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The Impact of Human Cytomegalovirus among Children Patients with Acute Leukemia Undergoing Chemotherapy in Sana'a City-Yemen

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Abstract

Human cytomegalovirus (HCMV) is a DNA virus categorized under the Herpesviridae family and is exclusively present in humans. This study aimed to identify HCMV antibodies and blood parameters in pediatric patients with pediatric leukemia patients with compromised immune systems in Sana'a - Yemen. A cross-sectional study was conducted to examine cytomegalovirus in pediatric leukemia cases are detecting HCMV antibodies and analyzing hematological parameters.in Sana'a city, Yemen, from June to October 2024. A total of 100 blood samples were collected from participants who had compromised immunity. Hematological parameters were evaluated and HCMV antibodies were alongside CMV detection using the ECLIA Cobas e 411 system. The majority of participants under the age of 12, 100% IgG positivity and this recent infection, 4% IgM positivity and this recent infection for HCMV in pediatric leukemia patients and the elevated WBC and PLT counts observed but no numerical data provided. These findings indicated that a high prevalence of HCMV antibodies in children with acute leukemia patients a significant increase of white blood cells (WBCs) and low platelet (PLT) counts in these patients.

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1. INTRODUCTION

Cytomegalovirus (CMV), a member of the herpes virus family, is specifically known as Human Cytomegalovirus (HCMV) and is designated as human herpesvirus 5 (HHV-5). It was first identified in the 1950s [1]. This virus is a double-stranded DNA entity that, like other herpesviruses, can cause latent infections—remaining dormant in the host—following the resolution of acute infections [2].

A key element of the immune system's response to CMV is the production of specific antibodies. These antibodies bind to the virus, thereby inhibiting its capacity to infect new cells and marking it for clearance from the body. The first antibody to emerge in response to CMV is IgM, which can be detected within a few days of the primary infection. While CMV IgG can persist for a lifetime, moderate to high levels of CMV IgM are typically observed during the initial may persist for months in some cases of infection [3]. Many seropositive individuals are asymptomatic but can still shed the virus. This shedding takes place via contact with infected bodily fluids or through organ donation [4, 5]. Typically, the initial exposure to CMV happens during childhood and is often asymptomatic [6]. Acute myeloid leukemia (AML) is a cancerous condition characterized by uncontrolled proliferation of immature myeloid cells in the bone marrow. This results from genetic mutations and chromosomal abnormalities, causing an accumulation of myeloblasts that disrupt normal hematopoiesis and may spread to peripheral tissues [7]. The leukemia accounted for the majority of hematological malignancies (HMs), with a prevalence rate of 94.16%. Among leukemia cases, acute forms (ALL and AML) were more frequently observed than chronic types (CML and CLL) [7].

2. LITERATURE REVIEW

Recent studies emphasize the clinical significance of cytomegalovirus (CMV) in hematological malignancies.[8] demonstrated that 30% of pediatric acute lymphoblastic leukemia (ALL) patients undergoing chemotherapy experienced CMV reactivation, which was strongly associated with febrile neutropenia, prolonged hospitalization, and adverse treatment outcomes. This underscores the need for systematic CMV monitoring in immunocompromised children. Similarly, [9] reported a 91.3% overall CMV seroprevalence in hematological patients, with leukemia cases showing 91% positivity. While their study highlighted age-related increases in CMV prevalence and identified anemia/ALL as risk factors for recurrence . In addition the findings align with [9] work to suggest that leukemia patients—particularly those with ALL—are at heightened risk for CMV-related complications. Together, these studies reinforce the critical role of CMV screening and early antiviral strategies in managing leukemia-associated immunosuppression, a priority relevant to populations with limited healthcare access, such as Yemen. This study aimed to identify HCMV antibodies and blood parameters in pediatric patients with pediatric leukemia patients with compromised immune systems in Sana'a - Yemen.

3. METHODOLOGY

A. Study design and area

The study is a cross-sectional that was carried out in Sana'a, Yemen, from June to October 2024 in Al Kuwait Hospital.

Table 1. Administrative Divisions of Yemen (Selected Governorates)

Governorate	Region	Major Districts/Cities
Amanat Al Asimah	Central Highlands	At Tahrir, Al Wahdah, Al Safiya
Sana'a	Central Highlands	Bani Matar, Hamdan, Arhab
Aden	Southern Coast	Crater, Al Mansoura, Khormaksar
Taiz	Southwest Highlands	Al Mudhaffar, Salah, Al Qahirah
Al Hudaydah	Red Sea Coast	Al Hudaydah City, Bajil, Zabid
Hadramaut	Eastern Desert	Mukalla, Seiyun, Shibam
Marib	Northeast	Marib City, Raghwan, Al Jubah

Study population and sample size

The sample size was calculated using Epi Info (Version 7.2) software, a statistical tool developed by the CDC for epidemiological studies. The following parameters were applied: Confidence level: 95%, expected prevalence of HCMV IgG: Based on prior regional studies, and margin of error: 5–10%. In Associative Analysis Chi-square tests used to identify correlations between HCMV serostatus (IgG/IgM) and hematological parameters (e.g., WBC, platelet counts).Confidence level: 95%, expected prevalence of HCMV IgG: Based on prior regional studies, and margin of error: 5–10%. In Associative Analysis Chi-square tests used to identify correlations between HCMV serostatus (IgG/IgM) and hematological parameters (e.g., WBC, platelet counts).

B. Data collection

An organized survey comprising sociodemographic information (age, sex, parents' educational attainment, and district name and income). The blood samples were collected from the Leukemia Center laboratory in Al-Kuwait Hospital. A questionnaire was made to collect data.

C. Inclusion and exclusion criteria

The children of immunocompromised individuals who presented to Sana'a from various public sectors within Yemen were suspected of exhibiting HCMV infection through the presence of IgG antibodies. The exclusion criteria stipulate that participants must be children above the age of 12 years.

D. Sample collection and analysis of Blood collection

Approximately 3 ml of venous blood was collected from each participant under aseptic conditions using sterile tubes. For hematological analysis, 3 mL of the sample was transferred to an EDTA-containing tube to prevent coagulation. The EDTA tube was then gently inverted 8–10 times (using a tube shaker or manual inversion) to ensure proper mixing with the anticoagulant. Processed for Complete Blood Count (CBC) using an automated hematology analyzer (e.g., MS 625). Centrifuged at 300 round/ min for 10 minutes to separate plasma from cellular components. The resulting plasma supernatant was aliquoted for cytomegalovirus (HCMV) antibody detection via electrochemiluminescence immunoassay (ECLIA) on the Cobas e411 system.

F. Blood hemoglobin assessment

Hematological parameters, such as total red blood cell count (RBC), hemoglobin (Hb) concentration, blood platelet count (PLT), and differential white blood cells (WBC), were measured using a fully automated hematology analyzer MS 625.

G. Detection of Human Cytomegalovirus (HCMV) antibodies

Anti-HCMV antibodies (IgG), IgM were detected serologically using an electrochemiluminescence immunoassay (ECLIA) by Cobas e411 [10].

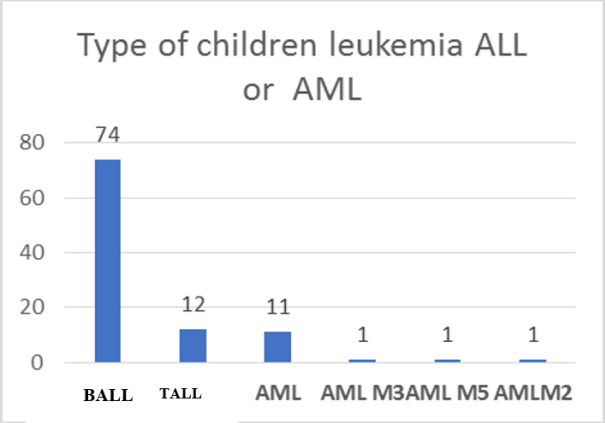

Figure 1. Type of children patients with acute leukemia ALL or AML

4. RESULTS

This study observed that the prevalence of CMV antibodies was equal between male and female participants, with approximately 50% of both sexes testing positive for CMV IgG. In contrast, the positivity rate for IgM was 2% for both males and females. The study also revealed no statistically significant correlation between HCMV antibodies and the age of pediatric leukemia patients,

During the show, figure 1 observed most of the patients ALL type(B). as indicated in Table 2, which shows a p-value of 0.308, exceeding the 0.05 threshold for statistical significance in CMV IgM positivity. Chemotherapy-induced effects induce profound immunosuppression, particularly affecting T-cell function, which is critical for controlling CMV reactivation. The higher IgG seropositivity during chemotherapy (71% vs. 29% before treatment) may reflect reactivation of latent CMV due to immunosuppression rather than new infections. Immune Suppression from Leukemia Itself Leukemia disrupts normal immune function even before chemotherapy, potentially altering CMV antibody dynamics. Impaired humoral immunity in some patients might lead to false-negative IgM results or delayed seroconversion. Socioeconomic Status (SES) and Environmental Exposure CMV seroprevalence is strongly linked to SES, with higher transmission in crowded or low-resource settings. If most patients in the study shared similar socioeconomic backgrounds, this could homogenize CMV exposure rates, masking potential demographic difference. The relationship between CMV infection and hematological parameters in leukemia patients is complex and may involve bidirectional interactions. Leukopenia and Lymphopenia Chemotherapy-induced leukopenia (particularly lymphopenia) is a major risk factor for CMV reactivation due to diminished immune surveillance. Patients with severe or prolonged neutropenia may exhibit higher CMV viral loads, even if serological markers (IgM/IgG) do not fully capture active infection. Thrombocytopenia and Anemia CMV infection can directly suppress bone marrow function, exacerbating chemotherapy-induced thrombocytopenia and anemia. In this study, if CMV reactivation occurs subclinically, it may contribute to delayed platelet and erythrocyte recovery, although serology alone cannot confirm this. The low IgM positivity (2%) suggests that acute CMV infections are rare, possibly due to limited new exposures or delayed IgM production in immunocompromised hosts.

Table 2. The prevalence of HCMV antibodies in different age of leukemia patients

Age Group	patient	IgM Negative	IgM Positive	P-value	IgG Positive	
	%	*No*	%		*No*	%
<5 Years	1.0%	35	35.0%	0.308	36	36.0%
5–9 Years	1.0%	40	40.0%		41	41.0%
>9 Years	2.0%	21	21.0%		23	23.0%
Total	4.0%	96	96.0%		100	100%

The study found that all tested patients were seropositive for CMV IgG, suggesting prior cytomegalovirus (CMV) exposure, which aligns with global seroprevalence data indicating high CMV infection rates, particularly in developing regions [11]. Although no p-value was reported for CMV IgG positivity, the universal seropositivity underscores CMV's endemic nature and potential role as a cofactor in hematological abnormalities.A significant correlation was observed between CMV seropositivity and hematological disturbances, including neutropenia, lymphocytosis, thrombocytopenia, and pancytopenia, whereas leukocytosis was less frequent. Notably, thrombocytopenia affected 54% of patients, consistent with prior studies linking CMV infection to bone marrow suppression and peripheral platelet destruction [12]. CMV-induced cytopenias may result from direct viral marrow infiltration, immune-mediated destruction, or cytokine dysregulation [13]. Additionally, the study highlights a high illiteracy rate among parents of pediatric leukemia patients, which may contribute to delayed diagnosis and poorer health outcomes due to limited health literacy and healthcare access [8]. Socioeconomic disparities are known to influence disease management and survival rates in pediatric oncology [14]. These findings emphasize the need for CMV screening in hematological disorders and targeted health education programs to improve early detection and treatment adherence in high-risk populations Additionally, there was a high percentage of illiteracy among the parents of pediatric leukemia patients.

Table 4 presents the illiteracy rates among the parents, while Table 5 indicates an increase in positive CMV antibodies in patients undergoing chemotherapy, with a sta-

Table 3. Frequency and Percentages of Hematological Parameters among leukemic patients with HCMV IgG Positivity.

Parameter	Category	Frequency (n)	Percentage (%)	P-value
Leukocytosis	Present	21	21.0	0.15
	Absent	79	79.0	
Leukopenia	Present	62	62.0	0.03*
	Absent	38	38.0	
Normal WBC Count	—	17	17.0	—
Pancytopenia	Present	34	34.0	0.21
	Absent	66	66.0	
Neutropenia	Present	62	62.0	0.01*
	Absent	38	38.0	
Lymphocytosis	Present	63	63.0	0.008*
	Absent	37	37.0	
Thrombocytopenia	Present	54	54.0	0.04*
	Absent	46	46.0	

Note *refers to statistical significant .

Table 4. Distribution of leukemia patients Positivity for HCMV regarding chemotherapy.

Education level to the parents patient	Educational level	Frequency	Percentage %
	Illiterate	**71**	**71.0%**
Education Mother	**Did not complete prim**	**10**	**10.0%**
	Secondary	**10**	**10.0%**
	complete primary	**5**	**5.0%**
	high school	**4**	**4.0%**
	Total	**100**	**100.0%**
	Illiterate	**45**	**45.0%**
Education Father	**Did not complete primary school**	**20**	**20.0%**
	complete primary school	**1**	**1..0%**
	secondary school	**21**	**21..0%**
	high school	**13**	**13.0%**

Table 5. Distribution CMV IgG, IgM between patients with use chemotherapy and before use the Chemotherapy.

Leukemia patients regarding chemotherapy	IgM Negative		p-value	IgM Positive		IgG Positive	
	N	%		N	%	N	%
Before chemotherapy	29	29%	0.248	0.0	0%	29	29%
During chemotherapy	67	67%		4	4%	71	71%

tistically significant relationship observed. The study also highlights the distribution of CMV IgG and IgM among patients who received chemotherapy compared to those who did not. A higher percentage of CMV IgG infection was found in patients receiving chemotherapy, although this was not statistically significant, as all patients, regardless of chemotherapy status, tested positive for CMV IgG antibodies. Conversely, CMV IgM positivity was noted in 4% of patients undergoing chemotherapy, with no prior CMV IgG infection detected, and the p-value remained statistically insignificant.

5. DISCUSSION

The study revealed a complete presence of HCMV antibodies among pediatric leukemia patients, patients, with all subjects testing positive for IgG. This observation is consistent with the findings of Loutfy and colleagues, who noted that all 68 leukemic patients in their study displayed anti-HCMV IgG antibodies [15]. These findings align with prior research investigating viral infections, such as human cytomegalovirus (HCMV), in hematological malignancies. Studies by [16, 17] have consistently demonstrated high HCMV seroprevalence in immunocompromised populations, including leukemia patients. For instance, [9] reported a 100% HCMV prevalence in Brazilian acute leukemia patients, mirroring the results of [18], who identified a strong association between viral infections (including HCMV) and chromosomal abnormalities in pediatric leukemia cases. This synergy across global studies underscores the potential role of viral triggers in leukemogenesis, possibly exacerbating hematological disruptions such as abnormal WBC differentials or thrombocytopenia, as observed in our results. The current study found no statistically significant difference in HCMV risk between male and female patients, a result that aligns with other research, including that of [15, 19]. Additionally, the results underscored a troubling level of illiteracy among the parents of these patients, a situation corroborated by [9, 20], who discovered that women without a university education were more likely to be CMV IgG seropositive than their educated peers. The study did not establish any correlation between HCMV and socioeconomic status, despite the high prevalence of HCMV infections among immunocompromised individuals, who are particularly susceptible to opportunistic infections through various transmission

routes, including saliva, blood transfusions, ear drops, kissing, and other bodily fluids. These findings align with established socio-economic correlations regarding CMV prevalence, as indicated in several studies that show individuals from lower socioeconomic backgrounds have higher CMV rates at any age [1]. Furthermore, a notable percentage of patients exhibited thrombocytopenia, which is attributed to the direct effects of CMV on megakaryocyte cells.

The observed **lymphocytosis** further supports an active viral process, as CMV and similar infections often trigger an expansion of lymphocyte populations [21]. In contrast, **leukocytosis** was less common (21%, *p=0.15*), indicating that bacterial co-infections or inflammatory conditions were not predominant in this cohort. Additionally, **pancytopenia** was present in 34% of cases (*p=0.21*), though not statistically significant. This finding may reflect severe or chronic infection, particularly in immunocompromised individuals, as documented in previous studies from Sana'a University [22].

6. CONCLUSION

This investigation revealed a widespread occurrence of Human Cytomegalovirus (HCMV) infection in leukemia patients, demonstrating a high prevalence of specific IgG antibodies (50%) among pediatric cases of acute leukemia. Cytomegalovirus (CMV) often causes fluctuations in hematopoietic conditions, especially in patients who are undergoing chemotherapy, which compromises the immune system. This vulnerability increases the risk of exposure to opportunistic pathogens, leading to the formulation of guidelines for prophylactic strategies, screening, and preemptive interventions for CMV infections. Additionally, CMV remains a significant concern in this population, with CMV antibodies identified in most chemotherapy recipients. HCMV is linked to variations in hematological parameters. It is essential to have a thorough understanding of CMV antibodies in samples from acute leukemia patients, and antiviral medications, such as Ganciclovir or Acyclovir, should be utilized for the prophylaxis of HCMV. These findings highlight the importance of hematological monitoring in patients with suspected viral infections, as leukopenia, neutropenia, and lymphocytosis may serve as key diagnostic indicators. Further research with larger cohorts is recommended to strengthen these associations.

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