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Abstract

To investigate the hemoglobin (Hb) concentration and related factors among maintenance hemodialysis (MHD) patients in Anhui province in 2020, so as to compare with the results in 2014. The cases of 3025 MHD patients were investigated in 27 hemodialysis centers of Anhui province from January 2020 to December 2020. The data of age, sex, primary disease, dialysis age, dialysis mode, drug use and laboratory tests were collected and analyzed. Compared with the survey in 2014, the average Hb level of MHD patients in Anhui province was increased (107.41 ± 20.40 g/L vs 100.2 ± 28.1 g/L), the anemia prevalence was decreased (65.9% vs 82.4%), and the percentage of patients with standard Hb level was increased significantly (47.1% vs 32.9%). Compared with low-Hb patients (Hb < 110 g/L), patients with Hb \geq 110 g/L had lower age, higher proportion of males, longer dialysis age, higher levels of serum Alb, creatinine, total cholesterol, triglyceride, low density lipoprotein, calcium, phosphorus, magnesium, and lower high-density lipoprotein (P < .05). The multivariate *logistic* regression analysis results showed that male, longer duration of dialysis therapy, treatment with iron, higher triglyceride and albumin were protective factors of anemia, but older age was independent risk factors. The anemia treatment in MHD patients in Anhui province was significantly improved. Male, long dialysis age, use of iron, high serum albumin and triglyceride levels may be protective factors for Hb reaching standard level, and old age may be an independent risk factor.

Abbreviations: Alb = albumin, BUN = urea nitrogen, Ca = blood calcium, CKD = chronic kidney disease, Cr = creatinine, ESAs = erythropoiesis stimulating agents, Hb = hemoglobin, HDL = high-density lipoprotein, LDL = low-density lipoprotein, Mg = blood magnesium, MHD = maintenance hemodialysis, P = blood phosphorus, TC = total cholesterol, TG = triglycerides, UA = uric acid.

Keywords: anemia, hemoglobin, maintenance hemodialysis

1. Introduction

Patients with end-stage renal disease require dialysis to remove accumulated solutes, toxins and excess fluid. Hemodialysis is the most common form of dialysis worldwide, thus, maintenance hemodialysis (MHD) is an important means for the treatment and maintenance of patients with end-stage renal disease. In recent years, the number of MHD patients in China has increased rapidly, and will continue to increase in the next few years.^[1]

Anemia is a complication of chronic kidney disease (CKD) and is caused by decreased synthesis of erythropoietin and altered iron metabolism in the impaired kidney.^[2] For patients on MHD, anemia is the most common complication, reaching 23% to 77%.^[3] Fortunately, timely correction of hemoglobin (Hb) concentration can improve the life quality and physiological function of MHD

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

patients, including shorter hospital stay and fewer complications. However, there are many factors that affect the decline of hemoglobin, including nutritional deficiencies, infection, inflammation, and genetic hemoglobin disorders.^[4] Especially in different disease backgrounds the influencing factors are not the same. Therefore, finding these influencing factors in MHD patients and conducting timely and effective interventions are effective means to relieve anemia in MHD patients in time.

Medicine

This research investigated the anemia and treatment of MHD patients in Anhui Province in 2020, analyzed related factors that affect Hb concentration, and compares with the survey results in Anhui Province in 2014^[5] to evaluate the effectiveness of the province's management of anemia in MHD patients in recent years. This study will provide a basis for the clinical prevention and treatment of MHD and anemia.

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2. Methods

2.1. Patients

The inclusion criteria were: ≥ 18 years of age; 2 to 3 times weekly dialysis for at least 3 mouths; and volunteer to participate in this research and sign the informed consent. The exclusion criteria were: patients with massive bleeding or blood transfusion, surgery, and severe trauma within 3 months before enrollment; patients with hemorrhagic or hemolytic diseases, bone marrow hematopoietic dysfunction caused by various causes; or patients with complications such as malignant tumors, liver cirrhosis, severe infections and severe heart failure.

2.2. Ethical statement

The research was approved by the Institutional Ethics Committee of the second hospital of Anhui medical university (ethical batch number: PJ-YX2020-006).

2.3. Data collection

This research is a multi-center, cross-sectional survey. Data entry and collection through Peking University's clinical data platform "Six Yuan Space." On-site training was conducted for participating doctors, nurses and graduate students before the questionnaire survey, and instructional videos for platform use were provided. The survey data were entered by the survey agency, and were checked by the quality controller. The main survey contents include: Basic information: gender, age, body mass index, smoking, drinking, education level, work and marital status, average monthly household income, diagnosis of primary disease and so on; Dialysis status: dialysis age, dialysis access, type of dialyzer; Drug treatment, erythropoiesis stimulating agents (ESAs) and iron application; and Biochemical indexes: Hb, alkaline phosphatase, creatinine (Cr), urea nitrogen (BUN), uric acid (UA), blood phosphorus (P), blood calcium (Ca), blood magnesium (Mg), full parathyroid hormone, albumin (Alb), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL).

2.4. Diagnostic criteria

According to the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD: Hb concentration < 130g/L in adult man, <120g/L in adult non-pregnant female, and < 110g/L in adult pregnant female were diagnosed as anemia.^[6]

2.5. Statistical analysis

All collected data were collected on the "six-element space" data platform. SPSS 23.0 was used for data analysis. The normality data was expressed by the mean \pm standard deviation and were analyzed by Student *t* test. The non-normality data were expressed by median (interquartile range) and the comparison between groups was analyzed by rank sum test. The qualitative data were represented by frequency (percentage), the comparison between groups of unordered classification data was by chi-square test, and the comparison between groups of ordered classification data was by Mann–Whitney *U* test. Logistic regression analysis was used to screen the factors that affect anemia in patients. Spearman correlation test was used to test the relationship between hemoglobin and various influencing factors. *P* < .05 was considered statistically significant.

3. Results

3.1. Characteristics of the patients

A total of 3025 patients were conformed to the criteria of inclusion and exclusion in this research, with an average age of 54.8 ± 12.8 years old, among which 1819 were male (60.1%). Primary diseases including chronic glomerulonephritis (n = 1225, 40.5%), diabetic nephropathy (n = 579, 19.1%), hypertensive nephropathy (n = 477, 15.8%), polycystic kidney disease (n = 131, 4.3%), 263 other cases (8.7%), such as gout, purpura, obstruction, interstitial nephritis, and 350 cases (11.6%) of unknown cause.

There are two main types of dialysis, 21.4% low-flux dialysis (n = 647), 51.4% high-flux dialysis (n = 1556). Dialysis access includes 88.0% autologous arteriovenous fistula (n = 2661), 9.2% semi-permanent venous catheters (n = 277), 1.2% temporary venous catheterization (n = 37), 0.9% grafted vascular fistulas (n = 26), 0.8% arteriovenous penetration (n = 24).

The usage rate of ESAs was 85.2%, and the median weekly dose of EPO was 8000 (4000, 10,000) U. The usage rate of iron was 43.3%.

3.2. Analysis of the patients' hemoglobin

In this study, the average Hb concentration of MHD patients was 107.41 ± 20.40 g/L, the prevalence of anemia was 65.9%, and the Hb compliance rate (Hb concentration ≥ 110 g/L) was 47.1%. Compared with the research results in Anhui Province in 2014, the average Hb concentration, normal Hb concentration (Hb concentration ≥ 110 g/L) rate and high-flux dialysis have increased

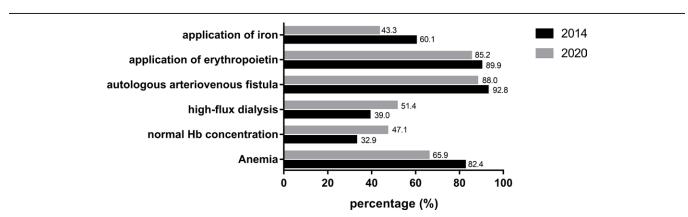


Figure 1. Comparison of anemia in MHD patients in Anhui Province in 2014 and 2020. Compared with the research results in 2014, the normal Hb concentration rate and high-flux dialysis have increased significantly, and the prevalence of anemia and the application of iron have decreased significantly, but the use of ESAs and autologous arteriovenous fistula have decreased slightly. Hb = hemoglobin, MHD = maintenance hemodialysis.

Table 1

Comparison of demographic characteristics, hemodialysis and drug treatment of the patients.

Index	Hb concentration substandard group	Normal Hb concentration group	P value
Male [n (%)]	866 (54.1%)	953 (66.9%)	<.001
Age	55.5 ± 12.9	54.0 ± 12.6	.003
BMI (kg/m ²)	21.45 (19.31, 23.88)	21.63 (19.54, 23.86)	.459
Educational level [n (%)]			
Illiteracy or semiliterate	321 (20.1%)	224 (15.7%)	<.001
Elementary school education	484 (30.4%)	347 (24.4%)	
Junior high school education	456 (28.5%)	465 (32.6%)	
High school education	236 (14.8%)	260 (18.2%)	
College education or higher	101 (6.3%)	129 (9.1%)	
Career			
Full-time job	82 (5.1%)	105 (7.4%)	.008
Work at home	186 (11.6%)	144 (10.1%)	
Retire	399 (24.9%)	390 (27.4%)	
Farmer	592 (37%)	467 (32.8%)	
Unemployment	341 (21.3%)	319 (22.4%)	
Family Residence [n (%)]			
Village	746 (46.6%)	606 (42.5%)	.039
Town	279 (17.4%)	246 (17.3%)	
City	575 (35.9%)	573 (40.2%)	
Average monthly total family income (¥)			
<2000	489 (30.6%)	458 (32.1%)	.038
2000-4000	791 (49.4%)	648 (45.5%)	.000
4001-8000	275 (17.2%)	257 (18.0%)	
>8000	45 (2.8%)	62 (4.4%)	
Smoking [n (%)]	209 (13.1%)	253 (17.8%)	<.001
Drinking [n (%)]	167 (10.4%)	193 (13.5%)	.008
Hypertension [n (%)]	1198 (74.9%)	1079 (75.7%)	.591
Diabetes [n (%)]	382 (23.9%)	350 (24.6%)	.660
Dialysis age [n (%)]	4.82 (2.36, 7.04)	5.04 (2.83, 7.90)	<.001
Dialysis access [n (%)]	1.02 (2.00, 1.07)	0.01 (2.00, 1.00)	2.001
Catheter	200 (12.5%)	114 (8.0%)	<.001
Internal fistula	1390 (86.9%)	1297 (91.1)	<.001
Type of dialysis [n (%)]			
Low-flux	403 (25.2%)	244 (17.1%)	<.001
High-flux	775 (48.4%)	781 (54.8%)	<.001
Hemodialysis	422 (26.4%)	400 (28.1%)	
Filtration (HDF $> 1/2$ wk)	122 (20.170)	400 (20.170)	
Use of iron (%)	49.0%	36.9%	<.001
Use of erythropoietin (%)	88.4%	81.5%	<.001
Weekly dosage of erythropoietin (U/W)	9000 (6000, 10,000)	6000 (3000, 9000)	<.001
Blood pressure	140.82 ± 21.23 mm Hg	$143.67 \pm 21.85 \text{ mm Hg}$.32
ACEI	9.7%	11.1%	.207
ARB	26.0%	25.8%	.912
עווע	20.070	20.070	.312

ACEI = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blockers, BMI = body mass index, Hb = hemoglobin.

significantly, and the prevalence of anemia and the application of iron have decreased significantly, but the use of ESAs and autologous arteriovenous fistula have decreased slightly (Fig. 1). Among the normal Hb concentration patients, 66.9% were males and 33.1% were females (P < .01). The normal Hb concentration rate of high-flux dialysis patients was significantly higher than that of low-flux dialysis patients (50.2% vs 37.7%, P < .01).

3.3. Analysis of factors affecting Hb concentration

Compared with the Hb concentration substandard group (Hb concentration < 110 g/L), there was higher proportion of men in the normal Hb concentration group (Hb concentration \geq 110 g/L). Similarly, the patients with high education, high income, city-resident, working or retirement have higher proportion in the normal Hb concentration group. The use of internal fistula dialysis and high-flux dialysis can also increase the rate of normal Hb concentration. However, compared with the Hb concentration substandard group, the usage of iron, ESAs, and weekly dose were lower in the normal Hb concentration group (P < .01) (Table 1).

Compared with the Hb concentration substandard group, the serum Cr, Alb, TG, TC, P, Ca, Mg, and LDL levels of the normal Hb concentration group were higher (P < .01), but the HDL level was lower (P < .01) (Table 2).

3.4. Correlation analysis of influencing factors of Hb

For the above factors that may affect the Hb of MHD patients, Pearson correlation or Spearman correlation analysis was used for further research, and the results showed that Hb concentration was positively correlated with dialysis age, the serum Alb, Cr, TC, TG, LDL, Ca, Mg, and P (P < .001). And it was negatively correlated with age, HDL, ESAs weekly dose (P < .01) (Table 3). The correlation coefficient is <0.3. There may be confounding factors masked the true relationship between the dependent variable and outcomes.

3.5. Analysis of multiple factors affecting Hb

Carrying out multivariate binary *Logisitc* regression analysis with Hb reaching normal concentration as the dependent

 Table 2

 Comparison of clinical biochemical indicators in the patients.

Indicators	Hb substandard group	Hb standard group	<i>P</i> value
BUN (mmol/L)	22.76 (17.30, 26.20)	22.04 (17.50, 25.46)	.052
Cr (µmol/L)	856.49 (675.35, 988.22)	856.49 (724.00, 1031.00)	<.001
UA (µmol/Ĺ)	393.86 (338.00, 451.00)	393.86 (343.00, 448.00)	.619
ALP [®] (U/L)	95.50 (70.00, 104.75)	92.00 (68.00, 105.00)	.359
Alb (g/L)	40.70 (37.00, 43.00)	41.60 (39.00, 44.90)	<.001
TC (mmol/L)	4.49 (3.47, 5.06)	4.66 (3.63, 5.06)	.003
TG (mmol/L)	1.92 (1.21, 1.92)	1.92 (1.32, 1.92)	<.001
HDL (mmol/L)	1.16 (1.00, 1.20)	1.16 (0.97, 1.16)	.012
LDL (mmol/L)	2.38 (1.78, 2.38)	2.38 (1.89, 2.38)	.005
Ca (mmol/L)	2.27 (2.12, 2.46)	2.33 (2.18, 2.50)	<.001
Mg (mmol/L)	1.17 (0.98, 1.28)	1.21 (1.02, 1.28)	<.001
P (mmol/L)	1.82 (1.45, 2.30)	1.91 (1.54, 2.37)	<.001
iPTH (pg/mL)	309.02 (140.88, 500.85)	321.60 (146.80, 535.85)	.210

Alb = albumin, ALP = alkaline phosphatase, BUN = urea nitrogen, Ca = blood calcium, Cr = creatinine, Hb = hemoglobin, HDL = high-density lipoprotein, iPTH = full parathyroid hormone, LDL = low-density lipoprotein, Mg = blood magnesium, P = blood phosphorus, TC = total cholesterol, TG = triglycerides, UA = uric acid.

<.001

< .001

Table 3						
Hb correlation in MHD patients.						
Factors	r	<i>P</i> value				
Age (yr)	-0.056	.002				
Dialysis age (yr)	0.110	<.001				
Abl (g/L)	0.212	<.001				
Cr (µmol/L)	0.090	<.001				
TC (mmol/L)	0.086	<.001				
TG (mmol/L)	0.110	<.001				
HDL (mmol/L)	-0.050	.006				
LDL (mmol/L)	0.070	<.001				
Ca (mmol/L)	0.132	<.001				
Mg (mmol/L)	0.104	<.001				

Alb = albumin, Ca = blood calcium, Cr = creatinine, Hb = hemoglobin, HDL = high-density lipoprotein, iPTH = full parathyroid hormone, LDL = low-density lipoprotein, MHD = maintenance hemodialysis, Mg = blood magnesium, P = blood phosphorus, TC = total cholesterol, TG = triglycerides,

0.099

-0.221

variable, and age, gender, dialysis age, treatment of iron, treatment of erythropoietin, Alb, BUN, Cr, UA, TC, TG, HDL, LDL, Ca, Mg, P levels as independent variables. The results showed that gender, age, dialysis age, treatment of iron, Alb and TG levels were the factors that affect the Hb of MHD patients (Table 4). We carried out multivariate binary Logistic regression analysis with Hb reaching normal concentration as the dependent variable, and the indicators with statistical significance above as independent variables.

4. Discussion

P (mmol/L)

iPTH (pg/mL)

Anemia, one of the most common complications and as an important predictor of poor prognosis of MHD patients, is closely related to the increase in hospitalization rate, length of stay, mortality, and medical expenses of MHD patients.^[3] The DOPPS research showed that for every 10g/L increase in Hb in MHD patients, the mortality and hospitalization rate were reduced by 10% and 12%, respectively. Therefore, it is of great significance to increase the Hb concentration of MHD patients and maintain long-term normal concentration.

Compared with the survey in Anhui Province in 2014, this research found that the average concentration of Hb and the rate of patients reaching standard Hb concentration in MHD patients in Anhui Province increased significantly. And the prevalence of anemia was reduced obviously, suggesting that Anhui Province has improved the management of anemia in MHD patients in recent years. And these achievements may be related to the following factors: The improvement of the medical security system and the increase the intensity of protection in recent years, thus, increasing patients adopt high-flux dialysis which make sure patients to receive adequate dialysis. Adequate dialysis and high-flux dialysis can also improve anemia by improving the patients' nutritional status. Lots of standardized training on the diagnosis and treatment for anemia in MHD patients has been conducted for doctors in recent years. Propaganda and education for patients and their families improved their cognition and increased compliance with treatment.

In 2021, China's DOPPS5 research showed that the rate of normal Hb concentration in MHD patients in Anhui (47.1%) was not worse than that in developed areas such as Beijing (49.6%), Shanghai (44.3%), Guangzhou (34.4%),^[7] however, it was lower than that of DOPPS member countries except Japan. There is still a gap in hemodialysis anemia management compared with American and European countries.

The KDGIO guidelines recommend that the target Hb concentration for patients with renal anemia should be 110 to 130 g/L and patients with hemodialysis renal anemia should use erythropoietin and iron to correct anemia. The usage rate of erythropoietin in Anhui was 85.2%, which is similar to that of DOPPS II member countries (83–94%), but was lower than that in 2014. The usage rate of iron in MHD patients was lower than that in 2014. At the same time, the results of this research showed that compared with the low Hb concentration group, the normal Hb concentration group's average weekly dose of erythropoietin and iron were lesser. It is possible that with the increase of Hb concentration and the correction of the anemia, the frequency and dosage of erythropoietin and iron use decreased gradually, and lower maintenance dose of the drug after reaching normal Hb concentration. Park H and his collages also found that the frequency and dose of ESAs in patients with chronic kidney disease have been reduced significantly in recent years.^[8] CHOIR (Correction of Hemoglobin and Outcomes in Renal Insufficiency, 2006),^[9] CREATE (Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta, 2006)^[10] and TREAT (Trial to Reduced Cardiovascular Events with Ananesp Therapy, 2009)^[11] three studies have shown that ESAs cannot reduce cardiovascular events and mortality in patients with chronic kidney disease. In addition, increasing the dose of ESAs is not only ineffective in increasing Hb concentration, but may increase the cost of treatment for patients, and the use of ESAs will increase the risk of stroke, heart attack, heart failure, blood clots, and death.^[11] In view of the increased risk of severe cardiovascular adverse reactions, stroke and death in patients with ESAs treatment to increase Hb concentration above 110 mg/L, the FAD recommends that under the premise

Table 4

Logistic regression analysis of multi-factors affecting Hb of MHD patients.

Factors	В	Wald	Р	OR	95% CI
Gender (ref: male)	0.501	41.48	<.001	1.651	1.417-1.922
Age (yr)	-0.008	7.245	.007	0.992	0.986-0.998
Educational level (ref: illiteracy or semiliterate)					
Elementary school education	-0.126	1.042	.307	0.881	0.692-1.123
Junior high school education	0.191	1.987	.159	1.210	0.928-1.578
High school education	0.216	1.755	.185	1.241	0.901-1.709
College education or higher	0.291	2.014	.156	1.338	0.895-2.000
Career (ref: full-time job)					
Work at home	-0.191	0.904	.342	0.826	0.557-1.225
Retire	-0.083	0.201	.654	0.920	0.640-1.323
Farmer	-0.197	0.933	.334	0.821	0.551-1.225
Unemployment	0.035	0.033	.856	1.035	0.712-1.505
Family residence (ref: village)					
Town	0.120	0.832	.362	1.127	0.872-1.458
City	0.177	1.909	.167	1.194	0.929-1.534
Average monthly total family income (ref: <2000)					
2000–4000	0.014	0.008	.928	1.014	0.753-1.364
4001-8000	0.097	0.046	.830	1.101	0.457-2.655
>8000	0.090	0.147	.702	1.094	0.690-1.736
Smoking (ref: no smoking)	0.156	1.792	.181	1.169	0.930-1.469
Drinking (ref: no drinking)	0.112	0.780	.377	1.118	0.873-1.433
Dialysis age	0.033	11.331	.001	1.003	1.014-1.053
Internal fistula (ref: catheter)	-0.145	2.715	.099	0.865	.728-1.028
Type of dialysis (low-flux)					
High-flux	0.889	1.600	.206	2.432	0.614-9.638
Hemodialysis Filtration (HDF $> 1/2$ wk)	0.146	1.527	.217	1.157	0.918-1.459
Use of iron (ref: no using)	0.538	48.358	<.001	1.713	1.472-1.993
Use of erythropoietin (ref: no using)	0.152	0.898	.343	1.164	0.850-1.593
Weekly dosage of erythropoietin (U/W)	-0.002	0.168	.682	0.998	0.991-1.006
Cr (µmol/L)	0.000	0.340	.560	1.000	1.000-1.000
Alb (g/L)	0.023	20.769	<.001	1.023	1.013-1.033
TC (mmol/L)	0.001	0.124	.725	1.001	0.996-1.006
TG (mmol/L)	0.090	5.743	.017	1.094	1.016-1.177
HDL (mmol/L)	-0.005	0.002	.960	0.995	0.818-1.211
LDL (mmol/L)	0.008	1.407	.236	1.008	0.995-1.021
Ca (mmol/L)	0.033	0.903	.342	1.034	0.965-1.108
Mg (mmol/L)	-0.016	0.933	.334	0.984	0.953-1.016
P (mmol/L)	-0.004	0.696	.404	0.996	0.987-1.005

Alb = albumin, Ca = blood calcium, Cr = creatinine, Hb = hemoglobin, HDL = high-density lipoprotein, LDL = low-density lipoprotein, MHD = maintenance hemodialysis, Mg = blood magnesium, P = blood phosphorus, TC = total cholesterol, TG = triglycerides.

of reducing the need for blood transfusions minimize the ESAs dose.^[12] This research found that the normal Hb concentration group used less ESAs, suggesting that maintaining normal Hb concentration can reduce the dose of ESAs and may reduce the adverse effects caused by the application of large doses of ESAs.

Compared with the low Hb concentration group, the Cr, Alb, TG, TC, P, Ca, Mg, LDL levels of the normal Hb group were higher, and positively correlated with Hb concentration. While the HDL level was lower and negatively correlated with Hb concentration. Zhao XJ and his collages also found that hypoproteinemia is an independent risk factor for anemia in MHD patients. Serum Alb can reflect the level of ferritin, and the reduction of serum Alb level in MHD patients will lead to a decrease in iron, which affects Hb synthesis and concentration. On the other hand, serum Alb is a biochemical indicator that reflects the nutritional status of patients. Increasing researches have confirmed that malnutrition is closely related to anemia.^[13] The increase in blood fat levels and rate of normal Hb concentration indicate that improving the nutrition of patients is conducive to increase Hb. And malnutrition and anemia can be corrected by maintaining caloric intake, high-quality protein diet, controlling inflammation, and reducing urine protein. Yu Shaobin et al found that parathyroid hormone is negatively correlated with Hb concentration, while Wu Fang et al believe that parathyroid hormone has nothing to do with Hb reaching the normal concentration, which is consistent with the results of this study.

The multivariate *logistic* regression analysis results suggested advanced age, low dialysis age, no iron use, low Alb and low TG levels are not conducive to normal Hb. Older patients are often accompanied with other comorbidities, and with age, bone marrow hematopoietic function gradually declines, Hb synthesis materials lost, leading to prone to anemia.^[14] Female patients are more likely to develop anemia, which may be related to women's repeated menstrual blood loss and insufficient iron intake.^[15] In addition, females have low levels of androgen and have lower stimulating effects on bone marrow hematopoiesis than males, which is one of the reasons why female patients are more likely to develop anemia than males. In this research, the rate of normal Hb concentration in high-flux dialysis patients was higher than that in low-flux dialysis patients. The high-flux dialysis can better remove large molecular toxins, improve chronic inflammation, enhance nutritional condition, and reduce erythropoietin resistance, which is more conducive to anemia.

This research found that the Hb concentration of MHD patients increased with the dialysis age increased. Liang et al^[16] have shown that compared with the normal Hb concentration group, patients with anemia have a younger age of dialysis and a lower weekly dialysis frequency. Hemodialysis can remove low-molecular erythropoietin inhibitors and improve the therapeutic effect of erythropoietin.^[17] Patients with short dialysis time often have electrolyte disturbances, insufficient removal of toxins, and large fluctuations in blood

volume. In addition, increased disease awareness after longterm dialysis, improved nutritional status, standardized anemia treatment and strengthened supervision form doctors, which have reduced the risk of anemia and increase the Hb to normal concentration.^[18]

Iron is the basic material for the synthesis of Hb. A variety of factors, including frequent blood tests, residual blood from dialyzers and dialysis tubes, dietary restrictions, taking calcium carbonate, electrolyte disorders, oxidative stress, micro-inflammatory conditions, which lead to the loss of iron or affect iron absorption will aggravate anemia in MHD patients.^[19] In addition, since EPO treatment stimulates red blood cell production, iron is consumed in large amounts. If iron is not supplemented in time and effectively, the therapeutic effect of EPO will decrease, and anemia will still not improve.^[20] Therefore, iron deficiency is the main cause of poor response to EPO treatment. And adequate iron supplementation can not only improve anemia, but also improve the treatment response of EPO and reduce the dosage of EPO.

This study is a multi-center, cross-sectional survey. The patient's anemia status and related indicators have not been dynamically analyzed, and the causal relationship between influencing factors and Hb cannot be confirmed. Laboratory examinations are completed by the laboratory of various hospitals, and different instruments and reagents were used, which may cause deviations between different hospitals.

In summary, the Hb concentration of MHD patients in Anhui Province was significantly higher than before, but there is still a gap compared with developed countries in Europe and America. Therefore, the comprehensive evaluation and follow-up of MHD patients should continue to be strengthened. There are many strategies to improve the patients' quality of life, reduce the mortality and hospitalization rate by removing the risk factors that affect Hb concentration, improving nutritional status, increasing Hb concentration through supplementing iron and erythropoietin.

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References

- Zhang LX, Zuo L. Current burden of end-stage kidney disease and its future trend in China. Clin Nephrol. 2016;86:S27–8.
- [2] Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc Nephrol. 2012;23:1631–4.
- [3] Pisoni RL, Bragg-Gresham JL, Young EW, et al. Anemia management and outcomes from 12 countries in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Am J Kidney Dis. 2004;44:94–111.
- [4] Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann N Y Acad Sci. 2019;1450:15–31.
- [5] Lei Y, Guixia Z, Yangyang H, et al. Epidemiological investigation on the prevalence of anemia and the standard-reaching rate of hemoglobin in patients with maintenance hemodialysis in Anhui province. Chin J Nephrol. 2016;32:264–70.
- [6] Kliger AS, Foley RN, Goldfarb DS, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for anemia in CKD. Am J Kidney Dis. 2013;62:849–59.
- [7] Zhao XJ, Niu QY, Gan LY, et al. Baseline data report of the China Dialysis Outcomes and Practice Patterns Study (DOPPS). Sci Rep Uk. 2021;11.
- [8] Park H, Liu XY, Henry L, Harman JRoss EA. Trends in anemia care in non-dialysis-dependent chronic kidney disease (CKD) patients in the United States (2006-2015). BMC Nephrol. 2018;19.
- [9] Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. New Engl J Med. 2006;355:2085–98.
- [10] Drueke TB, Locatelli F, Clyne N, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. New Engl J Med. 2006;355:2071–84.
- [11] Thamer M, Zhang Y, Kshirsagar O, Cotter DJ, Kaufman JS. Erythropoiesis-stimulating agent use among non-dialysis-dependent CKD patients before and after the trial to reduce cardiovascular events with aranesp therapy (TREAT) using a large US Health Plan Database. Am J Kidney Dis. 2014;64:706–13.
- [12] Administration UFaD. FDA drug safety communication: modified dosing recommendations to improve the safe use of erythopoiesis-stimulating agents (ESAs) in chronic kidney disease. 2011.
- [13] Green R, Datta Mitra A. Megaloblastic anemias: nutritional and other causes. Med Clin North Am. 2017;101:297–317.
- [14] Sanford AM, Morley JE. Editorial: anemia of old age. J Nutr Health Aging. 2019;23:602–5.
- [15] Tura MR, Egata G, Fage SGRoba KT. Prevalence of anemia and its associated factors among female adolescents in Ambo Town, West Shewa, Ethiopia. J Blood Med. 2020;7:279–87.
- [16] Liang MJ, Wu Y, Su N, et al. Prevalence, associated factors and cardiocerebral vascular prognosis of anaemia among patients on chronic haemodialysis in South Guangdong, China. J Int Med Res. 2020;48.
- [17] Meaney CJ, Karas S, Robinson B, et al. Definition and validation of a novel metric of erythropoiesis-stimulating agent response in hemodialysis patients. J Clin Pharmacol. 2019;59:418–26.
- [18] Nutrition and Hemodialysis. Indian J Nephrol. 2020:S55-66.
- [19] Cappellini MD, Musallam KM, Taher AT. Iron deficiency anaemia revisited. J Intern Med. 2020;287:153–70.
- [20] Whitehead L. Managing chemotherapy-induced anemia with erythropoiesis-stimulating agents plus iron. Am J Nurs. 2017;117:67.