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Evaluation of the necessity of revaccination with tetanus-toxoid-containing vaccines for childhood cancer survivors post-chemotherapy

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Abstract:

Objective: To evaluate serum tetanus IgG antibody levels in childhood cancer survivors (CCSs), investigate longitudinal dynamics pre- and post- chemotherapy, and determine the necessity of post-chemotherapy revaccination with tetanus-toxoid-containing vaccines (TTCVs). This aims to establish evidence-based guidelines for developing revaccination protocols in this vulnerable population. **Methods:** This cohort study enrolled CCSs (<15 years) hospitalized pre-chemotherapy at the Children's Hospital Affiliated to Zhejiang University School of Medicine between January 2022 and January 2023. Serial blood samples were collected at three critical timepoints: pre-chemotherapy baseline, and 1-month and 6-month post-chemotherapy intervals for the case group, alongside age-matched healthy controls recruited from community populations. Quantitative determination of tetanus-specific IgG antibodies utilized a standardized enzyme-linked immunosorbent assay (ELISA) (Verenserun kit V108.17). **Results:** The study included 379 CCSs and 379 healthy controls. Post-chemotherapy analysis unveiled a marked decline in tetanus IgG seropositivity compared to pre-treatment levels (70.45% vs 81.00%; $\chi^2=93.66$, $P<0.001$), with rates strikingly lower than healthy controls (82.69%; $\chi^2=15.54$, $P<0.001$). Geometric mean concentrations (GMC) demonstrated parallel reductions (0.73 ± 0.10 IU/mL post-chemotherapy vs 1.15 ± 0.16 IU/mL baseline, $t=5.00$, $P<0.001$; healthy controls: 1.10 ± 0.06 IU/mL, $t=3.09$, $P=0.002$), which was non-significantly different between CCSs pre-chemotherapy and healthy controls ($t=-0.33$, $P=0.745$). Longitudinal assessment at the 6-month follow-up ($n=88$) identified persistent seronegativity in 69.32% (61/88) of cases. Among 6 revaccinated patients receiving TTCVs, 66.67% (4/6) achieved seroconversion. **Conclusion:** Chemotherapeutic regimens significantly deplete tetanus IgG antibodies in CCSs, driving post-treatment titers below the World Health Organization (WHO) defined protective threshold (0.1 IU/mL). This serological evidence confirms treatment-induced erosion of pre-existing immune memory. Our data strongly advocate for structured revaccination protocols with TTCVs, initiated as soon as feasible under professional guidance following confirmed disease remission and immune function reconstitution. Such targeted immunological

rehabilitation strategies are vital to restore protective immunity and mitigate tetanus-associated morbidity within this high-risk group.

1. Introduction

The global pediatric cancer burden steadily escalates, now representing the second leading cause of childhood mortality (surpassed only by accidental injuries) across both industrialized and developing nations^[1,2]. In 2014, childhood cancer incidence in the United States stood at 16.0 per million, with a mortality rate of 2.0 per million^[3]; concurrently, China's national registry documented leukemia incidence at 42.9 per million among children aged 0-14 during 2016-2018^[4]. However, continuous therapeutic advancements have steadily improved the long-term survival rates for pediatric tumor patients^[5]. The 5-year survival rates now approach 80% in developed European and American countries^[6] and 72% in China^[7]. This profound epidemiological transition underscores the critical need for optimized survivors' care protocols to address acquired immunodeficiency states.

Childhood cancer survivors (CCSs) constitute a vulnerable population for vaccine-preventable infectious diseases (VPDs) (e.g., tetanus) owing to compromised long-term immunological integrity^[8,9], with a higher incidence of complications and mortality compared to the healthy population^[10-12]. Tetanus, an acute bacterial infection with high fatality rates caused by toxigenic strains of *Clostridium tetani* (C. tetani), can occur across all age groups but predominantly affects newborns and mothers with unhygienic childbirth practices and suboptimal postpartum health conditions^[13]. As a VPD associated with high mortality, the clinical necessity of tetanus-toxoid-containing vaccines (TTCVs) vaccination has garnered significant attention. Accumulating evidence indicates that chemotherapeutic agents (e.g., alkylating agents, antimetabolites) suppress B-cell and T-cell activity, impair memory immune responses, and diminish the efficacy of primary immunization^[14]. Abdolkarimi et al. conducted a study on 110 children who received immunosuppressive chemotherapy and found that the positive rate of tetanus antibodies in these children significantly decreased after chemotherapy. This indicates that for children with cancer who receive immunosuppressive chemotherapy, they should complete the supplementary vaccination, especially the tetanus vaccine, at least 6 months after the chemotherapy.^[15] Furthermore, immunosuppression in CCSs persists and exhibits delayed recovery even after months of immune reconstitution^[16,17]. Studies demonstrate that only 60% of CCSs achieve CD4+ T-cell recovery at 6 months post-chemotherapy, and early vaccination may result in suboptimal immune responses^[18]. Additionally, data regarding the long-term efficacy of revaccination remain limited: a cohort study involving 200 children revealed that the antibody decay rate was 1.8-fold higher in CCSs than in healthy children at 5 years after the second vaccination^[19].

The widespread adoption of childhood vaccination has driven the incidence of Vaccine-Preventable Diseases (VPDs) to historic lows. However, adherence to post-chemotherapy vaccination schedules among CCSs remains suboptimal^[20]. While the World Health Organization (WHO) advises evaluating revaccination needs 3-6 months after chemotherapy, no consensus exists on specific protocols^[13]. Divergent approaches prevail: U.S. Centers for Disease Control and Prevention (CDC) guidelines recommend restarting the entire primary immunization series, whereas the European Society of Paediatric Oncology (SIOP) advocates tailoring strategies to individual immune recovery^[21,22]. Standardized revaccination guidelines for CCSs are notably absent in China^[23]. In this study, we conducted a systematic

evaluation of tetanus antibody dynamics before and after chemotherapy, assessing the necessity for TTCVs revaccination in CCSs post-treatment. Our findings aim to offer evidence-based guidance for developing revaccination protocols in this vulnerable population.

2. Materials and methods

2.1 Subjects

The case group comprised all CCSs hospitalized at the Children's Hospital Affiliated to Zhejiang University School of Medicine between January 2022 and December 2023. Inclusion criteria specified children under 15 years old, diagnosed with tumors, and who provided blood samples at pre-chemotherapy baseline, as well as 1-month and 6-month post-chemotherapy intervals. The study excluded those not meeting these criteria or unwilling to participate. Community age-matched healthy individuals, recruited from the surrounding population, matching within +/- 6 months for those under 6 years old and within +/- 12 months for those over 7 years old, served as the control group. Control group inclusion required children under 15 years old who were healthy, without tumors or other diseases; exclusion applied to those not meeting these criteria or declining participation.

The formula for calculating equal-sized case and control groups determined the sample size^[24]. With the control group's tetanus IgG antibody positive rate at 76%^[25], p_0 was set to 70% to estimate the minimum requirement. Using parameters $RR = 2.0$, $\alpha = 0.05$, $\beta = 0.10$, $U_\alpha = 1.96$, and $U_\beta = 1.28$, the initial calculation yielded $n = 266$. Considering potential loss to follow-up, the sample size was expanded by 10%. Therefore, each group required 293 participants, resulting in 293 CCS cases and 293 healthy controls.

This study received approval from the Ethics Committee of Hangzhou CDC [No. (2021)18] and the Ethics Committee of Children's Hospital of Zhejiang University [2022-IRB-028]. Blood specimen collection and information acquisition obtained guardian consent.

2.2 Questionnaire Survey and Data Collection

The questionnaire survey on CCSs encompassed subjects' demographic profiles (gender, age, height, weight, etc.), prior vaccination records, histories of systemic diseases and allergies, family medical background, previous post-vaccination AEFI occurrences, and reasons for the current visit—all to investigate factors influencing immune response. This standardized questionnaire was meticulously prepared, refined through pilot testing and review, and then administered by specially trained medical staff who directly interviewed patient guardians to complete it. A dedicated quality control team rigorously performed logical checks and reviews on each returned form; any questionnaire failing to meet stringent quality standards was promptly returned for re-survey.

2.3 Specimen collection and laboratory testing

(1) Antibody level detection: At admission prior to chemotherapy, 2 ml of venous blood was drawn into a non-anticoagulant tube to establish the baseline IgG antibody level. Additional 2 ml venous blood samples were collected at 1 month and 6 months post-chemotherapy; similarly, 2 ml samples were obtained from control subjects and placed into non-anticoagulant tubes. Tetanus IgG antibody levels were quantified using an enzyme-linked immunosorbent assay (ELISA) with the German Verenserun Tetanus IgG antibody detection kit (Version V 108.17), following the manufacturer's instructions. At the time of sampling, the patient was not undergoing any treatment.

(2) Seropositivity assessment: A tetanus IgG antibody level ≥ 0.1 IU/mL was considered positive, while levels below 0.1 IU/mL were deemed negative..

2.4 Evaluation of Vaccination Recommendations

Comprehensive vaccination recommendations were formulated based on a thorough assessment of disease incidence, CCS diagnosis and treatment history, prior vaccination records, allergy history, family medical background, and previous adverse events following immunization (AEFI). This evaluation incorporated laboratory findings, including complete blood count, comprehensive immune function panels, electroencephalogram (EEG), electrocardiogram (ECG), and other significant positive test results.

2.5 Follow-up of Vaccination and Safety

In Hangzhou, primary vaccination of infants and young children consists of three doses of DTP in 3, 4 and 5 months old followed by a fourth dose at 18-24 months old, with DT booster doses being recommended at aged 6 y.

During rediagnosis, the vaccination certificates of CCSs were reviewed, and their immunization status was documented at follow-up visits. Concurrently, vaccination follow-up information was retrieved from the Hangzhou Vaccination Information Management System to supplement and analyze the overall vaccination status.

AEFI are reported through the Chinese National Immunization Information System (CNIIS). Which are classified as vaccine product-related reactions, coincidental events, immunization anxiety-related reactions, suspected immunization error-related reactions, or suspected vaccine quality defect-related reactions. Vaccine product-related reactions are further classified as common (usually minor) or rare (possibly serious) vaccine reactions. A serious AEFI is an AEFI that is life-threatening, results in permanent or significant disability, results in impairment of organ function, or leads to death.

2.6 Statistical Analysis

Data underwent initial screening and organization using basic Excel software. Subsequent statistical analysis was performed with SPSS 25.0. Normally distributed measurement data are expressed as mean $\pm$ standard deviation ($X \pm S$), with comparisons between two groups conducted using the T-test and comparisons among multiple groups using analysis of variance (ANOVA). Non-normally distributed measurement data are presented as median (interquartile range) [$M (P_{25}, P_{75})$], with group comparisons made via the rank sum test. The rank sum test between the two groups was conducted using the Mann-Whitney test to obtain the Z value, while for multiple groups, the Kruskal-Wallis test was used to obtain the chi-square value. Categorical data are expressed as rates or percentages, with group comparisons analyzed using the chi-square test ($\alpha = 0.05$). Multiple test correction performed (e.g., Bonferroni correction, correction $\alpha = 0.05/m$, $m = v(v-1)/2$, v means the number of comparison groups). Influencing factors were examined using a logistic regression model and Generalized Linear Model. A P -value $< \alpha$ was deemed statistically significant.

3. Results

3.1 Basic Characteristics

This study enrolled 379 CCSs and 379 matched controls. Participant demographics revealed a well-balanced gender and age distribution between the case and control groups. Within the CCSs group, 211 (55.67%) individuals were male and 168 (44.33%) were female,

yielding a male-to-female ratio of 1.26:1. The mean age stood at 6.37 ± 3.81 years. Among the CCSs, hematologic tumors were present in 339 (89.45%), while solid tumors affected 40 (10.55%). Additionally, 58 CCSs (15.30%) reported a history of allergies, and all were vaccinated with TTCVs. Notably, no CCS had a documented history of tetanus either before their primary diagnosis or during treatment.

In the control group, 209 participants (55.14%) were male and 170 (44.85%) were female, resulting in a male-to-female ratio of 1.23:1. Their mean age was 6.42 ± 4.13 years. All were vaccinated with TTCVs.. Furthermore, no control participant had a documented history of tetanus infection.

3.2 Tetanus IgG Antibody Levels in CCSs

3.2.1 Levels Pre- and One Month Post-Chemotherapy

The seroprevalence of protective tetanus IgG antibodies demonstrated significant chemotherapy-induced attenuation, plummeting from 81.00% (307/379) pre-treatment to a concerning 70.45% (267/379) one month post-chemotherapy ($\chi^2=93.66$, $P<0.001$). Concurrently, the geometric mean concentration (GMC) declined sharply from 1.15 ± 0.16 IU/mL to 0.73 ± 0.10 IU/mL ($t=5.00$, $P<0.001$).

3.2.1.2 Analysis of Factors Influencing Tetanus IgG Antibody Levels in CCSs Post-Chemotherapy

Univariate analysis revealed a significant decline in tetanus IgG antibody seroprevalence among CCSs after chemotherapy across various demographic and clinical strata ($P < \alpha$). This reduction affected groups defined by gender, specific age subgroups (3-4y, 7-9y, 10-15y), tumor types (leukemia versus solid tumors), history of allergy, active infections, the number of diseases time since last vaccination, and different treatment methods, including the number of chemotherapy cycles, solid organ transplantation, hematopoietic stem cell transplantation, radiotherapy, immunosuppressant use, targeted therapies, immunotherapy. No significant differences in the positive rate of tetanus IgG antibody emerged pre- and post-chemotherapy between other groups (Table 1).

The geometric mean concentrations (GMCs) of tetanus IgG antibody significantly declined in CCSs both before and after chemotherapy ($P < \alpha$) across diverse groups. These included different genders, age brackets (1y, 2y, 3-4y, 5-6y, 7-9y), tumor types (leukemia, other solid tumors), and histories of allergy, active infection, time since last vaccination, numbers of diseases and different treatment methods, including solid organ transplantation or hematopoietic stem cell transplantation, radiotherapy, immunosuppressant use, targeted therapies, immunotherapy, and as well as varying numbers of chemotherapy cycles. However, no significant pre- to post-chemotherapy GMC differences emerged in other groups (Table 1).

The ratio of GMC of tetanus IgG antibodies among CCSs post-chemotherapy to that among CCSs pre-chemotherapy being less than 1 were observed in different age subgroups, solid organ transplantation, and time since last vaccination ($P < 0.05$). No significant differences in the ratio emerged between other groups (Table 1).

Multivariate analysis identified distinct predictors for tetanus IgG antibody dynamics in CCSs following chemotherapy: levels of tetanus IgG antibodies in CCSs pre-chemotherapy, targeted therapies, immunotherapy, the number of chemotherapy cycles and time since last vaccination significantly affected the positive rate of tetanus IgG antibody; Concurrently, GMC of tetanus IgG antibodies in CCSs pre-chemotherapy, history of allergy, immunotherapy and the

number of chemotherapy cycles significantly affected the GMC of tetanus IgG antibody; And positive rate of tetanus IgG antibodies in CCSs pre-chemotherapy and history of allergy significantly affected the ratio of GMC of tetanus IgG antibodies among CCSs post-chemotherapy to that among CCSs pre-chemotherapy (Table 2).

3.2.2 Levels of tetanus IgG antibody in CCSs between pre-chemotherapy, one month post-chemotherapy and healthy children

The positive rate of tetanus IgG antibody among CCSs pre-chemotherapy (81.00%, 307/379) was no significant difference between that observed in healthy controls (82.59%, 313/379) ($\chi^2=0.32$, $P>0.05$). Furthermore, the geometric mean concentration (GMC) of tetanus IgG antibody in CCSs pre-chemotherapy (1.15 ± 0.16 IU/mL) was also no significant difference compared to controls (1.10 ± 0.06 IU/mL) ($t=0.33$, $P>0.05$). Across all subgroups analyzed—different genders, ages, and time since last vaccination—the healthy population consistently exhibited no significant difference of tetanus IgG antibody levels between CCSs post-chemotherapy (all P values > 0.05) (Table 3).

The positive rate of tetanus IgG antibody among CCSs post-chemotherapy (70.45%, 267/379) was significantly lower than that observed in healthy controls (82.59%, 313/379) ($\chi^2=15.54$, $P<0.001$). Furthermore, the geometric mean concentration (GMC) of tetanus IgG antibody in CCSs post-chemotherapy (0.73 ± 0.10 IU/mL) was also dramatically lower compared to controls (1.10 ± 0.06 IU/mL) ($t=3.09$, $P=0.002$). Across all subgroups analyzed—different genders, ages, and time since last vaccination—the healthy population consistently exhibited significantly higher tetanus IgG antibody levels than CCSs post-chemotherapy (all P values <0.05) (Table 4).

3.2.3 Level of tetanus IgG antibody in CCSs after 6 months of chemotherapy

Tetanus IgG antibody levels were measured in 88 CCSs six months after completing chemotherapy. Among these, only 27 cases (30.68%) tested positive for tetanus IgG antibody, while 61 cases (69.32%) were negative; it is recommended these negative individuals receive TTCVs.

3.3 Level of tetanus IgG antibody after revaccination in CCSs post-chemotherapy

Among the 61 CCSs who were negative for tetanus IgG antibodies six months post-treatment, six received TTCV boosters. Post-immunization monitoring revealed GMCs of tetanus IgG antibody as follows: 0.07 IU/mL, 0.16 IU/mL, 0.11 IU/mL, 0.03 IU/mL, 0.19 IU/mL, and 0.13 IU/mL. The positive rate achieved was 66.67% (4/6).

3.4 Safety monitoring of CCSs after revaccination post-chemotherapy

No adverse events following immunization (AEFI) were reported by any of the vaccinated individuals in the case group.

4. Discussion

The evolution of therapeutic modalities in CCSs has significantly improved long-term survival rates^[26]. Paradoxically, this therapeutic success, (especially chemotherapy, leads to a decline in the autoimmune function of CCSs, heightening their risk of infection^[26,27]. Our study revealed that tetanus IgG antibody levels in most CCSs decreased significantly post-chemotherapy compared to pre-chemotherapy levels and fell below those of the healthy population. CCSs receiving TTCVs within six months after treatment completion demonstrated both good efficacy and safety.

In this study, both the positive rate of tetanus IgG antibody and GMC in CCSs

post-chemotherapy (70.45%, 0.73 ± 0.10 IU/mL) were significantly lower than pre-chemotherapy levels (81.00%, 1.15 ± 0.16 IU/mL) and also markedly lower than the healthy population (82.59%, 1.10 ± 0.06 IU/mL). This aligns with the downward antibody trend reported by van der Sluis et al.^[15] The Ministry of Public Health's "Regulations on the Management of Planned Immunization Technology" stipulate that the proportion of tetanus IgG reaching protective levels must exceed 85%. Our results indicate the tetanus IgG levels here fell below this protective threshold and were lower than other domestic studies^[28,29]. Specifically, the post-chemotherapy positive rate of tetanus IgG antibody was less than 85%, and 69.32% of children exhibited negative antibodies six months post-treatment, underscoring the need for vaccination. Key factors influencing tetanus IgG antibody levels include age, chemotherapy exposure, and vaccination.

Age is a key determinant influencing tetanus IgG levels. Both domestic and international research has demonstrated that the positive rate of tetanus IgG declines with advancing age^[30]. This study identified marked differences in the tetanus antibody protection rate among CCSs across various age groups. The protection rate in the 1-6 year-old group was significantly higher than in both the 0-year-old group and the 7-15-year-old group, aligning with China's TTCV immunization program. According to the Childhood Immunization Schedule of National Immunization Program Vaccines and Instructions (2021 Version), China's primary vaccination for infants and young children comprises three doses of DTP administered at 3, 4, and 5 months old, followed by a fourth dose at 18-24 months old. Diphtheria-tetanus (DT) booster doses are then recommended at age 6, findings consistent with other domestic and international studies^[31,32]. This trend mirrors that observed in healthy children. However, in this study, before chemotherapy, the antibody levels of each age group in CCS were only lower in the 5-6 years old group compared to the healthy population. There was no statistically significant difference in antibody levels among the other age groups. But after chemotherapy, in each age group of CCS, except for the 5-6 years old group, the antibody levels of the 2-year-old and 7-9-year-old groups were also significantly lower than those of the healthy population. This also suggests age itself is not the primary driver of the specific attenuation in tetanus antibody levels among CCSs, but is intricately linked to post-chemotherapy immunosuppression. Crucially, the younger the child patient, the greater the risk of losing protective antibody levels after chemotherapy^[33]. This heightened vulnerability may stem from the immune system being particularly sensitive to chemotherapy during its formative stages^[10]. In this study, we found that among children aged 0 years, the percentage with protective antibodies increased after chemotherapy (from 50.00% to 70.00%), after Bonferroni correction, the P-values showed no statistically significant difference ($P < 0.002$ was considered statistically significant). This seems to be inconsistent with the conclusion drawn in this literature. The analysis might be related to the fact that the subjects in this age group were undergoing the immune program of TTCVs, or it might be due to the limited number of people in this age group in our study.

The results of this study suggest that the number of chemotherapy sessions perhaps impacts tetanus IgG antibody levels in CCSs post-chemotherapy. Similar research indicates that children with acute lymphoblastic leukemia face a heightened risk of losing protective antibodies, with the specific tumor treatment plan contributing substantially to this loss of protective humoral immunity^[10]. Studies confirm that some CCSs who underwent chemotherapy have indeed lost protective antibodies against Vaccine-Preventable Diseases (VPDs), a loss linked to chemotherapy-induced alterations within the immune system^[10,34]. Chemotherapy compromises the immune system by non-selectively destroying normal immunologically active cells and suppressing bone marrow function^[35,36]. Furthermore, the immunosuppressive effects triggered by treatment can persist long after therapy concludes. Although CCSs undergo months of immune reconstitution, their immune levels often remain suboptimal^[16,17]. Reilly et al.^[37] observed a significant decline in B-cell counts among children with leukemia following

post-chemotherapy vaccination. Across populations with solid tumors and lymphohematological malignancies, the functional recovery of B cells is typically delayed by at least one year post-chemotherapy^[23]. Impairments in memory B cells can consequently lead to common adverse vaccination reactions in these patients^[38]. Critically, variations between chemotherapy regimens may influence the severity of immunosuppression^[39], strongly suggesting that revaccination strategies require stratification based on the specific treatments received. This finding underscores the necessity for individualized analysis of treatment regimens, a principle emphatically reinforced by Haeusler et al.^[14].

Vaccination remains the most effective and reliable shield against tetanus. Zignol et al.^[40] demonstrated a notably high antibody positive conversion rate following single-dose vaccination in children with hematological malignancies whose tetanus antibodies had waned. Therefore, for CCSs completing chemotherapy, individual tetanus antibody level testing is strongly recommended. If protective antibody levels are insufficient, administering a TTCVs booster shot is advised^[41]; where testing is unavailable, considering a TTCVs booster also offers vital early protection for this vulnerable group. Significant international variations exist regarding the optimal timing for resuming CCS vaccinations and selecting appropriate vaccines post-chemotherapy. The United States endorses administering attenuated live vaccines 3 to 6 months after treatment^[42]. In contrast, China's expert consensus suggests inactivated vaccines at 6 months post-chemotherapy, with attenuated live vaccines considered only after immune function assessment at 12 months^[43]. The SIOP guidelines advocate for individualized delay strategies^[44], aligning with the immune reconstitution time window described by Meisel et al. (median CD4+ recovery time: 8.2 months)^[18]. Premature vaccination risks antigen-presenting cell dysfunction and ineffective memory B cell activation^[45]. However, the CDC's standardized re-vaccination program offers distinct advantages in operational simplicity, particularly for primary care settings^[21]. Balancing scientific rigor with practical accessibility demands further exploration through cost-benefit analysis^[46]. This study confirms that tetanus IgG antibodies plummet significantly in CCSs after chemotherapy, resulting in low protection rates. A comprehensive assessment incorporating chemotherapy intensity, bone marrow suppression severity, and lymphocyte count is crucial. Following clinical evaluation and exclusion of contraindications, administer TTCVs without delay. Crucially, intensified monitoring for post-vaccination adverse reactions is essential to minimize the risk of post-chemotherapy tetanus infection.

This study found that the level of serum tetanus IgG antibodies in CCSs who had a history of allergies with or underwent solid organ transplantation, hematopoietic stem cell transplantation, used anti-rejection drugs or targeted therapy decreased significantly 1 month after chemotherapy compared to before chemotherapy. The analysis suggested that this might be due to the fact that children who received treatments such as solid organ transplantation or hematopoietic stem cell transplantation usually require stronger immunosuppressive regimens and are in an immunosuppressed state; likewise, anti-rejection drugs (such as tacrolimus, cyclosporine, etc.) themselves have immunosuppressive effects and may have already caused the immune system to be in an inhibited state. The CCSs after transplantation may be in the process of immune reconstitution, and their immune system's response to chemotherapy may be different from that of non-transplanted children; targeted therapy may have a more specific mechanism of action and may have different effects on B cells and antibody production compared to conventional chemotherapy. CCSs who received transplantation or used

anti-rejection drugs usually receive more close clinical monitoring and management, including prophylactic infusion of immunoglobulin or other supportive treatments, which may affect antibody levels. Those who needed transplantation or used anti-rejection drugs usually had more severe diseases or more complex treatment histories, which may affect their immune system's response patterns. However, in this study, the sample size of children with solid organ transplantation, hematopoietic stem cell transplantation, anti-rejection drug use or targeted therapy was relatively small, and the statistical test power might be insufficient to detect statistical differences, and further studies with larger sample sizes are needed to further verify these findings.

Compared with other studies, the main advantage of this research lies in that, based on previous studies, it covers a wider range of CCSs and involves more subgroup analyses, to evaluate tetanus IgG antibody levels in CCSs, investigate the longitudinal dynamics before and after chemotherapy, and determine the necessity of post-chemotherapy revaccination with TTCVs. However, it also has some limitations, including: 1) A single-center design may constrain the generalizability of conclusions, though it is noteworthy that this center serves the overwhelming majority of CCSs throughout Zhejiang Province; 2) The scarcity of revaccination cases following chemotherapy restricts robust analysis of different procedures; 3) The size of each subgroup in this study is unbalanced, some subgroups have a relatively small sample size; 4) Cellular immune indicators, characterization of immunosuppressive therapies, etc.(such as T cell ELISpot, were not incorporated. Future research should significantly expand the sample size to compare the efficacy of diverse immune procedures, while incorporating multi-omics techniques — like single-cell sequencing — to elucidate the molecular characteristics underpinning immune memory reconstruction and identify targets for precise vaccination^[47].

5.Conclusion

In conclusion, this dynamic monitoring study revealed that tetanus IgG antibody levels in most CCSs plummeted significantly post-chemotherapy compared to pre-chemotherapy levels, falling below those observed in the healthy population. Continued follow-up further demonstrated that some CCSs tested negative for tetanus IgG antibodies just six months after completing chemotherapy. Importantly, the study found that CCSs receiving TTCVs within six months post-treatment demonstrated both efficacy and safety, with no serious AEFI reported. Therefore, individualized assessment is essential for CCSs. Once disease remission is confirmed and immune function reconstituted, TTCVs should be administered under professional guidance. Concurrently, strengthening doctor-patient communication and public health education is crucial. Through collaborative efforts among families, healthcare providers, and society, vaccination compliance can be enhanced, infection risk minimized, and the quality of life for these survivors significantly improved.

Table 1: Serum Tetanus IgG Antibody Levels Among CCSs Pre- and Post- Chemotherapy

Groups	Total	Qualitative results of tetanus IgG antibodies (N,%)				GMC of tetanus IgG antibodies (IU/mL)						Z/χ_2	P
		Positive pre-chemotherapy	Positive post-chemotherapy	χ^2	P	Pre-chemotherapy y	Post-chemotherapy y	t/F	P	AbT1/2 M (P_{25} , P_{75})			
Gender												-0.91	0.362
Male	211	162(76.78)	142(67.30)	53.14	<0.001	0.83±0.17	0.57±0.13	2.74	0.007	0.69(0.46,0.95)			
Female	168	145(82.30)	125(74.40)	38.81	<0.001	1.56±0.27	0.93±0.16	4.25	<0.001	0.64(0.43,0.98)			
Age (years) ^a												17.44	0.008
0~	10	5(50.00)	7(70.00)	4.29	0.038	0.64±0.22	0.49±0.12	0.87	0.408	0.79(0.48,5.53)			
1~	23	20(86.96)	19(82.61)	0.61	0.435	2.50±1.28	1.61±0.98	2.59	0.017	0.76(0.18,1.21)			
2~	49	47(95.92)	43(87.76)	0.29	0.590	2.01±0.67	0.94±0.27	2.42	0.019	0.51(0.37,0.84)			
3~4	94	87(92.55)	87(92.55)	0.00	1.000	1.82±0.35	1.21±0.25	4.38	<0.001	0.71(0.47,0.91)			
5~6	63	61(96.83)	45(71.43)	5.16	0.023	0.49±0.08	0.28±0.04	4.11	<0.001	0.62(0.45,0.76)			
7~9	58	45(77.59)	38(65.52)	18.64	<0.001	0.69±0.17	0.42±0.13	2.29	0.026	0.66(0.40,0.94)			
10~15	82	42(51.22)	28(34.15)	12.73	<0.001	0.41±0.15	0.41±0.16	0.02	0.987	0.83(0.56,1.12)			
Allergy history												-1.08	0.279
Yes	58	49(84.48)	45(77.59)	12.00	0.001	2.14±0.69	1.53±0.52	3.15	0.003	0.67(0.43,0.92)			
No	321	258(80.37)	222(69.16)	80.96	<0.001	0.98±0.13	0.59±0.08	4.16	<0.001	0.73(0.47,1.08)			
Number of diseases ^{b, c}												3.73	0.155
1	190	152(80.00)	135(71.05)	63.97	<0.001	1.48±0.26	0.89±0.16	3.77	<0.001	0.66(0.43,0.89)			
2	112	93(83.04)	80(71.43)	13.41	0.001	0.94±0.28	0.68±0.22	3.03	0.030	0.72(0.48,1.12)			
≥3	77	62(80.52)	52(67.53)	19.20	<0.001	0.64±0.10	0.42±0.08	3.65	<0.001	0.66(0.44,0.96)			
Tumor types												-0.07	0.943
Leukemia	339	282(83.19)	248(73.16)	76.56	<0.001	1.24±0.17	0.78±0.11	4.81	<0.001	0.67(0.45,0.95)			
Solid tumors	40	25(62.50)	19(47.50)	11.24	0.001	0.46±0.09	0.29±0.06	3.02	0.004	0.69(0.35,1.06)			
Active infection												-0.72	0.471
Yes	165	138(83.64)	120(72.73)	54.59	<0.001	0.97±0.21	0.57±0.15	5.12	<0.001	0.71(0.43,0.98)			
No	214	169(78.97)	147(68.69)	41.98	<0.001	1.30±0.22	0.86±0.14	3.20	0.002	0.66(0.46,0.93)			

Solid organ transplantation											-2.09	0.036
Yes	16	13(81.25)	13(81.25)	16.00	<0.001	0.44±0.08	0.38±0.07	1.11	0.286	0.67(0.43,0.94)		
No	363	294(80.99)	254(69.97)	83.33	<0.001	1.19±0.16	0.75±0.11	4.98	<0.001	0.90(0.67,1.09)		
Hematopoietic stem cell transplantation											-0.65	0.513
Yes	20	20(100.00)	20(100.00)	-	1.000	1.19±0.39	0.90±0.34	0.94	0.362	0.67(0.43,0.95)		
No	359	287(79.94)	247(68.80)	85.69	<0.001	1.15±0.16	0.72±0.11	4.91	<0.001	0.71(0.51,0.99)		
Radiotherapy											-0.34	0.735
Yes	30	28(93.33)	28(93.33)	30.00	<0.001	0.58±0.07	0.35±0.04	3.45	0.002	0.67(0.44,0.97)		
No	349	279(79.94)	239(68.48)	79.24	<0.001	1.20±0.17	0.76±0.11	4.80	<0.001	0.72(0.42,0.91)		
Number of chemotherapy sessions ^b											22.7 7	<0.001
1	131	107(81.68)	100(76.34)	57.91	<0.001	1.39±0.33	1.05±0.25	2.15	0.033	0.68(0.47,1.00)		
2	140	108(77.14)	93(66.43)	36.92	<0.001	0.87±0.18	0.55±0.11	3.37	0.001	0.73(0.55,1.00)		
3	108	92(85.19)	74(68.52)	8.38	<0.001	1.24±0.29	0.58±0.13	3.48	0.001	0.49(0.34,0.85)		
Immunosuppressant use											-0.72	0.473
Yes	7	7(100.00)	7(100.00)	-	1.000	2.42±1.00	1.74±0.93	0.75	0.480	0.67(0.44,0.97)		
No	372	300(80.65)	260(59.89)	90.88	<0.001	1.13±0.16	0.71±0.10	4.94	<0.001	0.51(0.39,0.75)		
Targeted therapy											-1.57	0.120
Yes	8	5(62.50)	7(87.50)	1.91	0.375	0.39±0.13	0.28±0.07	1.47	0.186	0.67(0.44,0.95)		
No	371	302(81.40)	260(70.08)	94.47	<0.001	1.17±0.16	0.74±0.11	4.97	<0.001	1.02(0.51,1.68)		
Immunotherapy											-0.87	0.390
Yes	27	21(77.78)	23(85.19)	2.10	0.148	2.85±1.03	2.23±0.79	2.13	0.043	0.67(0.44,0.97)		
No	352	286(81.25)	244(69.32)	94.04	<0.001	1.02±0.15	0.62±0.09	4.62	<0.001	0.70(0.49,0.94)		
Time since last vaccination (months) ^a											19.3 2	0.004
≤6	15	15(100.00)	10(66.67)	6.00	0.014	1.54±0.36	0.51±0.18	3.51	0.003	0.28(0.15,0.50)		
7~12	34	28(82.35)	23(67.65)	3.92	0.048	1.67±0.87	1.20±0.67	2.23	0.032	0.65(0.42,0.88)		
13~24	87	81(93.10)	72(82.76)	11.03	0.001	1.34±0.39	0.65±0.15	2.73	0.008	0.60(0.39,0.91)		
25~36	55	51(92.73)	53(96.36)	26.46	<0.001	2.03±0.53	1.46±0.41	3.26	0.002	0.67(0.49,0.87)		
37~48	66	55(83.33)	50(75.76)	6.60	0.010	0.90±0.24	0.54±0.13	2.75	0.008	0.67(0.46,0.85)		
49~60	50	40(80.00)	34(68.00)	4.50	0.034	0.46±0.11	0.25±0.03	2.66	0.010	0.71(0.48,0.95)		

≥61	72	37(51.39)	25(34.72)	25.29	<0.001	0.65±0.21	0.60±0.21	0.21	0.836	0.83(0.53,1.11)
Total	379	307(81.00)	267(70.45)	93.66	<0.001	1.15±0.16	0.73±0.10	5.00	<0.001	0.67(0.44,0.97)

Ab T1:GMC of tetanus IgG antibodies among CCSs Post-chemotherapy ; Ab T2: GMC of tetanus IgG antibodies among CCSs Pre-chemotherapy.

^a: Bonferroni correction, $m=7(7-1)/2=21$, correction $\alpha =0.05/21=0.002$; ^b: Bonferroni correction, $m=3(3-1)/2=3$, correction $\alpha =0.05/3=0.017$. ^c: "Number of diseases" refers to other diseases that are concurrently present, apart from tumors.

Table 2: Analysis of Factors Influencing Tetanus IgG Antibody Levels in CCSs
Post-Chemotherapy

Groups	Positive rate of tetanus IgG antibodies (N,%)			GMC of tetanus IgG antibodies (IU/mL)			AbT1/2		
	OR	95%CI	P	β	95%CI	P	β	95%CI	P
Gender									
Male	1			0			0		
Female	1.44	0.73-2.86	0.294	-0.05	-0.27-0.16	0.631	0.30	-0.82-1.41	0.603
Age (years)									
0~	1			0			0		
1~	0.42	0.02-8.90	0.577	0.38	-0.41-1.18	0.344	-3.61	-7.6-0.472	0.083
2~	0.52	0.03-9.31	0.657	0.01	-0.72-0.73	0.986	-1.11	-4.87-2.62	0.559
3~4	1.50	0.10-22.07	0.768	0.25	-0.44-0.95	0.479	-3.07	-6.63-0.50	0.091
5~6	0.41	0.03-6.38	0.521	0.24	-0.50-0.98	0.521	-2.18	-5.96-1.59	0.257
7~9	0.40	0.03-5.74	0.502	0.20	-0.51-0.90	0.588	-3.50	-7.13-0.13	0.059
10~15	0.25	0.02-3.31	0.293	0.20	-0.53-0.93	0.592	-2.68	-6.41-1.06	0.160
Rate of tetanus IgG antibodies in CCSs pre-chemotherapy									
Negative	1			0			0		
Positive	5.08	1.93-13.35	0.001	0.09	-0.20-0.39	0.531	-3.78	-5.29--2.27	<0.001
GMC of tetanus IgG antibodies in CCSs pre-chemotherapy (IU/mL)	10.69	3.25-35.12	<0.001	0.55	0.52-0.59	<0.001	-0.08	-0.26-0.10	0.380
Allergy history									
No	1			0			0		
Yes	1.64	0.61-4.43	0.326	0.35	0.06-0.65	0.018	1.91	0.41-3.42	0.013
Number of diseases ^a									
1	1			0			0		
2	1.12	0.49-2.55	0.794	0.06	-0.20-0.31	0.667	0.85	-0.44-2.14	0.197
≥ 3	1.12	0.47-2.63	0.804	-0.02	-0.3-0.25	0.863	-0.36	-1.78-1.05	0.614
Tumor types									
Leukemia	1			0			0		
Solid tumors	0.55	0.19-1.64	0.283	-0.10	-0.45-0.26	0.599	-0.37	-2.21-1.46	0.692
Active infection									
No	1			0			0		
Yes	0.67	0.33-1.34	0.253	-0.15	-0.36-0.06	0.167	-0.97	-2.06-0.13	0.083
Solid organ transplantation									
No	1			0			0		
Yes	0	0	0.999	-0.01	-1.18-1.16	0.989	-2.01	-8.01-3.99	0.512
Hematopoietic stem cell transplantation									
No	1			0			0		
Yes	0	0	0.999	0.38	-1.04-1.79	0.602	3.72	-3.51-10.96	0.313
Radiotherapy									
No	1			0			0		
Yes	5.19	0.42-63.68	0.198	-0.09	-0.60-0.41	0.716	-1.41	-4.01-1.20	0.290
Immunosuppressant use									
No	1			0			0		
Yes	0	0	0.999	-0.13	-1.75-1.48	0.874	-3.01	-11.30-5.28	0.476
Targeted therapy									
No	1			0			0		
Yes	20.97	1.80-244.60	0.015	-0.01	-0.73-0.72	0.983	-0.61	-4.33-3.11	0.749
Immunotherapy									
No	1			0			0		
Yes	8.87	1.61-48.98	0.012	0.47	0.06-0.89	0.024	-0.28	-2.39-1.83	0.793
Number of chemotherapy sessions									
1	1			0			0		
2	0.57	0.26-1.24	0.154	-0.21	-0.44-0.03	0.081	0.15	-1.07-1.35	0.812
3	0.40	0.17-0.90	0.027	-0.39	-0.64--0.15	0.002	-0.33	-1.60-0.93	0.605
Time since last vaccination (months)									
≤ 6	1			0			0		

7~12	7.07	0.65-76.91	0.108	0.59	-0.04-1.21	0.065	-0.40	-3.61-2.80	0.805
13~24	17.32	1.70-176.96	0.016	0.24	-0.33-0.80	0.411	1.15	-1.75-4.06	0.437
25~36	109.07	6.38-1865.49	0.001	0.59	-0.03-1.22	0.062	1.13	-2.07-4.33	0.488
37~48	16.16	1.45-179.95	0.024	0.39	-0.22-0.99	0.208	0.73	-2.38-3.84	0.645
49~60	19.92	1.67-237.71	0.018	0.27	-0.36-0.89	0.400	-0.91	-4.12-2.30	0.579
≥61	5.36	0.43-67.11	0.193	0.61	-0.10-1.31	0.092	-0.85	-4.47-2.77	0.644

Ab T1:GMC of tetanus IgG antibodies among CCSs Post-chemotherapy ; Ab T2: GMC of tetanus IgG antibodies among CCSs

Pre-chemotherapy.

^: "Number of diseases" refers to other diseases that are concurrently present, apart from tumors.

Table 3: Comparison of Tetanus IgG Antibody Levels Between CCSs Pre-Chemotherapy and Healthy Controls

Groups	Positive rate of tetanus IgG antibodies (N,%)				χ^2	<i>P</i>	GMC of tetanus IgG antibodies (,IU/mL)		t	<i>P</i>
	In CCSs pre-chemotherapy		In healthy controls				In CCSs pre-chemotherapy	In healthy controls		
	Total	Positive	Total	Positive						
Gender										
Male	211	162(76.78)	209	176(84.21)	3.69	0.055	0.84±0.17	1.14±0.08	1.58	0.113
Female	168	145(86.31)	170	137(80.59)	2.00	0.157	1.56±0.27	1.04±0.09	-1.79	0.336
Age (years) ^a										
0~	10	5(50.00)	10	9(90.00)	3.81	0.051	0.64±0.22	1.64±0.26	2.89	0.010
1~	23	20(86.96)	23	23(100.00)	3.21	0.073	2.50±1.28	2.11±0.27	-0.30	0.769
2~	49	47(95.92)	49	49(100.00)	2.04	0.153	2.01±0.67	2.04±0.16	0.05	0.958
3~4	94	87(92.55)	94	87(92.55)	-	1.000	1.82±0.35	1.35±0.13	-1.24	0.215
5~6	63	61(96.83)	63	56(88.89)	2.99	0.084	0.49±0.08	1.00±0.12	3.47	0.001
7~9	58	45(77.59)	58	53(91.38)	4.21	0.040	0.69±0.17	0.68±0.11	-0.07	0.948
10~15	82	42(51.22)	82	36(43.90)	0.88	0.348	0.41±0.15	0.28±0.06	-0.81	0.420
Time since last vaccination (months) ^a										
≤6	15	15(100.00)	31	31(100.00)	-	1.000	1.53±0.36	2.05±0.18	1.44	0.158
7~12	34	28(82.35)	42	40(95.24)	3.31	0.069	1.67±0.87	2.00±0.18	0.41	0.681
13~24	87	81(93.10)	87	81(93.10)	-	1.000	1.34±0.39	1.45±0.15	0.25	0.805
25~36	55	51(92.73)	54	49(90.74)	0.14	0.706	2.03±0.53	0.94±0.13	-1.99	0.051
37~48	66	55(83.33)	48	43(89.58)	0.90	0.343	0.90±0.24	0.88±0.14	-0.05	0.957
49~60	50	40(80.00)	44	38(86.36)	0.67	0.413	0.46±0.11	0.69±0.15	1.01	0.195
≥61	72	37(51.39)	73	31(42.47)	1.16	0.282	0.65±0.21	0.27±0.06	-1.79	0.076
Total	379	307(81.00)	379	313(82.59)	0.32	0.572	1.15±0.16	1.10±0.06	-0.33	0.745

^a: Bonferroni correction, $m=7(7-1)/2=21$, correction $\alpha=0.05/21=0.002$.

Table 4: Comparison of Tetanus IgG Antibody Levels Between CCSs Post-Chemotherapy and Healthy Controls

Groups	Positive rate of tetanus IgG antibodies (N,%)				χ^2	<i>P</i>	GMC of tetanus IgG antibodies (IU/mL)		<i>t</i>	<i>P</i>
	In CCSs post-chemotherapy		In healthy controls				In CCSs post-chemotherapy	In healthy controls		
	Total	Positive	Total	Positive						
Gender										
Male	211	142(67.30)	209	176(84.21)	16.33	<0.001	0.57±0.13	1.14±0.08	3.67	<0.001
Female	168	125(74.40)	170	137(80.59)	1.85	0.173	0.93±0.16	1.04±0.09	0.63	0.526
Age (years) ^a										
0~	10	7(70.00)	10	9(90.00)	1.25	0.264	0.49±0.12	1.64±0.26	3.92	0.002
1~	23	19(82.61)	23	23(100.00)	4.38	0.036	1.61±0.98	2.11±0.27	0.49	0.627
2~	49	43(87.76)	49	49(100.00)	6.39	0.011	0.94±0.27	2.04±0.16	3.53	<0.001
3~4	94	87(92.55)	94	87(92.55)	-	1.000	1.21±0.26	1.35±0.13	0.48	0.631
5~6	63	45(71.43)	63	56(88.89)	6.04	0.014	0.28±0.04	1.00±0.12	5.23	<0.001
7~9	58	38(65.51)	58	53(91.38)	11.47	<0.001	0.42±0.13	0.68±0.11	1.57	0.119
10~15	82	28(34.15)	82	36(43.90)	1.64	0.200	0.41±0.16	0.28±0.06	-0.76	0.448
Time since last vaccination (months) ^a										
≤6	15	10(66.67)	31	31(100.00)	11.59	0.001	0.51±0.18	2.05±0.18	5.37	<0.001
7~12	34	23(67.65)	42	40(95.24)	10.09	0.001	1.20±0.67	2.00±0.18	1.27	0.209
13~24	87	72(82.76)	87	81(93.10)	4.39	0.036	0.65±0.15	1.45±0.15	3.74	<0.001
25~36	55	53(96.36)	54	49(90.74)	1.43	0.231	1.46±0.41	0.94±0.13	-1.22	0.228
37~48	66	50(75.76)	48	43(89.58)	3.54	0.060	0.54±0.13	0.88±0.14	1.84	0.068
49~60	50	34(68.00)	44	38(86.36)	4.40	0.036	0.25±0.03	0.69±0.15	2.90	0.006
≥61	72	25(34.72)	73	31(42.47)	0.92	0.338	0.60±0.21	0.27±0.06	-1.57	0.121
Total	379	267(70.45)	379	313(82.59)	15.54	<0.001	0.73±0.10	1.10±0.06	3.09	0.002

^a: Bonferroni correction, $m=7(7-1)/2=21$, correction $\alpha=0.05/21=0.002$.

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Declaration of interests

No potential conflicts of interest were disclosed.

Authors' contributions

The contributions of authors as following: Writing – original draft: Yuyang Xu, Yan Liu, Chai Ji, Heping Shen, Mingyan Li, Xinren Che, Xuechao Zhang ; Writing – review & editing: Yuyang Xu, Yan Liu, Chai Ji, Heping Shen, Mingyan Li, Xinren Che, Xuechao Zhang ; Conceptualization: Yuyang Xu ; Data curation : Yuyang Xu ; Formal Analysis : Yuyang Xu ; Funding acquisition : Yuyang Xu ; Investigation : Chai Ji, Heping Shen, Mingyan Li, Xuechao Zhang ; Methodology : Yuyang Xu, Yan Liu ; Project administration : Jian Du ; Resources : Yuyang Xu, Yan Liu, Chai Ji, Heping Shen, Mingyan Li ; Software : Yuyang Xu, Yan Liu, Xinren Che, Xuechao Zhang ; Supervision : Jian Du ; Validation : Jian Du ; Visualization : Yuyang Xu, Yan Liu.

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Figures and Tables legends

Table 1: Serum Tetanus IgG Antibody Levels Among CCSs Pre- and Post- Chemotherapy

Ab T1: GMC of tetanus IgG antibodies among CCSs Post-chemotherapy ; Ab T2: GMC of tetanus IgG antibodies among CCSs Pre-chemotherapy.

^a: Bonferroni correction $m=7(7-1)/2=21$, correction $\alpha=0.05/21=0.002$;

^b: Bonferroni correction $m=3(3-1)/2=3$, correction $\alpha=0.05/3=0.017$.

^c: "Number of diseases" refers to other diseases that are concurrently present, apart from tumors.

Comparisons analyzed between Positive of tetanus IgG antibodies pre- chemotherapy and post- chemotherapy using the chi-square test, results are presented as χ^2 values and P values; Comparisons analyzed between GMC of tetanus IgG antibodies pre- chemotherapy and post- chemotherapy using T test (two groups) or ANOVA test (multiple groups), results are presented as t/F values and P values; Comparisons analyzed between Ab T1/2 using the rank sum test: using Mann-Whitney test (two groups) to obtain the Z values and P values, while using Kruskal-Wallis test (multiple groups) to obtain the chi-square values and P values.

Table 2: Analysis of Factors Influencing Tetanus IgG Antibody Levels in CCSs Post-Chemotherapy

Ab T1: GMC of tetanus IgG antibodies among CCSs Post-chemotherapy ; Ab T2: GMC of tetanus IgG antibodies among CCSs Pre-chemotherapy.

^a: "Number of diseases" refers to other diseases that are concurrently present, apart from tumors.

Analysis of Factors Influencing of Positive rate of tetanus IgG antibodies using a logistic regression model to obtain the OR, 95%CI values and P values; Analysis of Factors Influencing of GMC of tetanus IgG antibodies and Ab T1/2 using Generalized Linear Model to obtain the β , 95%CI values and P values.

Table 3: Comparison of Tetanus IgG Antibody Levels Between CCSs Pre-Chemotherapy and Healthy Control

^a: Bonferroni correction, $m=7(7-1)/2=21$, correction $\alpha=0.05/21=0.002$.

Comparisons analyzed between Positive of tetanus IgG antibodies pre- chemotherapy and Healthy Controls using the chi-square test, results are presented as χ^2 values and P values; Comparisons analyzed between GMC of tetanus IgG antibodies pre- chemotherapy and Healthy Controls using T test (two groups) or ANOVA test (multiple groups), results are presented as t/F values and P values.

Table 4: Comparison of Tetanus IgG Antibody Levels Between CCSs Post-Chemotherapy and Healthy Controls

^a: Bonferroni correction, $m=7(7-1)/2=21$, correction $\alpha=0.05/21=0.002$.

Comparisons analyzed between Positive of tetanus IgG antibodies post- chemotherapy and Healthy Controls using the chi-square test, results are presented as χ^2 values and P values; Comparisons analyzed between GMC of tetanus IgG antibodies post- chemotherapy and Healthy Controls using T test (two groups) or ANOVA test (multiple groups), results are presented as t/F values and P values.