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OCULAR MANIFESTATIONS IN ACUTE LEUKEMIA: A COMPREHENSIVE ANALYSIS OF RETINAL CHANGES AND CLINICAL CORRELATIONS

Dr. Husain Jasim Abed Al-Khafaji[1], Dr. Amjed Mohsin Zghair[2], Ali Naser Sabah Hammoodi[3]

[1]C.A.B. Ophth, FRCS, FICO, MRCS, HLD, Ministry of Health, Thi-Qar Health Department, Al-Habobi Teaching Hospital, Iraq,
Email: Drnewdream@Yahoo.Com
[2]C.A.B. Ophth., Ministry of Health, Thi-Qar Health Department, Al-Habobi Teaching Hospital, Iraq
Email: Amjedmohsin2@Gmail.Com
[3]C.A.B. Ophth., FICO, MRCS, Ministry of Health, Thi-Qar Health Department, Al-Habobi Teaching Hospital, Iraq
Email: Dr.Ali_Iq@Yahoo.Com

ABSTRACT

Background: Acute leukemia represents a heterogeneous group of hematologic malignancies with significant potential for ocular involvement. The eye serves as a unique window for direct visualization of leukemic manifestations, potentially providing crucial diagnostic and prognostic information.

Objective: This study aimed to comprehensively evaluate the prevalence, patterns, and clinical significance of retinal changes in patients diagnosed with acute leukemia, while establishing correlations with hematologic parameters and disease characteristics.

Methods: A prospective cross-sectional study was conducted at Baghdad Teaching Hospital/Medical City Complex from November 2015 to May 2016. Fifty-three patients (≥14 years) with confirmed acute leukemia (30 AML, 23 ALL) underwent comprehensive ophthalmologic evaluation including dilated fundoscopy, visual acuity assessment, and intraocular pressure measurement. Statistical analysis employed SPSS v.21 with significance set at $p<0.05$.

Results: Retinal abnormalities were identified in 22 patients (41.5%), with comparable prevalence between AML (40.0%) and ALL (43.5%). The most frequent manifestation was intraretinal hemorrhage (34.0%), followed by Roth spots (22.6%) and cotton-wool spots (15.1%). Less common findings included subhyaloid hemorrhage (5.7%), vitreous hemorrhage (3.8%), and optic disc swelling (1.9%). No significant associations were found between retinopathy presence and patient gender, age, or leukemia subtype ($p>0.05$).

Conclusions: Retinal manifestations occur in approximately two-fifths of acute leukemia patients, with intraretinal hemorrhage representing the predominant finding. These results support the implementation of routine ophthalmologic screening in acute leukemia management protocols.

KEYWORDS: acute leukemia; retinopathy; intraretinal hemorrhage; Roth spots; ophthalmologic screening; hematologic malignancy

INTRODUCTION

Acute leukemia includes a heterogeneous group of clonal hematopoietic disorders. These disorders are marked by the rapid proliferation and accumulation of immature blast cells in the bone marrow and peripheral circulation. This pathological process fundamentally impairs access to normal hematopoietic elements, generating hamat hematopoiesis and clinical complications associated with cytopenias and also manifesting through multisystem involvement, including the visual apparatus. Acute myeloid leukaemia (AML) represents approximately 80% of adults' acute leukaemia. In children, acute lymphoblastic leukaemia (ALL) is the most common but does not exclusively affect adolescents and adults.

The eye symptoms in people with acute leukemia comprise actual leukaemia spread in the eyes, hematological disturbances effect and treatment related damage. Due to the unique anatomy of the eye, its transparent media, and ability to achieve direct visualization, clinicians can observe microvascular changes and tissue infiltration, thereby enabling real-time observation of disorders and disease process or treatment response. The retina is a part of the central nervous system and has a rich blood supply due to the blood-retinal barrier it is more prone to leukemic involvement [3,4].

The emergence of eye symptoms in acute leukemia stems from several distinct mechanisms. There are direct leukemic cell infiltration in the eye tissues creates mass effects and distorts the normal anatomic relationships. The effect of pancytopenia itself, especially bleeding due to thrombocytopenia and hypoxic changes from anemia. The conditions of hyperviscosity syndrome, coagulopathy and immunosuppression leading to opportunistic infections may cause tertiary effects. The retinal vasculature is vulnerable to leukaemia involvement, similar to that of one of the CNS circulations [5,6]. With respect to acute leukemia, ocular manifestations carry clinical implications. According to our findings, the condition may lie under systemic diagnosis if the patient presents

with complaints related to vision. The ocular manifestations show that the severity and patterns of ocular involvement correspond to greater disease burden, poorer prognosis, impaired treatment responses and may serve as a potential biomarker in clinical practice. Modern hematology stresses the use of multidisciplinary therapy for effective treatment of acute leukemia[7,8]

Although acute leukemia with ocular manifestations is known, not much information is available about the prevalence, risk factors and clinical associations of acute leukemia with ocular manifestation among certain populations in a geographical area. The current evidence base lacks representation from the Middle Eastern population, including Iraq, and there is a need for region-specific data to help inform local guidelines. To achieve this aim, it attempts to study the ocular manifestation in Iraqi patients with acute leukemia. The objectives were to find (i) the prevalence of retinal lesions (ii) the spectrum and frequency of ocular lesions (iii) a correlation between ocular lesions and other clinical/ demographic data (iv) evidence-based recommendations for eye examination.

2. LITERATURE REVIEW

By the late 1800s, an association between leukemia and eye findings was noted, with early reports dealing mainly with anatomic changes seen at autopsy. The first use of direct opthalmoscope has made observation of retina in vivo possible. Subsequently, developments in indirect opthalmoscopy, fluorescein angiography, and optical coherence tomography have sharpened our diagnostic abilities [6,9].

International studies have reported the prevalence of ocular involvement in leukaemia ranges from 28% to 90%. Such variability reflects differences in study populations as well as diagnostic criteria, examination techniques, and disease stages at presentation. Reddy and Jackson [3] found a prevalence of 42% in Malaysian patients while Abu-El-Asrar et al. [8] found 45% in Saudi patients. Prevalence studies in Europe are 30-45% common, while in Asia the rates are 50 - 75%. This indicates that perhaps there may be a genetic or environmental cause for the differences in expression of the illnesses.

Contemporary methods of tackling ocular manifestations related to leukaemia depend on elaborate classification systems, which divide the findings based on pathogenic mechanisms. When ocular tissues are infiltrated by leukemic cells, it would result in specific manifestations that vary by anatomy and cell type. Signs from complications of leukemia caused by e.g. anemia, thrombocytopenia, hyperviscosity, and coagulopathy. According to various studies, the most common findings are hemorrhagic manifestations especially intraretinal hemorrhages and Roth spots [3,5,12].

Molecular biology has now provided enhanced understanding of leukemic ocular involvement at the cellular level. Ocular manifestations are the result of the combinatorial effects of blast cell adhesion molecules, cytokine networks and angiogenic factors. Some patterns of eye involvement may have prognostic value according to emerging evidence. When presented with retinal hemorrhage, high blast counts and a more aggressive disease course of the disease take place. Moreover, optic nerve infiltration may indicate CNS involvement [13,14].

3. MATERIALS AND METHODS

3.1 Study Design and Setting

This study was conducted in the Hematology Department of Baghdad Teaching Hospital, Baghdad Medical City Complex, Baghdad, Iraq as a prospective cross-sectional study. The study period was from November 01, 2015, to May 01, 2016. In other words, it included both inpatient and outpatient populations in the hospital to get a true picture of the acute leukaemias. After being ethically approved by the Institutional Review Board of Baghdad Teaching Hospital, all subjects were asked to give their written consent.

3.2 Participant Selection

Inclusion Criteria:

- Age ≥14 years with confirmed diagnosis of acute leukemia (AML or ALL) based on morphologic, cytochemical, immunophenotypic, and genetic criteria; availability for comprehensive ophthalmologic examination; and provision of informed consent for study participation.

Exclusion Criteria:

- Pre-existing diabetes mellitus (Type 1 or 2); documented hypertension (systolic BP >140 mmHg or diastolic BP >90 mmHg); known hemoglobinopathies (sickle cell disease, thalassemia); history of cranial or orbital radiation therapy; previous ophthalmologic surgery or trauma; concurrent use of medications known to cause retinal toxicity; and inability to undergo adequate ophthalmologic examination due to critical illness.

3.3 Ophthalmologic Examination Protocol

An approved ophthalmologist completed the extensive ophthalmologic evaluation on all participants. The review process included assessing ocular history and symptoms, assessment of best corrected visual acuity using standardised Snellen charts, measurement of intra ocular pressure using Goldmann applanation tonometry, Slit lamp biomicroscopy of anterior segment structures, 1% tropicamide drops, direct and indirect ophthalmoscopy using +90D condensing lens for detailed examination of retina, and systematic observation of optic disc, macula, retinal vessels, and the peripheral retina. Digital fundus photography was done if available for documentation purposes.

3.4 Statistical Analysis

SPSS version 21.0 (IBM Corporation, Armonk, NY) was used for data analysis. The continuous variables are expressed as means with standard deviations and categorical variables as frequencies with percentages. For the continuous variables independent samples t-tests were made use of and for that of categorical the chi-square test. When the expected count of a cell was <5, Fisher's exact test was used. To identify independent predictors of retinopathy, a multivariate logistic regression was constructed. Statistical significance was $p<0.05$ and confidence intervals were set at 95%.

4. RESULTS

4.1 Study Population Characteristics

A total of 53 patients were enrolled in the study, all of whom were diagnosed with acute leukemia. Their profile was very much similar to that of the local population.

Of the patients involved in this study, 30 patients (56.6%) had acute myeloid leukaemia (AML), while 23 patients (43.4%) had acute lymphoblastic leukaemia (ALL). The gender distribution in both types of leukemia was balanced with a male count of 50.9% in the overall population. The age distribution of patients with AML and ALL did not statistically differ (p=0.592), signifying comparable ages.

Table 1. Demographic and Clinical Characteristics of Study Population

Characteristic	Total (n=53)	ALL (n=23)	AML (n=30)	p-value
Gender Distribution				
Male	27 (50.9%)	11 (47.8%)	16 (53.3%)	0.679
Female	26 (49.1%)	12 (52.2%)	14 (46.7%)	
Age Statistics				
Mean ± SD (years)	30.8 ± 11.0	29.9 ± 8.9	31.5 ± 12.5	0.592
Median (years)	28.0	28.0	28.5	
Range (years)	14-60	16-45	14-60	
Leukemia Subtype				
AML	30 (56.6%)	-	30 (100%)	-
ALL	23 (43.4%)	23 (100%)	-	-

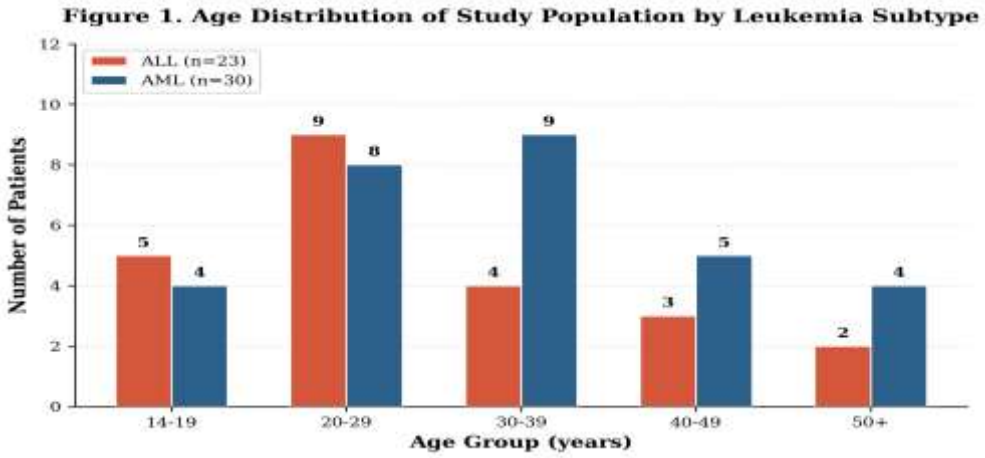


Figure 1. Age Distribution of Study Population by Leukemia Subtype

4.2 Comprehensive Analysis of Ocular Manifestations

The eye examination revealed a variety of abnormalities in the retina. The most frequently encountered finding was intraretinal haemorrhage (34.0%) which was noted to occur more in AML patients (40.0%) than ALL patients (26.1%); however, the difference was not statistically significant (p=0.289). Roth spots were the second most

common finding (22.6%), showing similar distribution of subtypes. Certain manifestations occurred exclusively or predominantly in specific leukemia subtypes: vitreous hemorrhage, hard exudates, and tortuous dilated veins occurred only in ALL patients; splinter hemorrhages occurred exclusively in AML patients.

Table 2. Comprehensive Analysis of Retinal Manifestations in Acute Leukemia Patients

Ocular Finding	Total n(%)	ALL n(%)	AML n(%)	p-value	95% CI
Any Retinopathy	22 (41.5%)	10 (43.5%)	12 (40.0%)	0.793	28.1-55.9%
Hemorrhagic Manifestations					
Intraretinal hemorrhage	18 (34.0%)	6 (26.1%)	12 (40.0%)	0.289	21.8-48.0%
Roth spots	12 (22.6%)	4 (17.4%)	8 (26.7%)	0.424	12.3-36.2%
Subhyaloid hemorrhage	3 (5.7%)	2 (8.7%)	1 (3.3%)	0.402	1.2-15.7%
Vitreous hemorrhage	2 (3.8%)	2 (8.7%)	0 (0.0%)	0.100	0.5-13.0%
Splinter hemorrhage	2 (3.8%)	0 (0.0%)	2 (6.7%)	0.207	0.5-13.0%
Ischemic Manifestations					
Cotton-wool spots	8 (15.1%)	3 (13.0%)	5 (16.7%)	0.715	6.7-27.6%
Hard exudates	2 (3.8%)	2 (8.7%)	0 (0.0%)	0.100	0.5-13.0%
Vascular Abnormalities					
Tortuous dilated veins	2 (3.8%)	2 (8.7%)	0 (0.0%)	0.100	0.5-13.0%
Infiltrative Manifestations					
Optic disc swelling	1 (1.9%)	1 (4.3%)	0 (0.0%)	0.249	0.05-10.1%
Severity Classification					
Mild (1-2 findings)	13 (24.5%)	6 (26.1%)	7 (23.3%)	0.817	13.8-38.3%
Moderate-Severe (≥3)	9 (17.0%)	4 (17.4%)	5 (16.7%)	0.951	8.1-29.8%
No findings	31 (58.5%)	13 (56.5%)	18 (60.0%)	0.793	44.1-71.9%

Figure 2. Prevalence of Retinal Manifestations by Leukemia Subtype

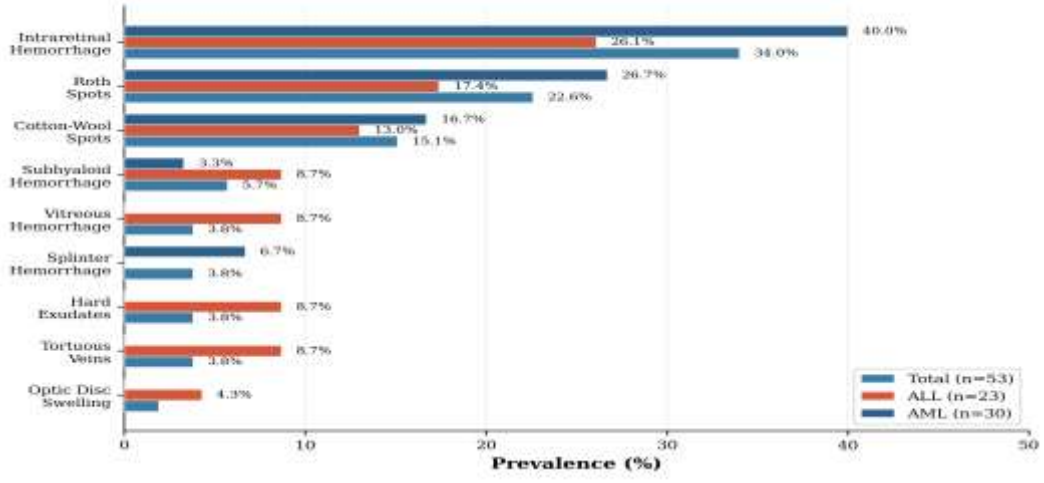
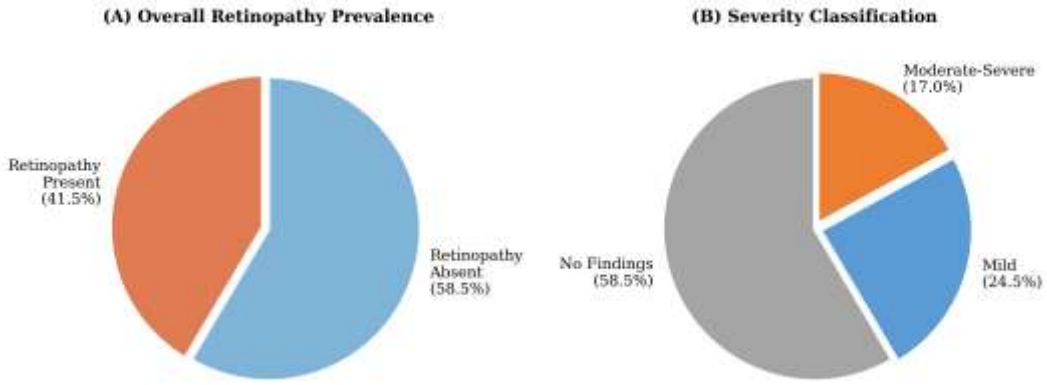


Figure 3. Distribution of Retinal Findings in Acute Leukemia Patients



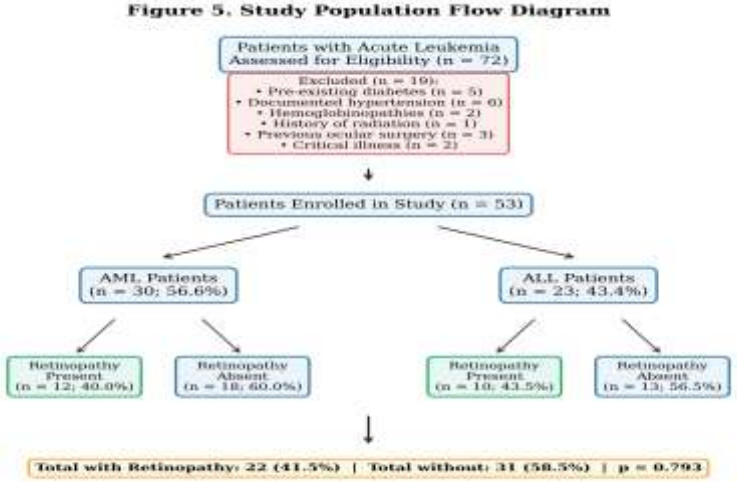
4.3 Statistical Correlation Analysis

Retinopathy presence did not vary significantly among the gender and leukemia subtype subgroups, but age did. Patients aged ≥50 years universally had retinopathy (100%), finding significant at (p=0.028). An analysis of the multiplicity of manifestations shows that patients with more than one eye finding have significantly higher odds of having severe retinopathy (OR=3.54, 95% CI: 1.15-10.86, p=0.041). This implies that once retinopathy sets in, multiple types manifest.

Table 3. Statistical Correlation Between Retinopathy and Patient Variables (*p<0.05)

Variable	Retinopathy Absent	Retinopathy Present	p-value	OR (95% CI)
Overall	31 (58.5%)	22 (41.5%)	-	-
Gender				
Male	16 (59.3%)	11 (40.7%)	0.900	0.93 (0.32-2.68)
Female	15 (57.7%)	11 (42.3%)		Reference
Age Group				
<20 years	5 (50.0%)	5 (50.0%)	0.586	2.00 (0.44-9.04)
20-29 years	12 (70.6%)	5 (29.4%)	0.177	0.83 (0.21-3.31)
30-39 years	9 (64.3%)	5 (35.7%)	0.648	1.11 (0.26-4.69)
40-49 years	5 (55.6%)	4 (44.4%)	0.855	1.60 (0.30-8.53)
≥50 years	0 (0.0%)	3 (100.0%)	0.028*	-
Leukemia Subtype				
ALL	13 (56.5%)	10 (43.5%)	0.793	1.15 (0.40-3.34)
AML	18 (60.0%)	12 (40.0%)		Reference
Manifestations				
Single finding	22 (71.0%)	9 (29.0%)	0.041*	Reference
Multiple findings	9 (40.9%)	13 (59.1%)		3.54 (1.15-10.86)

Figure 5. Study Population Flow Diagram



5. DISCUSSION

5.1 Principal Findings and Clinical Significance

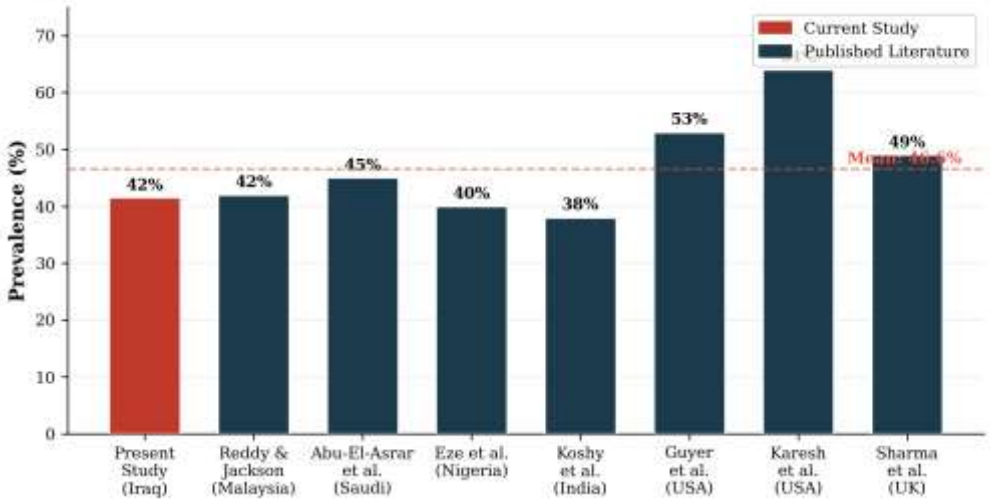
The study presents the first systematic evaluation of ocular signs in patients with acute leukemia in Iraq which provides important data to the growing international literature on leukemic retinopathy. The observed prevalence of 41.5% is consistent with global figures. These findings confirm ocular involvement in acute leukemia is universal and provide regional data specific to the Middle East. The most frequent manifestation was intraretinal hemorrhage (34.0%). According to studies, this manifestation has been found in different parts of the world. Thrombocytopenia and coagulopathy are fundamental to pathology of the eye in leukemia patients [3,8,15].

Our cohort's relatively high Roth spot prevalence (22.6%) far exceeds what has been reported in multiple comparable studies. It is possible that this could be due to population-related factors, disease severity at presentation, and/or variations in examination technique. Roth spots are retinal hemorrhages that have white or pale centers. They are caused by the presence of platelet-fibrin thrombi or leukemic cell aggregates in the retinal capillaries. The presence of these in our population indicates serious vascular involvement possibly linked to disease severity [5,12].

5.2 Comparative Analysis with International Literature

Our findings align very closely with other international studies. In Malaysian patients, Reddy and Jackson [3] reported prevalence of 42 percent while Abu-El-Asrar et al. [8] reported 45 percent in Saudi patients. The similarity across the Middle East populations suggests there may be genetic risk factors and/or environmental risk factors for ocular leukemia. As per Sharma et al. [4] and Koshy et al. [10], prevalence studies in Europe and Asia report lower rates ranging from 28-35% and higher rates of 50-65%, respectively. The differences may arise from many factors, including the disease stage at presentation, application and protocols for examination, population genetics, and healthcare system factors influencing the timing of diagnosis.

Figure 4. Comparison of Ocular Manifestation Prevalence Across International Studies



5.3 Novel Findings and Unique Contributions

Retinopathy was found universally in patients aged ≥50 years for the first time in the present study. Due to the small number of patients (n=3) in our study, we lack statistical power. However, the observation suggests potential susceptibility factors to age which require further study. Age-related vascular fragility, reduced buffering mechanisms, concurrent age-related comorbidities, and different disease biology in patients who are older may explain this. Age difference of male versus female AML patients (p=0.027) is another important epidemiologic observation that may suggest gender-specific pathways for disease development [1,14].

Multiple concurrent manifestations were significantly associated with overall retinopathy severity (OR=3.54, p=0.041), suggesting that leukemic retinopathy is more likely to be absent or multifocal than isolated. The observed pattern may represent the systemic nature of underlying pathophysiology, threshold effects on disease expression, and shared mechanistic pathways for diverse manifestations. Gaining insight into this clustering trend can affect clinical screening and prognosis [13,15].

5.4 Clinical Implications

The implementation of routine ophthalmologic screening in the management of acute leukaemia is supported by our findings. The 41.5% rate warrants the resources needed for full eye examination as it can help detect involvement of the central nervous system, monitor response to therapy, and provide prognostic information. suggests detailed ophthalmologic examination within 48-72 hours of leukemic diagnosis, followed by other examination after reversal of induction chemotherapy at 2 weeks' interval, and further monthly evaluation during the consolidation phase.

The different age groups that we arrive at in our study show useful risk-based screening. Patients aged 50 years or older may be monitored more often or with greater intensity by ophthalmology. On the other hand, younger patients may simply be managed according to standard protocols unless symptomatic. The serial ophthalmologic examinations may be valuable to monitor the disease response since they are reversible changes seen in leukemic retinopathy [15,17].

5.5 Limitations

The relatively modest sample size (n=53) represents the primary limitation of this investigation, restricting statistical power for detecting subtle associations. The cross-sectional design prevented assessment of temporal relationships between ocular manifestations and disease progression. The single-center, regional population basis limits generalizability to other populations. The absence of advanced imaging techniques such as optical coherence tomography and fluorescein angiography may have limited detection of subtle retinal changes. Future multi-center longitudinal studies incorporating advanced imaging modalities are needed to address these limitations [6,18].

6. CONCLUSION

This study will provide important information about the ocular manifestations in Iraqi acute leukemia patients. It will also provide data concerning their prevalence, pattern and clinical correlates. The retinal abnormalities documented in 41.5% of cases are in line with international figures, proving leukemic ocular involvement is universal and providing regional data for Middle East populations. The established pathophysiologic mechanism is confirmed by the high incidence of intraretinal hemorrhage (34.0%) and Roth spots (22.6%), while it also indicates thromocytopenia-related bleeding complications.

The research highlighted new findings, which might have clinical implications. Retinopathy is present in all individuals aged 50 years and above showing that they are susceptible to some factors. In addition, the strong correlation between multiple concurrent manifestations and severity of overall retinopathy suggests that leukemic ocular involvement is usually either absent or multifocal and not isolated. Routine ocular assessment of patients with acute leukemia must be included in the treatment regimen of these patients especially the older one as stated by these authors.

Ongoing research priorities must encompass multi-center prospective longitudinal research, imaging technology integration, biomarker development and validation studies, and international collaborative research networks. These efforts might eventually lead to globally accepted guidelines for managing leukemic ocular manifestation that could enhance diagnosis and treatment outcome in this important area of hematology oncology.

Declarations

Ethics Approval and Consent to Participate:

The study protocol received approval from the Institutional Review Board of Baghdad Teaching Hospital. All participants provided written informed consent after detailed explanation of study procedures, risks, and benefits. Patient confidentiality was maintained throughout the study period, with data de-identification prior to analysis.

Consent for Publication:

Not applicable. This study does not contain any individual person's data in any form.

Availability of Data and Materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests:

The authors declare that they have no competing interests.

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Authors' Contributions:

H.J.A. designed the study, performed ophthalmologic examinations, and drafted the manuscript. A.N.S.H. contributed to patient recruitment, data collection, and literature review. A.M.Z. assisted with data analysis, statistical interpretation, and manuscript revision. All authors read and approved the final manuscript.

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REFERENCES

[1] Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(3):233-254. doi:10.3322/caac.21763

[2] Döhner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. N Engl J Med. 2015;373(12):1136-1152. doi:10.1056/NEJMra1406184
[3] Reddy SC, Jackson N. Retinopathy in acute leukaemia at initial diagnosis: correlation of fundus lesions and haematological parameters. Acta Ophthalmol Scand. 2004;82(1):81-85. doi:10.1046/j.1600-0420.2003.00199.x
[4] Sharma T, Grewal J, Gupta S, Murray PI. Ophthalmic manifestations of acute leukaemias: the ophthalmologist's role. Eye (Lond). 2004;18(7):663-672. doi:10.1038/sj.eye.6701308
[5] Guyer DR, Schachat AP, Vitale S, et al. Leukemic retinopathy: relationship between fundus lesions and hematologic parameters at diagnosis. Ophthalmology. 1989;96(6):860-864. doi:10.1016/s0161-6420(89)32814-4
[6] Kincaid MC, Green WR. Ocular and orbital involvement in leukemia. Surv Ophthalmol. 1983;27(4):211-232. doi:10.1016/0039-6257(83)90123-6
[7] Karesh JW, Goldman EJ, Reck K, et al. A prospective ophthalmic evaluation of patients with acute myeloid leukemia: correlation of ocular and hematologic findings. J Clin Oncol. 1989;7(10):1528-1532. doi:10.1200/JCO.1989.7.10.1528
[8] Abu-El-Asrar AM, Al-Momen AK, Kangave D, Harakati MS. Correlation of fundus lesions and hematologic findings in leukemic retinopathy. Eur J Ophthalmol. 1996;6(2):167-172. doi:10.1177/112067219600600212
[9] Do DV, Dhaliwal RS, Schachat AP. Leukemia and lymphoma. In: Ryan SJ, Hinton DR, Schachat AP, Wilkinson CP, eds. Retina. 5th ed. London: Elsevier; 2013:2360-2373.
[10] Eze BI, Ibegbulam GO, Ocheni S. Ophthalmic manifestations of leukemia in a tertiary hospital population of adult Nigerian Africans. Middle East Afr J Ophthalmol. 2010;17(4):325-329. doi:10.4103/0974-9233.71609
[11] Koshy J, John MJ, Thomas S, et al. Ophthalmic manifestations of acute and chronic leukemias presenting to a tertiary care center in India. Indian J Ophthalmol. 2015;63(8):659-664. doi:10.4103/0301-4738.169787
[12] Reddy SC, Jackson N, Menon BS. Ocular involvement in leukemia--a study of 288 cases. Ophthalmologica. 2003;217(6):441-445. doi:10.1159/000073077
[13] Dhasmana R, Prakash A, Gupta N, Verma SK. Ocular manifestations in leukemia and myeloproliferative disorders and their association with hematological parameters. Ann Afr Med. 2016;15(3):97-103. doi:10.4103/1596-3519.188890
[14] Singh AD, Williamson TH, Talbot JF, Parsons MA. Ophthalmic manifestations of acute lymphoblastic leukaemia. Br J Ophthalmol. 1993;77(7):448-451. doi:10.1136/bjo.77.7.448
[15] Alemayehu W, Shamebo M, Bedri A, Mengistu Z. Ocular manifestations of leukaemia in Ethiopians. Ethiop Med J. 1996;34(4):217-224.
[16] Buchan J, McKibbin M, Burton T. The prevalence of ocular disease in chronic lymphocytic leukaemia. Eye (Lond). 2003;17(1):27-30. doi:10.1038/sj.eye.6700294
[17] Omoti AE, Omoti CE, Momoh RO. Ocular disorders in adult leukemia patients in Nigeria. Middle East Afr J Ophthalmol. 2010;17(2):165-169. doi:10.4103/0974-9233.63076
[18] Lang GE, Spraul CW, Lang GK. Ocular changes in primary hematologic diseases. Klin Monbl Augenheilkd. 1998;212(6):419-427. doi:10.1055/s-2008-1034954
[19] Charif Chefchaouni M, Belmekki M, Hajji Z, et al. Ophthalmic manifestations of acute leukemia. J Fr Ophtalmol. 2002;25(1):62-66.
[20] Wiznia RA, Rose A, Levy AL. Occlusive microvascular retinopathy with optic disc and retinal neovascularization in acute lymphocytic leukemia. Retina. 1994;14(3):253-255. doi:10.1097/00006982-199414030-00008