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Factors Associated with the Development of Retinopathy among Leukemia Patients in Khmer-Soviet Friendship Hospital in 2025: Correlation between Hematological Parameters with Retinopathy

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Abstract

Purpose: To identify the factors associated with the development of retinopathy among Leukemia patients in Khmer-Soviet Friendship Hospital in 2025. **Methods**: Prospective cross-sectional study evaluated the correlation between hematological parameters with Leukemia retinopathy. Patients presented with acute or chronic Leukemia which diagnosed and referred from Oncology department will be included in this study. Fisher's Exact Test was applied to examine the association between socio-demographic factors, hematologic parameters, and retinal manifestations among leukemia patients. **Result**: A total of 23 patients (46 eyes) were enrolled into our study, including 12 females (52.17%) and 11 males (47.83%). Median age of the patients was 40 years old ranged from 15 - 72 years old. IQR (Interquartile range) was 31.5 years old. The majority of retinal problems were intra-retinal hemorrhages 28 eyes (60.86%). Leukocytosis, anemia, and thrombocytopenia are the characteristic of leukemia and contribute to both systemic and retinal manifestations. Leukocytosis showed higher odds of intra retinal hemorrhage. In addition, low rate of hemoglobin and platelet count appeared to be associated with increased occurrence of intra retinal hemorrhage; however, the results are not statistically significant. **Conclusion**: Retinal manifestations of leukemia could be detected at initial presentations or relapse. While some manifestations are asymptomatic, others could affect a patient's visual acuity and change their quality of

life, or even the disease course. Cooperation between ophthalmologists and haemato-oncologists is essential for recognizing retinal involvement and disease management.

Keywords

Leukemia Retinopathy, Intra-Retinal Hemorrhage, Roth's Spot, Leukocytosis

1. Introduction

Leukemia is a life-threatening disease of blood and bone marrow malignant disorders which is caused by an abnormal proliferation of immature leukocytes [1] [3]. The data from WHO in 2020 reports 550 Cambodian deaths from leukemia, which accounts for 0.61% of total deaths [2]. Ocular involvement of Leukemia is vital for assessment because ocular symptoms may be the first indication of manifestation, relapse, or early worsening of the condition. Up to 90% of leukemia patients manifests ocular involvements, which commonly results in leukemic retinopathy [3].

In 2015, Jacob Koshy *et al.*, a study conducted in India reported the prevalence of Leukemic ophthalmic lesions were found in 43.8% [4]. Retinal and pre-retinal hemorrhage are commonly found in the posterior segment in Leukemia. Besides, Roth spots, white centered hemorrhages resulting from retinal capillary rupture and extrusion of whole blood, can be found in some cases of leukemic retinopathy. In leukemia, platelet adheres to the damaged endothelium, which initiates a coagulation cascade and forms a white lesion, platelet-fibrin thrombus, in the centre of the hemorrhage. The white centre corresponds to an accumulation of leukemic cells [3]. In 2022, Reza Mirshahi *et al.*, a study conducted in Iran reported low platelet count and low hemoglobin count were found to be associated with intraretinal hemorrhages. In patients with ocular signs, higher mortality rates were observed [5].

Despite these reports, there is very limited published data from Cambodia on the correlation between hematological parameters and retinal manifestations in leukemia. Understanding these associations is essential because retinal findings may serve as surrogate markers of systemic disease severity and prognosis. Identifying hematological parameters of retinopathy could help oncologists and hematologists anticipate ocular complications, initiate timely ophthalmic referral, and improve overall patient outcomes.

Therefore, this study aims to explore the factors associated with the development of retinopathy among acute and chronic leukemia patients at Khmer Soviet Friendship Hospital in 2025. Specifically, it examines the correlation between hematological parameters and the presence of retinopathy, thereby contributing local evidence to guide clinical practice and improve prognostic assessment in Cambodian leukemia patients.

2. Materials and Methods

This prospective cross-sectional was conducted at Oncology and Ophthalmology department of Khmer-Soviet Friendship Hospital from 1st February 2025 - 31st July 2025 (6 months). The study adhered to the principle of the Cambodian medical ethics and was approved by the National Ethics Committee for Health Research (NECHR) number 045. Inclusion criteria were: 1) patients of any age with a confirmed diagnosis of acute or chronic leukemia, 2) patients referred consecutively from the onco hematology service during the study period; 3) patients with complete hematological records (hemoglobin, total leukocyte count, platelet count). Patients with a history of diabetes, hypertension, any intraocular surgeries in the past 3 months, autoimmune disorders, vascular occlusions, or hematological disorders other than leukemia were excluded from the study.

Diagnosis was established through complete blood counts and peripheral smear examination; in cases where bone marrow aspiration was not feasible, persistent hematologic abnormalities (marked leukocytosis, anemia, and/or thrombocytopenia) together with compatible clinical features were accepted as diagnostic criteria.

Due to administrative delays in the initial study site, the research was relocated to Khmer-Soviet Friendship Hospital, which also contains oncology and ophthalmology services. As a result, the final sample size was limited to 23 patients.

All information of each patient was collected and recorded in a checklist. All data of the patients were collected under an informed consent form and will be kept confidentially.

Consent form was obtained from all patients who have received the eyes examination, including: name, gender, age, refractive status, history of ocular trauma or surgery, record of hematological parameters including hemoglobin (Hb), total leukocyte count (TLC), platelet count, duration of illness and treatment.

Visual acuity was assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, and vision categories were defined according to ETDRS scoring standards [6]. In addition, the value of complete blood count was based on the reference intervals provided by the clinical laboratory at Khmer Soviet Friendship Hospital, which are consistent with El Brihi J *et al.* [7].

The complete ophthalmic examination was done including best-corrected visual acuity (BCVA) on Snellen's chart, slit lamp biomicroscopy for the anterior segment and posterior segment evaluation by + 90 D (Volk Optical Inc.), and indirect ophthalmoscope (Keeler Ltd., Winsor, UK). Posterior segment examination was performed after pupillary dilation with 1% tropicamide eye drops (Auromide eye drops, India) by a Retina specialist.

Anterior and posterior segment photographs were taken for records except in patients unable to cooperate for clinical pictures. Intraocular pressure (IOP) was recorded with Air-puff tonometer (Kowa KT-800) except in patients unable to rest chin on the slit lamp, in whom IOP was measured by tonopFen (I-Care).

The primary outcome was the presence of leukemia retinopathy, defined as any

retinal abnormality attributable to leukemia (including intra-retinal hemorrhage, pre-retinal hemorrhage, Roth's spots, cotton wool spot, or vascular changes). Because leukemia is a systemic disease, both eyes of each patient were examined independently. Analyses were conducted at the eye level, with each eye considered a separate unit of analysis. The presence of retinopathy in an eye was sufficient to classify that eye as positive for the outcome.

Data Management and Analysis

All the data obtained were entered into Microsoft Excel and were analyzed by SPSS Version 27. Descriptive statistics were performed to summarize the characteristics of the study population. Continuous variables such as age and hematological parameters (hemoglobin, total leukocyte count, and platelet count) were presented as mean and standard deviation (SD). As the data were not normally distributed, these variables were summarized as median and interquartile range (IQR). Categorical variables, such as gender, occupation, diagnosis type, and retinal manifestations (intra-retinal hemorrhage, Roth's spots, and cotton-wool spots), were summarized as frequencies and percentages.

Due to the sample size is too small, all inferential analyses were conducted exclusively using the Fisher's Exact Test, which provides an exact p-value suitable for small datasets. The Fisher's Exact Test was applied to examine the association between socio-demographic factors, hematologic parameters, and retinal manifestations among leukemia patients. To measure the strength and direction of these associations, Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were calculated from 2× 2 contingency tables. The Fisher's Exact Test provided the p-value for statistical significance, while the Odds Ratio quantified the degree of association between each independent variable and the retinal outcomes. A p-value of less than 0.05 was considered statistically significant for this study.

Multivariate analysis was not performed due to the limited number of participants, which limited the statistical power and reliability of the regression model. Therefore, all reported results are based on Fisher's exact test results only, supported by odds ratios and 95% confidence intervals.

3. Result

3.1. Demographic Characteristics

During the period of study, 23 patients (46 eyes) were admitted in Oncology department and enrolled into this study. There were 12 females (52.17%) and 11 males (47.83%). Median age of the patients was 40 years old ranged from 15 - 72 years old. IQR (Interquartile range) was 31.5 years old. 10 patients (43.48%) were aged between 15 - 30 years old. 6 patients (26.09%) were 31 - 50 years old, and 7 patients (30.43%) were 51 - 72 years old.

Table 1 shows the demographic characteristics, hematological parameters and vision of the patients. Most of the patients live in Phnom Penh and 11 patients (47.83%) are from provinces. The most common occupation of the patients is

worker, which represent 8 patients (34.78%). The median visual acuity was 0.2 of logMAR in both eyes (A lower logMAR value indicates better visual acuity), IQR (Interquartile range) was 0.3 in the right eye and 0.77 in left eye. The duration of illness varies significantly, ranging from acute presentations 3 days to chronic cases lasting for 4 years. Acute Myeloid Leukemia (AML) represents 18 patients (78.26%) while 5 patients (21.74%) were diagnosed with Chronic Myeloid Leukemia [CML]. All of the patients, 11 patients (47.82%) receive the treatment such as chemotherapy, blood transfusion or platelet administration (8 patients received chemotherapy and 3 patients received both blood and platelet administration). An evaluation of the hematological profiles focusing on leukocyte count, hemoglobin level, and platelet count shows, the increasing mean of leukocyte counts (60.87%), reducing of hemoglobin (95.65%) and platelet count (91.30%).

Table 1. Socio-demographic characteristics, hematological parameters and vision of Leukemia patients.

Variable	Category	Total n (%)
Age group (Years)	15 - 31	10 (43.48%)
	31 - 50	6 (26.09%)
	51 - 72	7 (30.43%)
	Median	40
	IQR	31.5
Gender	Female	12 (52.17%)
	Male	11 (47.83%)
Occupation	Farmer	6 (26.09%)
	Student	6 (26.09%)
	Worker	8 (34.78%)
	Unemployment	3 (13.04%)
Diagnosis	Acute	18 (78.26%)
	Chronic	5 (21.74%)
Treatment status	Chemotherapy	8 (34.78%)
	Blood and Platelet infusion	3 (13.04%)
	No	12 (52.17%)
Leukocytes	Low (<4 × 10^9/l)	8 (34.78%)
	Normal (4 - 10 × 10^9/l)	1 (4.35%)
	High (>10 × 10^9/l)	14 (60.87%)
Hemoglobin	Low (<11.5 g/dl)	22 (95.65%)
	Normal (11.5 - 16.5 g/dl)	1 (4.35%)
Platelet	Low (< 150,000/mcl)	21 (91.30%)
	Normal (150,000 - 400,000/mcl)	2 (8.70%)

Continued

Vision Right Eye (LogMAR)	Mild Visual Impairment (0 - 0.4)	17 (73.91%)
	Moderate Visual Impairment (0.5 - 0.9)	2 (8.70%)
	Severe Visual Impairment (1 - 2)	4 (17.39%)
Vision Left Eye (LogMAR)	Mild Visual Impairment (0 - 0.4)	16 (69.56%)
	Moderate Visual Impairment (0.5 - 0.9)	1 (4.35%)
	Severe Visual Impairment (1 - 2)	6 (26.09%)

Note: n = number of participants, % = percentage.

3.2. Retinal Manifestations Base on Acute and Chronic Leukemia

Retinal involvement was seen in 14 patients or 28 eyes (60.86%). Most of the patients were asymptomatic and 6 patients (26.09%) have severe visual impairment; however, only 3 patients (13.04%) reported subjective complaints of vision deterioration. 1 patient presents with vitreous hemorrhage, 1 patient has pre and intra retinal hemorrhage involve macular and 1 patient has nucleus sclerosis cataract which is not relate to retinal problem. Table 2 shows the retinal manifestations of the patients. Retinal manifestations included intra-retinal hemorrhage in 28 eyes (60.86%) Figure 1, pre-retinal hemorrhage in 6 eyes (13.04%), Roth's spot in 12 eyes (26.08%) Figure 1, cotton wool spots in 5 eyes (10.86%), vitreous hemorrhage in 2 eyes (4.34%). One patient of the pre-retinal hemorrhage was breaking into the vitreous. There is no retinal vein occlusion and disc swelling found in the study.

Table 2. Retinal manifestations base on acute and chronic leukemia.

Retinal Manifestations	AML	CML	Total
Intra-retinal hemorrhage	20/36 (55.55%)	8/10 (80%)	28 (60.8%)
Pre-retinal hemorrhage	2/36 (5.55%)	4/10 (40%)	6 (13.04%)
Roth's Spots	8/36 (22.22%)	4/10 (40%)	12 (26.08%)
Cotton wool spot	5/36 (13.88%)	0	5 (10.86%)
Vitreous hemorrhage	2/36 (5.55%)	0	2 (4.34%)
Disc swelling	0	0	0
Retinal vein occlusion	0	0	0

Note: AML: Acute Myeloid Leukemia, CML: Chronic Myeloid Leukemia, Analyses were conducted at the eye level; percentages represent the proportion of eyes with lesions.

3.2.1. Association between Variable and Intra-Retinal Hemorrhage in Leukemia Retinopathy

A total of 23 patients were enrolled into this analysis. Fisher's Exact Test was used to examine the association of intra-retinal hemorrhage Figure 1 in Leukemia retinopathy related to demographic characteristics, hematological parameters and vision of the patients (Supplemental Table 1). Regarding age distribution, patients aged 31 - 50 years old demonstrated higher odds of intra-retinal hemorrhage com-

pared with those younger than 30 years (OR = 5.00, 95% CI: 0.41 - 59.65, P: 0.203), while those older than 51 years had an odd ratio of 1.33 (95% CI: 0.19 - 9.31, P: 0.772). No statistically significant association was observed between age group and the occurrence of intra-retinal hemorrhage (p = 0.405). In addition, Male patients also showed higher odds compared with females (OR = 3.60, 95% CI: 0.61 - 21.03, p = 0.147), but it is not statistically significant (OR = 3.6, 95% CI 0.61 - 21.03; P: 0.147).

The result also shows only occupation level was significantly associated with intra-retinal hemorrhage in Leukemia (P: 0.029). Compared to farmers, workers had lower odds of intra-retinal hemorrhage (OR = 0.33, 95% CI: 0.10 - 1.03, P: 0.015). While this association was statistically significant, the wide confidence interval indicates that the finding should be interpreted cautiously. Students and unemployed patients showed variable odds, but these results were not significant. The odds of intra-retinal hemorrhage were slightly higher among patients receiving chemotherapy (OR = 1.19, 95% CI: 0.19 - 7.45) and blood and platelet administration (OR = 1.42, 95% CI: 0.10 - 20.43) compared with untreated patients; however, these associations were not statistically significant (p = 1.000) (Supplemental Table S2).

In term of hematological parameters, high level of leukocyte counts was associated with higher odds of intra-retinal hemorrhage (OR = 6.1; 95% CI 0.89 - 41.59; P: 0.081) but it indicates this result is not statistically significant. Fisher's Exact Test also demonstrates low rate of hemoglobin and platelet count are likely developing intra-retinal hemorrhage; however, the analysis is not statically significant with p-value of 0.39 and 0.06 respectively. An evaluation of vison, severe loss of vision reports to develop of intra-retinal hemorrhage than those mild loss of vision (OR = 0.52; 95% CI 0.33 - 0.82; P: 0.131).

3.2.2. Association between Variable and Roth's Spot in Leukemia Retinopathy

In analysis of Supplemental Table S1, male patients appeared less likely to present Roth's spots Figure 1 compared with females (OR = 0.44, 95% CI 0.06 - 3.11; P: 0.408), but it is not statistically significant. For treatment status (Supplemental Table S2), Roth's spots were observed in 2 untreated patients (50%) and 2 patients (50%) who had received blood and platelet transfusion. The odds ratio suggested a possible trend toward increased occurrence in the transfusion group (OR = 10.00, 95% CI: 0.58 - 71.20, P: 0.154). However, this association did not reach statistical significance, and given the wide confidence interval, the finding should be interpreted as exploratory rather than confirmatory.

Regarding hematological parameters, high level of leukocyte counts showed higher odds of Roth's spots compared with those with lower counts (OR = 3.88; 95% CI 0.36 - 41.32; P: 0.351). This result suggests a possible relationship, but the wide confidence interval and non-significant p-value indicate that the finding is inconclusive. In term of vison, severe loss of vision in the right eye was associated with higher odds of Roth's spots compared with mild loss (OR = 14.00, 95% CI:

1.05 - 18.54, P: 0.053), while severe vison loss in the left eye showed a similar but non-significant (OR = 4.33, 95% CI: 0.56 - 33.12, P: 0.283). Although the right eye finding approached statistical significance, the small sample size and wide confidence intervals warrant cautious interpretation.

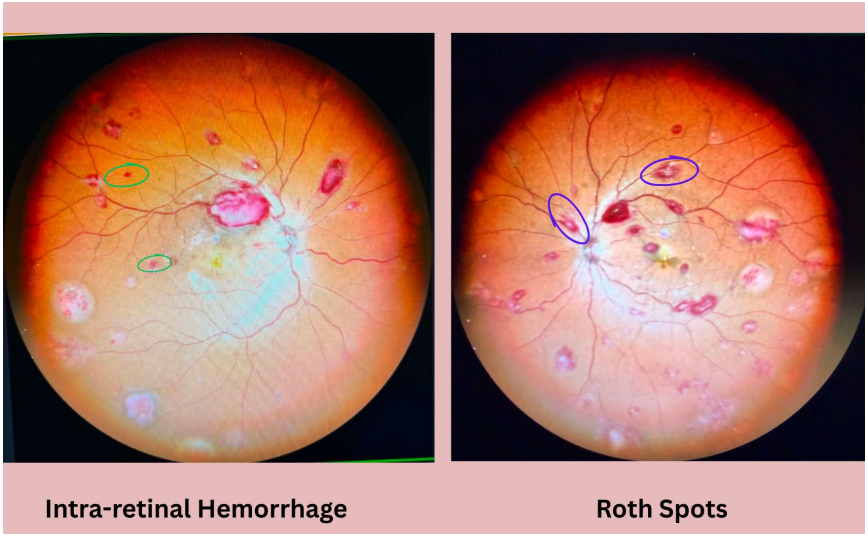

Figure 1. Fundus photo of a patient showing bilateral intra-retinal hemorrhage and Roth's Spots.

3.2.3. Association between Variable and Cotton Wool Spot in Leukemia Retinopathy

In analysis of Supplemental **Table S1**, the result demonstrated student and worker are slightly higher associated of cotton wool spot in Leukemia retinopathy than farmer (OR = 1.5, 95% CI 0.82 - 2.64; P: 0.455) and (OR = 1.14, 95% CI 0.88 - 1.48; P: 1.00), respectively.

In term of vision in the left eye, patients with moderate and severe vision loss had slightly lower odds ratios of cotton wool spots compared to those with mild vision loss (OR = 0.83, 95% CI 0.63 - 1.02; P: 1.00) and (OR = 0.81, 95% CI 0.64 - 1.02; P: 0.532), respectively.

4. Discussion

The current study demonstrates the factors associated with the development of retinopathy among acute and chronic Leukemia patients in Khmer-Soviet Friendship Hospital. Ocular involvement in leukemia is very frequent and 9% to 90% prevalence has been mentioned in various studies [8] [9]. In this study, Leukemia retinopathy was detected in 28 eyes (60.86%) of 23 patients. The majority of retinal problems were intra-retinal hemorrhages 28 eyes (60.86%). Roth's spots, the pathognomonic of Leukemia retinopathy represent 12 eyes (26.08%) of our study.

The prevalence of Leukemia retinopathy in present study is consistent with those reported by Koshy *et al.* [4], who documented leukemia retinopathy in 69% of patients and intra-retinal hemorrhage in 53.5% of cases, suggesting that retinal hemorrhages are a common sign in ocular involvement in leukemia (**Table 3**).

Interestingly, our study demonstrated the highest prevalence of Roth's spots (26.08%) among all reviewed studies. This may reflect differences in diagnostic sensitivity, patient demographics, or disease stage at presentation. Roth's spots may occur in other systemic conditions such as bacterial endocarditis, anemia, or vascular diseases. However, in our study, patients with diabetes, hypertension, autoimmune disorders, vascular occlusions, or hematological disorders other than leukemia were excluded. Therefore, the high prevalence of Roth's spots observed in our cross-sectional study is unlikely to be explained by other comorbid pathologies and more likely reflects the ocular vascular compromise associated with leukemia itself. Roth's spots, although less frequently identified in other studies, ranging from 6.3% in Jacob Koshy's study to 23% in A.M. Abu El-Asrar *et al.*, remain a significant indicator of retinal vascular compromise in leukemia [4] [10].

Cotton wool spots were mentioned in 10.86% of our patients, a rate that is intermediate compared to other studies. While A.M. Abu El-Asrar *et al.* [10] reported a higher prevalence (16%), other studies such as Dina N. Laimon *et al.* and Jihene Sayadi reported markedly lower rates (0.9% and 3.1%, respectively) [9] [11]. The variability in cotton wool spot detection may be attributed to differences in imaging techniques or clinical criteria used for diagnosis (**Table 3**).

Overall, the prevalence of leukemia retinopathy in our study (60.86%) aligns closely with the findings of Jacob Koshy [4] and Jihene Sayadi [11], reinforcing the notion that retinal involvement is a common and clinically relevant manifestation of leukemia. The relatively high rates of intra-retinal hemorrhage and Roth's spots observed in our study underscore the importance of routine ophthalmologic screening in leukemia patients, as early detection of retinal changes may provide insights into systemic disease activity and guide therapeutic interventions.

In our cross-sectional study of 23 leukemia patients, hematologic parameters revealed significant deviations from normal ranges, reflecting the systemic impact of the disease. Notably, leukocyte counts were elevated in the majority of patients, with 60.87% exhibiting leukocytosis. Hemoglobin levels were markedly reduced in nearly all patients, with 95.65% showing anemia. This high frequency highlights the common occurrence of marrow infiltration and impaired erythropoiesis in leukemia, leading to decreased oxygen-carrying capacity and associated clinical symptoms such as fatigue and pallor. Similarly, low platelet count (thrombocytopenia) was found in 91.30% of cases, which is indicative of a higher risk of bleeding problems and the suppression of megakaryocytic lineage. The low platelet count aligns with the high incidence of intra-retinal hemorrhages noted in our ophthalmologic findings (**Table 3**).

Previous studies [5] [10] [12] reported associations between anemia, thrombocytopenia, and retinal hemorrhages in patients with leukemia. In our study, we found similar patterns; however, these associations did not reach statistical significance due to the small sample size. Therefore, these findings should be considered exploratory.

These hematologic abnormalities including leukocytosis, anemia, and thrombocytopenia are characteristic of leukemia and contribute to both systemic and

ocular manifestations. Although lower platelet counts were observed frequently in patients with retinal hemorrhages, this association was not statistically significant. As a result, our report should be interpreted as exploratory and do not provide sufficient evidence to confirm a causal role of thrombocytopenia in leukemia retinopathy.

Table 3. Retinal manifestation in Leukemia retinopathy.

Authors	Number of patients	Intra-retinal hemorrhage	Roth's spots	Cotton wool spot	Leukemia Retinopathy
Our study	23	60.86%	26.08%	10.86%	60.86%
Koshy J *et al.* [4]	96	53.50%	6.30%	7.30%	69%
Laimon DN *et al.* [9]	222	19.80%	17.10%	0.90%	43.20%
Abu el-Asrar AM *et al.* [10]	74	38%	23%	16%	43%
Sayadi J *et al.* [11]	46	86.30%	17.70%	3.10%	50%

The correlation of hematologic parameters to retinopathy revealed high level of leukocyte counts showed higher odds of intra retinal hemorrhage, indicating a possible relationship between leukocytosis and retinal vascular changes, though this was not statistically significant. In addition, low rate of hemoglobin and platelet count were observed more frequent in intra retinal hemorrhage; however, the results are not statistically significant. Because the limited of sample size, these observations should be interpreted as exploratory rather than confirmatory. Correlation of Roth's spot in Leukemia retinopathy elevated leukocyte counts were associated with higher odds which suggest a potential link to retinopathy but the results are also not statistically significant.

In term of vision, 6 patients (26.09%) have severe visual impairment; however, only 3 patients (13.04%) reported subjective complaints of vision deterioration. Some patients with severe visual impairment may not recognize or report visual difficulties due to gradual adaptation with the fellow eye, systemic illness overshadowing ocular symptoms, or limited awareness of visual standards. Therefore, while objective testing revealed a higher prevalence of severe impairment, most patients were clinically asymptomatic from their own perspective. Dina N. Laimon *et al.* [9] also reported 8.6% complained of deterioration of vision, while 6.8% had impaired vision and 1.8% had complete visual loss. Reza Mirshahi *et al.* [5] also mentioned 10.6% patients complained of vision loss. These indicated, the visual disturbance.

5. Limitations

Our study has several limitations. First of all, the sample size is too small (23 cases) cannot cover all possibilities of all Leukemia patients in the study and it severely restricts the statistical power of the study. This is also a reason that we replace Fisher's Exact Test to calculate odd ratio for crude analysis to a standard logistic regression as planned in the research proposal. This minuscule sample size re-

sulted from the hospital's shifting, which left not much time for internal policies and documentations. Secondly, there is no bone marrow aspiration results to confirm a gold standard diagnosis in some patients which is not a strongly evidence of the diagnosis. However, the first-line diagnostic approach in developing countries, clinical signs, basic hematology test and peripheral blood smear also be the practical realities of Leukemia diagnosis. Thirdly, some patients are already received the treatment such as chemotherapy, blood transfusion or platelet administration before the eye's examination. These treatments may have improved hematological parameters and alleviated ocular signs and symptoms. This phenomenon may be described as temporal ambiguity, a limitation inherent in cross-sectional studies as it prevents clear determination of whether retinopathy was directly attributable to leukemia or influenced by treatment effects. Consequently, the observed correlations between hematological parameters and retinopathy should be interpreted with caution. However, this issue can be addressed through the future cohort studies.

6. Conclusions

Based on the result of our finding, we believe that retinal manifestations of leukemia could be detected at initial presentations or relapse. While some manifestations are asymptomatic, others could affect a patient's visual acuity and change their quality of life, or even the disease course. Intra-retinal hemorrhages were the most common reported in Leukemia patients. High level of leukocyte count (Leukocytosis), low level of hemoglobin (anemia), and low level of platelet (thrombocytopenia) are characteristic of leukemia and contribute to both systemic and ocular manifestations.

As study reported high leukocytes, low platelet and hemoglobin are likely risk to have intra-retinal hemorrhage, so cooperation between ophthalmologists and haemato-oncologists by conducting a blood test at each patient's appointment could facilitate the early detection or recognition of retinal manifestations resulting from abnormal hematological parameters. This approach can significantly enhance patient outcomes by allowing for timely interventions. Moreover, we need further evaluation of a larger cohort of acute and chronic leukemia patients especially for survival analysis to set the record for the prognostic value of Leukemia retinopathy in such neoplasms.

7. Recommendations

This study highlights several important factors that influence the prognosis factor of Leukemia patients. To medical professionals, this research identifies the benefit of eyes examination in Leukemia patients by early detection of relapse condition of disease and early worsening. In addition, it is an input contribute to assists Oncologist and Hematologist in prompting interventions, which benefits in better prognosis for patients. To patients, this present study demonstrates that a complete eyes examination with pupil dilation is a standard procedure in Leukemia

patients which is a non-invasive technique. Moreover, other eyes diseases could be diagnosed during this examination.

Author Contributions

All authors read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Krytha Tor: Conceptualization, study design, data collection, ophthalmic examination, data interpretation, manuscript drafting, and manuscript revision; Dyna Khuon: Study co-supervision, statistical analysis, data interpretation, and manuscript revision; Remy Tor: Data collection, literature review, and manuscript revision; Leakhena Or: Data collection and manuscript revision; Keanghak Taing: Data analysis and manuscript revision; Long Chhuor: Patient recruitment, facilitation of clinical examination, and manuscript revision; Chanvatanak Ly: Study supervision, methodology, data interpretation, and critical revision of the manuscript.

Artificial Intelligence Disclosure

The authors used ChatGPT to assist in purpose, improving the grammar, language, and readability of the manuscript after reviewers' comments. The AI tool was not used for data collection, data analysis, interpretation of results, or generation of scientific conclusions. All content was reviewed, verified, and approved by the authors, who take full responsibility for the accuracy and integrity of the manuscript.

Conflicts of Interest

The authors declare that they have no conflict of interest and the research was conducted independently, without any commercial or financial involvement that could be interpreted as a potential conflict of interest.

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Supplemental Table

Table S1. Association between variable, intra-retinal hemorrhage, Roth's spot and Cotton wool spot in Leukemia retinopathy.

Variable	Total n (%)	Variable and intra-retinal hemorrhage in Leukemia retinopathy		Variable and Roth's spot in Leukemia retinopathy		Variable and Cotton wool spot in Leukemia retinopathy	
		OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Age group			**0.405**		**0.828**		**0.513**
<30	10 (43.47%)	Ref		Ref		Ref	
31 - 50	6 (26.08%)	5.00 (0.41 - 59.65)	0.203	2.00 (0.20 - 19.91)	0.604	0.80 (0.58 - 1.09)	0.5
>51	7 (30.45%)	1.33 (0.19 - 9.31)	0.772	1.60 (0.16 - 15.27)	1	0.66 (0.04 - 9.18)	1
Gender			**0.147**		**0.408**		**0.59**
Female	12 (52.17%)	Ref		Ref		Ref	
Male	11 (47.83%)	3.60 (0.61 - 21.03)	0.147	0.44 (0.06 - 3.11)	0.408	0.50 (0.03 - 6.43)	1
Occupation			**0.029**		**0.183**		**0.317**
Farmer	6 (26.09%)	Ref		Ref		Ref	
Student	6 (26.09%)	1.00 (0.09 - 11.02)	1	1.50 (0.85 - 2.64)	0.455	1.50 (0.82 - 2.64)	0.455
Worker	8 (34.78%)	0.33 (0.10 - 1.03)	0.015	1.33 (0.89 - 1.98)	0.473	1.14 (0.88 - 1.48)	1
Unemployment	3 (13.04%)	4.00 (0.21 - 75.65)	0.524	3.00 (0.60 - 14.86)	0.083	1.00 (0.92 - 2.32)	1
Leukocytes			**0.073**		**0.408**		**0.918**
Low	8 (34.78%)	Ref		Ref		Ref	
Normal	1 (4.35%)	0.62 (0.36 - 1.06)	1	0.87 (0.67 - 1.13)	1	0.87 (0.67 - 1.13)	1
High	14 (60.87%)	6.10 (0.89 - 41.59)	0.081	3.88 (0.36 - 41.32)	0.351	1.16 (0.08 - 15.32)	1
Hemoglobin			**0.202**		**0.544**		**0.692**
Low	22 (95.65%)	Ref		Ref		Ref	
Normal	1 (4.35%)	0.36 (0.20 - 0.63)	0.391	0.94 (0.83 - 1.06)	1	0.86 (0.73 - 1.02)	1
Platelet			**0.065**		**0.379**		**0.567**
Low	21 (91.30%)	Ref		Ref		Ref	
Normal	2 (8.70%)	0.33 (0.18 - 0.61)	0.065	0.71 (0.54 - 0.93)	0.379	0.85 (0.72 - 1.02)	1
Vision Right Eye (LogMAR)			**0.21**		**0.043**		**0.544**
Mild	17 (73.91%)	Ref		Ref		Ref	
Moderate	2 (8.70%)	0.88 (0.40 - 16.66)	1	0.82 (0.66 - 1.02)	1	0.81 (0.60 - 1.07)	1
High	4 (17.39%)	0.52 (0.33 - 0.82)	0.131	14.00 (1.05 - 18.54)	0.053	0.82 (0.66 - 1.02)	1
Vision Left Eye (LogMAR)			**0.647**		**0.275**		**0.47**
Mild	16 (69.56%)	Ref		Ref		Ref	
Moderate	1 (4.35%)	1.11 (0.90 - 1.36)	1	0.81 (0.62 - 1.02)	1	0.83 (0.63 - 1.02)	1
High	6 (26.09%)	1.55 (0.21 - 11.08)	1	4.33 (0.56 - 33.12)	0.283	0.81 (0.64 - 1.02)	0.532

Note: OR = Odds Ratio, CI = Confidence Interval, statistically significant ($p < 0.05$), Analyses were conducted at the eye level; percentages represent the proportion of eyes with lesions.

Table S2. Associate variable with treatment status.

Variable	n (%)	OR (95% CI)	P-value
Intra-retinal Hemorrhage			**0.959**
No Treatment	7 (50%)	Ref	
Chemiotherapy	5 (35.7%)	1.19 (0.19 - 7.45)	1
Blood and Platelet infusion	2 (14.3%)	1.42 (0.10 - 20.43)	1
Roth's Spots			**0.080**
No Treatment	2 (50%)	Ref	
Blood and Platelet infusion	2 (50%)	10 (0.58 - 71.20)	0.154
Cotton Wool Spots			
No Treatment	2 (100%)		

Note: n = number of participants, % = percentage, Chi-square test used; Only variables with $p < 0.05$ in bivariate analysis proceed to multivariate analysis.