83–1.21)	1.7 (1.35–2.14)***
Mean (SD)‡	40.71 (15.98)		40.60 (15.81)		0.7661		
Job type					<0.0001		
Office workers	1994	51.91	2252	58.63		1	1
Manual workers	1435	37.36	1319	34.34		0.81 (0.74–0.9)***	0.84 (0.76–0.93)***
Others	412	10.73	270	7.03		0.58 (0.49–0.68)***	0.59 (0.5–0.7)***
Area					<0.0001		
Northern Taiwan	1856	48.32	1842	47.96		1	1
Central Taiwan	868	22.6	1001	26.06		1.16 (1.04–1.3)**	1.19 (1.07–1.34)**
Southern Taiwan	840	21.87	809	21.06		0.97 (0.86–1.09)	1.01 (0.9–1.14)
Eastern Taiwan and offshore islands	277	7.21	189	4.92		0.69 (0.57–0.84)***	0.75 (0.61–0.92)**
Baseline comorbidity							
Coronary artery disease					0.5796		
No	3584	93.31	3596	93.62		1	1
Yes	257	6.69	245	6.38		0.95 (0.79–1.14)	1.26 (1.02–1.57)*
Congestive heart failure					0.0016		
No	3719	96.82	3763	97.97		1	1
Yes	122	3.18	78	2.03		0.63 (0.47–0.84)**	0.79 (0.57–1.08)
Chronic liver disease and cirrhosis					0.4936		
No	3085	80.32	3061	79.69		1	1
Yes	756	19.68	780	20.31		1.04 (0.93–1.16)	1.11 (0.99–1.25)
Chronic kidney disease					<0.0001		
No	3604	93.83	3714	96.69		1	1
Yes	237	6.17	127	3.31		0.52 (0.42–0.65)***	0.76 (0.59–0.98)*
Chronic obstructive pulmonary disease					0.9234		
No	3271	85.16	3268	85.08		1	1
Yes	570	14.84	573	14.92		1.01 (0.89–1.14)	1.05 (0.92–1.2)
Diabetes mellitus					<0.0001		
No	3555	92.55	3714	96.69		1	1
Yes	286	7.45	127	3.31		0.43 (0.34–0.53)***	0.49 (0.38–0.63)***
Hypertensive disease					<0.0001		
No	3041	79.17	3302	85.97		1	1
Yes	800	20.83	539	14.03		0.62 (0.55–0.7)***	0.58 (0.49–0.68)***

*p < 0.05. **p < 0.01. ***p < 0.001, ‡Student's t test.
Abbreviate: CHM, Chinese herbal medicine; SD, standard deviation; OR, odds ratio; CI, confidence interval.
The mean (median) of follow-up duration was 1.67 (0.17) years and 5.48 (4.67) for case cohort and compared cohort.
Adjusted OR: multiple variable logistic regression adjusted by sex, age, job type, area and all comorbidities.

The top three single herbs prescribed were AM, SM and *Spatholobus suberectus* (SS), as shown in Table 2. AM prescription demonstrated the highest number of person-days (37,631), associated with 2 g average daily dose and 9.7 days of average duration of use for anemia patients. Prescriptions for SM and SS displayed the second and third highest numbers of person-days 36,386 and 29,999 respectively, with almost the same average daily dose and days of average duration. The most common formula prescribed for patients with anemia was GPT, associated with number of person-days (70,449), average daily dose (5.8 g) and days of average duration for prescription (10.6 days), as shown in Table 3. The second and third most commonly prescribed formulas were Jia-Wei-Xiao-Yao-San (JWXYS) and Ren-Shen-Yang-Rong-Tang (RSYRT), respectively. However, the number of person-days of both JWSYS and RSYRT were less than half of those recorded for GPT. The composition of the ten most common formulas is shown in Supplementary Table 1.As for the average daily dose and days of average duration among these three formulas, the prescription patterns were very similar (Table 3). There were 33.67% prescriptions which contain five or six CHM combinations in each treatment (Fig. 2). Prescriptions with three or four CHM combinations, as well as seven or eight CHM combinations for each treatment, were approximately one quarter among total prescriptions for patients with anemia. AM associated with AS or SM were the two most frequent TCM product combinations applied to patients (Fig. 3). The top five TCM single herbal products used in combinations were AM, SM, SS, AS and Asini gelatinum (AG) respectively. Meanwhile, GPT and SWT were the two major CHM formulas combinations prescribed to treat patients with anemia (Fig. 3). Collectively, AM increasing the qi, when associated with other CHM products improving the blood, played a significant role in activating the erythropoietic effect in patients with anemia.

Discussion

This is the first nationwide study to investigate a CHM network for the treatment of anemia by analyzing a cohort of one million beneficiaries from the NHIRD. As such, the study revealed several

Table 2
Ten most common single herbs prescribed for patients with anemia.

Prescription name (in Chinese)	Frequency	Number of person-days	Average daily dose (g)	Average duration for prescription (days)
***Astragalus membranaceus* (Huang Qi)**	3884	37,631	2	9.7
***Salvia miltiorrhiza* (Dan Shen)**	3439	36,386	1.6	10.6
***Spatholobus suberectus* (Ji Xue Teng)**	2790	29,999	1.6	10.8
***Asini gelatinum* (E Jiao)**	2275	24,829	2.1	10.9
***Eucommia ulmoides* (Du Zhong)**	2122	24,239	1.3	11.4
***Polygonum multiflorum* (He Shou Wu)**	1756	19,429	1.7	11.1
***Angelica sinensis* (Dang Gui)**	1746	17,642	1.4	10.1
***Rheum palmatum* (Da Huang)**	1637	17,374	0.7	10.6
***Dipsacus asperoides* (Xu Duan)**	1495	16,806	1.2	11.2
***Eclipta prostrate* (Han Lian Cao)**	1426	16,641	1.2	11.7

Table 3
Ten most common formulas prescribed for patients with anemia.

Prescription name (in Chinese)	Frequency	Number of person-days	Average daily dose (g)	Average duration for prescription (days)
Gui-Pi-Tang	6619	70,449	5.8	10.6
Jia-Wei Xiao-Yao-San	2905	31,605	5.3	10.9
Ren-Shen-Yang-Rong-Tang	2511	24,628	5.5	9.8
Bu-Zhong-Yi-Qi-Tang	2342	22,350	6.7	9.5
Szu-Wu-Tang	2434	19,217	5.8	7.9
Gui-Zhi-Fu-Ling-Wan	1282	15,638	4.8	12.2
Tian-Wang-Bu-Xin-Dan	1291	14,218	8	11
Sheng-Yu-Tang	1435	14,218	6.4	9.9
Dang-Gui –Shao-Yao-San	1374	13,778	4.5	10
Ma-Zi-Ren-Wan	1056	13,695	2.6	13

notable statistical and demographic characteristics, for example, approximately 67.1% of those patients with anemia were CHM users; however, only 17.2% of that number used CHM specifically for anemia treatment. In this study, women were more likely to have anemia in comparison with men. Women in their childbearing years had a higher tendency to iron-deficiency anemia due to blood loss from menstruation and increased blood supply demands during pregnancy. Furthermore, we found that young adult and middle-aged people, residing in urban centers, with white collar occupations had a higher inclination toward anemia. One hypothesis to explain the elevated tendency of patients with anemia residing in urbanized areas may be due to a higher density of doctors for medical consultation and accurate diagnosis [15]; while accessibility to CHM care and information concerning CHM treatment are more readily acquired from TCM practitioners in urbanized areas.

While there are several management and treatment methods available to anemia patients, the most common form of iron supplementation is orally; blood transfusions, on the other hand, should be reserved for those patients associated with severe anemia or hemodynamic instability. Chronic kidney disease (CKD) and congestive heart failure (CHF) are comorbidities of anemia which worsen the outcome of both associated conditions. Anemia often occurs during moderate (Stage 3) CKD, not only resulting from reduced erythropoietin production but also iron deficiency [16]. According to a recent study, one year of treatment with iron preparation to improve IDA severity, physical performance, and

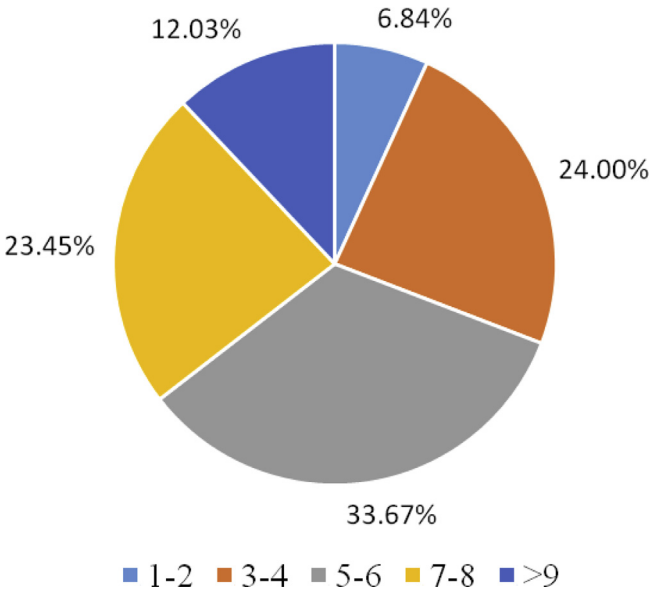

Fig. 2. Distribution of Chinese herbal products' combinations per single treatment for patients with anemia.

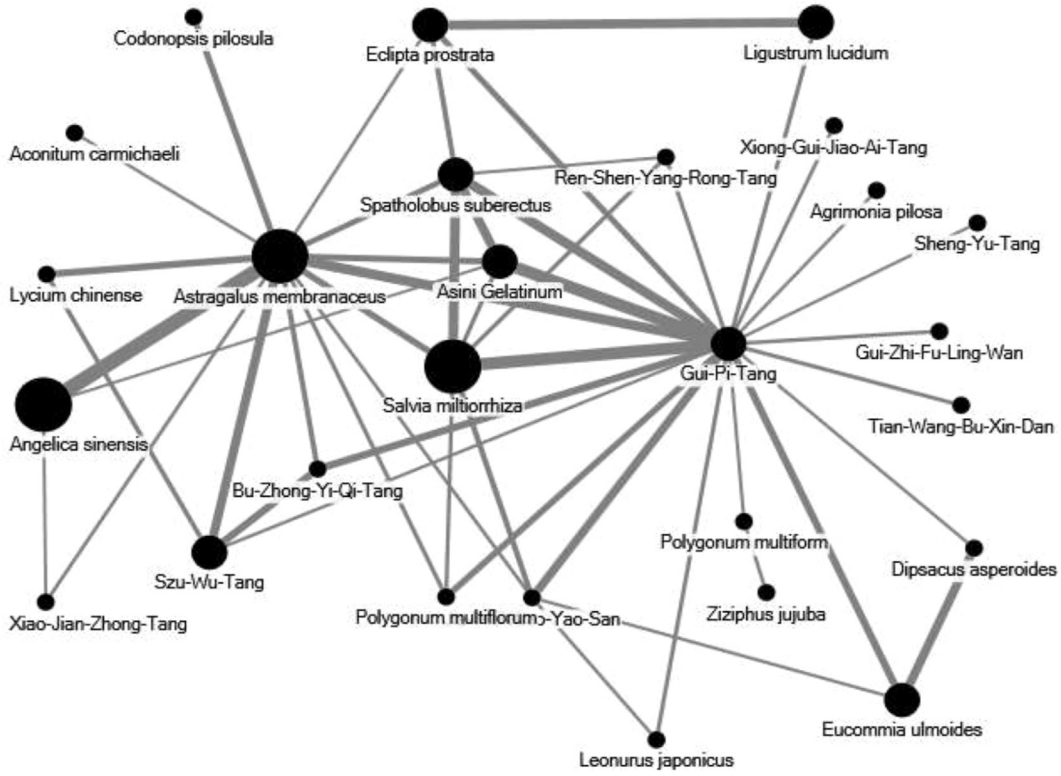

Fig. 3. Network analyses of the most frequent 30 herbs and formula combinations for patients with anemia.

quality of life was associated with a reduced risk of hospitalization due to chronic heart failure [6]. Oral iron therapy is a convenient, inexpensive, and effective means of treating patients with anemia, however side effects including nausea, vomiting, constipation, stomach pain and metallic taste limit its long-term use. Moreover, oral iron is poorly absorbed by intestinal tract due to upregulation of hepcidin, a peptide hormone that plays a central role in iron homeostasis [17].

With these limitations, an increasing number of patients with anemia look to CHM treatment to alleviate the adverse effects resulting from iron intake, or as an adjunct therapy used in combination with western treatments for improved outcomes. In accordance with TCM theory, Dang-Gui-Bu-Xue-Tang (DGBXT), composed of AM and AS with a ratio of 5:1, has long been used for the treatment of anemia. A recent an animal model study found that DGBXT combined with iron supplementation was effective at promoting the "qi" and invigorating the blood, thereby improving anemia [18]. Furthermore, DGBXT in combination with conventional western medicine (CWM) has been reported as superior to CWM alone for the treatment of renal anemia, with no adverse effects [19]. According to our analysis, AM and AS were included among the top ten single herbs used in prescriptions. The major ingredients of AM, such as polysaccharides, flavonoids, and saponins, have been reported to potentiate erythroid differentiation, and increase gamma-globin mRNA expression and fetal hemoglobin synthesis [20,21]. AS is further helpful for inducing hematopoietic effects by activating an inadequate response of recombinant human erythropoietin in patients with CKD [22]. Additionally, it has been observed to markedly suppress hepcidin expression by interrupting the JAK-STAT, BMPS-MAD, and ERK pathways in an animal model study of IDA [23]. Furthermore, recent research has noted that SS demonstrated antiplatelet activity, instead of anticoagulation effects, when applied to atherothromboietic diseases via the inhibition of the glycoprotein IIb/IIIa receptor, and partial inhibition of TXA2 formation [24]. Through network analysis, we herein include the top 50 combinations of herbal formulas and single herbs to show the core patterns associated with tonifying qi, enriching blood, nourishing yin, invigorating circulation, and lubricating the bowel. The present study therefore provides valuable information concerning current CHM clinical prescription patterns for the treatment of patients with anemia.

Regarding the prescription of herbal formulas in clinical practice and their respective functions, GPT was found to be the most frequently prescribed formula for IDA. According to TCM theory, GPT can augment qi and nourish the blood, effectively strengthening the spleen and heart meridians. As previously reported, it may improve the quantity and function of early hematopoietic stem cells by promoting the transition from the G0/G1 phase to the S phase, and from the S phase to the G2/M phase in the cellular cycle [25]. Similarly, RSYRT has been reported to induce immature erythroid progenitor cells in chemotherapy-induced anemia, and protect against hematotoxicity [26]. RSYRT decreases microinflammation and improve quality of life in patients associated with hemodialysis [27]. Another formula, Bu-Zhong-Yi-Qi-Tang (BZYQT), is often prescribed to manage symptoms of spleen-qi deficiency in patients with anemia, which commonly include inactivity, fatigue, and intolerance of exercise. One particular animal model study demonstrated that it functions by restoring endogenous metabolites, including valine, leucine, and O-acetyl-glycoprotein, as well as by inhibiting lactate production [28]. SWT has the effect of stimulating hematopoiesis in bone marrow so it can be used to activate red blood cell production [29–31]. SWT has also been demonstrated to have a regulatory effect on hepcidin iron metabolism in infant rats with IDA [32]. Gui-Zhi-Fu-Ling-Wan (GZFLW) is used to improve impaired microcirculation and congestion via inhibiting platelet aggregation [33], so it is applied in clinical practice to

ameliorate the symptoms of varicose veins of the lower extremity [34]. Dang-Gui-Shao-Yao-San (DGSYS) has been shown to provide cytoprotective effects against lipid peroxidation in rat liver homogenate. This protective effect extends to limiting human platelet aggregation induced by arachidonic acid and adenosine diphosphate, as well as mitomycin C-mediated hemolysis in human erythrocytes to decrease RBC consumption [35]. A key component of the above formulas, with the exception of BZYQT, is *Paeonia lactiflora* (PL), which exerts blood-enriching effects via regulation of immunological function to prevent blood deficiencies [36]. Based on TCM concepts, SM functions similarly to SWT, and is a very popular medicinal plant prescribed to treat various diseases, such as coronary heart diseases, and cerebrovascular diseases, and has been reported to be associated with antioxidative, neuroprotective, antifibrotic, anti-inflammatory, and antineoplastic activities [37]. The biological activities of single herbs or herbal formulas are illustrated in Supplementary Table 2.

Nearly the entire population of Taiwan is enrolled in the NHI program, therefore the NHIRD offers invaluable data to analyze TCM physicians' prescription patterns and to comprehensively summarize the usage of CHM; however, some limitations to the analysis remain. For instance, information regarding patients' TCM usage behavioral patterns, the practitioners' education and years of TCM experience are not included in the database for analysis. In particular, practitioner experience is considered to be a potential confounding factor, and the most important issue influencing the clinical efficacy of treatments. Furthermore, the study analysis did not include the patients' exact physical examinations, laboratory data (hemoglobin, hematocrit, platelet, white blood cell count, blood urine nitrogen, serum creatinine, electrolytes, albumin, etc.), or lifestyle details, as these factors are not recruited into the NHIRD; therefore there is a lack of exact clinical data to determine the severity of anemia. Thus, a prospective clinical study including these variables in the future is warranted. Nevertheless, this large-scale, population-based retrospective cohort analysis provides valuable information pertaining to CHM usage in patients with anemia.

Conclusions

Anemia is the most common illness affecting the circulatory system, marked by a decrease of red blood cells. In Taiwan, patients frequently use CHM to relieve the symptoms and signs associated with anemia. Higher percentages of CHM use are found in anemia patients between the ages of 20 and 59, and females. This study has revealed GPT as the most frequently used formula prescribed by TCM practitioners to treat anemia, while AM is the most frequently used single herb. The CHM formula combinations most commonly prescribed by TCM practitioners are GPT and SWT; meanwhile, AM, AS, and SM are the most commonly prescribed single herbs. It is important to note that well-designed clinical trials and pharmacological investigations will be necessary to further assess the effectiveness and side effects associated with CHM treatment in patients with anemia.

Conflicts of interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

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