Research Square

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The Burden of the Inflammatory State of Tuberculosis and Malnutrition on Anemia in Patients Undergoing Maintenance Hemodialysis

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Abstract

Background and Objective:

With the global rise in the incidence of chronic kidney disease (CKD), the number of patients receiving hemodialysis (HD) has also increased. These patients often exhibit immune dysfunction, making them more vulnerable to tuberculosis (TB) infection. Anemia is a common complication in both conditions. This study aims to investigate the clinical characteristics of TB in patients undergoing HD, and explore the relationships among inflammation, nutrition, and anemia.

Methods

This retrospective study included 95 HD patients diagnosed with TB (TB-HD group) and 152 HD patients without TB (NTB-HD group), all admitted to Changsha Central Hospital affiliated with the University of South China between January 2019 and September 2024.

Results

Significant differences in gender and HD duration were noted between the two groups ($P < 0.001$). Univariate analysis showed that TB-HD patients had significantly lower hemoglobin (Hb), red blood cell count, lymphocyte count and albumin (ALB), and higher C-reactive protein (CRP) (all $P < 0.05$). Multivariable analysis identified female sex (OR = 0.38, 95% CI: 0.17–0.88, $P < 0.001$) and ALB (OR = 0.78, 95% CI: 0.72–0.86, $P = 0.031$) as protective factors, while longer HD duration (OR = 1.31, 95% CI: 1.14–1.50, $P < 0.001$) and elevated CRP (OR = 1.03, 95% CI: 1.01–1.04, $P < 0.001$) increased TB infection risk in HD patients. TB-HD patients were stratified into four anemia categories by Hb levels (< 60, 60–90, 91–109, ≥ 110 g/L), with more severe anemia associated with higher CRP ($P < 0.001$). Correlation analysis showed a significant negative correlation between CRP and Hb (TB-HD: $R = -0.39$; NTB-HD: $R = -0.13$; both $P < 0.01$), with a stronger correlation in the TB-HD group. CRP was also negatively correlated with ALB (TB-HD: $R = -0.48$; NTB-HD: $R = -0.29$; both $P < 0.01$), while ALB was positively correlated with Hb (TB-HD: $R = 0.49$; NTB-HD: $R = 0.33$; both $P < 0.01$).

Conclusion

Patients on maintenance hemodialysis (MHD) who develop TB often experience worsened anemia, which is closely linked to systemic inflammation (elevated CRP) and malnutrition (reduced ALB). These factors contribute to a vicious cycle of **inflammation–malnutrition–anemia**.

1. Introduction

CKD and TB are two major global health challenges that pose significant threats to human well-being. With an aging global population and shifting lifestyles, the incidence of CKD continues to rise [1]. As CKD progresses to end-stage renal disease (ESRD), HD becomes an essential life-sustaining therapy [2]. Globally, more than 3.5 million individuals with chronic kidney failure rely on MHD [3]. However, impaired renal function and frequent exposure to the dialysis environment compromise the immune system in HD patients, increasing their susceptibility to infections particularly TB [4]. Studies have shown that the incidence of TB in dialysis patients is 6.9 to 52.5 times higher than in the general population [5].

TB, an ancient and highly detrimental infectious disease, has a markedly higher incidence among individuals with compromised immune function, such as those receiving HD [6]. According to the World Health Organization, approximately 10.8 million cases of TB were reported worldwide in 2023 [7]. Infection with *Mycobacterium tuberculosis* (MTB) triggers a cascade of complex immune responses, leading to systemic inflammation [8]. In HD patients, this inflammatory state may

exacerbate pre-existing low-grade inflammation, further destabilizing the body's internal environment [4]. Anemia is common in HD patients and is associated with increased morbidity and mortality, particularly from cardiovascular causes [9]. Notably, the inflammatory response induced by TB may significantly worsen anemia in this population. Studies have shown that TB-related inflammatory mediators can disrupt iron metabolism [10], suppress erythropoietin production and activity [11], and reduce the lifespan of red blood cells [12]. Additionally, TB leads to nutrient depletion, while chronic inflammation accelerates the catabolism of ALB and other essential nutrients, resulting in a deficiency of hematopoietic substrates [13]. Malnutrition, in turn, further amplifies the inflammatory response. These interrelated mechanisms contribute to the development of the so-called "inflammation–nutrition–anemia" syndrome [14, 15]. Collectively, they may further aggravate pre-existing anemia in HD patients, significantly impairing their quality of life and clinical outcomes.

Several previous studies have reported a higher incidence of TB among patients with ESRD and those undergoing HD [4, 16, 17]. However, there remains a significant lack of comprehensive and systematic research examining the specific physiological effects of TB in this population, particularly its impact on anemia. Therefore, the present study aims to evaluate whether TB worsens anemia in HD patients and to identify the key contributing factors.

2. Study Methodology

2.1 Study Design and Participants

This study strictly adheres to the ethical principles for medical research involving human subjects as stipulated in the World Medical Association Declaration of Helsinki. This retrospective study was approved by the Ethics Committee of Changsha Central Hospital Affiliated with the University of South China.Since the data were collected from the electronic medical record system, the Institutional Review Board (IRB) waived the requirement for informed consent from the participants. Data were collected from tuberculosis patients who underwent HD at the hospital between January 2019 and September 2024. The collected information included patient demographics (age, gender, smoking history, comorbidities), clinical characteristics related to HD (cause of ESRD, duration of HD), TB status (diagnostic methods, TB type, clinical presentation), and laboratory results (complete blood count, liver and renal function tests, serum calcium, and C-reactive protein levels). The inclusion and exclusion criteria for the study participants in the experimental group are as follows: Inclusion Criteria: (1) Age ≥ 18 years; (2) ESRD patients on MHD for more than 3 months; (3) Diagnosis of TB according to the guidelines outlined in WS 288 2017 for the Diagnosis of TB. The diagnostic criteria include clinical manifestations such as typical tuberculous symptoms persistent fever lasting more than two weeks, weight loss, fatigue, and night sweats. Laboratory confirmation must include at least one of the following: positive acid-fast bacillus staining, positive culture of *MTB*, or positive tuberculosis polymerase chain reaction (TB-PCR) results from blood, tissue, or other specimens. Pathological examination should show characteristic findings such as caseous granuloma. Imaging studies must reveal typical lesions, including pulmonary infiltration, cavities, fibrosis, or calcification, along with a favorable response to anti-tuberculous treatment. Exclusion Criteria: (1) Concurrent severe infections at other sites (e.g., intracranial infection); (2) History of malignancy or active cancer; (3) Active autoimmune diseases (e.g., systemic lupus erythematosus); (4) Receipt of blood transfusions within the past month. The control group consists of HD patients at this hospital during the same period with no history of tuberculosis, including no previous TB infection or treatment.

2.2 Data Collection and Sorting

Specialized data collection forms were developed for both the HD patients with TB (TB-HD) group and the non-tuberculosis hemodialysis (NTB-HD) group consisting of 152 patients. Trained researchers extracted relevant patient data from the hospital's electronic medical record system for both the experimental and control groups. Throughout the data collection process, each data point was carefully verified to ensure accuracy and completeness. Any missing or unclear information was supplemented and confirmed by reviewing original medical records and consulting with the attending physicians. After data collection was completed, the information was entered into a purpose-built Excel spreadsheet, and preliminary data

cleaning was performed using SPSS. This process involved checking for data consistency and removing duplicates. Given the non-normal distribution of the data, preprocessing steps including ranking the original data were carried out to prepare for subsequent Mann-Whitney U tests and Kruskal-Wallis rank sum tests. For categorical variables, frequencies and relative frequencies were calculated to facilitate chi-square (χ^2) tests.

2.3 Statistical Analysis Methods

We conducted data analysis and processing using SPSS 26. Descriptive statistical analysis was performed to assess the baseline demographic characteristics of the patients. Quantitative data with a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), while non-normally distributed data were presented as median (P25, P75). Qualitative data were described using frequency (percentage). The Mann-Whitney U test was used to compare two independent samples and assess significant differences in continuous variables, such as hemoglobin levels and red blood cell counts, between the experimental group (patients with TB undergoing HD) and the control group (HD patients without a history of TB). For comparisons involving multiple independent samples, the Kruskal-Wallis rank sum test was applied. When significant differences were found, Dunn's test was used for pairwise comparisons to identify specific groups with differences. For categorical variables, including patient sex, TB type, and comorbidities, the chi-square test (χ^2 test) was employed to analyze differences in group distributions. To further explore factors influencing outcomes such as anemia severity and TB infection status, variables significant in univariate analysis were included in a multivariate logistic regression model to identify independent predictors. Spearman's rank correlation test was used to analyze correlations between hemoglobin and CRP, as well as between hemoglobin and ALB, and ALB and CRP. A significance level of $\alpha = 0.05$ was set for all tests, with $P < 0.05$ considered statistically significant.

3. Results

3.1 Demographics of the participants

The study was conducted from January 2019 to September 2024, involving 95 TB-HD patients and 152 NTB-HD patients. The demographic characteristics and comorbidities of the two groups are presented in Table 1. The median age of the TB-HD group was 59.00 years (IQR: 51.00–67.00), with 74.74% (n=71) being male. These patients had a median hemodialysis duration of 3 years (IQR: 1–8), and 41.05% (n=39) had a history of smoking. TB infection mainly occurred more than one year after the initiation of hemodialysis. The primary cause of end-stage renal disease was identified as primary kidney disease, accounting for 71.58% (n=68) of cases. Among these, diabetic nephropathy accounted for 20.00% (n=19), hypertensive nephropathy for 1.05% (n=1), obstructive nephropathy for 3.16% (n=3), and polycystic kidney disease for 3.16% (n=3). The most prevalent comorbidities among patients were hypertension and diabetes. During the study period, 74.74% (n=71) had hypertension, 38.95% (n=37) had type 2 diabetes, 24.21% (n=23) had coronary heart disease (CHD), and 8.42% (n=8) had chronic obstructive pulmonary disease (COPD). In the NTB-HD group, the median age was 61.00 years (IQR: 52.00–70.00), with 54.61% (n=83) being male. The median duration of hemodialysis in the NTB-HD group was 0.6 years (IQR: 0.33–2.00). The primary causes of end-stage renal disease were mainly primary renal diseases, accounting for 49.34% (n=75) of cases. However, compared to the TB-HD group, the proportion of diabetic nephropathy among HD patients was higher at 32.89% (n=50). Obstructive nephropathy was present in 0.66% (n=1) of cases, and polycystic kidney disease accounted for 2.63% (n=3). Among the HD patients without tuberculosis during the study period, 86.18% (n=131) had hypertension, 40.13% (n=61) had type 2 diabetes mellitus, 25.00% (n=38) had CHD, and 4.61% (n=7) had COPD. Non-parametric tests revealed significant differences between TB-HD and NTB-HD patients in gender, causes of ESRD, and duration of hemodialysis ($P < 0.05$). Additionally, the data showed that tuberculosis infection in TB-HD patients mostly occurred more than one year after starting hemodialysis. Comparing the two groups, significant differences were observed in gender ($P < 0.001$), with a higher proportion of males in the TB-HD group. Differences in the causes of ESRD were also significant ($P < 0.05$), notably with a higher prevalence of diabetic nephropathy in the NTB-HD group. Hemodialysis duration differed significantly ($P < 0.001$), being longer in the TB-HD group. In contrast, age, smoking history, CKD duration, and most

comorbidities showed no significant differences (P > 0.05), except for a borderline difference in hypertension comorbidity (P = 0.054).

Table 1. Demographic characteristics between TB-HD group and NTB-HD group

Variables	TB-HD (N=95)	NTB-HD (N=152)	Z	P - value
Age (years, median [IQR])	59.00(51.00, 67.00)	61.00(52.00, 70.00)	-0.815	0.415
≥60 years	47 (49.47%)	80 (52.63%)	0.233	0.629
Sex (n, %)			10.093	<0.001
Male	71 (74.74%)	83 (54.61%)		
Female	24 (25.26%)	69 (45.39%)		
Smoking history (n, %)	39 (41.05%)	45 (29.61%)	3.414	0.065
Cause of ESRD (n, %)				
Primary kidney disease	68.00 (71.58%)	75.00(49.34%)	8.739	0.003
Diabetes	19.00 (20.00%)	50.00(32.89%)	4.829	0.028
Hypertension	1.00 (1.05%)	17.00(11.18%)	5.061	0.024
Obstructive Uropathy	3.00 (3.16%)	1.00 (0.66%)		0.411
Polycystic Kidney Disease	3.00 (3.16%)	4.00 (2.63%)	0.001	0.979
CKD duration (years, median [IQR])	3.00 (1.00, 8.00)	3.00(1.00,6.00)	-0.135	0.893
Hemodialysis duration (years, median [IQR])	3.00 (1.00, 6.00)	0.60(0.33,2.00)	-5.099	<0.001
<1	17 (17.89%)	25 (16.71%)		
1-5	44 (46.32%)	79 (52.24%)		
>5	34 (35.79%)	48 (31.05%)		
Comorbidities (n, %)				
CHD	23 (24.21%)	38 (25.00%)	0.218	0.641
Diabetes	37 (38.95%)	61 (40.13%)	0.034	0.853
Hypertension	71 (74.74%)	131 (86.18%)	3.720	0.054
COPD	8 (8.42%)	7 (4.61%)	5.368	0.229

Abbreviation: TB-HD: Tuberculosis combined with Hemodialysis; NTB-HD: Non – Tuberculosis combined with Hemodialysis; End-Stage Renal Disease; CKD: Chronic Kidney Disease; CHD: Coronary Heart Disease; COPD: Chronic Obstructive Pulmonary Disease

3.2 Comparisons of Laboratory Data between TB-HD group and NTB-HD group

The laboratory data revealed significant differences in inflammatory markers, biochemical parameters, and anemia indicators between the TB-HD group and the NTB-HD group (Table 2). Among the anemia indicators, the RBC in the TB-HD group was 3.08 × 10^{12}/L (2.59, 3.69) compared to 3.57 × 10^{12}/L (3.13, 4.07) in the NTB-HD group. Hemoglobin levels were

81.00 g/L (70.00, 102.00) versus 104.00 g/L (90.00, 117.00), hematocrit (HCT) was 26.30% (23.00, 32.30) versus 33.00% (28.65, 38.00), mean corpuscular volume (MCV) was 89.00 fL (84.00, 94.90) versus 93.00 fL (87.60, 97.00), and mean corpuscular hemoglobin (MCH) was 27.00 pg (26.00, 29.40) versus 29.00 pg (28.00, 31.00), all significantly lower in the TB-HD patients compared to the NTB-HD group ($P < 0.05$). Regarding inflammatory markers, the median CRP level was markedly elevated in the TB-HD group at 59.80 mg/L (19.30, 99.40) compared to 3.64 mg/L (3.14, 16.80) in the NTB-HD group ($P < 0.001$). The TB-HD group also showed significantly lower ALB, lymphocyte count, and lymphocyte percentage (L%, $P < 0.01$). The decreased albumin may indicate impaired liver synthetic function or increased protein loss, while the reduced lymphocyte percentage suggests immune suppression. These findings demonstrate that the TB-HD group suffered from more severe anemia, poorer nutritional status, and a heightened inflammatory state compared to the NTB-HD group. Univariate and multivariate analyses of the demographic and laboratory indicators were conducted (Table 3 and Figure 1). Univariate analysis showed that female gender (OR 0.41, 95% CI 0.25–0.58, $P < 0.001$), lower RBC (OR 0.38, 95% CI 0.25–0.58, $P < 0.001$), lower hemoglobin (OR 0.96, 95% CI 0.94–0.97, $P < 0.001$), lower L% (OR 0.92, 95% CI 0.89–0.96, $P < 0.001$), lower HCT (OR 0.90, 95% CI 0.86–0.94, $P < 0.001$), lower MCV (OR 0.95, 95% CI 0.91–0.98, $P = 0.002$), lower MCH (OR 0.82, 95% CI 0.74–0.91, $P < 0.001$), lower ALB (OR 0.76, 95% CI 0.71–0.82, $P < 0.001$), and higher CRP (OR 1.04, 95% CI 1.03–1.05, $P < 0.001$) were statistically significant. In the multivariate analysis, female gender (OR 0.38, 95% CI 0.17–0.88, $P < 0.001$) and ALB (OR 0.78, 95% CI 0.72–0.86, $P < 0.001$) were identified as protective factors, while CRP (OR 1.03, 95% CI 1.01–1.04, $P < 0.001$) and hemodialysis duration (OR 1.31, 95% CI 1.14–1.50, $P < 0.001$) were recognized as risk factors for active tuberculosis in patients undergoing hemodialysis.

Table 2. Comparisons of laboratory data between TB-HD group and NTB-HD group

Laboratory Data	TB-HD (N = 95)	NTB-HD (N = 152)	Z	P - value
WBC (×10⁹/L)	6.87 (4.63, 8.51)	5.89 (5.12, 6.89)	-1.939	0.053
RBC (×10¹²/L)	3.08 (2.59, 3.69)	3.57 (3.13, 4.07)	-5.003	<0.001
Hb (g/L)	81.00 (70.00, 102.00)	104.00 (90.00, 117.00)	-6.292	<0.001
PLT (×10⁹/L)	202.00(137.00,275.0)	201.00 (150.00, 242.00)	-0.234	0.815
N (×10⁹/L)	5.27 (3.34, 6.96)	4.20 (3.40, 5.12)	-2.794	0.005
L (×10⁹/L)	0.67 (0.47, 1.05)	1.02 (0.72, 1.31)	-4.868	<0.001
M (×10⁹/L)	0.47 (0.35, 0.60)	0.39 (0.30, 0.50)	-3.912	<0.001
L%	11.60 (7.20, 16.20)	17.30 (12.55, 22.05)	-5.833	<0.001
HCT (%)	26.30 (23.00, 32.30)	33.00 (28.65, 38.00)	-5.812	<0.001
MCV (fL)	89.00 (84.00, 94.90)	93.00 (87.60, 97.00)	-3.308	<0.001
MCH (pg)	27.00 (26.00, 29.40)	29.00 (28.00, 31.00)	-4.360	0.041
MCHC (g/L)	311.00(301.00,319.0)	313.00 (305.00, 322.00)	-2.041	0.041
CRP (mg/L)	59.80 (19.30, 99.40)	3.64 (3.14, 16.80)	-8.760	<0.001
TP(μmol/L)	63.00 (58.00, 67.30)	69.00 (64.00, 73.58)	-5.922	<0.001
ALB (g/L)	30.00 (26.00, 34.00)	37.69 (34.00, 41.00)	-8.913	<0.001
ALT(U/L)	8.00 (5.00,13.00)	12.00 (8.00,20.00)	-3.968	<0.001
AST(U/L)	16.00 (12.00,21.00)	15.00 (11.00,22.00)	-0.715	0.529
GLB (g/L)	31.00 (28.00, 35.00)	31.00 (27.00, 35.00)	-1.080	0.288
UA (μmol/L)	372.00(310.00,462.0)	367.00 (262.00,467.00)	-0.665	0.516
CR (μmol/L)	727.0 (570.00,898.00)	720.27 (565.00,906.00)	-0.293	0.771
UN (mmol/L)	16.98 (13.12,26.68)	18.95 (13.46,24.34)	-0.200	0.843
Ca (mmol/L)	2.28 (2.12,2.43)	2.19 (2.06,2.31)	-3.137	0.002

Abbreviation：TB-HD: Tuberculosis combined with Hemodialysis; NTB-HD: Non – Tuberculosis combined with Hemodialysis; WBC: White Blood Cell; RBC: Red Blood Cell; Hb: Hemoglobin; PLT: Platelet; N: Neutrophil; Lymphocyte; M: Monocyte; L%: Lymphocyte Percentage; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; TP: Total Protein; ALB: Albumin; ALT: Alanine Transaminase; AST: Aspartate Transaminase; GLB: Globulin; UA: Uric Acid; CR: Creatinine; UN: Urea Nitrogen; Ca: Calcium

Table 3. Univariate analysis of demographic and laboratory data in TB-HD group and NTB-HD group

Variables	OR	SE	Wald χ^2	P - value
Female	0.41(0.23,0.72)	0.287	-3.137	0.002
Hemodialysis duration(yr)	1.21(1.10,1.32)	0.046	16.757	<0.001
RBC ($\times10^{12}$/L)	0.38(0.25,0.58)	0.210	-4.557	<0.001
Hb (g/L)	0.96(0.94,0.97)	-5.988	243.000	<0.001
N ($\times10^{9}$/L)	1.19(1.05,1.34)	0.062	2.830	0.005
L ($\times10^{9}$/L)	1.06（0.93,1.20）	0.063	0.883	0.378
L%	0.92(0.89,0.96)	0.021	-3.918	<0.001
HCT (%)	0.90(0.86,0.94)	0.022	-4.993	<0.001
MCV (fL)	0.95(0.91,0.98)	0.018	-3.164	0.002
MCH (pg)	0.82(0.74,0.91)	0.052	-3.700	<0.001
MCHC (g/L)	0.99(0.99,1.00)	0.004	-1.367	0.173
CRP (mg/L)	1.04(1.03,1.05)	0.006	6.607	<0.001
TP(μmol/L)	0.89(0.85,0.93)	0.022	-5.238	<0.001
ALB (g/L)	0.76(0.71,0.82)	0.037	-7.426	<0.001
ALT (U/L)	0.98(0.96,1.00)	0.011	-1.918	0.059
Ca (mmol/L)	6.24(2.15,18.11)	0.541	3.387	0.001

Abbreviation：TB-HD: Tuberculosis combined with Hemodialysis; NTB-HD: Non-Tuberculosis combined with Hemodialysis; RBC: Red Blood Cell; Hb: Hemoglobin; N: Neutrophil; Lymphocyte; L%: Lymphocyte Percentage; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; CRP: C-Reactive Protein; TP: Total Protein; ALB: Albumin; ALT: Alanine Transaminase; Ca: Calcium.

3.3 The clinical features of hemoglobin at different levels

All tuberculosis and non-tuberculosis hemodialysis patients were divided into four groups based on hemoglobin levels (Table 4): Q1 group (Hb < 60 g/L, N = 6), Q2 group (Hb = 60–90 g/L, N = 93), Q3 group (Hb = 91–109 g/L, N = 76), and Q4 group (Hb ≥ 110 g/L, N = 74). Statistical analysis showed that the distribution of tuberculosis, as a complication, differed significantly among the four groups (Z = 38.54, P < 0.001). This suggests a close association between tuberculosis and the worsening of anemia in hemodialysis patients, indicating that TB may be an important contributing factor to anemia severity. The distribution of patients across hemoglobin levels was further analyzed between the TB-HD and NTB-HD groups (Table 5). In the TB-HD group, 6 patients (6.32%) had hemoglobin levels below 60 g/L, 54 patients (56.84%) had levels between 60 and 90 g/L, 19 patients (20.00%) had levels between 91 and 109 g/L, 16 patients (16.84%) had between 110 and 130 g/L, and none exceeded 130 g/L. In contrast, the NTB-HD group had no patients with hemoglobin below 60 g/L; 39 patients (25.66%) had levels between 60 and 90 g/L, 57 patients (37.50%) had levels from 91 to 109 g/L, 41 patients (26.97%) had levels between 110 and 130 g/L, and 15 patients (9.98%) had levels above 130 g/L. Notably, the TB-HD group was predominantly characterized by moderate anemia, while the NTB-HD group had a higher proportion of patients with mild anemia. The differences in the distribution of hemoglobin levels between the two groups were statistically significant (P < 0.05). Additionally, significant differences in age distribution were observed among the subgroups of dialysis patients with tuberculosis (Table 6, Table 7), classified by hemoglobin levels (P = 0.024). The median age of the Q4 group was 49.00 years, which was lower than that of the other groups. Among these subgroups, RBC, Hb, and HCT showed a gradual increase

from Q1 to Q4, with statistically significant differences ($P < 0.001$). Levels of MCV and MCH also increased significantly across the subgroups, particularly between Q1 and Q4 ($P < 0.05$). Albumin levels rose significantly with increasing Hb ($P < 0.001$), while CRP levels decreased significantly as Hb levels increased ($P < 0.001$). To investigate the relationships among inflammation, nutritional status, and anemia in hemodialysis patients, correlation analyses were conducted on key indicators in the tuberculosis-hemodialysis (TB-HD) and non-tuberculosis-hemodialysis (NTB-HD) groups (Figure 2). Regarding the association between CRP and hemoglobin, CRP was significantly negatively correlated with hemoglobin in both the TB-HD group ($R = -0.39$, $P < 0.01$) and the NTB-HD group ($R = -0.13$, $P < 0.01$), with a stronger negative correlation observed in the TB-HD group. Regarding the relationship between ALB and hemoglobin, ALB demonstrated a significant positive correlation with hemoglobin in both the TB-HD group ($R = 0.49$, $P < 0.01$) and the NTB-HD group ($R = 0.33$, $P < 0.01$), with the correlation being more pronounced in the TB-HD group. Similarly, CRP showed a significant negative correlation with ALB in both groups TB-HD ($R = -0.48$, $P < 0.01$) and NTB-HD ($R = -0.29$, $P < 0.01$) with a stronger inverse relationship observed in the TB-HD patients. These findings indicate that anemia in hemodialysis patients is closely linked to malnutrition and a chronic low-grade inflammatory state. Notably, in patients undergoing hemodialysis who also have tuberculosis, the interplay between inflammation, nutritional status, and anemia appears to be even more tightly connected, suggesting that tuberculosis infection may exacerbate these interactions.

Table 4. Demographic characteristic in four groups with different anemia severities for all HD patients

Variables	Q1*(N=6)	Q2*(N=93)	Q3*(N=76	Q4*(N=74)	Z	P-value
Age (years, median [IQR])	63.00 (53.50,71.25)	61.00 (52.00,69.50)	61.50 (54.75,70.25)	56.00 (47.00,69.00)	4.197	0.241
Sex (n, %)					7.416	0.053
Male	2 (33.33%)	59 (63.44%)	41 (53.95%)	52 (72.22%)		
Female	4 (66.67%)	34 (36.56%)	35 (46.05%)	20 (27.78%)		
Smoking history (n, %)	1 (16.67%)	28 (30.11%)	25 (32.89%)	30 (41.67%)	3.122	0.387
Cause of ESRD (n, %)						
Primary kidney disease	4 (66.67%)	58 (62.37%)	44 (57.89%)	42 (58.33%)	0.594	0.916
Diabetes	2 (33.33%)	22 (23.66%)	22 (28.95%)	23 (31.94%)	1.764	0.648
Hypertension	0 (0.00%)	9 (9.68%)	8 (10.53%)	3 (4.17%)	2.485	0.424
Obstructive Uropathy	0 (0.00%)	2 (2.15%)	1 (1.32%)	3 (4.17%)	1.746	0.647
Polycystic Kidney Disease	0 (0.00%)	3 (3.23%)	1 (1.32%)	5 (6.94%)	3.266	0.340
CKD duration (years, median [IQR])	7.00 (4.00,17.00)	3.00 (1.00,6.00)	5.00 (1.75,7.00)	3.00 (1.00,6.00)	5.506	0.138
Hemodialysis duration (years, median [IQR])	7.00 (4.00,17.00)	1.00 (0.50,4.50)	0.92 (0.33,4.00)	1.00 (0.33,3.00)	12.515	0.006
Comorbidities (n, %)						
CHD	1 (16.67%)	23 (24.73%)	23 (30.26%)	14 (19.44%)	2.42	0.501
Diabetes	4 (66.67%)	35 (37.63%)	31 (40.79%)	28 (38.89%)	2.023	0.575
Hypertension	5 (83.33%)	67 (72.04%)	68 (89.47%)	62 (86.11%)	9.469	0.019
COPD	0 (0.00%)	10 (10.75%)	2 (2.63%)	3 (4.17%)	4.929	0.156
Tuberculosis	6 (100.00%)	54 (58.06%)	19 (25.00%)	16 (21.62%)	38.54	<0.001

Abbreviation: ESRD: End-Stage Renal Disease; CKD: Chronic Kidney Disease; CHD: Coronary Heart Disease; COPD: Chronic Obstructive Pulmonary Disease

Q1*(Hb<60g/L,N=6Q2*(Hb=60-90g/L, N=93) Q3*(Hb=91-109g/L, N=76) Q4*(Hb≥110 g/L,N=74)

Table 5Comparison of hemoglobin levels between TB-HD group and NTB-HD group

Variables	TB-HD	NTB-HD	P-value
Hb<60g/L	6(6.32%)	0(0.00%)	0.003
Hb=60-90g/L	54(56.84%)	39(25.66%)	<0.001
Hb=91-109g/L	19(20.00%)	57(37.50%)	0.004
Hb≥110g/L	16(16.84%)	56(36.84%)	<0.001

Abbreviation: Hb: hemoglobin; TB-HD: Tuberculosis combined with Hemodialysis;

NTB-HD: Non-Tuberculosis combined with Hemodialysis.

Table 6. Demographic characteristic in four groups with different anemia severities for TB-HD patients

Variables	Q1(N=6)	Q2(N=54)	Q3(N=19)	Q4(N=16)	Z	P-value
Age (years, median [IQR])	63.00(57.00,70.00)	61.00(54.00,71.00)	63.00(56.00,66.0)	49.00(39.00,55.50$^{\#}$	9.397	0.024
Sex (n, %)					6.142	0.092
Male	2 (33.33%)	43 (79.63%)	13 (68.42%)	13 (81.25%)		
Female	4 (66.67%)	11 (20.37%)	6 (31.58%)	3 (18.75%)		
Smoking history (n, %)	1.00 (16.67%)	23.00 (42.59%)	8.00 (42.11%)	7.00 (43.75%)	1.478	0.714
Cause of ESRD (n, %)						
Primary kidney disease	4 (66.67%)	39 (72.22%)	14 (73.68%)	11 (68.75%)	0.441	0.982
Diabetes	2 (33.33%)	9 (16.67%)	5 (26.32%)	3 (18.75%)	1.965	0.595
Hypertension	0 (0%)	3 (5.56%)	0 (0%)	0 (0%)	1.443	0.804
Obstructive Uropathy	0 (0%)	1 (1.85%)	0 (0%)	0 (0%)	2.366	1
Polycystic Kidney Disease	0 (0%)	2 (3.70%)	0 (0%)	2 (12.50%)	3.014	0.414
CKD duration (years, median [IQR])	7.00(5.00,14.00)	2.50 (1.00, 6.00)	3.00 (1.00, 5.00)	1.00 (0.37, 6.50)	3.358	0.34
Hemodialysis duration (years, median [IQR])	7.00(5.00,14.00)	2.50 (1.00, 6.00)	3.00 (1.00, 5.00)	1.00 (0.37, 6.50)	5.427	0.143
Comorbidities (n, %)						
CHD	1 (16.67%)	14 (25.93%)	6 (31.58%)	2 (12.50%)	1.897	0.617
Diabetes	4 (66.67%)	21 (38.89%)	8 (42.11%)	4 (25%)	3.242	0.353
Hypertension	5 (83.33%)	38 (70.37%)	16 (84.21%)	12 (75%)	1.491	0.719
COPD	0 (0%)	8 (14.81%)	0 (0%)	0 (0%)	4.751	0.147

Abbreviation: TB-HD: Tuberculosis combined with Hemodialysis; ESRD: End-Stage Renal Disease; CKD: Chronic Kidney Disease; CHD: Coronary Heart Disease; COPD: Chronic Obstructive Pulmonary Disease; *Compared with Q1, #Compared with Q2, $Compared with Q3

Q1(Hb<60g/L,N=6） Q2(Hb=60-90g/L, N=54) Q3(Hb=91-109g/L, N=19) Q4(Hb≥110g/L,N=16)

Q1(Hb<60g/L,N=6） Q2(Hb=60-90g/L, N=54) Q3(Hb=91-109g/L, N=19) Q4(Hb≥110, g/L,N=16)

Table 7. Laboratory data among four groups with different anemia severities for TB-HD patients

Variables	Q1(N=6)	Q2(N=54)	Q3(N=19)	Q4(N=16)	Z	P-value
Laboratory Data						
WBC (×10⁹/L)	4.08 (1.64, 8.12)	7.14 (4.96, 9.51)	6.75 (4.63, 7.97)	5.93 (4.46, 7.43)	4.267	0.234
RBC (×10¹²/L)	2.00 (1.87, 2.14)	2.77 (2.49, 3.07)	3.55 (3.26, 3.73)*#	3.97 (3.79, 4.31)*#	64.052	<0.001
Hb (g/L)	51.00 (51.00, 58.00)	74.00 (67.00, 81.00)	100.00 (97.00, 105.00)*#	117.00(113.00,123.50)*#	75.576	<0.001
PLT (×10⁹/L)	115.50 (78.00, 185.00)	214.00 (161.00, 294.00)	147.00 (116.00, 251.00)	179.00 (163.00, 255.00)	6.671	0.083
N (×10⁹/L)	3.58 (1.23, 5.94)	5.76 (3.68, 7.40)	4.80 (3.52, 6.90)	4.27 (2.85, 5.83)	5.881	0.118
L (×10⁹/L)	0.28 (0.09, 0.82)	0.65 (0.49, 1.00)	0.62 (0.45, 1.05)	0.89 (0.66, 1.10)	6.705	0.082
M (×10⁹/L)	0.27 (0.14, 0.50)	0.50 (0.39, 0.68)	0.46 (0.38, 0.55)	0.46 (0.28, 0.59)	5.666	0.129
L%	12.25 (5.50, 17.10)	10.50 (6.80, 15.30)	11.00 (7.00, 15.00)	14.10 (11.10, 16.90)	4.594	0.204
HCT (%)	16.50 (16.00, 18.10)	24.00 (22.00, 26.00)	31.80 (31.00, 34.00)*#	37.55 (35.60, 38.55)*#	75.114	<0.001
MCV (fL)	86.00 (81.00, 94.00)	87.00 (82.00, 93.00)	92.90 (88.00, 96.00)	93.50 (89.00, 96.50)#	10.524	0.015
MCH (pg)	27.00 (25.00, 30.00)	27.00 (25.90, 28.00)	29.00 (27.00, 30.00)	29.80 (27.50, 30.00)#	14.846	0.002
MCHC (g/L)	313.50(305.00,315.00)	307.00 (297.00, 317.00)	312.00 (307.00, 319.00)	315.50 (308.50, 321.00)	5.878	0.118
CRP (mg/L)	70.20 (38.30, 142.00)	72.75 (46.40, 117.00)	31.50 (3.86, 88.50)	12.87 (3.36, 46.30)#	16.754	<0.001
TB (μmol/L)	55.20 (52.00, 60.00)	62.00 (58.00, 66.00)	63.00 (60.00, 71.00)	65.80 (61.60, 69.00)*	9.551	0.023
ALB (g/L)	27.00 (25.10, 28.00)	28.00 (25.30, 31.20)	33.00 (29.00, 35.00)#	37.00 (32.00, 40.00)*#	31.41	<0.001
ALT(U/L)	28.00 (26.00, 33.00)	32.00 (29.00, 38.00)	31.00 (28.00, 35.00)	28.00 (27.00, 32.00)#	8.115	0.044
AST(U/L)	8.00 (3.00, 12.00)	8.50 (5.00, 15.00)	8.00 (4.00, 12.00)	9.00 (8.00, 12.00)	1.136	0.768

GLB (g/L)	17.50 (12.00, 19.00)	16.00 (12.00, 23.00)	15.00 (12.00, 19.00)	14.00 (12.00, 20.00)	0.993	0.803
UA (μmol/L)	419.00(358.00,464.00)	393.00 (316.00, 467.00)	372.00 (226.00, 437.00)	334.00 (277.00, 406.00)	2.943	0.401
CR (μmol/L)	480.50(451.00,698.00)	716.00 (570.00, 880.00)	686.00 (527.00, 916.00)	898.00(725.00,1,094.00)*	11.195	0.011
UN (mmol/L)	15.15 (13.06, 20.68)	16.63 (12.98, 27.83)	19.41 (15.56, 43.43)	15.90 (11.15, 25.10)	3.473	0.324
Ca (mmol/L)	2.21 (2.02, 2.43)	2.29 (2.17, 2.42)	2.21 (2.14, 2.45)	2.28 (2.08, 2.48)	0.792	0.851

Abbreviation: TB-HD: Tuberculosis combined with Hemodialysis; WBC: White Blood Cell; RBC: Red Blood Cell; Hb: Hemoglobin ;PLT: Platelet; N: Neutrophil; Lymphocyte; M:Monocyte; L%: Lymphocyte Percentage; HCT: Hematocrit; MCV: Mean Corpuscular Volume ; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean; Corpuscular Hemoglobin Concentration ; CRP: C-Reactive Protein ; ESR: Erythrocyte Sedimentation Rate ; TP: Total Protein ; ALB: Albumin ; ALT: Alanine Transaminase ; AST: Aspartate Transaminase ; GLB: Globulin; UA: Uric Acid; CR: Creatinine; UN: Urea Nitrogen; Ca: Calcium; *Compared with Q1, #Compared with Q2, $Compared with Q3

Q1(Hb<60g/L,N=6 Q2(Hb=60-90g/L, N=54) Q3(Hb=91-109g/L, N=19) Q4(Hb≥110, g/L,N=16)

3.4 The initial symptoms after tuberculosis infection, types of tuberculosis, and tuberculosis detection in hemodialysis patients

The study documented a range of initial symptoms in hemodialysis patients following tuberculosis infection (Table 8). Fever (40%, N=38) and cough (64.21%, n=61) were the most common symptoms. Fatigue was reported by 15 patients (15.79%), whereas dyspnea was rare, observed in only 1 patient (1.05%). Hemoptysis occurred in 25 patients (26.32%), and gastrointestinal symptoms were present in 5 patients (5.26%). Additionally, 14 patients (14.74%) had lymphadenopathy, 2 (2.11%) experienced pain, and 6 (6.31%) exhibited genital swelling. One patient (1.05%) was asymptomatic during the initial phase of tuberculosis infection. Pulmonary tuberculosis was the predominant form among TB-HD patients. Fourteen patients (14.74%) were diagnosed with hematogenous disseminated tuberculosis, while secondary tuberculosis the most common subtype of pulmonary tuberculosis was identified in 66 patients (69.47%). Tuberculous pleuritis was diagnosed in 12 patients (12.63%). Extrapulmonary tuberculosis (EPTB) cases were also observed: 5 patients (5.26%) had tuberculous lymphadenitis, 5 (5.26%) had intestinal tuberculosis, and bone tuberculosis was found in only 1 patient (1.05%). Additionally, tracheobronchial tuberculosis was diagnosed in 3 patients (3.16%), tuberculous peritonitis in 6 (6.32%), genitourinary tuberculosis in 1 (1.05%), tuberculous pericarditis in 1 (1.05%), and joint tuberculosis in 2 patients (2.11%). Notably, 26 patients (27.37%) presented with two or more types of tuberculosis. Among initial symptoms, fever showed a significant association with anemia severity across the four TB-HD patient groups ($P < 0.001$). However, most tuberculosis types did not significantly correlate with anemia severity (Table 9). Tuberculosis laboratory tests were classified into bacteriological, immunological, serological, and molecular categories (Table 10). Bacteriological testing remains the cornerstone of tuberculosis diagnosis. All patients underwent acid-fast bacilli (AFB) staining and mycobacterial rapid culture (MGIT). However, the positive rates for these tests were relatively low: AFB was positive in 19 patients (20.00%), while MGIT yielded positive results in 37 patients (38.95%). Due to cost constraints and some patients' reluctance to cooperate, not all patients completed the full range of tuberculosis tests. For immunological testing, two methods were used: the Tuberculin Skin Test (TST) and the T-Spot TB test (T-SPOT). Fifty-seven patients completed the TST, with a positivity rate of 23%. Seventy-one patients underwent T-SPOT testing, which showed a notably higher positivity rate of 91.55%. In molecular diagnostics, three main methods were employed: Mycobacterium tuberculosis DNA (TB-DNA) testing, Xpert MTB/RIF assay (Xpert), and NGS.

Among those tested, 41 patients underwent TB-DNA testing, with a positive rate of 58.54%. Forty-three patients were tested using Xpert, which showed a positive rate of 53.49%. Only 14 patients underwent NGS testing, but this method demonstrated the highest positive rate at 92.86%, with 10 positive cases. While the positive and negative rates of these tuberculosis detection methods varied among different anemia groups (Table 11), no statistically significant differences were observed. The initial symptoms, types of tuberculosis, and detection methods in different groups of hemodialysis patients after tuberculosis infection are detailed in Figure 3.

Table 8 The initial symptoms and types of tuberculosis inTB-HD patients

Variables	N (%)
Initial Symptoms	
Fever	38 (40.00%)
Cough	61 (64.21%)
Fatigue	15 (15.79%)
Dyspnea	1 (1.05%)
Hemoptysis	25 (26.32%)
Gastrointestinal symptoms	5 (5.26%)
Lymph node enlargement	14 (14.74%)
Pain	2 (2.11%)
Genital swelling	6 (6.31%)
Asymptomatic	1 (1.05%)
Types of TB	
PTB	
Hematogenous Disseminated TB	14 (14.74%)
Secondary pulmonary TB	66 (69.47%)
Tuberculous Pleurisy	12 (12.63%)
EPTB	
Lymph Node TB	5 (5.26%)
Bone TB	1 (1.05%)
Tuberculous Meningitis	5 (5.26%)
Intestinal TB	5 (5.26%)
Tracheobronchial TB	3 (3.16%)
Tuberculous Peritonitis	6 (6.32%)
Genitourinary TB	1 (1.05%)
Tuberculous Pericarditis	1 (1.05%)
TB of Joints	2 (2.11%)
Combined with more than two types of TB	26 (27.37%)

Abbreviation: TB: Tuberculosis; PTB: Pulmonary Tuberculosis;

EPTB: Extra - pulmonary Tuberculosis

Table 9. The initial symptoms and types of tuberculosis in four groups with different anemia severities for TB-HD patients

Variables	Q1(N=6)	Q2(N=54)	Q3(N=19)	Q4(N=16)	Z	P-value
Initial Symptoms						
Fever	5 (83.33%)	29 (53.70%)	2 (10.53%)	2 (12.50%)	21.165	<0.001
Cough	2 (33.33%)	34 (62.96%)	15 (78.95%)	10 (62.50%)	4.129	0.237
Fatigue	1 (16.67%)	10 (18.52%)	1 (5.26%)	3 (18.75%)	2.156	0.552
Dyspnea	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	2.366	1
Hemoptysis	3 (50.00%)	16 (29.63%)	3 (15.79%)	3 (18.75%)	3.448	0.323
Gastrointestinal symptoms	0 (0.00%)	3 (5.56%)	1 (5.26%)	1 (6.25%)	0.616	1
Lymph node enlargement	0 (0.00%)	13 (24.07%)	1 (5.26%)	0 (0.00%)	7.521	0.036
Pain	1 (16.67%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	4.435	0.256
Genital swelling	1 (16.67%)	2 (3.70%)	2 (10.53%)	1 (6.25%)	3.246	0.264
Asymptomatic	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.25%)	4.798	0.232
Types of TB						
PTB						
Hematogenous Disseminated TB	2 (33.33%)	8 (14.81%)	4 (21.05%)	0 (0.00%)	5.411	0.114
Secondary pulmonary TB	4 (66.67%)	35 (64.81%)	13 (68.42%)	14 (87.50%)	3.15	0.401
Tuberculous Pleurisy	0 (0.00%)	8 (14.81%)	3 (15.79%)	1 (6.25%)	1.2	0.758
EPTB						
Lymph Node TB	1 (16.67%)	3 (5.56%)	1 (5.26%)	0 (0.00%)	2.578	0.376
Bone TB	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (6.25%)	4.798	0.232
Tuberculous Meningitis	0 (0.00%)	4 (7.41%)	1 (5.26%)	0 (0.00%)	1.07	0.87
Intestinal TB	1 (16.67%)	2 (3.70%)	1 (5.26%)	1 (6.25%)	2.738	0.327
Tracheobronchial TB	0 (0.00%)	1 (1.85%)	1 (5.26%)	1 (6.25%)	2.269	0.459
Tuberculous Peritonitis	0 (0.00%)	4 (7.41%)	1 (5.26%)	1 (6.25%)	0.428	1
Genitourinary TB	0 (0.00%)	0 (0.00%)	1 (5.26%)	0 (0.00%)	4.455	0.432
Tuberculous Pericarditis	0 (0.00%)	1 (1.85%)	0 (0.00%)	0 (0.00%)	2.366	1
TB of Joints	0 (0.00%)	2 (3.70%)	0 (0.00%)	0 (0.00%)	1.464	1
Combined with more than two types of TB	1 (16.67%)	17 (31.48%)	4 (21.05%)	4 (25.00%)	1.024	0.823

Abbreviation: TB: Tuberculosis; PTB: Pulmonary Tuberculosis; EPTB: Extra - pulmonary Tuberculosis

Table 10. Laboratory tests of tuberculosis in TB-HD patients

Variables	N (%)
Bacteriological Tests	
AFB	
Positive	19 (20.00%)
Negative	76 (80.00%)
MGIT	
Positive	37 (38.95%)
Negative	58 (61.05%)
Immunological Tests	
TST	
Positive	23 (40.35%)
Negative	34 (59.65%)
T – SPOT.TB	
Positive	65 (91.55%)
Negative	6 (8.45%)
Molecular Tests	
TB - DNA	
Positive	24 (58.54%)
Negative	17 (41.46%)
Xpert MTB/RIF	
Positive	23 (53.49%)
Negative	20 (46.51%)
NGS	
Positive	13 (92.86%)
Negative	1 (7.14%)

Abbreviation: TB-HD: Tuberculosis combined with Hemodialysis;

AFB: Acid-fast bacilli; MGIT: Mycobacteria growth indicator tube;

TST: Tuberculin skin test; T-SPOT.TB: T-cell spot of tuberculosis assay;

TB-DNA: Tuberculosis deoxyribonucleic acid detection;

Xpert MTB/RIF: Xpert MTB/RIF assay;

NGS: Next-generation sequencing.

Table 11. Laboratory tests of tuberculosis in four groups with different anemia severities for TB-HD patients

Variables	Q1(N=6)	Q2(N=54)	Q3(N=19)	Q4(N=16)	Z	P-value
Bacteriological Tests						
AFB					2.176	0.518
Positive	1 (16.67%)	10 (18.52%)	6 (31.58%)	2 (12.50%)		
Negative	5 (83.33%)	44 (81.48%)	13 (68.42%)	14 (87.50%)		
MGIT					0.915	0.849
Positive	3 (50.00%)	22 (40.74%)	7 (36.84%)	5 (31.25%)		
Negative	3 (50.00%)	32 (59.26%)	12 (63.16%)	11 (68.75%)		
Immunological Tests						
TST					4.185	0.225
Positive	1 (25.00%)	12 (33.33%)	5 (50.00%)	5 (71.43%)		
Negative	3 (75.00%)	24 (66.67%)	5 (50.00%)	2 (28.57%)		
T – SPOT.TB					3.463	0.27
Positive	2 (66.67%)	39 (90.70%)	13 (100.00%)	11 (91.67%)		
Negative	1 (33.33%)	4 (9.30%)	0 (0.00%)	1 (8.33%)		
Molecular Tests						
TB - DNA (PCR)					1.554	0.742
Positive	2 (100.00%)	14 (53.85%)	4 (66.67%)	4 (57.14%)		
Negative	0 (0.00%)	12 (46.15%)	2 (33.33%)	3 (42.86%)		
Xpert MTB/RIF					1.914	0.713
Positive	0 (0.00%)	13 (50.00%)	6 (66.67%)	4 (57.14%)		
Negative	1 (100.00%)	13 (50.00%)	3 (33.33%)	3 (42.86%)		
TNGS					3.194	0.429
Positive	3 (100.00%)	8 (100.00%)	0 (0.00%)	2 (66.67%)		
Negative	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (33.33%)		

Abbreviation: TB-HD: Tuberculosis combined with Hemodialysis; AFB: Acid-fast bacilli; MGIT: Mycobacteria growth indicator tube; TST: Tuberculin skin test; T-SPOT.TB: T-cell spot of tuberculosis assay; TB-DNA: Tuberculosis deoxyribonucleic acid detection; Xpert MTB/RIF: Xpert MTB/RIF assay; NGS: Next-generation sequencing.

Discussion

Anemia is a common and significant complication in patients with CKD, particularly those undergoing HD. In HD patients, anemia arises from multiple factors, including impaired red blood cell production, blood loss during dialysis, iron deficiency,

and inflammation [18],[19]. Additionally, HD patients are more susceptible to TB infections. This study examines the impact of inflammation and nutritional status related to active TB on anemia in patients receiving maintenance hemodialysis. Clinical data from 95 HD patients diagnosed with TB at Changsha Central Hospital affiliated with the University of South China were collected and compared with data from 152 HD patients without TB infection during the same period. The results show that patients with TB experienced more severe anemia, poorer nutritional status, and elevated levels of inflammation, suggesting that TB may worsen anemia through multiple mechanisms.

In this study, RBC, Hb, HCT, MCV, and MCH levels (all $P < 0.05$) were significantly lower in the TB-HD group compared to the control group, while CRP levels ($P < 0.001$) were significantly higher. MCV reflects the size of RBCs, MCH measures the amount of hemoglobin per RBC, and mean corpuscular hemoglobin concentration (MCHC) indicates the concentration of hemoglobin per unit volume [20]. These parameters, known as red cell indices, are key indicators of anemia when abnormal. Atoms et al. conducted a cross-sectional study comparing Hb, RBC, MCHC, MCV, and white blood cell (WBC) counts in TB patients and healthy controls [21]. Consistent with our findings, TB patients showed lower levels of CD4 cells, Hb, MCV, MCHC, and RBC counts. Generally, anemia associated with TB ranges from mild to moderate severity.

In this study, among the 95 TB patients, moderate anemia was the most common severity observed (N = 54, 56.84%), whereas patients without TB had a higher proportion of mild anemia (N = 57, 37.50%).

Multivariate analysis of TB-HD and NTB-HD patients identified ALB as a protective factor against TB infection (OR 0.78, 95% CI 0.72–0.86, $P = 0.031$), while CRP was a significant risk factor (OR 1.03, 95% CI 1.01–1.04, $P < 0.001$). Correlation analysis between CRP and hemoglobin revealed a significant negative relationship in both groups; the TB-HD group showed a moderate correlation ($R = -0.39$, $P < 0.01$), whereas the correlation in the NTB-HD group was weaker. Several studies have reported elevated CRP levels in patients with TB-related anemia [22],[23]. Furthermore, TB-HD patients were stratified into four groups based on hemoglobin levels: Q1 (Hb < 60 g/L, N = 6), Q2 (Hb 60–90 g/L, N = 54), Q3 (Hb 91–109 g/L, N = 19), and Q4 (Hb ≥ 110 g/L, N = 16). Across these groups, CRP levels decreased as anemia severity lessened. This pattern suggests that CRP production may be driven by inflammatory tissue damage induced by *Mycobacterium tuberculosis* (MTB) infection [23].

The pathogenesis of TB-associated anemia involves complex interactions among multiple factors, with inflammation playing a central role [24],[25]. The immune response triggered by *Mycobacterium tuberculosis* sets off a cascade amplification effect, resulting in a marked increase in pro-inflammatory cytokines such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) [26],[20]. These cytokines not only directly suppress the transcription and synthesis of erythropoietin (EPO) in the kidneys but also downregulate EPO receptor expression on bone marrow erythroid progenitor cells, thereby reducing their sensitivity to EPO and making anemia more difficult to treat clinically. This mechanism is further aggravated by the chronic low-grade inflammatory state frequently observed in hemodialysis patients [27]. In addition, complement activation and the cytokine storm induced by TB infection compromise the structural integrity of erythrocyte membranes [28],[29], significantly shortening red blood cell lifespan and accelerating hemolysis. Combined with declining renal function and the poor biocompatibility of certain dialysis membranes such as unmodified cellulose membranes this contributes to a persistent state of oxidative stress. Excessive production of reactive oxygen species (ROS) attacks lipids and proteins within erythrocyte membranes, triggering lipid peroxidation that further damages the cells [30]. As a result, erythrocyte destruction rates in TB-infected hemodialysis patients far exceed those seen in dialysis patients without TB. The interaction between hemodialysis and TB infection creates a vicious cycle of inflammation and anemia, adversely affecting both erythropoiesis and erythrocyte survival. Notably, dysregulation of iron metabolism mediated by IL-6 is especially pronounced in the hemodialysis population [31],[22]. In the inflammatory state induced by TB in dialysis patients, hepcidin expression is upregulated. This hormone not only inhibits iron absorption in the duodenum but also promotes the sequestration of iron by macrophages, leading to functional iron deficiency [32]. Moreover, the unavoidable blood loss associated with dialysis due to factors such as residual blood in the dialyzer and frequent blood sampling further depletes iron stores. This creates a vicious cycle of impaired iron utilization and ongoing loss, resulting in a shortage of essential substrates for hematopoiesis and severely limiting red blood cell production.

The findings of this study suggest that albumin serves as a protective factor in dialysis patients without TB infection and is closely linked to the severity of anemia in those with concurrent TB. Reduced serum albumin levels primarily result from inadequate intake, increased consumption, and decreased hepatic synthesis influenced by inflammatory mediators [14]. Malnutrition can cause deficiencies in essential nutrients for erythropoiesis, such as iron, folic acid, and vitamin B1. In TB patients, the heightened catabolic state driven by inflammation and the metabolic demands of TB accelerate protein breakdown [15], leading to a loss of body protein and worsening anemia in dialysis patients. Additionally, prolonged malnutrition results in an insufficient energy supply, which causes cellular damage and functional impairment, further triggering inflammatory responses. This bidirectional relationship between inflammation and malnutrition jointly exacerbates anemia in dialysis patients with TB, forming an intertwined “inflammation-malnutrition-anemia” syndrome.

This study also identified the duration of hemodialysis (OR 1.22, 95% CI 1.09–1.38, P < 0.001) as a risk factor for TB infection, aligning with findings from a similar study conducted in Turkey [33]. Patients on long-term dialysis experience severe renal dysfunction, which impairs the body’s ability to clear toxins and leads to immune system dysfunction. While dialysis partially compensates for kidney function, it cannot fully restore normal physiological conditions [34]. As dialysis duration increases, immune function further declines, reducing resistance to Mycobacterium tuberculosis and elevating the risk of TB infection [35]. Moreover, dialysis centers tend to be enclosed spaces with high patient density and frequent foot traffic. Long-term dialysis patients spend extended periods in these environments, increasing their exposure to potential TB carriers [36]. Poor ventilation and inadequate disinfection in these settings facilitate airborne transmission of Mycobacterium tuberculosis, further raising the risk of infection. To address this, the research center has established a dedicated HD purification unit for dialysis patients with TB, which has helped reduce the risk of cross-infection among patients.

Patients undergoing HD often exhibit subtle and atypical clinical manifestations following Mycobacterium tuberculosis infection [37]. In this study, most patients primarily presented with symptoms such as cough (N=61, 64.21%) and fever (N=38, 40%), which can easily be mistaken for dialysis-related complications or infections caused by other pathogens, thereby increasing the difficulty of clinical diagnosis. Meanwhile, traditional TB diagnostic methods, including AFB staining (20.00%), mycobacterial culture (MGIT) (38.95%), and the TST (40.35%), show clear limitations in the HD population. Both AFB and culture rely on sputum samples, but impaired immune function and reduced ciliary clearance in the respiratory tracts of HD patients significantly reduce the effectiveness of these methods [38]. Obtaining sputum specimens is often challenging, leading to low positive detection rates. The TST is also compromised by the chronic immunosuppressed state of HD patients, frequently resulting in false-negative results and markedly reduced sensitivity [39]. Given these limitations and the unique pathophysiology of HD patients, alternative diagnostic approaches are critical. This study found high positive rates for NGS (92.86%) and T-SPOT.TB (91.55%) tests. NGS can rapidly identify the entire genome sequence of Mycobacterium tuberculosis, overcoming the constraints of sample type [40]. Meanwhile, T-SPOT.TB effectively reduces the impact of immunosuppression on test results by detecting effector T cell responses to TB-specific antigens [41], [42].

Clinical vigilance is crucial regarding the risk of TB infection in patients undergoing HD and the associated inflammatory anemia. Optimizing TB screening protocols and prioritizing the use of advanced diagnostic technologies are essential steps. Additionally, enhancing infection control practices within dialysis centers and improving nutritional support for patients may help reduce TB incidence and anemia-related complications. These strategies offer promising intervention pathways to improve the quality of life for this vulnerable population. Future studies with larger sample sizes should further investigate the complex interactions between TB-induced inflammation and anemia in HD patients, providing stronger evidence to guide clinical management.

This study has several limitations. First, its retrospective design relies on historical data collection and analysis, which may introduce information bias. Second, the relatively small sample size comprising only 95 HD patients with active TB limits the statistical power of subgroup analyses, such as those stratified by hemoglobin levels. This limitation may affect the ability to detect true associations and increases the likelihood of random variation in the results. Future research should aim to

include larger cohorts to more thoroughly explore the mechanisms by which TB-related inflammation exacerbates anemia in HD patients, thereby strengthening the evidence base for clinical practice.

Conclusion

Patients on maintenance hemodialysis (MHD) who develop TB often experience worsened anemia, which is closely linked to systemic inflammation (elevated CRP) and malnutrition (reduced ALB). These factors contribute to a vicious cycle of **inflammation–malnutrition–anemia**. Comprehensive management including anti-TB therapy and nutritional support is critical to improving anemia outcomes in this population. Non-specific symptoms such as cough and fever are common early manifestations, while traditional diagnostic tests often lack sensitivity, leading to a high rate of missed diagnoses. For HD patients with suspected TB, timely testing with T-SPOT.TB or next-generation sequencing (NGS) is recommended. Routine TB screening should also be considered for all patients undergoing hemodialysis.

Abbreviations

CKD

Chronic kidney disease

HD

Hemodialysis

TB

Tuberculosis

Hb

Hemoglobin

ALB

Albumin

MTB

Mycobacterium tuberculosis

ESKD

End stage kidney disease

TB-PCR

Tuberculosis polymerase chain reaction

CHD

Coronary heart disease

COPD

Chronic obstructive pulmonary disease

PTB

Pulmonary tuberculosis

EPTB

Extra - pulmonary tuberculosis

AFB

Acid-fast bacilli

MGIT

Mycobacteria growth indicator tube

TST

Tuberculin skin test

T-SPOT.TB

T-cell spot of tuberculosis assay

TB-DNA

Tuberculosis deoxyribonucleic acid detection

NGS

Next-generation sequencing

Declarations

Authors' contributions

All authors read and approved the final manuscript

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Data availability

The datasets used and analyzed during the current study are available from Changsha Central Hospital Affiliated with the University of South China

This retrospective study was approved by the Ethics Committee of Changsha Central Hospital Affiliated with the University of South China and adhered to the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests

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Figures

Figure 1.

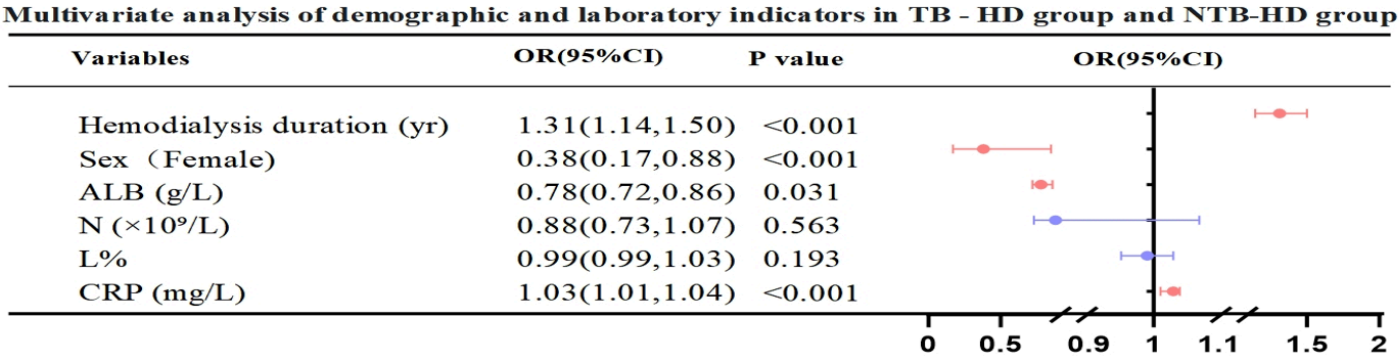


Figure 1

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Figure 2.

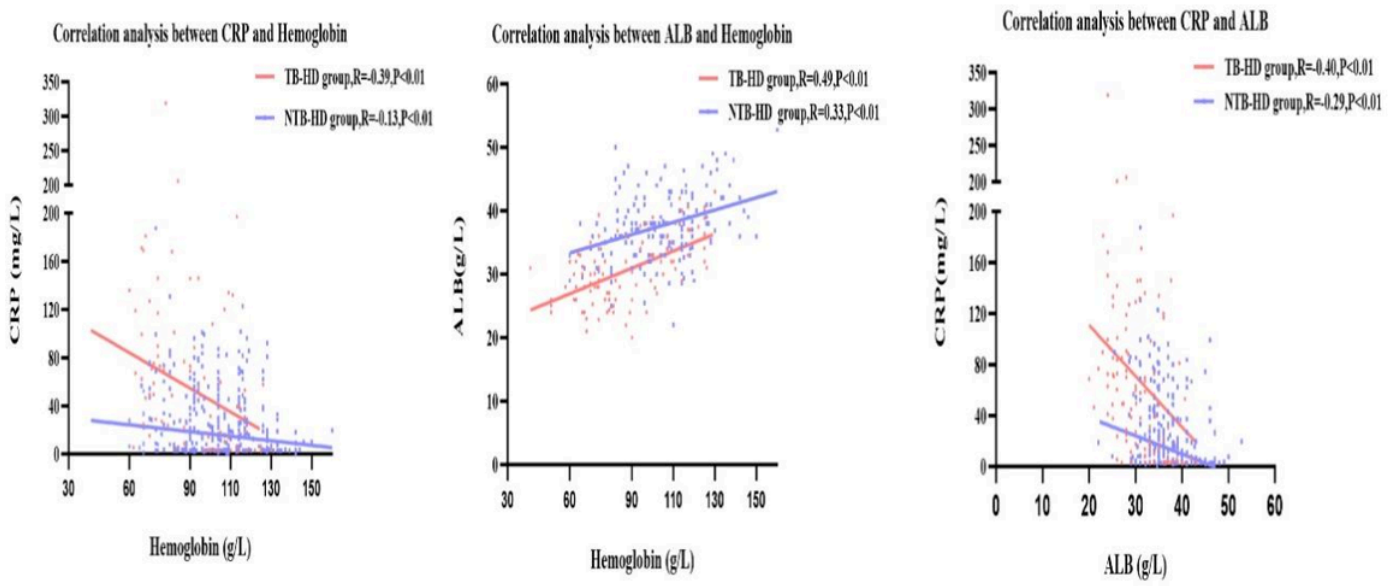


Figure 2

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Figure 3.

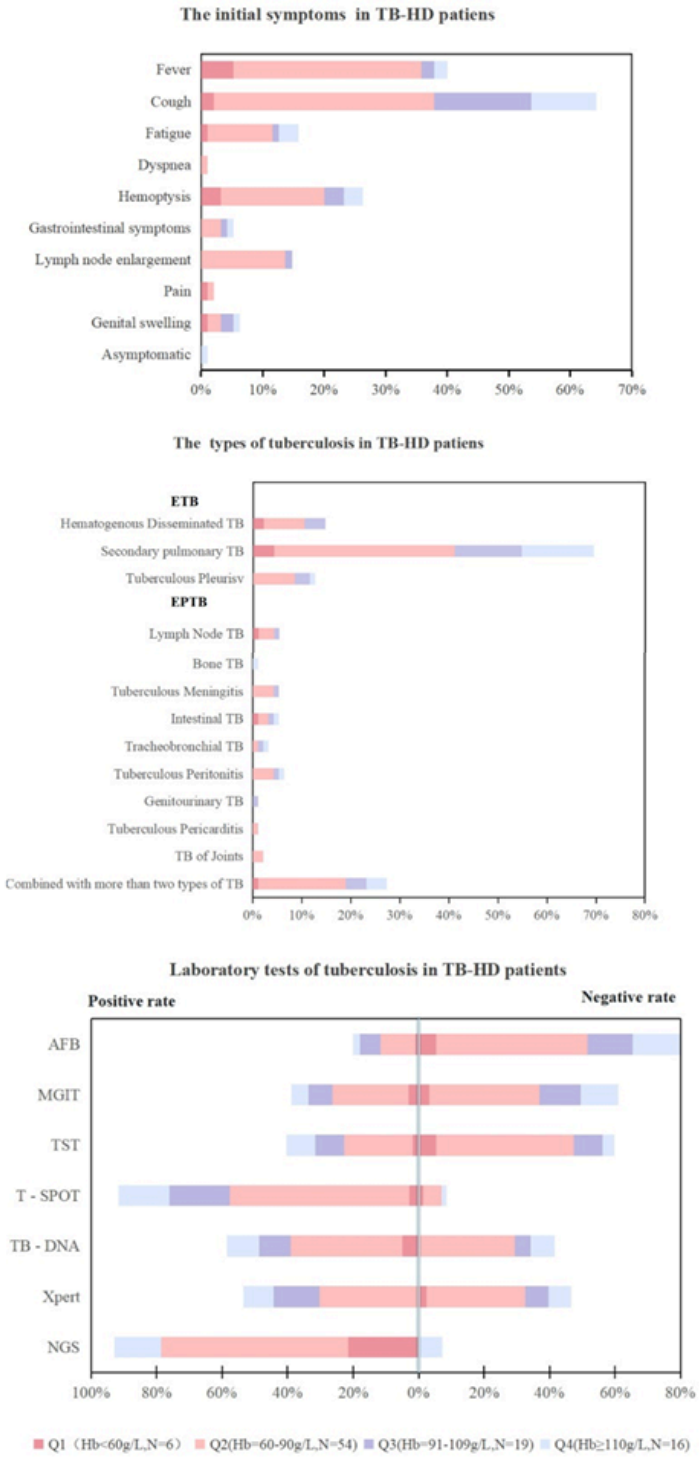


Figure 3

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