# Ocular fundus involvement and visual outcome of leukemia patients: Our experience in a Tertiary Hospital population of North India

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## Abstract

**Aims:** To study the posterior segment involvement pattern and visual outcome of leukemia patients in a tertiary care hospital population of north India

**Materials and Methods:** This is a prospective, observational case series study from a single centre. All leukemia patients coming to Ophthalmology department for routine check-up were screened. Those who had fundus involvement were included in the study after other retinal diseases ruled out. Detailed ophthalmological examination done. Investigations like Optical coherence tomography, B scan ultrasonography, fundus fluorescein angiography done when required. Various posterior segment ophthalmic manifestations were analysed. Ophthalmologic intervention done when required and all patients followed up for at least 6 months and visual outcome noted.

**Results:** There were 41 leukemia patients with fundus involvement (30 males and 11 females), age range 5 years to 60 years. The posterior segment findings was retinal venous tortuosity and stasis, haemorrhages, Roth spots, serous retinal detachment, optic nerve infiltration, papilledema, proliferative changes. At presentation 22 patints with leukemic retinopathy (53.6 %) had normal vision, 10 (24.4%) visual impairment and 9 (22%) had blindness. At 6 months 34 patients (82.92%) had normal vision, 5 (12.2%) had visual impairment and 2 (4.9%) remained blind. Visual improvement in normal and blind group was statistically significant ($p<0.05$)

**Conclusion:** Leukemic retinopathy responds well to modern chemotherapy. Optic nerve infiltration require prompt intervention, still has poor visual prognosis. Regular ophthalmological examinations are recommended in all leukemia patients to help in identifying relapses and optimize treatment outcome

**Keywords:** Leukemia, Leukemic retinopathy, Visual prognosis.

## Introduction

Ocular involvement in leukemia is very common.[(1)] It can be affected at any point in the course of the disease. The posterior segment is more often affected than anterior segment[(2-4)] and retina is most commonly involved ocular tissue in leukaemia. Prevalence of leukemic retinopathy can be very high, from 35.4% up to 77.8% in some countries has been reported.[(2-5)] Literature regarding ocular involvement in leukemia is plentiful but few studies has been done to assess the response to various systemic treatment modalities and visual outcome in leukemia patients except individual case reports.

So the purpose is to study leukemia patients, to note the diversities in leukemic retinopathy, to analyze their regression pattern and evaluate visual outcome in response to systemic chemotherapy and radiotherapy in a tertiary hospital population of north India.

## Materials and Methods

This is a prospective, observational case series study conducted between January 2012 to January 2015. Approval by our Institutional Ethics Committee obtained. All leukemia patients coming to Ophthalmology department of our hospital for routine check up were screened. Demographic data, type of leukemia, duration of illness, and modality of treatment were obtained from their hematology records and treatment protocol chart. Detailed history taking, careful checking of all systemic investigation reports done to rule out other causes of similar fundus involvement. Complete ophthalmological examination done including best corrected visual acuity with snellen distance visual acuity chart and landolt's C test, anterior segment examination, dilated fundus examination by slit lamp biomicroscopy using +78D lens and binocular indirect ophthalmoscope using +20D lens done. Those who had fundus involvement with or without decreased vision were included in the study. We categorized patients into three groups based on Best Corrected Visual Acuity (BCVA): Normal vision (BCVA ≥ 6/18 in better eye), Visual impairment (BCVA < 6/18 to 3/60 in better eye), blindness (BCVA < 3/60 in the better eye) (adapted from international statistical Classification of Diseases and Related Health problems, tenth revision. Geneva, World Health Organization, 1992. In developing country such as India, vision loss <3/60 classified as legal blindness) fundus photo documentd. Investigations like optical coherence tomography, B scan ultrasonography, fundus fluorescein angiography, visual field test done when required. Various posterior segment ophthalmic manifestations were analysed. Patients requiring optic nerve irradiation urgently referred for radiotherapy. All patients followed up 2 monthly for at least up to 6 months. Regression of fundus lesions in response to

systemic chemotherapy, radiotherapy analyzed and visual outcome at the end of 6 months noted.

*Statistical analysis*: Data was presented using frequency and percentage. McNemar chi-square test used to test the difference in proportion between baseline and 6 month visual acuity. P value < 0.05 was considered as statistically significant. Statistical package for social science, version 22 (SPSS-22, IBM, Chicago, USA) has been used to analyze the data.

*Exclusion criteria* were leukemia patients who require or already undergone bone marrow transplant (BMT), Patients with bilateral subhyaloid hemorrhage who required Nd-YAG hyaloidotomy at least in one eye for economic reason, those who did not have fundus involvement at baseline examination, very sick patients who could not come for complete ophthalmological check-up or follow up visit, patients with other associated systemic diseases.

## Results

There were 41 leukemic patients with fundus involvement including new and existing patients (30 males and 11 females), Mean age was 26.2±11.5 with age range 5 years to 60 years. Unilateral fundus lesion found in 5 patients, bilateral in 36 patients (1:7.2).

Out of 41 patients, 31 patients (75.6%) were having Acute Lymphoblastic Leukemia (ALL), 7 patients (17.1%) Chronic Myelocytic Leukemia (CML), 2 patients (4.9%) Acute Myeloblastic Leukemia (AML), 1 patient (2.4%) Chronic Lymphocytic Leukemia (CLL).

Most common fundus finding was vascular tortuosity and congestion in 90.24% cases, then retinal haemorrhage (flame shaped, intraretinal, subretinal and subhyaloid) in 82.93% cases among which macula was involved in 16 patients (39.02%). Other findings were retinal venous stasis and arterial occlusion, roth spots, perivascular sheathing, cotton wool spots, serous retinal detachment, optic nerve infiltration, papilledema, proliferative changes with neovascularisation. The major cause of vision loss was direct optic nerve infiltration, subhyaloid and intraretinal haemorrhage at macula. (Table 1)

**Table 1**: **Fundus findings at initial presentation**

| Fundus findings | No. of patients | Percentage (%) ( n = 41 ) |
|---|---|---|
| Venous tortuosity and congestion | 37 | 90.24 % |
| Intraretinal/subretinal /subhyaloid haemorrhage outside macula | 18 | 43.90 % |
| Intraretinal/subretinal/Subhyaloid haemorrhage including macula | 16 | 39.02 % |
| White centered hemorrhage | 5 | 12.19 % |
| Arterial blockage CRAO/BRAO | 4 | 9.76 % |
| Cotton wool spots | 4 | 9.76 % |
| Optic nerve infiltration | 3 | 7.32 % |
| Serous retinal detachment at macula | 2 | 4.88 % |
| Papilledema | 2 | 4.88 % |
| Proliferative changes | 1 | 2.44% |

The presenting and final visual acuity is shown in Table 2. Both normal vision and blindness group showed significant improvement in visual acuity ($p<0.001$ and $p= 0.016$ respectively) but in visual impairment group this improvement was not statistically significant ($p>0.05$). (Table 2)

**Table 2: Visual acuity at initial and 6 months**

| Category of patients based on BCVA* | BCVA in better eye | % at initial examination ( n= 41 ) | % at 6months (n= 41) | p value** |
|---|---|---|---|---|
| Normal Vision | ≥6/18 | 22 ( 53.6) | 34 (82.9) | <0.001* |
| Vision impairment | <6/18 to 3/60 | 10 (24.4) | 5 (12.2) | 0.063 |
| Blindness | <3/60 | 9 (22) | 2 ( 4.9) | 0.016* |
| *BCVA- Best Corrected Visual Acuity (Adapted from International Statistical Classification of Diseases and Related Health Problems, tenth revision. Geneva, World Health Organization, 1992) McNemar chi-square test used to test the difference in proportions between baseline and 6 months. **p value< 0.05 significant | | | | |

Among 16 patients of subhyloid and intraretinal haemorrhage at macula 5 patients showed some degree of residual vision defect with three patients having persistent haemorrhage at the time of follow up at 6 months. Serous retinal detachment in two patients resolved completely within three months. Two patients with papilledema recovered well. In rest 18 patients superficial and deep haemorrhages, venous tortuosity showed definite improvement during follow up period.

## Discussion

In our study both normal vision and blindness group showed significant improvement in visual acuity

($p<0.001$ and $p= 0.016$ respectively) but in visual impairment group this improvement was not statistically significant ($p>0.05$). We found that superficial and intraretinal haemorrhages, cotton wool spots, Roth spots, venous tortuosity and other venous stasis features responded very well to systemic chemotherapy. Complete resolution was noted at 6 months follow up. But subhyaloid hemorrhage at macula took longer time to resolve, in some patients they were persistent at final follow up. [Fig. 1 (a, b)] This failure in complete resolution of subhyaloid hemorrhage accounted for some residual visual defects in these patients.

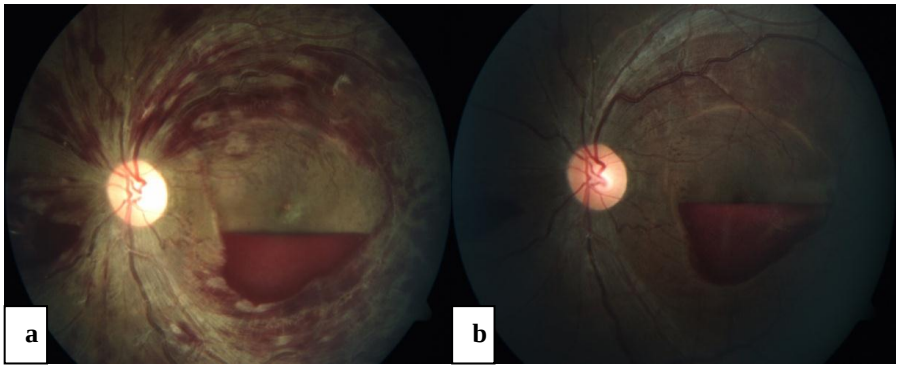


**Fig. 1: Photograph showing fundus picture of left eye of a patient with Acute Lymphoblastic Leukemia (ALL) a) vascular tortuosity, superficial and deep haemorrhages, subhyaloid haemorrhage at macula at initial examination; b) improvement in vascular tortuosity, congestion and resolution of all haemorrhages except subhyaloid haemorrhage at macula which seem to be increased at 6 month follow up.**

We have not included results of any intervention like Nd: Yag laser hyaloidotomy in this study, but in our experience this is a very good option specially in patients with bilateral subhyaloid haemorrhage who need early visual rehabilitation for economic reasons. Reports have shown that timely done Nd: Yag laser hyaloidotomy can give good results although dense clotted haemorrhage can cuase problem and procedure can be challenging in small children.[6,7]

Serous retinal detachment (SRD) is a less common ocular manifestation of leukemia, but can be a presenting feature of ALL.[8,9] Usually complete resolution occurs with chemotherapy. In our study also serous retinal detachment in two patients resolved within 3-4 months. Both were CML patients in chronic phase.

Microvascular blockage is common in leukemia patients. In eye optic nerve microvasculature, central retinal retinal vessels or branch vessel occlusion can be seen sometimes leading to severe ischemia and proliferative changes. In one CML patient we found neovascularisation at both periphery and optic disc. [Fig. 2 (a, b)]

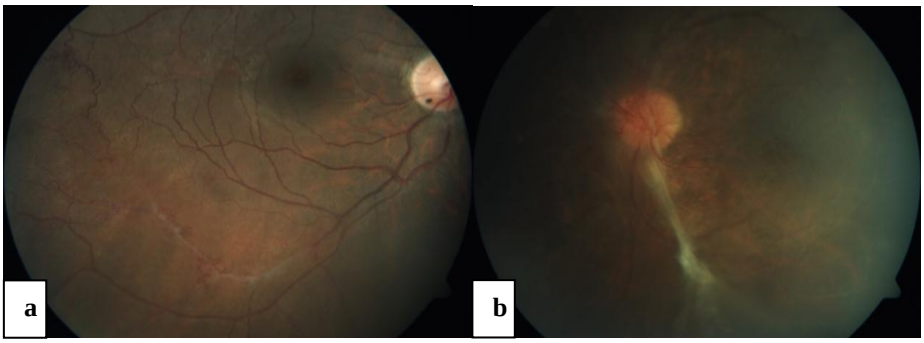


**Fig. 2: Photograph showing fundus picture of a patient with chronic myeloid leukemia a) right eye showing inferotemporal branch vein occlusion with neovascularisation; b) left eye showing neovascularisation at disc, fibrovascular traction with cystoid changes at macula**

Now-a–days we are getting more number of reports of central nervous system (CNS) infiltration in relapsing leukemia because of increased survival rate following improved treatment regimen.[10] Optic nerve infiltration can be the first manifestation of relapsing leukemia.[11]

In one of our case, a young girl with ALL on maintenance presented with unilateral isolated optic nerve relapse. Her other eye was absolutely normal and systemic condition was stable. Vision could not be salvaged in the affected eye despite prompt referral for

radiotherapy along with continuing chemotherapy. [Fig. 3 (a, b)]

Another case, a 5 year old child on Induction therapy for ALL referred to us for decrease vision both eyes. His vision was light perception one eye and counting finger at 1 meter other eye. He had CNS involvement and systemic condition was also deteriorating. He was given cranial and optic nerve radiation along with intrathecal and systemic chemotherapy but vision did not improve much, remained around counting finger at 2 meters. [ Fig. 4 (a, b, c, d)]

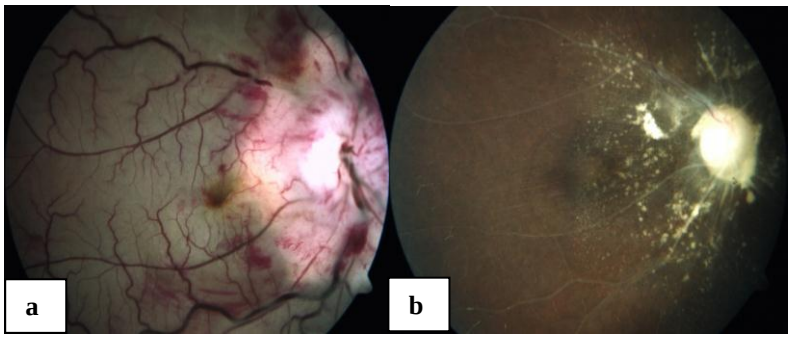


**Fig. 3**: **Photograph showing fundus picture of right eye of patient with Acute Lymphoblastic Leukemia (ALL) a) optic nerve infiltration, vascular tortuosity, superficial and deep haemorrhages at presentation b) at 6 months follow up after radiotherapy, intrathecal chemotherapy showing optic disc pallor, ischemic retina with ghost vessels, exudates and retinal folds.**

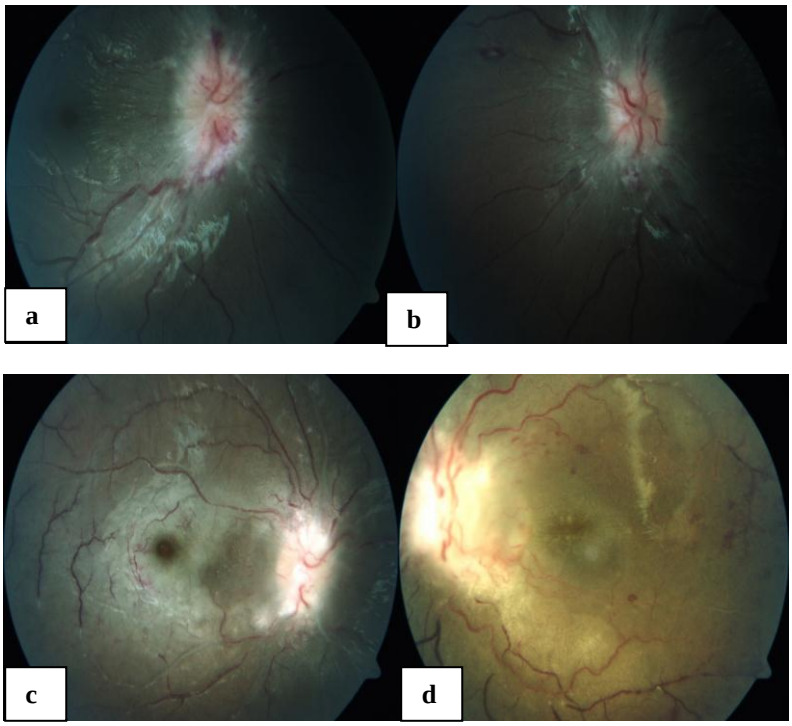


**Fig. 4: Photograph showing fundus picture of a child with acute lymphoblastic leukemia (a, b) fundus picture at in initial presentation optic nerve infiltration, vascular tortuosity and white centered haemorrhage; (c, d) Follow up at three months showing optic disc pallor, partial occlusion of vessels**

The third patient with optic nerve infiltration both eye improved with combined intrathecal chemotherapy and radiotherapy but remained in visual impairment group.

Variable results of radiotherapy for optic nerve infiltration can be found in some other series also.[12] Reports by Nikaido et al showed that optic atrophy continued in all eyes despite irradiation.[13] In some other reports residual visual defects remained after radiotherapy.[14] But many reports on optic nerve infiltration show favourable outcome with radiation therapy.[11,15-17]

While majority of reports support combined chemotherapy and radiotherapy for optic nerve infiltration, one case report shows improvement in vision after intrathecal and intravenous chemotherapy only.[18]

Many factors can contribute to poor visual recovery in a case of optic nerve infiltration like deteriorating systemic condition, associated central nervous system relapse, delayed presentation. Associated vascular occlusion, radiation optic neuropathy, effect of disc edema itself can also effect visual outcome.

**Drawback**

i. Our study population comprised only patients of leukemic retinopathy cases which were in various stages of their treatment and their blood parameters were also not correlated.
ii. The results of ocular laser therapy and surgical intervention was not taken into account.

## Conclusion

In our experience majority of patients with leukemic retinopathy responded well to modern chemotherapy. Those with optic nerve infiltration can have grave visual prognosis. Local irradiation along with intrathecal and systemic chemotherapy should be considered at earliest in these ophthalmic emergency cases. Regular ophthalmological examinations are recommended in all leukemia patients including those with maintenance therapy or having stable systemic conditions to help in identifying relapses and optimize treatment outcomes. Patient awareness is also very important in this regard so that they could seek ophthalmology consultation promptly when they develop any type of visual problem.

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