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ORIGINAL

EVALUATING INFECTION RISK FACTORS IN ATHLETES WITH ACUTE LYMPHOBLASTIC LEUKEMIA FOLLOWING CHEMOTHERAPY

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ABSTRACT

Objective: This study aims to investigate the risk factors associated with infections following chemotherapy in athletes diagnosed with adult acute lymphoblastic leukemia (ALL). **Methods:** We conducted a retrospective review of 215 adult ALL patients treated at our institution from January 2019 to January 2023. Patients were categorized into two groups: those who developed infections post-chemotherapy (n=135) and those who did not (n=80). Data collected included demographic details, treatment regimens, and common clinical indices such as white blood cells (WBC), neutrophils (NEU), platelets (PLT), hemoglobin (Hb), albumin (ALB), and D-dimer (DD) levels. Multivariate logistic regression was used to analyze the risk factors for post-chemotherapy infections. **Results:** The infection rate among the study cohort was 62.79%, with respiratory infections being predominant. There were no significant differences in gender, age, lifestyle factors, or seasonality between the two groups. Notably, body mass index values and the absence of community-acquired infections were significantly different in the infection group ($P<0.05$). Risk factors such as longer hospital stays, specific chemotherapy regimens, and critical hematological values (WBC <0.5 × 10^9/L, NEU ⩽0.1 × 10^9/L, PLT <30 × 10^9/L) were associated with higher infection rates. Protective factors included absence of community infections. **Conclusion:**

Infections remain a significant concern for athletes with ALL post-chemotherapy, particularly respiratory tract infections. Factors such as hospitalization duration, aggressive antibiotic usage, and critical decreases in hematological indices significantly contribute to infection risks. Understanding these risks is crucial for developing targeted strategies to prevent infections in this vulnerable population, ensuring safer chemotherapy outcomes and aiding in the overall management of athlete health during cancer treatment.

KEYWORDS: Adult; Acute lymphocytic leukemia; Chemotherapy; Infected; Risk factors

1. INTRODUCTION

Acute lymphoblastic leukemia (ALL) represents a significant medical challenge, particularly when compounded by the rigors of chemotherapy, which often leads to immunosuppression. This immunocompromised state exposes patients to a heightened risk of infections, a major cause of morbidity and mortality in this population. Understanding the risk factors associated with infection following chemotherapy is crucial for improving patient outcomes and guiding preventive care strategies. In athletes, the issue of managing ALL and its treatments takes on additional complexity. Athletes' bodies are subjected to extreme stresses, both from intense physical training and the demands of competition, which can complicate both the course of their leukemia treatment and their vulnerability to infection.

Moreover, the need to return to training and competition can pressure medical teams to balance effective treatment with the demands of maintaining peak physical condition(Brown et al., 2021; Shah et al., 2021). Identifying specific risk factors for infection in adult ALL patients after chemotherapy is essential for tailoring interventions that can mitigate these risks. Factors such as neutropenia (low white blood cell count), hospital stay duration, and specific treatment regimens are known contributors to infection risk. However, each patient's risk profile can vary significantly based on individual characteristics and treatment responses(Aamir et al., 2021; Roddie et al., 2021; Röst & Sadeghimanesh, 2023).

For athletes, the risk of infection also carries the potential for interrupted training and extended periods away from sport, which can have profound effects on career trajectory and psychological well-being. Thus, pinpointing the factors that contribute to infection in this specific population not only aids in clinical management but also supports the athlete’s overall career and life quality(Cook & Litzow, 2020; Qi et al., 2022). This study focuses on a retrospective analysis of 215 adults with ALL who underwent chemotherapy, comparing those who developed infections with those who did not. The aim is to explore correlations between clinical, demographic, and treatment-related

variables and the incidence of infections, thereby elucidating patterns that could inform more effective protective strategies in clinical practice(Radhakrishnan, Agrawal, Bagal, & Patel, 2021; Rüchel et al., 2022). By enhancing understanding of infection dynamics post-chemotherapy in athletes with ALL, this research aims to contribute to better health management protocols, tailored to the needs of this unique population. The insights gained could lead to improved strategies for infection prevention and management, ultimately enhancing treatment outcomes and quality of life for athletes facing this challenging cancer treatment (Ubillus, Neira-Montoya, Sedano-Gelvet, & Verona-Cueva, 2022).

2. Data and methods

2.1 General data

The clinical data of 215 adults ALL patients admitted to our hospital from January 2019 to January 2023 were retrospectively selected as the observation objects.

Inclusion criteria: ① The patients who were diagnosed as ALL according to cytogenetics, molecular biology and bone marrow cell morphology; ② The patients who were older than 18 years old; ③ All patients were treated with chemotherapy in our hospital, and all had more than one therapeutic effect; ④ The patients and their family members were informed, had good compliance, could cooperate with the examination and treatment, and signed the informed consent form.

Exclusion criteria: ① The patients with severe dysfunction of important organs; ② The patients were combined with other malignant tumors; ③ The patients were combined with bone marrow transplantation; ④ Transformation from chronic leukemia; ⑤ Women who were lactating or pregnant. According to the presence of infection, the patients were divided into infection group (n=135) and non-infection group (n=80). This experimental operation was approved by the hospital ethics committee.

2.2 Methods

Clinical data: the general data (gender, age, smoking, drinking, hypertension, diabetes, infection season, community infection, BMI value), pathological data (stimulators, length of stay, degree of bone marrow hyperplasia), treatment methods (immunosuppressants, stress application, chemotherapy cycle, chemotherapy stage, antibiotic application) and other data of the two groups of patients were collected.

Laboratory indicators: the fasting venous blood of the two groups of patients was collected, centrifuged for 10 min at 3000 r/min, the serum was

carefully collected, and stored it at - 40 ℃ at low temperature to avoid repeated freezing and thawing. The levels of white blood cells (WBC), neutrophils (NEU), platelets (PLT) and lymphocytes were detected by automatic blood cell analyzer. The levels of hemoglobin (Hb), albumin (ALB) and D-dimer (DD) of patients were detected by automatic biochemical analyzer.

2.3 Observation Indicators

(1) The general data, pathological data and treatment methods of patients in the two groups were compared. (2) The serum WBC, Hb, ALB, NEU, PLT, lymphocyte and DD levels of patients were compared between the two groups. (3) Multivariate logistic regression was used to analyze the risk factors of infection in adult ALL patients after chemotherapy.

2.4 Statistical Methods

SPSS20.0 software was used to analyze the experimental data in this study. The sex, hormone use, antibiotic use and the degree of bone marrow hyperplasia and other count data were expressed in (%), and χ^2 test was used. The statistical results of $P<0.05$ were indicated that the difference was statistically significant.

3. Results

3.1 Analysis of infection sites in acute lymphoblastic leukemia after chemotherapy

Of the 215 patients in this experiment, 135 patients were infected after chemotherapy, with the infection rate of 62.79%. Among the infected patients, lower respiratory tract infection and upper respiratory tract infection accounted for a relatively high proportion, with 42.22% and 35.56%, respectively. See Table 1 and Figure 1.

Table 1: Analysis of infection sites in acute lymphoblastic leukemia after chemotherapy (n, %)

POSITION	INFECTIONS	PROPORTION
LOWER RESPIRATORY TRACT INFECTION	57	42.22%
UPPER RESPIRATORY TRACT INFECTION	48	35.56%
PERIANAL INFECTION	9	6.67%
URINARY TRACT INFECTION	10	7.41%
SKIN INFECTION	4	2.96%
BLOOD INFECTION	4	2.96%
INTESTINAL INFECTION	3	2.22%
TOTAL	135	100%

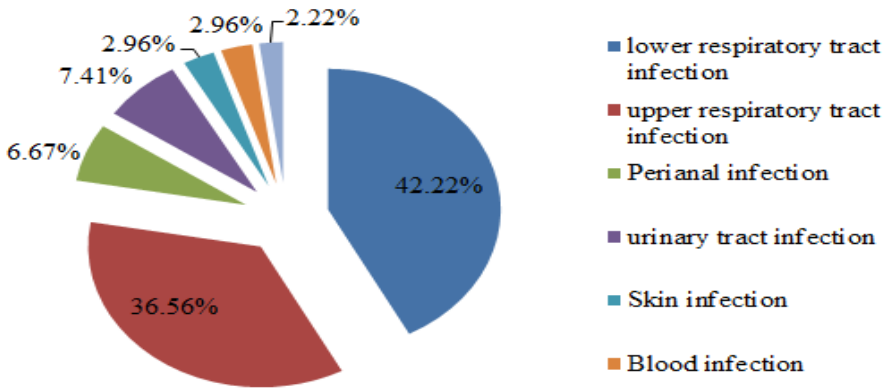

Figure 1: Analysis of infection sites in acute lymphoblastic leukemia after chemotherapy

3.2 Comparison of general data of two groups of patients

The difference in gender, age, smoking, drinking, hypertension, diabetes and infection season between the two groups was not statistically significant (P>0.05); the BMI value (18.51-24.99) kg/m^2 and the proportion of patients without community infection in the infected group were significantly higher than those in the non-infected group, and the difference was statistically significant (P<0.05). See Table 2.

Table 2 (a): Comparison of general data of two groups of patients (cases, %)

INDEX		INFECTION GROUP (N=135)	NON-INFECTION GROUP (N=80)	X^2	P
GENDER	Male	62（45.93）	31（38.75）	1.054	0.305
	Female	73（54.07）	49（61.25）		
AGE	18-40 years old	48（35.56）	39（48.75）	4.543	0.103
	41-60 years old	56（41.48）	30（37.50）		
	61-84 years old	31（22.96）	11（13.76）		

Table 2 (b): Comparison of general data of two groups of patients (cases, %)

INDEX		INFECTION GROUP (N=135)	NON-INFECTION GROUP (N=80)	X^2	*P*
BMI VALUE	15.63-18.50	15（11.11）	16（20.00）	7.614	0.022
	18.51-24.99	57（42.22）	20（25.00）		
	25.00-36.73	63（46.67）	44（55.00）		
SMOKING	Have	38（28.15）	26（32.50）	0.455	0.500
	Nothing	97（71.85）	54（67.50）		
DRINKING	Have	36（26.67）	23（28.75）	0.110	0.741
	Nothing	99（73.33）	57（71.25）		
HYPERTENSION	Have	25（18.52）	17（21.25）	0.238	0.625
	Nothing	110（81.48）	63（78.75）		
DIABETES	Have	31（22.96）	23（28.75）	0.894	0.344
	Nothing	104（77.04）	57（71.25）		
INFECTION SEASON	Spring	29（21.48）	23（28.75）	2.703	0.440
	Summer	30（22.22）	19（23.75）		
	Autumn	43（31.85）	18（22.50）		
	Winter	33（24.44）	20（25.00）		
COMMUNITY INFECTION	Have	52（38.52）	44（55.00）	5.521	0.019
	Nothing	83（61.48）	36（45.00）		

3.3 Comparison of pathology and treatment of two groups of patients

The difference in stimulating factors of patients between the two groups was not statistically significant ($P>0.05$); the proportions of patients without immunosuppressive agents, length of stay (31-75 days), hormone application, chemotherapy cycle (1-3), chemotherapy stage (induced remission stage), antibiotic application and myeloproliferative degree (proliferative active stage) in the infected group were significantly higher than those in the non-infected group, and the difference was statistically significant ($P<0.05$). See Table 3.

Table 3: Comparison of pathology and treatment of patients between the two groups (cases, %)

INDEX		INFECTION GROUP (N=135)	NON-INFECTION GROUP (N=80)	X^2	*P*
IMMUNOMODULATOR	Have	43（31.85）	57（71.25）	31.341	＜0.001
	Nothing	92（68.15）	23（28.75）		
LENGTH OF STAY	3-15 days	23（17.04）	30（37.50）	11.331	0.003
	16-30 days	44（32.59）	20（25.00）		
	31-75 days	68（50.37）	30（37.50）		
STIMULATING FACTOR	Have	72（53.33）	45（56.25）	0.172	0.678
	Nothing	63（46.67）	35（43.75）		
HORMONE APPLICATION	Have	23（17.04）	6（7.50）	3.915	0.048
	Nothing	112（82.96）	74（92.50）		
CHEMOTHERAPY CYCLE	1-3	114（84.44）	56（70.00）	6.333	0.012
	＞3	21（15.56）	24（30.00）		
CHEMOTHERAPY STAGE	Induced remission period	48（35.56）	15（18.75）	6.855	0.032
	Consolidation treatment period	57（42.22）	43（53.75）		
	Refractory recurrence period	30（22.22）	22（27.50）		
ANTIBIOTIC	Application	109（80.74）	48（60.00）	10.969	＜0.001
	Not applied	26（19.26）	32（40.00）		
DEGREE OF BONE MARROW HYPERPLASIA	Hyperplastic activity	99（73.33）	32（40.00）	26.427	＜0.001
	Hypoplasia	26（19.26）	26（32.50）		
	No bone puncture	10（7.41）	22（27.50）		

3.4 Comparison of laboratory indicators between two groups of patients

The proportions of WBC (<0.5 × 10^9/L）、Hb（30-60 g/L）、ALB（＜35g/L）、NEU（≤0.1 × 10^9/L）、PLT（＜30 × 10^9/L), lymphocytes (<0.8 × 10^9/L) and DD (＞ 0.55 μg/ml) of patients in infection group were significantly higher than those of non-infection group (*P*<0.05). See Table 4.

Table 4: Comparison of laboratory indicators between two groups of patients (cases, %)

INDEX		INFECTION GROUP (N=135)	NON-INFECTION GROUP (N=80)	X^2	P
WBC	＜0.5×10⁹/L	38（28.15）	10（12.50）	9.687	0.021
	0.5-1.0×10⁹/L	52（38.52）	46（57.50）		
	1-2×10⁹/L	29（21.48）	16（20.00）		
	≥2×10⁹/L	16（11.85）	8（10.00）		
HB	＜30 g/L	24（17.78）	8（10.00）	14.353	0.002
	30-60 g/L	52（38.52）	17（21.25）		
	60-90 g/L	39（28.89）	30（37.50）		
	≥90 g/L	20（14.81）	25（31.25）		
ALB	＜35g/L	94（69.63）	16（20.00）	49.518	＜0.001
	≥35g/L	41（30.37）	64（80.00）		
NEU	≤0.1×10⁹/L	76（56.30）	23（28.75）	15.343	＜0.001
	＞0.1×10⁹/L	59（43.70）	57（71.25）		
PLT	＜30×10⁹/L	78（57.78）	18（22.50）	25.296	＜0.001
	≥30×10⁹/L	57（42.22）	62（77.50）		
LYMPHOCYTE	＜0.8×10⁹/L	71（52.59）	26（32.50）	8.190	0.004
	＞3.5×10⁹/L	64（47.41）	54（67.50）		
DD	≤0.55 μ g/ml	26（19.26）	35（43.75）	14.826	＜0.001
	＞0.55 μ g/ml	109（80.74）	45（56.25）		

3.5 Multifactor analysis of infection after chemotherapy in acute lymphoblastic leukemia

The results of multivariate logistic regression analysis showed that the length of stay (31-75 days), antibiotic use, WBC<0.5 × 10⁹/L、NEU≤0.1 × 10⁹/L、PLT＜30 × 10⁹/L were the risk factors of infection in adult ALL patients after chemotherapy (*P*<0.05); community infection was the protective factor of infection in adult ALL patients after chemotherapy (*P*<0.05). See Table 5.

Table 5(a): Multi-factor analysis of infection after chemotherapy in acute lymphoblastic leukemia

INDEX	B	SE	WALD X^2 VALUE	P VALUE	OR VALUE	95%CI
BMI 18.51-24.99KG/M²	0.451	0.286	3.041	0.382	3.074	1.451-4.068
COMMUNITY INFECTION	-1.564	0.036	42.156	＜0.001	0.845	0.812-0.965
IMMUNOSUPPRESSANT	-2.078	0.415	5.164	0.052	0.816	0.795-0.942
HOSPITALIZATION DAYS (31-75 DAYS)	2.568	0.546	19.451	＜0.001	8.795	4.165-35.120

Table 5(b): Multi-factor analysis of infection after chemotherapy in acute lymphoblastic leukemia

INDEX	B	SE	WALD X^2 VALUE	P VALUE	OR VALUE	95%CI
HORMONE APPLICATION	1.254	0.216	3.069	0.302	2.154	1.784-3.066
CHEMOTHERAPY CYCLE (1-3)	1.325	0.216	2.498	0.412	3.015	2.095-4.115
CHEMOTHERAPY STAGE (INDUCED REMISSION STAGE)	1.845	0.185	3.102	0.382	4.052	2.151-6.231
APPLICATION OF ANTIBIOTICS	2.079	0.415	25.693	＜0.001	7.784	3.154-19.523
DEGREE OF BONE MARROW HYPERPLASIA (PROLIFERATIVE ACTIVE STAGE)	1.451	0.511	4.236	0.072	2.012	1.054-3.068
WBC＜0.5 × 10^9/L	0.495	0.125	21.561	＜0.001	1.854	1.326-3.458
HB30-60 G/L	0.854	0.326	4.085	0.085	2.794	2.155-4.008
ALB＜35G/L	0.381	0.401	3.157	0.166	2.846	1.147-3.018
NEU≤0.1 × 10^9/L	0.356	0.112	12.451	＜0.001	1.469	1.154-3.784
PLT＜30 × 10^9/L	0.489	0.104	21.568	＜0.001	1.645	1.325-6.451
LYMPHOCYTES ＜ 0.8 × 10^9/L	0.548	0.415	3.265	0.152	1.471	1.159-3.025
DD＞0.55 M G/ML	0.485	0.300	3.074	0.219	1.265	1.045-3.023

4. Discussion

ALL is a malignant tumor disease of the hematopoietic system caused by the malignant proliferation of lymphocytes in the early stage of differentiation in the body, which mainly occurs in children aged 1-4 years old and the elderly. With the increase of life pressure in recent years, the number of adult patients with ALL has gradually increased. Moreover, the statistics show that the prognosis of adult patients with ALL is relatively poor. Most patients die of infection and recurrence. The 5-year survival rate is only 30% - 45% (Benjamin et al., 2022; Colunga-Pedraza et al., 2022). Therefore, reducing the infection rate of adult ALL patients, improving the treatment effects and reducing the recurrence rate of ALL patients has become the focus of attention of medical

staffs in hematology department. Infection is a common complication and the main cause of death in ALL patients (Ribera et al., 2021; Zhang, Zhang, Wang, & Wang, 2022). Infection not only seriously affects the follow-up treatment and treatment effects of patients, endangers the life and health of patients, but also brings heavy medical and economic burden to families and society (Abdelmabood, Fouda, Boujettif, & Mansour, 2020; Aref et al., 2022). According to previous statistics, about 64% of ALL patients died of infection, especially those at the early stage of chemotherapy. According to the statistics of 215 patients in this experiment, 135 patients were infected after chemotherapy, with the infection rate of 62.79%, which is similar to the results of previous researches (Burke et al., 2020). At the same time, lower respiratory tract infection and upper respiratory tract infection accounted for 42.22% and 35.56% of the infected patients in this experiment, which may be related to the low immunity of ALL patients, the relatively poor ability to eliminate airway secretion, the use of drugs such as chemotherapy drugs and anti-biological drugs that damage the respiratory tract mucosal barrier to some extent, and other reasons. In addition, the Department of Hematology is a high incidence department of infection, and the pathogenic bacteria are more likely to enter the respiratory tract through droplet transmission to cause infection. Infection refers to the process of pathogenic microorganism or parasite invading human body and causing pathological reaction and damage to patients. When patients have one or some factors, the occurrence risk of infection will increase to a certain extent (Silva et al., 2022; Zhu et al., 2021). NEU is one of the human blood cells, mainly produced from bone marrow, and an important part of the human immune defense system, which can swallow and kill pathogens invading the human body (Los-Arcos et al., 2021; Mahmood, Abbas, Manzoor, Shahid, & Majeed, 2020). The function of human bone marrow will be inhibited to a certain extent, and the content of NEU in the blood will decrease during the chemotherapy stage. The decrease of NEU can lead to the decline of immunity, so the risk of infection will increase (Shahid et al., 2022; Singh et al., 2022). Oh, SM et al (Oh et al., 2021) showed that long-term NEU reduction is a risk factor for the occurrence of invasive fungal infection in ALL adults and children. Patients with NEU reduction should be screened early and given timely intervention to reduce the risk of invasive fungal infection. WBC is the general name of granulocyte, monocyte and lymphocyte. When the pathogen invades the body, WBC can gather in a large amount at the invasion site of the pathogen through deformation, and engulf the pathogen. In addition, some WBCs can also secrete cytokines such as interleukin and interferon, and regulate the inflammatory and immune responses of the body. The decrease of WBC level can increase the incidence of infection to a certain extent. Some studies have shown that bleeding can increase the risk of infection in patients (Azoulay et al., 2021; Ke et al., 2021). Bleeding will damage the skin and mucous membrane barrier of patients and increase the chance of pathogens invading the human body to cause infection, while the reduction of PLT level can increase the risk

of bleeding (Topp et al., 2021; Wang et al., 2021), so the reduction of PLT level can also increase the risk of infection. Previous studies have shown that there is a close relationship between the hospital infection rate and the length of stay of patients. The longer the length of stay of patients, the more invasive and nursing operations, the more contact with doctors, nurses and other patients, and the greater the probability of pathogenic bacteria invading the human body, so the higher the risk of infection (Hu et al., 2021; Nakagawa et al., 2021). With the abuse of antibiotics in recent years, some bacteria have developed drug resistance, the body's antibacterial ability has also declined, the body's normal flora has become disordered, and the incidence of infection is also difficult to control (Berger, Messina, Chandler, Amankwah, & Shaw, 2020; Bettelli et al., 2020). Multivariate logistic regression analysis was perfromed in this research, the results showed that the number of days in hospital (31-75 days), antibiotic use, WBC<0.5 × 10^9/L、NEU≤0.1 × 10^9/L、PLT＜30 ×10^9/L were the risk factors of infection in adult ALL patients after chemotherapy. Early screening of patients with high risk factors of infection and giving targeted preventive measures can help reduce the risk of infection, improve the treatment effects and improve the prognosis of patients. This experimental study also found that community infection was a protective factor for the infection of adult ALL patients after chemotherapy, which may be related to the improvement of immunity of patients with community infection to a certain extent. This study highlights the significant infection risks following chemotherapy in adults with acute lymphoblastic leukemia (ALL), particularly in athletes. Analyzing data from 215 patients revealed a high infection rate of 62.79%, predominantly respiratory infections. Key risk factors include prolonged hospital stays, specific chemotherapy protocols, and critical reductions in hematological indices such as white blood cells, neutrophils, and platelets. These insights underscore the need for tailored management strategies to mitigate infection risks and support recovery in athletes undergoing chemotherapy for ALL.

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