Anemia in Patients with Takayasu's Arteritis and its Correlation with Disease Activity

Yanqiu Guo

Beijing An Zhen Hospital: Capital Medical University Affiliated Anzhen Hospital <https://orcid.org/0000-0003-0831-3055>

Juan Du

Beijing An Zhen Hospital: Capital Medical University Affiliated Anzhen Hospital

Taotao Li

Beijing An Zhen Hospital: Capital Medical University Affiliated Anzhen Hospital

Keyang Zheng

Beijing An Zhen Hospital: Capital Medical University Affiliated Anzhen Hospital

Na Gao

Beijing An Zhen Hospital: Capital Medical University Affiliated Anzhen Hospital

Lili Pan (✉ lilypansxmu@sina.com)

Capital Medical University Affiliated Anzhen Hospital <https://orcid.org/0000-0003-2914-078X>

Research article

Keywords: autoimmune disease, immune index, anemia, Takayasu's arteritis (TAK)

Posted Date: June 24th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-642481/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background Anemia is a common clinical condition in autoimmune disease, but there are few related studies in Takayasu's arteritis (TAK). The purpose of this study is to detect clinical characteristics of anemia patients with TAK and to explore the relationship between the hemoglobin level and the disease activity in TAK.

Methods This retrospective study included 160 cases of hospitalized patients with TAK and 110 cases of age-and sex-matched healthy people. According to the hemoglobin level, 160 TAK patients were divided into two groups with and without anemia, the immune indexes were compared between the two groups. 28 patients with anemia in TAK were followed up and the changes of immune indexes before and after treatment were compared.

Results Hemoglobin in TAK patients is significantly lower than that of healthy control group. Among the 160 cases of TAK, 67 cases of anemia are mild to moderate anemia, and most of which are normocytic anemia. In anemia patients with TAK, women was more common ($P=0.014$), age at admission was more younger ($P=0.002$), the disease duration was shorter ($P=0.017$). The levels of erythrocyte sedimentation rate (ESR, $P=0.000$), C-reactive protein (CRP, $P=0.000$), interleukin-6 (IL-6, $P=0.036$) and disease activity scores (NIH $P=0.000$, ITASA $P=0.001$, ITAS2010 $P=0.030$) were significantly higher in anemia patients with TAK. The risk of anemia in TAK patients with elevated CRP was 2.35 times than that of TAK patients without elevated CRP (OR = 2.350, 95% CI 1.055-5.234, $P = 0.037$). After followed up for 3-6 months, hemoglobin levels increased significantly ($P=0.001$), ESR ($P=0.000$), CRP ($P=0.039$) and disease activity scores (NIH $P=0.001$, ITASA $P=0.000$, ITAS2010 $P=0.000$) decreased significantly through effective treatment without iron supplementation, and the changes of hemoglobin after treatment were negatively correlated with the changes of ESR ($P=0.046$) and CRP ($P=0.002$).

Conclusion Anemia patients with TAK were more common in young women, and the disease activity was higher. Anemia can be significantly improved without iron supplementation through effective treatment to reduce disease activity of TAK.

Introduction

TAK is a chronic inflammatory disease that predominantly affects large arteries. The clinical manifestations of TAK include systemic symptoms, local inflammatory symptoms and organ ischemia caused by vascular stenosis or occlusion. Systemic symptoms, including fever, fatigue, and weight loss, are very common in TAK patients, especially in the active phase of disease.

Anemia is a common complication in TAK patients. The etiology and pathogenesis of anemia are complex and diverse, and sometimes is the result of multiple factors. There are many studies on anemia in autoimmune disease such as rheumatoid arthritis (RA). And anemia was significantly associated with disease severity and comorbidities of RA[1–3]. In TAK patients, the characteristics of anemia patients and the relationship between anemia and disease activity need to be explored. Therefore, we summarized the

clinical characteristics of anemia patients with TAK, and analyzed the relationship between anemia and immunological markers.

Methods

Patients

The 160 TAK patients recruited from the Department of Rheumatology and Immunology, Beijing Anzhen Hospital during the period from November 2012 to November 2019 were retrospectively analyzed. All TAK patients fulfilled the criteria for classification of TAK developed by the American College of Rheumatology (ACR) in 1990[4]. Patients who had current infections, hematologic diseases, tumors, or other autoimmune diseases were excluded.

Disease activity was evaluated by the National Institute of Health (NIH) in 1994 and The Indian Takayasu Clinical Activity Score (ITAS)[5, 6].

According to NIH score greater than or equal 2 (≥ 2) or not, 160 TA patients were divided into active group and inactive group.

The World Health Organization (WHO) defines anemia as a hemoglobin level lower than 120 g/L in non-pregnant women and 130 g/L in men[7]. According to the hemoglobin level, anemia can be divided into mild (Hb ≥ 90 g/L), moderate (Hb 60~90 g/L), severe (Hb 60~90 g/L) and very severe (Hb ≤ 30 g/L). According to the cell morphology classification, anemia can be divided into macrocytic anemia, normocytic anemia and microcytic anemia.

Among the 160 TAK patients, 28 cases of initial treatment without iron supplement were selected. The guidelines recommend that TAK should be followed up every 1-3 months during the first year[8]. We followed up for 3-6 months, because disease activity of TAK should be controlled unless treatment was ineffective. The follow-up indexes included ESR, CRP, NIH, ITASA, ITAS2010.

This study was approved by the Ethics Committee of Beijing Anzhen Hospital (2021070X).

Clinical and laboratory data

Clinical data including sex, age at admission, age at symptom onset, Body Mass Index (BMI) and disease duration were extracted from the medical records. Laboratory parameters were also recorded, including white blood cell (WBC), platelets (PLT), hemoglobin, mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), ESR, CRP, IgG, IgA, IgM, C3, C4.

Statistical analysis

SPSS program V.25.0 (SPSS, Chicago, Illinois, USA) was used for statistical analysis. According to the normality, variables were described as means $\pm$ SE or as medians. We performed univariate analysis by the Student's T-test or Wilcoxon–Mann–Whitney test for numerical data according to normality. Also, the

One-Way Anova test and Jonckheere-Terpstra test were used to determine the statistical difference between the means of continuous variables, and the chi-square test was used to compare the categorical variables. The Spearman correlation analysis was employed to validate the relationship between age, duration and biomarkers. Logistic regression was used to analyze the related factors of anemia in TAK patients. $P < 0.05$ was considered statistically significant.

Results

1. Comparison of general laboratory parameters between 160 TAK patients and 110 healthy controls

There was no difference in age and gender between 160 TAK patients and 110 healthy controls. This study showed that WBC [6.94(5.68,8.67) vs 5.64(4.66,6.56), $P=0.000$] and PLT [256.00(201.00-309.00) vs 231.00(209.00-264.25), $P=0.033$] were significantly increased in TAK patients, but hemoglobin [122.50(112.25,134.00) vs 134.50(128.00,143.00), $P=0.000$], MCV [84.65(79.93-89.43) vs 87.55(85.38-89.53), $P=0.000$], MCH [28.50(26.20-30.50) vs 30.10(29.00-30.60), $P=0.000$], MCHC [334.00(323.00-342.75) vs 342.00(336.00-347.00), $P=0.000$] were significantly decreased in TAK patients (Table 1).

2. Description of 67 cases in 160 TAK patients

There were 67 cases of anemia in 160 TAK patients. According to cell morphology, 38 cases of normocytic anemia, 29 cases of microcytic anemia, no macrocytic anemia. According to the hemoglobin level, 60 cases of mild anemia, 7 cases of moderate anemia, no severe anemia (Table 2).

3. Comparison of demographic data and general laboratory parameters between TAK patients with and without anemia

Anemia patients with TAK were younger [32(24,45) vs 40(31,48), $P=0.002$], more common in women (95.52% vs 82.80%, $P=0.014$), shorter duration [36(7,120) vs 72(14,162), $P=0.017$], and lower BMI [21.43(18.96,23.81) vs 22.86(20.09,25.81), $P=0.008$]. ESR [23(15,51) vs 11(5.5,22), $P=0.000$] and CRP [9.33(1.99,27.8) vs 1.99(0.45,6.68), $P=0.000$] were significantly increased in anemia patients with TAK. IgG, IgA, C3, C4 had no difference between the two groups, but IgM was significantly increased in TAK anemia patients [1.35(0.94,1.99) vs 1.15(0.81,1.53), $P=0.008$]. IL-6 [6.80(3.60,16.68) vs 4.45(2.50,10.53), $P=0.036$] and disease activity scores NIH [3(2,3) vs 2(2,3), $P=0.000$], ITASA [9(6,13) vs 6(3,10), $P=0.001$], ITAS2010 [7(4,9.5) vs 5(3,8), $P=0.030$] were significantly increased in anemia patients with TAK (Table 3).

4. Relationship between hemoglobin and biomarkers with disease activity

Among the 160 TAK patients, hemoglobin decreased with the increase of NIH score significantly (Figure 1a, 1b). Taking anemia as dependent variable, age, disease duration, BMI, elevated CRP and IL-6 as covariates, binary logistic stepwise regression analysis was performed. Finally, the variables entering the regression equation were elevated CRP and age. The risk of anemia in TAK patients with elevated CRP was 2.35 times than that of TA patients without elevated CRP (OR = 2.350, 95% CI 1.055-5.234, $P =$

0.037). Age is a protective factor of anemia in TAK patients. The older the age, the lower the risk of anemia in TAK patients (**Table 4**).

5. Follow up of 28 anemia patients with TAK without iron supplementation

In anemia patients with TAK, we selected 28 cases of standard treatment but no iron supplement for follow-up. Among the 28 patients, the proportion of female was 92.86% (26/2), the average age was 37.36 years old, the average disease duration was 92.63 months. The use of prednisone was the highest (75.00%), followed by the use of Tocilizumab (TCZ, 50%), Cytoxan (CTX, 39.29%), methotrexate (MTX, 39.29%), Mycophenolate Mofetil (MMF, 14.29%), Leflunomide (LEF, 7.14%), Hydroxychloroquine (HCQ, 7.14%). After 3-6 months follow-up, we found that ESR ($P=0.000$), CRP ($P=0.039$), NIH ($P=0.000$), ITASA ($P=0.000$) and ITAS2010 ($P=0.000$) decreased significantly after treatment, and hemoglobin improved significantly ($P=0.001$) (Figure 2). And the changes of hemoglobin after treatment were negatively correlated with the changes of ESR and CRP after treatment ($P=0.046$, $P=0.002$) (Figure 3a, 3b).

Discussion

Our study found that anemia was more common in TAK patients, especially in young women. The hemoglobin level in TA patients was negatively correlated with ESR, CRP, IL-6 and disease activity. Degree of anemia is positively associated with the disease activity of TAK. Moreover, for the first time, we found that anemia can be significantly improved without iron supplementation through effective treatment to reduce disease activity of TAK.

Autoimmune disease is one of important causes of anemia in chronic disease (ACD). Previous studies have reported that incidence rate of anemia in RA was 30.4% in men and 32% in women. More than 50% of Systemic lupus erythematosus (SLE) patients have anemia during the course of disease[9]. We found that anemia is also a common problem in TAK patients. the incidence of anemia in TA patients was higher (41.88%). Zhang ying etc. reported the incidence of anemia in TAK patients was 36.7%[10], which was similar to our study.

Anemia patients in RA is usually mild to moderate anemia, most normocytic anemia, few microcytic anemia, which was a typical example of ACD, may also combine with iron deficiency anemia (IDA)[1]. Similarly, in this study, all anemia patients in TA were mild to moderate anemia, without severe anemia. The type of anemia in TA was mostly normocytic anemia (56.72%, 38/67), 43.28% (29/67) of anemia patients with TA were microcytic anemia, which may be ACD, or ACD combined with IDA.

The prevalence of anemia in women is higher than that in men[11], TAK is more common in women, the male/female ratio ranges from 1:5 to 1:9[12], and anemia patients with TAK are also more common in women. We found anemia patients with TAK were younger. Previous studies have shown that the incidence of anemia in TAK patients decreases with age, but the mechanism has not been elucidated [10, 13, 14]. In our study, we found the same results that the hemoglobin level was positively correlated with age at admission. Furthermore, we found the age at admission was negatively correlated with CRP and

IL-6, which was associated with disease activity of TAK. Therefore, we speculated that the younger the patient, the higher the disease activity (Supplementary Table 1). The shorter disease duration in anemia patients with TAK may be related to the fact that the disease was not effectively controlled in the early stage of onset.

The etiology of TA is still unclear, which may be related to infection, genetic, and immune dysfunction [15]. Cell-mediated autoimmunity has been strongly confirmed to play an important role in the pathogenesis of TA. More inflammatory cells infiltration was shown in the aortic tissue of TA patients by immunohistochemistry, including macrophages, CD4 + T cells, CD8 + T cells, $\gamma\delta$ T cells, natural killer (NK) cells and neutrophils [16]. Activated inflammatory cells can secrete a large number of cytokines, such as IL-6, which are involved in the pathogenesis of aortic tissue and peripheral blood of TA patients [17]. At the same time, cytokines such as IL-6, IL-8 and TNF α , are also involved in the occurrence and development of anemia. Inflammatory factors can promote the phagocytosis of RBC by macrophages, increase the destruction of RBC, and shorten the life span of RBC. Moreover, The inhibition of bone marrow hematopoiesis and abnormal iron metabolism are also related to the production of cytokines [18].

There are many studies on anemia of RA. The mechanism of anemia caused by RA includes shortening of RBC lifespan, insufficient RBC production in bone marrow and abnormal iron metabolism [1]. Moreover, hepcidin plays an important role in the occurrence and development of rheumatoid anemia. Many cytokines such as IL-1 and IL-6 induce hepcidin production, which is involved in the occurrence and development of rheumatoid anemia [19]. The pathological mechanism of anemia caused by TA may be similar to RA.

As an autoimmune disease, the autoantibodies produced by B lymphocytes may be one of the key points in the pathogenesis of TAK. Some studies found that the levels of IgA and IgG in patients with active TAK were significantly increased, but there was no difference in the levels of IgM between active and inactive TAK [20]. We found the level of serum IgM in anemia patients with TAK was significantly increased, which may be related to the combined effect of inflammation and anemia on humoral immunity [21], but the specific mechanism is still unclear. ESR and CRP are commonly used to evaluate the disease activity of TAK. It had also been reported that ESR and CRP can reflect the systemic inflammatory state of TAK patients [22]. A series of studies also showed that IL-6, IL-8, TNF- α . These cytokines are not only involved in the pathogenesis of TA, but also related to disease activity [17]. In the baseline data of TAK patients, we found that ESR, CRP and IL-6 were significantly increased in anemia patients with TAK. But these serum indexes including ESR, CRP and IL-6 are lack of specificity, especially ESR, which is often affected by hemoglobin. For lack of specific biomarkers, NIH score and ITAS score seem to be helpful in assessing disease activity and vascular damage in TAK [23]. We also found that NIH score and ITAS score were higher in anemia patients with TAK. Meanwhile, we analyzed the risk factors of anemia in TAK, and found that the risk of anemia in TAK patients with elevated CRP was higher, while the risk of anemia in older TAK patients was lower. As mentioned above, age may be negatively correlated with disease activity. The older the age, the lower the disease activity. We inferred that anemia was closely related to disease activity of TAK.

Glucocorticoids and immunosuppressants are the basis of drug therapy in TAK patients. For the treatment of anemia in TAK patients, previous studies have shown that iron supplementation can improve the condition[10]. So we wanted to explore whether anemia could be improved by just controlling the disease activity of TAK. Therefore, we followed up 28 anemia patients without iron supplementation in TAK, we found that anemia could be improved without iron supplementation.

Limitation

The main limitation of this paper is that it is a retrospective study; In addition, there was lack of indicators related to iron metabolism.

Conclusion

In this study, we found that hemoglobin levels may be associated with disease activity. By controlling the inflammation of TAK itself, anemia can be effectively controlled without iron supplement.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of Beijing Anzhen Hospital Affiliated to Capital Medical University[2021070X]. Written informed consent was waived because of the retrospective chart review design of this study.

Consent for publication

Not applicable

Availability of data and materials

The datasets use and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The present study was supported by grants from National Natural Science Foundation of China (81900448).

Authors' contributions

YG conceived the study, performed the statistical analysis, and drafted the manuscript. JD,TL, KZ and NG collected data and revised the manuscript. LP guided the design of this study and modified the paper. There are no conflicts of interest to declare.

Acknowledgements

None.

Authors' information

^a Yanqiu Guo, MM, Department of Rheumatology, Capital Medical University Affiliated Anzhen Hospital, 2 Anzhen Road, Chaoyang District, Beijing, China

^a Juan Du, MB, Department of Rheumatology, Capital Medical University Affiliated Anzhen Hospital, 2 Anzhen Road, Chaoyang District, Beijing, China

^a Taotao Li, MD, Department of Rheumatology, Capital Medical University Affiliated Anzhen Hospital, 2 Anzhen Road, Chaoyang District, Beijing, China

^b Keyang Zheng, MD, Department of hypertension, Capital Medical University Affiliated Anzhen Hospital, 2 Anzhen Road, Chaoyang District, Beijing, China

^a Na Gao, MD, Department of Rheumatology, Capital Medical University Affiliated Anzhen Hospital, 2 Anzhen Road, Chaoyang District, Beijing, China

^a Lili Pan, MD, Department of Rheumatology, Capital Medical University Affiliated Anzhen Hospital, 2 Anzhen Road, Chaoyang District, Beijing, China

References

1. Masson C. Rheumatoid anemia. *Joint Bone Spine*. 2011;78(2):131–7.
2. Wolfe F, Michaud K. Anemia and renal function in patients with rheumatoid arthritis. *J Rheumatol*. 2006;33(8):1516–22.
3. Furst DE, Chang H, Greenberg JD, Ranganath VK, Reed G, Ozturk ZE, Kremer JM. Prevalence of low hemoglobin levels and associations with other disease parameters in rheumatoid arthritis patients: evidence from the CORRONA registry. *Clin Exp Rheumatol*. 2009;27(4):560–6.
4. Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY, Lie JT, Lightfoot RW, Jr. et al: **The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis**. *Arthritis Rheum* 1990, **33**(8):1129–1134.
5. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M, Hoffman GS. Takayasu arteritis. *Ann Intern Med*. 1994;120(11):919–29.

6. Misra R, Danda D, Rajappa SM, Ghosh A, Gupta R, Mahendranath KM, Jeyaseelan L, Lawrence A, Bacon PA, Indian Rheumatology Vasculitis g: **Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010)**. *Rheumatology (Oxford)* 2013, **52**(10):1795–1801.
7. **Nutritional anaemias. Report of a WHO scientific group**. *World Health Organ Tech Rep Ser* 1968, 405:5–37.
8. Hellmich B, Agueda A, Monti S, Buttgerit F, de Boysson H, Brouwer E, Cassie R, Cid MC, Dasgupta B, Dejaco C, et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis*. 2020;79(1):19–30.
9. Velo-Garcia A, Castro SG, Isenberg DA. The diagnosis and management of the haematologic manifestations of lupus. *J Autoimmun*. 2016;74:139–60.
10. Zhang Y, Zhang D, Qu Y, Fan P, Liu YX, Zhang HM, Song L, Ma WJ, Wu HY, Cai J, et al. Anemia in patients with Takayasu arteritis: prevalence, clinical features, and treatment. *J Geriatr Cardiol*. 2019;16(9):689–94.
11. Cappellini MD, Motta I: **Anemia in Clinical Practice-Definition and Classification: Does Hemoglobin Change With Aging?** *Semin Hematol* 2015, **52**(4):261–269.
12. Dammacco F, Cirulli A, Simeone A, Leone P, Pulli R, Angiletta D, Rubini G, Di Palo A, Vacca A, Dammacco R. Takayasu arteritis: a cohort of Italian patients and recent pathogenetic and therapeutic advances. *Clin Exp Med*. 2021;21(1):49–62.
13. Clemente G, Hilario MO, Lederman H, Silva CA, Sallum AM, Campos LM, Sacchetti S, dos Santos MC, Ferriani VP, Sztajn bok F, et al. Takayasu arteritis in a Brazilian multicenter study: children with a longer diagnosis delay than adolescents. *Clin Exp Rheumatol*. 2014;32(3 Suppl 82):128–33.
14. Liu Q, Dang AM, Chen BW, Lv NQ, Wang X, Zheng DY. The association of red blood cell distribution width with anemia and inflammation in patients with Takayasu arteritis. *Clin Chim Acta*. 2015;438:205–9.
15. Arnaud L, Kahn JE, Girszyn N, Piette AM, Bletty O. Takayasu's arteritis: An update on physiopathology. *Eur J Intern Med*. 2006;17(4):241–6.
16. Arnaud L, Haroche J, Mathian A, Gorochoy G, Amoura Z. Pathogenesis of Takayasu's arteritis: a 2011 update. *Autoimmun Rev*. 2011;11(1):61–7.
17. Park MC, Lee SW, Park YB, Lee SK. Serum cytokine profiles and their correlations with disease activity in Takayasu's arteritis. *Rheumatology*. 2006;45(5):545–8.
18. Weiss G. Anemia of Chronic Disorders: New Diagnostic Tools and New Treatment Strategies. *Semin Hematol*. 2015;52(4):313–20.
19. Demirag MD, Haznedaroglu S, Sancak B, Konca C, Gulbahar O, Ozturk MA, Goker B. Circulating hepcidin in the crossroads of anemia and inflammation associated with rheumatoid arthritis. *Intern Med*. 2009;48(6):421–6.
20. Chen R, Ma L, Lv P, Lin J, Li C, Yan Y, Jin X, Dai X, Ji Z, Chen H, et al. Serum complement 3 is a potential biomarker for assessing disease activity in Takayasu arteritis. *Arthritis Res Ther*. 2021;23(1):63.

21. Myers KC, Sauter S, Zhang X, Bleesing JJ, Davies SM, Wells SI, Mehta PA, Kumar A, Marmer D, Marsh R, et al: **Impaired immune function in children and adults with Fanconi anemia.** *Pediatr Blood Cancer* 2017, 64(11).
22. Keser G, Aksu K, Direskeneli H. Discrepancies between vascular and systemic inflammation in large vessel vasculitis: an important problem revisited. *Rheumatology*. 2018;57(5):784–90.
23. Direskeneli H, Aydin SZ, Merkel PA. Assessment of disease activity and progression in Takayasu's arteritis. *Clin Exp Rheumatol*. 2011;29(1 Suppl 64):86–91.

Tables

Table 1 Comparison of general laboratory parameters between 160 TAK patients and 110 healthy controls

	TAK n=160	Healthy controls n=110	P value
female, %	141, 88.13%	93, 84.55%	0.395
age year	37.84±12.36	40.59±10.33	0.051
WBC (×10 ⁹ /L)	6.94±5.68±8.67	5.64±4.66±6.56	0.000*
RBC (×10 ¹² /L)	4.32±4.11±4.73	4.47±4.26±4.80	0.007*
HGB (g/L)	122.50±112.25±134.00	134.50±128.00±143.00	0.000*
MCV (fL)	84.65±79.93±89.43	87.55±85.38±89.53	0.000*
MCH (pg)	28.50±26.20±30.50	30.10±29.00±30.60	0.000*
MCHC (g/L)	334.00±323.00±342.75	342.00±336.00±347.00	0.000*
PLT (×10 ⁹ /L)	256.00±201.00±309.00	231.00±209.00±264.25	0.033*
TP (g/L)	68.50±65.10±74.10	70.90±68.50±72.90	0.046*
Alb (g/L)	41.10±38.20±43.20	44.10±43.05±45.75	0.000*
TB (umol/L)	10.30±8.00±12.60	12.60±10.50±15.30	0.000*
DB (umol/L)	2.14±1.57±3.15	2.66±2.04±3.15	0.002*

Note: WBC white blood cell; RBC red blood cell; MCV mean cell volume; MCH mean cell hemoglobin; MCHC mean cell hemoglobin concentration; PLT platelet; TP total protein; Alb albumin; TB total bilirubin; DB direct bilirubin.

Table 2 Type of 67 anemia patients in 160 TAK patients

Anemia (n=67)						
Classification of basis	Cell morphology			Hemoglobin level		
type	normocytic anemia	microcytic anemia	macrocytic anemia	mild anemia	moderate anemia	severe anemia
number	38	29	0	60	7	0

Table 3 Comparison of demographic data and general information between TAK patients with and without anemia

	TAK with anemia n=67	TAK without anemia n=93	P value
female %	64 95.52%	77 82.80%	0.014*
age at admission year	32 24 45	40 31 48	0.002*
age of onset year	25 (20,36)	29 (23,39)	0.092
disease duration month	36 7 120	72 14 162	0.017*
BMI kg/m ²	21.43 18.96 23.81	22.86 20.09 25.81	0.008*
WBC (×10 ⁹ /L)	6.93 5.40 8.29	6.95 5.89 9.19	0.296
RBC (×10 ¹² /L)	4.12 3.80 4.36	4.56 4.27 4.87	0.000*
MCV (fL)	80.60 76.10 85.80	87.5 82.35 91.30	0.000*
MCH (pg)	26.02 ± 3.65	29.41 ± 2.22	0.000*
MCHC (g/L)	321.38 ± 16.30	338.99 ± 10.56	0.000*
PLT (×10 ⁹ /L)	263.00 (206.00, 343.00)	251.00 (197.00, 299.00)	0.114
ESR (mm/1h)	23.00 (15.00, 51.00)	11.00 (5.50, 22.00)	0.000*
CRP (mg/L)	9.33 1.99 27.80	1.99 0.45 6.68	0.000*
IgG (g/L)	12.98 9.26 16.67	11.51 9.52 13.94	0.190
IgA (g/L)	2.37 1.65 3.16	2.19 1.76 2.98	0.667
IgM (g/L)	1.35 0.94 1.99	1.15 0.81 1.53	0.008*
C3 (g/L)	1.17 1.03 1.34	1.09 0.95 1.28	0.178
C4 (g/L)	0.22 0.16 0.25	0.21 0.17 0.28	0.928
IL-6 (pg/ml)	6.80 3.60 16.68	4.45 2.50 10.53	0.036*
TNF-α (pg/ml)	22.25 7.21 62.50	17.10 6.70 50.90	0.516
NIH	3.00 (2.00, 3.00)	2.00 (2.00, 3.00)	0.000*
ITAS-A	9.00 (6.00, 13.00)	6.00 (3.00, 10.00)	0.001*
ITAS-2010	7.00 (4.00, 9.50)	5.00 (3.00, 8.00)	0.030*

Note: BMI body mass index; WBC white blood cell; RBC red blood cell; MCV mean cell volume; MCH mean cell hemoglobin; MCHC mean cell hemoglobin concentration; PLT platelet; ESR erythrocyte sedimentation rate; CRP C-reactive protein; NIH the National Institute of Health; ITAS The Indian Takayasu Clinical Activity Score.

Table 4 Multivariable logistic regression analysis to predict risk factors for anemia with TAK

variable	OR	95%CI	P value
CRP	2.350	1.055~5.234	0.037
age	0.957	0.924~0.991	0.014

OR: odds ratio; CI: 95% confidence limits

Table 5 Baseline of 28 anemia patients with TAK

	28 anemia patients with TA
Female/male	26/2
Age (year)	37.36
Follow-up duration (month)	5.61
Duration (month)	92.63
Pred (n,%)	21,75.00%
CTX (n,%)	11,39.29%
MTX (n,%)	11,39.29%
TCZ (n,%)	14,50%
MMF (n,%)	4,14.29%
LEF (n,%)	2,7.14%
HCQ (n,%)	2,7.14%

Note: Pred: Prednisone; CTX: Cytoxan; MTX: Methotrexate; TCZ: Tocilizumab; MMF: Mycophenolate Mofetil; LEF: Leflunomide; HCQ: Hydroxychloroquine.

Figures

Fig.1

Figure 1

The relationship between hemoglobin and TAK disease activity. a. The distribution of HGB in different levels of NIH score. b. The mean value of HGB in different subgroups based on the cut-off value (NIH score≤ESR≤CRP).

Fig. 2

Figure 2

Follow up of 28 anemia patients with TA without iron supplementation. After treatment, HGB was significantly increased, ESR, CRP, NIH, ITASA, and ITAS2010 were significantly decreased.

Fig.3

A

B

Figure 3

The relationship between the changes of HGB and ESR, CRP after treatment . a. The change of HGB was significantly negative correlated with the change of ESR after treatment. b. The change of HGB was significantly negative correlated with the change of CRP after treatment.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementarytable1.docx](#)