Research Article

Analysis of Multiple Vitamins Serum Levels and Disease-Related Factors in Children with Acute Leukemia

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Objective. To explore the relationship between vitamins levels and disease-related indicators in children with acute leukemia (AL).

Methods. A total of 107 hospitalized children with AL were enrolled in this study and assigned to one group in each of the following categories: infected group (n = 52) and noninfected group (n = 55); treatment remission group (n = 56) and nonremission group (n = 51); high-risk (HR) group (n = 44), intermediate risk (IR) group (n = 53), and slight risk (SR) group (n = 8); cyclophosphamide + cytosine arabinoside + 6-mercaptopurine + pegaspargase group (CAML, n = 15); methotrexate group (MTX, n = 9); and vindesine + daunomycin + L-asparaginase + prednisone (VALP, n = 38). Hematological and serological parameters, hepatic and renal function, and changes in vitamins A, B1, B2, B6, B9, B12, C, D, and E serum content in children with AL were analyzed to investigate their relationship with AL disease-related factors.

Results. The vitamin D level was significantly higher in the noninfected group than in the infected group (P < 0.05). Compared with the nonremission group, the level of vitamin B1 in the treatment remission group was significantly higher, while the levels of vitamin B6 and B12 were notably lower (P < 0.05). The levels of vitamins B6 and B12 were notably different among the treatment groups. Multivariate analysis showed that hemoglobin (Hb) and C-reactive protein (CRP) were predisposing factors of AL in children. The disease type (acute lymphoblastic leukemia/acute myelogenous leukemia) was the factor affecting remission in AL children. Abnormal kidney function and the occurrence of icterus were the influencing factors for the risk degree in AL children. Platelet (PLT) count, activated partial thromboplastin time (APTT), neutrophils (N), and immunophenotype were shown to affect the choice of therapeutic regimens. Conclusion. There are notable vitamins imbalances in children with AL. The imbalances influence disease-related factors and therefore provide some references for the prognosis and treatment of AL.

1. Introduction

Leukemia, a general term for malignant clonal disease of hematopoietic stem cells, is divided into myeloid and lymphoid according to cell types. Acute leukemia (AL) is the most common childhood hematological malignancy and is the leading cause of malignancy-related mortality in children [1]. Approximately 80% of children’s AL cases are acute lymphoblastic leukemia (ALL) and 17% are acute myelogenous leukemia (AML) [2]. While a variety of factors have been suggested to be etiologically involved in leukemia, the etiology of leukemia is still unclear. Vitamins are essential nutrients for the human metabolism. As coenzymes or enzymes, vitamins play an important role in many important physiological processes, which contribute to normal body functions. In addition, vitamins have been reported to have preventive and therapeutic effects on some cancers [3, 4]. In children with AL, malnutrition is a common complication of the diseases and chemotherapy. Consequently, the resultant vitamins deficiency has been reported to negatively influence treatment response and disease prognosis [5]. It is reported that vitamin supplementation, particularly carotenoids and glutathione, may play a protective role against AL [3]. AL-caused oxidative stress response leads to increased concentration of vitamin C (VC) in leukocytes [4–6]. However, there are only a few studies on...
the effects of serum vitamin content on the pathogenesis or treatment of AL in children. Therefore, this study investigated the relationship between the serum vitamin content and disease-related indicators in children with AL.

2. Subjects and Methods

2.1. Study Subjects and Grouping. A total of 107 hospitalized children with AL (from June 2018 to December 2020) were enrolled in this study. The children were divided into the infected group (n = 52) and noninfected group (n = 55), according to the presence of infection. Bone marrow examination was conducted to evaluate remission and residual disease, and according to the examination results, the children were divided into the treatment remission group (no residual disease, n = 56) and nonremission group (with residual disease, n = 51). According to clinical risks and treatment responses, the children were divided into the high-risk (HR) group (n = 44), intermediate risk (IR) group (n = 53), and slight risk (SR) group (n = 8). According to different therapeutic regimens, the children were divided into three groups: cyclophosphamide + cytosine arabinoside + 6-mercaptopurine + pegaspargase group (CAML, n = 15), methotrexate group (MTX, n = 9), and vindesine + daunomycin + L-asparaginase + prednisone (VALP, n = 38). Some other treatment groups (n = 45) were also set. The results in all the different groups were analyzed.

2.2. Methods. The fasting venous blood of all the study subjects was collected in the morning and stored at ambient temperatures for 1 h. Then, blood was centrifuged at 3000 rpm/min for 10 min. After that, serum was collected and stored in the fridge at –20°C. The serum vitamin content and blood-related disease indicators were determined using chemiluminescence with a vitamin detector (LK3000VI). Venous whole blood was collected for the routine blood analysis.

The disease-related indicators were as follows. (1) General information: age, body mass index (BMI), gender, diagnostic result type, immunophenotyping, abnormal liver and kidney function, and occurrence of icterus. (2) Biochemical indicators: alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LD), and hydroxybutyric dehydrogenase (HBDH). (3) Serological and hematological parameters: white blood count (WBC), neutrophils (N), lymphocyte (L), hemoglobin (Hb), platelet count (PLT), C-reactive protein (CRP), activated partial thromboplastin time (APTT), and troponin (Tn). (4) Vitamin (V) indicators: vitamin A (VA), VB1, VB2, VB6, VB9, VB12, VC, VD, and VE levels.

2.3. Statistical Methods. Statistical analysis was done using SPSS 21.0 software. Data were expressed as mean ± standard deviation (SD). If the data obeyed normal distribution and homogeneity of variance, the t-test or repeated measures analysis of variance was applied; otherwise, a nonparametric test was utilized. Multivariate analysis was performed using binary logistic regression. P < 0.05 was considered statistically significant.

3. Results

3.1. Analysis of Infection-Related Influencing Factors in Children with Acute Leukemia. The clinical general conditions of the children in infected and noninfected groups are shown in Table 1. There were no significant differences in age, BMI, gender, diagnostic result type, immunophenotyping, abnormal liver and kidney function, and occurrence of icterus between the two groups (P > 0.05). LD and HBDH blood levels were significantly higher in the infected group than in the noninfected group (P < 0.05). Among the serological and hematological disease indicators, WBC, L, and CRP were significantly higher, while Hb and PLT were significantly lower in the infected group than in the noninfected group (P < 0.05). For various serum vitamins level, only VD was significantly lower in the infected group than that in the noninfected group (P < 0.05). Furthermore, multivariate regression analysis (Table 2) showed that Hb and CRP might be AL predisposing factors in children.

3.2. Analysis of Remission-Related Influencing Factors in Children with Acute Leukemia. Based on the disease status, the children were divided into the treatment remission group and nonremission group. There were no significant differences in age, BMI, gender, abnormal renal function, and occurrence of icterus between the two groups (P > 0.05). However, there were statistically significant differences in the diagnostic results, immunophenotype, liver function, and infection incidence (P < 0.05). The level of LD in the treatment remission group was significantly lower than that in the nonremission group (P < 0.05). Among the serological and hematological disease indicators, the levels of Hb, PLT, APTT, and Tn were significantly higher, while the levels of WBC and L were significantly lower in the treatment remission group than in the nonremission group (P < 0.05). For the serum vitamin levels, there was a statistically significant difference (P < 0.05) in VB1, VB6, and VB12 levels between the two groups (Table 3). Furthermore, the results of multivariate regression analysis showed that the type of leukemia (ALL or AML) may be a factor affecting AL remission in children (Table 4).

3.3. Analysis of Factors Influencing Different Risk Degrees in Children with Acute Leukemia. There were no significant differences in age, BMI, gender, diagnostic results, immunophenotype, and abnormal liver function among the general conditions (Table 5) among the HR, IR, and SR groups (P > 0.05). However, there were statistically significant differences in the occurrence of renal function and icterus (P < 0.05). There was a statistically significant difference in PLT among the three groups (P < 0.05). There were no statistically significant differences in serological and hematological parameters and vitamins levels (P < 0.05). The results of the multivariate regression analysis confirmed that abnormal renal function and icterus incidence were the influencing factors for risk degree in children with AL (Table 6).
| Indicators                          | Infected group (n = 52) | Noninfected group (n = 55) | t/χ² | P value |
|-----------------------------------|-------------------------|-----------------------------|------|---------|
| Age                               | 7.54 ± 8.83             | 8.96 ± 16.95                | 0.901| 0.370   |
| BMI                               | 16.88 ± 2.89            | 16.15 ± 2.76                | 1.335| 0.100   |
| Gender                            |                         |                             |      |         |
| Male                              | 31 (59.6)               | 30 (54.5)                   | 0.280| 0.596   |
| Female                            | 21 (40.4)               | 25 (45.5)                   |      |         |
| Diagnostic results                |                         |                             |      |         |
| ALL                               | 42 (80.8)               | 42 (76.4)                   | 0.307| 0.579   |
| AML                               | 10 (19.2)               | 13 (23.6)                   |      |         |
| AML                               | 9 (17.3)                | 13 (23.6)                   |      |         |
| Immunophenotype                   |                         |                             |      |         |
| B                                 | 38 (73.1)               | 38 (69.1)                   | 3.028| 0.220   |
| T                                 | 5 (9.6)                 | 4 (7.3)                     |      |         |
| Liver function (missing = 1)      |                         |                             |      |         |
| Abnormal                          | 17 (32.7)               | 12 (22.2)                   | 1.461| 0.227   |
| Normal                            | 35 (67.3)               | 42 (77.7)                   |      |         |
| Kidney function                   |                         |                             |      |         |
| Abnormal                          | 12(23.1)                | 7 (12.7)                    | 1.960| 0.161   |
| Normal                            | 40 (76.9)               | 48 (87.3)                   |      |         |
| Icterus                            |                         |                             |      |         |
| Yes                               | 2 (3.8)                 | 6 (10.9)                    |      |         |
| No                                | 50 (96.2)               | 49 (89.1)                   |      |         |
| Biochemical indicators            |                         |                             |      |         |
| Lactate dehydrogenase (LD, U/L)   | 661.63 ± 1371.89        | 223.91 ± 65.42              | 2.364| 0.020   |
| Hydroxybutyric dehydrogenase (HBDH, U/L) | 474.55 ± 906.57 | 168.80 ± 50.27              | 2.498| 0.014   |
| White blood count (WBC, 10⁹/L)    | 14.99 ± 24.83           | 4.30 ± 4.53                 | 3.139| 0.002   |
| Neutrophils (N, 10⁹/L)            | 3.66 ± 6.24             | 2.32 ± 2.19                 | 1.489| 0.140   |
| Hemoglobin (Hb, g/L)              | 80.17 ± 16.49           | 100.53 ± 20.85              | 5.581| <0.001  |
| Platelet count (PLT, 10⁹/L)       | 108.46 ± 94.2           | 209.11 ± 112.59             | 5.000| <0.001  |
| Lymphocyte (L, 10⁹/L)             | 7.57 ± 15.34            | 14.6 ± 2.16                 | 2.928| 0.044   |
| C-reactive protein (CRP, mg/L)    | 13.87 ± 27.82           | 2.40 ± 8.59                 | 2.361| 0.020   |
| Activated partial thromboplastin time (APTT, s) | 29.22 ± 5.38 | 31.61 ± 7.16                | 1.930| 0.056   |
| Troponin (Tn)                     | 7.36 ± 9.68             | 6.49 ± 7.82                 | 0.430| 0.668   |
| Vitamin A (VA, μmol/L)            | 0.73 ± 0.26             | 0.74 ± 0.18                 | 0.400| 0.690   |
| Vitamin B1 (VB1, nmol/L)          | 98.47 ± 11.71           | 100.05 ± 13.05              | 0.660| 0.511   |
| Vitamin B2 (VB2, μg/L)            | 5.45 ± 1.94             | 5.71 ± 1.75                 | 0.732| 0.466   |
| Vitamin B6 (VB6, nmol/L)          | 33.85 ± 14.54           | 33.80 ± 15.04               | 0.016| 0.987   |
| Vitamin B9 (VB9, nmol/L)          | 20.19 ± 5.83            | 19.38 ± 5.76                | 0.723| 0.471   |
| Vitamin B12 (VB12, pg/mL)         | 485.32 ± 102.97         | 472.17 ± 79.12              | 0.738| 0.462   |
| Vitamin C (VC, μmol/L)            | 39.22 ± 6.47            | 38.43 ± 4.54                | 0.728| 0.469   |
| Vitamin D (VD, nmol/L)            | 37.96 ± 14.78           | 45.67 ± 19.97               | 2.259| 0.026   |
| Vitamin E (VE, µg/mL)             | 10.76 ± 0.90            | 10.62 ± 0.56                | 0.956| 0.341   |

Data were mean ± SD or n (%). *P < 0.05. AML, acute myeloid leukemia; BMI, body mass index.

| Table 2: Multivariate regression analysis of influencing factors for infection in children with acute leukemia. |
|-------------------------------------------------|-------------------------------------------------|---------------------------------|------------------------------|-----------------|-----------------|-----------------|-----------------|
| B                                               | Wald χ²  | Exp (B) | 95% of Exp (B) confidence interval | P                      |
|                                                 |         |         | Lower limit | Upper limit |                  |                  |                  |
| Lactate dehydrogenase (LD)                       | 0.002   | 0.022   | 1.002       | 0.975        | 1.031 | 0.881 |
| Hydroxybutyric dehydrogenase (HBDH)             | 0.007   | 0.176   | 1.007       | 0.974        | 1.042 | 0.675 |
| White blood cell count (WBC)                     | 0.054   | 0.236   | 1.056       | 0.849        | 1.313 | 0.627 |
| Hemoglobin (Hb)                                  | −0.048  | 6.105   | 0.953       | 0.917        | 0.99  | 0.013* |
| Platelet count (PLT)                             | −0.002  | 0.215   | 0.998       | 0.992        | 1.005 | 0.643 |
| Lymphocyte (L)                                   | −0.009  | 0.004   | 0.991       | 0.76         | 1.292 | 0.949 |
| C-reactive protein (CRP)                         | 0.065   | 7.003   | 1.067       | 1.017        | 1.12  | 0.008* |
| Vitamin D (VD)                                   | −0.039  | 3.35    | 0.961       | 0.922        | 1.003 | 0.067 |
| Constant                                         | 3.205   | 4.53    | 24.654      |                   |                  | 0.033 |

*P < 0.05.
### Table 3: Analysis of the factors influencing progression of acute leukemia in children.

| Indicators                     | Treatment remission group (n = 56) | Nonremission group (n = 51) | t/χ²      | P     |
|-------------------------------|------------------------------------|----------------------------|----------|-------|
| Age                           | 6.32 ± 3.72                        | 5.66 ± 3.40                | 0.955    | 0.342 |
| BMI                           | 16.02 ± 2.51                       | 17.03 ± 3.09               | 1.848    | 0.060 |
| Gender                        |                                    |                            |          |       |
| Male                          | 31 (55.4)                          | 30 (58.8)                  | 0.131    | 0.718 |
| Female                        | 25 (44.6)                          | 21 (41.2)                  |          |       |
| Diagnostic results            |                                    |                            |          |       |
| ALL                           | 49 (87.5)                          | 48 (94.2)                  | 6.309    | 0.043 |
| AML                           | 7 (12.5)                           | 2 (3.9)                    |          |       |
| Immunophenotype               |                                    |                            |          |       |
| B                              | 42 (75.0)                          | 34 (66.7)                  |          |       |
| T                              | 7 (12.5)                           | 2 (3.9)                    |          |       |
| Liver function                |                                    |                            |          |       |
| Abnormal                      | 20 (36.4)                          | 9 (17.6)                   | 4.664    | 0.030 |
| Kidney function               |                                    |                            |          |       |
| Normal                        | 36 (63.6)                          | 42 (82.4)                  |          |       |
| Abnormal                      | 13 (23.2)                          | 6 (11.8)                   |          |       |
| Icterus                       |                                    |                            |          |       |
| Normal                        | 43 (76.8)                          | 45 (88.2)                  | 2.396    | 0.122 |
| Infection                     |                                    |                            |          |       |
| Yes                           | 4 (7.1)                            | 4 (7.8)                    | 0.019    | 0.890 |
| No                            | 52 (92.9)                          | 47 (92.2)                  |          |       |
| Infection                     |                                    |                            |          |       |
| Yes                           | 18 (32.1)                          | 34 (66.7)                  |          |       |
| No                            | 38 (67.9)                          | 17 (33.3)                  |          |       |
| Alanine aminotransferase (ALT, mmol/L) | 42.93 ± 51.65                   | 34.24 ± 90.83              | 0.610    | 0.543 |
| Biochemical indicators        |                                    |                            |          |       |
| Aspartate aminotransferase (AST, mmol/L) | 39.93 ± 40.17                   | 29.50 ± 32.30              | 1.457    | 0.148 |
| Lactate dehydrogenase (LD, U/L) | 231.11 ± 80.66                    | 656.14 ± 1373.01           | 2.207    | 0.032 |
| Hydroxybutyric dehydrogenase (HBDH, U/L) | 170.00 ± 59.74                   | 475.02 ± 906.01            | 2.399    | 0.200 |
| White blood cell count (WBC, 10⁹/L) | 4.16 ± 3.50                     | 15.34 ± 25.14              | 3.149    | 0.003 |
| Serological indicators        |                                    |                            |          |       |
| Neutrophils (N, 10⁹/L)        | 2.73 ± 2.50                        | 3.24 ± 6.24                | 0.547    | 0.587 |
| Hemoglobin (Hb, g/L)          | 99.79 ± 20.05                      | 80.59 ± 18.14              | 5.175    | <0.001 |
| Platelet count (PLT)          | 183.00 ± 102.30                    | 135.16 ± 124.19            | 2.182    | 0.031 |
| Lymphocyte (L, 10⁹/L)         | 1.05 ± 1.16                        | 8.14 ± 15.39               | 3.286    | 0.002 |
| C-reactive protein (CRP, mg/L) | 7.14 ± 15.54                      | 8.89 ± 25.93               | 0.426    | 0.671 |
| (PLT, 10⁹/L)                  | 32.76 ± 7.29                       | 28.03 ± 4.24               | 4.118    | <0.001 |
| Activated partial thromboplastin time (APTT, s) | 9.24 ± 10.03 | 5.20 ± 5.33 | 2.533 | 0.01 |
| Troponin (Tn)                 | 0.74 ± 0.18                        | 0.73 ± 0.26                | 0.141    | 0.888 |
| Vitamin A (VA, μmol/L)        | 102.58 ± 12.53                     | 95.67 ± 11.27              | 3.003    | 0.003 |
| Vitamin B1 (VB1, nmol/L)      | 5.72 ± 1.81                        | 5.44 ± 1.88                | 0.793    | 0.430 |
| Vitamin B2 (VB2, μg/L)        | 30.41 ± 13.29                      | 37.58 ± 15.81              | 2.547    | 0.012 |
| Vitamin B6 (VB6, nmol/L)      | 20.55 ± 5.78                       | 18.92 ± 5.71               | 1.468    | 0.145 |
| Vitamin B9 (VB9, nmol/L)      | 453.54 ± 73.62                     | 506.03 ± 101.17            | 3.043    | 0.003 |
| Vitamin B12 (VB12, pg/mL)     | 39.57 ± 5.77                       | 37.99 ± 5.23               | 1.482    | 0.141 |
| Vitamin C (VC, μmol/L)        | 44.93 ± 20.64                      | 38.63 ± 13.98              | 1.828    | 0.070 |
| Vitamin D (VD, nmol/L)        | 10.69 ± 0.75                       | 10.70 ± 0.75               | 0.057    | 0.955 |
| Vitamin E (VE, μg/mL)         |                                    |                            |          |       |

Data were mean ± SD or n (%). * P < 0.05. AML, acute myeloid leukemia; BMI, body mass index.

3.4. Analysis of Treatment Regimen-Related Factors in Children with Acute Leukemia. There was no significant difference in age, BMI, gender, abnormal liver function, abnormal renal function, and icterus among the three therapeutic regimen groups (P < 0.05) (Table 7). However, there were statistically significant differences in immunophenotype and type of diagnosis (P < 0.05). For serological and hematological parameters, there were significant differences in N, PLT, and APTT among the three groups (P < 0.05). For serum vitamin levels, there was a statistically significant difference between VB6 and VB12 (P < 0.05). Furthermore, results from multivariate regression analysis showed that PLT was significantly higher and N was significantly lower in the CAML group than in the other regimen groups. The immunophenotype of the MTX group was statistically different from the other regimens. The VDL group had lower APTT and higher VB6 compared to other regimens (P < 0.05). These results confirmed that PLT, N, immunophenotype, APTT, and VB6 were the factors that influenced the choice of AML treatment regimen in children (Table 8).

4. Discussion

In this study, a total of 107 AL children were included, and their vitamin content and clinical parameters were analyzed in relation to infection, disease status, and clinical risk and treatment regimens. According to the analysis results, the level of serum VD in the infected group was significantly lower than that in the noninfected group. Compared with
Table 4: Multivariate regression analysis of factors affecting remission in children with acute leukemia.

| Factors                        | B      | Standard error | Wald $X^2$ | $P$     | Exp (B) |
|--------------------------------|--------|----------------|------------|---------|---------|
| Diagnostic results             | 2.372  | 0.924          | 6.596      | **0.01**| 10.724  |
| Abnormal liver function        | 0.395  | 1.065          | 0.137      | 0.711   | 1.484   |
| Infection                      | 1.501  | 1.032          | 2.117      | 0.146   | 4.486   |
| Lactate dehydrogenase (LD)     | 0      | 0              | 0.056      | 0.813   | 1       |
| White blood cell count (WBC)   | 0.029  | 0.026          | 1.291      | 0.256   | 1.03    |
| Hemoglobin (Hb)                | 0.027  | 0.026          | 1.059      | 0.304   | 1.028   |
| Platelet count (PLT)           | -0.001 | 0.005          | 0.035      | 0.851   | 0.999   |
| Lymphocyte (L)                 | -0.033 | 0.052          | 0.394      | 0.53    | 0.968   |
| Activated partial thromboplastin time (APTT) | -0.009 | 0.074          | 0.015      | 0.904   | 0.991   |
| Troponin (Tn)                  | -0.043 | 0.037          | 1.389      | 0.239   | 0.958   |
| Vitamin B1 (VB1)               | -0.012 | 0.035          | 0.129      | 0.719   | 0.988   |
| Vitamin B6 (VB6)               | 0.001  | 0.033          | 0.002      | 0.968   | 1.001   |
| Vitamin B12 (VB12)             | -0.011 | 0.006          | 3.777      | 0.052   | 0.989   |
| Constant                       | 3.355  | 4.885          | 0.472      | 0.492   | 28.655  |

The value with $P > 0.05$ is indicated in bold.

Table 5: Analysis of factors influencing different risk degrees in children with acute leukemia.

| Indicators                        | HR group ($n = 44$) | IR group ($n = 53$) | SR group ($n = 8$) | $X^2$ | $P$       |
|-----------------------------------|---------------------|---------------------|--------------------|-------|-----------|
| Age                               | 8.18 ± 10.83        | 8.98 ± 16.57        | 5.25 ± 2.92        | 0.261 | 0.771     |
| BMI                               | 16.85 ± 2.78        | 16.58 ± 2.88        | 14.43 ± 2.5        | 0.883 | 0.417     |
| Gender                            | Male                | 22 (50)             | 33 (62.3)          | 4 (50.0) | 1.604 | 0.448     |
|                                  | Female              | 22 (50)             | 20 (37.7)          | 4 (50.0) |          |           |
| Diagnostic results                | ALL                 | 35 (79.5)           | 40 (75.5)          | 7 (85.7) | 0.681 | 0.711     |
|                                  | AML                 | 9 (20.5)            | 13 (24.5)          | 1 (12.5) |          |           |
| Immunophenotype                   | B                   | 32 (72.7)           | 36 (67.9)          | 6 (75.0) | 1.084 | 0.897     |
|                                  | T                   | 4 (9.1)             | 4 (7.5)            | 1 (12.5) |          |           |
| Liver function                    | Normal              | 34 (77.3)           | 36 (69.2)          | 7 (87.5) | 2.119 | 0.347     |
|                                  | Abnormal            | 10 (22.7)           | 16 (30.8)          | 1 (12.5) |          |           |
| Renal function                    | Normal              | 40 (90.9)           | 42 (79.2)          | 4 (50.0) | 9.869 | 0.007*    |
|                                  | Icterus             | Yes                 | 5 (11.4)           | 8 (15.1) | 0       | 8.496 | 0.014*    |
| Biochemical indicator             |                     |                     |                    |       |           |
| Lactate dehydrogenase (LD, U/L)   | 534.66 ± 281.05     | 363.04 ± 278.54     | 303.86 ± 181.69    | 0.426 | 0.654     |
| Hydroxybutyric dehydrogenase (HBDH, U/L) | 386.91 ± 841.45   | 262.06 ± 491.06     | 239.14 ± 161.26    | 0.487 | 0.616     |
| Serological indicators            |                     |                     |                    |       |           |
| White blood cell count (WBC, 10^9/L) | 6.99 ± 11.62       | 12.37 ± 23.50       | 5.83 ± 4.62        | 1.203 | 0.304     |
| Neutrophils (N, 10^9/L)           | 3.33 ± 5.50         | 2.80 ± 4.29         | 2.72 ± 1.66        | 0.168 | 0.846     |
| Hemoglobin (Hb, g/L)              | 87.89 ± 18.32       | 92.45 ± 22.68       | 97.88 ± 28.54      | 0.997 | 0.373     |
| Platelet count (PLT)              | 125.39 ± 87.45      | 189.85 ± 132.01     | 170.63 ± 92.35     | 3.964 | 0.022*    |
| Lymphocyte (L, 10^9/L)            | 2.76 ± 6.16         | 6.18 ± 14.67        | 2.63 ± 3.98        | 1.224 | 0.298     |
| C-reactive protein (CRP, mg/L)    | 9.63 ± 25.49        | 9.15 ± 19.36        | 9.21 ± 14.44       | 0.006 | 0.994     |
| Activated partial thromboplastin time (APTT, s) | 30.73 ± 7.70     | 30.61 ± 5.76        | 28.36 ± 2.57       | 0.411 | 0.664     |
| Troponin (Tn)                     | 6.79 ± 8.58         | 5.68 ± 8.62         | 6.28 ± 11.67       | 0.192 | 0.926     |
| Vitamin A (VA, μmol/L)            | 0.71 ± 0.18         | 0.76 ± 0.24         | 0.71 ± 0.24        | 0.944 | 0.392     |
| Vitamin B1 (VB1, nmol/L)          | 98.32 ± 13.29       | 99.91 ± 12.16       | 101.67 ± 10.33     | 0.336 | 0.715     |
| Vitamin B2 (VB2, μg/L)            | 5.42 ± 1.33         | 5.78 ± 2.25         | 5.50 ± 1.37        | 0.466 | 0.629     |
| Vitamin B6 (VB6, nmol/L)          | 34.77 ± 17.05       | 32.86 ± 13.23       | 36.43 ± 15.96      | 0.309 | 0.735     |
| Vitamin B9 (VB9, nmol/L)          | 20.49 ± 6.73        | 19.54 ± 5.04        | 18.14 ± 4.94       | 0.688 | 0.505     |
| Vitamin B12 (VB12, pg/mL)         | 484.54 ± 91.76      | 474.32 ± 90.16      | 446.55 ± 76.09     | 0.635 | 0.532     |
| Vitamin C (VC, μmol/L)            | 38.69 ± 5.26        | 39.22 ± 6.10        | 37.51 ± 3.45       | 0.358 | 0.700     |
| Vitamin D (VD, nmol/L)            | 40.85 ± 15.11       | 44.04 ± 21.09       | 36.56 ± 4.02       | 0.785 | 0.459     |
| Vitamin E (VE, μg/mL)             | 10.77 ± 0.83        | 10.62 ± 0.68        | 10.77 ± 0.87       | 0.520 | 0.596     |

Data were mean ± SD or n (%). Missing = 2. *$P < 0.05$. AML, acute myeloid leukemia; BMI, body mass index; HR, high risk; IR, intermediate risk; SR, slight risk.
Table 6: Multivariate regression analysis of factors influencing different risk degrees in children with acute leukemia.

| Slight risk (SR = 0) | B   | Wald X² | Exp (B) | 95% of Exp (B) confidence interval | P       |
|---------------------|-----|---------|---------|-----------------------------------|---------|
|                     |     |         |         | Lower limit | Upper limit |         |
| HR                  |     |         |         |           |           |         |
| Platelet count (PLT, 10⁹/L) | −0.006 | 0.004 | 0.997 | 0.987 | 1.002 | 0.167 |
| Abnormal renal function = 1.00 | −2.558 | 7.247 | 0.077 | 0.012 | 0.499 | 0.007* |
| Icterus = 1.00      | 19.288 | 372.102 | 237982258.740 | 33530638.034 | 1689068827.669 | <0.001* |
| Constant            | 2.968 |         |         |           |           |         |
| IR                  |     |         |         |           |           |         |
| Platelet count (PLT, 10⁹/L) | 0.001 | 0.103 | 1.001 | 0.994 | 1.008 | 0.749 |
| Abnormal renal function = 1.00 | −1.356 | 2.970 | 0.258 | 0.055 | 1.205 | 0.085 |
| Icterus = 1.00      | 17.149 | 0.000 | 28035276.423 | 28035276.422843 | 28035276.423 | <0.001* |
| Constant            | 2.106 |         |         |           |           |         |

* P < 0.05. HR, high risk; IR, intermediate risk; SR, slight risk.

Table 7: Analysis of factors influencing different treatment regimens in children with acute leukemia.

| Indicators | CAML group (n = 15) | MTX group (n = 9) | VDLP group (n = 38) | Other groups (n = 45) | F/X² | P       |
|------------|---------------------|------------------|--------------------|-----------------------|------|---------|
| Age        | 6.22 ± 4.46         | 4.93 ± 2.67      | 5.18 ± 2.95        | 6.92 ± 3.63           | 2.483 | 0.065   |
| BMI        | 16.54 ± 3.28        | 16.24 ± 2.51     | 16.59 ± 2.90       | 16.45 ± 2.77          | 0.043 | 0.988   |
| Gender     | Male                | 7 (46.67)        | 4 (44.44)          | 23 (60.53)            | 27 (60.00) | 1.590 | 0.662   |
|            | Female              | 8 (53.33)        | 5 (55.55)          | 15 (39.47)            | 18 (40.00) |       |         |
| Diagnostic results | AML               | 0                | 1 (11.11)          | 0                     | 22 (48.89) | 35.098 | <0.001* |
|            | ALL                 | 15 (100.00)      | 8 (88.89)          | 38 (100.00)           | 23 (51.11) |       |         |
|            | B                   | 15 (100.00)      | 5 (55.55)          | 37 (97.37)            | 19 (42.22) |       |         |
| Immunophenotype | T                 | 0                | 3 (33.33)          | 1 (2.63)              | 5 (11.11) | 47.056 | <0.001* |
|            | AML                 | 0                | 1 (11.11)          | 0 (2.9)               | 21 (46.67) |       |         |
| Liver function | Abnormal         | 2 (26.67)        | 3 (33.33)          | 9 (23.68)             | 15 (33.33) |       | 2.908  | 0.406   |
|            | Normal              | 13 (73.33)       | 6 (66.67)          | 29 (76.32)            | 29 (64.44) |       |         |
| Renal function | Abnormal         | 6 (40.00)        | 2 (22.22)          | 6 (15.79)             | 5 (11.11) | 6.666  | 0.083   |
|            | Normal              | 9 (60.00)        | 7 (77.78)          | 32 (84.21)            | 40 (88.89) |       |         |
| Icterus     | Yes                 | 1 (6.67)         | 1 (11.11)          | 1 (2.63)              | 5 (11.11) |       |         |
|            | No                  | 14 (93.33)       | 8 (88.89)          | 37 (97.37)            | 40 (88.89) |       |         |
| Biochemical indicator | Alanine aminotransferase (ALT, mmol/L) | 20.68 ± 14.95 | 40.89 ± 23.79 | 47.79 ± 104.97 | 37.56 ± 55.13 | 0.502 | 0.682 |
|            | Aspartate aminotransferase (AST, mmol/L) | 22.66 ± 5.71 | 37.66 ± 14.25 | 33.11 ± 39.72 | 40.75 ± 42.94 | 0.953 | 0.418 |
|            | Lactate dehydrogenase (LD, U/L) | 215.33 ± 44.06 | 235.67 ± 41.50 | 374.24 ± 307.76 | 601.95 ± 1473.89 | 0.858 | 0.465 |
|            | Hydroxybutyric dehydrogenase (HBDH, U/L) | 164.67 ± 36.99 | 2.36 ± 3.30 | 293.61 ± 223.21 | 414.68 ± 974.95 | 0.763 | 0.517 |
| White blood cell count (WBC, 10⁹/L) | 2.27 ± 1.75 | 4.32 ± 1.33 | 10.30 ± 18.23 | 12.25 ± 22.29 | 1.394 | 0.249 |
| Neutrophils (N, 10⁹/L) | 1.46 ± 1.22 | 3.22 ± 1.61 | 1.57 ± 1.74 | 4.61 ± 6.59 | 3.846 | 0.012* |
| Hemoglobin (Hb, g/L) | 9.09 ± 1.67 | 98.56 ± 16.30 | 84.68 ± 20.73 | 94.00 ± 23.88 | 1.807 | 0.051 |
| Platelet (PLT, 10⁹/L) | 2.26 ± 1.09 | 171.11 ± 88.49 | 171.00 ± 133.53 | 126.84 ± 94.98 | 3.233 | 0.025* |
| Lymphocyte (L, 10⁹/L) | 0.62 ± 0.46 | 0.85 ± 0.42 | 7.53 ± 14.78 | 3.80 ± 10.06 | 1.961 | 0.124 |
| C-reactive protein (CRP, mg/L) | 7.67 ± 17.66 | 5.60 ± 11.21 | 6.99 ± 26.19 | 10.43 ± 20.52 | 0.225 | 0.879 |
| Activated partial thromboplastin time (APTT, s) | 35.31 ± 9.31 | 31.26 ± 4.89 | 26.63 ± 3.54 | 31.96 ± 5.88 | 10.267 | <0.001* |
| Troponin (Tn) | 8.92 ± 4.17 | 13.88 ± 13.80 | 5.02 ± 2.91 | 10.43 ± 10.97 | 1.370 | 0.261 |
tumor cell proliferation, and participating in the development and progression of tumor cells [3, 4]. VD deficiency is a common malnutrition case. It affects approximately 30%–50% of the population worldwide, and most people are common malnutrition case. It affects approximately 30%–50% of the population worldwide, and most people are

| Table 7: Continued. |
|---------------------|
| Vitamin level      |
| Vitamin A (VA, μmol/L) | 0.81 ± 0.20 | 0.79 ± 0.16 | 0.70 ± 0.27 | 0.73 ± 0.18 | 1.173 ± 0.324 |
| Vitamin B1 (VB1, nmol/L) | 101.03 ± 13.23 | 100.91 ± 14.64 | 95.16 ± 11.22 | 101.85 ± 12.08 | 2.279 ± 0.084 |
| Vitamin B2 (VB2, μg/L) | 5.29 ± 0.88 | 4.73 ± 0.66 | 5.53 ± 0.68 | 5.90 ± 2.28 | 1.247 ± 0.297 |
| Vitamin B6 (VB6, nmol/L) | 32.83 ± 13.74 | 21.76 ± 7.45 | 18.53 ± 5.28 | 20.14 ± 5.93 | 1.113 ± 0.347 |
| Vitamin B9 (VB9, nmol/L) | 2.06 ± 5.36 | 1.85 ± 0.16 | 1.72 ± 0.24 | 1.60 ± 0.39 | 1.146 ± 0.312 |
| Vitamin D (VD, pg/mL) | 434.05 ± 54.62 | 435.39 ± 74.77 | 515.39 ± 98.76 | 470.93 ± 87.31 | 4.415 ± 0.006* |

Data were mean ± SD or n (%). Missing = 13. AML, acute myeloid leukemia; BMI, body mass index; CAML, cyclophosphamide + cytosine arabinoside+6-mercaptopurine + pegaspargase; MTX, methotrexate; VDLP, vindesine + daunomycin + L-asparaginase + prednisone. The value with P > 0.05 is indicated in bold.

| Table 8: Multivariate analysis of factors influencing different treatment regimens in children with acute leukemia. |
|---------------------------------------------------------------|
| Regimen (others = 0)                                           | B     | Wald X² | Exp (B) | 95% of Exp (B) confidence interval | P     |
|                                                              |       |         |         | Lower limit | Upper limit |
| CAML                                                          |       |         |         |             |           |
| Intercept                                                     | 0.548 | 0       | 1       |             |           |
| Platelet count (PLT)                                          | 0.01  | 4.682   | 1.01    | 1.001       | 1.019    |
| Neutrophils (N)                                               | −0.801| 4.969   | 0.449   | 0.222       | 0.908    |
| Activated partial thromboplastin time (APTT)                  | 0.022 | 0.148   | 1.022   | 0.915       | 1.141    |
| Vitamin B6 (VB6)                                              | −0.013| 0.177   | 0.987   | 0.927       | 1.074    |
| Vitamin B12 (VB12)                                            | −0.003| 0.471   | 0.997   | 0.987       | 1.006    |
| Immunophenotype = 0.00*                                       | 0.165 | 0       | 1.18E + 0 | 0          | 1.00E + 0 |
| Immunophenotype = 1.00*                                       | −17.98| 0       | 1.55E - 0 | 0          | 9.99E - 01 |
| Diagnosis = 0                                                 | −17.335| 0 | 2.96E - 0 | 0          | 0.999    |
| MTX                                                           |       |         |         |             |           |
| Intercept                                                     | 19.84 | 20.885  | 0       |             |           |
| Platelet count (PLT)                                          | 0.002 | 0.369   | 1.002   | 0.995       | 1.01     |
| Neutrophils (N)                                               | 0.005 | 0.002   | 1.005   | 0.799       | 1.264    |
| Activated partial thromboplastin time (APTT)                  | −0.078| 0.86    | 0.925   | 0.784       | 1.091    |
| Vitamin B6 (VB6)                                              | −0.016| 0.23    | 0.984   | 0.921       | 1.052    |
| Vitamin B12 (VB12)                                            | −0.005| 0.849   | 0.995   | 0.984       | 1.006    |
| Immunophenotype = 0.00*                                       | −16.297| 177.051 | 8.37E - 0 | 7.59E - 0  | <0.001*  |
| Immunophenotype = 1.00*                                       | −15.147| 125.811 | 2.64E - 0 | 1.87E - 0  | <0.001*  |
| Diagnosis = 0                                                 | −17.91 | 0   | 1.67E - 0 | 1.67E + 0  | 0.06     |
| VDLP                                                          |       |         |         |             |           |
| Intercept                                                     | 10.317| 0       |         |             | 0.999    |
| Platelet count (PLT)                                          | 0.001 | 0.143   | 1.001   | 0.994       | 1.008    |
| Neutrophils (N)                                               | −0.499| 5.798   | 0.607   | 0.405       | 0.911    |
| Activated partial thromboplastin time (APTT)                  | −0.412| 10.908  | 0.662   | 0.518       | 0.846    |
| Vitamin B6 (VB6)                                              | 0.065 | 4.721   | 1.067   | 1.006       | 1.131    |
| Vitamin B12 (VB12)                                            | 0.007 | 2.348   | 1.007   | 0.998       | 1.016    |
| Immunophenotype = 0.00*                                       | −2.274| 0       | 0.103   | 0           | 0.1      |
| Immunophenotype = 1.00*                                       | −3.488| 0       | 0.031   | 0           | 0.1      |
| Diagnosis = 0                                                 | −20.163| 0 | 1.75E - 0 | 0           | 0.998    |

* P < 0.05. *AML was considered as the control group of immunophenotype, B cell type: immunophenotype = 0.00; *MT cell type: immunophenotype = 1.00; *ALL acted as the control group of diagnostic results, AML: diagnosis = 0. CAML, cyclophosphamide + cytosine arabinoside+6-mercaptopurine + pegaspargase; MTX, methotrexate group; VDLP, vindesine + daunomycin + L-asparaginase + prednisone. The value with P > 0.05 is indicated in bold.

the nonremission group, the serum levels of VB6 and VB12 in the treatment remission group were significantly decreased, while the level of VB1 was notably increased. Additionally, there were notable differences in the levels of VB6 and VB12 among treatment regimen groups.

Recently, it has been shown that vitamins have non-classical effects such as regulating body immunity, inhibiting
Previous scholars have found that a decrease in VB6, VB9, and VB12 blood levels increases cancer risk, and epidemiological studies findings reported that adequate intake of folate, VB6, and VB12 may prevent breast cancer [10–12]. But the specific mechanism of action is not clear. However, these findings are not consistent with the results of this study. In our study, VB6 and VB12 serum levels were lower in the AL treatment remission group than in the nonremission group. Based on our analysis, since VB is involved in cell division as a coenzyme in the synthesis of purine and thymic acid for DNA synthesis [12], after treatment and remission of the patients, tumor cell division activity was reduced, so the level of VB6 and VB12 was significantly decreased in patients in the treatment remission group. Johansson et al. [13] measured the folic acid and VB12 blood concentrations in 869 patients and 1174 controls and concluded that VB12 may be associated with an increased risk of advanced prostate cancer. Chandy et al. [14] found that VB12 could increase colorectal cancer risk. Brasky et al. [15] demonstrated that the use of VB6 and VB12 alone without other vitamins increased the risk of lung cancer up to 30%–40% in men. In agreement with the present study, Pais et al. [16] showed that vitamin B6 levels were significantly higher in newly diagnosed childhood leukemia than in the control group. The possibility that folate has a dual regulatory effect depends on its timing and dose of administration. Folate supplementation before the onset of precancerous lesions may prevent tumor development, but increased folate in the presence of lesions may increase tumorigenesis [17, 18].

Giovannucci’ study [19] showed that higher VD plays a protective role against the development of colorectal cancer and adenoma. There was a significant negative linear relationship between plasma VD and colorectal cancer risk [20]. Giovannucci et al. [21] showed that a 25 nmol/L increase in VD was associated with a 17% reduction in total cancer incidence, a 29% reduction in total cancer mortality, and a 43% and 45% reduction in digestive system cancer incidence and mortality, respectively. Together, the results of the above studies showed the protective effects of VD on tumorigenesis. In addition, a number of epidemiological studies were conducted in adults and children, and the results showed that VD deficiency was associated with an increased risk and severity of infections, especially respiratory infections [22]. Similarly, the results of this study also showed that VD levels were significantly lower in the infected group than in the noninfected group. Brasky et al. [15] also found that the level of VD in AL patients was significantly lower than the normal level.

PLT is the smallest cell fragment produced by mega-karyocytes in the bone marrow. Under physiological conditions, PLT exerts the functions of adhesion, aggregation, release, and contraction to ensure smooth progress of the normal hemostatic process. PLT is also associated with pathological thrombosis, tumor metastasis, inflammation, and immune response [23]. AL is a common malignant proliferative tumor of the hematopoietic system. Bleeding is one of the common symptoms and causes of death in AL. The mechanism through which bleeding occurs is complex, involving various factors such as infiltration of leukemia cells into the vessel walls, the reduction of PLT production, and abnormal coagulation and anticoagulant functions. Among them, reduction of PLT production is the major cause of bleeding [24]. Studies have found that reduced PLT count in all types of AL may lead to abnormal PLT function [25, 26]. In this study, PLT count and Hb levels in the infected group were lower than those of in the noninfected group. The PLT count and Hb levels in the treatment remission group were significantly increased than those in the nonremission group. The PLT count also varied among the three risk degrees in children with AL. Together, these results indicate that low PLT count and Hb levels are associated with poor treatment outcomes and prognosis. Furthermore, the results of multivariate analysis showed that PLT was an influencing factor for the choice of AML treatment regimen.

CRP is commonly applied in the diagnosis of multiple systemic inflammatory diseases [27]. It has been reported that CRP can act as a marker of fever, bloodstream infection, and sepsis in immunocompromised patients [28–30]. Shimony et al. [31] demonstrated that CRP level was significantly elevated in AL, and as a sensitive biomarker, CRP preceded bloodstream infection. In this study, the level of CRP in the infected group was higher than that in the noninfected group. The level of CRP was lower in the treatment remission group than that in the nonremission group, but the differences were not significant. Multivariate analysis also confirmed that CRP level was a risk factor for the occurrence of infection in children with AL.

In this study, multivariate regression analysis results showed that abnormal renal function and icterus were effective prediction factors of different risk degrees in AL children, and L count, immunophenotype, and APTT were the influencing factors for the choice of therapeutic regimen. Overall, close attention to vitamin levels in AL children at different stages of chemotherapy, improvement of nutritional status, minimized complications, and especially reduction of the incidence of infection are important means to improve the survival rate and quality of life of AL children. However, due to the small sample size included in this study, some indicators had no significant changes at different stages of disease development in children with AL. Therefore, further studies with larger sample sizes are needed.

To sum up, this study has found imbalances in serum vitamins levels in AL children, which provide some references for AL diagnosis and treatment. The results of this study suggest that close attention to vitamins levels changes and maintaining vitamin level balance (through timely supplementation or cessation of vitamin intake) can contribute to successful treatment outcomes in children with AL. In addition, HB and CRP were found to be the main factors influencing infection in children with AL. Since low HB is likely in AL patients, the risk of infections is high, and therefore, antinfective treatment should be considered in the treatment of AL.
Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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