Comparative analysis of hematology parameters after Human cytomegalovirus infection in children of different ages

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Abstract

Background: Children vulnerable to Human cytomegalovirus (HCMV) infection, most of them are recessive infection, easy to lead to missed diagnosis. However, missing early diagnosis and treatment may have adverse consequences for the child. Therefore, the purpose of this study was to evaluate the hematological parameters in HCMV-infected infants or children less than 6 years. **Method:**A retrospective analysis of 223 children aged 0-6 years who had accepted urine HCMV-DNA testing in Luohu People's Hospital. The children were divided into 0 day-21 days, 22 days-6 months, 7 months-11 months, 12 months-23 months, and 2 years-6 years groups according to their age when they were tested, and total white blood cell count (WBC), lymphocyte percentage (L%), lymphocyte count (LYM), alanine transaminsase (ALT), aspartate transaminase (AST), γ-glutamy1 transferase (GGT), urea nitrogen (UREA), and creatinine (CREA) of different age groups were compared. **Results:** The L% and LYM of HCMV-infected children aged 0d-6y were significantly higher than those of the control group ($P<0.05$); The ALT and GGT of HCMV-infected children aged 0-12m and AST of HCMV-infected children aged 0d-2y were significantly higher than control group ($P<0.05$), but this difference did not show up among older children ($P<0.05$); Compared with control group, there was no significant difference in UREA and CREA of HCMV-infected children aged 0d-6y ($P>0.05$). In addition, we found that GGT was highest in HCMV-infected children aged 0-21d and decreased with the increase of age. **Conclusion:**HCMV infection can increase lymphocytes in the peripheral blood of children from 0 to 6 years old, and cause more serious hepatobiliary injury to younger children. However, renal damage caused by HCMV is rare in childhood.

1. Introduction

Human cytomegalovirus (HCMV) is a double-stranded DNA virus belonging to the β-herpesviridae family [1]. HCMV infection is common globally, with approximately 60% of people in developed countries having HCMV specific IgG antibodies, while in many developing countries this proportion exceeds 90% [2]. This high prevalence rate of HCMV infection is mainly due to the fact that can be efected at any age through body fluids (i.e., urine, saliva, and human breast milk) from-infected individuals [3], and HCMV persists for the lifetime of the host after primary infection [4]. HCMV infection in adults with normal immune function will not cause obvious clinical symptoms,however, primary infection usually occur in early childhood. A survey of HCMV infection found that HCMV seroprevalence reached 75% in children less than 6 years [5].

Due to the immature development of immune function of young children[6], HCMV infection may cause diseases of liver, blood, digestive tract, kidney, lung and other organs [7-12], and young children have no specific clinical symptoms in the early stage of HCMV infection. Therefore, we need to investigate the hematology parameters (i.e., WBC, L%, LYM, ALT, AST, GGT, UREA, and CREA) of young children of different ages to provide a reference basis for diagnosis and treatment of infants infected with HCMV.

2. Materials and methods

2.1 Study population

This retrospective study collected data from the children (aged 0-6 years) who underwent examine HCMV-DNA at the Department of Medical Laboratory, Luohu People's Hospital, Shenzhen, China, from July 2019 to April 2023. This study was approved by the Reproductive Medicine Ethics Committee of Shenzhen Luohu People's Hospital (2023-LHQRMYY-KYLL-028).

A total of 223 children were included in the study, including 132 HCMV-infected children and 91 non-HCMV-infected children. According to reference intervals of blood cell analysis for children in People's Republic of China (PRC) health industry standard WS/T 779-2021[13], Children were divided into five subgroups (i.e., children at 0 to 21 days (0d-21d, children at 22 days to 6 months (22d-6m, only children younger than 6 months were recruited in this group), children at 7 months to 11 months (7m-11m, only children younger than 1 year were recruited in this group), children at 12 months to 23 months (12m-23m, only children younger than 2 years were recruited in this group), and children at 2 years to 6 years (2y-6y, only children younger than 6 years were recruited in this group) based on the age at which HCMV-DNA was detected. The newborn with HCMV-DNA positive detected in saliva and/or urine of infants aged 0d-21d can be considered as congenital HCMV infection [14].

Inclusion and exclusion criteria are as follows:

Inclusion criteria: (1) HCMV-infected group:HCMV-DNA [?] 4.0×10^2 copies/ml in the urine of child, and the child has not received antiviral treatment; (2) Control group (no-HCMV-infected):HCMV-DNA $<$ 4.0 x 10^2copies/ml in the urine of children and diagnosed as HCMV-infected.

Exclusion criteria: All subjects in this experiment should meet the following exclusion criteria: (1) active or known chronic infection (such as autoimmune disease, diabetes, and cardiovascular disease); (2) infectious diseases (hepatitis virus, herpes virus, rubella virus, rubella virus, mycoplasma, chlamydia, AIDS, syphilis, toxoplasma gondii, and other infections); (3) serious blood disease; (4) history of malignancy.

2.2 Detection of urine HCMV-DNA

This technique is based on TaqMan PCR- Fluorescence probe technology, 1ml of urine specimen was centrifuged at 12000 rpm for 5 min. Urine supernatant was discarded, and the pellet was collected and mixed with 50 μl of DNA extraction solution. Putting the10 μl of the above mixture, 10 μl of the treated negative-positive control,and 10 μl $\times$ 4 of the quantitative reference substance were respectively added into each individual tube with the 40μl PCR mixture (Quantitative Diagnostic Kit for HCMV-DNA, Hunan, China) and centrifuged for 10s, PCR was performed using the 7500 real-time PCR system (Applied Biosystem, CA, USA) Under the following conditions: one cycle of 5for 2 min and 94 for 5 min; followed by 45 cycles of 94 for 15 s and 57 for 31 s; one cycle of 25 for 10 s. The fluorescence signal emitted by fluorescein-labeled probe is collected by PCR instrument, and the amplification curve and Ct value are judged. HCMV DNA [?] 4.0 for 10^2 copies/ml of specimen was regarded as positive.

2.3 Detection of hematological parameters

2.3.1 Detection of White blood cells

2 ml of venous blood of the subjects was drawn into a vacuum blood collection tube containing EDTA-K2 anticoagulant. Blood cells were automatically absorbed, diluted, stained, and measured by routine analyzer (XN-1000, SYSMEX) to obtain the information of blood cells, and then the WBC, L%, and LYM were recorded.

2.3.2 Detection of Liver and kidney function

The venous blood was drawn in a vacuum blood collection tube without anticoagulant. After standing at room temperature for 30 min, the blood was centrifuged at 3500 rpm for 5 min to obtain serum. If the specimen can't be detected in time, refrigerate the centrifuged specimen in a refrigerator at 2-8. The liver and renal function were detected in Automatic biochemical analyzer (COBASC 701, Roche), and then ALT, AST, GGT, UREA, and CREA were recorded.

2.4 Statistical analyses

Statistical analysis was performed using the SPSS ver. 26.0 software (SPSS, Inc., Chicago, IL, USA). Quantitative data (such as WBC, L%, LYM, ALT, AST, GGT, UREA, CREA) with normal distribution or approximate normal distribution were expressed as mean ± standard deviation. T test or Mann-Whitney test was used to compare the data between the two groups. Comparing the data among multiple groups, the analysis of variance or Kruskal Wallis test is adopted. A P -value < 0.05 was considered to be statistically significant.

3. Results

3.1 Patient characteristics

A total of 223 children were enrolled the investigation (Table 1). Out of these, 42 children aged 0d-21d (HCMV infection group (n=20) and control group (n=22)), 98 children aged 22d-6m (HCMV infection group (n=74) and control group (n=24)), 35 children aged 7m-11m (HCMV infection group (n=17) and control group (n=18)), 17 children aged 12m-23m (HCMV infection group (n=6) and control group (n=11)), 31 children aged 2y-6y (HCMV infection group (n=15) and control group (n=16)). The characteristics of all children are shown in Table 1.

3.2 White blood cells related parameters characteristics after HCMV infection in children of different age

To analyze the effect of HCMV infection on white blood cells, we compared the changes of the WBC, L% and LYM in HCMV-infected children and corresponding control group (Table 2). Compared with the corresponding control group the L% and LYM of HCMV-infected children increased significantly in 0d-21d, 22d-6m, 7m-11m, 12m-23m, and 2y-6y groups (P <0.05) (Table 2). The change of WBC is complicated, in the age groups of 22d-6m, 7m-11m and 2y-6y, the WBC of children infected with HCMV is higher than that of their control groups (Table 2). However, there was no significant increase in WBC in groups 0d-21d and 12m-23m compared with the control groups (P <0.05) (Table 2). The results showed that HCMV infection can cause increase lymphocytes in children's peripheral blood, but not all WBC of HCMV-infected children aged 0d-6y were elevated.

3.3 Liver function related parameters characteristics after HCMV infection in children of different ages

To further ascertain the effect of HCMV-infection on Liver function, we compared the changes of the ALT, AST and GGT in HCMV-infected children and control group (Table 3). The ALT of HCMV-infected children within 6 months were significantly higher than their control groups (P <0.05),but there was no significant difference in ALT between HCMV-infected children aged 7m-6y and their control groups (P >0.05) (Table 3). The AST of HCMV-infected children within 2 years was significantly higher than that of their corresponding control groups (P <0.05),but there was no significant difference in AST between HCMV-infected children aged 2y-6y and their control groups (P >0.05) (Table 3). The GGT of HCMV-infected children within 1 years were significantly higher than their corresponding control groups (P <0.05),but there was no significant difference in GGT between HCMV-infected children aged 12m-6y and their corresponding control groups (P >0.05) (Table 3). Therefore, we speculate that HCMV infection has more damage to the liver of younger children than older children.

3.4 Renal function related parameters characteristics after HCMV infection in children of different ages

In order to investigate the effect of HCMV infection on renal function, the changes of CREA and UREA were investigated (Table 4). We found that there was no significant difference in CREA and UREA between HCMV-infected groups aged from 0 to 6y and their control groups (P >0.05) (Table 4). However, CREA levels were significantly higher than normal in three HCMV-infected children aged 0d-21d (Table 4). Therefore, we speculate that HCMV infection has little influence on children aged 0d-6y, or the probability that

HCMV infection has influence on CREA or UREA is rare.

3.5 Hematological parameters of infants and children with HCMV infection in different age groups

There is no significant difference in white blood cells among different age groups except that L% and LYM in group 0-21d are slightly lower than those in group 22d-6m (P <0.05) (Table 5). In addition, HCMV infection in children of different ages can have different effects on liver function, among which the results of ALT in children aged 0d-21d are the lowest, however, infants of 22d-6m are the highest, and then decrease with the increase of children's age (Table 5). AST of 22d-6m and 7m-11m groups was significantly higher than that in 0d-21d, 12m-23m, and 2y-6y groups (P <0.05) (Table 5). The GGT of HCMV-infected children aged 0d-21d was the highest, and then decreased with age (Table 5), which means that CMV may cause less hepatobiliary damage in older children in the 22d-6y age group. And children with 0-21d are special. Because the ALT of Infants aged 0d-21d is lower than other age groups, but GGT is significantly higher than other age groups, which suggests that the injuries of children aged 0d-21d may mainly come from gallbladder and bile duct. As for the effect of HCMV on renal function, UREA had no significant difference among different age groups, but CREA of 0d-21d group was significantly higher than that in other age groups(P <0.05) (Table 5). which indicating that children of 0d-21d age group may have a higher risk of kidney disease after being infected with HCMV.

4. Discussion

Infants or children infected with HCMV are prone to missed diagnosis because the vast majority of infants and children are mainly characterized by occult infection. However, CMV can cause some infants with corresponding complications such as low cellular immune function, deafness and mental retardation.

In the process of HCMV infection, the number, distribution and proportion of WBC in peripheral blood may change. In a retrospective study, it was found that WBC and L% in pneumonia children with HCMV infection within 6 years were higher than those respiratory infection caused by other viruses but no bacterial infection [15]. Moreover, in HCMV-infected children within 3 months,their WBC and LYM were higher than those in normal group (P <0.01)[16]. In this study, we found that the LYM and L% of HCMV-infected children aged 0d-6y were higher than control group, but not all WBC of HCMV-infected children aged 0d-6y were higher than control group. We speculate that the reason may be related to the occurrence of autoimmune neutropenia after HCMV infection or neutropenia caused by ganciclovir treatment [17, 18]. Further studies have found that HCMV can induce specific changes in lymphocyte subsets, which mainly show that HCMV-positive people have more lymphocytes, CD8+T cells and CD28+T cells, and the ratio of CD4+/ CD8+ cells decrease [19]. Moreover, some scholars believe that CD4+ and CD8+T lymphocyte reaction is related to HCMV infection rate and mortality [20], so lymphocyte response plays an important role in controlling HCMV infection.

CMV has a wide tropism to cells, and the liver and gallbladder are also the prone organs of CMV infection. The main manifestations of HCMV liver injury in children are jaundice, hepatomegaly and cholestasis. A significant association between HCMV antibodies and liver enzymes (ALT, AST, and GGT) was found in a HCMV-screening of 455 patients with liver dysfunction [21]. In 49 children with HCMV between 7 days and 32 months of age, Alt and AST were elevated in all patients and 26.5% suffered from cholestasis [22]. Goel et al. found that 52% newborns with cholestasis had HCMV in their liver[23], and a report showed that HCMV can also cause acute cholecystitis in adults with normal immunity [24]. These results suggest that HCMV infection may cause liver and biliary system damage in children. In our study, HCMV-infected childrens' GGT, ALT, and AST were significantly higher than their corresponding control group. But not all children infected with HCMV showed abnormal liver function. About 50% of infants who have been exposed to cervical and vaginal secretions containing HCMV during perinatal period and 50%-60% of infants who have eaten breast milk containing HCMV after birth will develop HCMV infection [25]. In addition, our data showed that the damage of HCMV to gallbladder and bile duct in children aged 0-21d is greater than that to liver, and the damage of HCMV to liver and gallbladder will be weakened with the growth of infant age.

we speculate the reason may be related to the maturation of the infant immune system.

HCMV can replicate in the renal tubules of congenital HCMV-infected children and excrete in urine, which suggests that kidney is the target organ of HCMV [26]. Infants and children are generally susceptible to CMV, but there are few reports about kidney damage caused by CMV infection in infants and children [27]. It is now known that HCMV infection is part of major infection complications following kidney transplantation [28]. In addition, it has been found that HCMV reactivation can lead to an increase in UREA and CREA in patients with sepsis, and these variables are correlated with viral load, but infection with the virus may not be associated with an increased risk of renal malformation [29]. Our data showed that the renal function was no statistical difference between HCMV-infected childrens' and their control groups. Therefore, it can be considered that renal dysfunction caused by HCMV infection is a rare event. In addition, it can also be considered that the degree of renal damage caused by HCMV infection is relatively light, and some more sensitive indicators are needed to monitor.

In addition, the CREA of HCMV-infected children aged 0d-21d was significantly higher than other age groups, but it was no significant difference compared with control group. The reason may be that the CREA of the newborn reflects the state of the mother's renal function, and within 1-2 weeks after the baby is born, CREA will gradually decrease and turn into the real creatinine of the baby [30]。

5. Conclusions

In conclusion, the current analysis reveals that HCMV infection can cause the increase of lymphocytes in children aged 0-6y. The damage of HCMV to liver and gallbladder gradually decreases with age. HCMV infection may have little effect on renal function or be rare cases. Serum creatinine cannot be used to evaluate neonatal renal function because it is affected by maternal renal function. And we anticipate to provide diagnostic value for children infected with HCMV in different age groups through these common hematology parameters.

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Potential Conflict of interest

There are no relevant financial or non-financial competing interests to report.

Author Contributions

Y.Y.W and Z.Z conceived and designed the study; X.M.Z acquired funding; Y.Y.W and Z.Z performed the analysis; D.X contributed analytic tools; D.X and L.J.K supervised the work; Y.Y.W and Z.Z wrote the original draft, reviewed and edited the paper. All authors have read and agreed to the published version of the manuscript.

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References

1 Connolly SA, Jardetzky TS, Longnecker R. The structural basis of herpesvirus entry. Nat Rev Microbiol. 2021;19(2):110-121. doi:10.1038/s41579-020-00448-w.

2 Gugliesi F, Coscia A, Griffante G, et al. Where do we Stand after Decades of Studying Human Cytomegalovirus?. Microorganisms. 2020;8(5):685. doi:10.3390/microorganisms8050685.

3 Fulkerson HL, Nogalski MT, Collins-McMillen D,et al. Overview of Human Cytomegalovirus Pathogenesis. Methods Mol Biol. 2021;2244:1-18. doi:10.1007/978-1-0716-1111-1_1.

4 Krishna BA, Wills MR, Sinclair JH. Advances in the treatment of cytomegalovirus. Br Med Bull. 2019;131(1):5-17. doi:10.1093/bmb/ldz031.

5 Voigt S, Schaffrath Rosario A, Mankertz A. Cytomegalovirus Seroprevalence Among Children and Adolescents in Germany: Data From the German Health Interview and Examination Survey for Children and Adolescents (KiGGS), 2003-2006. Open Forum Infect Dis. 2015;3(1):ofv193. doi:10.1093/ofid/ofv193.

6 Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. Proc Biol Sci. 2015;282(1821):20143085. doi:10.1098/rspb.2014.3085

7 Kabani N, Ross SA. Congenital Cytomegalovirus Infection. J Infect Dis. 2020;221(Suppl 1):S9-S14. doi:10.1093/infdis/jiz446.

8 Hu H, Cheng Y, Peng Q, et al. Clinical Features, Treatment Courses, and Distribution of Cytomegalovirus Genotypes among Thrombocytopenia Patients Aged Younger than 12 Months. Am J Perinatol. 2021;38(13):1403-1411. doi:10.1055/s-0040-1713001

9 Chen J, Zhou Y, Tang J, et al. Minimal adverse outcomes of postnatal cytomegalovirus infection in term or moderate and late preterm infants. Front Pediatr. 2023;11:1048282. doi:10.3389/fped.2023.1048282.

10 Wiemels JL, Talbäck M, Francis S, Feychting M. Early Infection with Cytomegalovirus and Risk of Childhood Hematologic Malignancies. Cancer Epidemiol Biomarkers Prev. 2019;28(6):1024-1027. doi:10.1158/1055-9965.EPI-19-0044.

11 Lee SM, Mitchell R, Knight JA, et al. Early-childhood cytomegalovirus infection and children's neurocognitive development. Int J Epidemiol. 2021;50(2):538-549. doi:10.1093/ije/dyaa232.

12 Degli-Esposti MA, Hill GR. Immune control of cytomegalovirus reactivation in stem cell transplantation. Blood. 2022;139(9):1277-1288. doi:10.1182/blood.2020010028.

13 Ministry of Health of the People's Republic of China. Reference intervals of blood cell analysis for children [J]. WS/T 779-2021.0. Beijing, China: China Standard Press; 2021.

14 Rawlinson WD, Boppana SB, Fowler KB, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. Lancet Infect Dis. 2017;17(6):e177-e188. doi:10.1016/S1473-3099(17)30143-3.

15 Liu Z, Zhang P, Tang S, et al. Urine real-time polymerase chain reaction detection for children virus pneumonia with acute human cytomegalovirus infection. BMC Infect Dis. 2014;14:245. Published 2014 May 8. doi:10.1186/1471-2334-14-245.

16 Zhan C, Wang W, Chen L. Predictive significance of neutrophil-to-lymphocyte and platelet-to-lymphocyte for cytomegalovirus infection in infants less than 3 months: A retrospective study. J Clin Lab Anal. 2022;36(1):e24131. doi:10.1002/jcla.24131.

17 Ross SA, Kimberlin D. Clinical outcome and the role of antivirals in congenital cytomegalovirus infection. Antiviral Res. 2021;191:105083. doi:10.1016/j.antiviral.2021.105083.

18 Penner J, Chan CS, Burns JE, Ali S, Lyall H. Congenital Cytomegalovirus and Autoimmune Neutropenia: Cause or Coincidence?. Pediatr Infect Dis J. 2020;39(4):336-338. doi:10.1097/INF.0000000000002583.

19 Jackson SE, Sedikides GX, Okecha G, et al. Latent Cytomegalovirus (CMV) Infection Does Not Detrimentally Alter T Cell Responses in the Healthy Old, But Increased Latent CMV Carriage Is Related to Expanded CMV-Specific T Cells. Front Immunol. 2017;8:733. doi:10.3389/fimmu.2017.00733.

20 Britt WJ. Maternal Immunity and the Natural History of Congenital Human Cytomegalovirus Infection. Viruses. 2018;10(8):405. Published 2018 Aug 3. doi:10.3390/v10080405.

21 Farag R M A, Alayobi D, Alsaleh K A, et al. Study the Impact of Cytomegalovirus (CMV) Infection and the Risk Factor for Liver Dysfunction in Saudi Patients [J]. Journal of Pure and Applied Microbiology, 2018, 12(3): 1255-66. doi: 10.22207/JPAM.12.3.27.

22 Tezer H, Kanık Yüksek S, Gülhan B, Özkaya Parlakay AN, Tuna Kırsaçlıoğlu C. Cytomegalovirus hepatitis in 49 pediatric patients with normal immunity. Turk J Med Sci. 2016;46(6):1629-1633. doi:10.3906/sag-1507-161.

23 Goel A, Chaudhari S, Sutar J, et al. Detection of Cytomegalovirus in Liver Tissue by Polymerase Chain Reaction in Infants With Neonatal Cholestasis. Pediatr Infect Dis J. 2018;37(7):632-636. doi:10.1097/INF.0000000000001889.

24 Tseng M, Syed T, Prater A, et al. S3469 Cytomegalovirus (CMV) Infection Presenting as Acute Cholecystitis in an Immunocompetent Patient[J]. Am J Gastroenterol, 2021, 116():p S1429. doi: 10.14309/01.ajg.0000787408.62364.22.

25 Kadambari S, Whittaker E, Lyall H. Postnatally acquired cytomegalovirus infection in extremely premature infants: how best to manage?. Arch Dis Child Fetal Neonatal Ed. 2020;105(3):334-339. doi:10.1136/archdischild-2019-317650.

26 Ríos-Barnés M, Fortuny C, Alarcón A, Noguera-Julian A. Renal Involvement in Congenital Cytomegalovirus Infection: A Systematic Review. Microorganisms. 2021;9(6):1304. Published 2021 Jun 15. doi:10.3390/microorganisms9061304.

27 Murugananth S, Padmaraj R, Gopalakrishnan N, et al. Isolated renal involvement of cytomegalovirus inclusion disease in an infant. Saudi J Kidney Dis Transpl. 2018;29(1):198-201. doi:10.4103/1319-2442.225176.

28 Ruan Y, Guo W, Liang S, Xu Z, Niu T. Diagnostic performance of cytomegalovirus (CMV) immune monitoring with ELISPOT and QuantiFERON-CMV assay in kidney transplantation: A PRISMA-compliant article. Medicine (Baltimore). 2019;98(16):e15228. doi:10.1097/MD.0000000000015228.

29 Ríos-Barnés M, Fortuny C, Alarcón A, Noguera-Julian A. Renal Involvement in Congenital Cytomegalovirus Infection: A Systematic Review. Microorganisms. 2021;9(6):1304. Published 2021 Jun 15. doi:10.3390/microorganisms9061304.

30 Mohr Lytsen R, Taageby Nielsen S, Kongsgaard Hansen M, et al. Markers of Kidney Function in Early Childhood and Association With Maternal Comorbidity. JAMA Netw Open. 2022;5(11):e2243146. Published 2022 Nov 1. doi:10.1001/jamanetworkopen.2022.43146.

Table 1. The baseline characteristics of 223 children

Factors	N (%)	HCMV-infected	Control groups
Gender			
Male	125(56.05%)		
Female	98(43.95%)		
Age			
0d-21d	42(18.83%)	20	22
22d-6m	98(43.95%)	74	24
7m-11m	35(15.70%)	17	18
12m-23m	17(7.62%)	6	11
2y-6y	31(13.90%)	15	16
Total	223	132	91

Table 2. Comparison of white blood cell parameters after HCMV infection in children of different ages

	WBC	**WBC**	**WBC**	**L%**	**L%**	**L%**	**LYM**	**LYM**	**LYM**
group	HCMV	Control	*P value*	HCMV	Control	*P value*	HCMV	Control	*P value*
0d-21d	11.86±3.65	12.91±3.18	ns	54.61±15.84	28.15±7.72	<0.01	5.96±1.85	3.4±1.00	<0.01
22d-6m	10.65±3.89	8.26±1.77	<0.01	67.62±10.45	53.55±12.5	<0.01	7.21±3.04	4.22±1.24	<0.01
7m-11m	10.23±2.64	8.48±1.30	<0.05	64.84±11.68	51.81±16.04	<0.05	6.59±1.57	4.31±1.29	<0.01
12m-23m	9.98±3.67	7.42±1.49	ns	64.25±9.34	43.48±9.00	<0.01	6.24±1.83	3.12±0.86	<0.01
2y-6y	10.82±3.23	8.37±1.14	<0.05	61.55±11.73	42.13±7.03	<0.01	6.24±2.39	3.43±0.55	<0.01

Table 3. Comparison of hepatobiliary injury-related parameters after HCMV infection in children of different ages

	ALT	**ALT**	**ALT**	**AST**	**AST**	**AST**	**GGT**	**GGT**
group	HCMV	Control	*P value*	HCMV	Control	*P value*	HCMV	Control
0d-21d	13.48±9.28	8.75±3.15	<0.05	50.81±23.11	33.85±11.81	<0.01	274.64±130.81	107.14±44.75
22d-6m	43.33±33.08	17.18±8.54	<0.01	57.00.±29.8	30.78±14.88	<0.01	62.61±52.2	36.8±25.45
7m-11m	38.22±33.27	22.16±5.01	ns	57.54±26.9	31.95±7.39	<0.01	24.93±19.23	10.83±3.68
12m-23m	28.83±24.24	16.68±5.00	ns	43.3±10.59	29.07±8.25	<0.01	8.25±3.77	12.03±3.07
2y-6y	20.5±16.58	13.66±5.36	ns	33.23±8.51	28.11±5.86	ns	16.81±15.42	12.07±2.98

Table 4. Comparison of kidney injury-related parameters after HCMV infection in children of different ages

	UREA	**UREA**	**UREA**	**CREA**	**CREA**	**CREA**
group	HCMV	Control	*P value*	HCMV	Control	*P value*
0d-21d	3.25±1.51	2.59±1.69	ns	49.31±18.19	41.85±12.07	ns
22d-6m	2.26±0.99	2.45±1.05	ns	25.47±10.60	23.04±6.39	ns
7m-11m	2.47±1.25	3.05±0.94	ns	28.14±5.44	30.64±7.71	ns
12m-23m	4.28±0.75	4.2±1.06	ns	27.88±7.18	26.39±8.43	ns
2y-6y	3.94±1.26	3.97±0.83	ns	32.47±3.95	32.6±8.88	ns

Table 5. Hematological parameters of children with HCMV infection in different age groups

	WBC	**L%**	**LYM**	**ALT**	**AST**	**GGT**	**GGT**	**U**
0d-21d	11.86 ± 3.65^{a}	54.61 ± 15.84^{a}	5.96 ± 1.85^{a}	13.48 ± 9.28^{a}	50.81 ± 23.11^{a}	274.64 ± 130.81^{d}	3.23 ± 1.58^{ab}	3.2
22d-6m	10.65 ± 3.89^{a}	67.62 ± 10.45^{b}	7.21 ± 3.04^{a}	43.33 ± 33.08^{d}	57.00 ± 29.8^{b}	62.61 ± 52.2^{c}	2.45 ± 1.01^{a}	2.4
7m-11m	10.23 ± 2.64^{a}	64.84 ± 11.68^{a}	6.59 ± 1.57^{a}	38.22 ± 33.27^{c}	57.54 ± 26.9^{b}	24.93 ± 19.23^{b}	2.47 ± 1.25^{a}	2.4
12m-23m	9.98 ± 3.67^{a}	64.25 ± 9.34^{a}	6.24 ± 1.83^{a}	28.83 ± 24.24^{b}	43.3 ± 10.59^{a}	8.25 ± 3.77^{a}	4.28 ± 0.75^{b}	4.2
2y-6y	10.82 ± 3.23^{a}	61.55 ± 11.73^{a}	6.24 ± 2.39^{a}	20.50 ± 16.58^{a}	33.23 ± 8.51^{a}	16.81 ± 15.42^{ab}	3.94 ± 1.26^{b}	3.9