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Ocular Manifestations in Children with Acute Leukemia during Chemotherapy: A Correlation with Hematological Parameters

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Abstract

Aim: Thus study aimed to determine the association between hematological parameters (hemoglobin, leukocyte count, and platelet count) and ocular manifestations in children diagnosed with acute leukemia.

Settings and Design: A Cross-sectional design was conducted at the Medan Pediatric Oncology Foundation involving pediatric patients undergoing chemotherapy.

Materials and Methods: Fifty children aged 5 to 18 years with confirmed acute leukemiawew enrolled.Data collection included interviews and comprehensive ophthalmologic examinations (anterior and posterior segment). Hematological parameters assessed were Hb, leukocyte, and platelet counts.

Statistical Analysis: Data were analyzed using descriptive stats and t-test/Mann–Whitney U to compare hematological parameters by ocular status ($p < 0.05$).

Results: A total of 50 patients (27 males [54%], 23 females [46%]) participated. Acute lymphoblastic leukemia (ALL) was diagnosed in 41 patients (82%), and acute myeloid leukemia (AML) in 9 patients (18%). Most children were in the induction phase of chemotherapy (60%). The mean visual acuity was 0.2 Logarithm of the Minimum Angle of Resolution (LogMAR) in the right eye and 0.19 LogMAR in the left eye. Anterior manifestations included subconjunctival hemorrhage (8%), and posterior segment manifestations included retinal exudates and Roth spots (7%). Hemoglobin and platelet levels were significantly associated with ocular manifestations, but not leukocyte counts.

Conclusion: Ocular manifestations are common in children with acute leukemia and are significantly correlated with low Hb and platelet levels. Periodic ophthalmologic evaluations are essential for early detection of ocular complications in this population.

What is already known

Ocular manifestations are frequent in leukemic patients and may correlate with hematologic abnormalities, particularly anemia and thrombocytopenia.

What is new in this study: This study specifically highlights the correlation between reduced hemoglobin and platelet levels with both anterior and posterior ocular manifestations in Indonesian pediatric leukemia patients, underscoring the need for routine eye examinations during chemotherapy to prevent visual complications.

INTRODUCTION

Childhood cancer is one of the non-communicable diseases that has become a significant public health concern globally, including in Indonesia. The World Health Organization (WHO) reports that childhood cancer accounts for 2–4% of all cancer cases in humans. In Indonesia, data from the Cancer Registry System (SriKanDi) from 2005–2007 estimated the incidence of cancer in children aged 0–17 years at 9 per 100,000, with leukemia being the most common type, at 2.8 per 100,000.[1]

Acute leukemia is the most common type of cancer in children under the age of 15, with a global incidence rate of 46.4 per million per year among children aged 0–14 years and 28.5 per million among adolescents aged 15–19 years.[1] Leukemia represents 27% of pediatric cancers in the United States, 30% in Ireland and France, 33% in Germany, and 35% in Shanghai, China. [2] Acute Lymphoblastic Leukemia (ALL) is commonly diagnosed in children and adolescents, while Acute Myeloid Leukemia (AML) is the most frequent acute leukemia among adults.[3] In developing countries, approximately 83% of leukemia cases are classified as ALL, and 17% as AML. In Indonesia, the same data indicated that leukemia ranked first among pediatric cancers, with 4,370 cases (35.2%) in children aged 0–19 years.[4] A study by Sinaga *et al*. (2017) revealed that the highest proportion of leukemia patients were aged 5–14 years (25.6%), and the majority were male (56.8%).[5]

Ocular manifestations in leukemia are important to assess, as they may indicate the initial presentation, relapse, or worsening of the disease.[7]

A study by Bitirgen *et al.* (2018) also reported a significant relationship between low platelet counts and ophthalmic manifestations.[10] Additionally, research by Abu Bukhari *et al*. (2020) found that retinal hemorrhage was more frequently observed in anemic patients. [11]

Therefore, routine eye exams are essential for leukemia patients to monitor potential complications and improve outcomes. This study aims to investigate the ocular manifestations in patients with acute leukemia and their correlation with hematological parameters, emphasizing the importance of early detection and prevention of visual morbidity.

MATERIALS AND METHODS

This study was a Cross-sectional design conducted at the Medan Pediatric Oncology Foundation involving pediatric patients undergoing chemotherapy prospective observational design. The study commencement in August 2024 and informed written consent was obtained from all patients.

Methodology

Patients with acute leukemia who underwent eye examinations were recruited for this study. Patient selection was based on inclusion and exclusion criteria. After the required, total of 50 patients were included in the study. Each patient underwent a comprehensive initial evaluation, including demographic

data, systemic examination, hematological assessment, and ophthalmologic evaluation by an ophthalmologist.

Inclusion Criteria

Inclusion criteria were: (1) pediatric patients aged 5–18 years who had been diagnosed with acute leukemia; (2) patients undergoing chemotherapy for acute leukemia; and (3) patients who provided informed consent to participate in the study.

Exclusion Criteria

Exclusion criteria were: (1) patients with a history of prior ocular surgery; (2) pediatric patients with systemic diseases; and (3) patients whose parents or guardians did not provide consent for participation in the study.

Procedure

Patients and their families were informed about the objectives and procedures of the study. All patients meeting the inclusion criteria had their identities recorded. Visual acuity was assessed using a Snellen chart. Anterior segment examination was performed using a portable slit lamp. Tropicamide 0.5% eye drops were instilled to induce pupil dilation. Posterior segment evaluation was conducted using a fundus camera and Ullmann indirect ophthalmoscopy with a 20D condensing lens. The results of all examinations were documented. Data processing and analysis were subsequently carried out.

Statistical Analysis

Data analysis was conducted analytically and presented in tabular form. Categorical variables were described using frequency distributions, while numerical data were presented as mean ± standard deviation for normally distributed data, or as median (minimum–maximum) for non-normally distributed data. The average values of hematological parameters, including hemoglobin, leukocyte, and platelet counts, were compared based on the presence or absence of ocular manifestations. To determine the relationship between hematological parameters and ocular manifestations in children with acute leukemia undergoing chemotherapy, statistical tests including the t-test and Mann–Whitney U test were used. A p-value < 0.05 was considered statistically significant.

RESULTS

Study Characteristics

The study included 50 pediatric patients with acute leukemia undergoing chemotherapy at the Medan Pediatric Oncology Foundation participated in this study, all of whom met the inclusion criteria presented in Tabel 1.

Correlation Hematological Parameters and Ocular Manifestation

The diagnosed ALL type of leukemia, accounting for 41 patients (82%), and most were undergoing the induction phase of chemotherapy (30 patients, 60%). The average visual acuity was 0.2 LogMAR in the right eye and 0.19 LogMAR in the left eye. The most common complaint was blurred vision (11 patients), followed by red eyes (5 patients, 10%).

Tabel 1. Demographic Characteristics of Pediatric Patients with Acute Leukemia Undergoing Chemotherapy	
Demographic Characteristic	**n = 50**
Sex, n (%)	
Male	27 (54)
Female	23 (46)
Age, years	
Mean (SD)	10,48 (2,9)
Median (Min – Max)	10 (6 – 16)
Type of Leukemia, n (%)	
ALL	41 (82)
AML	9 (18)
Type of Chemotherapy, n (%)	
Induction	30 (60)
Intensification	4 (8)
Consolidation	3 (6)
Maintenance	13 (26)
Visual Acuity OD (Right Eye)	
Mean (SD)	0,2 (0,3)
Median (Min – Max)	0 (0 – 1,1)
Visual Acuity OS (Left Eye)	
Mean (SD)	0,19 (0,4)
Median (Min – Max)	0 (0 – 2,48)
Subjective Complaints, n (%)	
Red eye	5 (10)
Blurred vision	11 (22)
Red, itchy, and watery eyes	1 (2)
Blurred vision and red eye	1 (2)
None	32 (64)

Types of Ocular Abnormalities		n = 100
Anterior Segment		
Ecchymosis		2 (2)
Conjunctivitis		2 (2)
Subconjunctival hemorrhage		8 (8)
Subconjunctival hemorrhage and ecchymosis		4 (4)
None		84 (84)
Posterior Segment		
Retinal exudates		7 (7)
Papilledema		4 (4)
Roth spots		7 (7)
Splinter hemorrhages		2 (2)
Splinter hemorrhages and papilledema		3 (3)
Cotton wool spots		1 (1)
Subhyaloid hemorrhage		1 (1)
Retinal detachment		1 (1)
None		74 (74)
Hematological Parameters	**Mean (SD)**	**Median (Min-Max)**
Haemoglobin, g/dL	10,94 (2,95)	12,1 (6 – 14,7)
Leucocyte, cell/µL	24790 (36610,51)	11000 (1410-172550)
Thrombocyte, thousand/µL	245,67 (161,9)	148,5 (13 – 670)

The most common anterior segment abnormality was subconjunctival hemorrhage in 8 children (8%), while the most frequent posterior segment findings were retinal exudates and Roth spots, each observed in 7 children (7%).

The mean hemoglobin level was 10.94 g/dL, ranging from 6 to 14.7 g/dL. The mean leukocyte count was 24,790/µL, with a minimum of 1,410/µL and a maximum of 172,550/µL. The mean platelet count was 245.67 × 10^3/µL, ranging from 13 × 10^3/µL to 670 × 10^3/µL.

The median hemoglobin level in pediatric patients with acute leukemia and anterior segment ocular manifestations was 8 g/dL, while the median hemoglobin level in those without ocular manifestations was 12.3 g/dL. Using the Mann-Whitney test, a significant relationship was found between hemoglobin

levels and anterior segment ocular manifestations in pediatric patients with acute leukemia undergoing chemotherapy (p=0.007).

The median leukocyte count in patients with anterior segment ocular manifestations was 13,000/µL, while the median in those without ocular manifestations was 11,000/µL. The Mann-Whitney test showed no significant relationship between leukocyte levels and anterior segment ocular manifestations (p=0.910).

The median platelet count in patients with ocular manifestations was 100,000/µL, while the median platelet count in patients without ocular manifestations was 260,000/µL. Using the Mann-Whitney test, a significant relationship was found between platelet count and anterior segment ocular manifestations in pediatric patients with acute leukemia undergoing chemotherapy (p=0.011).

The median hemoglobin level in children with acute leukemia and posterior segment ocular manifestations was 7 g/dL, while in children without ocular manifestations, it was 12.4 g/dL. Using the Mann-Whitney test, a significant relationship was found between hemoglobin levels and posterior segment ocular manifestations in children undergoing chemotherapy (p<0.001).

The median leukocyte count in children with acute leukemia and posterior segment ocular manifestations was 11,000/µL, while in children without ocular manifestations, it was also 11,000/µL. The Mann-Whitney test showed no significant relationship between leukocyte levels and posterior segment ocular manifestations in these patients (p=0.314).

Table 2. The Correlation Between Hematological Parameters and Anterior Posterior Segment Ocular Manifestations in Children with Acute Leukemia Undergoing Chemotherapy

Variable	Ocular Manifestations in the Anterior Segment		p*	Ocular Manifestations in the Posterior Segment		p*
	Present (n=26)	Absent (n=74)		Present (n=26)	Absent (n=74)	
Haemoglobin, g/dL						
Mean (SD)	9,13 (2,88)	11,29 (2,83)	,007	8,05 (2,34)	11,96 (2,4)	<0,001
Median (Min–Max)	8 (6-14,4)	12,3 (6 – 14,7)		7 (6 – 13,8)	12,4 (6-14,7)	
Leucocyte, thousand/µL						
Mean (SD)	17,29 (16,99)	26,2 2 (38,95)	0,910	40,96 (55,2)	19,11 (25,1)	00,314
Median (Min – Max)	13 (1,66-56)	11 (1,41-172,55)		12 (1,41-172,55)	11 (1,41-113)	
Thrombocyte, thousand/µL						
Mean (SD)	153,13 (159,49)	263, 29 (156,16)	0,011	103,19 (93,82)	295,72 (149,68)	<<0,001
Median (Min – Max)	100 (13 – 512)	260 (28 – 670)		69,5 (13-369)	282 (28-670)	

**Mann Whitney*

The median platelet count in children with acute leukemia and posterior segment ocular manifestations was 69,500/µL, while in children without ocular manifestations, it was 282,000/µL.

The Mann-Whitney test revealed a significant relationship between platelet levels and posterior segment ocular manifestations in these children undergoing chemotherapy ($p<0.001$).

Among 50 patients, 8 individuals (13.3%) in the induction phase had anterior segment ocular manifestations. In the intensification phase, 2 out of 8 patients (25%) presented with ocular findings, while 1 out of 6 patients (16.7%) in the consolidation phase had similar manifestations.

Table 3. Correlation Between Chemotherapy Phases and Anterior Posterior Segment Ocular Manifestations in Children with Acute Leukemia Undergoing Chemotherapy

Chemotherapy Phase	Ocular Manifestations in the Anterior Segment		p*	Ocular Manifestations in the Posterior Segment		p*
	Present (n=16)	Absent (n=84)		Present (n=26)	Absent (n=74)	
Induction	8 (13,3)	52 (86,7)	0,803	18 (30)	42 (70)	0,313
Intensification	2 (25)	6 (75)		0	8 (100)	
Consolidation	1 (16,7)	5 (83,3)		2 (33,3)	4 (66,7)	
Maintenance	5 (19,2)	21 (80,8)		6 (23,1)	20 (76,9)	
*Kruskal Wallis						

50 patients in the induction phase, 18 (30%) exhibited posterior segment ocular manifestations. No cases were identified in the intensification phase. In the consolidation phase, 2 of 6 patients (33.3%) had posterior ocular involvement, while in the maintenance phase, 6 of 26 patients (23.1%) presented such findings.

Statistical analysis using the Kruskal-Wallis test revealed no significant relationship between the chemotherapy phase and the presence of posterior segment ocular manifestations (p=0.313).

DISCUSSION

The gender distribution in this study showed a male predominance (54%), consistent with findings by Cristiano *et al*. (55.6%) and Bukhari *et al.* (54.5%).[7,11] Most children in this study were in the induction phase of chemotherapy (60%), which is the initial treatment stage aimed at achieving remission by suppressing leukemic cell proliferation. Overall, visual acuity in both eyes among the subjects fell within the normal range, with a mean visual acuity of 0.2 LogMAR in the right eye and 0.19 LogMAR in the left eye. These findings align with Laimon et al., who reported good visual acuity in 91.4% of cases.[13]

The most commonly reported symptom among children with acute leukemia undergoing chemotherapy was blurred vision (22%), followed by red eyes (10%).[14] These findings align with the study by Isawumi *et al.,* which noted that visual disturbances were the most frequent ocular complaint, occurring in 34% of pediatric leukemia patients. [14] Blurred vision in children with acute lymphoblastic leukemia (ALL) may be attributed to several factors, including anemia, retinal hemorrhage, or papilledema resulting from increased intracranial pressure. Red eyes, on the other hand, are often related to conjunctival hemorrhage caused by thrombocytopenia or inflammatory reactions secondary to leukemic infiltration. [14] The consistency of these findings with previous research highlights the critical role of regular

ophthalmologic evaluations in children with acute leukemia to ensure early detection and management of visual complications that may affect the patient's quality of life.

The most common ocular finding in the anterior segment was subconjunctival hemorrhage, which is associated with thrombocytopenia—a common complication in acute leukemia due to leukemic cell infiltration in the bone marrow that impairs platelet production. In the posterior segment, retinal exudates and Roth spots (each found in 7% of patients) may result from microembolism or vasculopathy related to coagulopathy often seen in leukemia. Papilledema, observed in 4% of patients, could be linked to increased intracranial pressure caused either by central nervous system involvement of leukemic cells or as a secondary effect of therapy. These findings are consistent with the study by Putra et al. (2024), which also noted that retinal hemorrhage in ALL is relatively uncommon—possibly due to vascular compensatory mechanisms or variations in patient characteristics.[15]

This study also identified posterior segment abnormalities, including splinter hemorrhages, cotton wool spots, subhyaloid hemorrhage, and retinal detachment. These findings are consistent with Mirshahi et al., who reported that subhyaloid hemorrhage occurred in approximately 9.5% of children with acute leukemia.[16] The average hemoglobin level found in this study was 10.94 g/dL, suggesting that most children did not present with severe anemia. However, the lowest recorded value of 6 g/dL indicates the possibility of significant bone marrow suppression, likely due to leukemic cell infiltration or the adverse effects of chemotherapy.[17]

Supporting this, El-Zine *et al.* (2024), in the *Universal Journal of Pharmaceutical Research*, observed a post-induction rise in hemoglobin levels in children with acute leukemia—from 8.8 g/dL to 10.8 g/dL—highlighting a positive hematologic response to treatment.[17] In addition, a study by Wicaksono et al. (2023) also reported a significant increase in hemoglobin levels following induction chemotherapy ($p<0.05$), indicating the therapy's effectiveness in improving erythrocyte production.[18]

This study found significant associations between anterior ocular manifestations and both hemoglobin and platelet levels in children with acute leukemia undergoing chemotherapy. Patients with ocular signs had lower mean hemoglobin (9.13 vs. 11.29 g/dL; $p=0.007$) and platelet counts (100,000 vs. 260,000/µL; $p=0.011$). These findings support previous research indicating that anemia and thrombocytopenia increase the risk of intraocular hemorrhage. Leukocyte levels showed no significant association ($p=0.910$), suggesting a limited role in anterior segment involvement.[19]

Hun *et al.* (2021) also reported that higher hemoglobin and platelet levels may offer protective effects against Posterior Reversible Encephalopathy Syndrome (PRES), a common neurological complication in pediatric leukemia patients undergoing chemotherapy.[20]

This study highlights the clinical importance of monitoring ocular signs in children with acute leukemia, as low hemoglobin and platelet levels are linked to higher risk of intraocular complications. Regular hematologic and ophthalmologic evaluations can aid in early detection and treatment adjustments.

However, limitations include a small sample size and difficulty distinguishing disease effects from treatment outcomes.

CONCLUSION

Ocular involvement is a common complication in pediatric patients with acute leukemia, particularly during chemotherapy. This study reinforces existing evidence that anemia and thrombocytopenia are strongly associated with intraocular manifestations such as subconjunctival hemorrhage and retinal findings. However, leukocyte levels and chemotherapy phase showed no significant correlation with ocular outcomes.

Declarations

Funding:

Not applicable

Data Availability Statement

The data supporting this study are available from the corresponding author upon reasonable request.

Conflict of Interest

None declared.

Ethical Approval

This study was conducted in accordance with the principles of the Declaration of Helsinki and relevant national regulations. The study protocol was reviewed and approved by the Institutional Review Board/Ethics Committee of University of North Sumatera (Approval No: 1102/KEPK/USU/2024). Written informed consent was obtained from all participants and/or their legal guardians prior to inclusion in the study.

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