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Lymphocyte levels in Crohn's disease patients in clinical remission are significantly lower than those in healthy people

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Abstract

Background and purpose Inflammatory bowel disease (IBD) is a chronic, non-specific inflammatory bowel disease caused by multiple causes. Lymphocytes migration is involved in the pathogenesis of IBD. The purpose of this study was to evaluate whether there were differences in blood lymphocytes levels between IBD patients in clinical remission and healthy people.

Patients and methods A total of 94 Crohn's disease (CD) and 20 ulcerative colitis (UC) patients were included in this study. Ninety-four people who underwent physical examination in our hospital were randomly selected as controls. We analyzed whether there were differences in white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count, lymphocyte percentage between CD patients, UC patients, and healthy people.

Results There were significant differences in lymphocyte count ($P<0.001$), lymphocyte percentage ($P<0.001$), neutrophil count ($P=0.038$), and neutrophil percentage ($P<0.001$) between CD patients and normal people, but no statistically significant differences in sex ($P=0.216$), age ($P=0.745$), and white blood cell count ($P=0.757$). UC patients had significant differences in white blood cell count ($P=0.005$), lymphocyte count ($P=0.010$), and neutrophil count ($P=0.023$), but no difference in lymphocyte percentage ($P=0.968$) and neutrophil percentage ($P=0.461$).

Conclusions The white blood cell count of CD patients was not significantly different from that of normal people, but the lymphocyte count and lymphocyte percentage were significantly different from that of healthy people. Similar results were not found in UC patients.

Keywords Crohn's disease, Lymphocyte migration, Lymphocyte count, Lymphocyte percentage

Introduction

Inflammatory bowel disease (IBD) is a chronic, non-specific inflammatory bowel disease that includes Crohn's disease (CD) and ulcerative colitis (UC). The pathogenesis of IBD is still unknown and is thought to be caused by a combination of susceptibility genes, environmental factors, an excessive immune response, and intestinal microbiome disturbances [1–4]. In recent years, the incidence of IBD has been on the rise.

CD frequently occurs in young people. Based on Chinese statistics, the age of peak incidence is between 18 and 35 years old, with a slightly higher prevalence in males than in females (the male/female ratio is approximately 1.5:1). [5]. The clinical manifestations were varied, including gastrointestinal manifestations, systemic manifestations, parenteral manifestations (such as arthritis, primary sclerosing cholangitis, and scleritis), and complications. Gastrointestinal manifestations mainly include diarrhea and abdominal pain, may have bloody stool.

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Weight reduction, fever, loss of appetite, fatigue, anemia, and other symptoms were the main systemic manifestations. Meanwhile, the common complications consisted of fistula, abdominal abscess, stenosis of the intestinal lumen, intestinal obstruction, and perianal lesions (including perianal abscess, perianal fistula, skin superfluity, and anal fissure). UC most often occurs in young adults. According to Chinese statistics, the peak age of onset is 20–49 years old, and the gender difference is not obvious [6, 7]. The clinical manifestations are persistent or recurrent diarrhea, mucous, pus and blood stools with abdominal pain, and tenesmus with different degrees of systemic symptoms, and the course of the disease is more than 4 to 6 weeks.

Crohn's disease activity index (CDAI) was used to assess the severity of disease activity and evaluate the efficacy. The CDAI calculation method of Best et al. is widely used in clinical and scientific research [8]. Modified Mayo score is commonly used to assess disease activity in UC [9]. Laboratory tests such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and fecal calcarein are also commonly used to assess disease activity for CD and UC. Mucosal healing (MH) is an objective indicator of drug efficacy of CD, and MH is associated with the reduction of clinical recurrence rate [10]. Given that the intestinal tissue of IBD patients harbors a significant infiltration of chronic inflammatory cells, including lymphocytes and plasma cells [11], a question arises: do the blood lymphocyte levels of CD and UC patients in clinical remission vary from those of healthy individuals? Thus, this study aimed to assess the disparities in blood lymphocyte levels between CD and UC patients in clinical remission and healthy people.

Methods

Ethical considerations

This research was performed according to the Declaration of Helsinki including patients' consent. This study was approved by the local Ethics Committee.

Patients and study design

In this prospective study, a total of 94 CD patients and 20 UC patients were evaluated (March 2024–May 2024) in the Department of Gastroenterology of the First Affiliated Hospital of Wannan Medical College. The IBD diagnosis was made in accordance with the European Crohn's and Colitis Organisation (ECCO) guidelines [11, 12]. Of the 94 patients with CD, 67 patients were male and 27 patients were female. Of the 20 UC patients, 10 patients were women and 10 patients were men. The inclusion criteria were as follows: (1) patients who meet the diagnostic criteria for IBD, and were admitted to the hospital for treatment with biological agent; (2) IBD patients in clinical remission. The exclusion criteria were as follows: (1) IBD patients with infection, or tumor, or blood system diseases, (2) IBD patients who refused blood tests, (3) IBD patients using steroids, azathioprine, and other drugs that affect white blood cells and lymphocytes. Gender and age were recorded in the 94 CD patients and 20 UC patients when they were first admitted to hospital. On the second day of hospitalization, blood was drawn to check white blood cells, neutrophil count, neutrophil percentage, lymphocyte count, and lymphocyte percentage. CDAI < 150 indicates clinical remission of CD patients [8]. The modified Mayo score ≤ 2 and no single sub-score > 1 were classified as clinical remission of UC patients [9].

To investigate differences in white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count, lymphocyte percentage between IBD patients, and healthy people, 94 patients who underwent physical examination in our hospital from March 2024 to May 2024 were randomly selected and their age, sex, and white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count, and lymphocyte percentage were recorded.

Firstly, the differences in white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count, and lymphocyte percentage were compared between CD patients and healthy people. Then 20 of the 94 normal subjects were randomly selected to compare the difference in white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count, and lymphocyte percentage with UC patients. Finally, the difference of above parameters between CD patients and UC patients was compared.

Statistical analysis

Descriptive data are expressed in terms of median (interquartile) or percentage. All numerical variables were tested for normal distribution. Mann–Whitney *U* test was used for non-parametric tests, and Chi-square test or Fisher's exact test was used for categorical variables. SPSS 21.0 software was used for statistical analysis. A *P*-value < 0.05 indicated statistical significance.

Results

Lymphocyte levels in CD patients group were significantly lower than those in control group

To investigate differences in white blood cell count, neutrophil count, neutrophil percentage, lymphocyte count, and lymphocyte percentage between CD patients and normal people, a random sample of 94 healthy patients who underwent physical examination in our hospital from March 2024 to May 2024 served as a control group. The two groups showed no

statistically significant differences in sex ($P=0.216$), age ($P=0.745$), and white blood cell count ($P=0.757$). Nevertheless, there were significant differences in lymphocyte count ($P<0.001$), lymphocyte percentage ($P<0.001$), neutrophil count ($P=0.038$), and neutrophil percentage ($P<0.001$). Moreover, the lymphocyte count and percentage in the CD patients group were significantly lower than those in the control group. (Table 1).

Analysis of the differences of above parameters between UC group and control group

A total of 20 UC patients were included in this study. So 20 of the 94 normal subjects were randomly selected as control group to compare the difference. There were no statistically significant differences regarding sex ($P=0.752$), age ($P=0.947$), lymphocyte percentage ($P=0.968$), and neutrophil percentage ($P=0.461$) when comparing the two groups. In contrast, significant differences were observed in white blood cell count ($P=0.005$), lymphocyte count ($P=0.010$), and neutrophil count ($P=0.023$). Overall, the cell counts differed significantly between the two groups, but the cell percentages did not (Table 1).

Analysis of the differences between CD group and UC group

There were no statistically significant differences in sex ($P=0.065$), lymphocyte percentage ($P=0.226$), and neutrophil count ($P=0.239$) between the two groups. There were significant differences in age ($P=0.009$), white blood cell count ($P=0.023$), lymphocyte count ($P=0.002$), and neutrophil percentage ($P=0.040$) between the two groups (Table 2).

Discussion

IBD is a group of chronic inflammatory bowel diseases that are caused by genetic, environmental, immune, microbial, and other factors. Current research suggests that lymphocytes travel to the intestine is involved in the pathogenesis of IBD. The chemokines secreted by various organs in the body bind to the chemokine receptors expressed by lymphocytes, thereby facilitating the binding of the surface homing receptors of lymphocytes to specific address hormones and subsequently completing the migration of lymphocytes to specific tissues and organs. Studies [13, 14] have shown that homing receptors involved in the migration of lymphocytes to the gut mainly include α4β7α4β1 and αLβ2 of the integrin family, and the corresponding address hormones MadCAM-1, VCAM-1, ICAM-1, etc. The main chemokines

Table 1 Analysis of the differences between CD group and control group, UC group and control group

	CD group *n* = 94	Control group *n* = 94	*P*	UC group *n* = 20	Control group *n* = 20	*P*
Sex: female, *n* (%)	27 (28.70%)	36 (38.20%)	0.216	10 (50.00%)	11 (57.80%)	0.752
Age (years):M (QR)	31.00 (23.00–43.50)	31.50 (22.00–48.25)	0.745	48.50 (34.50–55.50)	49.00 (35.50–53.00)	0.947
White blood cell: M (QR), $\times 10^9$/L	6.50 (4.90–7.10)	5.90 (5.20–7.03)	0.757	7.05 (5.85–8.87)	5.75 (4.90–6.28)	0.005
Lymphocyte count: M (QR), $\times 10^9$/L	1.80 (1.40–2.80)	2.10 (1.78–2.50)	< 0.001	2.30 (1.90–2.98)	1.75 (1.60–2.10)	0.010
Lymphocyte percentage: %	29.35 (23.10–36.95)	34.75 (31.10–39.55)	< 0.001	32.70 (28.05–38.43)	31.50 (28.70–35.80)	0.968
Neutrophil count: M (QR), $\times 10^9$/L	3.70 (2.80–4.63)	3.40 (2.70–4.10)	0.038	4.30 (3.03–5.10)	3.15 (2.55–3.93)	0.023
Neutrophil percentage: %	61.40 (53.75–68.35)	55.70 (51.33–59.43)	< 0.001	56.20 (50.50–61.65)	59.00 (52.20–61.08)	0.461

M median, *QR* quartile range, *CD* Crohn's disease, *UC* ulcerative colitis

Table 2 Analysis of the differences between CD group and UC group

	CD group *n* = 94 (IFX/Vedolizumab:83/11)	UC group *n* = 20 (IFX/Vedolizumab:11/9)	*P*
Sex: female, *n* (%)	27 (28.70%)	10 (50.00%)	0.065
Age (years):M (QR)	31.00 (23.00–43.50)	48.50 (34.50–55.50)	0.009
White blood cell: M(QR), $\times 10^9$/L	6.50(4.90–7.10)	7.05(5.85–8.87)	0.023
Lymphocyte count: M (QR), $\times 10^9$/L	1.80 (1.40–2.80)	2.30 (1.90–2.98)	0.002
Lymphocyte percentage: %	29.35 (23.10–36.95)	32.70 (28.05–38.43)	0.226
Neutrophil count: M (QR), $\times 10^9$/L	3.70 (2.80–4.63)	4.30 (3.03–5.10)	0.239
Neutrophil percentage: %	61.40 (53.75–68.35)	56.20 (50.50–61.65)	0.040

M median, *QR* Quartile range, *CD* Crohn's disease, *UC* Ulcerative colitis, *IFX* Infliximab

involved in the migration of lymphocytes to the gut are CCL25 and CXCL10, whose receptors are CCR9 and CXCR3, respectively. A study by Habtezion et al. [15] indicates that MadCAM-1 molecule is considerably upregulated in the intestinal tract of patients with active IBD. This alteration can facilitate the migration of circulating α4β7 + T lymphocytes to the intestinal tract, thus worsening chronic intestinal inflammation. Only 1% of lymphocytes in human peripheral blood expressed integrin αEβ7, but transforming growth factor-beta (TGF-β) could induce T lymphocytes to express integrin αEβ7 after lymphocytes homed to the intestine. Lymphocytes expressing integrin αEβ7 colonize the intestinal epithelium in the form of IELs, which may be involved in the persistence of inflammation [16].

Because of the migration of lymphocytes from the blood to the intestinal tissue in IBD patients, will the number and percentage of lymphocytes in the blood be lower than those in healthy people? Therefore, 94 patients with CD in clinical remission and 20 patients with UC in clinical remission were included in this study. The results showed that although the total number of white blood cells in CD patients in clinical remission was not significantly different from that of healthy people, the lymphocyte count and percentage were significantly lower than those of healthy people. Due to the small number of UC patients in clinical remission, there were differences in white blood cell count and lymphocyte count between UC patients and healthy people, but no difference in lymphocyte percentage, thus rendering the results meaningless. Similarly, the results between CD patients and UC patients were not clinically significant.

The primary goal of early clinical treatment is to alleviate symptoms, but this cannot completely change the course of IBD. In clinical practice, it has been observed that some IBD patients with remitted clinical symptoms still exhibit mucosal damage and mucosal inflammation to varying degrees, and the persistent intestinal inflammatory response can further lead to irreversible changes in intestinal structure [17]. There is a growing consensus and clinical guidelines regarding MH as a new therapeutic target, and MH may improve IBD outcomes [18]. However, there are still varying degrees of inflammation in the intestinal mucosal tissues of MH patients, so a higher therapeutic goal is proposed on the basis of MH, that is deep remission (DR) [19]. The DR concept is that the activity of the disease is fully controlled at the clinical, biological, endoscopic, and histological levels [20–22]. Therefore, IBD patients who are in clinical remission may still have inflammation of the intestinal tissue. This is why the blood lymphocyte count and percentage of CD patients in clinical remission are lower than those of healthy people, which may be related to the existence of lymphocyte migration. Since the white blood cell count, lymphocyte count, and percentage of CD patients in this study were generally within the normal range, thus, it is highly likely that the significantly lower lymphocyte count and percentage compared to healthy individuals were not caused by therapeutic drugs.Due to the small number of patients enrolled in UC, similar results were not observed.

This study has certain limitations. First, this study only compared IBD patients in clinical remission, and did not include a comparison IBD patients in endoscopic remission. Secondly, since most of the hospitalized IBD patients in our hospital were in clinical remission, and few patients were in the active stage, there was no comparison of IBD patients in the active stage. Last, in this study, there were only 20 UC patients, the sample size was too small, and it was a single-center study. Therefore, it is hoped that further studies will be carried out in future and more patients will be included. Whether monitoring blood lymphocyte count and percentage can be used to determine whether CD patients are in deep remission and whether blocking lymphocyte migration can be utilized to treat CD patients remains to be explored in future.

In conclusion, the results of this study are hold great clinical significance. Even though CD patients are in clinical remission, their blood lymphocyte counts and percentages are lower than those of normal individuals. Due to the small sample size of UC patients, no similar results have been observed.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-025-02352-6.

Supplementary Material 1.

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None.

Author contributions

Asi He and Linzhen Li conceived and designed the paper and extracted data; Linzhen Li wrote the manuscript. Asi He and Tulan Hu analyzed the data and completed the tables.

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Availability of data and materials

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

The study protocol was in accordance with the Declaration of Helsinki Ethical Guidelines and this study was approved by the institutional review board of Wannan medical college (No.12, 2021). All participants give informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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